

## AMENDMENT OF SOLICITATION

Solicitation Number: PHS 2015-1

Amendment Number: 2

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### AMENDMENT TWO (2)

Issued by:

National Institute of Allergy and Infectious Diseases (NIAID)  
Office of Acquisitions  
6700-B Rockledge Drive, Suite 300  
Bethesda, MD 20892

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**The hour and date specified for receipt of Offers remains unchanged, 4:30 PM Eastern  
Prevailing Time on November 5, 2014.**

**Offerors MUST acknowledge receipt of the amendment by Amendment number(s) and date  
of the amendment.**

**FAILURE OF YOUR ACKNOWLEDEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER.**

Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full force and effect.

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**PURPOSE OF SOLICITATION AMENDMENT**

The purpose of this amendment is to provide revisions to Section 12 of the subject solicitation and to respond to questions. Accordingly, Solicitation PHS 2015-1 is revised as follows:

**Section 12 Component Instructions and Technical Topic Descriptions, National Cancer Institute (NCI), Topic 335 Development of Advanced Culture Systems for Expansion of Cancer Stem Cells** is revised to make the following correction to page 66 of Solicitation PHS 2015-1, as attached to Amendment One:

- Culture CSC population isolated from tumor biospecimens (human or mouse) to a minimum of **10<sup>7</sup>** cells.

**Section 12 Component Instructions and Technical Topic Descriptions, National Institute of Allergy and Infectious Diseases (NIAID), Topic 031: Inhaled Delivery of Clofazimine (CFZ) – An Important Anti-tuberculosis Drug** is revised to make the following changes to the Project Goal and Phase I Activities on page 97 of Solicitation PHS 2015-1, as attached to Amendment One:

***Project Goal***

The goal of this solicitation is to develop an inexpensive, easy-to-use, inhaled delivery system for clofazimine to **eventually** be used **in humans** with combinations of systemic anti-tubercular drugs to improve the treatment of MDR and DS TB.

***Phase I activities***

- Development of an inhaled formulation of clofazimine.
- Development of an inexpensive, hand-held, self-contained platform for delivery of this formulation **that is developed enough to test on animals with a design that is scalable for humans.**
- Initial testing to quantitatively assess for drug **toxicity, and pharmacokinetics in serum and tissues in uninfected animals and any relevant** in-vitro studies.

**Section 12 Component Instructions and Technical Topic Descriptions, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Topic 043: Yeast-derived Candidate of Hepatitis E Virus Vaccine** is revised to make the following correction to the Project Goal and Deliverables on page 107 of Solicitation PHS 2015-1, as attached to Amendment One:

### *Project Goal*

The purpose of this project is to express the HEV ORF2 protein of **4 HEV genotypes (genotypes 1,2,3, and 4)** in yeast and purify the expressed proteins. Considering that the antigens are planned to be evaluated as vaccine candidates, it is important to show that the purified proteins model the fully functional HEV neutralizing epitope.

### *Deliverables*

- Genetic constructs expressing HEV proteins of **4 HEV genotypes (genotypes 1,2,3, and 4)** in yeast, *Hansenula polymorpha* or *Pichia pastoris*, and yeast strains expressing and secreting the antigens in the immunologically active form.

## **GENERAL QUESTIONS**

The Government's responses to questions received regarding this solicitation are as follows:

**Question: I do not know the difference between a grant and a contract. Can we submit a request for funding and have it considered ahead of the November 5 deadline?**

*Answer:* Proposals will not be considered until after the closing date of the solicitation. Please refer to Section 6 of this solicitation for a description of how proposals for contracts will be evaluated under this solicitation.

**Question: How should receipt of amendments to this solicitation be acknowledged?**

*Answer:* Include acknowledgement within the proposal being submitted.

**Question: Is there any possibility to resubmit the contract application if not funded initially?**

*Answer:* Proposals may not be resubmitted under this solicitation. You may review future SBIR solicitations for funding opportunities of interest.

**Question: Will any topics contained in this solicitation be re-issued in future funding opportunities?**

*Answer:* Information concerning topics to be included in future SBIR funding opportunities is not available.

**Question: We are currently operating under Business Name X and we'll be applying for a Phase I under that name. It is very likely we will have a change to a new entity in the next month or two. How are these events treated under the SBIR program?**

*Answer:* If you are notified by an HHS Component that your proposal is being considered for award, please alert the Point of Contact named in that notification of any anticipated changes to your entity, prior to award. Any changes made post-award would be handled in accordance with the Federal Acquisition Regulations. You may also refer to <http://sbir.gov/faq/company-registry> for guidance on updating your SBIR/STTR Company Registration.

**Question: Do you keep the SBIR award archives in any database? Where can I find this information?**

*Answer:* Searchable information is available at [projectreporter.nih.gov](http://projectreporter.nih.gov).

**Question: Are letters of support for your proposal a requirement?**

*Answer:* Inclusion of letters of support/commitment is discussed in various places throughout the solicitation. Please adhere to the instructions provided therein.

### **Section 1 Introduction**

**Question 1: If you were successful with Phase I, how do you apply for Phase II? Are there Phase II contracts available in 2015 and 2016? If so, has that schedule been published?**

*Answer 1:* As stated in Section 1 of the solicitation, “HHS Components will notify Phase I awardees of the Phase II proposal submission requirements. Submission of Phase II proposals will be in accordance with dates provided by individual Component instructions. The details on the due date, content, and submission requirements of the Phase II proposal will be provided by the awarding HHS Component either in the Phase I award or by subsequent notification. All SBIR/STTR Phase II awards made on topics from solicitations prior to FY13 will be conducted in accordance with the procedures specified in those solicitations.”

**Question 2: Is there a table which shows Phase I, FAST TRACK or Direct to Phase II opportunities? How many of each are available?**

*Answer 2:* Please refer to Section 1 of the solicitation, which provides a table identifying Fast Track and Direct to Phase II opportunities by Topic number.

