

**AMENDMENT OF NIAID SOLICITATION No.  
BAA-NIAID-DAIDS-NIHAI2008027  
“Rapid HIV Point-of-Care Diagnostic Device for Resource-Limited Settings”**

**Solicitation Number:** BAA-NIAID-DAIDS-NIHAI2008027

**Amendment Number:** One (1)

**Amendment Issue Date:** Monday, October 17, 2008

**Proposal Due Date:** **Unchanged** **Tuesday, December 2, 2008 at 3:00 PM, Local Time**

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**This amendment provides answers to questions regarding the solicitation from prospective offerors and notifies offerors that there is a cut off date for receipt of questions regarding the BAA (see question no. 1).**

**Offerors must acknowledge receipt of this Amendment by identifying this amendment number and date of the amendment on each copy of the offer submitted. Failure to receive your acknowledgement may result in the rejection of your offer. Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full force and effect.**

**Questions and Answers:**

1. To reconfirm, are you awarding up to \$1.5M/year for up to 5 years of work?

**Response:** Yes, this information is included in Attachment 3, Broad Agency Announcement (BAA) Description, Attachment 8, Uniform Cost Assumptions and Section L.1.c.

2. Is it a desire/aspiration for the MDx device to be handheld per the specifications? Or can one build an integrated sample-to-answer system (bench top footprint – i.e., much smaller than Cepheid GeneXpert)?

**Response:** Ideally, a handheld portable device would be best. However, a small portable machine would be adequate if it meets the specifications outlined in the BAA. Power consumption, transportation and durability would need to be addressed. Please refer to the specifications listed in Attachment 5, Research and Technical Objectives, Table 1.

3. Further to question 2, 120min TAT seems to be at odds for a handheld device in a resource limited setting. Is greater emphasis placed on the device or the TAT?

**Response:** As indicated in Attachment 5, Research and Technical Objectives, Table 1, the Government's preference is 2 hours time to results because of patient management and sample throughput. However, we realize that specifications need to be balanced to take advantage of the strengths of the technology.

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4. Who are developing the candidate vaccines? And is there an ability for the POC maker to partner with said group(s)?

**Response:** The discovery and development of an HIV/AIDS vaccine for the prevention of HIV infection is one of the top priorities at the NIAID. As such, the DAIDS Vaccine Research Program (VRP) supports basic, preclinical, and clinical research of candidate vaccines through the following activities:

- (1) Oversees grants, contracts, and cooperative agreements that support preclinical and clinical vaccine research, including the HIV Vaccine Trials Network (HVTN) and Center for HIV/AIDS Immunology (CHAVI)
- (2) Fosters evaluation of the safety and efficacy of vaccine candidates
- (3) Promotes research programs to discover novel vaccine strategies for the treatment of HIV
- (4) Coordinates research activities in consultation and/or collaboration with other government agencies, international organizations, and other Institutes at the National Institutes of Health
- (5) Works with the pharmaceutical industry and the Food and Drug Administration to facilitate the evaluation and approval of new vaccines
- (6) Provides scientific guidance to grantees and contractors

Therefore, by definition, the offeror will be partnering with a vaccine developer.

5. How many samples do you envision testing with the device? 1 sample? Batching of multiple samples? Multiple samples with random access?

**Response:** We envision testing for 1 sample will be sufficient. If successful, alternatives may be explored such as pooling and multisample units if the need is present.

6. For the option of developing a test that informs treatment decisions, are you implying multiplexing of resistance genes as an example?

**Response:** Not necessarily, often times loss of virological control (i.e., increase in viral load) can signal the need to alter treatment therapy. Further details can be found on page 3 of Attachment 5, Research and Technical Objectives.

7. Did you work with any parties in pulling together the project scope and specifications in writing this RFP? If so, whom?

