Document Coversheet

Study Title: Efficacy of the OrthoApnea NOA® Mandibular Advancement Device in the Management of Obstructive Sleep Apnea. Clinical Trial and Retrospective Comparison Study

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	2/3/2023
NCT Number:	NCT05139303
IRB Number	71295
Coversheet created:	8/1/2024

Which IRB

◉ Medical ○ NonMedical

Protocol Process Type

○ Exemption
◉ Expedited (Must be risk level 1)
○ Full

IMPORTANT NOTE: You will not be able to change your selections for "Which IRB" and "Protocol Process Type" after saving this section. If you select the wrong IRB or Protocol Process Type, you may need to create a new application.

See below for guidance on these options, or refer to ORI's "Getting Started" page. Please contact the Office of Research Integrity (ORI) at 859-257-9428 with any questions prior to saving your selections.

Which IRB

The **Medical IRB** reviews research from the Colleges of:

- Dentistry
- Health Sciences
- Medicine
- Nursing
- Pharmacy and Health Sciences
- and Public Health.

The **Nonmedical IRB** reviews research from the Colleges of:

- Agriculture
- Arts and Sciences
- Business and Economics
- Communication and Information
- Design; Education
- Fine Arts
- Law
- and Social Work

Note: Studies that involve administration of drugs, testing safety or effectiveness of medical devices, or invasive medical procedures must be reviewed by the **Medical IRB** regardless of the college from which the application originates.

Which Protocol Process Type

Under federal regulations, the IRB can process an application to conduct research involving human subjects in one of three ways:

- by exemption certification
- by expedited review.
- by full review;

The investigator makes the preliminary determination of the type of review for which a study is eligible. Please refer to ORI's "Getting Started" page for more information about which activities are eligible for each type of review.

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

Efficacy of the OrthoApnea NOA® mandibular advancement device in the management of obstructive sleep apnea. Clinical trial and retrospective comparison study.

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

Mandibular advancement device for OSA

Anticipated Ending Date of Research Project: 7/31/2023

Maximum number of human subjects (or records/specimens to be reviewed) 50

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? (•) Yes ( ) No

PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	Isabel	Room# & Bldg:	OFP
Last Name:	Moreno Hay	Speed Sort#:	40536
Middle Name			
Department:	Dentistry Oral Health Science …	Dept Code:	7A800
PI's Employee/Student ID#:	10752795	Rank:	Division Chief
PI's Telephone #:	8593235500	Degree:	DDS MS PhD
PI's e-mail address:	imo226@uky.edu	PI's FAX Number:	
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	8/2/2022
		RCR Trained:	Yes

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- (●) (Risk Level 1) Not greater than minimal risk
- ( ) (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- ( ) (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ( ) (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

For Expedited and Exempt Applications, the research activities must be Risk Level 1 (no more than minimal risk to human subjects).

Refer to UK's guidance document on assessing the research risk for additional information.

SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc.) 18 to 80

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

For the prospective section, based on the effect sizes of the mandibular advancement device (MAD) based on past meta-analyses, we conducted a GPower which revealed that obtaining a sample size of 45 participants to would provide us 80% power to detect the anticipated effects. To compensate for dropout/attrition, we aim to recruit 50 participants.

No specific population will be targeted in terms of sex/gender or racial/ethnic background. The age range considers patients between 18 and 80 y.o. with a diagnosis of obstructive sleep apnea (OSA). Participants will be recruited from the consecutive patients referred to the Orofacial Pain Clinic for the management of OSA with a MAD.

Inclusion criteria:
- Age: >18 and <80 years old.
- No history of previous use of a MAD.
- Diagnosis of OSA by a sleep physician based on a PSG or HSAT (done >12 months before - evaluation date or > 12 months with >10% variation of BMI).
- Upon clinical examination: >8 teeth per arch; range of anteroposterior mandibular mobility >5 mm.
- Informed consent to participate in the study.

Exclusion criteria:
- Patients with concomitant diagnosed sleep disorders (i.e. insomnia, narcolepsy, restless legs syndrome, rapid eye movement sleep behavior disorder).
- History of previous allergic reaction to the appliance material (Polyamide 12).
- Patients using combination therapy for the management of OSA (i.e. PAP therapy or positional therapy).
- Upon clinical examination: periodontal disease (>4 mm on periodontal probing, with bleeding on probing, visual signs of periodontal inflammation); tooth horizontal mobility >1 mm, vertical mobility, and unfavorable crown to root ratio; open cavities, loose or fractured restorations, or patient undergoing restorative dental treatments.
- Exaggerated gag reflex.
- Lack of coordination or dexterity.
- Inadequate English comprehension.

For the retrospective section, the same inclusion and exclusion criteria will be considered when doing the data extraction.

The proposed dates of enrolment are from October/November 2021 to October/November 2022 (12 months since the starting date).

Attachments

Attach Type	File Name
StudyPopulation	Protocol NOA DEVICE 09202021.docx

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:	0	0		
Asian:	1	1		
Black/African American:	3	3		
Latinx:	1	1		
Native Hawaiian/Pacific Islander:	0	0		
White:	20	20		

American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:	0	0		

If unknown, please explain why:

Participants will be recruited from the patients referred to the Orofacial Pain Clinic (College of Dentistry, UK Kentucky Clinic), not targeting any specific population.

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking (translated long or short form)
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☑ Patients
- ☐ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a "Reliance Consent Form" so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a PDF.**
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☑ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☐ Stamped Consent Doc(s) Not Needed

Attachments

Attach Type	File Name
Informed Consent/HIPAA Combined Form	Informed ConsentHIPAA Combined Form_08.11.2022.pdf

Informed Consent Process:

Using active voice, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)
- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

PROSPECTIVE SECTION:
We will recruit participants from the consecutive patients referred to the Orofacial Pain Clinic (OFPC) for the management of obstructive sleep apnea (OSA) with a mandibular advancement device (MAD). As part of the standard clinical protocols, these patients are initially evaluated for eligibility to start OSA therapy with a mandibular advancement device by the residents under supervision of an attending provider of the Orofacial Pain Division (College of Dentistry – University of Kentucky) at the OFPC. After the evaluation, if the patient is eligible to start MAD therapy, the study will be offered as an option for their treatment or they can continue with the standard of care provided at the clinic. If the patient expresses interest in participating in the study, they will be evaluated for eligibility by having an initial assessment done by Dr. Diego Fernandez Vial, Dr. Fernanda Yanez Regonesi or by Dr. Isabel Moreno Hay. If the patient is eligible and agrees verbally to participate, they will be given the consent form to read.