### **Section 2 Program Description**

**Question 1: Are there any regulations to prevent us from applying for a Direct to Phase II award following a traditional Phase II award?**

*Answer 1:* Under this solicitation, a project that has already received a Phase II award will not be considered for a Direct to Phase II award. Note that, as stated in Section 4.18, if there is any question of the proposed project being essentially the same in nature as a project supported by a prior award, it must be disclosed to the soliciting agency or agencies as early as possible.

You may, however, consider Section 2.3 of this solicitation, which provides information regarding Phase IIB Competing Renewal Awards.

**Question 2: Can a project that was supported by a FAST-TRACK STTR award, with published efficacy data, in the final stages of updating and revision, be considered for a Direct to Phase II award?**

*Answer 2:* As set forth in Section 3 Definitions, for this solicitation, a project will only be considered for Direct to Phase II funding if it has not received Phase I SBIR/STTR funding.

**Question 3: Can a project that was supported by a Phase I award from an agency other than NIH be considered for a Direct to Phase II award for follow on research under this solicitation?**

*Answer 3:* As set forth in Section 3 Definitions, for this solicitation, a project will only be considered for Direct to Phase II funding if it has not received Phase I SBIR/STTR funding.

**Question 4: I am in the final stage of a SBIR Phase II project. If I am going to apply for SBIR Phase IIB, do I still need to write SBIR Phase II final report?**

*Answer 4:* This question is outside the scope of this solicitation. You are advised to contact the Contracting Officer for your current SBIR Phase II project.

**Question 5: Section 2 of the solicitation and the “Purpose” section of Announcement NOT-OD-14-120 say that Phase I awards have a budget of \$150,000 and a duration of 6 months. However, specific Topic X says that it has a different budget and/or a different duration. Please clarify.**

*Answer 5:* Section 2 of the solicitation and the “Purpose” section of Announcement NOT-OD-14-120 only set forth general guidelines of the SBIR program. However, each individual Topic contained in the solicitation can differ somewhat from these guidelines. As stated in Section 2.2, refer to the individual Topic that you are proposing under, listed in Section 12.0, for specific, applicable budget and contract durations.

#### **Section 4.2 Offeror Eligibility and Performance Requirements**

**Question 1: Are contract solicitations subject to limitations regarding the use of American institutions for sub-awards?**

*Answer 1:* As stated in Section 4.2 of this solicitation, “For both Phase I and Phase II, all research or research and development work must be performed by the small business concern and its subcontractors in the United States.”

**Question 2: Are public companies eligible to receive SBIR/STTR grants or contracts, assuming other eligibility requirements are met?**

*Answer 2:* Public companies are eligible under this solicitation, provided that all other eligibility requirements are met.

**Question 3: I own a sole proprietorship. I am not sure if I would qualify as a "Small Business Concern."**

*Answer 3:* Please refer to the definition of “Small Business Concern” set forth in Section 3 Definitions of this solicitation.

**Question 4: We are planning on moving our company to the US this Fall, but have not figured out all of the legal questions yet. I see that registration requires an EIN. Can we apply for an SBIR award under this solicitation?**

*Answer 4:* In accordance with 13 C.F.R. §121.702, referenced in Section 4.2. of the solicitation, a company must meet United States ownership and control eligibility requirements “[t]o be eligible to compete for award of funding agreements in SBA’s Small Business Innovation Research (SBIR) program . . .” Proposals will not be considered unless United States ownership and eligibility requirements are met by the closing date of this solicitation.

**Question 5: Can the small business work with an academic partner to carry out the contract? If so, is the budget done with a subcontract to the academic partner? Are F&A costs allowed for the academic partner?**

*Answer 5:* Collaboration with academic partners is not prohibited. You may account for such collaborations in the “Subcontractors/Consultants” section of Appendix C – Contract Pricing Proposal. F&A costs of subcontractors may be included in the Contract Pricing Proposal.

**Question 6: Is there a requirement that 50% of the total costs be budgeted to the small business? In determining the 50% total cost allocation to the small business vs. subcontractor, I know the total cost is the crucial number. Must 50% of the total cost go to the small business in each of the 2 years, or is the 50% rule calculated overall for the two years of funding?**

*Answer 6:* Section 4.2. of the solicitation states: “For Phase I, a minimum of two-thirds of the research or analytical effort must be performed by the awardee. For Phase II, a minimum of one-half of the research or analytical effort must be performed by the awardee. The percentage of work will be measured by total contract costs. Offeror’s [sic] planning to subcontract a significant fraction of their work should verify how it will be measured with their HHS Component contracting officer during contract negotiations.”

**Question 7: One of the SBIR requirements is that the PI should spend at least 51% of his/her time on the project. If there are two co-PIs, is it OK if both of them combined meet the 51% requirement? (For example, with 25/26% split).**

*Answer 7:* As set forth in Section 4.2 of the solicitation, “For both Phase I and II, the principal investigator must be primarily employed with the small business firm or the research institution. Primary employment means that more than one half (50%) of the employee's time is spent with the small business. Primary employment with a small business concern precludes full-time employment at another organization.” Thus, the percentage requirement applies to how much time the PI commits to the small business in total, not how much time the PI commits to the specific project being proposed.

#### **Section 4.4 Joint Ventures**

**Question: Can contracts be small business and non-profit joint applications?**

*Answer:* Refer to Section 4.4 of the solicitation, as well as to the definitions of “Joint Venture” and “Small Business Concern” set forth in Section 3 Definitions.

#### **Section 4.9 OMB Clearance**

**Question:** Can you speak to OMB Approval, how that should be addressed in the proposals, and specifically for Fast Tracks and the direct to Phase II proposals?

*Answer:* Refer to Section 4.9 of the solicitation.

#### **Section 4.13 Debriefing**

**Question:** In the case where an applicant is not awarded a contract, what is the process to request feedback or reviewer comments?

*Answer:* Refer to Section 4.13 of the solicitation.

#### **Section 4.16 Registrations and Certifications**

**Question:** We are registered in grants.gov and have a commons account. Do we have to also be registered in any other databases?

