
# Research Announcement

# for

# Somnus

# Biological Technologies Office

DARPARA2402

April 29, 2024

This Research Announcement (RA) constitutes a public notice of a competitive funding opportunity as described in 2 CFR § 200.203. Any resultant negotiations and/or awards will follow all laws and regulations applicable to the specific award instrument(s) available under this RA.

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## 1. Overview Information

- **Federal Agency Name** – Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office (BTO)
- **Funding Opportunity Title** – Somnus
- **Announcement Type** – Research Announcement (RA)
- **Funding Opportunity Number** – DARPARA2402
- **NAICS Code**: 541714, 541715, 541720;
- **Dates** (All times listed herein are Eastern Time.)
  - **Posting Date: April 29, 2024**
  - **Question Submittal Closed: June 5, 2024, at 4:00 p.m.**
  - **Proposal Due Date: June 17, 2024, at 4:00 p.m.**
- **Concise description of the funding opportunity:**
  This Research Announcement represents a Solicitation for a research thrust, entitled Somnus, that will focus on the identification of molecules and mechanisms of host interactions with the gut microbiome that are associated with the restorative effect of sleep on cognitive performance. DARPA's Biological Technologies Office (BTO) solicits rapid, targeted and limited scope investments through our Research Announcements.
- **Anticipated individual awards** – Multiple awards may be awarded.
- **Types of instruments that may be awarded** – Cooperative Agreements and Research Other Transactions awards under the authority of 10 U.S.C. § 4021.

**Funding limitation**: DARPA will issue a Research Other Transaction or a cooperative agreement award instrument, with a total award value limited to a maximum of $2,000,000 in Government funding to only cover the cost of the proposed full time equivalent (FTE) and required materials, equipment, and Other Direct Costs. Under no circumstances will profit be authorized. While resource sharing is not expected, it may be offered in the proposal. Any proposed resource share must be directly applicable to effort. The total award value for this effort is limited to $2,000,000. This limit applies to the sum of the Government's funding and any performer cost share (if proposed). The maximum period of performance is 18 months. Should the proposer request and is granted a Research OT or cooperative agreement by the Agreements or Grants Officer, the selected proposer will have 15 calendar days from the issue date to agree to the terms of the OT or Cooperative Agreement, sign, and return the agreement to DARPA. If the proposer fails to sign and return the OT or cooperative agreement within 15 calendar days, DARPA will withdraw its OT or cooperative agreement award.

- **Agency contact**
  - **Technical PoC:** Matthew J. Pava, Ph.D., Program Manager, DARPA/BTO
  - **Agreements/Grants Officer:** Ms. Belinda Nwanguma, DARPA/CMO
  - **Email:** Somnus@darpa.mil
  - **Mailing Address:**
    DARPA/BTO
    ATTN: DARPARA2402
    675 N. Randolph Street
    Arlington, VA 22203-1714

# 2. Funding Opportunity Description

## 2.1 Introduction

This Research Announcement (RA), entitled Somnus (DARPARA2402), focuses on the identification of molecules and mechanisms of host interactions with the gut microbiome that are associated with the restorative effect of sleep on cognitive performance. To achieve this goal, funded studies will utilize an animal model of acute sleep deprivation and recovery, perform cognitive assessments that empirically assess the impact of sleep deprivation on performance, and collect biospecimens to generate a dataset that enables identification of pathways between the gut and the brain that correlate with changes in sleep pressure and cognitive function.

This RA is designed to enable a rapid investigation of this topic with targeted and limited scope investments. Ras enable DARPA to initiate a new investment in less than 120 calendar days after the proposal submission window for this RA closes. To this end, proposals may be submitted in response to this RA for a maximum of 45 days from publication at https://sam.gov/.[1] The following sections of this solicitation will (1) identify specific details regarding the research topic of interest, including the technical goals and metrics; and (2) provide proposal content and submission instructions, including the due date for proposal submissions (see Section 3.2 for submission instructions). Proposals submitted in response to Somnus will be evaluated and selected in accordance with Section 4 of this RA. A checklist is included in Appendix A as a tool to help proposers in designing their experiments and drafting their proposals. This checklist can be used to ensure that all the requirements in the Somnus solicitation have been met, but the checklist should **not** be submitted with the proposal and cost documents.

### 2.1.1 Somnus Overview:

Insufficient sleep is highly prevalent in the military and has multiple causes ranging from environmental factors to disease processes. According to a recent DoD study, 64% of US service members reported less than seven hours of sleep per night, compared to 28-37% of adults in civilian population. Irrespective of its etiology, sleep loss has negative effects on health and performance that are poorly addressed by existing therapeutic interventions. Acute sleep loss has been found to result in cognitive and social dysfunction, as well as dysregulation of molecular pathways underlying immune and metabolic function. While the deleterious effects of acute sleep loss may be reversed by subsequent recovery sleep, the efficacy of recovery sleep may be stymied by suboptimal environmental or disease-related conditions, leading to chronic sleep loss. The deleterious effects of chronic sleep loss are systemic and include metabolic dysregulation (insulin resistance, diabetes, and obesity), immune dysfunction (increased risk of infection, neurodegeneration, and autoimmune diseases) and neuropsychiatric disorders (PTSD, depression, and increased risk of suicide). Furthermore, even acute sleep loss reduces the ability to execute complex cognitive tasks, effective communication, rapid decision making, and maintenance of vigilance and alertness required to carry out assigned duties.

The propensity to sleep and the subjective experience of sleepiness accumulate with increased time spent awake, but the biological mechanisms regulating this drive to sleep, or “sleep pressure,” have not been characterized. Recent studies have identified various changes in gut

[1] Because DARPA is soliciting proposals for the award of Other Transactions (OTs), and OTs are not subject to the Federal Acquisition Regulation (FAR), the 45-day response time required at FAR 5.203 does not apply.

microbiota associated with sleep deprivation and/or insomnia in humans, as well as in animal models. Evidence suggests that the gut microbiomes of insomnia patients compared to healthy controls are characterized by lower microbial richness and diversity, as well as depletion of anaerobes and short-chain fatty acid (SCFA)-producing bacteria. Additionally, gut bacterial metabolites and components of the bacterial cell wall have been shown to serve in sleep signaling through peripheral pathways, such as the hepatoportal vein and the vagus nerve. Notably, however, these observed associations have not been tied to changes in cognitive function following sleep deprivation. Thus, it is unknown whether such observed changes in the gut ecological environment lead to deleterious effects of sleep deprivation on health and performance, or whether they are involved in compensatory mechanisms to recover physiological function following sleep deprivation. Moreover, while studies have suggested that modulating the gut microbiome via mechanisms such as administration of prebiotics, butyrate (a gut bacterial metabolite) or lipopolysaccharide (a bacterial cell wall component) can modulate sleep/wake states in animal models, the underlying mechanisms have not been fully elucidated, and the impacts of these interventions on health and functional performance following sleep deprivation have not yet been explored.

Somnus seeks to identify molecules and mechanisms of host interactions with the gut microbiome that are associated with the impact of acute sleep deprivation and restorative effect of sleep on cognitive performance in a mammalian animal model.

### 2.1.2 Somnus Objective:

DARPA seeks to identify gut microbiota and downstream biomolecules (e.g., metabolites, lipids, peptides, nucleic acids, etc.), and host-microbiome interactions associated with acute sleep deprivation and recovery and corresponding changes in cognitive function. Successful proposals must adhere to validated and published methods of acute sleep deprivation protocols and must include cognitive assessments with demonstrable sensitivity to sleep deprivation, as reported in published literature. Proposals to develop novel paradigms to induce sleep deprivation and/or assess cognitive function are *not* in-scope. Respondents must clearly describe and provide technical and statistical rationale for their selected experimental methodologies, mammalian animal model, group size, outcome measures, and quantitative analyses for proposed experiments designed to induce acute sleep deprivation and to measure sleep pressure and cognitive function. Rationale for these proposed approaches must address throughput, ease of implementation, probability of reliable outcome measures, statistical power, and future translatability to humans. Proposers must address potential challenges inherent to the proposed approaches, along with corresponding risk mitigation strategies.

