RFP-NIH-NIAID-DMID-07-05
Amendment 4 (Questions and Answers, 1st Posting)

This Amendment provides questions submitted by potential offerors and the responses provided by the NIAID. The responses are offered for information only and do not modify or become part of this solicitation. This Amendment will be updated as necessary to add any further questions and their related responses.

"DEVELOPMENT OF A THIRD GENERATION ANTHRAX VACCINE"

Amendment Issue Date:	August 15, 2006 (Questions 1 - 29)
Proposal Due Date/Time: (UNCHANGED)	September 18, 2006 at 4:00 PM Local Time
Issued By: (UNCHANGED)	Ross Kelley Contracting Officer OA/DEA/NIAID/NIH/DHHS 6700-B Rockledge Drive, Room 3214, Bethesda, Maryland 20892-7612 RKelley@niaid.nih.gov
Point of Contact: (UNCHANGED)	Ross Kelley Contracting Officer RKelley@niaid.nih.gov

Offerors must acknowledge receipt of this Amendment 4 (Questions and Answers, 1st Posting), on each copy of the proposal submitted. Failure to receive your acknowledgment of this Amendment may result in the rejection of your proposal.

The hour and date specified for receipt of proposals HAS NOT been extended.

THE FOLLOWING PAGES PROVIDE ANSWERS CONCERNING INQUIRIES WE RECEIVED FOR THE ABOVE-NUMBERED SOLICITATION:

Question 1:

Is it required that the final delivery device be used for vaccination during the proposed Phase 1 dose-escalation and Phase 2a schedule optimization trials or would conventional needle and syringe dosing suffice?

Answer 1:

If a device is proposed, the Offeror must satisfy the Mandatory Criteria for a device. The development path for the vaccine, and in this case including a device, should be described in the proposal and will be evaluated by a review panel.

Question 2:

Is the ability to be given post exposure an absolute requirement?

Answer 2:

To submit a proposal an Offeror must satisfy the Mandatory Criteria. An external review panel will evaluate accepted proposals for responsiveness to the RFP objectives using the evaluation criteria.

Question 3:

Would a Drug Master File submitted with CBER suffice to meet the requirements for an IDE exemption?

Answer 3:

There is no exemption or exception to the Mandatory Qualification Criteria. An Offeror must meet the criteria as specified in the RFP at the time of proposal submission.

Question 4**:**

Similarly we are unclear about the level of detail required in the cost proposal for activities such as the clinical trial option where a protocol is not yet required to be submitted but the budget would necessarily depend on the final trial design.

Answer 4:

We believe there is sufficient information in the solicitation to prepare a cost proposal. Please keep in mind the solicitation is for the award of a Cost-Reimbursement contract and will be based on estimated cost.

Question 5:

Does the rPA used in the efficacy study need to be rPA manufactured with the final process for the first clinical lot?

Answer 5:

The candidate vaccine must have been tested in an anthrax spore challenge model. The candidate vaccine includes all vaccine components in the combined final drug product (FDP) form proposed to be produced and tested in the proposal. An rPA component should therefore be from the same source as intended to be taken forward in an Offeror's proposal.

Question 6:

Please can you clarify what constitutes "filed"?

Answer 6:

Filed means that the appropriate documentation has been submitted to the FDA and the FDA has provided comments.

Question 7:

Is there a total amount budgeted for the RFP award?

Answer 7:

There is a Government Cost Estimate but I could not share this information with you.

Question 8:

Is there an estimated # of awards to be granted for the base years? Option years?

Answer 8:

There is no specific number of awards estimated at this time. That is other than there will be multiple awards.

Question 9:

Will 07-05 likely be a recurring solicitation?

Answer 9:

Sorry but at this time I do not have any information concerning future solicitations.

Question 10:

Do FTE estimates include subcontractor and consultant costs?

Answer 10:

The FTE estimate is for the entire project. But - please be advised that the estimate of FTE's is the Governments Estimate and it is provided as guidance. It is not a requirement.

Question 11:

Are there any requirements / preferences for the animal efficacy model used to establish “proof-of-concept efficacy” for the “vaccine candidate”? Species of animal (mouse, rabbit, etc) Route of challenge (aerosol, dermal, oral, etc.) Challenge strain (e.g. Ames, Stern)

Answer 11:

Any mammalian species is acceptable for the "proof-of-concept" studies.

