AWARD NUMBER: W81XWH-22-C-0051

TITLE: Wearable Neurotechnology for Treatment of Insomnia

PRINCIPAL INVESTIGATOR: Dr. Stephen Simons

CONTRACTING ORGANIZATION: Teledyne Scientific & Imaging, LLC

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PREPARED FOR: U.S. Army Medical Research and Development Command
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5e. TASK NUMBER

5f. WORK UNIT NUMBER

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Teledyne Scientific & Imaging, 19 TW Alexander Drive, Durham, NC 27703

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Over the previous year, Teledyne developed, built, tested and delivered 20 prototype PeakSleep wearable headsets to Geneva for use in the current clinical trial. IRB approval was obtained on June 8th, 2023 and the Human Research Protections Office for the Department of Defense waived their jurisdiction of the study since it was reviewed by an existing DoD IRB at the Uniformed Services University for Health Science. Enrollment is slated to begin in October 2023 following several required minor amendments to the protocol.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:	17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

   This program is focused on the traditional feasibility clinical trial of a new therapeutic approach to treat insomnia using transcranial electrical stimulation (tES). We will test delivery of 30 minutes of short duration repetitive tES at 0.75 Hz immediately before bedtime in a population of 60 active duty military. The study will be conducted by Dr. Kent Werner at the Uniformed Services University of Health Science (USUHS) using Teledyne's PeakSleep™ wearable device.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

   Insomnia, transcranial electrical stimulation, PeakSleep, clinical trial

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

   What were the major goals of the project?
   List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

   The major aims of the Phase 1 Base are:
   1) To obtain the necessary regulatory approvals to begin clinical trial work by 8 months after contract (MAC)
   2) To execute a traditional feasibility clinical trial to investigate the safety and efficacy of the Teledyne PeakSleep™ device to treat insomnia in at least 48 patients (enrolling 60).

   Phase 1 milestones by task:

   Prepare Regulatory Documents and Research Protocols
   3 MAC - IRB approval at USUHS. Completed 9 MAC.
   7 MAC – OHRO approval for clinical protocol. Completed 10 MAC.
   8 MAC – Any required FDA approvals for any protocol changes (now unnecessary because the FDA determined this was a non-significant risk study). N/A.

   Clinical Trial Preparation
   7 MAC – 20 quality-control tested PeakSleep™ devices delivered to USUHS. Completed 6 MAC.
   8 MAC – Research staff trained in data collection. Completed 8 MAC.

   Clinical Trial Execution
   15 MAC – Intermediate analyses exploring initial efficacy of PeakSleep™
   20 MAC – Enrollment complete, with 48 complete and analyzable datasets
   24 MAC – Final analyses of impact of intervention on sleep onset latency, accompanying subjective measures of sleep and brain-based biomarkers of PeakSleep™

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Teledyne completed the development and testing of 20 PeakSleep^{TM} devices during the first 6 MAC. The devices were delivered to USUHS in April of 2023 by Dr. Stephen Simons during a program review to go over clinical procedures and test the devices. Following multiple requested revisions by the USUHS IRB, approval was granted in June 2023. OHRO waived jurisdiction of the protocol to the USUHS IRB in July 2023. Multiple small amendments have since been filed with the USUHS IRB and enrollment is anticipated to begin in October 2023.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Our focus over the coming year will be to enroll and complete as many patients as possible towards our goal of 48 complete. There is considerable interest among the patient population at USUHS with over 25 individuals already expressing interest in participation. We anticipate that enrollment will ramp quickly once it has begun.

Remaining goals:

Clinical Trial Execution
15 MAC – Intermediate analyses exploring initial efficacy of PeakSleep™
20 MAC – Enrollment complete, with 48 complete and analyzable datasets
24 MAC – Final analyses of impact of intervention on sleep onset latency, accompanying subjective measures of sleep and brain-based biomarkers of PeakSleep™

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Initially, we had planned for Walter Reed National Military Medical Center (WRNMMC) to be the clinical trial site. In early 2023, due to concerns about the length of time to obtain IRB approvals through the WRNMMC IRB, we decided to change the clinical trial site to USUHS but recruit at both WRNMMC and USUHS. This required USUHS IRB approval only, and the change is not anticipated to affect recruitment rates. On 24 Feb 2023, we received a request from USAMRAA for an updated proposal and budget reflecting this change. On 1 May 2023, contract modification P00001 was fully executed which incorporated Teledyne's revised research proposal, budget, and Statement of Work. The only changes to the Statement of Work are the addition of USUHS as a third research site where the clinical trial will take place, and only recruitment will occur at WRNMMC.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

IRB by USUHS and subsequent regulatory steps including for a data sharing agreement have taken considerably longer than anticipated. The original protocol was filed in December of 2022, however the USUHS IRB required 3 separate revisions with full board review, prior to approval in June. As a result of this and additional delays due to secondary regulatory steps (e.g. data sharing agreement review, OHRO) enrollment has been delayed. We anticipate that completion of our interim and final data analysis milestones will be delayed and expect that a no-cost extension will be requested sometime in 2024.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Cumulative expenditures to date are much lower compared to the original plan, due to the significant delay in obtaining regulatory approvals. We had anticipated being able to run participants by 8 MAC which would correspond to an increase in activity.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects
Nothing to report; human subject enrollment has not begun.