Somnus aims to test the hypothesis that molecular/biochemical pathways between the gut and the brain are associated with sleep-deprivation induced cognitive performance deficits. To this end, selected performer team(s) will be responsible for carrying out experiment including acute sleep deprivation and recovery with integrated cognitive task assessments and biospecimen collection. Selected team(s) will also perform data analyses to measure changes in sleep pressure across baseline, sleep deprivation, and recovery conditions, and to assess the effects of varying sleep pressure on cognitive performance. The team(s) will also harvest and ship collected blood and tissue biospecimens to a Somnus government resource partner, identified by DARPA, who will perform one or more of the following multiomic analyses on each of the provided biospecimens (Figure 1): shotgun metagenomics, metabolomics, untargeted proteomics, host transcriptomics,

metatranscriptomics, and lipidomics. Collaborative engagement between the selected performer team(s) and the government resource partner is anticipated to enable further analysis of the multiomics results by the government resource partner in the context of varying sleep pressure and cognitive performance.

*Experimental and analytical design*

Proposers must clearly describe – and schematically depict – an experimental design that enables the investigation and quantification of a dose-response effect of sleep deprivation and recovery on cognitive function, as well as on corresponding host-microbiome interactions in a mammalian model. The experimental design must include the following components, with additional guidance provided in the sections below: 1) mammalian animal model, 2) acute sleep deprivation, 3) cognitive assessment, 4) blood, fecal, and tissue biospecimen collection, and, optionally, 5) additional data collection and analysis. Somnus is seeking to identify gut-brain pathways associated with cognitive deficits arising from increased sleep pressure, so proposals should justify how their experimental design will support this key aim. For example, some biospecimens are only obtainable at terminal timepoints, and proposals must describe how these biospecimens may be obtained at key timepoints (e.g., baseline, sleep-deprived, and recovered states). While data collection at terminal time points will necessitate between-group comparisons across experimental conditions (i.e., following periods of sleep deprivation and recovery) and matched control groups, the proposed experimental design must also allow for within-subjects comparisons of cognitive performance and non-terminal biospecimens across sleep-deprived and non-sleep-deprived states, such that inter-individual effects of sleep deprivation and recovery on both cognitive performance and corresponding host-microbiome interactions may be assessed.

As the complexity of an experimental design and its corresponding analyses increases, the number of animal subjects required to achieve statistical significance also increases. Proposers are encouraged to minimize the complexity of their experimental design where possible, in order to achieve statistically robust results that address the goals of Somnus. Moreover, proposers must clearly describe their planned analytical and statistical approaches to quantify sleep pressure across baseline, sleep deprived, and recovered states, and to assess the impact of sleep pressure on behavioral performance of one or more cognitive tasks. Proposers must also specify the number of animals included in each of the proposed experimental and control groups, along with a power analysis to justify the proposed group size.

Proposers must present a schedule of data collection from the proposed cohorts and groups and address potential confounds such as batch effects and seasonal effects. Proposals also must include a description of potential challenges inherent to the proposed experimental design, along with corresponding risk mitigation strategies. Of note, the proposed data collection schedule must adhere to the timeframe depicted in Figure 2.

To verify quality and accuracy of both the raw behavioral and physiological data and the results (e.g., scores) derived from these data, proposals must include a detailed quality assurance and quality control (QA/QC) plan that describes: 1) quality assurance (QA) measures for all data collection (e.g., manual scoring by two independent analysts, or human oversight of data streams from automated recording systems), and 2) quality control (QC) protocols for an independent review of either the entire dataset or a randomized subset of at least 10% of the data.

*Mammalian animal model*

Proposers must select a mammalian animal model based on published literature describing the use of the animal model with the selected acute sleep deprivation protocols and cognitive task(s), as well as volume and mass requirements for blood, fecal, and tissue biospecimens (see *Biospecimen Collection* section below). Genetic diversity of the animal model is also important to DARPA with regard to future translation of Somnus outcomes to humans. Thus, proposed experimental groups must contain equal numbers of male and female animals, although tracking of estrous (or similar) cycles is not of interest for Somnus.

*Acute sleep deprivation*

Proposals must include a description of one or more validated approaches, along with citations of peer-reviewed published literature, to induce acute sleep deprivation in a mammalian animal model. Proposed durations of sleep deprivation and recovery, and their alignment with respect to circadian phase, must be selected on the basis of published literature regarding the sensitivity of the proposed cognitive task to these sleep deprivation and recovery parameters.

Proposers must describe rationale for the selected sleep deprivation protocol(s) with respect to throughput, ease of implementation, probability of reliable outcome measures, and, importantly, their inherent trade-offs in the context of the Somnus goals. For instance, forced locomotion paradigms can be automated and are therefore relatively easy to implement across long durations of sleep deprivation; however, these paradigms have been found to induce relatively high levels of stress to the animal, which could present a confounding variable in the context of gut microbiome activity in sleep-deprived vs. non-sleep-deprived animals. In contrast, the gentle handling approach to induce acute sleep deprivation is relatively less stressful for the animals but is also less feasible to implement over longer periods of sleep deprivation, due to the requirement for frequent manual intervention by trained research personnel. Proposers must carefully consider their approach(es) to induce acute sleep deprivation and describe rationale for the selected sleep deprivation approach(es), addressing experimental considerations such as durations of sleep deprivation, circadian phase alignment, and data collection time points. Moreover, proposers must describe how the sleep deprivation protocol will be incorporated into the overall experimental design and how the design of experimental and control groups will account for any potential confounding variables such as stress.

Selected proposer team(s) will also be responsible for characterizing sleep quality and assessing changes in sleep pressure. Respondents must describe how they will implement gold-standard methods for assessing sleep stages (e.g., polysomnography), along with their proposed approaches to characterize sleep pressure across sleep and/or wakefulness.

*Cognitive assessment*

Proposers must clearly describe the implementation of one or more behavioral tasks to assess cognitive function at baseline, sleep deprived, and recovered states in the context of their experimental design. Proposals should include citations of peer-reviewed references from published literature to justify the sensitivity of measurable behavioral outcomes to the proposed

durations of acute sleep deprivation. Rationale for the proposed cognitive task(s) and corresponding behavioral assessments should also address throughput, ease of implementation, and future translatability to humans. Importantly, proposers must provide rationale for use of the proposed cognitive task(s) within the overall context of analyzing host-microbiome interactions across conditions of varying sleep pressure. For instance, a task that produces confounding effects on gut microbiome content due to variable ingestion of food or other sugar-based rewards across animals (e.g., based on behavioral performance) would be unacceptable.

At minimum, cognitive performance must be assessed: 1) at baseline, 2) following sleep deprivation, and 3) following recovery. Proposers must describe the schedule and duration of the cognitive assessments in the context of their proposed sleep deprivation schedule, along with any required training of the animals prior to implementation of the assessments. Importantly, cognitive assessments must be aligned within and across groups with respect to circadian phase to account for potential circadian effects on cognitive performance.

Proposers must also provide justification regarding the suitability of the selected behavioral task for repeated testing, allowing for within-subject comparisons of cognitive performance across baseline, sleep deprivation, and recovery time points. If additional training and/or testing with the behavioral task is required, for instance, to habituate the animals to the task, to control for differences across experimental and control groups due to circadian effects, or to pilot task parameters, proposals must include a clear description of these aspects of the study design.

*Blood, fecal, and tissue biospecimen collection*

Proposals must describe approaches to acquire biospecimens across baseline, sleep deprived, and recovered states in an animal model. Additionally, proposals must include plans to transfer biospecimens and associated experimental data to the government resource partner. Selected performer(s) will be expected to enter into a material transfer agreement and data sharing agreement with Somnus government resource team members in order to facilitate transfer of biospecimens and data generated under Somnus. DARPA anticipates two government resource organizations supporting the program. Example agreement documents from these organizations are included in Appendix B as a reference. These documents will be completed following award finalization. Proposers should not return completed agreements with their proposal submissions. Proposers should budget for approximately three batch shipments of biospecimens to the government resource team. The proposed experimental schedule will likely dictate optimal timing of each shipment, and proposers must include these shipments and associated timing as milestones in their proposed task description document (TDD). Using the biospecimens, the government resource team will characterize differences in gut microbiota and associated biomolecules – including circulating molecules detectable in blood samples – corresponding to inter-individual and between-group differences in the physiological, behavioral, and cognitive effects of sleep pressure as it fluctuates between sleep deprived and recovered states.

