<div align="center">AMENDMENT THREE (3)</div>

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PURPOSE OF SOLICITATION AMENDMENT

 The purpose of this amendment is to:

- Provide slides, recording, and transcript of the pre-proposal conference; and,
- Remove and replace Page 41 of the solicitation, to revise Section 6.2 Denial of award as attached; and,
- Respond to Questions received regarding the solicitation.

The hour and date specified for receipt of Offers remains unchanged.
Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full effect.

A recording of the pre-proposal conference and associated materials have been posted on the NIH SBIR/STTR SEED webpage and are also made available below:

- Watch the recording.
- Access the transcript.
- Access the slides.

<u>General Solicitation Questions</u>

Question 1: **For our SAMs account we selected to focus on grant applications and not governmental contracts. Is this something we can still apply for?**

Answer 1: Your company must have an active registration in SAMs that reflects "purpose of registration: All Awards" not "Federal Assistance Awards Only." Please review Section 4.12 of the solicitation for more information.

Question 2: **In section 4.17, it states that "Advance payments may be requested and approved on a case-by-case basis, and are dependent on Agency procedures. Offerors should indicate the need for advanced payments in Appendix C – Contract Pricing Proposal, Section III."**

We will indicate "Yes" and then "Advance payments" in Section III. Is there anything further we need to do to indicate the amount of the advance payment?

Answer 2: Indicating the need for advance payments by checking the box in Section III of Appendix C is all that is needed at the time of proposal. Once the Contracting Officer notifies that the proposal is being considered for award, details about advance payment can be discussed.

Question 3: **Do we have to provide cost proposal justification other than some details required in Appendix C? In the SBIR grant application there is a budget justification document. For the SBIR contract, where should we justify the expected costs in more detail?**

Answer 3: In Appendix C, page 2 under Item Description, there are instructions on what to include for cost/price justification. If more space is needed, please add pages to this appendix and label clearly.

Question 4: **Are there any examples of the awarded SBIR contract proposals available? I only found SBIR grant proposal examples on the NIA website.**

Answer 4: NIH does not have a copy of a funded SBIR contract proposal as an example.

Question 5: **For a Phase II contract, will it still be a firm-fixed price contract, or is it a cost-reimbursable contract?**

Answer 5: Phase II funding type will vary among each topic. Therefore, it is important for the proposing firms to review the topics description and reach out to the specific Contracting Officer in the agency for that topic.

Question 6: **Can a PI/company submit two proposals to a solicitation this time?**

Answer 6: Yes, a company is allowed to submit more than one proposal under the same topic, if the proposals represent separate and distinct projects.

Note that for proposal submission in eCPS, the company would need to create entirely separate submission packages. The company would go through the eCPS submission process for the 1st submission and then repeat the process for the next submission. If a company is planning to submit more than one proposal under the same topic, it is recommended that the Company differentiates between their different Phase I proposals by using a unique identifier in the file names/naming conventions. For example: if each submission has a different PI, include the PI name in the submission file names, etc., to ensure reviewers will be aware that the submissions are different proposals from the same vendor not a duplicate submission of the same proposal.

Question 7: **What are the timelines (e.g., award notification and project kick-off) after November submission?**

Answer 7: The timelines will be different for each agency. Please review the estimated timelines in the solicitation, Section 9, which contains projected dates for when the review and award will take place.

Question 8: **What is the process for NIH and CDC to make decisions? Is it the same review process as SBIR grant?**

Answer 8: The requirements are identified and described specifically under each of these research topics. The way that the review will be conducted is that each awarding component will assemble a panel of peer reviewers, which is similar to grants review in the sense that it's a peer review. However, the expertise that's gathered for those panels is going to be collected based on the needs and requirements of the specific topic. So, proposals submitted under a topic will be reviewed together by a peer review panel that's reviewing against the criteria that's stated in the Solicitation. Please review section 6 of the solicitation for information.

Question 9: **Does "outsource" mean subcontracting?**

Answer 9: Outsource can be a subcontractor or any contract/agreement with a third party for activities being conducted in the Statement of Work.

Question 10: **Could you please elaborate the criteria for a Fast Track contract?**

Answer 10: A Fast Track submission may result in award for Phase I with a contractual option for Phase II. The Government is not obligated to fund the Phase II portion unless and until the awarding HHS Component exercises that option. Performance requirements are specific to each contract, and will be addressed by the awarding component's Contracting Officer for proposals identified for negotiation.

Question 11: **What if there are multiple PIs? All need to be 50% employed by company?**

Answer 11: At least one proposed PI must be primarily employed with the applicant, as discussed in Section 4.2 "Offeror Eligibility and Performance Requirements."

Question 12: **How is this RFP different from the one closing on Jan5?**

Answer 12:   The January 5th receipt date is for SBIR and STTR grants. In general, the majority of our grants are submitted through the omnibus solicitations. You can find those at: seed.nih.gov.

Question 13:   Are there restrictions on eligibility for SBIR/STTR funding if the applying company is owned more than 50% by a non-profit organization?

Answer 13:   Small Businesses must meet the eligibility criteria listed here: https://seed.nih.gov/small-business-funding/small-business-program-basics/eligibility-criteria

Question 14:   Are there suggested page lengths for the sections of the proposals? Does this page limit include biosketches? resource pages etc?