*Answer:* Refer to Section 4.16 of the solicitation in particular, and review the entire solicitation for other registrations and certifications that may be required depending on the specific parameters of the project proposed.

#### **Section 4.18 Prior, Current, or Pending Support of Similar Proposals or Awards**

**Question:** If the subject meets a topic of the contract solicitation, can we apply to both the grant solicitation and the contract solicitation?

*Answer:* Refer to Section 4.18 of the solicitation.

#### **Section 4.21 Payment**

**Question 1:** Do contracts pay only at the time of reports? Or monthly regardless of reports??

*Answer 1:* Please refer to solicitation section 4.21 Payment, for information regarding payments on resulting contracts.

**Question 2:** In Sec. 4.21 Payment, it states that payment is based on completion of deliverables but that advanced payments can be made on a case-by-case basis. What are the criteria to qualify for advanced payments?

*Answer 2:* Offerors should indicate the need for advanced payments in Appendix C – Contract Pricing Proposal, Section III. If you are notified by an HHS Component that your proposal is being considered for award, communicate with the point of contact named in that notification regarding procedures for advanced payment approval.

## **Section 6 Method of Evaluation**

**Question:** If I submit a FAST TRACK proposal (combining Phase I and Phase II proposals), but it is only viewed as appropriate for Phase I, does the proposal get reassigned or given the chance for Phase I?

*Answer:* Section 6 of the solicitation states: “If the NIH Component has indicated in the topic description that FAST Track proposals are accepted under a specific topic, and the offeror wishes to be considered for a FAST Track award, they must submit a Phase I and Phase II (FAST Track) proposal for concurrent peer review and evaluation. The Phase I and Fast Track Proposals will be evaluated and scored individually. Consequently, if a Phase I proposal is evaluated and found to be Technically Unacceptable; the Fast Track proposal will not be evaluated.”

As referred to in Section 8.3 of the solicitation, proposals found unsuitable for FAST TRACK will be redirected for Phase I consideration only.

## **Section 6.1 Evaluation Process**

**Question:** What is the mix of reviewers (how many from within NIH) vs. not-employed there and what are their backgrounds?

*Answer:* Refer to Section 6.1. of the solicitation for information pertaining to the review process.

## **Section 7.2 Limitation on the Length of the Technical Proposal**

**Question:** It is stated that the entire Phase I technical proposal shall not exceed 50 pages, but no particular page limit was stated for the sub-topics of the technical proposal. Are there individual page limits for sub-topics?

*Answer:* Section 7.2 of the solicitation states that “Item 1,” of Phase I proposals shall not exceed 50 pages. Section 8 of the solicitation provides further instructions on what “Item 1: Technical Element” must contain; however, the components of “Item 1” do not have individual page limits. “Item 1,” as a whole, may not exceed 50 pages.

## **Section 8.7 Content of the Pricing Proposal**

**Question:** Is the Budget set forth under each topic for direct costs or all costs?

*Answer:* The Budget for each topic is inclusive of all costs.

## **Section 9 Summary of HHS Components Anticipated Number of Awards**

**Question 1:** What is the timeline for review and award under this solicitation?

*Answer 1:* Refer to the table in Section 9 of the solicitation for anticipated review and award dates.

**Question 2:** What are the start dates for awards made under this solicitation?



*Answer 2:* Periods of Performance have not yet been determined for awards made under this solicitation. Refer to the table in Section 9 of the solicitation for anticipated award dates. Start dates will be designated in each contract award document.

## **Section 10 Contracting Officers and Addresses for Delivery of Contract Proposals**

**Question:** How do you identify the contracting officer representing a specific Institute and project?

*Answer:* Please refer to Section 10 of the solicitation.

### **SPECIFIC TOPIC QUESTIONS**

The Government's responses to questions received regarding this solicitation are as follows:

*National Cancer Institute (NCI),*

#### **Topic 334: Vacutubes to Preserve the Viability of Circulating Tumor Cells**

**Question 1:** In regards to the Phase II activities, if we are interested in a FAST TRACK proposal, how detailed do our manufacturing plans have to be for the product?

*Answer 1:* Use your professional judgment, following the general FAST TRACK Proposal instructions set forth in Section 8.3 of this solicitation.

**Question 2:** If we have the time and funding, would we be able to conduct additional evaluations in addition to the technologies emphasized in the solicitation?

*Answer 2:* You may propose relevant experiments in addition to the required work listed as deliverables in the topic if they fit within the published project duration and budget.

**Question 3:** The approach regarding CTC viability included in the solicitation involves the use of proprietary formulations and may be outside the suggested factors for this topic. Would this approach fit under the guidelines of the contract?

*Answer 3:* Any technical solution that addresses the preservation of CTC viability for the time period prescribed in the published topic, that is compatible with the use of human blood vacutubes, and that enriches CTCs from whole human blood in some way is acceptable. The suggested types of solutions included in solicitation are just examples and are not meant to include all possible solutions.

*National Cancer Institute (NCI),*

#### **Topic 335: Development of Advanced Culture Systems for Expansion of Cancer Stem Cells**

**Question 1:** Please clarify as to what is required by the instructions, "specify SOP and biomarkers (cell marker or assays) used to identify CSC population." Does this mean that the applicant needs to specify by which biomarkers the cell population will be identified?

*Answer 1:* The applicant needs to specify the biomarkers they intend to use to identify or isolate the CSC population in their proposal. The solicitation does not specify which

biomarkers to use since this will be dependent on the cell lines or biospecimens proposed.

**Question 2: Please clarify as to what is required by the instructions, "Specify SOP for assays used to define CSC phenotype". Does this mean that the applicant needs to elaborate what assays were used to define the CSC population – e.g., FACS, western blot, PCR? Or is the requirement here to specifically define the phenotype of the population? In this case, should one assume there's a difference between phenotype and the cell surface markers expressed on the surface of the specific population?**

*Answer 2:* The applicant needs to specify the assays that will be employed to characterize the CSC phenotype. Cell surface markers can be used to identify or enrich for the CSC population, but the applicants will need to demonstrate that the cells they are calling CSCs in fact display the CSC phenotype using suitable assays. The solicitation does not specify which biomarkers or assays to use since this will be dependent on the cell lines or biospecimens proposed.