Blood and fecal biospecimens must be collected within subjects at baseline, following acute sleep deprivation, and, where applicable, following recovery. Due to volume requirements for government partner -omics analyses of the blood biospecimens, a minimum volume of 1.3 Ml blood must be collected per animal, per collection timepoint. Proposers must demonstrate that the proposed timing and volume of blood draws adhere to their organization's IACUC guidelines

regarding the maximum volume of blood collection that may take place per animal across a given amount of time. To facilitate necessary spacing of blood draws between baseline and experimental time points, proposers are encouraged to consider strategies for spacing the collection of baseline blood biospecimens prior to the onset of the proposed sleep deprivation protocol. Sample collection plans must show how confounds associated with circadian phase are avoided across experimental groups (e.g., controls vs. sleep-deprived, tissues obtained at different terminal endpoints, etc.) and timepoints (e.g., baseline, sleep-deprived, and recovered states). As intestinal motility and gut transit time will impact the timing of fecal sample excretion and terminal intestinal tissue state with respect to baseline (non-sleep deprived), sleep deprived, and recovered states, proposers must also describe how their proposed timing of biospecimen collection accounts for these varying states of sleep pressure. For each proposed timepoint, a minimum of 1-2 fecal pellets per subject must be collected.

Brain and intestinal tissue biospecimens must be collected following acute sleep deprivation and, in separate cohorts, following recovery, as well as in control cohorts who do not undergo sleep deprivation, enabling between-subjects comparisons across these conditions. Proposers must select two brain regions for tissue collection, on the basis of their involvement in sleep-wake regulation, cognitive function, and any known sensitivity to circulating factors, particularly those originating from the gut. Proposers must also select one intestinal region for tissue collection and provide justification for the selected region in the context of its involvement in sleep and/or circadian rhythm, immune response, and host-microbiome interface. Proposers must clearly describe their proposed methodologies for harvesting the intestinal and brain tissue specimens.

Due to tissue mass requirements for planned -omics analyses on terminal tissue biospecimens by a government resource partner, proposed approaches must include the collection of 200 mg brain tissue per sample in each region, as well as 400 mg intestinal tissue per sample (~100 mg per planned -omics analysis for each brain and intestinal tissue specimen; see Figure 1 for planned analyses for each tissue type). Depending on the tissue regions selected, samples may need to be pooled across animals. In this case, proposers must provide clear rationale for choosing the selected region despite the lack of inter-individual resolution that the tissue biospecimens will provide. Moreover, proposers must clearly describe how samples will be pooled across animals in the context of the experimental design and analysis of sleep pressure and cognitive performance.

*Additional data collection and analysis*

While not required, proposers may also choose to collect and analyze complementary biospecimens and/or data on neural and/or physiological underpinnings of acute sleep deprivation and recovery, as well as associated cognitive function. Proposers must clearly describe any additional proposed biospecimen collection, data collection, and/or analytical activities, as well as associated scientific rationale with regard to how these activities will complement the primary goals of Somnus. Importantly, any complementary biospecimen and/or data collection must not interfere with implementation of the sleep deprivation and cognitive assessment protocols, or the acquisition of blood and tissue biospecimens, as described in this solicitation. Any additional biospecimen and/or data collection and analyses must be included in separate task(s) in the TDD, with associated milestones and costs broken out by task; the total proposed budget, inclusive of any of these additional task(s), must not exceed $2M.

### 2.1.3 Anticipated Structure:

The Somnus study will assess the impact of gut microbiota on sleep-wake states and cognitive function across acute sleep deprivation and recovery according to an 18-month structure, consisting of a performer-led period of performance of 18 months and an overlapping government resource-led period of performance of 12 months as described below.

The performer-led period of performance (PoP) includes obtaining local Institutional Animal Care and Use Committee (IACUC) and U.S. Army Medical Research and Development Command Animal Care and Use Review Office (ACURO) approvals, as well as successfully implementing animal studies consisting of published acute sleep deprivation protocols, cognitive tasks with published demonstration to be sensitive to sleep deprivation, and collection of biospecimens (as specified below).

This study will involve data collection from mammalian animal models only; any proposed efforts to collect human data will be considered out of scope. A government resource team, identified by DARPA, will analyze biospecimens collected by the selected performer team(s) to characterize molecules and mechanisms of host interactions with the gut microbiome that are associated with the impact of acute sleep deprivation and restorative effect of sleep on cognitive performance. Multiomic analyses to be performed on the different types of biospecimens collected by proposers are represented in Figure 1.

Figure 1: Multiomic analyses to be performed by government resource team

| | | Biospecimen | | | | | |
|---|---|---|---|---|---|---|---|
| | | Blood (Venous, non-terminal) | Fecal Sample | Terminal Blood (Venous) | Brain Tissue (region 1) | Brain Tissue (region 2) | Intestinal Tissue * |
| Analysis Type | Shotgun metagenomics | | X | | | | |
| | Metabolomics | X | X | X | | | X |
| | Untargeted proteomics | | | X | X | X | X |
| | mRNA host transcriptomics | X | | X | X | X | X |
| | Metatranscriptomics | | X | | | | |
| | Lipidomics | X | X | X | | | X |

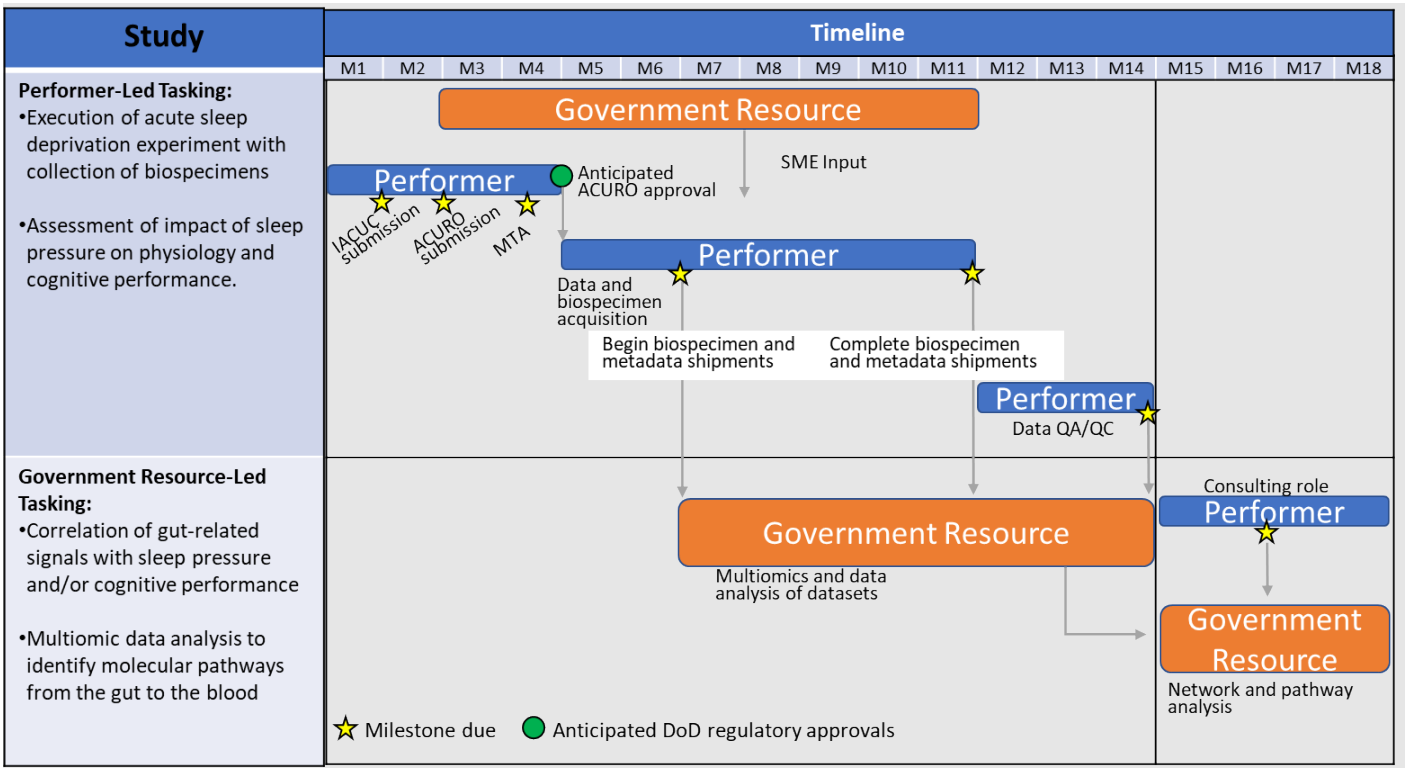
* Depending on the intestinal region chosen by proposer, additional analysis may be performed on the intestinal lavage (fluid from flushing the tissue) to include shotgun metagenomics and metatranscriptomics.

