

**AMENDMENT NO. 3, NIAID SOLICITATION No.
BAA-NIAID-DAIDS-NIHAI2008027
“Rapid HIV Point-of-Care Diagnostic Device for Resource-Limited Settings”**

Solicitation Number: BAA-NIAID-DAIDS-AI2008027
Amendment Number: Three (3)
Amendment Issue Date: August 1, 2008
Proposal Due Date: (Changed) Wednesday, December 17, 2008 at 3:00 PM, Local Time

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The purpose of this amendment is to make changes to the solicitation as a result of: 1) making available to offerors the option of using fresh blood specimens and collecting specimens specifically for the contract work. After further consideration, the NIAID feels it would be better to use fresh blood rather than plasma or frozen cells since this is a Point of Care device; and 2) removing the requirement for FDA submission of the device. We have learned that companies are unwilling to file paperwork for FDA approval as the regulatory requirements for US approval of a device are costly.

The date specified for receipt of proposals has been extended to Wednesday, December 17, 2008 at 3:00 p.m. local time.

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.

PART I, THE SCHEDULE, SECTION H, is hereby modified to replace ARTICLE H.1., HUMAN SUBJECTS, with the following.

ARTICLE H.1. HUMAN SUBJECTS

Research involving human subjects shall not be conducted under this contract until written notice of approval has been provided by the Contracting Officer, and the Contractor has provided to the Contracting Officer a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310) certifying IRB review and approval of the protocol. The human subject certification can be met by submission of the Contractor's self designated form, provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310).

When research involving Human Subjects will take place at collaborating sites or other performance sites, the Contractor shall obtain, and keep on file, a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310) certifying IRB review and approval of the research.

In addition, SECTION H is modified to add the following provisions:

ARTICLE H.23. REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

NIH policy requires education on the protection of human subject participants for all investigators receiving NIH contract awards for research involving human subjects. For a complete description of the NIH Policy announcement on required education in the protection of human subject participants, the Contractor should access the [NIH Guide for Grants and Contracts](#) Announcement dated June 5, 2000 at the following website:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

The information below is a summary of the NIH Policy Announcement:

The Contractor shall maintain the following information: (1) a list of the names and titles of the principal investigator and any other individuals working under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program(s) in the protection of human subjects that has been completed for each named personnel and; (3) a one sentence description of the educational program(s) listed in (2) above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Prior to any substitution of the Principal Investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the Contractor shall provide the following written information to the Contracting Officer: the title of the education program and a one sentence description of the program that has been completed by the replacement.

ARTICLE H.24. RESTRICTION ON ABORTIONS

Pursuant to the current HHS annual appropriations act, the Contractor shall not use contract funds for any abortion.

ARTICLE H.25. PRIVACY ACT, HHSAR 352.270-11 (January 2006)

This contract requires the Contractor to perform one or more of the following: (a) Design; (b) develop; or (c) operate a Federal agency system of records to accomplish an agency function in accordance with the Privacy Act of 1974 (Act) (5 U.S.C. 552a(m)(1)) and applicable agency regulations. The term "system of records" means a group of any records under the control of any agency from which information is retrieved by the name of the individual or by some identifying number, symbol, or other identifying particular assigned to the individual.

Violations of the Act by the Contractor and/or its employees may result in the imposition of criminal penalties (5 U.S.C. 552a(i)). The Contractor shall ensure that each of its employees knows the prescribed rules of conduct and that each employee is aware that he/she is subject to criminal penalties for violation of the Act to the same extent as HHS employees. These provisions also apply to all subcontracts awarded under this contract which require the design, development or operation of the designated system(s) of records (5 U.S.C. 552a(m)(1)).

The contract work statement: (a) Identifies the system(s) of records and the design, development, or operation work to be performed by the Contractor; and (b) specifies the disposition to be made of such records upon completion of contract performance.

(End of clause)

45 CFR Part 5b contains additional information which includes the rules of conduct and other Privacy Act requirements and can be found at: http://www.access.gpo.gov/nara/cfr/waisidx_06/45cfr5b_06.html. The Privacy Act System of Records applicable to this project is Number 09-25-0200 . This document is incorporated into this contract as an Attachment in SECTION J of this contract. This document is also available at: <http://oma.od.nih.gov/ms/privacy/pa-files/read02systems.htm> .