**Question 3: In Activities and Expected Deliverables, can a patient tumor biopsy be used in Phase I as the preliminary data for isolation and enrichment of CSCs from a heterogeneous cell population?**

*Answer 3:* Yes.

**Question 4: In Activities and Expected Deliverables, can existing patient-derived cancer stem cell lines be used for Phase I deliverables in lieu of those presented as examples?**

*Answer 4:* Patient derived cell lines may be used in the phase I studies.

*National Cancer Institute (NCI),*

**Topic 337: Cell-Free Nucleic Acid-Based Assay Development for Cancer Diagnosis**

**Question 1: Phase 1 deliverables require developing an assay to differentiate a specific type of cancer from healthy samples and from other types of cancer. Does NCI or any other NIH agency provide access to characterized biological blood plasma samples that can be used to develop these assays?**

*Answer 1:* Access to characterized biological blood samples will not be provided upon award of a contract under this solicitation. You will need to find a source of blood / serum / plasma samples on your own. You may explore developing a collaboration with investigator(s) at NCI/NIH at your own discretion.

**Question 2: Will NCI be able to provide any clinical cancer samples during any stage of the project, Phase I and/or Phase II?**

*Answer 2:* No, NCI will not provide any samples.

**Question 3: Does the project need to develop a new assay for one or a set of validated cfNA markers?**

*Answer 3:* An offeror should develop an assay that targets either one or a panel of cfNA-based biomarkers. The biomarker(s) has/have to be the one(s) that are already validated.

**Question 4: Does the project need to develop a new technology assay? Innovative assay? Or can the project use any technology to develop an assay that targets cfNA-biomarker? Is clinical validation is required?**

*Answer 4:* An offeror can propose using either existing technologies or new technologies to develop an assay that targets cfNA-based biomarkers. However, the assay itself has to be innovative. The goal is to develop an assay for clinical application.

**Question 5: If we have to demonstrate our system with validated biomarkers, does it mean the biomarker has to be published before?**

*Answer 5:* A validated biomarker means the biomarker is published, or patented, or validated with your own preliminary / proprietary data.

**Question 6: The solicitation states the following: If you intend to propose surveys or other data collections in a Phase I project, you should refrain from proposing more than 9 respondents. Does this 9 respondent maximum apply to human subjects data as well?**

*Answer 6:* Human subjects work goes through the IRB approval process, if it is needed. In this case, NCI does not develop the instrument nor instruct the contractor on how to develop the instrument. NCI will not collect, receive, or maintain the data. Therefore, the 9 respondent maximum does not apply in this situation.

**Question 7: Will submitting an SOP at the end of contract performance interfere with our IP?**

*Answer 7:* You may exclude IP-related items in your SOP.

**Question 8: Could you clarify what is meant by the need to file a regulatory application?**

*Answer 8:* Filing a regulatory application means seeking an FDA approval for the assay that you will develop.

**Question 9: We would like to focus on one cancer type for the Phase I, and expand it to multiple cancer types in the Phase II. Are there any cancer types of particular interests to NCI that we should focus on?**

*Answer 9:* Any type of cancer can be targeted in this topic. There is no preference for any particular cancer type. It is permissible to focus on one cancer and move to multiple cancer types.

**Question 10: Does the sponsor prefer an assay platform using one type of assay on multiple genetic loci to pinpoint the cancer (sub)types, or multiple mechanically different assays on multiple biomarkers?**

*Answer 10:* You only need to develop one assay for this contract topic.

**Question 11: The solicitation states that “the technology platform should be portable”. Does it mean that the technology can be easily transferred to detect additional cancer types, or the platform/instrument should be physically portable?**

*Answer 11:* It is meant that the technology can be easily transferred to detect additional cancer types in the future. You are not required to have a physically portable device.

**Question 12: Is it ok if we incorporate into our assay process an instrument/platform that is already commercially available?**

*Answer 12:* Yes.

**Question 13: For the assay process/platform development, especially for Phase II, what is the TRL (technology readiness level) requirement?**

*Answer 13:* Demonstrate that the assay enables a test to be finished within one day. Validate the assay in the clinical setting. Submit a regulatory application to obtain approval for clinical application.

**Question 14: The solicitation seems to be written primarily for cell-free DNA detection. Our assay detects differences in RNA splicing. Is this concept within the solicitation intent and needs?**

*Answer 14:* Yes, this topic will accept applications for detection of cell-free RNAs.

**Question 15: Do we need to have the IRB submitted along with the proposal or can we submit it if we win the contract?**

*Answer 15:* You do not need to submit IRB approval with the proposal. You need to have FWA and IRB at the time of a contract award, although a company may be allowed to sign a contract with IRB pending if the Human Subjects work starts at a late stage.

**Question 16: We have a platform for cfNA-based assay for clinical use in the evaluation of cancer diagnosis, prognosis, and /or response to therapy. Do you think work using the platform for validation of the cfNA-based biomarkers aligns with this NIH solicitation topic?**

*Answer 16:* Yes.

*National Cancer Institute (NCI),*

**Topic 338: Predictive Biomarkers of Adverse Reactions to Radiation Treatment**

**Question 1: Is finding a biomarker that will predict adverse reaction to radiation, independently of its efficiency at treating cancer and recurrence, within scope of Topic 338?**

*Answer 1:* Yes, this is within scope.

**Question 2: Is NIH looking for predictive biomarker/s (already identified/discovered, for e.g. TGF-beta) which can be used to detect radiation induced hypersensitivity or radiation-induced fibrosis? Or, is NIH looking to identify/discover, develop and**

**validate cost-effective biomarker-based tests to rapidly assess inter-individual differences in radiation sensitivity?**

*Answer 2:* This Topic is seeking novel biomarkers that can identify (and develop and validate and commercialize) which subset of patients have radio-sensitivity. Using an existing platform to validate an existing marker may not be responsive to the Topic.