As previously stated in this document, a minimum of 1.3 ml of blood per each collection timepoint is required, to be collected as 1 ml of whole blood directly in EDTA tubes for plasma separation and 0.3 ml whole blood to be aliquoted into a tube containing 0.828 ml RNA stabilizing agent. If applicable, the intestinal tissue will be harvested by the proposer and sent to the government resource team who will perform the lavage and collect the resulting fluid. Further specific biospecimen collection guidelines, including volumes and storage conditions, will be communicated to proposers by the government resource team at the beginning of the

study.

Proposers shall develop a milestone-driven work plan, incorporating metrics and deliverables into the 18-month period of performance. Proposals must describe measurement methodology (devices, collection approach, etc.) for achieving the Somnus study goals according to the timeline shown in Figure 2.

Figure 2: Timeline of Somnus performer and government resource activities




### 2.1.4 Somnus Milestones:

Periodic milestones will direct efforts to meet the final goal of the Somnus study. A minimum set of these milestones are described below in the context of key tasks associated with Somnus goals. Proposals should describe any additional milestones required to achieve the study goals and milestones described below using the Task Description Document (TDD) for Other Transactions and Research Description Document (RDD) for cooperative agreements. The TDD can be found in the Model Research Other Transaction (OT) (see Attachment 6, "Model Research Other Transaction (OT)"). Please note that the naming convention for the TDD and RDD are based on the award instrument type and there are no differences. The schedule of milestones and payments, milestone and task descriptions, agreement deliverables and reporting requirements should assist in generating the proposal costs and timeline.

**(Months 1-4) Preparation and Submission of Animal Use Protocols and Negotiation of Material Transfer Agreements.**

Submission of required protocols (IACUC & ACURO) for all animal studies to be conducted

during the performer-led base period.

*Month 1:* Submit animal use protocol packages for IACUC review and approval.

Animal use protocols must describe experimental protocols for acute sleep deprivation, restorative sleep, and assessment of cognitive function.

Negotiation of material and data sharing agreements. Proposers shall collaborate with government resource team and any other relevant parties to negotiate a materials transfer/sharing agreement and data sharing protocols for transfer of animal study results and biospecimen analysis results across the government resource and proposing teams.

*Month 2*: Upon receipt of IACUC approval, submit animal use protocol packages for ACURO review and approval.

*Month 3*: Provide briefing to DARPA against planned technical objectives.

*Month 4*: Obtain signed material transfer and data sharing agreement(s) with government resource team prior to data collection and biospecimen acquisition.

**(Months 5-11) Animal Study of Sleep Deprivation and Restorative Sleep Impact on Cognitive Function.**

*Month 5:* Acquire biospecimens and other physiological measures across sleep deprived and non-sleep deprived states in a mammalian model. Acquire biospecimens from the gut microbiome and blood within-subjects across periods of acute sleep deprivation and recovery in a mammalian model.

- Obtain physiological measures associated with changes in sleep pressure over the course of acute sleep deprivation.
- Quantify physiological correlates of recovery sleep following acute sleep deprivation.
- Assess behavioral performance on cognitive tasks across baseline and acute sleep deprivation conditions, as well as following recovery sleep.
- Collect biospecimens from animals across baseline, sleep deprivation, and recovery sleep conditions. Biospecimens to include venous blood and fecal samples.
- Collect additional biospecimens from animals after recovery sleep and/or at terminal timepoints. Biospecimens to include venous blood, intestinal tissue, and brain tissue from two regions.

*Month 6*: Provide briefing to DARPA against planned technical objectives.

*Month 7:* Begin transfer of biospecimens and associated metadata and results to government resource team. This is a placeholder milestone and may be changed based on the proposed experimental schedule that will likely dictate optimal timing of each shipment. Proposers must include these shipments and associated timing as milestones in their proposed task description document (TDD).

*Month 8*: Provide briefing to DARPA against planned technical objectives.

*Month 9*: Provide briefing to DARPA against planned technical objectives.

*Month 10*: Provide briefing to DARPA against planned technical objectives.

*Month 11:* Complete transfer of biospecimens and associated metadata and results to government resource team.

- Metadata and results must include on a per-animal basis (but are not limited to) sleep staging break-out (e.g., as determined by polysomnography), accumulated sleep pressure based on physiological measurements, and cognitive assessment results at each timepoint.
- Government resource team will perform one or more of the following multiomic analyses on each of the provided biospecimens (Figure 1): shotgun metagenomics, metabolomics, untargeted proteomics, Mrna host transcriptomics, metatranscriptomics, and lipidomics.

**(Months 12-14)** Perform quality control (QC) assessments on physiological and behavioral data across sleep deprivation and cognitive task performance to ensure standardization of scoring and uniformity of treatment for all collected measurements, as described in the performer's quality assurance and quality control (QA/QC) plan. Deliver all processed results to government resource team by end of month 14.

*Month 12*: Provide briefing to DARPA against planned technical objectives.

*Month 13*: Provide briefing to DARPA against planned technical objectives.

*Month 14*: Provide briefing to DARPA against planned technical objectives.

**(Months 15-18)** Provide subject matter expertise support to government resource team with respect to experimental biospecimens, metadata, and results.

*Month 15*: Provide briefing to DARPA against planned technical objectives.

*Month 16*: Provide briefing to DARPA against planned technical objectives.

*Month 17*: Provide briefing to DARPA against planned technical objectives.

*Month 18*: Provide briefing to DARPA against planned technical objectives.

The government resource team will further conduct extended, system-level analyses of datasets obtained in the Base Period, with the goal of identifying putative molecular/biochemical pathways associated with host-microbiome interaction in the gut and resultant molecules in the blood that correspond to sleep pressure and its effects on cognitive function. The selected proposers will provide up to five hours per month (total) of subject matter expertise support to the government resourceteam to include email correspondence and/or phone communication to respond to questions pertaining to collected biospecimens and experimental results. The proposers may also include additional tasking to extend their analysis of the physiological and behavioral data beyond simple quantification of sleep stages and pressure and cognitive deficits generated in months 5-14.

### 2.2 Proposal Information and Structure

Proposals submitted in response to Somnus must be UNCLASSIFIED and must address all tasking outlined in section 2.1. The period of performance for this effort is 18 months. Specific technical objectives to be achieved, task descriptions, intellectual property rights, milestone payment schedules, and deliverables will be addressed according to the guidelines outlined in this RA.

The total award value for this effort is limited to $2,000,000. This limit applies to the sum of the Government's funding and any performer cost share (if proposed). All awards issued under this RA will be Other Transactions (Ots) awarded under the authority of 10 U.S.C. § 4021 or cooperative agreements under the authority of 10 U.S.C. § 4001.

Proposers must only propose an OT with fixed payable milestones or a cooperative agreement.

Note that fixed payable milestones are fixed payments based on successful completion of the milestone accomplishments agreed to in the milestone plan. Specific milestones will be based on the detailed tasking outlined in the Somnus solicitation in section 2.1.

**Cost Sharing/Matching**

Cost sharing is not required; however, it will be carefully considered where there is an applicable statutory condition relating to the selected funding instrument (e.g., OTs under the authority of 10 U.S.C. § 4021). Cost sharing is encouraged where there is a reasonable probability of a potential commercial application related to the proposed research and development effort.

The flexibility of the OT award instrument is beneficial to the program because the performer will be able to apply its best practices as required to carry out the research project that may be outside of the Federal Acquisition Regulation (FAR) process-driven requirements. Streamlined practices, such as milestone-driven performance measures, will be used and intended to reduce time and effort on award administration tasks and permit performers to focus on the research effort and rapid prototyping. OTs provide the Government and the proposer the flexibility to create an award instrument that contains terms and conditions that promote commercial transition, reduce some administratively burdensome acquisition regulations, and meet BTO program goals.