**Response:** The NIAID held a workshop entitled "Novel Technologies in Rapid HIV-1 Viral Detection" at NIH on July 12-13, 2007 where we sought input from the research community regarding the state of the art. However, these researchers did not participate in the development of the scope or specifications for this BAA requirement.

8. The RFP describes a diagnostic POC assay that can differentiate between individuals who have been exposed to an HIV vaccine only versus those who have an HIV infection. Such an assay most likely will be based on detection of differentiating antibodies. In addition, the HIV POC assay described in the RFP should be able to detect acute infections in adults and infections, almost certainly acute, in newborns. The latter two applications will require detection of the virus (e.g. HIV RNA or viral proteins). Thus, it appears that the RFP is describing either two assays in one or two separate assays that might be employed sequentially with a decision-algorithm. Are these assumptions correct?

**Response:** No, since a vaccine will likely consist of most, if not all major HIV genes, then a serological assay would not be appropriate. In addition, since we do have an HIV vaccine, nor know what components a

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successful vaccine might include, it would be prudent to move away from an indirect serological assay and implement an assay that will require the direct detection of virus.

9. The assay for direct detection of HIV should have an (analytical) sensitivity (i.e. LoD) of 200-1000 copies/mL. If a sample volume of 0.1-0.2 mL is employed, this means that there could be as few as 20 copies in the input volume (0.1 mL at 200 copies/mL). Today, the very best, FDA-approved assays are non-CLIA-waived, require advanced laboratory infrastructure, and are considered to be high complexity (i.e. required lab technicians with specialized training). These assays, COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test and Abbott RealTime HIV-1, can only detect as few as 48 input copies or 40 input copies, respectively. Thus, achieving the desired analytical sensitivity in a POC assay, usually less sensitive than a lab-based test, will be very difficult. Could you please respond to our observations?

**Response:** True, 20 copies would be lower limit. We realize that this would be a tall order and have the upper limit set at 1000 copies/ml in 0.2 ml in the solicitation. Therefore, the upper range limit of the assay would be 200 input copies. This would still be satisfactory. However, if your assay is not that sensitive then you could argue that it is offset by having other advantages (specificity, time to result, sample type, cost, etc.) that we've outlined in the specifications. We realize that all these specifications are interrelated and that each application could address them differently since each technology has its own strengths. However, the final product is something that meets the needs of patients and volunteers in limited-resource settings. Please note, as indicated in the BAA, the Statement of Work is developed by you and the terms are negotiable.

10. The assay for direct detection of HIV is indicated for use in acutely-infected patients, both adults and newborns. Since viral loads are very high in acute infections, the desired (clinical) sensitivity (90-95% in ATTACHMENT 5, page 2, Table 1 of the RFP) may be achieved with an assay that has an LoD considerably higher than 200-1000 copies/mL. Would an assay that does not achieve the desired LoD, but achieves the desired sensitivity be satisfactory?

**Response:** Although a higher LOD would be fine to detect acute infections and for infant diagnosis, a limit of 1000 copies per ml was chosen not only for a vaccine need but is also a monitoring threshold that the WHO uses to switch ART. Again, if the offeror specifies a higher LOD, then an argument for another advantage should be made to compensate for falling outside of the set target range as defined in the BAA.

11. The RFP describes development of a CLIA-waived HIV POC test that might be used in the home among other sites. Thus, the user must understand how to use the assay by following simple, easy-to-follow diagrams/instructions with the assay. Training of  $\leq 1$  hr to  $\leq 8$  hrs (see ATTACHMENT 5, page 2, Table 1) seems inconsistent with the intended sites for use of the device. Could you please respond to our observations?

**Response:** The intended sites for use include non-medical professionals or those with limited-medical training. This device would be used in VTC centers, rural clinics and drop in centers much the same way that current rapid antibody-based HIV tests are used today. There is no mention that this type of device would be licensed for home use since the regulatory aspects of such a device would be difficult to address at this time.

