

## RESEARCH PLAN

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### 1. PROJECT TITLE

The Efficacy of Intra-oral Neuromuscular Stimulation Training on Snoring in Individuals with Primary Snoring

### 2. PRINCIPAL INVESTIGATOR

Prof Bhik Kotecha, Chief Investigator

### 3. FACILITIES

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### 4. ESTIMATED DURATION OF THE STUDY

Up to 2 years

### 5. LAY LANGUAGE SUMMARY OR SYNOPSIS

Snoring is part of a spectrum of conditions called Sleep Disordered Breathing (SDB) which spans from Simple Snoring to Severe Sleep apnea. SDB and snoring has multiple underlying mechanisms but often the common pathway is excessive loss of muscle tone in the throat and pharynx. These patients may be amenable to upper airway muscle training exercises using neuromuscular stimulation techniques. Over the last decade, there have been several publications on the use of upper airway training exercises and electrical neurostimulation of the upper airway for treatment of Snoring and OSA. Based on this background, we seek to test the hypothesis that daytime upper airway tongue muscle training using transoral surface neuromuscular electrical stimulation (SnooZeal Device) may have benefits to patients with Simple Snoring.

### 6. SPECIFIC AIMS

#### Primary Objective:

Assess the efficacy of daytime trans-oral neuromuscular stimulation training on nocturnal snoring.

#### Secondary Objectives:

Assess the efficacy of daytime trans-oral daytime neuromuscular stimulation training on sleep quality and its safety.

#### Primary Endpoint:

- A. Reduction of 20 % in the percentage of time spent snoring at levels greater than 40 dB. This will be achieved using WatchPat (510K - K161579) sleep studies
- B. Reduction of 40% in bed partner VAS assessment of snoring.

#### Secondary Endpoints:

- A. Reduction in the Epworth Sleepiness Scale (validated hypersomnolence questionnaire) and Pittsburgh Sleep Index (validated sleep quality questionnaire with 7 domains).
- B. Assess safety of device (record and investigate adverse events, oral status and monitor device integrity through use)

### 7. BACKGROUND AND SIGNIFICANCE

Forty five percent of the male population snore, 25% habitually (daily). Sleep disordered breathing (SDB) (partial or total obstruction of the upper airway during sleep) is a spectrum of conditions (Fig 1) ranging from simple snoring to obstructive sleep apnea-hypopnea syndrome (OSAHS)<sup>1</sup>. The latter affects at least 4-6% of the population and is associated with increased incidence of hypertension, cardiac (heart attacks) and cerebral events (strokes). Although the gold standard of treatment for OSAHS is Continuous Positive Airway Pressure (CPAP), a variety of treatments are offered for simple snoring.

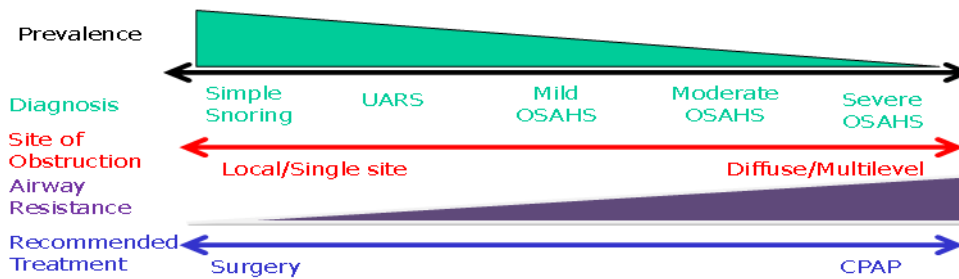


Figure 1: spectrum of sleep disordered related breathing ranging from simple snoring to severe obstructive sleep apnea syndrome (OSAHS: obstructive sleep apnea hypopnea syndrome, CPAP: continuous positive airway pressure)

Although there are several lifestyle practices associated with snoring (smoking, obesity, drinking etc.), a significant proportion of individuals may snore despite not being associated with these.