*National Cancer Institute (NCI),*

**Topic 339: Systemic Targeted Radionuclide Therapy For Cancer Treatment**

**Question:** Would it be possible to include Phase I trial in our application?

*Answer:* Yes, it is permissible so long as it fits within the budget and duration caps of this contract topic.

*National Cancer Institute (NCI),*

**Topic 340: Validation of Mobile Technologies for Clinical Assessment, Monitoring, and Intervention**

**Question 1:** The solicitation says "Products in beta version are particularly appropriate for this effort." Are products in early beta which still require additional programming to implement all features also considered particularly appropriate? Less appropriate? Unresponsive? Modification seems necessary based on feedback from validation testing before product release. Would a budget that uses SBIR funds for final development of the product before, during, and after testing be considered unresponsive?

*Answer 1:* The approaches indicated would be responsive.

**Question 2:** Does the complete IRB approval, which is listed as a Phase II activity and deliverable, need to be in place by the time that proposals are due for this solicitation?

*Answer 2:* No, the complete IRB approval does not need to be in place before the proposal due date. If a proposal is selected for an award, the IRB approval is expected before any human subjects work may begin.

**Question 3:** Much of the topic solicitation refers to wireless tracking. Must we have a wireless tracking component?

*Answer 3:* You do not need to have a wireless tracking component.

**Question 4:** Should the kickoff presentation be more or less completely outlined in the contract proposal—or is that a deliverable to be produced in the first months of funding?

*Answer 4:* The kickoff presentation is a deliverable to be produced in the first month of funding. The kickoff presentation describes what the contractor will do in the project, so essentially it is a summary of the project.

**Topic 030: Methods of Clinical Sample Preparation for Rapid Detection of Bacterial Pathogens**

**Question 1: Should the sample preparation device be compatible with a specific diagnostics tool or a few diagnostics tools? Please give some examples. Are these tools already in clinical practice? Is it OK to propose the development of an integrated system that includes both sample preparation and diagnostics?**

*Answer 1:* Please utilize your professional judgment to determine the business model for your clinical sample prototype – either to be compatible with a specific diagnostic platform, or to be modular with the potential for incorporation into multiple platforms. There are existing integrated clinical sample-to-answer diagnostic systems for some infectious diseases, but not for detection of gram negative bacteria directly from clinical samples without the need for culture. Proposing the development of a clinical sample processing prototype during the Phase I performance period, for integration into a specific system during a potential Phase II period, is permissible.

**Question 2: Are there specific requirements for sample preparation given diverse variation in sampling fluids and concentration of pathogen?**

*Answer 2:* No. Offerors should gather this information via discussions with potential end-users of their product.

**Question 3: Any guidelines concerning sample preparation time? For example, less than 10 minutes?**

*Answer 3:* No. Offerors should use their professional judgment to determine this parameter via discussions with potential end-users of your product.

**Question 4: Any information about the starter sample size, for each kind of sample, i.e. blood, urine, bronchoalveolar lavage (BAL), sputum and CSF?**

*Answer 4:* Please use your professional judgment in establishing this parameter via discussions with potential end-users of your product.

**Question 5: For certain samples, esp. BAL and sputum, it may be most cost effective, yet efficient, to perform initial sample preparation manually, so the sample is a flowable liquid before it is introduced into a final sample preparation device. Is it acceptable?**

*Answer 5:* The goal of this Topic is to develop rapid, modular clinical sample processing technologies that can be integrated into closed sample-to-answer infectious disease diagnostic platforms. Thus, development of a manual clinical sample preparation process would not be acceptable.

**Question 6: Would the rapid separation of e.g. salmonella or e-coli O157:H7 from stool samples be considered as a potential target of the call? Would the separation of the same pathogens from food (e.g. ground meat) be considered? Could it be considered as an indirect diagnosing tool?**

*Answer 6:* The call of this Topic is for ‘proposed sample processing technology...designed to rapidly extract the analyte from normally sterile sample types, such as blood, cerebral spinal fluid (CSF), and bronchoalveolar lavage’. As the examples provided in your questions below refer to stool samples and food samples, neither of which are sterile human samples, they would not be considered responsive for this topic.

**Question 7: Would a proposal focused on fecal specimens be responsive? In addition, would it would be advantageous to include method for extraction of nucleic acid, and its application in various test formats?**

*Answer 7:* Although a proposal focusing on fecal samples will be considered unresponsive, a proposal will be considered responsive if it can explain/justify how the proposed technology, regardless of the application it was developed for, could be applied for the isolation of bacteria from whole blood or other normally sterile fluids.

**Question 8: Can you clarify the technology you have in mind when asking for a sample processing method?**

*Answer 8:* If the proposed method/technology can reproducibly detect very low numbers of colony forming units in whole blood or other normally sterile fluids, without the need for culture enrichment, the proposal will be considered responsive.

*National Institute of Allergy and Infectious Diseases (NIAID),*

**Topic 031: Inhaled Delivery of Clofazimine (CFZ) – An Important Anti-tuberculosis Drug**

**Question 1: For the Phase I activity, “development of an inexpensive hand-held contained platform for delivery of this formulation,” do we need to design such a device to be tested on animals or would this be a design for people?**

*Answer 1:* A prototype should be developed that can be tested in animals and then scaled up for human use later.

**Question 2: Does a working prototype need to be produced as part of the Phase I work or do we simply need a design concept?**

*Answer 2:* During Phase I, a prototype should be developed enough to test on animals with a design that is scalable for humans.

**Question 3: One of the list of activities to be carried out during Phase I is, “Initial testing to quantitatively assess for drug efficacy, toxicity, and pharmacokinetics including required in vitro studies.” Typically, pharmacokinetic studies are performed in vivo, so is the offeror required to do the in vivo work on the Phase I to assess pharmacokinetics?**

*Answer 3:* Yes, in vivo work to assess pharmacokinetics should be part of the Phase I work.