The consent form will be offered electronically (in-person) using an iPad associated to EPIC (UK Healthcare). The patient will be allowed to take as much time as needed to read the information and a printed copy will be provided (contact information included in the copy). The patient will sign the electronic form using a digital signature on the iPad (in-person), or in paper format if any technical difficulty occurs. The hand-signed consent forms will be stored at the OFP clinic along with the rest of the paper data collection forms (locker Kentucky Clinic room E214). Only English speaking subjects will be considered as potential participants. Consequently, the consent form will be available in an English version only. If English is a second-language for the prospective subject, only those who routinely read and sign UK Healthcare documents in English will be considered eligible. During the recruitment process, the subject will be evaluated by the investigator(s) present for comprehension and will be asked to paraphrase their understanding of different aspects of the study (i.e, objectives of the study, potential risks, procedures, etc.). If patient demonstrates inadequate comprehension, they will not be considered eligible to participate in the study.

RETROSPECTIVE SECTION:
Archival data will be extracted from the records of patients that started MAD therapy for OSA at the Orofacial Pain Clinic (University of Kentucky) between 01/01/2010 and 08/17/2021. An active study involving MAD therapy outcomes (protocol #46643; same PI, Dr. Isabel Moreno Hay) includes a consent form for the retrospective participants to collect retrospective data that allows to use the obtained data in future research projects.
For the prospective section, the copy of the consent form that will be provided to the participants will include the the following information:
- PI: Dr. Isabel Moreno Hay: (859) 323 55 00; UK Kentucky Clinic. 740 S. Limestone, Second Floor, Wing C, Room E214, Lexington, KY 40536.
- ORI/IRB between business hours of 8 am and 5 pm EST, Monday- Friday at 859- 257-9428 or toll free at 1-866-400-9428.

For the retrospective section, since this is a retrospective chart review, we do not anticipate having to address participant complaints.

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except

for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

- Private information/specimens are “identifiable” if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the 18 HIPAA identifiers including dates of service.
- If not using identifiable private information or identifiable biospecimens, insert N/A below.

☐ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the ***Cover Letter Template*** *as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

○ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

(•) Yes ( ) No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Bailey	Autum	Data Analysis/Processing	SP	N	N	HHS major	P	Y	08/27/2022	Y	N	02/02/2023	N
Boggero	Ian	Project Assistance/Support	DP	N	Y	PhD	P	Y	07/14/2020	Y	N	10/18/2021	N
Dawson	Dawn	Project Assistance/Support	DP	Y	Y	RDH CCRC	P	Y	10/12/2022	Y	N	10/18/2021	N
Fernandez Vial	Diego	Co-Investigator	DP	Y	Y	DDS	P	Y	12/17/2020	Y	N	10/18/2021	N
Pasha	Sara	Project Assistance/Support	SP	N	N	MD	P	Y	10/13/2020	Y	N	10/18/2021	N
Yanez Regonesi	Fernanda	Co-Investigator	SP	Y	N	DDS, MS	P	Y	10/20/2022	Y	N	05/23/2022	N

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

Multiple mandibular advancement devices (MAD) are available on the market and have been used for the management of obstructive sleep apnea (OSA). They are specifically used to prevent upper airway collapse by protruding the mandible forward, thus altering the jaw and tongue position. The models vary regarding the titratability and the level of customization [1]. Titratable devices are thought to increase treatment success by allowing gradual adaptation to optimal protrusion [2] [3]. The effective degree of mandibular protrusion used in published studies has been highly variable, ranging from 50% to 80% of maximal protrusion [1] [4] [5] [6]. In mild to moderate cases of OSA, no differences were found between 50% and 75% of protrusion [5], whereas in severe cases of OSA, 75% of protrusion demonstrated to be more efficacious than 50% [6].

Oral appliance therapy has been associated with various short and long-term side effects. In relation to the short-term adverse effects: hyper-salivation [7], dry mouth [7], dental pain [7], gingival irritation [7], and temporomandibular disorders [7] [8] has been reported at an incidence rate ranging between 6% to 86%. The long-term side effects include: temporomandibular disorders [7] [8], occlusal changes (ie: a reduction in overjet [9] [10], overbite [9] [10], and development of posterior open bite [8] [10] among others) and range between 0% and 75% of patients [7] [9] [10]. In a recent meta-analysis, the odds of experiencing a side effect leading to discontinuation of therapy with an oral appliances was 6.65:1 (95% CI) [1]. In previous studies, it has been demonstrated that an increase in side effects could be expected at larger advancement levels [11] [12], especially with more than 50% of mandibular protrusion [11]. Therefore, having a MAD design that requires less degree of mandibular advancement to reach an adequate management of OSA represents a great benefit for the patients, and can lead to better compliance.

In the case of the Orthoapnea NOA® device, the customization level is reached with a personalized approach based on clinical pictures, digital dental scans, and radiographic studies. Therefore, this allows a design that guides the mouth opening with a forward mandibular motion. The main target is to move the jaw forward progressively, so that the more the mouth is opened, the more forward the mandible can be positioned. Therefore, the Orthoapnea NOA® device is thought to require a less degree of advancement to be effective in the management of OSA than other designs. Consequently, comparing this particular characteristic of the Orthoapnea NOA® with the other available device design is hypothesized to be correlated with a lower incidence of side effects and better patient compliance.

FDA approved use: "NOA SLEEP APNEA AND SNORING DEVICE is a mandibular advance device (MAD) indicated for obstructive sleep apnea (OSA) and to alleviate or reduce snoring in adults." (FDA K202651 ; https://www.accessdata.fda.gov/cdrh_docs/pdf20/K202651.pdf). See attachments.

