Pharmacotherapies for Alcohol and Substance Use Disorder Alliance (PASA)
Study Research Planning Program (SRPP)
Expansion Award Application
Request for Application (RFA) #7d: [FY23; Round 1]

Release: June 2, 2023

SUBMISSION AND REVIEW DATES

• Letter of Intent Due	6/30/2023
• Full Application Due	7/14/2023
• Peer Review Process Ends	8/14/2023
• Programmatic Panel Review	Late September 2023
• Notification of Award Recommendations	Early October 2023
• Award Negotiations Begin	Mid-October 2023

Request for Application (RFA) #7d: [FY23; Round 1]
Synopsis

Expansion award to support the continued research of highly impactful studies that were funded by the Pharmacotherapies for Alcohol and Substance Abuse Use Disorder Alliance (PASA) Study Research Planning Program (SRPP).

Additional details and associated templates for this RFA are available at:
https://pasa-research.org/funding-opportunities

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I. Funding Opportunity Description

A. Introduction and Intent of Award Mechanism

The **P**harmacotherapies for **A**lcohol and **S**ubstance Use Disorder **A**lliance (PASA) is funded by the Congressionally Directed Medical Research Programs (CDMRP) (https://cdmrp.health.mil/) as part of its Alcohol and Substance Use Disorders Research Program (ASUDRP) consortium awards (W81XWH-17-ASADRP-CA and W81XWH-21-ASADRP-CA). The PASA's goal is to fund study applications that explore integrated approaches to address ASUD especially comorbid ASUD with PTSD and other psychological disorders and reduce the number of opioid and other substance use-related deaths through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols and enhanced quality of life for service members, Veterans, and the American public. Studies of military and Veteran populations are encouraged. These medications will ideally address the comorbidity between ASUDs and PTSD or other psychological disorders as these comorbidities are common in the military and veteran populations. Alcohol use disorder (AUD) is the most common ASUD in the military, but opiate use disorder also has developed significant clinical importance because of prolonged pain treatments with opiates. Commercialization linked to FDA approval for these new medications or combinations of medications is critical so that early linkages to pharmaceutical companies are considered strengths of any application for PASA funding.

The PASA SRPP is requesting applications for expansion awards to support the continuation or extension of previously funded PASA research to further compound identification, assessment, and/or development. Separate RFAs are available for new non-clinical basic science research studies, basic science pre-clinical animal research studies, and planning awards for human participant clinical trials.

B. Program Description

The PASA is administered by a PASA Core led by RTI International in collaboration with the Baylor College of Medicine (BCM). The PASA Leadership team consists of Principal Investigator Tracy Nolen, DrPH from RTI and co-Principal Investigators Tom Kosten, MD, from BCM and Nathan Vandergrift, PhD, from RTI. Oversight of PASA is provided by a Programmatic Panel assembled by the CDMRP.

The goal of the PASA is to fund study applications for developing new medications that can be brought to therapeutic use to improve treatment outcomes for ASUD, especially as related to PTSD and other psychological disorders. These medications will ideally address the comorbidity between ASUD and other psychological disorders.

C. PASA Core

The PASA Core is responsible for soliciting and prioritizing applications. Successful applications will be recommended for funding by Programmatic Panel assembled by the CDMRP. The PASA Core will provide oversight and coordination for future proof-of-principle non-clinical basic research studies, receive all relevant study data in a timely manner and act as a data repository, and provide analytic support in study design and analyses.

The PASA Core will provide the administrative, protocol development and review, regulatory, statistical, resource, and data management/storage functions necessary to facilitate rapid development of research that would perhaps not otherwise be feasible without the PASA Core support. The PASA Core contains multidisciplinary expertise and experience in support of ASUD research. Additional information about PASA is available on its website (https://pasa-research.org).

II. Research Focus

A. Research Aims

The PASA has three broad aims:

1. Discover: Test new chemical entities and repurpose existing medications in strictly pre-clinical and non-clinical models of ASUD with comorbid PTSD and other psychological disorders.
2. Phase 1 First-in-Human Safety: Conduct clinical trials of potential medications that include assessment of medical safety and doses for potential efficacy in subjects with ASUD and comorbid PTSD and other psychological disorders.
3. Phase 2 Efficacy: Conduct multiple site clinical trials to test preliminary efficacy and safety of potential medications or medication combinations in humans with ASUD and comorbid PTSD and other psychological disorders, and to also explore precision medicine tools for matching patients to these medications.