12. We have been considering the potential budget (potential of \$1.5 MM per year for five years) for this RFP. We believe that the total potential amount described in the RFP would not cover product development (following Quality Systems Regulations and GMP) to early-stages (i.e. Pre-IDE presentation and early-stage PMA) for an FDA-approvable product.

**Response:** Remember that the funds listed are not for basic research to support the initial development of the diagnostic device. Importantly, the funds will not cover clinical or field trials which typically are resource intense. This material can be made available by requesting it through the mechanism outlined in the BAA.

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Our initial assessment showed that this level of funding should be sufficient and that one assay can be developed to meet all the milestones of this RFP.

13. If our assumption that the HIV POC device described in this RFP might actually require development of two assays, would NIAID consider our submitting a separate proposal for each of the two assays?

**Response:** You must submit a proposal that meets all the requirements of the BAA.

14. According to our understanding, the objective of this program is to develop a device which can be used to distinguish patients with HIV infection from vaccination at resource-limited areas. Is this correct?

**Response:** The offeror should evaluate the BAA and whether their technology meets the specifications listed in Table 1 of the BAA and decide whether to submit a proposal.

15. What type of technology is “ideal”?

**Response:** If we had an answer to that question, we would not be advertising this solicitation. We would have written a contract requesting a specific type of deliverable.

16. What are the limitations for the current commercial available technologies and what technologies are promising for this task?

**Response:** We anticipate you are the experts in this area and it is up to you to review the literature and make that determination. NIAID sponsored a workshop in July 2007 on Rapid Technologies. This BAA was written as a result of gaps identified during this workshop.

17. It's mentioned in the solicitation for a viral loading measurement. Two methods can be used for virus detection including immunoassay and nucleic acid based assay. Which method do you think is more preferred and why?

**Response:** Either method is suitable as long as it is used to detect virus directly. Again, we refer you to the specifications of the device listed in Table 1 to help you decide which type of technology would meet the needs of a POC diagnostic device.

18. Is the RFP really intended for an industrial company?

**Response:** The RFP is intended for all interested parties. There are no restrictions about who may submit a proposal.

19. I understand that it encourages broad involvement, but reading the RFP we got a sense that you were really seeking a large scale diagnostics company, rather than a collection of academic efforts.

**Response:** Quite the contrary. We encourage a collaborative effort as you eluded.

20. Has there been further clarification of whether one or two grants were going to be offered?

**Response:** No grants will be awarded as a result of the BAA. We anticipate awarding 1-2 contracts.

21. Most of the researchers who read the RFP, based on the detail included in the specifications, were left with the opinion that they were written with a product already in development in mind.

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**Response:** The assumption of the researcher's is not the case in actuality. The rationale for using the Broad Agency Announcement was so that there could be creative latitude for the successful offeror to develop the desired device. The solicitation was not written with any specific pre-existing product in mind.

22. Is the Dec 2nd date for final applications or is it for letters of intent (LOI)? Has there been discussion of soliciting LOIs first?

**Response:** December 2, 2008 is the deadline for submission of proposals. This is not a deadline for letters of intent (LOI). The BAA requests that interested parties submit a Proposal Intent Response Sheet (see Attachment 2) by no later than November 3, 2008. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

23. Although the RFP seems to indicate that technology at any stage of development will be considered, we got the sense that the focus was more on building and commercialization of an existing approach. Can you give any better sense of how far along the technology needs to be?

**Response:** We anticipate that this BAA will work toward a product that can be used as a POC diagnostic device. A timeline for advancing the diagnostic device is provided as Table 2, Attachment 7. If your technology is still in the R & D phase, it would not qualify as we anticipate this contract will generate a diagnostic device that meets the specifications listed in Table 1, Attachment 5. If a diagnostic device exists for another purpose and you wish to transition this activity to HIV/AIDS, that type of technology transfer would be appropriate.

**END OF AMENDMENT #1 to RFP-NIAID-DAIDS-NIHAI2008027**