REFERENCES:

1. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015. J Clin Sleep Med. 2015 Jul 15;11(7):773-827. doi: 10.5664/jcsm.4858. PMID: 26094920; PMCID: PMC4481062.
2. Fleury B, Rakotonanahary D, Petelle B, Vincent G, Pelletier Fleury N, Meyer B, Lebeau B. Mandibular advancement titration for obstructive sleep apnea: optimization of the procedure by combining clinical and oximetric parameters. Chest. 2004 May;125(5):1761-7. doi: 10.1378/chest.125.5.1761. PMID: 15136388.
3. Ngiam J, Balasubramaniam R, Darendeliler MA, Cheng AT, Waters K, Sullivan CE. Clinical guidelines for oral appliance therapy in the treatment of snoring and obstructive sleep apnoea. Aust Dent J. 2013 Dec;58(4):408-19. doi: 10.1111/adj.12111. PMID: 24320895.
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Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

1. To assess the efficacy of the Orthoapnea NOA® mandibular advancement device and describe the percentage of advancement (%) needed to reach efficacy, and to retrospectively compare with other MAD designs in the management of obstructive sleep apnea.
2. Describe patient compliance and adherence to the therapy with the Orthoapnea NOA® device.
3. To assess the incidence and prevalence of signs, symptoms, and diagnosis of temporomandibular disorders (TMD) associated to the use of the Orthoapnea NOA® mandibular advancement device.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.
- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

This study will incorporate a prospective and a retrospective section:

The prospective study will be an uncontrolled open-label clinical trial.

The retrospective component will extract previously collected archival data from medical records of patients that started MAD therapy for OSA at the Orofacial Pain Clinic (Kentucky Clinic). These subjects had a second sleep study performed to assess the effectiveness of the mandibular advancement devices.

Attachments

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

PROSPECTIVE SECTION:

We will recruit participants from the consecutive patients referred to the Orofacial Pain Clinic (OFPC) for the management of obstructive sleep apnea (OSA) with a mandibular advancement device (MAD). As part of the standard clinical protocols, these patients are initially evaluated for eligibility to start OSA therapy with a mandibular advancement device by the residents under supervision of an attending (provider) of the Orofacial Pain Division (College of Dentistry – University of Kentucky) at the OFPC. The PI, Dr. Isabel Moreno-Hay is one of the attendings. After this evaluation, if the patient is eligible to start MAD therapy, they will be offered to continue with the standard of care at the clinic or to be evaluated to participate in this study. If the patient decides to proceed and evaluated for eligibility for this study, the initial assessment will be done by Dr. Diego Fernandez Vial, or by Dr. Isabel Moreno Hay, or by Dr. Fernanda Yanez Regonesi. If the patient is eligible and agrees to participate, verbal consent will be obtained and all forms will be completed. After consent, the following sessions will be performed at the OFPC (UK Kentucky Clinic) or at the Delta Dental of Kentucky Clinical Research Center (College of Dentistry - University of Kentucky).

In order to offer the Orthoapnea NOA® device to eligible subjects that might like to participate, a report will be requested from Clinical data routinely collected in RedCap to identify patients that were evaluated within the last 3 yrs and referred to Dr. Isabel Moreno Hay for MAD therapy but did not return to start treatment. Those patients will be contacted via phone by Dr. Isabel Moreno Hay or by Dr. Diego Fernandez Vial (see phone script attached) to explain the study. If the patient is interested in participating in the study, an appointment will be scheduled to do an evaluation and initial assessment for eligibility for with Dr. Diego Fernandez Vial or with Dr. Isabel Moreno Hay. The treatment relationship that Dr. Isabel Moreno Hay has with those patient was only based on the initial evaluation performed, with no other sessions nor procedures conducted. There is no treatment relationship between Dr. Diego Fernandez Vial and those patients. Historically, there is a considerable number of patients that never started treatment because it was not covered by their insurance. So this recruitment will target and benefit a population with less access to health care. Contact with the participants for recruitment, scheduling and clinical sessions, will be carried out by Dr. Diego Fernandez Vial, Dr. Fernanda Yanez Regonesi and/or Dr. Isabel Moreno Hay.

All the information will be collected via paper questionnaires and data collection forms, and then transferred to an Excel spreadsheet that will be stored on a desktop computer (at the Oral Facial Pain Clinic). This desktop computer is password protected and is a only accessible to Dr. Diego Fernandez Vial (located in Kentucky Clinic room E214). The spreadsheet will capture the subject's de-identified data and it will be numbered consecutively starting with NOA -1 to NOA -50. After recruitment has been completed, the statistician (Dr. Ian Boggero) and the PI (Dr. Isabel Moreno Hay) will be given access to the information in the de-identified spreadsheet. All the paper questionnaires and data collection forms will be stored in a keyed locker at the Kentucky Clinic room E214, for back up and data verification, until the data analysis has been completed. The PI will maintain and store all the study documents for a minimum of six (6) years in the same location.

RETROSPECTIVE SECTION:

Archival data will be extracted from records of subject's that started MAD therapy for OSA at the Orofacial Pain Clinic (University of Kentucky) and were consented between 01/01/2010 and 08/17/2021 under protocol # 46643. The data collection process for this previously approved study is been conducted using REDCap (CCTS - University of Kentucky). Using this software, we plan to obtain a report to identify subjects that started MAD therapy and that had a second sleep study performed to assess the effectiveness of the MAD. Demographic data (age, gender, BMI), OSA diagnosis, sleep parameters (AHI, RDI, minimum and average oxygen saturation), level of advancement of the MAD (%) prior to the second sleep study, and compliance of use will be extracted. Thus creating a deidentified "report" (spreadsheet) from the REDCap database (assigning progressive numbers (starting with M-51)).
Print advertisements: The study will recruit subjects through flyers, brochures, posters, Research Spotlights, ads placed on campus and in the surrounding community and region (Study Team will place/remove ads), including but not limited to the UK Medical Center, UK Clinics, Good Samaritan Hospital, Student Center, UHS, the 5 UK Center for Clinical and Translational Research wall mounts, Cardinal Hill, monitor screens, and area facilities and businesses.

Internet and Social Media: This study will be advertised on recruitment internet webpages in digital or video form (e.g., UKclinicalresearch.com, ResearchMatch.org, UK Public Relations and HealthCare, CCTS and may utilize Google Adwords). The study will be promoted via social media, including Facebook boost ads, UK_CCTS Facebook, UK_CCTS Twitter, UK_CCTS Instagram, UKclinicalresearch_YouTube, UK and UKHC social media, and departmental/lab pages. If advertised on UKClinicalresearch.com, the online study flyer will include an option for interested individuals to enter and submit their contact information, they will be asked whether study team can contact them (Yes or No) via study related text messages, and CCTS will also ask, 'How did you learn about the study? Internet and social media recruitment will follow the terms of use for each site utilized. The study will also be promoted through UK HC monitor screens.