B. Research Areas of Emphasis

1. Improved formulations to treat ASUD with comorbid substance use
2. Improved formulations to treat ASUD with comorbid PTSD and other psychological disorders
3. Stronger, longer-duration formulations to counteract opioid (including fentanyl analogs) overdose
4. New formulations and/or combinations of existing medications to improve treatment compliance, prevent relapse, and reduce risk of misuse
5. Novel medications and immunotherapies to treat substance and/or ASUD
6. New medication targets for the treatment of substance and/or ASUD

For this RFA, we are soliciting for expansions of current or previously funded PASA studies (all Aims). Separate RFAs are available for new non-clinical basic science research studies (Aim 1), basic science pre-clinical, animal research studies (Aim 1) and planning awards for human participant clinical trials (Aims 2 and 3). The research expansion award must address at least one research area of emphasis.

C. Expansion Award Information

This award is designed to support expansion of current or previously funded research by PASA.

III. Submission Information

This award will support continued research and further development of research projects previously funded by the PASA SRPP. The awards are intended to fund work that is a next step or an expansion on currently funded work. The expansion award may be used to support non-clinical or pre-clinical basic science or clinical research. The total funded amount and period of performance should align with the proposed work.

A. Types of Studies to be Awarded

Type	Period of Performance	Maximum Total Cost (Direct and Indirect)
Expansion Award	12-24 months	$250,000-$750,000

Note: ***Maximum total cost includes direct and indirect costs***. Deviations from these time and funding limits will require written permission from PASA Leadership. Please contact PASA_RFA@rti.org.

B. Application

All applications must include the following elements (as applicable) in the order as listed in this announcement. Page limits are noted where applicable. Failure to include a required element may result in the application not being reviewed. Start each component on a new page with the component title, PI name, and study title at the top of the first page.

All applications should include details on the objective and results of the previously funded PASA project. The description should include how these results or accomplishments relate to this application.

Questions about the application process will be received; with answers provided on a rolling basis and posted on a FAQ page of the PASA website.

B.1 Letter of Intent

A letter of intent (LOI) must be submitted prior to submission of the full application. The LOI shall not exceed four pages and provide:

- The title of the application;
- The name(s) and affiliation(s) of the PI and, if any, co-PIs;
- The address, phone number, and e-mail address of the PI;
- A brief overview of the previous research and accomplishments of the previously funded project by PASA.
- A brief overview of the expansion study including research aims and objectives; and
- A list of the sites where the study will be conducted.

All LOIs must be submitted as a PDF file by e-mail no later than 11:59 PM Eastern Time June 30, **2023;** to:
PASA_RFA@rti.org

The LOIs are for planning purposes only and no response from the PASA Core is required to proceed with the full application. If any concerns or questions are identified upon review of the LOI, the PASA Core will contact the listed investigators.

B.2 Expansion Award Application Submission Requirements

All full applications must be submitted as a PDF file by e-mail no later than **July 14, 2023;** to:
PASA_RFA@rti.org

The full application consists of the following components:

Item	Description
Proposal Cover Sheet	See Appendix A for this template.
Title	Provide the title of the proposed project.