Answer 14:   SBIR Phase I Technical Proposals (Item 1) shall not exceed 50 pages. SBIR Phase II Technical Proposals (Item 1) shall not exceed 150 pages. The Technical Proposal shall not exceed the page limits stated, inclusive of all pages, cover sheet, tables, CVs, resumes, references, pictures/graphics, appendices, attachments, etc.

Question 15:   Do Phase IIs follow the same due dates listed in the funding opportunity announcement or are awarded Phase I agencies notified of Phase II requirements individually? Do you typically apply for Phase I and Phase II at the same time?

Answer 15:   Please refer the solicitation Section 8.4 'Phase II Proposal Instructions', for information regarding Phase II proposal's (either as part of a FAST TRACK or Direct to Phase II). This will depend on the topic and fast track applications.

Question 16:   If we are a startup just incorporated, can we use 40% indirect rate for budget?

Answer 16:   SBIR offerors who propose a G&A/IDC rate of 40 percent of total direct costs or less will not be required to negotiate Final Indirect Rates with the NIH Division of Financial Advisory Services (DFAS), or other cognizant auditing agency. However, awarding Contracting Officers may require offerors to document how they calculated their IDC rate(s) in order to determine that these costs are fair and reasonable.

Question 17:   How should I determine and document indirect rates?

Answer 17:   The solicitation allows for small business to charge indirect costs at a rate of up to 40% of total direct costs without requiring that the small business negotiate an indirect rate agreement with the NIH Division of Financial Advisory Services (DFAS).

However, this does not mean that an indirect rate of 40% will be acceptable for every business.

Your business should complete a table such as the one found at the website below to be able to justify your rate (of up to 40%), and include this information in your Business Proposal:
- https://oamp.od.nih.gov/dfas/indirect-cost-branch/indirect-cost-submission/indirect-cost-definition-and- example

After reviewing the DFAS website above, if you have further questions, you are encouraged to contact the DFAS staff at dfas-idc@nih.gov for assistance in understanding how to determine an appropriate indirect rate.

Question 18: **Can you explain the difference between grants vs contracts?**

Answer 18: A contract is a legally binding agreement between the two parties, your organization and the government. There will be specific performance requirements in the statement of work and details of deliverable schedule that will include dated that are expected for performance.

Question 19: **Are we required to submit Pricing proposal form other than in Appendix C? Or are there any other detailed forms needed?**

Answer 19: Appendix C is the pricing proposals that is required.

Question 20: **Do we have to submit the letter of intent before the submission?**

Answer 20: As this is not a requirement, it is recommended.

Question 21: **Are letters of support required? If so, how many and from whom (ex. researchers, doctors, potential end users, etc)?**

Answer 21: When a subcontractor or consultant collaborator is proposed, a letter must be included from each individual confirming his/her role in the project and extent of involvement; when facilities other than those of the applicant are proposed, a letter must be included stating that leasing/rental arrangements have been negotiated and will be available for the use of the SBIR applicant; and, for Phase II proposals under a Fast Track submission, letters should be included in the Finance Plan section of your Commercialization Plan.

In addition, some of the specific Topic Descriptions in Section 12 refer to additional and/or more specialized letter requirements, so check your individual Topic of interest carefully.

All of these letters should be included in your Technical Proposal to ensure that they are reviewed by all reviewers.

In addition, costs associated with collaborators should be addressed in Appendix C of the Business Proposal, and letters that discuss or confirm financial information for collaborators can also be included in the Business Proposal to support the evaluation of the proposed project budget. For NIH Topics, please

note that information submitted in the Business Proposal, however, will not be seen by all evaluators, some of whom will only review the Technical Proposal.

Question 22: **Are both grants and contracts available for For-Profit entities?**

Answer 22: Yes, both SBIR contracts and grants must go to for-profit entities.

Question 23: **With SBIR, do you have to be with a university?**

Answer 23: You do not have to be affiliated with a university to submit an SBIR.

Question 24: **Is a company allowed to submit more than one proposal to the same topic, assuming the proposals represent clearly different approaches, under the PHS 2024-1 SBIR Contracts solicitation?**

Answer 24: Yes, a company is allowed to submit more than one proposal under the same topic if the proposals represent separate and distinct projects.

Note that for proposal submission in eCPS, the company would need to create entirely separate submission packages. The company would go through the eCPS submission process for the 1st submission and then repeat the process for the next submission. If a company is planning to submit more than one proposal under the same topic, it is recommended that the Company differentiates between their different Phase I proposals by using a unique identifier in the file names/naming conventions. For example: if each submission has a different PI, include the PI name in the submission file names, etc., to ensure reviewers will be aware that the submissions are different proposals from the same vendor not a duplicate submission of the same proposal.

Question 25: **In general, how guaranteed are the funds stated in the topics?**

Answer 25: NIH/CDC will not fund a proposal for more than the budget listed for each topic (with the exception of potential Technical and Business Assistance funding, as described in that section of the solicitation).
The Agency is under no obligation to fund any proposals or any specific number of proposals in a given topic.