Research Participant Registries: Potential participants may be identified from registry databases, including but not limited to ResearchMatch.org*, WellnessHealthandYou.org, Sanders Brown Center on Aging, Infectious Disease, Dentistry, and the Markey Cancer Center. *ResearchMatch.org/uky will be utilized as a recruitment tool for this protocol. ResearchMatch.org/uky is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University as an IRB approved data repository (Vanderbilt University IRB #090207)." Once UK IRB approval is obtained the researcher or proxy will upload a flyer with no contact information via ResearchMatch email to selected de-identified participants in the ResearchMatch registry. If the de-identified participant selects "Yes, I'm interested!" the researcher or proxy will receive information about participant and they may contact them with more information about their research study. If the participant selects "No, thanks", researcher or proxy will not receive any information from de-identified participant.

Outreach activities: The CCTS attends outreach activities to promote research participation in general (e.g., Roots & Heritage Festival, Latino Festival, Eastern Kentucky University, Transylvania Health fairs, etc.) and will brings all relevant study flyers that are enrolling participants.

E-Newsletters and ListServs: This study may also go out on email distribution, listservs, or enewsletters, e.g., the CCTS list serv, Markey Cancer Affiliates list servs, ResearchMatch.org, Wednesday's Word, Kentucky Office of Rural Health (KORH), Appalachian Translational Research Network (ATRN), etc. Physician referral letters to community physicians for patient recruitment.

UK Public Relations (College/Dept. PR personnel) and UK HealthCare venues: Articles and interviews about the researchers and research study may be promoted via UKNow, Kentucky living, and other media outlets. Research and study-related articles published on UKNow may contain standard language directing interested individuals on where to read more about research and current studies: You can make a difference through participating in research and discovery. To find more information, including a list of current studies at UK and access to studies nationwide, please visit UKclinicalresearch.com or call 859.257.7856 or join the ResearchMatch.org or wellnesshealthandyou.org registries to be matched today. UKPR, UK HealthCare marketing or the CCTS PRS may create videos to promote research, researchers and their studies to local, regional and national media venues and on internal hospital monitors. UK HealthCare may place study recruitment flyers on their internal and external racks (e.g., UK pharmacies, clinics, UK Libraries and Lexington Libraries) or on digital monitors. Participants may be recruited using newsletters, such as In the Loop, Health Matters, Making a difference, and external news letters. The study may also be advertised through UKPR and UKHC outreach activities. UKHC and CCTS have booths at many events, and researchers and coordinators are invited to attend any events that pertain to their study populations. Researchers may participate in radio or TV interviews. General information about their research may be presented with a phone number or website url for more study specify information. Consenting members of the research team and/or consenting participants may be interviewed about the study for print, radio, or video which may be distributed via the aforementioned activities.

Attachments

Attach Type	File Name
Advertising	Advertisements 71295.docx
Advertising	DENT-036 MON stamped.pdf
Advertising	DENT-036 MON.pdf
Advertising	DENT-036 research match stamped.pdf
Advertising	DENT-036 research match.pdf
Advertising	DENT-036 social media stamped.pdf
Advertising	DENT-036_ flyer.pdf
Advertising	DENT-036 social media.pdf
Advertising	DENT-036_ flyer_stamped.pdf

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

PROSPECTIVE SECTION:
An Orthoapnea NOA® (OrthoApnea® laboratory, Malaga, Spain; FDA K202651) appliance will be custom made for each participant. Digital impressions (scanner 3Shape TRIOS® 3 (does not involve any form of radiation)), protrusive records will be obtained at 50% from maximum retrusion (5 mm fork and George GaugeTM, and clinical pictures will be obtained following the protocol recommended by the manufacturer. Maximum opening will be measured adding the interincisal distance to the overbite (in millimeters, using TheraBite® Range of Motion ruler). Information will be uploaded in the laboratory software (Apneadock®) to order the appliance. The MAD will be fabricated at an initial protrusion of 50%, with subsequent progressive mandibular components of additional 10% of protrusion until 80% of the maximum protrusive is achieved. Lastly, a full coverage morning deprogrammer (TAP® AM Aligner - Airway Management Inc) will be fabricated for all the participants to be used for 10 minutes upon removal of the MAD. Verbal and written instructions will be provided.

At the device delivery appointment, we will fabricate an aligner for the patient to wear for 10 minutes each morning after waking and removing the OrthoApnea NOA® oral appliance. The morning aligner (TAP® AM Aligner) is a record of the patient's habitual bite (the way the teeth come together normally) that will reposition their mandible back into its normal position. It is part of the standard of care for patients undergoing mandibular advancement (MAD) therapy. The aligner is constructed from a thermoplastic material that, when heated, can be molded by hand onto the upper or lower teeth. Once the thermoplastic material is molded around the teeth, they will be instructed to bite down while it is still soft. This will create indentations for the opposing teeth and allow them to be set at their 'normal' and proper biting position. After the molded thermoplastic material has hardened at normal temperature, it is removed from the mouth and trimmed, if needed.

Follow up sessions will be scheduled every two weeks until maximum therapeutic benefit is achieved. At each follow up visit patients will be asked to fill out a questionnaire and further advancement of the MAD will be determined by changes in patients' symptoms and Epworth Sleepiness Scale (ESS). Measures of successful management include: ESS < 10, and >70% reduction or absence of snoring, observed apneic events, and daytime fatigue, to be assessed via questionnaire using a numerical rating scale (NRS). Once the patient has obtained successful management of symptoms, 80% of maximum protrusive or is unable to tolerate the advancement, a home sleep apnea test (Alice NightOne, Phillips Respironics©) will be provided to the patient to perform one night while wearing the appliance to determine the efficacy of the MAD. We will verbally instruct the patient how to operate the machine, and a printed copy of the manufacturer protocol for patients will be provided. Additionally, we will provide our contact number if any question arise. An appointment will be scheduled in the following 2-3 days to return the machine, and to further advance the appliance if needed. Sleep parameters including: AHI, RDI, minimum and average oxygen saturation will be extracted from the initial PSG, and by a trained technician from the final home sleep apnea test, which will be scored following the American Academy of Sleep Medicine Scoring Manual.