The most notable change that occurs in the physiology of humans during sleep is the reduction in the tone of the muscles and increased collapsibility of the throat (pharynx) and tongue. Notably, there is evidence to show that the collapsibility is significantly higher in patients who obstruct (OSAHS) and marginally higher in patients who snore (simple snoring) when compared to individuals who don't snore (Fig 2)<sup>2</sup>. As demonstrated in the graph below, it has been shown that when compared to "normal" individuals, the breathing passage in snorers and sleep apnea individuals collapses at a positive rather than negative airway pressure.

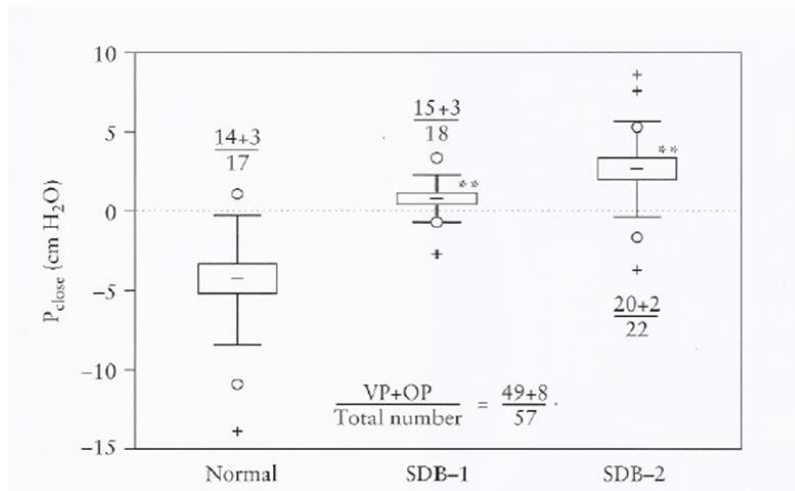
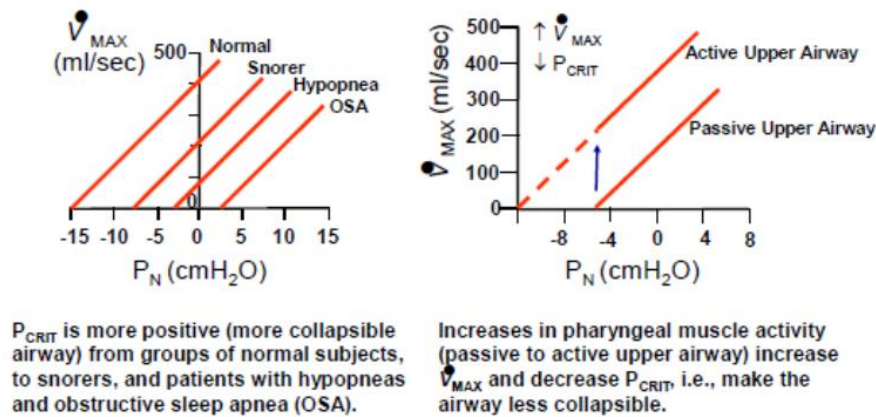


Figure 2: critical closing pressure in healthy subjects, snorers and patients with OSA (SDB-1 = snorers, SDB-2 = Sleep Apnea), (according to Isono et al. 2)

Research has demonstrated that increasing the pharyngeal muscle activity or tone, reduces the collapsibility of the airway as demonstrated by the graphs below (Figure 3). It is the reduction of throat/pharynx/tongue muscle tone that leads to this partial or complete obstruction.