**Question 4: In addition, if in vivo studies are required, would a preliminary evaluation in a non-infected model suffice or should an infected in vivo model be included?**

*Answer 4:* Yes, a non-infected in vivo model will suffice.

**Topic 032: Simple, Inexpensive Unit for Removing Cells from Small Amounts of Blood in Resource-Limited Settings**

**Question 1: Is the ability to easily collect a separated blood sample in a remote area a benefit? Is stability at ambient temperature a bonus or not needed?**

*Answer 1:* The solicitation states that we are interested in something that will give us plasma to immediately put into a point of care test. We are not interested in stability or shipping the sample since we want to test immediately. We are definitely interested in the ability to collect a separated blood sample in a remote area. We are not interested in stability at ambient temperature since we do not plan to store or ship the sample; it will go immediately into a viral load test while the patient waits for their result.

**Question 2: The background section of this solicitation indicates that the removal of cells should be performed "...without the need for electricity...". Does this preclude portable concepts that are battery operated?**

*Answer 2:* Portable concepts that are battery operated are acceptable.

**Question 3: If we aim for a device that can process maximum 300ul of blood, would that be adequate, or do you need it to accommodate up to 500ul of blood?**

*Answer 3:* We are interested in a product that can give plasma in a sufficient amount and of sufficient quality to be used with a point-of-care viral load test. The solicitation states "approximately 500 ul" of blood, but as long as the unit produces a volume of plasma that can be used with a viral load test, lower volumes may be acceptable.

**Question 4: Would the blood be in a collection tube with anti coagulates or directly from the patient's hand?**

*Answer 4:* Blood will be directly from the patient's hand (we specify "finger stick blood samples"), not collected in a tube, since many point-of-care facilities do not have blood collection capabilities.

**Question 5: Do we need to accurately meter the blood or develop a collection device too for this call or can we use existing off-the shelf products?**

*Answer 5:* Unless it is important to the method you propose, it is not important to meter the blood.

**Question 6: Amount of plasma required from the device: Is there a % recovery requirement?**

*Answer 6:* We are interested in a product that can give plasma in a sufficient amount and of sufficient quality to be used with a point-of-care viral load test. The solicitation states "approximately 500 ul" of blood, but as long as the unit produces a volume of plasma that can be used with a viral load test, lower volumes may be acceptable.

**Question 7: Amount of time for separation: Would 1-2 minutes be acceptable?**



*Answer 7:* The Research Topic information included in this solicitation does not specify an appropriate amount of time, but it should be appropriate for point-of-care so the testing can be completed while the patient is at the clinic.

**Question 8: Quality of the plasma - % red cells, and white cells and platelets acceptable? % cell membrane fragments acceptable? Would 98% red blood count and plasma, 99% white blood count, be acceptable if the offeror can prove equivalent performance to centrifuge separated plasma with spiked blood?**

*Answer 8:* We are interested in a product that can give plasma in a sufficient amount and of sufficient quality to be used with a point-of-care viral load test. The solicitation states “approximately 500 ul” of blood, but as long as the unit produces a volume of plasma that can be used with a viral load test, lower volumes may be acceptable.

**Question 9: For spiked blood with HIV subtypes, are there any specific requirements on type and concentration?**

*Answer 9:* The information included in the solicitation for this Research Topic doesn’t specify the HIV subtypes to use, but the tests will be used in resource limited settings (which is stated) and the prevalent subtypes in those areas are well-known.

*National Institute on Drug Abuse (NIDA),*

**Topic 157: Mobile Technologies Extending Reach of Primary Care for Substance-Use-Disorders**

**Question 1: Does the population of “patients determined to be at a high-risk for substance use disorders (SUD)” include A) people who do not yet have an SUD or B) people who have an SUD but have not yet been identified as having an SUD or C) both?**

*Answer 1:* Per the solicitation, risk is “determined by validated screening and assessment tools.” Therefore, “patients determined to be at a high-risk for SUD” are those in a “high-risk” category as determined by a “validated screening and assessment tool suitable for primary care settings.”

**Question 2: The deliverable "Building in incentives for meeting treatment-plan-adherence goals" seems to involve a population already in treatment, unlike the deliverable "Test the application on 8 patients screened and determined to be at a high-risk for SUD." How do these two reconcile and would it unresponsive to propose Phase I testing with a population who already have treatment plan adherence goals because they are already in treatment?**

*Answer 2:* To clarify, “treatment-plan adherence goals” refer to “treatment plans” established by primary care providers (PCPs). With implementation of the Final Rule of the Mental Health Parity and Addiction Equity Act and Patient Protection and Affordable Care Act, many more PCPs in general medical settings are expected to offer integrated, patient-centered care and treatment plans (e.g., patient-centered medical homes (PCMHs), accountable care organizations, coordinated care organizations, federally qualified health centers, etc.) and intervene accordingly in patient populations at a high-risk for SUD. Thus, these two deliverables are fully consistent for an increasing number of PCPs within these healthcare delivery settings offering patient-centered treatments.

**Question 3: Do the "8 patients screened and determined to be at a high-risk for SUD" need to come from a primary care setting? Would it be unresponsive to test a population derived from sources other than a primary care provider, like people with DUIs referred to sessions at a treatment center because of a concern they are high-risk for SUD?**

*Answer 3:* Per the solicitation, "high-risk" needs to be operationalized "using a validated screening and assessment tool suitable for primary care settings." Similarly, to be responsive to this solicitation, patients referred to a treatment center should be determined to be at "a high-risk for SUD" based upon a valid method using a "validated screening and assessment tool suitable for primary care settings."