The efficacy of the appliance for the management of OSA will be stablished based on two criteria. Criterion I: > 50% reduction of AHI/RDI. Criterion II: AHI/RDI < 5 events/hour or <15 events/hour with a significative reduction of OSA associates symptoms as defined before. Therapeutic failure will be established when at 100% of advancement of the device, there is less than 50% of reduction of the AHI/RDI with a residual AHI/RDI >5 events/hour with OSA associates symptoms.

If the criteria for success is reached, the participation of the patient in the present study will be ended. The subject will be offered to continue with standard of care in the OFPC for future follow-ups, and a report will be provided and sent to the treating sleep physician. The subject will be allowed to keep the appliance after the study is completed. If participants do not reach a successful management of OSA at 100% of advancement, they will be referred back to their referring sleep physician to consider another treatment option.

The participation in this research will last between seven to sixteen weeks depending on the time for each patient's individual improvement. The initial visit will last 45-60 minutes, and the follow-up sessions will take about 30-45 minutes. After participation in the study is completed, the participants will be allowed to keep the MAD and all the accessories provided by the manufacturer

RETROSPECTIVE SECTION:
Archival data will be extracted from records of patients that started MAD therapy for OSA at the Orofacial Pain Clinic (University of Kentucky) between 01/01/2010 and 08/17/2021. An active study involving MAD therapy outcomes (protocol #46643; same PI, Dr. Isabel Moreno Hay) includes a consent form for the retrospective participants to collect retrospective data and future use of that data in future research projects. The data collection process of the previous study is being conducted using RED Cap (CCTS - University of Kentucky), and through that software, we intend to obtain a report to identify subjects that started MAD therapy and had a second sleep study performed to assess the effectiveness of the MAD. Data regarding demographic characteristics (age, gender, BMI and OSA

diagnosis), sleep parameters (AHI, RDI, minimum and average oxygen saturation), level of advancement of the MAD (%) prior to the second sleep study, and compliance of use will be extracted creating a deidentified "report" (spreadsheet) from the RED Cap database (assigning progressive numbers (starting with M51)).

Attachments

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

This study has a prospective and a retrospective component. (SEE ANNEX IN ATTACHMENTS)

1) Prospective study: data will be obtained using paper questionnaires:
- Demographic information regarding age, race, gender and comorbidities will be extracted from the initial questionnaire (Annex 1).
- The self-reported use of MAD will be assessed at each follow-up via questionnaire on a five-point checklist (number hours per night and nights per week) (to be extracted from Annex 6).
- Epworth sleepiness scale (ESS) (Annex 1 and 6)
- Snoring, observed apneic events, and daytime fatigue, to be assessed via questionnaire using a numerical rating scale (NRS) (to be extracted from Annex 1 and 6).
- Sleep parameters including: AHI, RDI, minimum and average oxygen saturation will be extracted from the initial PSG, and by a trained technician from the final home sleep apnea test.
- The presence of signs, symptoms of TMD will be assessed following the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) Symptom Questionnaire and Examination Form (Annex 2 and 4).
- Additional parameters will be controlled, including the presence of morning headaches (to be evaluated via questionnaire at baseline and at each follow-up using NRS), waking up during the night to urinate (to be evaluated at baseline and at each follow-up via questionnaire using continuous numeric scale), and the sleep quality (will be assessed at baseline and when performing the home sleep apnea test, using the Pittsburgh Sleep Quality Index (PSQI) questionnaire). Patients subjective perception of improvement will be assessed at each follow up using visual analog scale (to be extracted from Annex 6).
- Incidence of side effects will be assessed at each follow-up session, including subjective increase/decrease salivation (measured via questionnaire using numeric rating scale), increase/decrease teeth mobility, changes in occlusal contacts (measured in habitual occlusion using 0.01 mm occlusal registration strips (ARTUS corporation®) (to be extracted from Annex 6&7).
- Problems related to the appliance will be measured at each follow up session, considering appliance breaks, cracks, deformation, retention changes, wear, discoloration changes and calculus accumulation (to be extracted from Annex 7).

2) Retrospective study: Archival data will be extracted from from records of patients that started MAD therapy for OSA at the Orofacial Pain Clinic (University of Kentucky) between 01/01/2010 and 08/17/2021. An active study involving MAD therapy outcomes (protocol #46643; same PI, Dr. Isabel Moreno Hay) includes a consent form for the retrospective participants to collect retrospective data that allows to use the obtained data in future research projects. The data collection process of the previous study is being conducted using RED Cap (CCTS - University of Kentucky), and through that software, we pretend to obtain a report to identify subjects that started MAD therapy and that had a second sleep study performed to assess the effectiveness of the MAD. Data regarding demographic characteristics (age, gender, BMI and OSA diagnosis), sleep parameters (AHI, RDI, minimum and average oxygen saturation), level of advancement of the MAD (%) prior to the second sleep study, and compliance of use will be extracted creating a deidentified "report" (spreadsheet) from the RED Cap database (assigning progressive numbers (starting with M51)).

Attachments

Attach Type	File Name
DataCollection	Annex MP Orthoapnea.docx

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

a) Staff and personnel:
- Dr. Isabel Moreno Hay DDS PhD ABOP ABDSM (PI): participation in the recruitment of patients, clinical procedures and data

collection.
- Dr. Diego Fernandez Vial, DDS (Co-Investigator): participation in the recruitment of patients, clinical procedures and data collection.
- Dawn Dawson, RDH, CCRC: Study coordinator.
- Dr. Ian Boggero PhD: Project Assistance/Support and biostatistician.
- Dr. Sara Pasha MD: Project Assistance/Support.
- Dr. Fernanda Yanez Regonesi, DDS Ms (Co-Investigator): participation in the recruitment of patients, clinical procedures and data collection.

b) Facilities:
- Primary center: Orofacial Pain clinic (UK Kentucky Clinic. 740 S. Limestone, Second Floor, Wing C, Room E214, Lexington, KY 40536)
- Secondary center (to be used only if there is no availability at the primary): Center for Oral Health Research (414 Health Sciences Research Bldg. Lexington, KY. 40536-0305College of Dentistry - University of Kentucky).