Redrawn from Smith and Schwartz, *Sleep Apnea: Pathogenesis, Diagnosis and Treatment*, 2002

Figure 3: Upper airway collapsibility and critical closing pressure in sleeping individuals (according to Schwartz et al.<sup>3</sup>)

Several studies have shown that implanting electrical nerve stimulators (for the tongue and limited numbers for diaphragm) are effective in treatment of OSA. However, these stimulators involve operations and implantation of the device<sup>4,5,6,7</sup>. Furthermore, studies involving apnea-triggered nocturnal stimulation reportedly disturb the patient sleep by arousals due to the electrical stimulation<sup>7</sup>. Also, similar to implanted pacemakers, there are multiple maintenance and logistic complications (battery replacement, unable to be in electromagnetic fields, cannot have other external electrical circuits attached, detected by external detection devices like airport security etc. etc.).

There is a considerable body of knowledge, literature and evidence to state that use of transcutaneous electrical stimulation in paralyzed or inactive limbs (muscles with low or absent muscle tone) significantly improves muscle power and tone recovery<sup>8</sup>. Considering the muscles of the throat, pharynx and tongue are of the same muscle type as of the limbs (skeletal muscle), the hypothesis is electrical stimulation of the pharyngeal and tongue muscles would lead to a similar effect of increased resting muscle tone and muscle tone during sleep.

Studies show that training the upper airway muscles either by playing a wind instrument (didgeridoo)<sup>9</sup> or oropharyngeal exercises<sup>10,11,16</sup> can ameliorate moderate OSA and snoring. A recent meta-analysis demonstrated that oropharyngeal exercises provide a reduction in apnea-hypopnea index (AHI) of 50% in adults and decreases snoring<sup>12</sup>. Oropharyngeal exercises are, therefore, a viable option to treat patients suffering from snoring and OSA. The presumption is that these changes are due to improvement in pharyngeal muscle tone.

In a placebo controlled randomized study of tongue stimulation for OSA, although the OSA index did not significantly improve, there was a significant reduction in the snoring<sup>13</sup>. The number of snoring epochs decreased in the training group (baseline  $63.9 \pm 23.1$  epochs per hour versus  $47.5 \pm 31.2$ ;  $P < .05$ ).

Unlike the above-mentioned study, the SnooZel device uses an entirely intra-oral stimulation device with an aim of reducing snoring in individuals with primary snoring. The mouth piece will be placed with two electrodes below and two above the tongue for muscle stimulation, with no transcutaneous component as in the previous studies.

A preliminary study with this trial product has been undertaken in 27 patients in Germany<sup>14</sup>. SnooZeal device was used twice a day for 20 minutes each time during the 6 week training period. The study showed that the mean snoring reduced from 6.4 to 3.1 ( $p=0.001$ ) on bed partner Visual analogue score rating of snoring ((6.4 to 2.7 in the primary snoring subgroup ( $p=0.001$ ) versus a drop from 6.6 to 3.6 in the mild OSA subgroup ( $p=0.001$ )). There was a statistically significant improvement in 2 of 7 components of the Pittsburgh Sleep Questionnaire inventory supporting an improvement the snorer's sleep quality with the use of the device. This study has been accepted for presentation and subsequent publication in Chest 2018.

## 8. PROGRESS REPORT

N/A

## 9. RESEARCH DESIGN AND METHODS

### Introduction to device

Indications: The Snoozeal transoral neurostimulation device is a prescription only, home use device. Its primary indication is for use in primary snoring.

The TMS system is to be a reusable device that produces muscular stimulation via electrodes connected to the tongue muscles. It is to be considered a single medical device with three components; one controller, a washable electrode mouthpiece, and a remote control/mobile application (Figure 4).