ARTICLE H.26. OMB CLEARANCE

In accordance with HHSAR 352.270-7, Paperwork Reduction Act, the Contractor shall not proceed with surveys or interviews until such time as Office of Management and Budget (OMB) Clearance for conducting interviews has been obtained by the Project Officer and the Contracting Officer has issued written approval to proceed.

PART II, CONTRACT CLAUSES, SECTION I.3. ADDITIONAL CONTRACT CLAUSES, is hereby amended as follows:

Paragraph b, **DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CHAPTER 3) CLAUSES**, is hereby revised to add:

5. HHSAR Clause **352.270-7, Paperwork Reduction Act** (January 2006).
6. HHSAR Clause **352.270-8(b), Protection of Human Subjects** (January 2006).

Paragraph c, **NATIONAL INSTITUTES OF HEALTH (NIH) RESEARCH CONTRACTING (RC) CLAUSES**, is hereby revised to add the following:

2. **NIH(RC)-11, Research Patient Care Costs (4/1/84)**

PART III – LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS, is hereby revised as follows:

TECHNICAL PROPOSAL ATTACHMENTS, is hereby amended to add:

Attachment 13: Targeted/Planned Enrollment Table <http://rcb.cancer.gov/rcb-internet/forms/enroll-table.pdf>

As a result of the aforementioned change, the BUSINESS PROPOSAL ATTACHMENTS and INFORMATIONAL ATTACHMENTS are renumbered accordingly.

PART IV, SECTION L – INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS, paragraph 2, INSTRUCTIONS TO OFFERORS, paragraph b, TECHNICAL PROPOSAL INSTRUCTIONS, subparagraph 5, HUMAN SUBJECTS, is hereby added to read as follows:

IMPORTANT NOTE TO OFFERORS: The following paragraphs (5) through (15) through shall be addressed, as applicable, in a SEPARATE SECTION of the Technical Proposal entitled, "HUMAN SUBJECTS."

5. Human Subjects

The following notice is applicable when contract performance is expected to involve risk to human subjects: Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects, HHSAR 352.270-8(a) (January 2006)

(a) Copies of the Department of Health and Human Services (HHS) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Bethesda, Maryland 20892. The regulations provide a systematic means,

based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the HHS.

(b) The regulations define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information. The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable State and local law and is not directly regulated by 45 CFR Part 46.

(c) Activities in which the only involvement of human subjects will be in one or more of the categories set forth in 45 CFR 46.101(b)(1-6) are exempt from coverage.

(d) Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research in a project may result in delays in the review of a proposal. The OPDIV will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal. In doubtful cases, prior consultation with OHRP, (telephone: 301-496-7014), is recommended.

(e) In accordance with 45 CFR Part 46, prospective Contractors being considered for award shall be required to file with OHRP an acceptable Assurance of Compliance with the regulations, specifying review procedures and assigning responsibilities for the protection of human subjects. The initial and continuing review of a research project by an institutional review board shall assure that the rights and welfare of the human subjects involved are adequately protected, that the risks to the subjects are reasonable in relation to the potential benefits, if any, to the subjects and the importance of the knowledge to be gained, and that informed consent will be obtained by methods that are adequate and appropriate. HHS regulations for the protection of human subjects (45 CFR Part 46), information regarding OHRP registration and assurance requirements/processes, and OHRP contact information can be accessed at the OHRP Web site: <http://www.hhs.gov/ohrp/>.

(f) It is recommended that OHRP be consulted for advice or guidance concerning either regulatory requirements or ethical issues pertaining to research involving human subjects."

(End of provision)

6. Instructions to Offerors Regarding Protection of Human Subjects

Offerors must address the following human subjects protections issues if this contract will be for research involving human subjects (note: under each of the following points below, the offeror should indicate whether the information provided relates to the primary research site, or to a collaborating performance site(s), or to all sites:

a. Risks to the subjects

- Human Subjects Involvement and Characteristics:
 - Describe the proposed involvement of human subjects in response to the solicitation.
 - Describe the characteristics of the subject population, including their anticipated number, age range, and health status.
 - Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable populations.
- Sources of Materials:

- Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.
 - Potential Risks:
 - Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects.
 - Describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures, to participants in the proposed research, where appropriate.
- b. Adequacy of Protection Against Risks
- Recruitment and Informed Consent:
 - Describe plans for the recruitment of subjects and the procedures for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. The informed consent document for the Contractor and any collaborating sites should be submitted only if requested elsewhere in the solicitation. Be aware that an IRB-approved informed consent document for the Contractor and any participating collaborative sites must be provided to the Government prior to patient accrual or participant enrollment.
 - Protection Against Risk:
 - Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.
 - Discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects where appropriate.
 - In studies that involve interventions, describe the provisions for data and safety monitoring of the research to ensure the safety of subjects.
- c. Potential Benefits of the Proposed Research to the Subjects and Others
- Discuss the potential benefits of the research to the subjects and others.
 - Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.
 - Describe treatments and procedures that are alternatives to those provided to the participants by the proposed research, where appropriate.
- d. Importance of the Knowledge to be Gained
- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.
 - Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that may reasonably be expected to result.

Note : If a test article (investigational new drug, device, or biologic) is involved, name the test article and state whether the 30-day interval between submission of offeror's certification to the Food and Drug Administration (FDA) and its response has elapsed or has been waived and/or whether the FDA has withheld or restricted use of the test article.

Collaborating Site(s)

When research involving human subjects will take place at collaborating site(s) or other performance site(s), the offeror must provide in this section of its proposal a list of the collaborating sites and their assurance numbers. Further, if you are awarded a contract, you must obtain in writing, and keep on file, an assurance from each site that the

previous points have been adequately addressed at a level of attention that is at least as high as that documented at your organization. Site(s) added after an award is made must also adhere to the above requirements.

7. Required Education in the Protection of Human Research Participants

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for contracts for research involving human subjects. This policy announcement is found in the NIH Guide for Grants and Contracts Announcement dated June 5, 2000 at the following website: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html> . Offerors should review the policy announcement prior to submission of their offers. The following is a summary of the Policy Announcement:

For any solicitation for research involving human subjects, the offeror shall provide in its technical proposal the following information: (1) a list of the names of the principal investigator and any other individuals proposed under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program completed (or to be completed prior to the award of the contract) for each named personnel; (3) a one sentence description of the program(s) listed in (2) above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Curricula that are readily available and meet the educational requirement include the NIH on-line tutorial, titled "Protection of Human Research Subjects: Computer-Based Training for Researchers," available at <http://ohsr.od.nih.gov/cbt/> . You may download the information at this site at no cost and modify it, if desired. The University of Rochester has made its training program available for individual investigators. Completion of this program will also satisfy the educational requirement. The University of Rochester manual can be obtained through Centerwatch, Inc. at http://www.centerwatch.com/order/pubs_profs_protect.html .

In addition, the NCI sponsors an online training course at: <http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp> . If an institution already has developed educational programs on the protection of research participants, completion of these programs also will satisfy the educational requirement.

In addition, prior to the substitution of the principal investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the Contractor shall provide the contracting officer with the title of the education program and a one sentence description of the program that the replacement has completed.

8. Inclusion of Women and Minorities in Research Involving Human Subjects

It is NIH policy that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. The Director, NIH, may determine that exclusion under other circumstances is acceptable, upon the recommendation of an Institute/Center Director, based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43), and applies to research subjects of all ages.

All investigators proposing research involving human subjects should read the UPDATED "NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, Amended

October 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 at the following web site:

http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

These guidelines contain a definition of clinical research adopted in June 2001, as: "(1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) Epidemiologic and behavioral studies; and (3) Outcomes research and health services research," at:

(<http://www.nih.gov/news/crp/97report/execsum.htm>).

9. Information Required for ALL Clinical Research Proposals

This solicitation contains a review criterion addressing the adequacy of: (1) the offeror's plans for inclusion of women and minorities in the research proposed; or (2) the offeror's justification(s) for exclusion of one or both groups from the research proposed.

Provide information on the composition of the proposed study population in terms of sex/gender and racial/ethnic groups and provide a rationale for selection of such subjects in response to the requirements of the solicitation. The description may include (but is not limited to) information on the population characteristics of the disease or condition being studied in the planned research, and/or described in the statement of work, national and local demography, knowledge of the racial/ethnic/cultural characteristics of the population, prior experience and collaborations in recruitment and retention of the populations and subpopulations to be studied, and the plans, arrangements and letters of commitment from relevant community groups and organizations for the planned research.