Question 26: **Are contracts eligible for Technical and Business Assistance (TABA)?**

Answer 26: Section 4.16 provides guidance on State Assistance and Technical Assistance. NIH offers distinct technical assistance programs to NIH SBIR and STTR Phase I and Phase II awardees. These programs offer specialized, strategic business training and provide access to a vast network of industry experts which is made possible by the efficiencies of scale accomplished through providing this service through the Government.

Note for CDC offerors: CDC does not participate in the NIH TABA Program. If you are a CDC offeror and wish to utilize your own technical assistance provider, you are required to include these costs in your budget and to provide a detailed

budget justification. You may request up to $6,500 per year for a Phase I and up to $50,000 per Phase II project (across all years) for assistance.

Refer to Section 8 for how to include this in your Pricing Proposal. Please note, if funds are requested to utilize your own technical assistance vendor and an award is made, the awardee is not eligible to apply for the NIH-provided technical assistance program for the phase awarded.

Question 27: Are contracts eligible for a diversity supplement?

Answer 27:   No, that program is not applicable to Federal contracts.

Question 28: Can a new corporation apply for a direct-to-phase II contract using the results of the previous LLC? The team and resources remain the same, the company structure and name are the only changes.

Answer 28:   There should not be an issue with changing company structure.

https://www.sbir.gov/faqs/all states:
What happens if we change our corporate structure and change our EIN or DUNS number, are we considered new company or existing company?

If you change your corporate structure, EIN, or DUNS, you would add a new record to the already existing company for data and recordkeeping purposes.

Question 29: Are you able to provide the contact information for the program managers/contract officers for the different Topics?

Answer 29:   All inquiries must be addressed to Contracting Office personnel, as set forth in Section 10 of the solicitation.

Question 30: Are the contract topics ever repeated? In case a company is unable to apply before the deadline, would there be another opportunity to apply for a similar topic?

Answer 30:   An SBIR contract topic may or may not be repeated in future years. If the topic of interest is not repeated, applicants may consider applying for the SBIR/STTR Omnibus solicitations. Link:
https://seed.nih.gov/sites/default/files/HHS_Program_Descriptions.pdf.

Question 31: We are having issues finding the funding component when it comes to naming conventions? Where can we find the funding component to insert in the highlighted title?
                    Phase I FAST TRACK_XYZ Company_NIAID_Topic_049

Answer 31:   The funding component is the awarding component that will be awarding the contract. As highlighted above, NIAID will be awarding Topic 049. The Awarding Component can be found in the solicitation under each topic within the title.

NATIONAL CANCER INSTITUTE (NCI)
NCI Topic 455: Point-of-Care Detection of Prostate Specific Antigen

Question 1: **In regards to the following deliverable listed in the solicitation: 'Conduct initial clinical testing with at least one of the current FDA-approved PSA assays to demonstrate accuracy of PSA measurement compared to a gold standard test.' Must this "initial clinical testing" be conducted under an IRB with an open-enrollment, prospective clinical trial?**

Answer 1: No, it does not need to be a prospective clinical trial.

NCI Topic 456: Rapid and Affordable Point-of-Care HPV Diagnostics for Cervical Cancer Control

Question 1: **Our will be doing all the R&D in the US, but will need to purchase RPA reagents from a UK subsidiary. Would this be allowed under the SBIR contract?**

Answer 1: Recombinase Polymerase Amplification (RPA) is done by a lot of sources now, and while your company's particular reagent is proprietary, there are other reagents manufactured that are readily available. If you choose to submit a proposal, please include a justification on why you cannot develop your home HPV molecular test using these other reagents.

Question 2: **The Phase I and II deliverables listed in the solicitation appear to be a "must" requirement – as in, if we do not propose these, we would not be eligible??**

Answer 2: Yes, that is correct. Deliverables are "must" requirements.

Question 3: **If awarded, will this contract fund: a) "Clinical validation trials in other locations than in the US? In a LMIC setting b) local manufacturers in LMICs to produce the diagnostic tool locally c) Wider public health campaigns and education and training materials for local health systems and ministries of health OR d) In addition to self sampling, self testing for a positive or negative result?**

Answer 3: a) Yes, but LMICs only, and applicants are required to include a statement in their proposals on why these resources are not available in the US. It should be also noted that NIH has implemented a new Due Diligence process to review foreign components for contract proposals and the collaborations & relationships that contract applicants have or had before awards are made.
b) No.
c) No, unless the work is related to R&D technology development such as user or patients tests.
d) Yes.

Question 4: **If collaborating with a company in New Delhi, India that has highly affordable tests for the rapid detection of viral genes such, what would be the specific requirements for the company and myself to be a co-partner?**

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The company has a branch in the USA that will provide the materials and technical know-how. I will coordinate all the procurement and the laboratory work.

Answer 4:   The applicant must be a for-profit US small business based in the US with the work performed in the US. There are additional details about the company ownership that can be found on our website here: https://sbir.cancer.gov/small-business-funding/application-process. For projects where the technology has already been developed, the applicant should consider Direct to Phase II since the deliverable focuses on supporting a larger validation study.

NCI Topic 457: Technologies for Detecting Tumor-Derived Cell Clusters

Question 1:   Are these deliverables examples of what is expected from the proposed project or are <u>all</u> the deliverables expected to be addressed in the proposal? For example, are both *in vivo* (e.g. monitoring) and *in vitro* deliverables required or would a technology focusing on the in vitro aspects have enough merit to be considered for funding for this opportunity?