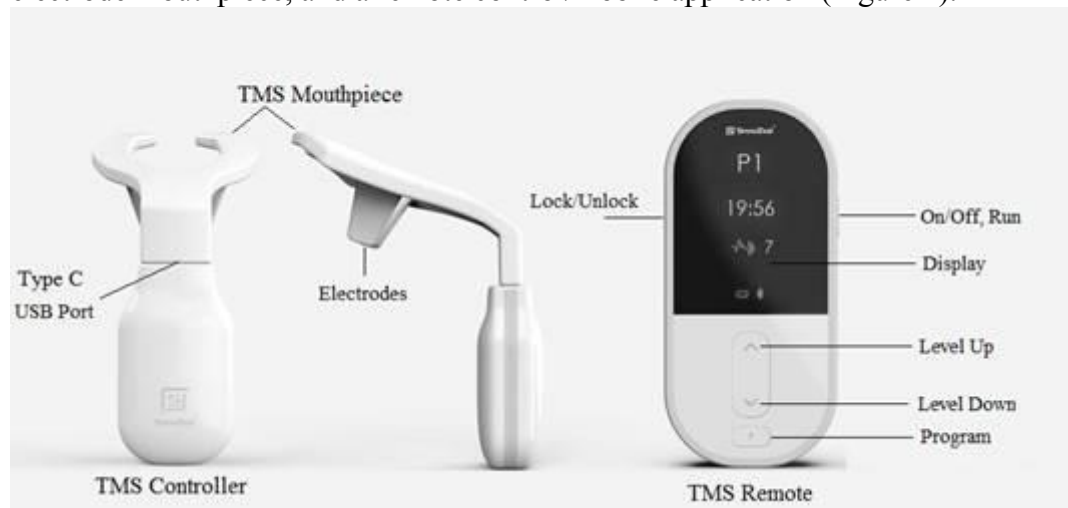


Figure 4. SnooZeal transoral neurostimulation device.

The mouthpiece is connected to the control unit via a USB port and Bluetooth connection is established between the control unit and remote control/app. This allows the remote control/app control over the current level and on/off functionality of the control unit and mouth piece.

The mouthpiece is placed in the mouth, with two electrodes located above and two electrodes below the tongue. The therapy consists of a series of pulse bursts with the basic characteristic of 6 secs burst and 4 seconds rest. During the 20 mins therapy period the pulse frequency will change every 5 mins in a defined sequence (through 3, 10, 20 and 3 Hz frequencies). The product is to be used once daily (20 min therapy session), during the day, for a period of six weeks to get the desired improvement.

## Research Method:

The study plans to investigate the change in snoring sound, sleep quality and the safe use of intraoral neuromuscular stimulation using SnooZeal device. After appropriate screening and assessment, the recruited participants will proceed through three phases of the trial. The Pre-Trial phase collects data on the pretreatment state of the participant, after which they will enter the Therapy phase where they use the device once daily for a six week period whilst continuing to record the required data. The participant will stop using the device at the end of this stage and have a follow up phase for two weeks, during which trial indices will continue to be recorded. The trial period for each participant will be 10 weeks.

### A. Screening

Participants will be identified from Queen's Hospital, Barking, Havering and Redbridge NHS Trust. There will be a screening phone call to ensure suitability based on an inclusion criterion and offer first line information about the trial. If suitable, patients will be given a written information sheet and invited to undertake a 2 day home sleep study (using WatchPAT). If the average AHI from these 2 days is below 15/h, the participants will be invited for a clinical examination.

### B. Recruitment visit

- Clinical airway examination by ENT surgeon (Appendix 5)
- Review of inclusion and exclusion criteria (section 10)
- Informed consent (Appendix 7)
- Inclusion into trial

### C. Pre-therapy period (day -14 to -1):

- Bed partner daily subjective assessment of snoring (Visual Analog Scale). Participant's bed partner will be required to complete daily visual analogue scoring of the participant's snoring, with 1 being "no snoring" and 10 being "intolerable snoring".
- Oral examination (Detailed examination by Dentists to document pretreatment oral state – Appendix 5)
- Participant and bed partner to complete sleep quality questionnaires (Pittsburgh Sleep Quality Index, Epworth sleepiness score and subjective sleep quality questionnaire) on Day -1 (Appendix 4)

### D. Therapy phase (day 1-42)

- Face-to-face meeting, instruction on use of the intraoral device
- Participant to use the Snoozeal device for 20 minutes once daily
- Bed partner daily subjective assessment of snoring (VAS)
- Participant daily assessment of side effects/adverse events and time of use
- Participant and bed partner to complete Sleep quality Questionnaires (Pittsburgh Sleep Quality Index, Epworth sleepiness score and subjective sleep quality questionnaire) at day 42
- Weekly follow up phone call from research team to confirm compliance. Compliance will also be cross checked using the total time of use recorded by the device.