The proposal must include the following information:

- A description of the subject selection criteria
- The proposed dates of enrollment (beginning and end)
- A description of the proposed outreach programs for recruiting women and minorities as subjects
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group
- The proposed sample composition using the "Targeted/Planned Enrollment Table"(see Section J, Attachments)

NOTE 1 : *For all proposals, use the ethnic and racial categories and complete the "Targeted/Planned Enrollment Table in accordance with the Office of Management and Budget (OMB) Directive No. 15, which may be found at :*
<http://www.whitehouse.gov/OMB/fedreg/ombdir15.html> .

NOTE 2 : *If this is an Indefinite Delivery, Indefinite Quantity (IDIQ) or Requirements contract as defined in FAR 16.5, the proposal should describe in general terms how it will comply with each bulleted item above for each task order. When the Government issues a task order request for proposal, each of the bulleted information items must be fully and specifically addressed in the proposal.*

Standards for Collecting Data . When you, as a contractor, are planning data collection items on race and ethnicity, you shall use, at a minimum, the categories identified in OMB Directive No. 15. The collection of greater detail is encouraged. However, you

should design any additional, more detailed items so that they can be aggregated into these required categories. Self-reporting or self-identification using two separate questions is the preferred method for collecting data on race and ethnicity. When you collect race and ethnicity separately, you must collect ethnicity first. You shall offer respondents the option of selecting one or more racial designations. When you collect data on race and ethnicity separately, you shall also make provisions to report the number of respondents in each racial category who are Hispanic or Latino. When you present aggregate data, you shall provide the number of respondents who selected only one category, for each of the five racial categories. If you collapse data on multiple responses, you shall make available, at a minimum, the total number of respondents reporting "more than one race." Federal agencies shall not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

In addition to the above requirements, solicitations for NIH defined Phase III clinical trials * require that: a) all proposals and/or protocols provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide:

http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm , Definitions - Significant Difference).

*The definition of an " NIH-Defined Phase III clinical trial " can also be found at this website.)

by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable; and b) all contractors to report annually cumulative subject accrual, and progress in conducting analyses for sex/gender and race/ethnicity differences.

Offerors may obtain copies of the Updated Guidelines from the sources above or from the contact person listed in the solicitation.

Also, the proposal must include one of the following plans:

- Plans to conduct valid analysis to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups,

OR

- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups,

OR

- Plans to conduct valid analyses of the intervention effect in sex/gender and/or racial/ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect between subgroups.

Use the form entitled, "Targeted/Planned Enrollment Table," when preparing your response to the solicitation requirements for inclusion of women and minorities. (See Section J-List of Documents, Exhibits and Other Attachments of the RFP)

Unless otherwise specified in this solicitation, the Government has determined that the work required by this solicitation does not involve a sex/gender specific study or a single

or limited number of minority population groups. Therefore, the NIH believes that the inclusion of women and minority populations is appropriate for this project. (See Section M of this RFP for more information about evaluation factors for award.)

Use the form entitled, "Inclusion Enrollment Report," for reporting in the resultant contract .

10. Inclusion of Children in Research Involving Human Subjects

It is NIH policy that children (defined below) must be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are clear and compelling reasons not to include them. (See examples of Justifications for Exclusion of Children below).

For the purposes of this policy, contracts involving human subjects include categories that would otherwise be exempt from the DHHS Policy for Protection of Human Research Subjects (sections 101(b) and 401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

For purposes of this policy, a child is defined as an individual under the age of 21 years.

All offerors proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts on March 6, 1998 and is available at the following URL address:

<http://www.nih.gov/grants/guide/notice-files/not98-024.html>

Offerors also may obtain copies from the contact person listed in the RFP.

Inclusion of children as participants in research must be in compliance with all applicable subparts of 45 CFR 46 as well as other pertinent laws and regulations whether or not such research is otherwise exempted from 45 CFR 46. Therefore, any proposals must include a description of plans for including children, unless the offeror presents clear and convincing justification for an exclusion. The "Human Subjects" section of your technical proposal should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. This solicitation contains a review criterion addressing the adequacy of: (1) the plans for including children as appropriate for the scientific goals of the research; and/or (2) the justification of exclusion of children or exclusion of a specific age range of children.