Answer 1:   The contract topic welcomes technologies that monitor TDCCs using either an in vivo <u>or</u> in vitro modality. Offerors should follow the deliverables relevant to the modality of their proposed technology, including the deliverables listed that are common to all modalities (listed below the section which specifies the deliverables for in vivo and in vitro).

NCI Topic 461: Ultra-Fast Dose Rate (FLASH) Radiation Detectors and Safety Systems for Cancer Treatment

Question 1:   How many NEW awards are anticipated for 2024? How many continuing awards are anticipated?

Answer 1:   At the end, within each topic description and Section 9 provides information regarding anticipated awards.

NCI Topic 462: Organ-on-Chip for Preclinical and Translational Radiobiological Studies

**Question 1:   Regarding a Phase I deliverable for Topic 462, it states to provide detailed plans for "Irradiation with dosimetry traceable to the national standard and demonstration of compatibilities with radiation and drug radiation combination experiments."
Is there a requirement/preference for the radiation source used (i.e. Cs-137 vs. X-ray)? Could either be used if appropriate dosimetry can be demonstrated?**

Answer 1:   Dosimetry influences research outcome. There is no preference for dosimetry to one vs. other. But dosimetry should be traceable to a standard.

NCI Topic 463: Translation of Novel Cancer-specific Imaging Agents and Techniques to Mediate Successful Image-guided Cancer Interventions

Question 1:   Even if the IRB has been approved, the human trial including patients' recruitment cannot be started before the IND approval by FDA as. "Sponsors may submit research to be conducted under an IND to an IRB at

any time before or after the IND is in effect. However, the research itself (including study-specific recruitment) may not begin until after the IND is in effect, even if the IRB has approved the research".

How can we reconcile Contract Phase II deliverables with the lack of IND approval?

Answer 1: IRB approval and IND filing with FDA are required before the initiation of clinical trials. These activities should be achieved before proposal of Phase II objectives focused on clinical testing.

Question 2: Regarding the Phase I activities and deliverables, in the second bullet point, it is stated "Refine a GMP grade selected probe to yield maximal biological safety and validate very small volume tumor detection of primary and metastatic cancers in selected animal models."   Does this mean that applicants are expected to already have a GMP-grade probe in hand when submitting the proposal?

Answer 2: Yes, GMP batch manufacture can be a phase I objective under this topic solicitation.

Question 3: Does the cancer-specific imaging agents discussed in Topic 463 need to be "activatable" at the tumor site?

Answer 3: The major goal of this contract topic solicitation is to bring highly sensitive cancer imaging agents and technologies capable of detecting very small volume (1 mm^3) tumors in human to clinical utility. There is a clinical need for techniques that improve image contrast between tumors and surrounding normal tissue. As long as the proposed technology can address these points it is considered within scope for this solicitation.

Question 4: Do we need to find a medical center to provide us with the required data prior to the SBIR phase I submission or in the phase I should we provide a proof of concept on the technology. In the phase II, should we partner with a medical facility to gather data for testing the software?

Answer 4: This topic solicitation is focused on translation of developing technologies for small tumor detection in human subjects. The bulk of the proposed research must focus on translating improvements in imaging sensitivity to a clinical environment. It is not intended to support continued major development and testing of techniques or novel agents in a nonclinical setting. Working with clinical samples in Phase I is recommended.

Question 5: Does the imaging agent technology need to demonstrate detection of both primary and metastatic tumors to be eligible for review and funding?

Answer 5: The technology can be used for primary and/or metastatic tumor sites.

Question 6: Could experimental animal demonstration of laparoscopic pressurized aerosol dispersion and detection of small tumors by MTTI's fluorogenic pH-sensitive dye be performed at CROs or academic centers ex-US and paid using SBIR Phase I Contract funds?

Answer 6:   All SBIR work and dollars spent must be within the US. Waivers for this are incredibly rare and the only case must be that the work is unable to be performed in the US. This contract topic is focused on bringing highly sensitive cancer-specific imaging agents and technologies capable of detecting very small volume (1 mm3) tumors in humans to clinical utility. It is not intended to support continued major nonclinical development and testing of techniques or novel agents.

Question 7:   Can the duration period of the Phase II Contract period be extended by a year if the FDA requires a second species GLP safety/toxicology study be performed before initiating clinical studies in the US?

Answer 7:   SBIR Phase II deliverables for this contract topic should be limited to clinical work (FIH dose escalation or validation study

NCI Topic 464: Cloud-Based Multimodal Data Analysis Software for the Cancer Research Data Commons

Question 1:   Does 'multimodal' in Topic 464 imply omic data AND imaging data, or can we interpret 'multimodal' to also mean different classes of variants detected using different modalities (many of which are quite challenging to automatically annotate)?

Answer 1:   Multimodal' in the SBIR topic 464 means different omics, imaging, and/or spatial omics datasets.