Should a proposer request a Research Other Transaction, please note that any intellectual property is developed or generated under these agreements, the Performer shall retain title of any subject invention. DARPA shall retain a nonexclusive, nontransferable, irrevocable, paid-up Limited Rights license in the subject invention throughout the world, regardless of the protection method chosen (Refer to Attachment 6, Model Research Other Transaction (OT), which defines in more detail the allocation of principal rights).

The performer shall agree to adhere to the DoD Research and Development (R&D) General Terms and Conditions incorporated into Attachment 7: Model Cooperative Agreement.

Intellectual property rights will not be negotiated in the award regardless of award instrument. Any Proposer who is not prepared to grant the Government a limited license right should not submit a proposal under this Research Announcement.

The Government will only award either a cooperative agreement or a Research OT agreement

under this solicitation and will not consider any other award instruments. Refer to the model OT agreement provided as an attachment to this RA for additional information (Attachment 6 – Model Research Other Transaction (OT)). Specific milestones will be based on the Research Project Objectives detailed in the Research Announcement and Somnus. No other negotiated changes to the OT terms and conditions and the cooperative agreement are expected. The milestone payments will be contingent on the proposed individual(s) continuing work on the proposed RA idea for the entire Period of Performance at their proposed level-of-effort (LOE).

Please see http://www.darpa.mil/work-with-us/contract-management for more information on Ots and DARPA's OT authority.

## 3. Evaluation Criteria

Proposals will be evaluated using the following evaluation criteria, listed in descending order of importance.

### 3.1 Overall Scientific and Technical Merit

The proposed technical approach is feasible, achievable, and complete. Detailed technical rationale is provided, delineating why the proposed approach can achieve the program goals and metrics. The proposed technical team has the expertise and experience to accomplish the proposed tasks, and the proposal includes a plan to efficiently integrate technologies from proposed subcontractors, if any. The expertise of the technical team is documented in peer-reviewed publications, and the team possesses the facilities and equipment necessary to conduct the proposed tasks. Task descriptions and associated technical elements provided are completed and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of award. The proposal identifies and directly addresses the key technical challenges in achieving the program goals and metrics for the proposed approach. The proposal identifies major technical risks, and planned mitigation efforts are clearly defined and feasible.

### 3.2 Potential Contribution and Relevance to the DARPA Mission

The potential contributions of the proposed effort bolster the defense technology base, and support DARPA and BTO's mission to make pivotal early investments in technologies that may lead to groundbreaking impact on national security. The proposed intellectual property restrictions (if any) will not significantly impact the Government's ability to transition the technology.

### 3.3 Cost Realism

The proposed cost represents a practical understanding of the effort, and this cost is based on meeting the key technical challenges in an efficient manner.

A cost evaluation will be conducted to ensure that the proposed cost is realistic. As described in this RA, satisfactory cost competition is anticipated to establish cost realism. If needed, the Government may use various cost evaluation techniques and methodologies to ensure the proposed cost is realistic.

A cost should be sufficiently detailed to demonstrate its realism. The burden of demonstrating cost realism rests with the proposer. An assessment that the proposal cost is not realistic may result in the proposal being non-selectable for award. This Research Announcement has a Not To Exceed amount of $2,000,000.

Unless otherwise specified in this announcement, for additional information on how DARPA reviews and evaluates proposals through the Scientific Review Process, please visit: Proposer Instructions and General Terms and Conditions

## 4. Submission Information

### 4.1 Proposal Submission Information

This announcement allows for the following award instrument types: Cooperative Agreements and Research Other Transactions. The following websites are incorporated by reference and contain additional information regarding overall proposer instructions, general terms and conditions, and each specific award instrument type.

- **Proposer Instructions and General Terms and Conditions**: Proposer Instructions and General Terms and Conditions
- **Assistance (Grants and Cooperative Agreements)**: Proposer Instructions: Grants/Cooperative Agreements
- **Other Transaction Agreements**: Proposer Instructions: Other Transactions

- Full proposals are due **June 17, 2024 at 4:00 p.m.** as stated in the Overview section.
- **Attachments 1 through 6** contain specific instructions and templates and constitute a full proposal submission for proposers requesting an Other Transactions for Research.
- **Attachments 1 through 5, and 7** contain specific instructions and templates and constitute a full proposal submission for proposers requesting a Cooperative Agreement.
- Please visit Proposer Instructions: General Terms and Conditions for General Terms and Conditions for all requested contract types. Visit Proposer Instructions: Other Transactions for submission instructions for proposers requesting Other Transactions. Visit Proposer Instructions: Grants/Cooperative Agreements for submission instructions for proposers requesting Cooperative Agreements. (Proposers requesting Other Transactions for Research must submit proposals through the Broad Agency Announcement Tool. If requesting a Cooperative Agreement, proposals must be submitted through grants.gov.)
- **RA Attachments**:
  - **(Required)** Attachment 1: Proposal Template – Volume 1: Technical Slide
  - **(Required)** Attachment 2: Proposal Template – Volume 1: Technical & Management Volume Template
  - **(Required)** Attachment 3: Proposal Template – Volume 2: Cost Volume Template
  - **(Required)** Attachment 4: Proposal Template – Volume 2: DARPA Standard Cost Proposal Spreadsheet
  - **(Required)** Attachment 5: Proposal Template – Volume 3: Administrative & National Policy Requirements
  - **(Required if Requesting a Research OT)** Attachment 6: Model Research Other Transaction (OT)
  - **(Required if Requesting a Cooperative Agreement)** Attachment 7: Model Cooperative Agreement

## 5. Special Considerations

- This announcement, stated attachments, and websites incorporated by reference constitute the entire solicitation. In the event of a discrepancy between the announcement, attachments, or websites, the announcement takes precedence.
- All responsible sources capable of satisfying the Government's needs, including both U.S. and non-U.S. sources, may submit a proposal DARPA will consider. Historically Black Colleges and Universities, small businesses, small-disadvantaged businesses, and minority institutions are encouraged to submit proposals and join others in submitting proposals; however, no portion of this announcement will be set aside for these organizations' participation due to the impracticality of reserving discrete or severable areas of this research for exclusive competition among these entities. Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances.
- As of the time of publication of this solicitation, all proposal submissions are anticipated to be unclassified.
- FFRDCs, UARCs, and Government entities interested in participating in the Somnus program or proposing to this BAA should first contact the agency point of contact listed in the Overview section prior to the proposal due date to discuss eligibility. Complete information regarding eligibility can be found at Proposer Instructions: General Terms and Conditions.
- DARPA's Fundamental Research Risk-Based Security Review Process (formerly CFIP) is an adaptive risk management security program designed to help protect the critical technology and performer intellectual property associated with DARPA's research projects by identifying the possible vectors of undue foreign influence. DARPA will create risk assessments of all proposed senior/key personnel selected for negotiation of a fundamental research grant or cooperative agreement award. The DARPA risk assessment process will be conducted separately from the DARPA scientific review process and adjudicated prior to final award. For additional information on this process, please visit Proposer Instructions: Grants/Cooperative Agreements.
- As of the date of publication of this solicitation, the Government expects program goals as described herein may be met by proposed efforts for fundamental research and non-fundamental research. Some proposed research may present a high likelihood of disclosing performance characteristics of military systems or manufacturing technologies unique and critical to defense. Based on the anticipated type of proposer (e.g., university or industry) and the nature of the solicited work, the Government expects some awards will include restrictions on the resultant research requiring the awardee seek DARPA permission before publishing any information or results relative to the program. For additional information on fundamental research, please visit Proposer Instructions: General Terms and Conditions.
- Proposers should indicate in their proposal whether they believe the scope of the research included in their proposal is fundamental or not. While proposers should clearly explain the intended results of their research, the Government shall have sole discretion to determine whether the proposed research shall be considered fundamental and to select the award

instrument type. Appropriate language will be included in resultant awards for non-fundamental research to prescribe publication requirements and other restrictions, as appropriate. This language can be found at Proposer Instructions: General Terms and Conditions.