### E. End of Therapy Review (day 43 – 49)

- Review of device integrity by visual inspection

- Oral examination (Detailed examination by Dentists to document pretreatment oral state – see examination record sheets – Appendix 5)
- Repeat Sleep Study – 2 night sleep study with WatchPAT

#### F. Follow Up phase (day 43-56)

- Participant advised to stop using device
- Bed partner daily subjective assessment of snoring (VAS)
- Subject and bed partner to complete Sleep quality Questionnaires (Pittsburgh Sleep Quality Index, Epworth sleepiness score and subjective sleep quality questionnaire) at day 56

#### G. Post Therapy Review (day 57)

- Face-to-face meeting and feedback
- Collection of participant data sheets
- Participant subjective overall assessment

### Data Analysis

The pre and post sleep studies will be performed using WatchPAT.  
Parameters recorded: saturation, AHI, snoring sound parameters.

AHI will be identified and analyzed by WatchPAT data and software. The WatchPat is an approved FDA sleep study device with 510K - K161579. Snoring will be quantified subjectively by both the bed partner using a visual analog score, and objectively during the home sleep study as frequency of snores (number of snores / hours of sleep) and % total sleep time spent snoring. Sleep quality will be quantified subjectively by PSQI score. Sleepiness will be quantified subjectively by ESS score.

### Snoring Sound

- 1) Objective: WatchPat Sleep study: Comparative analysis of % total sleep time spent snoring will be undertaken between the 2 day sleep study pre and post therapy phase. To ensure consistency, the WatchPAT microphone will be placed in the same position, just below the suprasternal notch, in both pre and post sleep studies.
- 2) VAS: Partner reported change will be assessed using VAS. Therapy efficacy will be based on statistical analysis of average VAS scores for the three periods – pre-therapy (2 weeks), therapy phase (last 2 weeks) and follow up phase (2 weeks).  
Although data will be collected for the whole of the six-week therapy phase, comparative analysis will be limited to the last two weeks of the therapy phase to exclude any transitional changes. The six-week therapy stage data will undergo temporal analysis to establish if there is a progressive change in the indices measured.
- 3) Number of nights sleeping together recorded in Subjective sleep quality questionnaire will be assessed for the pre-therapy, therapy phase and follow up phase.

### Sleep Quality

- 1) Epworth sleepiness score will be assessed for both Snorer and Bed partner for the pre-therapy, therapy phase and follow up phase.
- 2) Pittsburgh Sleep Quality Index will be assessed for both Snorer and Bed partner for the pre-therapy, therapy phase and follow up phase.

- 3) Subjective sleep quality questionnaire will be assessed for both Snorer and Bed partner for the pre-therapy, therapy phase and follow up phase.

### **See Appendix 1 for endpoint assessment and validation**

#### Safety

- 1) Any side effects or adverse events to be recorded in research record sheets and will be collated for assessment
- 2) Pre and post therapy WatchPat sleep studies will be assessed for change in parameters of saturation and AHI.
- 3) The pre and post oral examination clinical sheets will be scrutinized for any change in oral status.