Item	Description
Abstract	Include an abstract for the proposed expansion award.
Personnel (3-page limit)	Demonstrate that the PIs, collaborators, and other researchers are well suited to the project and have an ongoing record of accomplishments. Describe any collaboration between civilian, DoD, or VA personnel. Include an organizational chart and briefly describe the roles and responsibilities of the study personnel.
Background (3-page limit)	Detail the objective and results of the previously funded PASA project. Please include published and/or unpublished data.
Research Rationale (1-page limit)	Detail rationale that the previously funded PASA project is ready for the next phase of development. Include how the proposed project will builds upon previous research.
Research Aims & Objectives (1-page limit)	Research aims and objectives should be clearly defined and sensibly tied to a definite research question. A clear endpoint or set of endpoints should be tied to each objective.
Research Strategy and Feasibility (10-page limit)	The overall strategy, methodology, statistical plan, and analyses should be well reasoned and appropriate to accomplish the specific aims of the project. A sample size estimate must be included and supported by a power analysis or other justification that demonstrates the adequacy of the sample size.
Impact and Innovation (1-page limit)	State how the project has the potential to significantly inform military or VA health care and practice and promote a greater understanding of the treatment of ASUD comorbid with PTSD or other psychological conditions and reduce the number of opioid and other substance related deaths. A successful application will also describe how the proposed research: • Meaningfully expands on the previous PASA study without overlapping existing research/current studies. • Uniquely contributes to the understanding of ASUD comorbid with PTSD or other psychological conditions and not replicate current studies but move beyond with an innovative approach or objectives. • Promotes the development of improvements in pharmacotherapies for ASUD comorbid with PTSD or other psychological conditions leading to approval and marketing.
Environment (1-page limit)	Applicants should describe how the project benefits from unique features of the scientific environment, or collaborative arrangements. A description of all locations should also be provided. Also describe how each proposed site contributes to the study and how these sites will be able to complete the study protocol.
Pharmaceutical Company Collaboration/Regulatory Pathway Progression Potential *(clinical research studies only)*	Address the proposed collaboration with a pharmaceutical company or other institution that would be used to provide continuity of development to inform study design, sample size and dosing needed to move this compound through the regulatory pathway in support of

Item	Description
(1-page limit)	future clinical trials leading to a to a new label/indication if the study where to be successful.
Laboratory Animals (pre-clinical basic science studies only)	Each animal protocol must include: 1. A justification for using animals, the number of animals to be used, and the species chosen; 2. The procedures or drugs to be used to eliminate or minimize pain and discomfort; 3. A description of the methods and sources used to search for alternatives to painful procedures; and 4. A description of the search used to ensure that the experiment does not unnecessarily duplicate previous research.
Human Subject Recruitment and Safety Procedures *(clinical research studies only)*	This section should address the following topics: • Study Population: Describe the population at the study sites including the approximate number and pertinent demographic characteristics of the population from which participants will be recruited. • Describe how the application addresses ethnic and gender diversity and access to the appropriate populations. • Inclusion/Exclusion Criteria • Description of the Recruitment Process: Describe the methods for identification of potential human subjects (e.g., medical records review, health care provider identification, etc.) • Description of the Informed Consent Process: (1) Describe who is responsible for explaining the study and answering questions; (2) when and where informed consent will be obtained; (3) address issues of mental capacity • Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, patient histories or physical examinations) that are required to determine study eligibility. • Risks and Benefit Assessment
Research and Related Budget and Budget Justification	A budget justification which describes the labor and other direct costs necessary to complete the project must be included here. The budget should reflect yearly direct costs for each year over the entire period of performance. Because PASA project funding is available through a DoD award, all study subaward funds will be subject to policies and restrictions based on the DoD source of this funding. • Budget to be submitted using R&R Budget form • Forms are available on the PASA website
Quad Chart	All applications must include a quad chart (separate from the application) briefly describing the study including rationale, population

Item	Description
	to be studied, sample size, study sites, methods, total budget, and a picture or other graphic describing the study. An example of a CDMRP-compliant quad chart can be found at: https://ebrap.org/eBRAP/public/Program.htm
Supporting Documentation	Start each document on a new page with complete header information. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.
	• **References Cited:** List the references cited in the Research Methods (including URLs if available) using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
	• **List of Abbreviations, Acronyms, and Symbols:** Provide a list of all abbreviations, acronyms, and symbols used in the application.
	• **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable.
	• **Publications or Patent Abstracts** *(three-document limit)*: Include relevant publication URLs or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included here. Extra items will not be reviewed.
	• **Letters of Organizational Support** *(two-page limit per letter)***:** Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, reflecting the institution's commitment to the completion of the trial, including laboratory space, equipment, and other resources available for the project.
	• **Letters of Collaboration (if applicable)** *(two-page limit per letter)***:** Provide a signed letter from each collaborating individual