No route of challenge has been specified for the "proof-of-concept" studies (so it is up to the offeror). (Alternative routes suggested to be used in a proposal, if different than the "proof-of-concept study(s), would be evaluated by reviewers; but would not prevent submission of a proposal).

Challenge strain has also not been specified in the MQC since only certain strains will work in a mouse model, strain use justification should be provided with the 'proof-of-concept' study data.

Question: 12
Will the candidate vaccine(s) containing native PA as opposed to recombinant PA be considered for funding?

Answer: 12
The MQC requires a "PA component", there is no specification for source of the PA component.

Question 13:
Does “vaccine candidate” and demonstrated efficacy of vaccine candidate against spore challenge refer **only** to the active vaccine ingredients / components (i.e. antigen – PA and any adjuvant(s) / immunomodulators) as delivered by the proposed route of administration or does the efficacy of vaccine candidate need to have been demonstrated in animals using proposed delivery device?

Answer 13:

The candidate vaccine is all the vaccine components that the Offeror is proposing to take forward in the RFP proposal. It is not required that a novel device be used in the "proof-of-concept" study. (Please refer to Amendment 1 regarding device criteria.)

Question 14:

Could you confirm our understanding of 'vaccine candidate'? Is this the entirety of the new drug product? For example, if the drug product had improved stability, improved efficacy and was delivered using a needle-free device the whole would be considered as the 'vaccine candidate'.

Answer 14:

As indicated in the RFP, contract funds may be spent on formulating the candidate to a device, if one is proposed. The candidate vaccine may not yet have been used with a novel device and therefore not a part of the definition of the candidate vaccine. All other components that are intended to be in the final vaccine product to be developed under this RFP define the proposed candidate vaccine. Improved stability, improved efficacy, and a final presentation that would be amenable to mass inoculation are all objectives of the RFP, not MQC. Data included in a proposal to support the objectives are a part of the Evaluation Criteria.

Question 15:

Could you confirm that to be compliant, and using the above example, proof-of-concept data would have to be provided whereby the vaccine with improved stability and efficacy had been delivered using the needle-free delivery device in the animal model? That is the complete construct would have to be shown to be efficacious.

Answer 15:

See response to above regarding a proposed vaccine candidate.

Question 16:

Consider a vaccine candidate that has improved efficacy and stability. Would a proposal for this vaccine candidate be compliant if proof-of-concept was provided separately for each improvement? That is, the improvements have been shown to be efficacious in isolation but not in combination.

Answer 16:

See response to the first question regarding what comprises a vaccine candidate relative to what are objectives of the RFP. The proposed candidate vaccine must have proof-of-concept anthrax spore challenge efficacy data in an animal model.

Question 17:

Does Clause 5, 'Alternate Proposals', on page 38 of the RFP mean that we could submit more than one proposal? For example, one that addresses stabilty and a second that addresses efficacy?

Answer 17:

The answer to your question is yes. But please keep in mind that an Alternate Proposals is just a proposal for an alternative way to complete the entire Statement of Work.

Question 19:

On the FTE question, are the projected FTE's a guideline or a "hard" ceiling?

Answer 19:

They are only a guide.

Question 20:

I suppose my question 2 below depends on the definition of "vaccine candidate." If we define vaccine candidate as a topical patch vaccine containing PA, then we have 2 published studies, with 2 different sources of PA, demonstrating protective efficacy in an animal challenge model. But for business reasons, we may use a 3rd source of PA for our proposal, for which there is no animal efficacy studies. We would contend that our vaccine candidate has already been shown efficacious in the animal model with two different sources of PA, and therefore meets the mandatory criteria, even if we use a 3rd PA in the proposal. Would this be NIAID's interpretation?

Answer 20:

The candidate vaccine must have been tested in an anthrax spore challenge model. The candidate vaccine includes all vaccine components in the combined final drug product (FDP) form proposed to be produced and tested in the proposal. An rPA component should therefore be from the same source as intended to be taken forward in an Offeror's proposal.