Significant changes in use or care of vertebrate animals
N/A. No animal research is being conducted.

Significant changes in use of biohazards and/or select agents
N/A. No biohazards planned or used.

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Authors: Caswell, K., Motoni, C., Roe, G., Odafe, E., Shimizu, R., Simons, S., Werner, J.K.
  Title: Wearable neurotechnology for treatment of insomnia: Study protocol of a prospective, placebo-controlled, double-blind, crossover clinical trial of a transcranial electrical stimulation device.
  Journal: To be submitted to Contemporary Clinical Trials.
  Status: In preparation.
  Acknowledgment of federal support: Yes

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to report.

  Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

  > Werner, J.K., Caswell, K., Lee, A., Simons, S., Schelp, S. (2023, Jun). Transcranial electrical stimulation therapy for insomnia: Evidence for target engagement for a future clinical trial. Poster presentation at the Johns Hopkins Sleep & Circadian Research Day, Baltimore, MD.

  Dr. Werner presented the planned study in the context of his larger portfolio in the following presentation and poster:

Werner, J. K. Uniformed Services University Glymphatics Team. Oral presentation at the annual Military Health System Research Symposium MTEC Glymphatic Talk, Kissimmee, FL.

Werner, J. K., Metzger, E., Coon, W., Marinelli, L., Simons, S., Schelp, S., Amyot, F. (2023, August). Applying Non-Invasive Technology to Measure and Modulate Sleep Physiology in U.S. Warfighters. Poster presentation at the annual Military Health System Research Symposium MTEC Spotlight, Kissimmee, FL.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

  Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

  Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

  Nothing to report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*

- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name:	Stephen Simons
Project Role:	Prime: PI / Sponsor
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	2
Contribution to Project:	Oversaw human subjects research protocol updates, IRB resubmission, PeakSleep™ device testing and delivery, and administered study training to Dr. Werner's team

Name:	Renee Shimizu
Project Role:	Prime: Program Manager
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	<1
Contribution to Project:	Project oversight and reporting, supported regulatory submissions

Name:	Maria Provo
Project Role:	Prime: Research Assistant
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Created and tested data processing pipelines in preparation for study data analyses. Supported training of Dr. Werner's team.

Name: Kent Werner
Project Role: Subcontractor PI / Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0001-9858-2931
Nearest person month worked: 1
Contribution to Project: Edited protocol and helped oversee resubmission to IRB, maintain communication with IRB, advocated for study support at meetings with colleagues

Name: Sonja Skeete
Project Role: Subcontractor: Site Program Manager
Researcher Identifier (e.g. ORCID ID): 0000-0002-5252-8419
Nearest person month worked: 3
Contribution to Project: Supported IRB and other regulatory submissions, reporting and other management activities, assisted with study start-up activities

Name: Elizabeth Metzger
Project Role: Subcontractor: Scientific Program Manager
Researcher Identifier (e.g. ORCID ID): 0000-0003-0714-2637
Nearest person month worked: 1
Contribution to Project: Project oversight, reporting and other management activities

Name: Colin Dawkins
Project Role: Subcontractor: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID): 0000-0002-8772-1032
Nearest person month worked: 6
Contribution to Project: Support IRB submissions, trained to run study, study start up activities

Name: Adriana Penafiel
Project Role: Subcontractor: Study Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Supported study start-up activities and documentation

Name: Keenan Caswell
Project Role: Subcontractor: Study Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Built instruments into REDCap.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); andOther.*

Organization Name: The Geneva Foundation
Location of Organization: (if foreign location list country): Tacoma, WA (headquarters)
Partner's contribution to the project: Subcontractor. Provided project staff (research assistants, project manager) at research site.

Organization Name: The Uniformed Services University of the Health Sciences (USUHS)
Location of Organization: (if foreign location list country): Bethesda, MD
Partner's contribution to the project: Subcontractor PI/Investigator and facilities for project activities.

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) should be updated and submitted with attachments.*

See associated quad chart submission on eBRAP.

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

None attached.