Question 2:   For the topic NIH/NCI 464 – Cloud-Based Multimodal Data Analysis Software for the Cancer Research Data Commons, I noticed there was a very similar one in 2020's solicitation, "NIH/NCI 428 - Cloud-Based Multi-Omic and Imaging Software for the Cancer Research Data Commons (in PHS 2021-1)". How is the solicitation in this year different from the one in 2020? What is the emphasis for this year?

Answer 2:   The topic 464 is the reissuance of the topic 428. They both have the same goal, which is to provide support for the development and implementation of innovative solutions for continued advancement and evolution of cloud-based multimodal informatics tools to integrate with the CRDC for broader user community engagement. However, there are a few minor changes in the new contract topic. Applicants should follow the new solicitation regarding Phase I&II deliverables.

Question 3:   Can we submit two proposals to NIH/NCI 464 – Cloud-Based Multimodal Data Analysis Software for the Cancer Research Data Commons in the same round with the due date of Nov 14, 2023?

Answer 3:   An applicant can submit two different contract proposals if the aims/objectives of the two projects are distinctly different.

Question 4:   In reference to business models, is it acceptable to charge a license fee to tool users? Or should we be pursuing other models that make tools freely available to academic researchers?

Answer 4:   Contract applicants decide what business models that they want to use to market their technologies. Charging a license fee to tool users is acceptable.

NCI Topic 465: Cancer Prevention and Treatment Clinical Trials Tools for Recruitment and Retention of Diverse Populations

Question 1:   Does a tech-enabled service that integrates tech+providers qualify as "tools" if the service is designed to address gaps in clinical trials recruitment and retention?

Answer 1:   Tech-enabled service that integrates tech+providers would qualify as "tools" if the service is designed to address gaps in clinical trials recruitment and retention.".

NATIONAL INSTITUTE ON AGING (NIA)

NIA TOPIC 010 – Technology to facilitate characterization of the exposome in under-resourced populations for AD/ADRD Studies

Question 1:   For the SBIR contract PHS-2024-1, the topic for NIH/NIA 010 is different in different places in the solicitation and on eCPS. Could you please clarify if the topic is "Technology to Facilitate Characterization of the _Exposome_ in Under-Resourced Populations for AD/ADRD Studies" or "Technology to Facilitate Characterization of the _Exosome_ in Under-Resourced Populations for AD/ADRD Studies"?

Answer 1:   The correct topic title is "Technology to Facilitate Characterization of the **_Exposome_** in Under-Resourced Populations for AD/ADRD Studies."

Question 2:   Is there a link to a description of what this topic covers? Specifically, I am trying to understand what the word "exposome" covers.

Answer 2:   We define the exposome exposures, such as chemicals, radiation, infectious agents, and lifestyle factors, as occurring outside the body. However, a person's response to these exposures is determined by how the exposures interact with their normal biological systems, particularly metabolic processes and the microbiome. Ideally, the samples collected will enable both environmental exposure assessment, but also detection of biologic effect as reflected in various -omic measures (e.g. genomics, metabolomics, proteomics, etc.). Self-collection of these measures is paramount to enable broad participation in diverse populations across the life course.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

General Question:

Question 1:   Since 126 and 127 both include POC HIV detection, (although topic 127 also detects HCV, HBV), are they going to be reviewed in the same panel?

Answer 1:   Each topic will be evaluated by separate review panels.

NIAID TOPIC 124 - Development of Next-Generation Devices and Materials-Based Platforms for the Administration of HIV-1 Broadly Neutralizing Antibodies

Question 1: **The solicitation mostly speaks to dermal patches and implantable devices, but at the end mentions that nucleic acids are a potential modality for bNAb delivery. I was wondering if you thought viral vector-based approaches would be responsive to this contract topic or just mRNA/DNA?**

Answer 1: Yes, viral vector-based approaches are responsive, as long as they are intended to enhance sustained release, bioavailability, and/or protective durability.

NIAID TOPIC 126 - Rapid Diagnostic Assays for Self-Monitoring of Acute or Rebound HIV-1 Infection

Question 1: **Is it possible to obtain funding for similar, but not overlapping, projects for home HIV RNA testing through both the NIAID 126 and NIMH 001 solicitations?**

Answer 1: It is permissible to submit proposals containing similar work with no overlapping to two different topics. Two separate and different proposals must be submitted to each topic to be evaluated separately under each IC.

Question 2: **Please confirm if semi-quantitative HIV-1 RNA tests (reported as above or below a cutoff without a true viral load result) are acceptable under this contract.**

Answer 2: Yes, this is correct – the solicitation Topic 126, Project Goals (2nd bullet) indicates the assay should be a semiquantitative antigen or molecular test and indicates a target sensitivity for RNA.

NIAID Topic 127 - Multiplexed Patient Administered Diagnostics for Hepatitis B, Hepatitis C, and HIV

Question 1: **For HIV testing, is it necessary to detect both HIV-1 and HIV-2?**

Answer 1: Both HIV-1/2 are preferred.

Question 2: **If only HIV-1, is it necessary to detect strains outside of group M?**

Answer 2: No, it is not necessary to detect strains outside of group M.

Question 3: **What is the desired pricing for the multiplexed test (assuming antigen/immunoassay format for dual/multiplexed detection of 2 or 3 targets).**

Answer 3: It is not the Governments place to provide pricing for testing. Please propose a reasonable price for the testing and provide justification for the proposed amount.

