AMENDMENT THREE (3)

OFFICE OF ACQUISITIONS
National Institute of Allergy and Infectious Diseases (NIAID)
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Division of Allergy, Immunology, and Transplantation (DAIT)

Research Area 001: Adjuvant Development Program
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Research Area 002: Development of Radiation/Nuclear Medical Countermeasures;
Research Area 003: Development of Radiation/Nuclear Predictive Biomarkers and Biodosimetric Devices
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Division of Microbiology and Infectious Diseases (DMID)

Research Area 004: Development of Broad Spectrum Therapeutic Products for Biodefense, Anti-microbial
Resistant Infections and Emerging Infectious Diseases;
Research Area 005: Advanced Development of Vaccine Candidates for Biodefense and Emerging
Infectious Diseases
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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.

PURPOSE OF SOLICITATION AMENDMENT

The purpose of this amendment is to provide responses to questions received regarding the solicitation. The responses are offered for information only and do not modify or become part of this solicitation. Additional amendments may be provided as needed to address further questions and their related responses. All potential offerors are advised to refer back to all previous amendments for additional questions and clarification.

SPECIFIC RESEARCH AREA QUESTIONS

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

Division of Allergy, Immunology, and Transplantation (DAIT)
Research Area 001: Adjuvant Development Program

Question 1: Will this Research Area support the following IND-enabling activities?

- Determining whether the addition of the adjuvant to commercially available vaccines augments the serologic response sufficiently to reduce the vaccine dose and number of immunizations required.
- Determining whether the addition of our adjuvant results a change in the type of immune response induced.
- Manufacture of cGMP grade adjuvant and adjuvant:vaccine.
- Formal pharmacology and toxicology and stability analysis.

Answer 1:
- This Research Area will support the conduct of Preclinical IND-enabling studies of novel vaccine:adjuvant combinations. The use of already licensed vaccines is acceptable, but the offeror is required to provide documentation that the offeror has IP protection and/or proprietary freedom to develop the adjuvant:vaccine (see “Project Management”, paragraph 8).
- This Research Area “supports the development of more effective vaccines to replace or supplement those with suboptimal efficacy”. Optimization of a vaccine may include strategies that reduce the dose and/or number of immunizations as well as the modulation of immune responses to induce responses associated with protective immunity.
- cGMP manufacturing of adjuvant or adjuvant:vaccine is an IND-enabling activity and, therefore, supported by this Research Area (see “Technical Objectives”)

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• Toxicology and pharmacokinetics/absorption studies are IND-enabling activities and, therefore, supported by this Research Area (see “Technical Objectives”)

**Question 2:** I gather responses should be for 2-5 years and up to $2,000,000 per year. Is that correct?

**Answer 2:** The solicitation states: "This initiative supports the development of adjuvants through immunological characterization studies and compound optimization, up to and including IND-enabling studies, for a period not to exceed 5 (five) years." Therefore, 5 years is the maximum period of performance. "The NIAID estimates that the average annual total cost (direct and indirect costs combined) is approximately $2.0M per award." Again, this amount is only an estimate.

**Question 3:** If an IND submission can be accomplished in less than 5 years, would this Research Area support a Phase I clinical trial?

**Answer 3:** The solicitation “supports the development of adjuvants through immunological characterization studies and compound optimization, up to and including IND-enabling studies, for a period not to exceed 5 (five) years”, but will “not provide funds to support the design and conduct of clinical trials” (see “Technical Approach”).

Please also see, “Provide a summary of the Product Development Plan for the adjuvant selected for further development, outlining its intended use and specifications, approaches for carrying out each stage of the overall product development pathway, and clearly defined milestones and timelines necessary to complete and deliver an adjuvant suitable for future clinical studies within the 5-year contract performance period.”