c) Resources:
- Desk computer at the Orofacial Pain Clinic (Kentucky Clinic room E214; UK Healthcare system; J066143): This computer will be used for data entering, collection and analysis. Access only by Dr. Diego Fernandez Vial (protected with password). Files (Microsoft Word and Excel) will be protected with a password.
- External USB flash drive: For data back-up. A back-up of the data will be performed every week. The drive will have Endpoint Encryption. Files (Microsoft Word and Excel) will be protected with a password. The flash drive will be stored in a key locked locker at the OFPC (access only by Diego Fernandez Vial).
- Land line phone (at the OFPC): will be the primary way of communication with participants. UKY annex #83135.
- Email: the email of Dr. Diego Fernandez Vial (dfe@uky.edu) may be used as an alternative to the land line phone if it is needed to communicate with the participants.
- Digital scanner and computer: 3Shape TRIOS® 3 (at the OFPC). The scans will be obtained and sent to the lab from the computer that is associated to the scanner.
- Home sleep apnea test (HSAT): Alice NightOne, Phillips Respironics©.
- EPIC

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

Initially, when explaining the consent form, the patient will be informed regarding the potential side effects associated to the oral appliance therapy for OSA, and will be instructed to contact us (via phone call or email) if they have any question or if they notice any side effects. The incidence of side effects will be assessed at each follow-up session, including subjective increase/decrease salivation (measured via questionnaire using numeric rating scale), increase/decrease teeth mobility, changes in occlusal contacts (measured in habitual occlusion using 0.01 mm occlusal registration strips (ARTUS corporation®). Problems related to the appliance will be measured at each follow up session, considering appliance breaks, cracks, deformation, retention changes, wear, discoloration changes and calculus accumulation.

The use of the home sleep apnea test machine do not represent significant risks for the subjects. The nasal canula and tape to be used are one-time use, and each patient will be provided with a new one. The machine will be disinfected once is returned, and will stay at least one day without use between different patients. The potential risk to participating in an at home sleep study is disrupted sleep and possible cheek irritation from the medical tape placed on the nasal tubing to keep it in place overnight. Participants might find it challenging to sleep with the additional equipment, so sleep disturbances might occur.
BACKGROUND: Patients with untreated OSA may be at increased risk of developing cardiovascular disease, including difficulty to control blood pressure, coronary artery disease, congestive heart failure, arrhythmias, and stroke. OSA is also associated with metabolic dysregulation, affecting glucose control and risk for diabetes. Continuous positive air pressure (CPAP) is the main therapeutic option in patients with OSA, but the use of mandibular advancement devices has markedly increased in the last decades, and have been associated with higher levels of compliance than CPAP. When comparing CPAP versus mandibular advancement devices (MAD), there was found to be no significant difference between MAD and CPAP in the percentage of mild OSA patients

achieving their target AHI/RDI/ REI after treatment.

BENEFITS: In previous studies, it has been demonstrated that an increase in side effects could be expected at larger advancement levels, especially with more than 50% of mandibular protrusion. Therefore, having a MAD design that requires less degree of mandibular advancement to reach an adequate management of OSA represents a great benefit for the patients, and can lead to better compliance. That's why the MAD that will be tested in this study represent a potential benefit to the patients with OSA, which is a life-threatening condition when is not properly managed.

RISKS: Oral appliance therapy is associated with short and long-term side effects. In relation to the short-term adverse effects, usually mild and transient, it has been reported hypersalivation, dry mouth, dental pain, gingival irritation, and temporomandibular disorders. Regarding the long-term side effects, we can expect: temporomandibular disorders, occlusal changes including: a reduction in overjet, overbite, and development of posterior open bite among others.

BENEFITS vs. RISKS: This therapeutic option can be associated with minimal and non life-threatening risks, and the risks to subjects are reasonable in relation to the anticipated benefits. The mandibular advancement devices are considered as a standard care option for the management of OSA.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

Continuous positive air pressure (CPAP) is the main therapeutic option in patients with OSA. Reduced symptoms of sleepiness improved health-related quality of life, cardiovascular outcomes such as hypertension, dyslipidemia, and insulin resistance after CPAP treatment have been reported. In the last few decades, the clinical use of oral appliances for the management of snoring and obstructive sleep apnea has markedly increased. When comparing CPAP versus mandibular advancement devices (MAD), there was found to be no significant difference between MAD and CPAP in the percentage of mild OSA patients achieving their target AHI/RDI/ REI after treatment. However, for patients with moderate to severe OSA the odds of achieving the target AHI were significantly greater with CPAP than with MAD.
The patients referred to the Orofacial Pain Clinic for MAD therapy, the ones that will be targeted to be recruited for this study, are patients that were not able to tolerate previous therapeutic options.

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Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies
Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

PROSPECTIVE SECTION: Information will be mostly obtained via questionnaires (see protocol and annex attached). Demographic information and past reports of diagnostic sleep study will be obtained from EPIC.

RETROSPECTIVE SECTION: Archival data will be extracted from from records of patients that started MAD therapy for OSA at the Orofacial Pain Clinic (University of Kentucky) between 01/01/2010 and 08/17/2021. An active study involving MAD therapy outcomes (protocol #46643; same PI, Dr. Isabel Moreno Hay) includes a consent form for the retrospective participants to collect retrospective data that allows to use the obtained data in future research projects. The data collection process of the previous study is being conducted using RED Cap (CCTS - University of Kentucky), and through that software, we pretend to obtain a report to identify subjects that started MAD therapy and that had a second sleep study performed to assess the effectiveness of the MAD. Data

regarding demographic characteristics (age, gender, BMI and OSA diagnosis), sleep parameters (AHI, RDI, minimum and average oxygen saturation), level of advancement of the MAD (%) prior to the second sleep study, and compliance of use will be extracted creating a deidentified "report" (spreadsheet) from the RED Cap database (assigning progressive numbers (starting with M51)).
All the information will be collected via paper questionnaires and forms, and then transferred to an Excel spreadsheet (protected with pasword) that will be stored in a desktop computer (UK Kentucky Clinic room E214; UK Healthcare system; J066143), to which initially only Dr. Diego Fernandez Vial will have access. In the spreadsheet, the patients will be identified with consecutive numbers (NOA1-NOA50) and their dates of birth. After the recruitment period, the statistician (Dr. Ian Boggero) and Dr. Isabel Moreno Hay will have access to the spreadsheet. All the paper questionnaires and forms will be stored (for back up and data verification if needed) in a key locked locker (access only by Dr. Diego Fernandez Vial and Dr. Isabel Moreno Hay). Data will be retained for 6 years after study closure and deleted using UK Policy(s) A13-050 and A05-055.

