AMENDMENT TWO (2)

OFFICE OF ACQUISITONS
National Institute of Allergy and Infectious Diseases (NIAID)
5601 Fishers Lane, Room 3D35, MSC 9821
Rockville, MD 20852

Solicitation Number:	PHS2016-1
Date of Solicitation Issuance:	07/24/2015
Date of Amendment No.1 Issuance:	08/11/2015
Date of Amendment No.2 Issuance:	09/17/2015
Number of Pages:	13

NIAID Points of Contact:

Tiffany Chadwick, Contracting Officer
Email: tiffany.chadwick@nih.gov
Phone: 240-669-5171

George Kennedy, Contracting Officer
Email: kennedyg@mail.nih.gov
Phone: 240-669-5170

The hour and date specified for receipt of Offers remains unchanged.

Offerors must acknowledge receipt of the amendment by Amendment number(s) and date of the amendment. Include a statement of acknowledgement in your proposal submission. Failure of acknowledgement 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.

Note: A recording of the pre-proposal conference and associated materials have been posted on http://grants.nih.gov/grants/webinar_docs/webinar_20150813.htm.

PURPOSE OF SOLICITATION AMENDMENT

The purpose of this amendment is to provide revisions to Sections 7, 8, 10 & 12 of the subject solicitation and to respond to questions. Accordingly, Solicitation PHS 2016-1 is revised as follows:

Section 7.3 Limitation on the Length of the Technical Proposal (Item 1) is revised to add a requirement for page margins, as follows:

> All pages shall be single-sided, single-spaced pages for the entire proposal, all inclusive [including all pages, cover sheet(s), tables, CVs, resumes, references, pictures/graphics, and all enclosures, appendices or

attachments, etc.]. **Page margins must be at least one inch on all sides.** Proposal pages shall be numbered "Page 1 of 50," "Page 2 of 50," and so on. Pages shall be of standard size (8.5" X 11") with a font size of 11 points (or larger). Two sided pages count as two pages. There are NO exclusions to the page limit – the technical proposal shall not exceed 50 pages for Phase I, and 150 pages for Phase II. Pages in excess of the page limitation will be removed from the proposal and will not be considered or evaluated.

Section 8.15 Dual Use Research of Concern is added, as follows:

8.15 Dual Use Research of Concern

The offeror shall demonstrate compliance with the United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf) or "DURC" policy. If the offeror proposes using an agent or toxin subject to the DURC policy, the offeror shall provide in its technical proposal each of the following items:

a. Identification of the agents or toxins subject to the DURC policy.
   - The following agents or toxins are subject to the DURC policy:
     - Avian influenza virus (highly pathogenic)
     - *Bacillus anthracis*
     - Botulinum neurotoxin
     - *Burkholderia pseudomallei*
     - Ebola virus
     - Foot-and-mouth disease virus
     - *Francisella tularensis*
     - Marburg virus
     - Reconstructed 1918 influenza virus
     - Rinderpest virus
     - Toxin-producing strains of *Clostridium botulinum*
     - Variola major virus
     - Variola minor virus
     - *Yersinia pestis*

b. A description of the categories of experiments in which the identified agents or toxins produces or aims to produce or can be reasonably anticipated to produce one or more of the effects identified in Section 6 of the DURC policy.

c. For projects involving any of the agents listed in the DURC policy and that involve or are anticipated to involve any of the categories of experiments listed in the DURC policy, an indication of whether or not the project meets the definition of "dual use research of concern" in Section 4C of the policy.

d. For projects meeting the definition of "dual use research of concern," a draft risk mitigation plan.

e. Certification that the offeror is or will be in compliance with all aspects of the DURC policy prior to use of pertinent agents or toxins.

If the offeror does not propose using an agent or toxin subject to the DURC policy, the offeror shall make a statement to this effect in its technical proposal.

The Government shall not award a contract to an offeror who fails to certify compliance or whose draft risk mitigation plan is unsatisfactory to the Government. If selected for award, an approved risk mitigation plan shall be incorporated into the contract.