Item	Description
	or organization that will demonstrate that the PI has the support or resources necessary for the proposed work. Letters of support from a collaborating pharmaceutical company are welcomed and desired.
	• **Letters Confirming Access to Military or VA Patient Populations or Resources (if applicable; not applicable for non-clinical nor pre-clinical basic research**): If the proposed research plan involves access to active-duty military and/or VA patient populations or resources, include a letter of support, signed by the lowest ranking person with approval authority, confirming such access. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources.
	• **Research & Related Senior/Key Person Profile: All applications must include:** o PI Biographical Sketch (4-*page limit*) o PI Previous/Current/Pending Support (*no page limit*) o Key Personnel Biographical Sketches (4-*page limit each*) o Key Personnel Previous/Current/Pending Support (*no page limit*) Forms available on the PASA website.

B.3 Full Application Format

All applications should be submitted as a single PDF file, except for the full budget PDF form, which should be a separate file. All text should be in Calibri with a font size of no less than 11. All margins should be at least one inch. Inclusion of URLs to provide additional information is prohibited in all sections.

IV. Full Application Review and Selection Process

A. Peer Review

To determine technical merit, all applications will be evaluated by a peer-review committee according to the following scored criteria, which are of equal importance. For multisite studies, feasibility, personnel, and environment will be evaluated across all sites.

- **Personnel**
  - How the background and expertise of the PI(s) and other key personnel demonstrate their abilities to perform the proposed work.

- How the levels of effort by the PI(s) and other co-investigators are appropriate to ensure the successful conduct of the project.
- How the PI(s)'s and co-investigators' record(s) of accomplishment demonstrate their abilities to accomplish the proposed work.

Research Rationale

- How the proposed expansion clearly builds on the existing/previous PASA research studies.
- How well the scientific rationale supports research on the proposed compound(s) for treatment of ASUD comorbid with PTSD or other psychological disorders. The feasibility of such research, as demonstrated by previous work and critical review and analysis of the literature, supporting data, and logical reasoning.
- How well the application describes existing non-clinical, pre-clinical and/or clinical trial research of the proposed compound(s) and justifies additional study for treatment of ASUD comorbid with PTSD or psychological disorders.

- **Strategy and Feasibility**
  - To what extent the overall strategy, methodology, statistical plan, and analyses are reasonable and appropriate to accomplish the specific aims of the project. To what degree the sample size is supported by a power analysis or other justification that demonstrates the adequacy of the sample size.
  - How well the application defines the aims and objectives of the research and the necessary endpoints.
  - How well the application assesses the likely next steps needed for continuing the compound along the regulatory pathway (*for clinical research studies*).
  - Whether the investigators demonstrate an ability via pharmaceutical collaboration or otherwise for compound to continue to progress long term on regulatory pathway (*for clinical research studies*).
  - How well the application acknowledges potential problems or delays and addresses alternative approaches and solutions.

- **Impact and Innovation**
  - How the proposed research, if successful, will:
    - Promote greater understanding of the treatment of ASUD comorbid with PTSD or other psychological disorders and reduce the number of opioid and other substance use-related deaths.
    - Promote the development of improvements in pharmacotherapies for ASUD comorbid with PTSD or other psychological disorders.
    - Support potential approval and marketing of pharmacotherapies for ASUD comorbid with PTSD or other psychological disorders.
  - How the proposed research uniquely contributes to the understanding of ASUD comorbid with PTSD or other psychological conditions using an innovative approach or objectives.

- **Expansion**
  - If the current research is not yet completed, how the expansion is justified with the information available and how the expansion operationally aligns with current research timeline
  - Whether the next proposed research plan/development is feasible

- **Environment**
  - How the scientific environment is appropriate for the proposed research.
  - How the research requirements are supported by the availability of and accessibility to facilities and resources.
  - How the quality and extent of organizational support are appropriate for the proposed research.

- **Laboratory Animal Protocol (if applicable)**
  - How well the animal protocol provides a justification for the animal used, the procedures or drugs used to minimize discomfort and a description of the search used to ensure that the experiment does not unnecessarily duplicate previous research.