Questions 4: **What is the desired pricing for a multiplexed RNA test? For RNA tests, what is an acceptable price for the reader/analyzer?**

Answer 4: It is not the Governments place to provide pricing for testing. Please propose a reasonable price for the testing and provide justification for the proposed amount.

Questions 5: **When you say "self-administered test", can the test be a self-collection and ship to a lab test, or an at-home self collection and self-run test?**

Answer 5: "Self-administered test" refers to at home self-collection/self-run test.

Question 6: **Can these SBIR funds pay for a foreign clinical site for resource-limited settings in the developing world?**

Answer 6: No, the funding for this topic is not intended for a foreign clinical site.

Question 7: **Does the test have to be developed under ISO13485?**

Answer 7: No, the test does not have to be developed under ISO13485.

Question 8: **Will the funds pay for Quality system setup and maintenance, and Quality personnel?**

Answer 8: No, the funding for this topic is not intended for Quality system setup/maintenance or Quality Personnel

NIAID TOPIC 128 - Adjuvant Development for Vaccines for Infectious and Immune-Mediated Diseases

Question 1: **We've identified a vaccine adjuvant and would like to screen structural variations of the adjuvant (e.g., -R groups, numbers of covalently linked chains of the adjuvant) to improve adjuvant activity. Should this project be submitted to Topic NIH/NIAID 130 (Adjuvant discovery) or 128 (Adjuvant development)?**

Answer 1: Topic NIH/NIAID 130 (Adjuvant discovery) supports 1) the screening for new vaccine adjuvant candidates against infectious diseases or for tolerogenic adjuvants for the treatment of autoimmune or allergic diseases, or 2) the down-selection of adjuvants to support the subsequent development of novel adjuvanted vaccines. Topic NIH/NIAID 128 (Adjuvant development) will support the optimization of an identified adjuvant, including structural alterations of the adjuvant. Topic NIH/NIAID 128 (Adjuvant development) may support a Phase I proposal that includes screens of structural variations of an identified adjuvant (e.g., -R groups, numbers of covalently linked chains of the adjuvant) to improve adjuvant activity.

Question 2: **What is the difference between a Phase II under Topic NIH/NIAID 130 (Adjuvant discovery) and a Phase I or II under Topic NIH/NIAID 128 (Adjuvant development)?**

Answer 2: A Phase II under Topic NIH/NIAID 130 (Adjuvant discovery) would support continued high-throughput screening, validation of possible candidate vaccine adjuvants, and activities to identify lead adjuvant candidates. Topic NIH/NIAID 128 (Adjuvant development) will support continued development of an identified lead adjuvant candidate, which may include evaluating the effect of structural modifications to that lead core adjuvant compound.

NIAID TOPIC 129 - Reagents for Immunologic Analysis of Non-mammalian and Underrepresented Mammalian Models

General amendment/clarification to Topic 129:

> While the solicitation requires the comprehensive evaluation of (a) specificity, (b) functional utility, and (c) cross-reactivity (off-target binding) of antibodies/reagents based on the use of (a) flow cytometry and (b) any two of the following - Western blotting, Immunoprecipitation, immunofluorescent staining, immunohistochemistry, or ELISA (including ELISPOT) -, Offerors may propose to replace flow cytometry as the primary assay as long as they provide a strong justification for why flow cytometry is not an appropriate assay for specific target antigens and would not be a useful assay format for end-users of the reagent.

Question 1: **The technical topic description for this topic states the requirement to do flow cytometry, which doesn't make sense for some of the analytes, such as IP-10. Can Elispot be used instead of flow?**

Answer 1: Offerors may propose to use other assay formats to replace flow cytometry as their primary assay for comprehensive evaluation of their antibodies/reagents, as long as they provide a strong justification for why flow cytometry is not an appropriate assay for their targets.

NIAID TOPIC 130 - Adjuvant Discovery and Down-Selection for Vaccines against Infectious and Immune-Mediated Diseases

Question 1: **We've identified a vaccine adjuvant and would like to screen structural variations of the adjuvant (e.g., -R groups, numbers of covalently linked chains of the adjuvant) to improve adjuvant activity. Should this project be submitted to Topic NIH/NIAID 130 (Adjuvant discovery) or 128 (Adjuvant development)?**

Answer 1: Topic NIH/NIAID 130 (Adjuvant discovery) supports 1) the screening for new vaccine adjuvant candidates against infectious diseases or for tolerogenic adjuvants for the treatment of autoimmune or allergic diseases, or 2) the down-selection of adjuvants to support the subsequent development of novel adjuvanted vaccines. Topic NIH/NIAID 128 (Adjuvant development) will support the optimization of an identified adjuvant, including structural alterations of the adjuvant. Topic NIH/NIAID 128 (Adjuvant development) may support a Phase I proposal that includes screens of structural variations of an identified adjuvant (e.g., -R groups, numbers of covalently linked chains of the adjuvant) to improve adjuvant activity.