Section 10 CONTRACTING OFFICER POINTS OF CONTACT FOR QUESTIONS RELATED TO SPECIFIC TOPICS is revised to replace the Point of Contact for NIAAA and to correct a typo in the e-mail address for Mr. Charles Jackson, as follows:

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

Erin Goldstein, MBA, CPCM, CFCM
Acting Branch Chief
Contracts Management Branch, NIAAA
E-mail: egoldstein@nih.gov

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

Charles H. Jackson, Jr.
Contracting Officer
Office of Acquisitions, DEA
National Institute of Allergy and Infectious Diseases
National Institutes of Health, DHHS
Phone: (240) 669-5175
Email: Charles.Jackson@nih.gov

Section 12 Component Instructions and Technical Topic Descriptions,
National Cancer Institute (NCI), Topic 344 Technologies for Differential Isolation of Exosomes and Oncosomes is revised to correct the Phase II budget:

344 Technologies for Differential Isolation of Exosomes and Oncosomes

(Fast-Track proposals will not be accepted.)

(Direct to Phase II will not be accepted.)

Phase II budget and duration information is provided to assist Phase I offerors with their long-term strategic planning.

Number of anticipated awards: 2 – 3

Budget (total costs, per award): Phase I: up to $300,000 for up to 9 months
Phase II: **up to $2,000,000** for up to 2 years

PROPOSALS THAT EXCEED THE BUDGET OR PROJECT DURATION LISTED ABOVE MAY NOT BE FUNDED.

Section 12 Component Instructions and Technical Topic Descriptions,
National Institute of Allergy & Infectious Diseases (NIAID), Topic 036 Simple, Inexpensive Device to Purify DNA from Sputum for Tuberculosis Testing is revised modify the Phase I Activities description, as follows:

Phase I activities

- Development of a method for processing sputum to purify DNA for TB testing.
  a. **Sample processing time must be no more than 30 minutes.**
  b. DNA recovery must be at least 50% compared to a gold standard laboratory method and must allow detection of Mtb in sputum containing at least 5-20 CFU/ml using a standard molecular detection method.
  c. The CV for inter-operator variability must be no more than 20%.
  d. Processed specimens must be stable for at least 7 days at temperatures ranging from 5 to 50^0C.

- Initial evaluation of the product compared to DNA obtained using standard laboratory methods with at least one molecular TB test technology

GENERAL QUESTIONS

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

Question 1: If my organization has already accomplished some of the deliverables listed under a Topic, prior to receiving any funding, does this hurt our proposal's chances of getting funded under the Topic?

Answer 1: In general, the "Activities and Deliverables" descriptions under each Topic are written to accommodate projects at various stages of product development. It will not hurt an organization to be further along in that process. Provide the data for all Activities and Deliverables published under a Topic that you have already completed, and propose a new set of Activities and Deliverables that may advance the product to a stage beyond what was included in the solicitation. Proposed Activities and Deliverables must still be consistent with the allowed budget and duration listed for the Topic.

Question 2: For our other applications, there has been a technical point-of-contact who I've been able to discuss our approach with in order to assess whether he/she thinks our technology is a good fit. Is there a technical point-of-contact for this solicitation?

Answer 2: Solicitations for contract awards, such as this one, are conducted in a different manner than the grant application process, in part because different laws and regulations related to fairness in competition apply. For this contract solicitation, technical staff are not allowed to speak directly with interested organizations. Questions from interested organizations were accepted and are answered through this solicitation amendment. The solicitation and its amendments include all the information necessary to prepare and submit a proposal for funding consideration.

Question 3: Do we have to submit the application as formatted as form SF424? In the "proposal preparation and instruction", it did not specify certain forms or format need to be followed.

Answer 3: Please refer to Section 7, Proposal Submission, and Section 8, Proposal Preparation and Instructions, for information regarding the format and content of a proposal. Also refer to Section 13, Appendices, where forms to be used for proposal submission can be found.

Section 1 Introduction

Question 1: It is our understanding that the SBIR contract solicitation is issued once per year and the same research topics are not normally repeated the next year. If we are awarded a Phase I contract and complete the work next year, but the same research topic is not included in next year's SBIR solicitation, can we still apply for the Phase II next year?

Answer 1: As noted in Section 1 of the solicitation, "All firms that are awarded Phase I contracts originating from this solicitation will be eligible to participate in Phases II and III. 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."

Section 2.3 Fast Track Proposals

Question 1: What is the page limit for a Fast Track proposal?