- **Human Subject Recruitment and Safety Procedures (if applicable)**
  - How well the application describes the population at the study sites including the approximate number and pertinent demographic characteristics of the population from which participants will be recruited.
  - How well the inclusion/exclusion criteria are described.
  - How well the recruitment process is described.
  - How well the informed consent process is described: who is responsible for explaining the study and answering questions? (2) when and where the informed consent will be obtained and (3) to what degree is the issue of mental capacity addressed?
  - How well the screening procedures are described.
  - To what degree the risks and benefit are assessed.
  - If applicable, how well the application addresses ethnic and gender diversity and provides evidence of availability of and access to the necessary study populations or resources.

- **Pharmaceutical Collaboration/ Regulatory Pathway Progression**
  - Whether collaborations with industry or other institutions exist that will be used to provide continuity of development to inform study design, sample size, and dosing for future clinical trials.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the funding limitations.

- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the ease of review and the understanding of the reviewers.

B. Programmatic Review

Following the Peer Review, the PASA Core leaders will present the applications to the Programmatic Panel for their review. The Programmatic Panel will make funding recommendations using the following criteria:

- Ratings and evaluations of the peer reviewers
- Relevance to the goal of PASA, as evidenced by the following:
  - Relative impact
  - Program portfolio composition
  - Programmatic relevance
  - Adherence to the intent of the award mechanism

Final recommendation of research awards to be funded will be made by the Programmatic Panel.

V. Award Negotiation

If your application is recommended for funding by the Programmatic Panel, award negotiations will be held between your institution and the PASA Core to establish the scope of the final award consistent with the recommendations of the Programmatic Panel and subject to final approval of the Programmatic Panel. All official negotiations of the budget, terms, and conditions of any resulting award will be conducted between the Business Official of your institution and the RTI Subcontracts Specialist. All subawards, and changes to all subawards that result in substantive changes to the budget, including major modifications of subawards and changes across cost categories, require approval from the United States Army Medical Research Acquisition Agency.

VI. Post-Award Requirements

A. Protocol

Within 4 months of study award, all studies shall finalize a protocol based on the proposal in conjunction with the Management Core and submit for review and approval by the PASA Leadership and obtain necessary approvals (Intuitional Review Board (IRB), Human Research Protection Office [HRPO], Institutional Animal Care and Use Committee [IACUC)], and/or Animal Care and Use Review Office [ACURO]. The protocol must follow the PASA Protocol Template on the PASA website.

B. Study Manual of Procedures

In addition to the study protocol, a study manual of procedures (MOP) will be developed by the study team in conjunction with the Management Core and submitted to the PASA Leadership for review and approval. The MOP must be approved in writing by the PASA Leadership prior to the initiation of study activities.

Most studies funded by PASA must be conducted in accordance with GCP and/or GLP requirements. Some basic science studies may not require adherence to GLP, and a determination will be made concerning GLP in consultation between the PI and the PASA Core.

C. Reporting

Quarterly and annual progress reports will be required in the format shown on the PASA website. In addition to written progress reports, oral presentations may be requested, particularly to the Programmatic Panel.

D. Quality Assurance

During MOP development, a quality assurance plan must be developed in line with PASA's quality assurance guidelines. This plan will include details of records maintenance at the site, timely data recording, verification, and routine reporting/submission of data to the PASA Core and planned checks for data consistency.

E. Publications

A PASA priority is the rapid publication and presentation of study results in high quality peer reviewed journals and venues. Investigators should adhere to PASA publication policy which is available on the PASA website. A primary manuscript should be completed in a timely fashion. PASA Leadership will implement corrective action when 3 months have passed between final analysis and first draft, or 6 months have passed between final analysis and submission to a peer-reviewed journal; and an extension has not been requested or awarded.

Appendix A: Proposal Cover Sheet

Project Title:

Principal Investigator's Name:
Position/Title:
Department:
Organization Name:
Street:
City:
State:
Zip:
E-mail:
Phone:

Direct costs:
Indirects:
Total costs:

Proposed Start Date:

Proposed End Date:

PASA target disorders: (please list all that apply)

- Alcohol
- Opiates
- Marijuana
- Stimulants
- Other substance (specify)
- PTSD
- TBI
- Other psychological disorders (specify)