- For certain research projects, it may be possible that although the research to be performed by a potential awardee is non-fundamental research, their proposed subawardee's effort may be fundamental research. It is also possible the research performed by a potential awardee is fundamental research while their proposed subawardee's effort may be non-fundamental research. In all cases, it is the potential awardee's responsibility to explain in their proposal which proposed efforts are fundamental research and why the proposed efforts should be considered fundamental research.
- DARPAConnect offers free resources to potential performers to help them navigate DARPA, including "Understanding DARPA Award Vehicles and Solicitations," "Making the Most of Proposers Days," and "Tips for DARPA Proposal Success." Join DARPAConnect at www.DARPAConnect.us to leverage on-demand learning and networking resources.
- DARPA has streamlined our RAs and is interested in your feedback on this new format. Please send any comments to DARPAsolicitations@darpa.mil.

## 6. Appendix A: Checklist

DARPA encourages the use of this checklist to ensure that your proposal is responsive to the Somnus solicitation. This checklist is for your own use only, do not submit it with the proposal and cost documents.

**This checklist does not represent evaluation criteria that DARPA will use to review proposals received in response to the Somnus RA. These evaluation criteria are listed and described in Section 4 of the Somnus RA. Rather, this checklist is only included as a tool to help respondents ensure their proposals conform to the Somnus RA. Conforming proposals address all aspects of the RA, and this table calls attention to all instances where "must", "should", "shall", "all", and "encouraged to" language is used.**

| **Experimental and analytical design** | | |
|---|---|---|
| | Does the proposal clearly describe and provide technical and statistical rationale for their selected experimental methodologies, mammalian animal model, group size, outcome measures, and quantitative analyses for proposed experiments designed to induce acute sleep deprivation and to measure sleep pressure and cognitive function | Yes No |
| | Does the proposal include rationale for the proposed approaches that addresses throughput, ease of implementation, probability of reliable outcome measures, statistical power, and future translatability to humans? | Yes No |

| | | | |
|---|---|---|---|
| | Does the proposal address potential challenges inherent to the proposed approaches, along with corresponding risk mitigation strategies | Yes | No |
| | Does the proposal clearly describe – and schematically depict – an experimental design that enables the investigation and quantification of a dose-response effect of sleep deprivation and recovery on cognitive function, as well as on corresponding host-microbiome interactions in a mammalian model? | Yes | No |
| | Does the proposed experimental design include the following components: 1) mammalian animal model, 2) acute sleep deprivation, 3) cognitive assessment, 4) blood, fecal, and tissue biospecimen collection, and, optionally, 5) additional data collection and analysis? | Yes | No |
| | Does the proposal justify how their experimental design will support the aim to identify gut-brain pathways associated with cognitive deficits arising from increased sleep pressure? | Yes | No |
| | Does the proposal describe how terminal biospecimens may be obtained at key timepoints (e.g., baseline, sleep-deprived, and recovered states)? | Yes | No |
| | Does the proposed experimental design allow for within-subjects comparisons of cognitive performance and non-terminal biospecimens across sleep-deprived and non-sleep-deprived states, such that inter-individual effects of sleep deprivation and recovery on both cognitive performance and corresponding host-microbiome interactions may be assessed? | Yes | No |
| | Is the complexity of the proposed experimental design minimized where possible, in order to achieve statistically robust results that address the goals of Somnus? | Yes | No |
| | Does the proposal include a description of planned analytical and statistical approaches to quantify sleep pressure across baseline, sleep deprived, and recovered states, and to assess the impact of sleep pressure on behavioral performance of one or more cognitive tasks? | Yes | No |
| | Does the proposal include the number of animals to be included in each of the proposed experimental and control groups, along with a power analysis to justify the proposed group size? | Yes | No |
| | Does the proposal contain a schedule of data collection from the proposed cohorts and groups? | Yes | No |
| | Does the description of the proposed experimental design address potential confounds such as batch effects and seasonal effects? | Yes | No |

| | | | |
|---|---|---|---|
| | Does the proposal include a description of potential challenges inherent to the proposed experimental design, along with corresponding risk mitigation strategies? | Yes | No |
| | Does the proposed data collection schedule adhere to the timeframe depicted in Figure 2 of the Somnus Research Announcement? | Yes | No |
| | Does the proposal include a detailed quality assurance and quality control (QA/QC) plan that describes: 1) quality assurance (QA) measures for all data collection (e.g., manual scoring by two independent analysts, or human oversight of data streams from automated recording systems), and 2) quality control (QC) protocols for an independent review of either the entire dataset or a randomized subset of at least 10% of the data? | Yes | No |
| **Mammalian animal model** | | | |
| | Is the proposed animal model a **mammalian** model? | Yes | No |
| | Does the proposal include rationale for the selected mammalian model based on published literature describing the use of the animal model with the selected acute sleep deprivation protocols and cognitive task(s)? | Yes | No |
| | Does the proposal include rationale for the selected mammalian model based on volume and mass requirements for blood, fecal, and tissue biospecimens? | Yes | No |
| | Do proposed experimental groups contain equal numbers of male and female animals? | Yes | No |
| **Acute sleep deprivation** | | | |
| | Does the proposal adhere to validated and published methods of acute sleep deprivation protocols? | Yes | No |
| | Does the proposal include a description of one or more validated approaches, along with citations of peer-reviewed published literature, to induce acute sleep deprivation in a mammalian animal model? | Yes | No |
| | Were the proposed durations of sleep deprivation and recovery, and their alignment with respect to circadian phase, selected on the basis of published literature regarding the sensitivity of the proposed cognitive task to these sleep deprivation and recovery parameters?? | Yes | No |
| | Does the description of the selected sleep deprivation protocol(s) include rationale with respect to throughput, ease of implementation, probability of reliable outcome measures, and, importantly, their inherent trade-offs in the context of the Somnus goals? | Yes | No |

| | | |
|---|---|---|
| | Does the proposal include rationale for the selected sleep deprivation approach(es), addressing experimental considerations such as durations of sleep deprivation, circadian phase alignment, and data collection time points? | Yes No |
| | Does the proposal describe how the sleep deprivation protocol will be incorporated into the overall experimental design and how the design of experimental and control groups will account for any potential confounding variables such as stress? | Yes No |
| | Does the proposal describe how gold-standard methods will be implemented to assess sleep stages (e.g., polysomnography)? | Yes No |
| | Does the proposal include a description of approaches to characterize sleep pressure across sleep and/or wakefulness? | Yes No |
| **Cognitive assessment** | | |
| | Does the proposal clearly describe the implementation of one or more behavioral tasks to assess cognitive function at baseline, sleep deprived, and recovered states in the context of the proposed experimental design? | Yes No |
| | Does the proposal include citations of peer-reviewed references from published literature to justify the sensitivity of measurable behavioral outcomes to the proposed durations of acute sleep deprivation? | Yes No |
| | Does the proposal include rationale for the proposed cognitive task(s) and corresponding behavioral assessments that address throughput, ease of implementation, and future translatability to humans? | Yes No |
| | Does the proposal include rationale for use of the proposed cognitive task(s) within the overall context of analyzing host-microbiome interactions across conditions of varying sleep pressure? | Yes No |
| | Does the proposal avoid tasks that would produce confounding effects on gut microbiome content due to variable ingestion of food or other sugar-based rewards across animals (e.g., based on behavioral performance)? | Yes No |
| | Does the proposed approach include assessment of cognitive performance, at minimum, 1) at baseline, 2) following sleep deprivation, and 3) following recovery? | Yes No |
| | Does the proposal describe the schedule and duration of the cognitive assessments in the context of the proposed sleep deprivation schedule, along with any required training of the animals prior to implementation of the assessments? | Yes No |