Answer 1: A Fast Track proposal consists of a complete Phase I proposal and a complete Phase II proposal. Page limitations for the Technical Element (Item 1) for Phase I and Phase II proposals are set forth in Section 7.3 of the solicitation.

Section 3.2 Definitions (Relating to R&D)

Question 1: Regarding use of human subjects, is an Exemption allowed if samples will be purchased from a commercial company where the patients are not identified by name, but described in terms of age, gender, ethnic group, and pathological details of their malignancy? The instructions say that Human Subjects are defined as living individuals; does it make any difference, when samples will be purchased from a company, whether the donors are still living or deceased?

Answer 1: If the samples are publically available and are fully de-identified, such that they cannot be linked to specific individuals by the investigator either directly or indirectly through coding systems, then use of the samples would fall under an exemption and regulations pertaining to Research Involving Human Subjects would not apply.

Section 4.2 Offeror Eligibility and Performance Requirements

Question 1: Can we use subcontractors or consultants to do some of the research?

Answer 1: Yes, however please note the limitations on subcontracting and consulting set forth in Section 4.2. of the solicitation.

Question 2: Regarding the minimum percentages of research effort for Phase I and Phase II performed by the awardee (2/3rds in Phase I and 1/2 in Phase II), can we use the amount of contract funds distributed between the awardee (Direct + Indirect + G&A + Profit/Fixed Fee) compared against consultant and sub-contract amounts to determine this? Or is there another preferred method?

Answer 2: As set forth in Section 4.2 of the solicitation, "The percentage of work will be measured by total contracts costs." It is correct to combine all types of costs and to determine eligibility based on the overall dollar amount that will be paid out to all subcontractors, consultants, etc., versus the overall dollar amount to be retained by the awardee.

Question 3: Regarding use of contract funds for subcontractors and consultants: is there any requirement that such funds must be spent on domestic consultants, or could they be used for consultants in foreign countries? The group that reported the biomarkers we would like to use for our assay development is in a European country.

Answer 3: Section 4.2 of the solicitation states, "For both Phase I and Phase II, all research or research and development work must be performed by the SBC and its subcontractors in the United States." SBIR funds may only be used to pay United States subcontractors, consultants, etc. The Offeror may propose to cost-share any portion of its research, through its own or other non-SBIR resources, which would benefit from paid collaboration with non-U.S. entities.

Section 4.3 Multiple Principal Investigators

Question: Can we have co-PIs on a direct to Phase 2?

Answer: The solicitation allows for Multiple Principal Investigators. See Section 4.3 of the solicitation. Your proposal's Research Plan (a part of the Technical Element) must include a Multiple PD/PI Leadership Plan, as discussed in Section 8.8.

Section 4.14 Phase I Award Information &
Section 4.15 Phase II Award Information (For Fast Track and Direct to Phase II Proposals)

Question 1: What is a 'normal profit margin'?

Answer 1: A fixed amount of money may be included in an organization's pricing proposal for profit/fee to represent that element of the potential total remuneration that contractors may receive for contract performance over and above allowable costs.

See HHSAR 315.404-4 (d) for a description of Profit Analysis factors that are used to determine if the proposed amount of profit/fee is reasonable for the work to be performed, available at: http://www.hhs.gov/grants/contracts/contract-policies-regulations/hhsar/subpart315/index.html#315.404-4Profit.

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

Question 1: May I submit a proposal or application for the same research project under multiple solicitations?

Answer 1: You may submit the same or essentially equivalent proposal under a non-NIH/CDC solicitation to other agencies. You may not submit the same or essentially equivalent proposal to more than one active NIH/CDC solicitation.

Question 2: I applied for a Topic in a certain research area last year, however the reviewer misunderstood several parts of my application and turned me down. May I resubmit my application?

Answer 2: If you submitted a grant application last year that was not funded, and the grant cycle is complete, you may submit a proposal pertaining to the same research project under this contract solicitation. You may not submit a proposal for a research project that is pending funding consideration for an NIH/CDC grant funding announcement. Additionally, your proposal must fall within one of the Topics specifically set forth in this contract solicitation, and your proposal should be tailored to align with the Project Goals, Objectives, Activities & Deliverables set forth under the Topic of interest in this contract solicitation.