Question 2: **What is the difference between a Phase II under Topic NIH/NIAID 130 (Adjuvant discovery) and a Phase I or II under Topic NIH/NIAID 128 (Adjuvant development)?**

Answer 2: A Phase II under Topic NIH/NIAID 130 (Adjuvant discovery) would support continued high-throughput screening, validation of possible candidate vaccine

adjuvants, and activities to identify lead adjuvant candidates. Topic NIH/NIAID 128 (Adjuvant development) will support continued development of an identified lead adjuvant candidate, which may include evaluating the effect of structural modifications to that lead core adjuvant compound.

NIAID TOPIC 132 – Novel Diagnostic Biomarker Discovery and Validation for Malaria and Select Neglected Tropical Diseases (NTDs)

Question 1: **NIAID lists a total of 5 NTDs under this topic. Is an offeror allowed to submit multiple separate applications, addressing discovery and development of biomarkers for different NTDs?**
   a. Or alternatively, can we submit a phase I application for biomarker discovery for multiple pathogens and then proceed to develop the most promising marker for a single pathogen?

Answer 1: There is no prohibition on organizing the proposal around a single pathogen or multiple pathogens. It is allowable for the Offeror to use a down selection strategy during the Phase I application. This would need to be made clear in the proposal such that the Technical Evaluation Panel would have the opportunity to assess the merits of this approach. It is also allowable for an Offeror to submit a Phase I application focused on multiple pathogens followed by a Phase II application focused on the single most promising pathogen.

NIAID TOPIC 133 - Development of a Serological Test for Herpes Simplex Types 1 and 2 Infections

Questions 1: **What is the unmet diagnostic need in the current market that NIH is looking to address?**

Answer 1: The unmet need is a well-performing, widely available, serological assay to aid in the diagnosis of genital herpes.

Question 2: **Is NIAID interested in Rapid Test or ELISA? The solicitation does not clarify the intended use setting but does mention the need for the test to be distributed for broad use.**

Answer 2: Yes, NIAID is interested in those types of tests and any others that would provide broad use. As stated, current serological tests are critical when patients are asymptomatic, but herpes is suspected. This situation occurs in many patient-provider locations, both public and private.

Question 3: **Is NIAID anticipating that the final device will be FDA approved? Is it only serotype differentiation?**

Answer 3: FDA approval of the final device would be anticipated; however it is not a required deliverable of this solicitation. Not clear what "it" is referring to, but the test needs to distinguish between HSV-1 and-2.

Question 4: **Are there specific patient/sample populations that NIH is interested in targeting: Sexually active adults>=18 y/o, pregnant women, etc.?**

Answer 4:   Population target research should be done by the Offeror, but in general NIH supports the development of diagnostics for infectious diseases to those most at risk. For herpes in particular, patients who are asymptomatic but are suspected of having herpes are of highest concern. Under-performing serological tests are routinely not used for these patients for fear of delivering a false-positive result.

NIAID TOPIC 135 – Software or Web Services to Automate Metadata Enrichment and Standardization for Data on Infectious and Immune – Mediated Diseases

Question 1:   **Are there high-value examples of ontologies or data sites that NIAID would benefit the most from regarding the creation and enrichment of metadata?**

Answer 1:   There are several examples, and it is up to the offeror to identify high-value ontologies or data sites. Sites for reference include, but are not limited to:
NIAID Data Ecosystem Portal: https://data.niaid.nih.gov/
   ▪ Associated schema: https://discovery.biothings.io/ns/nde
NIH supported repositories: https://sharing.nih.gov/data-management-and-sharing-policy/sharing-scientific-data/repositories-for-sharing-scientific-data
Ontology example: https://ontobee.org/ontology/IDO

Question2:   **Do you know how many data sources you are interested in automating metadata enrichment and standardization from?**

Answer 2:   The scope of the effort should align with the proposed budget by the offeror. However, the priority should be on data resources that align with NIAID mission.

Question 3:   **Can you provide further details as to the expected inputs to the proposed web service? Should it primarily be unstructured documents? Raw structured datasets in a variety of formats?**

Answer 3:   The input could be either unstructured or structured data or both; the (meta)data will focus on Infectious and Immune-mediated Disease (IID) data.

Question 4:   **Will sample data be provided to support development of the prototypes?**

Answer 4:   Program believes that there is sufficient number of repositories pertaining to IID with (meta)data openly available for prototype development.

Question 5:   **We did find this BMIC maintained <u>list of repositories</u>. Are these repositories representative of the ones envisioned for scientists to be interfacing within this effort?**

Answer 5:   Yes; A few other resources to reference are:
   • NIAID Data Ecosystem Portal: https://data.niaid.nih.gov/
      • Associated schema: https://discovery.biothings.io/ns/nde
   • NIH supported repositories: https://sharing.nih.gov/data-management-and-sharing-policy/sharing-scientific-data/repositories-for-sharing-scientific-data

Question 6: **Is there any preference toward a particular cloud platform (AWS, Azure, Google)?**

Answer 6: There is no endorsement of one cloud platform over another as long as it meets the requirements of the topic.

Question 7: **Can you provide details on any existing software? Are there already middleware components that need improving? Are there already moving pieces that need to be aligned to?**

Answer 7: NIAID currently supports a metadata search portal for NIAID mission related areas. Alignment with the portal would be a plus. Details are provided below:
- NIAID Data Ecosystem Portal: https://data.niaid.nih.gov/
  - Associated schema: https://discovery.biothings.io/ns/nde

Question 8: **One of the requirements described "Hardening and improving user-friendliness." Does this imply primarily user experience development, or security and privacy controls as well?**

Answer 8: This would include all aspects of the user experience and is one example of a potential activity in phase I.