#### Statistical Considerations

Sample size: 50 participants

Data will be analyzed based on two tailed paired t-test, with 80% power.  $P < 0.05$  will be considered significant. Multiple regression analysis will be used to identify which of the following factors has a causal relationship with the outcome - age, sex, BMI, neck size, AHI group (<5 and 5-15) and clinical examination characteristics (Endoscopy staging, Muller Maneuver, Friedman Classification, Tonsil size)

Power analysis:

- AHI reduction >50% and AHI <10: sample size required 17,
- VAS change of 40%, (i.e. average snoring score to drop from 6.4 to 3.8 on 10 point scale): sample size required 4. Standard deviations extrapolated from Verse et al.<sup>15</sup>.
- To calculate the required sample size for the paired observations of pre and post treatment for proportion of sleeping time snoring more than 40 dB; first the correlation between proportions before and after treatment was estimated by using provided pilot data. The required sample size of the patients with snoring more than 40 dB was then calculated such that the one-sided statistical test would be able to detect 20% reduction in snoring time from 50% to 30% with 80% power. (See Appendix 1 for validation of parameters)

## **10. HUMAN SUBJECTS**

### **Subjects**

50 primary snorers (AHI <15/hr) will be recruited from Queen's Hospital, Romford (Barking, Havering and Redbridge NHS Trust), UK.

Inclusion criteria

- Age 18 years and above (adult population) at entry into study
- Subjects must have a live-in partner as the assessment includes partners report
- More than six month history of habitual snoring (i.e. >5 days per week as reported by partner)

Exclusion criteria

- BMI > 35 kg/m<sup>2</sup>
- AHI >15/h, i.e. evidence of moderate to severe OSA from sleep study
- ESS > 10 in participants with AHI 5-15/h (symptomatic mild sleep apnea should be treated with CPAP)
- Symptomatic nasal pathology i.e. septal deviation, nasal polyposis or chronic rhinosinusitis
- Tonsil Hypertrophy (Tonsil size – Grade 3 or greater)
- Tongue or lip piercing
- Pacemaker or implanted medical electrical devices
- Previous oral surgery for snoring
- Relevant facial skeletal abnormalities (i.e. syndromic facial deficiencies, severe micrognathia etc.)
- Oral disease/conditions (see Appendix 3)
- Any criteria that, in the opinion of the investigator, would make the participant unsuitable for the study due to inability to complete required study procedures

#### **11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH**

Participants will be identified from the sleep clinic at the Department of Otorhinolaryngology, Head and Neck Surgery in Queen’s Hospital, Barking, Havering and Redbridge University Hospitals NHS Trust. Patients may be referred to this service from dental practices.

Participants considered to be suitable for the study will be invited to undergo a 2 night sleep study, performed at home using a WatchPAT device, to determine average AHI. If the AHI is less than 15, the participant will be invited to attend a clinic assessment for upper airway and to undertake an oral assessment.

If all inclusion criteria and none of the exclusion criteria are met, full informed consent will be taken by the Chief Investigator or a delegated member of the research team.

Participants will be on the study for a total of 10 weeks.

#### **12. INFORMED CONSENT**

All informed consent is completely voluntary. Participants and their partners will be given full information regarding the study prior to obtaining consent. Participants will be given the written patient information pack and provided with the full details of the study and its purpose. Participants will be given more than 24 hours to consider their participation in the study and to ask any questions they may have. Participants will be assessed for capacity to consent during the consent process. If lack of capacity is deemed, these participants will not be considered for the study.

#### **13. ALTERNATIVES TO STUDY PARTICIPATION**

Participation will not alter or influence patient’s normal clinical treatment. Participants do not have to take part in the study and if they do decide to, they are able to withdraw at any point.

#### **14. POTENTIAL RISKS**

We believe that this study and the Snoozeal device to be low risk. The investigative tool, the WatchPAT, for the sleep study is routine practice undertaken by thousands of patients and has FDA approval (510K - K161579). The Snoozeal device has been used in a pilot study of 27 patients, which revealed no significant adverse events<sup>14</sup>.