Section 4.21 Payment

Question 1: Regarding the payment of the award, do I understand correctly that Phase I contracts are paid upon completion of deliverables? Would this be done when ALL deliverables are completed (i.e. at the end of the phase I period) or each time that a single deliverable is completed?

Answer 1: Yes, contract award payments are tied to the completion of deliverables. A payment schedule may be discussed with the Contracting Officer handling the negotiation and award of your contract, from the appropriate Awarding Component, once an organization receives notification that it is being considered for award. Payment tied to several interim reports and/or deliverables, which are to be submitted as the performance period progresses, is often feasible.

Section 7.3 Limitation on the Length of the Technical Proposal (Item 1)

Question 1: Regarding the limitations on length of the Technical Proposal, does the 50 page limit include the Business Proposal? If not, what is the length limitation for the Business Proposal?

Answer 1: The page limitation only applies to the Technical Proposal (Item 1). The Business Proposal is not included in this page limitation. There is no page limitation on the Business Proposal. The Business Proposal consists only of Appendix C (the Pricing Proposal form), along with any supporting cost/price information (see Section 8.13 of the solicitation), as well as Proof of Registration in the

SBA Company Registry (see Section 4.16 of the solicitation), and VCOC Certification, if applicable (see Section 4.5 of the solicitation).

Section 8.8 Content of Technical Element (Item 1)

Question 1: The solicitation does not specify the format of biosketches to be used for the personnel (or even if there needs to be a biosketch, per se). Does the Senior/Key Personnel and Bibliography of Directly Related Work need to be written in the biosketch format typical of grant applications to the NIH? Will you be accepting the previous format used until May, 2015, or does it need to be in the new format that started in May (with Contributions to Science instead of a list of publications)?

Answer 1: A specific format is not required for the "Senior/Key Personnel and Bibliography of Directly Related Work" portion of the Phase I Research Plan, or the "Personnel" portion of the Phase II Research Plan. You may use the format of your choice. Keep in mind the overall page limitations for the entire Technical Element (Item 1).

Section 9 Summary of HHS Components Anticipated Number of Awards

Question 1: Regarding the anticipated award dates provided in the table in Section 9 of the solicitation: what would the award date be dependent on? A window from August 2016 to March 2017 is listed for National Cancer Institute awards, for instance.

Answer 1: Factors may include the dates of the peer review meetings, workload distribution, and funding availability.

Section 10 Contracting Officers and Addresses for Delivery of Contract Proposals

Question 1: My organization is interesting in submitting more than one SBIR proposal under this solicitation, from more than one Institute (Awarding Component). Should my organization provide a written notice of intent to each of the appropriate Contracting Officers – or should I choose the most likely target and only send a single written notice of intent?

Answer 1: Organizations are advised to provide a notice of intent to the Contracting Officer for each Awarding Component that is handling a Topic that the organization is interested in submitting a proposal for. Notices of intent are not required, but can be helpful in ensuring that your organization is notified of any changes to the status of the solicitation.

SPECIFIC TOPIC QUESTIONS

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

National Cancer Institute (NCI),
Topic 342: Validation of Mobile Technologies for Clinical Assessment, Monitoring and Intervention

Question 1: The same Topic was included in last year's SBIR solicitation (PHS 2015-1). Why is the Topic repeated in this year's SBIR solicitation (PHS 2016-1)?

Answer 1: The technical advisory group decided to reissue this Topic due to the importance of this area of technology and the potential for commercialization.

National Cancer Institute (NCI),
Topic 344: Technologies for Differential Isolation of Exosomes and Oncosomes

Question 1: If our organization had a method that could easily, quickly, and for low cost, separate Large Oncosomes from all exosomes (from tissue and tumor), would you be interested in that?

Answer 1: Yes, the research that you describe would be considered for award under this Topic.

Question 2: Would you consider a technology that uses centrifugation as a processing step?

Answer 2: Yes, the research that you describe would be considered for award under this Topic.

National Cancer Institute (NCI),
Topic 346: Molecularly Targeted Radiation Therapy For Cancer Treatment

Question 1: I am developing a new molecule and I am wondering if this molecule fits this topic?

Answer 1: Approaches to anti-cancer therapy that lack a radionuclide and do not involve a cancer-specific binding agent will not be considered for award under this Topic. Investigators are encouraged to consider submitting an SBIR grant application to the Omnibus SBIR Program announcement, for which any topic that is cancer-relevant is appropriate. The next two deadlines are September 5 and January 5. Here is a link to that funding opportunity: http://grants.nih.gov/grants/guide/pa-files/PA-15-269.html.