**Question 4:** Can a non-US organization as prime investigator come into consideration for funding in this call?

**Answer 4:** Yes, non-US organization may apply as long as they are not one of the prohibited sources identified in FAR 25.7. [https://www.acquisition.gov/sites/default/files/current/far/html/Subpart%2025_7.html](https://www.acquisition.gov/sites/default/files/current/far/html/Subpart%2025_7.html)

**Question 5:** Can an NIH investigator be part of an application?

**Answer 5:** NIH investigators may be a part of the application as long the NIH Policy on Cooperative Research and Development Agreements (CRADAs) is followed. Information regarding this policy can be found here: [https://www.ott.nih.gov/cradas](https://www.ott.nih.gov/cradas)

**Question 6:** May the statement of work include development of the antigen?

**Answer 6:** The contract will not support the development and/or optimization of a pathogen-specific vaccine component, but will support the production of vaccine to be used for the conduct of the contract project including pilot lot or cGMP manufacturing.

**Question 7:** I saw that a proposal intent response form is required but I could not find the submission date of this form.

**Answer 7:** There is no due date for the proposal intent response form, yet. You may submit this form at your earliest convenience.

**Question 8:** Would it be acceptable for us to submit two applications? We have two different adjuvant combinations that we believe would be responsive and according to the recent Amendment Two (2), we could not combine them into one application.
**Answer 8:** Yes, offerors are always allowed to submit more than one application. First, you must upload your technical/business proposal. Then, click on “alternate proposal” and upload that one with a different proposal name.

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**Division of Allergy, Immunology, and Transplantation (DAIT)**

**Research Area 002: Development of Radiation/Nuclear Medical Countermeasures**

**Question 1:** Is there an allowable way to exceed $2 Million USD? In the second amendment - it states that for Research Area 002: Development of Radiation/Nuclear Medical Countermeasures "NIAID anticipates up to 2 awards to be issued as a result of the solicitation, for up to $2 million across all contracts, on an annual basis; a total of $6M for a 3-year period across all awards. The $2M includes direct and indirect costs of all contracts issued under Research Area 2." If two awards are given, with a spend of $2M/year, over three years - this would be $3M per award over three years. Can you confirm/clarify this?

**Answer 1:** The total budget for up to 2 awards for the 3-year period is $6M. The total cost for each award(s) may vary depending upon the scope of the proposed project and the technical objectives of the award(s).

**Question 2:** What are “key biological or chemical resources”?

Per page 71 of the solicitation, “…. Key biological and/or chemical resources may or may not be generated with NIH funds”.

**Answer 2:** “Key biological or chemical resources” is interpreted as anything having to do with your IPW5371 drug and the vehicle.

**Question 3:** Is it allowable for funds from this contract to be used for the synthesis of study drug, IPW-5371?

**Answer 3:** Yes. Please refer to page 18 of the solicitation, item 2. Manufacturing. The contract will provide funds to support the following activities:

2. Manufacturing, including:

   a. Formulation development, stability, and production scale-up.

   b. Physicochemical and bioanalytical methods development.

   c. Current Good Manufacturing Practice (cGMP) Manufacturing development and scale-up support.

   d. Stability studies.

   e. Manufacture of pilot lots of candidate product in amounts sufficient to carry out proposed non-clinical research.

**Question 4:** Page 76 of solicitation – with reference to “…to the Base and each Option proposed…” What are Base? And Option?

**Answer 4:** The award will be funded only the Base period (year 1) at the time of award with options for two additional one-year periods. According to FAR 52.217-9, the Government may extend the term of the contract by written notice to the contractor.
Question 5: Are modifications to the proposal after submission allowable? Can budget details be added?

Answer 5: The Government may enter into negotiations with an Offeror whose proposal is found Technically Acceptable, at which time the offeror will be provided an opportunity to submit a revised proposal (technical and cost) in response to the government’s technical and business questions. During the negotiation offeror will be asked to make adjustment(s) to the initial proposed cost that may result from their responses to the technical and cost questions.

Question 6: We are working on the Business Proposal for BAA # HHS-NIH-NIAID-BAA2017-1. We are of course following all uniform cost assumptions for Research Area 002; however, I was wondering if the budget and cost data for the Travel uniform cost assumptions need to be included in 'SECTION 3 - UNIFORM COST ASSUMPTIONS' in the business proposal or if it can be included in 'SECTION 2 - COST OR PRICE SUPPORT' with the other cost data.