Question 9: **Are there existing cloud-based services, custom tools, etc. already in use for monitoring performance of the system (existing or new)?**

Answer 9: No

Question 10: **For phase 1, will access to specific repositories be necessary? Are there generally common authentication mechanisms?**

Answer 10: There are a sufficient number of open-source repositories to initiate work. Should permissions be required, that can be obtained from the performer and/or in consultation with NIAID.

Question 11: **Is there an expected scale of the user-based testing? Number of users, query concurrency, etc.?**

Answer 11: The scale and scope of effort should match the proposed budget.

Question 12: **Are there existing NLP libraries the team has leveraged in the past in this area? Are there potentially available compute resources (GPUs, etc.) for more intensive approaches (LLM perhaps)?**

Answer 12: The performer should leverage resources available to them to deliver the product. NIAID will not make any internal compute resources available to the offerors.

NIAID TOPIC 136 – Software or Web Services to Re-Represent Existing Scientific Data and Knowledge into a Knowledge Graph Format

Question 1:   **What type(s) of knowledge graphs would be of the highest value to the NIAID community?**

Answer 1:   Knowledge graphs pertaining to NIAID mission areas such as Infectious Diseases, Immunology, HIV would be considered high priority by program. These could be derived from biomedical literature, biomedical datasets or combine both.

Question 2:   **Which relationships would be of the highest importance?**

Answer 2:   It is incumbent on the offeror to identify relevant relationships and their priority. Below are a few examples, in no particular order of importance (NOTE: this is **NOT** a comprehensive list):
- Association
- Interactions (drug, gene, protein, regulatory areas)
- Bioprocess
- Disease – biomarker for outcomes
- Disease – causative agent
- Drug- disease
- Drug – mechanism of action
- Drug – target
- Regulates
- Phenotypes

Question 3:   **Could you provide an example of a knowledge graph that NIAID would like to integrate this new knowledge graph into?**

Answer 3:   There are no existing knowledge graphs that NIAID expects the offeror to integrate their new product into, if integration into an existing research work environment is proposed. The offeror would need to identify such an environment and delineate mechanisms for increased adoption by a broad user community.

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

NIMH TOPIC 001 - Point-of-Care HIV Viral Load and Drug Adherence Assays
Question 1:   **Is it possible to obtain funding for unique projects involving home HIV RNA testing through both the NIAID 126 and NIMH 001 solicitations?**

Answer 1:   The projects should be distinct and tailored to the requirements in the solicitation-the approach can involve HIV RNA testing for both the solicitations.

Question 2:   **Please confirm if semi-quantitative HIV-1 RNA tests (reported as above or below a cutoff without a true viral load result) are acceptable under this contract.**

Answer 2:   Semi-quantitative HIV-1 RNA tests the based on the WHO/CDC recommended cutoffs are acceptable.

Question 3:   What is the minimum number of sample matrices that should be evaluated during Phase I? Five different samples are named (blood, DBS, urine, saliva, and hair) - is there any preference for which samples should be addressed during Phase I?

Answer 3:   Any samples that can give validated results related to long term adherence to antiretrovirals are acceptable.

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6.2   Award Decisions

The Awarding Component will make awards to the offerors who provide the best overall value to the Government, considering the following:

- Ratings resulting from the technical evaluation;
- Areas of high program relevance;
- Program balance (i.e., balance among areas of research);
- Availability of funds; and,
- Cost/Price
- Security risk as assessed by the HHS Due Diligence Program.

Denial of Awards

Offerors are encouraged to consider whether their entity's relationships with foreign countries of concern will pose a security risk. Prior to issuing an award, NIH, CDC and FDA will determine whether the SBC submitting the proposal:

- has an owner or covered individual that is party to a malign foreign talent recruitment program;
- has a business entity, parent company, or subsidiary located in the People's Republic of China or another foreign country of concern; or
- has an owner or covered individual that has a foreign affiliation with a research institution located in the People's Republic of China or another foreign country of concern.

A finding of foreign involvement with countries of concern will not necessarily disqualify an offeror. Final award determinations will be based on whether the applicant's involvement falls within any of the following risk criteria, per the SBIR and STTR Extension Act of 2022:

- interfere with the capacity for activities supported by NIH, CDC, or FDA to be carried out; or
- create duplication with activities supported by NIH, CDC, or FDA; or
- present concerns about conflicts of interest; or
- were not appropriately disclosed to NIH, CDC, or FDA; or
- violate Federal law or terms and conditions of NIH, CDC, or FDA; or
- pose a risk to national security.

NIH or CDC will not issue an award under the SBIR program if the covered relationship with a foreign country of concern identified in this guidance is determined to fall under any of the criteria provided above.

The Government anticipates that prospective offerors will develop unique proposals in response to the topics of research set forth in this solicitation. The agency is not under any obligation to fund any proposal or make any specific number of contract awards in a given research topic area. The agency may also elect to fund several or none of the proposals received within a given topic area.