**Question 4: We notice on page 100 of the RFP (page 104 of the PDF), the final bullet in the Phase I Activities and Expected Deliverables section is:**

- **Demonstrate acceptability, feasibility, and preliminary efficacy in improving patient linkage to and engagement in indicated follow-up SUD specialty care. Test the application on 8 patients screened and determined to be at a high-risk for SUD, using a validated screening and assessment tool suitable for primary care settings, to gather preliminary data regarding the reliability of the application and its ease of use by patients and providers.**

**In our experience, a 6-month Phase I SBIR requires a very tight turn-around time in which it is difficult to apply for and receive IRB approval (required for any human-use testing), and complete any data collection. Could you elaborate on what is expected under this deliverable?**

*Answer 4:* The timeframe for such testing appears feasible for a Phase I SBIR. There is precedence suggesting the feasibility of completing testing in a small number of patients in a Phase I SBIR. For instance, see a similar timeframe of an acceptability, feasibility, and preliminary efficacy testing deliverable in a previous Phase I SBIR solicitation NIDA issued in PHS 2013-1, Topic 147, page 93.

**Question 5: Is there a specific targeted SUD that NIDA is interested in or is the objective of the NIDA topic to find a generic SUD application?**

*Answer 5:* Since the target patient population mentioned in the solicitation is patients "screened and determined to be at a high-risk for SUD" using a "validated screening and assessment tool suitable for primary care settings", a responsive application would target the application toward the types of SUDs encountered in these "high-risk" patients in primary care settings.

**Question 6: Since we are submitting a Phase I application, do we have to demonstrate efficacy? The announcement states "Demonstrate acceptability, feasibility, and preliminary efficacy in improving patient linkage to and engagement in indicated follow-up SUD specialty care." It has been our experience in other NIH SBIR that the efficacy was reserved for Phase II while acceptability and feasibility are for Phase I objectives. Could you clarify?**

*Answer 6:* This type of deliverable has been specified in prior SBIR Phase I solicitations NIDA has issued. For instance, see an acceptability, feasibility, and preliminary efficacy testing deliverable in a previous Phase I SBIR solicitation NIDA issued in PHS 2013-1, Topic 147, page 93. “Preliminary efficacy” means pilot data sufficient to justify conducting future evaluation of efficacy (e.g., such as consistent with deliverables mentioned in Phase II) in a later clinical research study.

**Question 7: The scope of the topic and the deliverables seem large for the \$150K budget. Does NIDA want the solution to address all the deliverables listed in the announcement?**

*Answer 7:* Yes, NIDA expects the solution to address all the deliverables listed in the announcement. Completion of these deliverables is needed to strengthen this application, both in terms of scientific merit and commercialization potential / likelihood it would result in a marketable product. In terms of scope and number of deliverables, there is precedence from previous Phase I SBIR solicitations NIDA issued suggesting it is not too large for a Phase I SBIR solicitation (e.g., see PHS 2013-1, Topic 147, pp. 91-93).

***National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP),  
Topic 037: Optical Character Recognition Software for Scanning Nutrition Facts Panel***

**Question 1: Are there any additional features that NCCDPHP would like to have in such a system?**

*Answer 1:* The solicitation addresses the need for information from the Nutrition Facts Panel; additional features were not indicated. Applicants may determine the approach that best achieves the goal of the announcement.

**Question 2: Would information regarding GMO/not GMO product be useful?**

*Answer 2:* GMO’s were not addressed as part of the solicitation. Thus, applicants may determine the approach that best achieves the goal of the topic: to develop a deliverable that has OCR technology that has the ability to read and interpret NFPs and can be integrated into other mobile applications.

**Question 3: Are there any specific requirements to the database (e.g., who should be responsible for the database, how the database should be maintained, etc.)?**

*Answer 3:* The solicitation addresses the need for information from the Nutrition Facts Panel. Additional specifications were not provided thus applicants may determine the approach that best achieves the goal of the announcement.

**Question 4: What features are lacking from the existing solutions? (such as <http://www.expervision.com/find-ocr-software-by-document-types/ocr-software-for-label-processing-1>)**

*Answer 4:* The deliverable expected would need to read and interpret Nutrition Facts Panels from various smart devices, demonstrate the potential to be integrated with other health and wellness applications, and prove to be reliable on a variety of packaging formats (box, bag, can, etc.).

**Question 5: For Phase I, does the system have a mobile front end, or would it be sufficient to demonstrate a back-end solution that will then be integrated with a front end in subsequent phases?**

*Answer 5:* The solicitation does not prescribe a specific approach, thus a variety of approaches are welcome. The goal of the topic is: to develop a deliverable that has OCR technology that has the ability to read and interpret NFPs and can be integrated into other mobile applications.

**Question 6: If a mobile component needs to be developed in Phase I, could some of the processing be done on a server, rather than on the phone/tablet?**

*Answer 6:* The solicitation does not address this aspect, thus applicants may determine the approach that best achieves the goal of the announcement. The goal of this topic is: to develop a deliverable that has OCR technology that has the ability to read and interpret NFPs and can be integrated into other mobile applications.

**Question 7: Is the system expected to identify food items by their UPC codes, or by using computer vision techniques to actually recognize the food item through analysis of its appearance and/or packaging?**

*Answer 7:* In the background section of the solicitation, it describes that some existing Apps trigger an option to take and submit pictures after a UPC is scanned by the consumer and no results are yielded. The solicitation is seeking technology that has the ability to read and interpret NFPs (Nutrition Facts Panels).

**Question 8: In the third paragraph, it says that “Software, such as Optical Character Recognition (OCR) that can scan the photo or the NFP as opposed to bar codes can assist in two areas”. The user can scan “the photo” or the user can scan “the NFP”. If the user chose to scan “the photo”, what would this photo contain? Is the software expected to recognize the food item from a photo of the food (which may or may not contain an NFP or UPC)?**

*Answer 8:* The solicitation suggests that one solution may be technology to read and interpret the photos and a second solution may be ability to read directly from a user scanning the product. The solicitation is seeking technology that has the ability to read and interpret NFPs (Nutrition Facts Panels).

**Question 9: A large part of what makes this topic challenging is the need to perform OCR on warped or distorted surfaces (cans, bags) as opposed to the more traditional page/flat-surface-based OCR. Would you agree with this statement?**

*Answer 9:* The solicitation asks that the technology proves to be reliable on a variety of packaging formats (box, bag, can, etc.).