When children are included, the plan also must include a description of: (1) the expertise of the investigative team for dealing with children at the ages included; (2) the appropriateness of the available facilities to accommodate the children; and, (3) the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose/objective of the solicitation.

Justifications for Exclusion of Children

It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified:

- The objective of the solicitation is not relevant to children.
 - There are laws or regulations barring the inclusion of children in the research to be conducted under the solicitation.
 - The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant. You should provide documentation of other studies justifying the exclusion.

- A separate, age-specific study in children is warranted and preferable. Examples include:
 - The relative rarity of the condition in children, as compared with adults (in that extraordinary effort would be needed to include children); or
 - The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
 - Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages of different age-related metabolic processes); or
 - Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). While children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis; or
 - Study designs aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children);
 - Other special cases justified by the offeror and found acceptable to the review group and the Institute Director

Definition of a Child

For the purpose of this solicitation, a child is defined as an individual under the age of 21 years.

The definition of child described above will pertain to this solicitation (notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states). Generally, State laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, State laws vary, and many do not address when a child can consent to participate in research. Federal Regulations (45 CFR 46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under State law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

11. Research Involving Prisoners as Subjects

- a. HHS Regulations at 45 CFR Part 46, Subpart C provide additional protections pertaining to biomedical and behavioral research involving prisoners or those individuals who, during the period of the contract become prisoners, as subjects. These regulations also set forth the duties of the Institutional Review Board (IRB) where prisoners are involved in the research. HHS funded research involving prisoners as subjects may not proceed until the Office for Human Research Protections (OHRP) issues approval, in writing, as required by 45 CFR 46.306(a)(2). In addition, OHRP Guidance on the Involvement of Prisoners in Research may be found at: <http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.pdf> .
- b. HHS Waiver for Epidemiological Research Involving Prisoners as Subjects

On June 20, 2003 the Secretary of HHS waived the applicability of certain provisions of Subpart C of 45 CFR Part 46, (Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects) to specific types of epidemiological research involving prisoners as subjects.

The applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain epidemiological research conducted or funded by DHHS is waived when:

1. The sole purposes are:
 - a. to describe the prevalence or incidence of a disease by identifying all cases, or
 - b. to study potential risk factor associations for a disease, and
2. The Institution responsible for the conduct of the research certifies to the OHRP that the Institutional Review Board (IRB) approved the research and fulfilled its duties under 45 CFR 46.305(a)(2 7) and determined and documented that:
 - c. the research presents no more than minimal risk, and
 - d. no more than inconvenience to the prisoner subjects, and
 - e. prisoners are not a particular focus of the research.

For more information about this Waiver see

[http://www.hhs.gov/ohrp/special/prisoners/Prisoner waiver 6-20-03.pdf](http://www.hhs.gov/ohrp/special/prisoners/Prisoner%20waiver%206-20-03.pdf)

12. Research Involving Human Fetal Tissue

Human Fetal Tissue means tissue or cells obtained from a dead human fetus, including human embryonic stem cells, human pluripotent stem cells and human embryonic germ cells.

The governing federal statute is the Public Health Service Act, 42 U.S.C. 289g 1 and 289g 2. Implementing regulations and guidance for conducting research on human fetal tissue may be found at 45 CFR 46, Subpart B and <http://grants1.nih.gov/grants/guide/notice-files/not93-235.html> and any subsequent revisions to this NIH Guide to Grants and Contracts ("Guide") Notice.

By signing the face page of the proposal, the offeror (authorized institutional official) certifies that researchers using human fetal tissue are in compliance with 42 USC 289g 2. This statute specifically prohibits any person from knowingly acquiring, receiving, or transferring any human fetal tissue for valuable consideration. "Valuable consideration" is a concept similar to profit, and does not include reasonable payment for costs associated with the collection processing, preservation, storage, quality control or transportation of these tissues.

Research involving the transplantation of human fetal tissue must be conducted in accordance with applicable Federal, State and local law.

13. Research Involving Recombinant DNA Molecules (including Human Gene Transfer Research)

Recombinant DNA Molecules are either 1) molecules that are constructed outside of living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or 2) DNA molecules that result from the replication of those described in 1).