Question 21:

Will there be a public proposers' conference where such questions might be asked and answered?

Answer 21:

There are no plans for a conference.

Question 22:

In the RFP it states that it is required to include "Data and results from a proof-of-concept study of the vaccine candidate in an anthrax spore challenge model which has demonstrated vaccine efficacy." Does this mean that efficacy data in models other than rabbit and NHP (i.e. mouse spore challenge model) will be accepted, or will only rabbit data be accepted. (Of course in the proposed studies, as required, immunogenicity and efficacy trials will be performed in the rabbit (and NHP) model).

Answer 22:

The proof of concept anthrax spore challenge proof-of-concept model can be in any species including mice.

Question 23:

Does this Amendment intentionally specify biological products? Would a device that is in clinical testing or FDA licensed for a chemical or pharmaceutical product qualify? I believe the intent of MQC (b) is to show that the device is at least at the clinical-use development stage thus it would seem any device, as part of an IND or FDA licensed, would qualify.

Answer 23:

Biological in this context refers to any therapeutic product. You are correct - the intent of MQC (b) is to show that the device is at least at the clinical-use development stage.

Question 24:
Regarding the "Estimate of Effort" on page 35 please can you confirm that the expected FTE numbers in the proposal only apply to the prime contractor?

Answer 24:
The estimate of effort is for the entire project. Please keep in mind this is the Governments estimate and is included for guidance purposes and is not a requirement.

Question 25:

Please can we confirm that the Milestone 2 requirement (Attachment 4 page 3) "Stability Data Reports - Submit Monthly Stability Data Reports..." requires us to update you on the stability programmed monthly through the monthly reporting process. We are assuming that there is no requirement to produce additional data on monthly time points outside our proposed stability plan which will include periodic measurements of stability/potency on schedules used previously e.g. 0,1,3,6,9,12, 18, 24 etc. etc. months.

Answer 25:

The Offeror should propose a stability plan in the proposal. The appropriateness of time points, assays, etc. will be evaluated by a review panel.

Question 26:

Please can you clarify what is meant by "a model organism"? This is in Section 7D (Which is effectively Section 8D as it is the second Section 7) which is at Attachment 6 page 10 "Sharing of Model Organisms for Biomedical Research"

Answer 26:

A "model organism" is defined as follows: Animal, plant, or other organism used to study basic biologic processes to provide insight into the workings of other organisms.

Question 27:

Clarification of Clinical Trials requirements i) For the clinical trials, there is no explicit requests for GUP and PEP trials. Does this mean that it would be equally compliant with the
RFP to run either separate GUP and PEP trials, or a combined GUP/PEP trial? This obviously means that we would have to ensure that both indications are addressed in our proposed trial?

Answer 27:

The Offeror should propose a clinical trial plan that they feel is most appropriate for their vaccine candidate and its intended use.

Question 28:

ii) The statement under option 1 (Attachment 4 Page 14) says that the contract will consist of paragraphs 1 through 7 of the Statement of Work, unless option 1 is exercised. Are we correct in taking that to mean the numbered sections on page 2 - 13 of attachment 4 (ie 1. Product development milestones, 2. Manufacturing and non-clinical biocontainment facilities, safety and training, 3. Animal care and use, 4.... etc) ?

Answer 28:

If Option 1 is exercised then the Statement of Work will include items 1-7 and item number 8. If Option 2 is exercised then the Statement of Work will include items 1-8 and item number 9.

Question 29:
How can I obtain information about this (the rabbit PEP) model as well as the monkey PEP model?

Answer: 29

Regarding a rabbit post-exposure prophylaxis (PEP) model:

'Rabbits may be intolerant to certain antibiotics, and therefore may be of limited use to study post-exposure prophylaxis. The IASG has developed a PEP model in the rabbit using Levofloxacin as the antibiotic. This model has been successfully applied to demonstrate added benefit of anthrax vaccine when given in conjunction with antibiotics. The PEP rabbit model uses groups that, following spore challenge, receive a single dose of Levofloxacin for 7 days and either with or without 2 vaccine doses. Several dilutions of vaccine which resulted in a range of increased survival.'

And

Regarding non-human primate PEP model development:

Currently, NHP model development is in progress.