Besides a statement that we are following all Uniform Cost Assumptions for Research Area 002, what other information needs to be included in Section 3 of the business proposal?

Answer 6: The budget and cost data for the travel uniform cost assumptions should be included in Section 3 – Uniform Cost Assumptions.

Please refer to page 24 of the solicitation, item 5. Uniform Cost Assumptions and pages 76-80 of the solicitation, Section C. Business Proposal Instructions, and follow the instructions to prepare your proposal accordingly.

Division of Allergy, Immunology, and Transplantation (DAIT)
Research Area 003: Development of Radiation/Nuclear Predictive Biomarkers and Biodosimetric Devices

Question 1: NIAID anticipates that one or two awards may be issued for a total of up to $2 million for the non-severable base work across all contracts (direct and indirect costs combined), depending on the number of technically meritorious proposals, importance to agency programs, and availability of funds. The total cost for each award(s) may vary depending upon the scope of the project and the technical objectives of the award(s).

How much would you recommend?

Answer 1: According to the solicitation, NIAID anticipated to award up to 2 contracts for a total cost of up to $2 million per year across all contracts (direct and indirect costs combined). The total cost for each award(s) may vary depending upon the scope of the proposed project and the technical objectives of the award(s).

NIAID does not make recommendation as to how much a proposed budget should be. The proposed budget must be reasonable and corresponding to the proposed scope of the project and/or study.

Division of Microbiology and Infectious Diseases (DMID),
Research Area 004: Development of Broad Spectrum Therapeutic Products for Biodefense, Anti-Microbial Resistant Infections and Emerging Infectious Diseases

Question 1: The solicitation states that "...a biological product...intended for use in the...treatment of two or more bacterial or viral pathogens...", and that the candidate product must display activity against the pathogens listed on the 2013 CDC Antibiotic Resistance Threats list and on page 27. Would a bacteriophage cocktail that infects two species on the required lists be considered
responsive? Bacteriophages are viruses that target and kill specific bacteria while not harming the beneficial bacteria, such as the gut flora, in the host.

**Answer 1:** This Research Area does not specify therapeutic bacteriophages as agents that are NOT supported, as listed on page 30; a bacteriophage product is a biological product under FDA regulation, and will be responsive to this BAA if it satisfies the definition of a broad-spectrum candidate for antibacterial or antiviral therapeutics provided on page 29 of the solicitation, Research Area 004, Technical Approach, as follows: a single agent that meets all of the following criteria:

a. A drug (synthetic or natural product) or a biological product (e.g. monoclonal antibodies, recombinant proteins) intended for use in the cure, mitigation, or treatment of two or more bacterial or viral pathogens;

b. An agent with demonstrated in vivo activity in an appropriate therapeutic model of disease; and

c. An agent that will complete evaluation in a Phase 1 clinical trial within the 5-year proposed period of performance. Phase 1 clinical trial completion is defined as completion of a Final Clinical Study Report following International Conference on Harmonization (ICH) Guidelines on Structure and Content of Clinical Study Reports E3.

**Question 2:** The solicitation states that the candidate product must display activity against the pathogens listed on the 2013 CDC Antibiotic Resistance Threats list and the list of bacterial pathogens on page 27. Would a therapeutic that affects only two bacterial pathogens listed on the required lists (one from each) be considered broad-spectrum under this announcement?

**Answer 2:** Page 29 of the solicitation, Research Area 004, Section 1. Antibacterial Broad-spectrum Therapeutics, states that candidate antibacterial therapeutic products must meet all of the criteria identified. Thus, a candidate therapeutic that displays activity against one or more of the bacterial threats listed in the 2013 CDC Antibiotic Resistance Threats report, must also display activity against the effects of one of the identified bacterial pathogens in Section 1.b. to be considered responsive.

**Question 3:** Does the efficacy of an anti-CHIKV antibody to neutralize multiple strains of CHIKV satisfy criterion (Section 2a.), or would we need to include in the BAA proposal data establishing cross-neutralization of at least one other Alphavirus?