*National Center for Emerging Zoonotic and Infectious Diseases (NCEZID),*  
**Topic 011: Development of Nanoparticle Dengue Diagnostic Tests**

**Question 1: In the solicitation, only the Phase I budget amounts are indicated. Does this suggest that only Phase I contracts will be awarded or is there the potential for a Phase II SBIR contract under this topic?**

*Answer 1:* This solicitation topic is only for Phase I awards.

**Question 2: Test with clinical samples? Do we need clinical samples?**

*Answer 2:* Yes and Yes.

**Question 3: 80% sensitivity or specificity?**

*Answer 3:* 80% sensitivity when RT-PCR is used as the reference test.

**Question 4: What kind of SERS device do we use (portable only or )?**

*Answer 4:* SERS device is not limited to those which are only portable.

**Question 5: Do we need nucleic acid amplification?**

*Answer 5:* Yes, for the reference test for NS1.

**Question 6: The topic describes the use SERS in what we imagine to be a clinical setting. Is there any desire to investigate methods that may be implemented in the field?**

*Answer 6:* The instrument can be for either clinical settings or field settings.

**Question 7: How fast is a shot-turn-around diagnostic result?**

*Answer 7:* A short-turn around diagnostic should be less than 3 hours, which is the approximate time it takes for real time RT-PCR.

**Question 8: What would be examples of resource constrained settings? If this is for field, then what would a realistic size or sensitivity be that would allow the end goal to be reached?**

*Answer 8:* A resource constrained setting would be most developing countries where there is variable technology. We want the instrument to be affordable, similar in price to a conventional ELISA plate reader. The sensitivity of a field test needs to be greater than or equal to 80%, which is about 10% higher than currently available rapid diagnostic tests (RDTs) for nonstructural DENV antigen (NS1).

*National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP),*  
**Topic 043: Yeast-derived Candidate of Hepatitis E Virus Vaccine**

**Question 1: Are we supposed to make constructs of genotypes 1, 2, 3 but express and purify only 1 and 3?**

*Answer 1:* Please see revision included on Page 2 of this Amendment.

**Question 2: Is this a topic that is based on an established technology platform to which a proposal should be focused, or is this topic open to proposals to develop the technology for the topic?**

*Answer 2:* This proposal is to develop and evaluate a yeast-derived candidate of hepatitis E virus vaccine rather than to develop a new technology platform.

**Question 3: Page#3 for HepE in Pichia from NCHHSTP states scientific and technical merit review: May-June 2014 and anticipated award date: August 2014. Please confirm the actual dates.**

*Answer 3:* These dates have been corrected in Section 9 Summary of HHS Components Anticipated Number of Awards of the solicitation document attached to Amendment 1.

***National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP),  
Topic 044: Multiplex Assay for Simultaneous Detection of Hepatitis and Other Viruses***

**Question 1: In the solicitation, only the Phase I budget amounts are indicated. Does this suggest that only Phase I contracts will be awarded or is there the potential for a Phase II SBIR contract under this topic?**

*Answer 1:* This solicitation topic is only for Phase I awards

**Question 2: The solicitation states that the technology should not be electrically driven. Does this include battery or solar-powered electricity generation?**

*Answer 2:* As long as batteries are standard or solar panels easily available/transportable to remote locations, we will consider the proposals.

**Question 3: By “multiplex” we gather that the assay should distinguish between the five different viruses. Does it matter if this is performed in one reaction or different reactions / locations?**

*Answer 3:* One vs. multiple reactions is optional. However, low sample volume and low cost of the assays should be kept in mind since we are looking for technologies we can use in resource poor countries.

**Question 4: If Phase I does not require multiplex detection of all 5 types of viruses, are there strains of particular interest that we should include in the initial studies?**

*Answer 4:* We are interested in detecting genomes of all five hepatitis viruses. If there is an assay that meets most of our criteria for just one of the viruses, we will still consider it if assay development for the additional viruses can be achieved within phase II of the project. Applicants should state what steps would need to be taken for development of the missing assays.

**Question 5: Should the output be quantitative (giving an indication of viral copies) or qualitative (showing that it has surpassed a certain threshold)?**

*Answer 5:* We will consider a qualitative assay if it meets most of our other criteria (low cost, no electricity, etc), but quantitative would be a plus.

**Question 6: What sensitivity, assay duration, cost and sample size requirements are there?**

*Answer 6:* The sensitivity requirements should be similar or better than the ones published in the Journal Clinical Virology 2014;61:260-4 by Kodani et al on this SBIR contract topic. There are no specific requirements on the duration of the assay, cost and sample size, but we would like to be able to run a large number of samples at a low cost because this assay is intended for use in resource poor countries. In addition, scalability is important, so that reagents are not wasted when only a few samples are run.

*National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP),*  
**Topic 045: Improved Antibody Preparation for Post-Exposure Prophylaxis Against Hepatitis A**

**Question 1: The topic number is listed as 045 on the web page, but 033 in the pdf of the Program Solicitation. Which number should be used in the application?**

*Answer 1:* The topic number is 045.

**Question 2: If the goal is to develop a neutralizing mAb for eventual use in humans, is clonal expression of HAV candidate antigens really a necessary deliverable? That sounds more like the deliverable for a vaccine.**

*Answer 2:* The ultimate goal of this project is to develop a neutralizing mAb for eventual use in humans as an alternative to the current IG preparations PEP against HAV infection and Hepatitis A. The production of neutralizing antibody from the candidate's antigens is not expected to occur in Phase I. The candidate antigens are not intended to be used for a vaccine.

**Question 3: The title and description are focused on antibody, but the activity section asked for antigen. Could you please clarify for us? Is antibody or antigen requested?**

*Answer 3:* Antigen is being requested in Phase I.

**Question 4: If a process to produce antibodies is already available can the proposal skip antigen production?**

*Answer 4:* No, the deliverables for Phase I only specify the production of antigens.

*National Center for Immunization and Respiratory Diseases (NCIRD),*  
**Topic 029: Thermostable Dry Vaccine Formulation for Microneedle Administration**

**Question: Do we need include animal efficacy study in the Phase I stage?**

*Answer:* No.