National Cancer Institute (NCI),
Topic 347: Signal Amplification to Enable Attomolar Quantitation in Slide-Based or ELISA Biomarker Immunoassays

Question 1: The description of Topic 347 discusses 3 specific technologies based on recently published work as methods for addressing the key technical goals of the proposal. Since it seems only 2-3 awards will be given, should I assume that my company's technology, which is different from those 3 technologies discussed, is better suited for an SBIR grant application?

Answer 1: Proposals involving technology different from the cited examples will still be considered for award. Make certain to align your proposal to the Project Goals and Objectives clearly laid out in the Topic description. Also, the research plan must show that you can meet the expected Activities and Deliverables. In addition, make sure to use the correct samples specifically asked for in the Topic description.

National Cancer Institute (NCI),
Topic 348: Identification and Capture of Enriched Tumor Zones with Preservation of Labile Biomarkers from Ultra-Cold Biopsies

Question 1: Does the proposed method need to bring an innovative optical/microscopic approach or would the above workflow satisfy the requirements of the solicitation?

Answer 1: A novel way to visualize and/or identify the tumor zones is a key component of the goal of this topic. Thus, technologies focused on removing tissue sections but not visualizing/identify tumors will not be considered for award.

Question 2: Does the system need to be stand-alone (all needed component packaged into a single instrument box) or what are the expectations for the "most common microscopic/microdissections systems" that it needs to work with?

Answer 2: It does not need to be a stand-alone system, and there is no strict list of systems it needs to work with, although these factors may be taken into account during the evaluation process.

Question 3: What is the best method to start the dialog with NCI about tissue procurement and arranging for a validation laboratory?

Answer 3: NCI can make recommendations regarding tissue procurement at the time of award; however, there is no commitment to provide tissues. NCI may be able to perform some validation, and those discussions would occur during negotiations or at the time of award.

Question 4: Our method would allow for thin tissue sections to be collected and individually stained for H&E and other biomarkers, and the data would be 3D registered and aligned to the tissue block. Is this within the scope? Or is the goal to determine an alternative to traditional imaging methods?

Answer 4: The degree that the technology enables visualization would be a key criterion of review as it is listed as the goal of the Topic. Without seeing all the technology details, it is hard to determine if the research that you describe adheres to the Topic's goal. Offerors must focus on the visualization component as well as the capture/dissection components.

National Cancer Institute (NCI),
Topic 353: Cell-Free Nucleic Acid-Based Assay Development for Cancer Diagnosis

Question 1: In the announcement it says: "Select one or a set of validated cfNA markers with samples of a choice (e.g., plasma, serum or/and urine) for detection of a cancer or subtype." Would an assay detecting several types of cancer be appropriate for this topic or should we specifically focus on one cancer type or a subtype?

Answer 1: The assay must specific to one type of cancer or a subtype. The technology that will be developed can be expanded to other types of cancer in the future.

Question 2: Could you please clarify whether the development of an automated method for isolation of cell-free DNA and RNA from plasma for use with any cancer target would be an appropriate proposal topic? Should we also include co-development of a specific detection assay, or is the solicitation intended to be solely for detection methods?

Answer 2: Proposals should focus on the assay development. It is acceptable to include the development of an automated method for isolation of cell-free DNA and RNA from plasma as a part of the assay development. However, the cfNA that will be isolated needs to be specific to certain/one type of cancer or subtype.

Question 3: Regarding the requirement to develop assays using validated cfDNA markers: if we select markers reported in the open scientific literature, how do we address intellectual property concerns?

Answer 3: Your proposal should address licensing or working out a path towards a license, if this is the case. Take care to address the status of a license and potential patentability in a way that enables evaluation under the Technical Evaluation Criterion regarding commercial application and commercialization, set forth in Sections 6.2 and 6.3 of the solicitation.

Question 4: Regarding the deliverable related to demonstrating a plan necessary to file regulatory application: our company is not a clinical lab and we don't have CLIA certification. We do however have strong record for developing and commercializing technology that is relevant to achieving the technical goals of the project. Given these circumstances, are we at a disadvantage

in having our proposal funded? Would it be reasonable for us to propose to collaborate with a clinical entity in Phase 2, to eventually obtain clinical approval of the assay we develop? If so, would we need to identify the clinical partner for the Phase 1 submission, and get letters of intent to work with us?