**Answer 3:** For the purpose of this Research Area, the candidate broad-spectrum therapeutic antiviral shall have activity against more than one virus family or have activity against two or more virus species from the same virus family, within the different virus families listed in Sections 2a and 2b on page 29.

**Question 4:** Requirement as listed in the BAA: ‘Display activity against infection caused by two or more viruses from the following families: Flaviviruses (esp. Zika and Dengue virus)’. (Page 29)

Would a compound series showing activity against Dengue and activity against other Flaviviruses (including Zika) meet the criteria? Is it necessary to exhibit activity against other non-Flavivirus families e.g. activity against Coronaviruses or Filoviruses?

**Answer 4:** For the purpose of this BAA, the candidate broad-spectrum therapeutic antiviral shall have activity against more than one virus family or have activity against two or more virus species from the same virus family or within the different virus families listed in Sections 2a and 2b on page 29. Therefore, having antiviral activities against more than two virus from the Flavivirus family meets the definition of broad spectrum.
Question 5: Requirement as listed in the BAA: ‘Therapeutic activity is defined as the cure or mitigation of disease once signs and symptoms of infection are evident’. (Page 28)

For infections with a limited therapeutic window for small molecules against flaviviruses, such as Dengue, would a feasibility study examining prophylactic approaches meet with the criteria outlined in the BAA?

If developing the prophylactic approach while in parallel assessing the feasibility of the therapeutic approach, would it be possible to submit a proposal that addresses both approaches, or will only therapeutic approaches be considered?

Answer 5: The BAA does not limit the intended use of the drug to treatment. As stated on page 28, “The objective of Research Area 004 is the development of broad-spectrum therapeutic products for use in post-event settings following the intentional release of a NIAID Category A, B, or C Priority Pathogen, or in response to naturally-occurring outbreaks of infectious diseases caused by these pathogens or Zika virus”. Further, this BAA will support a drug candidate as long as it is “intended for use in the cure, mitigation, or treatment of two or more bacterial or viral pathogens”, as stated on page 29.

Question 6: As Dengue is still a major unmet medical need, is it considered to be in scope of the BAA, work to support the development of a first in class compound?

Answer 6: Dengue is listed as one of the viral pathogens on Section 2a and 2b, on page 29, Technical Approach that are supported under this Research Area.

Division of Microbiology and Infectious Diseases (DMID), Research Area 005: Advanced Development of Vaccine Candidates for Biodefense and Emerging Infectious Diseases

Question 1: Regarding research area 005 of the BAA HHS-NIH-NIAID-BAA2017-1, would development of an intranasal adjuvanted vaccine against Entamoeba histolytica be considered responsive? In particular, would an intranasal adjuvanted vaccine be considered relevant to technical objective #3: Enhanced Vaccine Performance (strategies for ease and simplicity of delivery etc.)?

Answer 1: As stated on page 31, ‘Technical Objectives’, of the solicitation, only proposed candidate products aimed at a NIAID Category A, B, or C Priority Pathogen, or in response to naturally-occurring outbreaks of infectious diseases caused by these pathogens or Zika virus, are eligible. In order to be considered responsive, a proposal must also meet the description for one or more of the categories identified on pages 31 and 32 under ‘Technical Approach’: (1. Vaccines Against Antimicrobial Resistance Threats; 2. Technology Gaps that Slow Progression to Clinical Testing; 3. Enhanced Vaccine Performance; 4. Novel Vaccine “Plug-and-Play” Technologies); as well as satisfy the ‘Additional Requirements’ identified on page 32 of the solicitation.

Question 2: The BAA states that animal protection data is a minimal requirement. Would a technology having protection data for pandemic-like candidates (H5, H7), but not the seasonal flu vaccine, be eligible?

Answer 2: Page 32 of the solicitation, Research Area 005, ‘Additional Requirements’, states that lead candidates must possess all of the following characteristics: -Demonstrated feasibility of manufacturing, -In vitro and in vivo evidence of efficacy, and -Sufficient characterization to allow the development of a draft target product profile.
Page 32 of the solicitation further states that contracts awarded under this Research Area will not support development of candidates/products that have not demonstrated vaccine efficacy in a relevant animal model of disease.