Snoozeal device: The pilot study of the Snoozeal device involved 27 patients who used the device twice daily (double the planned utilization in this trial). The only side effects were feeling tingling of the tongue for a short period (up to 5 minutes) after using the device, excessive saliva production and gum discomfort during use as shown in Table 2. As these symptoms were in keeping with anticipated effects of device use and were not



persistent, we consider this to be a non-significant risk device. The mouthpiece has been modified since the original trial to address any gum contact and discomfort. Compared to RCTs on snoring, quoted in the American Sleep medicine guideline (TheraSnore™), the Snoozeal device has less severe and less prevalent side effects.

A full risk assessment can be found in the DFMEA.

*Table 1: Side effects of the TheraSnore™ appliance (Cooke ME, Battagel JM)*

Side Effect (n = 23)	Non-advanced MAD		Advanced MAD	
	Short term (%)	Long term (%)	Short term (%)	Long term (%)
Muscular discomfort	39	13	74	26
Temporomandibular joint discomfort	26	9	61	22
Abnormal bite on waking	39	9	57	17
Excessive salivation	65	26	65	22
Dry mouth	21	52	26	70

*Table 2: Side effects of the Snoozeal device*

Side Effect (n = 27)	Short term (%)
Tingling sensation	33
Excessive salivation	26
Gum discomfort	19
Feeling of change in speech	4

Sleep Study with WatchPAT:

Participants may experience poorer sleep quality and minor discomfort related to the use of the WatchPAT device due to the larger size (compared to a normal wrist watch) and finger probe. However, we are expecting the level of discomfort to be significantly less when compared with a laboratory based polysomnography. Hypoallergenic tape will be used to minimize risk of skin irritation.

Data Handling: There is a risk of loss of subject confidentiality. This study will comply with the Data Protection Act 1998 and Caldicott Principles as laid out in the privacy and confidentiality considerations below.

**15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES**

Research Ethics Committee (REC) review & reports

Ethical approval for this study has been granted by Stanmore Research Ethics Committee (REC) using the Integrated Research Application System (IRAS project ID: 219271). All correspondence with the REC will be retained. The Chief Investigator (CI) will notify the REC at the end of the study. It is also the CI's responsibility to produce the final report of the study with the results including any publication and submit to the REC.

Safety reporting

All Adverse Events and Reactions will be logged in data sheet or reported to CI and have cause analysis and assessment performed. If the AE is not defined as serious, the AE will be recorded in the study documents and the participant followed up by the research team. The AE will be documented in the participants' source documents.

Adverse Events (AEs) - any untoward medical occurrence in a participant to whom an intervention has been administered, including occurrences which are not necessarily caused by or related to that intervention. An AE can therefore be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with study activities.

Adverse Reaction (ARs) - any untoward and unintended response in a participant to an intervention. All adverse events judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to the intervention qualify as adverse reactions. The expression 'reasonable causal relationship' means in general that there is evidence or an argument to suggest a causal relationship.

Should any events arise during a therapy session, the session should be terminated immediately. If this does not resolve the issue, the participant should contact the research team, or in case of emergency, seek urgent medical attention.

#### Serious Adverse Events (SAEs)

Serious Adverse Events (SAEs) that are considered to be 'related' and 'unexpected' will be reported to the sponsor within 24 hours of learning of the event, and to the REC within 15 days in line with the required timeframe using the form shown in Appendix 6.

A serious adverse event (SAE) is defined as an untoward occurrence that:

- Results in death,
- Is life-threatening,
- Requires hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability or incapacity,
- Consists of a congenital anomaly or birth defect, or
- Is otherwise considered medically significant by the investigator.

SAEs will be reported to the REC where in the opinion of the Chief Investigator the event was serious and:

- Related (it may have resulted from administration of any of the research interventions), and
- Unexpected (the type of event is not listed in the protocol or other Reference Safety Information as an expected occurrence).

#### Device Defects

Should an issue arise with the device, either mechanical or software related, participants are advised to contact the study team for troubleshooting advice. Should this occur during a therapy session, participants will be told to discontinue use immediately. If the error cannot be fixed through guided troubleshooting, the device will be replaced (at no cost to the participant). The defective device will be returned to the sponsor and sent to the manufacturer to undertake root cause analysis.