| | | |
|---|---|---|
| | Are proposed cognitive assessments aligned within and across groups with respect to circadian phase to account for potential circadian effects on cognitive performance? | Yes No |
| | Does the proposal provide justification regarding the suitability of the selected behavioral task for repeated testing, allowing for within-subject comparisons of cognitive performance across baseline, sleep deprivation, and recovery time points? | Yes No |
| | If additional training and/or testing with the behavioral task is required, does the proposal include a clear description of these aspects of the study design? | Yes No<br>N/A |
| **Blood, fecal, and tissue biospecimen collection** | | |
| | Does the proposal describe approaches to acquire biospecimens across baseline, sleep deprived, and recovered states in an animal model? | Yes No |
| | Does the proposal include plans to transfer biospecimens and associated experimental data to a government resource partner? | Yes No |
| | Does the proposal budget for approximately three batch shipments of biospecimens to the government resource team? | Yes No |
| | Does the proposed Task Description Document (TDD) / Research Description Document (RDD) include biospecimen shipments and associated timing as milestones? | Yes No |
| | Does the proposed approach include collection of blood and fecal biospecimens within subjects at baseline, following acute sleep deprivation, and, where applicable, following recovery? | Yes No |
| | Do proposed blood biospecimens include a minimum volume of 1.3 mL blood per animal, per collection timepoint? | Yes No |
| | Does the proposal demonstrate that the proposed timing and volume of blood draws adhere to their organization's IACUC guidelines regarding the maximum volume of blood collection that may take place per animal across a given amount of time? | Yes No |
| | Does the proposal include strategies for spacing the collection of baseline blood biospecimens prior to the onset of the proposed sleep deprivation protocol, to facilitate necessary spacing of blood draws between baseline and experimental time points? | Yes No |
| | Do proposed sample collection plans show how confounds associated with circadian phase are avoided across experimental groups (e.g., controls vs. sleep-deprived, tissues obtained at different terminal | Yes No |

| | | |
|---|---|---|
| | endpoints, etc.) and timepoints (e.g., baseline, sleep-deprived, and recovered states)? | |
| | Does the proposal describe how the proposed timing of biospecimen collection accounts for intestinal motility and gut transit time with respect to varying states of sleep pressure across baseline, sleep deprived, and recovered states? | Yes No |
| | Does each proposed fecal collection timepoint include collection of a minimum of 1-2 fecal pellets per subject? | Yes No |
| | Does the proposed approach include collection of brain and intestinal tissue biospecimens following acute sleep deprivation and, in separate cohorts, following recovery, as well as in control cohorts who do not undergo sleep deprivation, enabling between-subjects comparisons across these conditions? | Yes No |
| | Do the proposed terminal biospecimens include tissue collection from two brain regions, on the basis of their involvement in sleep-wake regulation, cognitive function, and any known sensitivity to circulating factors, particularly those originating from the gut? | Yes No |
| | Do the proposed terminal biospecimens include tissue collection from one intestinal region, and was justification provided for the selection of this region in the context of its involvement in sleep and/or circadian rhythm, immune response, and host-microbiome interface? | Yes No |
| | Does the proposal include a description of proposed methodologies for harvesting the intestinal and brain tissue specimens? | Yes No |
| | Do the proposed terminal tissue biospecimens include at least 200 mg brain tissue per sample in each region, as well as 400 mg intestinal tissue per sample? | Yes No |
| | Do proposed tissue biospecimens need to be pooled across animals to meet the minimum per-sample mass requirements, and if so, are the pooling approach and rationale for choosing the selected region despite the lack of inter-individual resolution clearly described? | Yes No<br>N/A |
| **Additional data collection and analysis** | | |
| | If the proposal includes optional complementary data collection and analyses, are the approaches and scientific rationale described, and are separate tasks and associated milestones included in the proposed Task Description Document (TDD) / Research Description Document (RDD)? | Yes No<br>N/A |
| | If the proposal includes collection of additional biospecimens, was justification provided, and are | Yes No |

| | | |
|---|---|---|
| | separate tasks and associated milestones included in the proposed TDD / RDD? | N/A |
| | If the proposal includes optional complementary biospecimen and/or data collection, do the proposers ensure that these approaches will not interfere with implementation of the sleep deprivation and cognitive assessment protocols, or the acquisition of blood and tissue biospecimens, as described in this Somnus research announcement? | Yes No<br><br>N/A |
| **Cost** | | |
| | Is the total proposed cost at or under $2M? | Yes No |

## 7. Appendix B: Material and sharing agreements

The following agreement templates are provided to prospective Somnus proposers as examples for situational awareness. Selected Somnus performer(s) will be expected to enter agreements with government resource partners with regard to transfer of biospecimens for analysis by government partners. Proposers do not need to submit these agreements with their proposal materials. Agreement templates are subject to modification, as per negotiation between Somnus performer(s) and Somnus government resource organizations. Proposers selected for award will receive copies and further instructions.

**WRAIR Office of Technology Transfer**
**Agreement Request Form & Division Director's Checklist**

| **FOR ORTA USE ONLY** | | | |
|---|---|---|---|
| **Type of Agreement** | **New:** | | |
| **ORTA Internal Database Number** | | | |
| **ORTA POC** | | | |
| **WRAIR Principal Investigator (PI) & Division** | | | |
| *Instructions for adding more than one WRAIR PI & Division:*<br>1. *Click anywhere on the section below*<br>2. *A plus sign should automatically appear at bottom right-hand corner*<br>3. *Click on the plus sign and an additional WRAIR PI & Division section should appear* | | | |
| **WRAIR Division** | | **Division Director** | |
| **PI Name** | | **PI Title** | |
| **Contact information** | Phone:<br>Email: | | |
| **If PI is <u>not</u> a US Govt. employee please complete this section** | Employed through a Contract, Cooperative Agreement, or OTA (identify one):<br><br>Other:<br>GOR/COR:<br>Email: | | |
| **Name(s) of Partner Organization(s)** | | | |
| *Instructions for adding more than one partner organization:*<br>1. *Click anywhere on the section below*<br>2. *A plus sign should automatically appear at bottom right-hand corner*<br>3. *Click on the plus sign and an additional Partner Organization section should appear* | | | |
| **Organization Name** | | | |
| **Address** | | | |
| **Organization Type** | | | |
| **POCs** | <u>PI/Scientific POC</u><br>Name:<br>Title:<br>Phone:<br>Email:<br><br><u>POC for Agreements</u><br>Name:<br>Title: | | |

| | |
|---|---|
| | Phone:<br>Email:<br><br>POC for Invoices (*only if funding is involved*)<br>Name:<br>Title:<br>Phone:<br>Email: |

| **Research Project Budget-Related Information** |
|---|
| WRAIR Division/Dept./Lab POC for Budget: |
| Will WRAIR receive funds through the agreement? **Yes*** **No****<br>****The direct, indirect and total $ amount(s) and overhead % are required (see below)***<br>*****Proposal Number/Title or a valid WBS number, and approximate $ amount are required (see below)*** |
| Will WRAIR provide funds to another US Govt. agency? Yes No |
| Will WRAIR receive funds from another US Govt. agency? Yes No |

| **Funding Amount & Source (Required for Submission to WRAIR ARC)** | | |
|---|---|---|
| **Partner Funding (fill in this section if WRAIR will receive funds from Partner)** | **TOTAL($):**<br>**Direct ($):**<br>**Indirect ($):** | **Overhead %:** |
| **Non-Partner Funding Source** (fill in this *mandatory* section if WRAIR will not receive funds from Partner) | **Amount ($):** | **Funding Source(s):**<br><br>**WBS Internal Project Number & Title:** |

| **Research Project Title & SOW & Agreement Term** | | | | | | |
|---|---|---|---|---|---|---|
| **Project Location(s)** | WRAIR (FGA) | AFRIMS | USAMRD-A | USAMRD-G | USAMRD-W | OTHER |

Title:

Background:

Purpose/Goal:

WRAIR will:

Partner/Cooperator will:

Both Parties will:

Proposed Agreement Term (Years):

| **Data/Information/Research Materials to be Shared by WRAIR** |
|---|

Data/Information/Research Materials:

Owned solely by WRAIR – may be shared with partner organization(s)

Developed or received through third party collaboration(s) – list collaboration(s) below:

Prior approval from third party(ies) REQUIRED to share with partner organization(s)

Prior approval from third party(ies) NOT required to share with partner organization(s)

Data/Information:

Must be kept confidential by partner organization(s)

May be published by partner organization(s)

| | | | |
|---|---|---|---|
| **WRAIR Intellectual Property** | Yes<br>No | Notes/Comments: | |
| **Human Subjects/ Biospecimens** | Yes<br>No | Protocol Number(s) | Notes/Comments: |
| **Animal Use** | Yes<br>No | Protocol Number(s) | Notes/Comments: |

**Director's Checklist & Signature/Approval**

I confirm the following:

- This effort aligns with WRAIR's strategic plan
- Appropriate source of funding is available to support this work
- Completion and compliance with human subjects regulatory requirements will be met prior to work beginning
- Completion with animal use regulatory requirements will be met prior to work beginning
- There has been determination of WRAIR IP
- If a contract vehicle will be used to execute incoming funds, an acquisition plan will be in place

*Instructions for adding the Division/Dept./Lab Director signature:*

1. *Save document to computer to enable editing and digital signature*
2. ***Please DO NOT convert this Word document to a PDF***
3. *Double click on the signature line below and a signature window should appear*
4. *Type your name in the signature window and save*

***Note: Once the signature is saved, any edits to the document will automatically delete the signature***

**Director's Signature***

_____

**Director**

***Although a signature is preferred, an email concurrence from the Division/Dept./Lab Director is acceptable***

NIH COLLABORATION AGREEMENT

This Agreement is made by and between the _____, an agency of the United States Government, (hereinafter referred to as "**[IC acronym]"**), and _____,_____ (hereinafter referred to as "Entity"). Collectively or individually, the **[IC]** and Entity shall also be referred to as "Parties" or "Party."