Answer 4: Generally, the proposal should discuss an available pathway forward towards a regulatory submission. Consider the Technical Evaluation Criterion set forth in Sections 6.2 and 6.3 of the solicitation when deciding what information and content to include in your proposal.

National Cancer Institute (NCI),
Topic 354: Companion Diagnostics for Cancer Immunotherapies

Question 1: If we just submit for Phase I, do we need to have a letter of support from a company or clinical institution that could provide clinical trials specimens or this is optional?

Answer 1: For Phase I, all Offerors must establish a collaboration or partnership with a diagnostic and/or pharmaceutical company and/or clinical/research institution that can provide relevant clinical trial specimens. For the Phase I proposal, providing a letter of support from the partnering organization is optional. For the Phase II proposal, providing a letter of support from the partnering organization is required.

Question 2: Regarding the Phase I Activities and Expected Deliverables, do all activities and deliverables listed have to be completed during Phase 1?

Answer 2: Yes.

Question 3: Is it required that the therapeutic for which the diagnostic is being developed as companion be in the clinic as a cancer drug? I ask this because my company has an immunotherapy drug being evaluated in the clinic for another indication but is being developed (not yet in the clinic) as a cancer therapy. There is strong *in vivo* indication that the drug will be effective against many cancer types and its safety has been demonstrated in the other indication.

Answer 3: The goal of Topic 354 is to develop companion diagnostics for immunotherapy regimens in clinical development for cancer indications. However, because the drug has entered clinical development for another (non-cancer) indication, this research would be considered for award under this Topic. The Offeror is strongly encouraged to highlight the *in vivo* data demonstrating the efficacy of the drug in pre-clinical cancer models.

National Institute of Allergy and Infectious Diseases (NIAID),
Topic 036: Simple, Inexpensive Device to Purify DNA from Sputum for Tuberculosis Testing

Question 1: Is the $10 price point intended to cover the cost per test or per device?

Answer 1: The indicated price goal of < $10 is intended per test.

Question 2: Will technologies with more than 3 user steps be accepted if it is easy to use?

Answer 2: The solicitation currently states under Phase I activities: "Sample processing time must be no more than 30 minutes with no more than 2-3 steps performed by the operator." It is now revised to read "Sample processing time must be no more than 30 minutes." We are deleting the requirement regarding the number of operator steps.

Question 3: Are there biosafety and/or disinfection requirements for processing the sample?

Answer 3: Organizations are advised to consult with TB clinicians regarding this matter and include information in the proposal on biosafety and/or disinfection steps deemed necessary to carry out the research.

Question 4: Does the molecular MTB test used for evaluation of the extraction performance need to include drug sensitivity?

Answer 4: The solicitation states "Initial evaluation of the product compared to DNA obtained using standard laboratory methods with at least one molecular TB test technology." Offerors should make choices regarding the TB test technology based on their knowledge of the field and proposal budget considerations.

National Institute of Allergy and Infectious Diseases (NIAID),
Topic 037: Telemonitoring for Infectious Diseases: A Remote System for Assessing Patient Parameters and Specimen Analysis

Question 1: We would like to better understand the priorities of your agency in connection to Topic 038 in terms of target antiviral compounds (or class) that might be most relevant in the clinics and in a global health context (e.g. delivery of products in developing countries)?

Answer 1: NIAID does not want to limit proposal research areas and would like to leave this up to the small business Offeror to propose. The Offeror may propose the development of oral formulations for any antimicrobial (or antiviral) compound(s) that meet the criteria of the Topic. The Offeror should provide adequate justification in its proposal for the antimicrobial (or antiviral) compounds chosen and should include appropriate infectious disease expertise to understand the current limitations and address the needs in this research area. Consider the Background and Project Goal for this Topic, as well as the Technical Evaluation Criteria set forth in Sections 6.2 and 6.3 of the solicitation.

National Institute of Allergy and Infectious Diseases (NIAID),
Topic 038: Innovative Oral Formulations for Anti-Infective Drugs

Question 1: What constitutes an infectious disease for this Topic? I see the solicitation gives an example of RSV disease, but are there any infectious diseases in particular the NIAID are seeking telehealth monitoring capabilities for?