### Protocol compliance

Any accidental protocol deviations that occur will be documented and reported to the Chief Investigator and Sponsor immediately.

## **16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT**

For this research, only the direct healthcare team has access to participant's medical records. All collected data will be stored on NHS computers. Manual files will be kept safe within a locked cupboard in a coded room in the hospital office.

The manual files of this study including completed consent forms, questionnaires and pro forma will be kept in a locked cupboard of a coded room in the ENT outpatient department in Queen's Hospital, where medical notes are kept. Only the healthcare team within the department has access to the room.

All electronic data will be password protected and stored on a NHS computer in the ENT outpatients department in Queen's Hospital under personal logins of the research team. Therefore, no one else apart from the direct research team and the health care team will have access to the data.

Personal data will be regarded as strictly confidential. This study will comply with the Data Protection Act 1998 and Caldicott Principles. Action will be taken to ensure research team who will be handling the patient identifiable information are made fully aware of their responsibilities and obligations to respect patient confidentiality. All research team members are required to adhere to Trust/ University codes of conduct.

The confidentiality is ensured through anonymization of data. The Trial register will allocate a Trial Number (e.g. SN001) which will be the only data associated with the patient collected data. Presentation of results will not include any subject identifiable details. Written reports of the study will include only anonymized data.

Throughout the study, only the direct health care team who are also the research team members, which includes the Chief Investigator, Professor Bhik Kotecha will have access to the participants' personal data during the study.

Local research NHS Trust R&D personnel may require access to study records for the purpose of inspection and/or audit. Patient will be asked to consent to this on the consent form.

The data generated will be analyzed within Queen's Hospital, Romford. Only anonymized data will be available outside the hospital.

## **17. POTENTIAL BENEFITS**

It is anticipated that the participant will experience improvement in snoring and sleep quality. They can continue to use the device if they choose to after the completion of the study and can participate in on going Post Market Surveillance. They can also be considered for other treatment modalities post completion of trial if appropriate.

## **18. RISK/BENEFIT RATIO**

Due to the low risk nature and transient use of the device there is minimal risk to participants in this study. This device is the only one of its kind that aims to combat the cause of snoring, rather than merely treating the symptom, therefore we feel the benefits far out way the risks.

## **19. EXPENSE TO PARTICIPANT**

There will be no cost to the subject for participating in this study. All the tests and procedures that will be done for this research will be paid for by study funds.

#### **20. COMPENSATION FOR PARTICIPATION**

Participants will be reimbursed for their time and any travel costs with a flat fee of £500.

#### **21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES**

All physicians performing physical exams and taking medical histories are GMC registered and able to practice in the UK.

- Prof Bhik Kotecha is an ENT consultant at Queen's Hospital, Romford and has worked in the field for over 20 years. He will be the PI of this study.
- Karon Thurgood is an ENT nurse at Queen's Hospital, Romford who leads the ENT and maxilla-facial out-patients departments. She will assist Prof Kotecha in the review and recruitment of participants.
- Gurs Selma is a qualified dentist with extensive experience in dental implant surgery, he will be performing dental examinations before and after device therapy period.

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**23. FUNDING SUPPORT FOR THIS STUDY**

SnooZeal

**24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT**

NA

**25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER**

NA

**26. IMPACT ON STAFF**

NA

**27. CONFLICT OF INTEREST**

The CI and the research team do not have any financial interests or other conflicts related to this study.

This protocol was written by Professor Anshul Sama, who is an expert from SnooZeal Ltd. (sponsor).

The protocol has been reviewed by the Chief investigator, Professor Bhik Kotecha, who is an independent expert in the field of Sleep Surgery based at the institution of the study.

**28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES**

NA

**29. OTHER APPROVALS/REGULATED MATERIALS**

NA

**30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT**

NA