Each Party is interested in collaborating on a joint project described by the Research Plan attached as Appendix A, and the Parties agree as follows:

1. Each Party may transfer Research Material to the other Party as described in the Research Plan. Each Party retains title to its Research Material.

2. To the extent both Parties decide to transfer material not already described in the Research Plan, each such transfer must be documented in writing and notice must be copied to each Party prior to the transfer of the additional material and such material will be treated as Research Material under this Agreement. The Parties will not transfer Human Material under this Agreement. "Human Material" means material that is directly obtained from human subjects (including genomic DNA and isolated RNA) and derivatives of material originally obtained from human subjects that are identified or coded (including infectious agents).

3. THE RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. Recipient agrees to comply with all U.S. Federal rules and regulations applicable to the research project and the handling of the Research Material.

4. A Party that receives Research Material ("Recipient") from the other Party ("Provider") agrees to retain control over the Research Material and will not transfer the Research Material to third parties, except Recipient's contractors or agents, without advance written approval of the Provider. Research Material will only be used to conduct the research outlined in the Research Plan by Recipient's investigator, contractors, or agents who have a need to use the Research Material in connection with the Research Plan and whose obligations of use are consistent with, but no less stringent than, the terms of this Agreement. Recipient will not use Provider's Research Material in a for-profit manner such as for production or for sales of the Research Material. When the research is completed or within thirty (30) days of termination of this Agreement, whichever occurs first, Recipient will dispose of the Provider's Research Material as directed by Provider.

5. For the purposes of this Agreement, “Proprietary Information” includes any information relating to the Research Plan that a Party transfers to a receiving Party and asserts is confidential and proprietary. Proprietary Information shall not include information that:

    a) is generated by either Party under the Research Plan (“Research Results”), which, for clarity, shall be maintained in confidence unless disclosed in accordance with Paragraph 9;
    b) has been published or otherwise publicly available at the time of disclosure to the receiving Party;
    c) becomes publicly known, by publication or otherwise, not due to any unauthorized act by the receiving Party;
    d) was in the possession of or was readily available to the receiving Party without being subject to a confidentiality obligation from another source prior to the disclosure;
    e) the receiving Party can demonstrate it developed independently, or it acquired without reference to or reliance upon such Proprietary Information; or
    f) is required to be disclosed by law, regulation or court order.

6. All information to be deemed proprietary under this Agreement shall be clearly marked "**PROPRIETARY**" by the disclosing Party. Any Proprietary Information that is orally disclosed must be reduced to writing and marked "**PROPRIETARY**" by the disclosing Party, and such notice must be provided to the receiving Party within thirty (30) days of the oral disclosure.

7. Each Party agrees to accept the Proprietary Information and employ all reasonable efforts to maintain the Proprietary Information of the other Party confidential, such efforts to be no less than the degree of care employed by each Party to preserve and safeguard its own proprietary information. The Proprietary Information of the disclosing Party shall not be disclosed, revealed, or given to anyone by the receiving Party, except employees, contractors, or agents of the receiving Party who have a need for the Proprietary Information in connection with the receiving Party's activities under this Agreement, and who are under confidentiality obligations to the receiving Party that are consistent with, but no less stringent than, this Agreement. Such employees, contractors, and agents shall be advised by the receiving Party of the confidential nature of the Proprietary Information and that the Proprietary Information shall be treated accordingly. The obligations of this Paragraph 7 shall continue for five (5) years from the execution of this Agreement.

8. “Modifications” means substances created under the Research Plan by one Party which contain/incorporate Research Material of the other Party. The Parties agree to share Modifications with each other as available and upon request. Either Party can use Modifications for their own internal research purposes. Either Party may make Modifications available to non-profit entities for research purposes only. A Party that wishes to distribute Modifications to for-profit entities for any purpose or to any third party for commercial purposes agrees that it will not do so unless it has first notified the other Party.

9. The Parties agree to exchange all Research Results. The Parties agree to work together to make Research Results publicly available and will use reasonable efforts to keep the Research Results confidential until published or until a corresponding patent application has been filed, whichever occurs first. Before either Party submits a paper or abstract for publication, the other Party shall have thirty (30) days to review the proposed publication to ensure that Proprietary Information or any intellectual property therein is protected. The reviewing Party may request in writing that the proposed publication be delayed for up to thirty (30) additional days as necessary to file a patent application. Each Party will be given seven (7) days to review and provide comments on any press releases relating to this Agreement. Each Party agrees not to claim, infer, or imply endorsement of itself, its research, or any of its products or services, by the other Party or any of its employees or subunits.

10. This Agreement shall remain in force for three (3) years or until the research has been completed, whichever occurs first. The term may be extended and the provisions of this Agreement may be modified only by amendment signed by the duly authorized signatory for each Party. The Agreement may be terminated by either Party for any reason by providing written notice at least thirty (30) days prior to the desired termination date.

11. Each Party shall retain title to any intellectual property rights in inventions and works of authorship made by its employees in the course of the research. The Parties understand that nothing herein shall be deemed to constitute, by implication or otherwise, the grant to either Party by the other of any license or other rights under any patent, patent application, or other intellectual property right or interest. NIH will seriously consider Entity's request for a license to any invention made in whole or in part by [IC] under the research described in the attached Research Plan, subject to the terms of 35 U.S.C. Section 207-209 and 37 C.F.R. Part 404.

12. THE PROVIDER OFFERS NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. The Party providing Research Material or Proprietary Information makes no representations that the use thereof will not infringe any patent or proprietary rights of third parties. No indemnification for any loss, claim, or liability is intended or provided by either Party under this Agreement.

13. This Agreement constitutes the entire understanding between the Parties concerning the subject matter of this collaboration and supersedes any prior understanding or written or oral agreement. The illegality or invalidity of any provision of this Agreement shall not impair, affect or invalidate the other provisions of this Agreement. The relationship of the Parties is that of independent contractors and not agents of each other or joint venturers or partners. Each Party shall maintain sole and exclusive control over its personnel and operations.

14. Each Party expressly certifies and affirms that the contents of any statements made herein are truthful and accurate to the best of its knowledge and belief, and each official signing this Agreement on behalf of a Party further certifies and affirms that the official has the authority to do so.

**ACCEPTED AND AGREED**

**FOR THE [Full Name IC] _____**

_____ _____
(Authorized Signatory for **[IC]**) Date
(Printed Name)
(Title of Signatory)
**[IC]**, National Institutes of Health

Address for Notices:

**READ AND UNDERSTOOD:**

_____ _____
([IC] Investigator Name) Date

**FOR THE ENTITY**

_____ _____
(Authorized Signatory for Entity) Date
(Printed Name)
(Title of Signatory)

Address for Notices:

**READ AND UNDERSTOOD:**

_____ _____
(Entity Investigator Name) Date

# Research Plan
**[Title]**

IC Investigator:
Mailing Address:
Telephone #:

Entity Investigator:
Mailing Address:
Telephone #:

## I. Research Material and Proprietary Information to be exchanged between the Parties

**For the [IC]:**

Research Material provided by the [IC]:

Proprietary Information provided by the [IC]:

**For the Entity:**

Research Material provided by the Entity:

Proprietary Information provided by the Entity:

## II. Project Description

## III. Goals:

## IV. Activities of the Parties

**[IC]:**

**Entity:**

**Both Parties jointly:**