Answer 1: NIAID does not want to limit proposal research areas and would like to leave this up to the small business Offeror to propose. The Offeror should provide adequate justification in its proposal for why its research is targeting a particular infectious disease in response to this Topic. Consider the Background and Project Goal for this Topic, as well as the Technical Evaluation Criteria set forth in Sections 6.2 and 6.3 of the solicitation.

National Institute of Allergy and Infectious Diseases (NIAID),
Topic 039: Vaccines against Pathogens with Small Market Potential

Question 1: Can you please expand on the list of targets of interest that might fall under this Topic and especially what would fall under "vaccines for selected high risk populations"? You list Coccidioidomycosis/San Joaquin Valley Fever (VF), and Lyme disease. A few more examples would help us delineate if our target of interest may fall under this small market category.

Answer 1: NIAID does not want to limit proposal research areas and would like to leave this up to the small business Offeror to propose. The Offeror may propose the development of any vaccine that falls within the scope of this topic. The Offeror should provide adequate justification in its proposal for how it has determined that the proposed vaccine candidate fits the Topic, regarding both small market potential and selected high risk populations. Consider the Background and Project Goal for this Topic, as well as the Technical Evaluation Criteria set forth in Sections 6.2 and 6.3 of the solicitation.

Question 2: Is this Topic limited to pathogens that are endemic to parts of the US?

Answer 2: No.

Question 3: It seems that the primary focus of this Topic is in small markets confined to the US. Is that an appropriate assessment?

Answer 3: The focus of this Topic is to develop vaccines against pathogens affecting a relatively small segment of the US population. The pathogen does not necessarily need to be confined to the US population.

Question 4: Would an application be considered for award if the pathogen target had a high chance of jumping into the US because of the proximity to the endemic area or because of the movement of workers from those endemic areas to the US?

Answer 4: Yes.

Question 5: Would an antibody-based approach, rather than active vaccine development, be considered for award under this Topic?

Answer 5: For Topic 039, NIAID is focusing on research areas of active vaccination that stimulate a robust host immune response. Passive immunization approaches are, however, of general interest to NIAID, and investigators interested in this type of research are encouraged to consider other SBIR funding opportunities, which can be found at https://sbir.nih.gov/funding.

National Center for Immunization and Respiratory Diseases (NCIRD),
Topic 013: Detecting Lower Intestinal Microbiome Disruption and Multidrug Resistant Organisms

Question 1: What is "clinically meaningful" sensitivity and specificity?

Answer 1: The assay should be designed to reliably detect MDRO colonization in human stool at an organism load that would detect all or most MDRO-colonized patients, or, if this is not possible, at least that subset of MDRO-colonized patients most likely to transmit to other patients. A sensitivity and specificity similar to current FDA-approved molecular assays for detection of bacterial pathogens in a stool matrix would be considered reliable detection at such an organism load. Higher sensitivities and specificities at a lower organism load are advantageous, especially if some measure of quantitation is also possible.

Question 2: What is a "clinically useful" turnaround time?

Answer 2: The assay should be developed with a turnaround time that is comparable to or shorter than current commonly used assays to detect MDRO-colonization. Thus, a turnaround time should be no longer than current commonly used culture methods for a given MDRO, with shorter turnaround times being advantageous.

National Center for Immunization and Respiratory Diseases (NCIRD),
Topic 032: Thermostable Dry Powder Live Attenuated Influenza Vaccine for Nasal Delivery

Question 1: Would investigational live flu vaccines be considered or does LAIV specifically mean FluMist or Leningrad cold-adapted vaccine?

Answer 1: Yes, investigational live attenuated flu vaccines would be considered for award under this Topic.

Question 2: Would liquid stable LAIV formulations that meet the potency and thermostability requirements be considered?

Answer 2: Yes, liquid stable LAIV formulations would be considered for award under this Topic.

Question 3: Would CDC consider a proposal under Topic 032 for a Thermostable Dry Powder Recombinant Influenza Vaccine for Nasal Delivery?

Answer 3: Only proposals using Live Attenuated Influenza Vaccine will be considered for award under this Topic; recombinant protein vaccines will not be considered for award.