Special protection:
- Desk computer at the Orofacial Pain Clinic (UK Kentucky Clinic room E214; UK Healthcare system; J066143): This computer will be used for data entering, collection and analysis. Access only by Dr. Diego Fernandez Vial (protected with password). Files (Microsoft Word and Excel) will be protected with a password.
- External USB flash drive (Endpoint Encryption): For data back-up. A back-up of the data will be performed every week. Files (Microsoft Word and Excel) will be protected with a password. The flash drive will be stored in a key locked locker at the OFPC (access only by Dr. Diego Fernandez Vial; Kentucky Clinic room E214).
- Digital scanner and computer: 3Shape TRIOS® 3 (at the OFPC). The scans will be obtained and sent to the lab from the computer that is associated to the scanner. Access protected with password.
The side effects associated to the oral appliance therapy for the management of obstructive sleep apnea are minimum and not associated with life-threatening events. The patient will be informed regarding the potential side effects associated to the oral appliance therapy for OSA, and will be instructed to contact us (via phone call or email) if they have any question or if they notice any side effects. The incidence of side effects will be assessed at each follow-up session.

Active contact with the participants for recruitment, scheduling and clinical sessions, will be carried only by Dr. Diego Fernandez Vial, Dr. Fernanda Yanez Regonesi and/or Dr. Isabel Moreno Hay. All the information will be collected via paper questionnaires and forms, and then transferred to an Excel spreadsheet (password protected) that will be stored in a desktop computer (Kentucky Clinic room E214; UK Healthcare system; J066143), to which initially only Dr. Diego Fernandez Vial will have access. In the spreadsheet, the patients will be identified with consecutive numbers (NOA1-NOA50) and their dates of birth. After the recruitment period, the statistician (Dr. Ian Boggero), Dr. Fernanda Yanez Regonesi and Dr. Isabel Moreno Hay will have access to the deidentified spreadsheet. All the paper questionnaires and forms will be stored (for back up and data verification if needed) in a key locked locker (at Orofacial Pain Clinic, UK Kentucky Clinic, Room E214). Data will be retained for 6 years after study closure and deleted using UK Policy(s) A13-050 and A05-055, under the responsibility of the primary investigator (Dr. Isabel Moreno Hay). A back-up of the data will be performed every week using a flash drive (Endpoint Encryption) that will be stored in a key locked locker at the OFPC (access only by Dr. Diego Fernandez Vial; Kentucky Clinic room E214).

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Do you confirm that you will retain all IRB-related records for a minimum of 6 years after study closure?
◉ Yes ○ No

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Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

No monetary payment will be offered. The device and the confirmatory sleep study will be provided with no cost for the participants.

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is “standard” – and thus not covered by the sponsor/study – unless you tell them.

No monetary payment will be offered. The device and the confirmatory sleep study will be provided with no cost for the participants. The participant will be responsible for the expenses for commuting to the research place (parking costs, gas, transportation, etc).

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.

- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

This study is considered as not greater than minimal risk (Risk Level 1), so should not require a data and safety monitoring board. The DSM Plan will consist in that the PI will be responsible for the study to review safety, progress, compliance, quality, and data-integrity on an ongoing basis.

The clinical component of this research will be carried out by Dr. Fernandez Vial. At each session, the patient will be asked via questionnaire about the occurrence of any side effect or problems related to the appliance (se previous description in protocol). Additionally, the patient will be instructed to contact us if any harm is detected (contact information will be provided). If the occurrence of any of the expected minor side effects previously described is reported by the patient, or detected by Dr. Fernandez Vial during the examination, the patient will be notified, and if wants to continue in the study, no other measures will be taken. If any injury, or potential injury, is detected, the PI will be informed immediately in order to stablish the most beneficial management for the patient. Additionally, the IRB will be notified. If required, the participation of the subject in the study will be ended, and patient will be recommended to continue with standard care. Additionally, every six months, or beforehand if needed, all the members of the research team will meet to discuss progress and any concern that may arise.

This is an independent study and there is no conflict of interest nor economic profit for any of the members of the research team.

Future Use and Sharing of Research Data

If the results of this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

All the information collected will be kept for six years after the study closure and will be available to be used in other research studies for that period. The data entered in the excel spreadsheet that will be used for the statistical analysis in this study does not contain identifiable information of any participant. Instead, are coded using consecutive numbers (NOA1-NOA50). As specified in previous sections, the USB flash drive (Endpoint encryption) containing the digital copy of the spreadsheet will be stored together with the other documents collected and only the PI (Isabel Moreno-Hay) will have access. At the present time, there are no research studies planned for which the data collected in this study may be used. If in the future any research study requires the data collected in this study, it will count with the participation of the PI of this study (Isabel Moreno-Hay) and will be related to retrospective research on the topic of dental sleep medicine and temporomandibular disorders. In that scenario, the PI will share the information with the statistician (spreadsheet downloaded from the encrypted USB flash drive) of that study and the copy of the file will be protected following the IRB protocols planed for that research for data storage and use. The USB flash drive will be returned to the original storage place. The future use of the spreadsheet does not represent any risk to the participant's confidentiality.

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant

for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the "Additional Information/Materials" section. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?
○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:
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1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?

○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for all investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?
○ Yes ○ No

If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

If yes, check below all that apply and attach the applicable document(s):

☐ HIPAA De-identification Certification Form
☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐		Held By:	
Investigator: ☐		Held By:	
Other: ☐		Held By:	

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer "no" above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ○ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor's authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Medical Device SOP.

Does the intended use of any research device being tested (not clinically observed) in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) as used in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- No. All devices, as used in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky, at sites that are geographically separate from UK, or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK

sites.

- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

List all other non-UK owned/operated locations where the research will be conducted:

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Attachments

B) Is this a multi-site study for which **you are the lead investigator or UK is the lead site**? ○ Yes ◉ No

If YES, describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

C) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

RESEARCH ATTRIBUTES

0 unresolved comment(s)

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

	For additional requirements and information:
☑ Academic Degree/Required Research	• Cancer Research (MCC PRMC)
☐ Alcohol/Drug/Substance Abuse Research	• Certificate of Confidentiality (look up "Confidentiality/Privacy...")
☐ Biological Specimen Bank Creation (for sharing)	• CCTS (Center for Clinical and Translational Science)
☐ Cancer Research	• Clinical Research (look up "What is the definition of....)
☐ CCTS-Center for Clinical & Translational Science	• Clinical Trial
☐ Certificate of Confidentiality	• Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
☑ Clinical Research	• Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
☐ Clinical Trial - Phase 1	• Community-Based Participatory Research (look up "Community-Engaged...")
☑ Clinical Trial	• Data & Safety Monitoring Board (DSMB)
☐ Collection of Biological Specimens for internal banking and use (not sharing)	*For Medical IRB: Service Request Form for CCTS DSMB
☐ Community-Based Participatory Research	• Data & Safety Monitoring Plan
☐ Deception	• Deception*
☐ Educational/Student Records (e.g., GPA, test scores)	*For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Emergency Use (Single Patient)	• Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
☐ Gene Transfer	• Genetic Research (look up "Specimen/Tissue Collection...")
☐ Genetic Research	• Gene Transfer
☐ GWAS (Genome-Wide Association Study) or NIH Genomic Data Sharing (GDS)	• HIV/AIDS Research (look up "Reportable Diseases/Conditions")
☐ Human Cells, Tissues, and Cellular and Tissue Based Products	• Screening for Reportable Diseases [E2.0000] (PDF)
☐ Individual Expanded Access or Compassionate Use	• International Research (look up "International & Non-English Speaking")
☐ International Research	• NIH Genomic Data Sharing (GDS) Policy (PDF)
☐ Planned Emergency Research Involving Exception from Informed Consent	• Planned Emergency Research Involving Waiver of Informed Consent*
☐ Recombinant DNA	*For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Registry or data repository creation	• Use, storage and disposal of radioactive material and radiation producing devices
☐ Stem Cell Research	
☐ Suicide Ideation or Behavior Research	
☐ Survey Research	
☐ Transplants	
☐ Use, storage and disposal of radioactive material and radiation producing devices	
☐ Vaccine Trials	

FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

☐ Grant application pending
☐ (HHS) Dept. of Health & Human Services
☐ (NIH) National Institutes of Health
☐ (CDC) Centers for Disease Control & Prevention
☐ (HRSA) Health Resources and Services Administration
☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
☐ (DoJ) Department of Justice or Bureau of Prisons
☐ (DoE) Department of Energy
☐ (EPA) Environmental Protection Agency
☐ Federal Agencies Other Than Those Listed Here
☑ Industry (Other than Pharmaceutical Companies)
☐ Internal Grant Program w/ proposal
☐ Internal Grant Program w/o proposal
☐ National Science Foundation
☐ Other Institutions of Higher Education
☐ Pharmaceutical Company
☐ Private Foundation/Association
☐ U.S. Department of Education
☐ State

Other:

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

The laboratory (OrthoApnea® laboratory, Malaga, Spain) that produces the device (NOA SLEEP APNEA AND SNORING DEVICE) will provide the devices at no cost for the research team nor to the patient, along with a home sleep apnea test machine (Alice Nightone, Phillips). No direct economical contribution will be provided to the research team nor to the patients.
This will be an independent study, with no participation of laboratory representatives.

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.

If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

Additional Information

- ☐ Institutional Biosafety Committee
- ☐ Radiation Safety Committee
- ☐ Radioactive Drug Research Committee
- ☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
- ☐ Graduate Medical Education Committee (GME)
- ☐ Office of Medical Education (OME)

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

Do you want specific information inserted into your approval letter? ○ Yes ◉ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☑ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Other Documents

Protocol/Other Attachments

Attach Type	File Name
Other	K202651.pdf
Protocol	Protocol NOA DEVICE 09202021.docx

NOTE: [Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
Isabel	Moreno Hay	Principal Investigator	Dentistry Oral Health Science	08/19/2021 03:45 PM	View/Sign
Melvyn	Yeoh	Department Authorization	Dentistry Oral Health Science	06/08/2022 08:45 AM	View/Sign

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Please notify the personnel required for signing your IRB application after sending for signatures. Once all signatures have been recorded, you will need to return to this section to submit your application to ORI.

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

SUBMISSION INFORMATION

0 unresolved comment(s)

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Your protocol has been submitted.

STATISTICAL METHODS: For the prospective section, a power analysis was conducted based on effect sizes or efficacy of other MAD appliances as previously reported in the literature. Based on the effect sizes of the MAD based on the meta-analyses (d = -2.063),(9) we conducted a meta-analysis using GPower which revealed that obtaining a sample size of 33 participants would provide us 80% power to detect the anticipated effects.

Aim 1.1 was to assess the efficacy of the NOA® mandibular advancement device. To do this, we had two different criteria for success as defined before. For each of these criteria, we calculated the proportion of patients who "succeeded" vs. "failed." As exploratory analyses, we used independent samples t-test or chi-square testes (as appropriate) to compare baseline demographic characteristics between those who succeeded and failed for each of the criteria. **Aim 1.2** was to describe the percentage of advancement (%) needed to reach efficacy for the NOA® appliance in the management of obstructive sleep apnea. For this aim, we only examined the data of those who "succeeded" in Aim 1.1. Paired samples t-tests were carried out to detect the possible statistically significant differences in each of the parameters studied before and after receiving the treatment. The sociodemographic characteristics and other variables of interest of the patients included in the prospective and retrospective studies were described (n, mean ± SD).

Aim 2 was to describe patient compliance to the NOA® device in the management of obstructive sleep apnea. Using the definition of compliance provided above, we computed the proportion of study participants who complied with the NOA® appliance and described the use in terms of nights per week and hours per night (n, mean ± SD).

Aim 3 was to assess the incidence and prevalence of temporomandibular disorder (TMD) diagnoses, morning headaches, possible sleep bruxism, nighttime voids, sleep quality, side effects, and of problems related to the NOA® appliance during the titration process by using paired samples t-test or chi-square testes (as appropriate) to compare baseline and final values between those who succeeded and failed for each of the criteria.

Mean and standard deviation and other centralization measures were calculated for quantitative variables, frequencies, and percentage values were calculated for categorical variables. The McNemar test was used as a significance test, with which assessed if there were significant changes. Statistical significance was defined by p <0.05. All analyses were conducted using SPSS version 29.