**Question 3:** For manufacturing capability, does the offeror need to have its own GMP manufacturing facility? Will a consortium with a contracting manufacturing organization (CMO) meet this requirement?

**Answer 3:** Proposals will be evaluated by a peer review group in accordance with the criteria stated in Solicitation Section V, Evaluation Factors for Award. Please refer to the solicitation, and use your professional judgement in preparing a proposal, considering the best balance of risk and likelihood of success to achieve proposal and BAA objectives.

**Question 4:** Would NIH consider establishing IAA for an FDA portion of a budget if a contract is awarded?

**Answer 4:** In the event a proposal includes costs for a Government entity, the decision to use an IAA would be dictated by the specific authority under which appropriated funds are transferred between Government Agencies, and the specific funding authority granted to the entity in question.

**Question 5:** For a proposal focused against a Group 2 influenza vaccine to protect against multiple subtypes influenza subtypes using a live-attenuated influenza vaccine (LAIV) prime followed by inactivated influenza vaccine (IIV) with adjuvant boost be responsive?

**Answer 5:** Influenza is a NIAID priority pathogen, as required on page 31, ‘Technical Objectives’, of the solicitation. In order to be considered responsive, a proposal must also meet the description for one or more of the categories identified on pages 31 and 32 under ‘Technical Approach’: (1. Vaccines Against Antimicrobial Resistance Threats; 2. Technology Gaps that Slow Progression to Clinical Testing; 3. Enhanced Vaccine Performance; 4. Novel Vaccine “Plug-and-Play” Technologies); as well as satisfy the ‘Additional Requirements’ identified on page 32 of the solicitation.

**Question 6:** Would development of combined oral Shigella and ETEC vaccine candidates with a novel protein adjuvant be considered responsive?

**Answer 6:** Shigella is a NIAID priority pathogen, as required on page 31, ‘Technical Objectives’, of the solicitation. In order to be considered responsive, a proposal must also meet the description for one or more of the categories identified on pages 31 and 32 under ‘Technical Approach’: (1. Vaccines Against Antimicrobial Resistance Threats; 2. Technology Gaps that Slow Progression to Clinical Testing; 3. Enhanced Vaccine Performance; 4. Novel Vaccine “Plug-and-Play” Technologies); as well as satisfy the ‘Additional Requirements’ identified on page 32 of the solicitation.

**Question 7:** Please confirm that NIAID is seeking proposals that address a minimum of one (and not ALL) of the following four subtopic areas:

i. Vaccines against antimicrobial resistant threats
ii. Technology gaps that slow progression to clinical testing
iii. Enhanced vaccine performance
iv. Novel vaccine plug-and-play technologies

**Answer 7:** Yes, this is correct.

**Question 8:** The “Additional Requirements” Section on page 32 of this BAA Research Area states that proposals should feature a lead vaccine candidate and proceeds to define “lead candidate.” Does
this requirement apply only to sub-area #1 on page 33? Are there similar requirements for the maturity level required for sub-areas #2-4 (technologies to accelerate development, approaches to optimizing performance, plug-and-play platforms, respectively)? If so, can you provide that guidance?

Answer 8: Research Area 005 is for advanced vaccine development. The ‘Additional Requirements’ section described on page 32 applies to all sub areas of the Research Area.

Question 9: Can you please advise if the types of activities NOT supported by this topic area (pages 32 and 33) also may be better described with reference to each of the subtopics. (e.g., it seems demonstrating the utility of a plug-and-play platform [subtopic 4] may require expanding the platform to include antigens for protection in a new disease not previously demonstrated in a relevant animal model of disease).

Answer 9: The primary objective of a proposal must satisfy the requirements set forth for this Research Area on pages 31-32 of the solicitation. Proposals with an objective identified under the section “Contract awarded under this Research Area will NOT support:” are not considered responsive.