The NIH Guidelines for Research Involving Recombinant DNA Molecules at:

(<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html> and the May 28, 2002 Notice, Compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules at:

(<http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html>) and any subsequent revisions to the Guide Notice) stipulates biosafety and containment measures for

recombinant DNA research and delineates critical, ethical principles and key safety reporting requirements for human gene transfer research (See Appendix M of the NIH Guidelines). These guidelines apply to both basic and clinical research studies.

The Recombinant DNA Advisory Committee (RAC) is charged with the safety of manipulation of genetic material through the use of recombinant DNA techniques. Prior to beginning any clinical trials involving the transfer of recombinant DNA to humans, the trial must be registered with the RAC. If this contract involves new protocols that contain unique and/or novel issues, the RAC must discuss them in a public forum and then the Institutional Biosafety Committee (IBC), the Institutional Review Board (IRB), and the Project Officer and Contracting Officer must approve the protocol prior to the start of the research.

Failure to comply with these requirements may result in suspension, limitation, or termination of NIH funding for any work related to Recombinant DNA Research or a requirement for the Contracting Officer's prior approval of any or all Recombinant DNA projects under any contract awarded from this solicitation. This includes the requirements of the Standing Institutional Biosafety Committee (IBC) (See <http://www4.od.nih.gov/oba/IBC/IBCindexpg.htm>).

As specified in Appendix M 1 C 4 of the NIH Guidelines, any serious adverse event must be reported immediately to the IRB, the IBC, the Office for Human Research Protections (if applicable), and the NIH Office for Biotechnology Activities (OBA), followed by the filing of a written report with each office/group and copies to the Project Officer and Contracting Officer, at: (http://www4.od.nih.gov/oba/rac/guidelines_02/Appendix_M.htm#_Toc7255836).

14. Human Embryonic Germ Cell (HEGC) Research

1) Guidelines.

Research use of human embryonic germ cells derived from fetal tissue with Federal funds requires review of compliance with the NIH Guidelines for Research Using Human Pluripotent Stem Cells (<http://stemcells.nih.gov/policy/guidelines.asp>) (only the information regarding human embryonic germ cells is relevant). Embryonic germ cells are pluripotent stem cells derived from human embryos. See NIH Guide for Grants and Contracts Notice NOT OD 02 049, requiring that offerors/contractors submit certain documents to the Human Pluripotent Stem Cell Review Group (HPSCRG), which will be reviewed in a public meeting. Research using human embryonic germ cells may not be performed prior to approval by the HPSCRG.

All offerors should read the "NIH Guidelines" (<http://stemcells.nih.gov/policy/guidelines.asp>) if they either: (1) propose to respond to the Statement of Work requirements by conducting research that uses human embryonic germ cells or, (2) are responding to a Statement of Work that requires the use of human embryonic germ cells.

Offerors may obtain copies of these Guidelines from the website above or from the contact person listed in this solicitation.

2) Procedure for Review by Human Pluripotent Stem Cell Review Group (HPSCRG)

If, in response to the solicitation, the offeror proposes to use human embryonic germ cells, it must submit, as a separate attachment to its proposal, an original and two copies of the documentation and assurances that address the areas covered in the "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells" at: (<http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html>).

Prior to any award made under this solicitation, the documentation and assurances will be subject to review by the HPSCRG, which meets in a public meeting. No research involving the use of human embryonic germ cells may begin prior to HPSCRG approval.

Offerors are encouraged to review issues pertaining to informed consent processes described in Section II.B.2.b of the NIH Guidelines. Offerors should also review the March 19, 2002, DHHS Office of Human Research Protection's document titled "Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, and Stem Cell Derived Test Articles," at (<http://stemcells.nih.gov/StaticResources/news/newsArchives/stemcell.pdf>)

15. Human Embryonic Stem Cell (HESC) Research

On August 9, 2001, the President announced the criteria that must be met for Federal funds to be used for research on existing human embryonic stem cell lines. These criteria were subsequently published by the NIH at: <http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html> . The following eligibility criteria must be met:

1. The derivation process (which commences with the removal of the inner cell mass from the blastocyst) must have already been initiated prior to August 9, 2001;
2. Prior to August 9, 2001, the embryo from which the stem cell line was derived no longer had the possibility of development as a human being;
3. The stem cells must have been derived from an embryo that was created for reproductive purposes;
4. The embryo was no longer needed for these purposes;
5. Informed consent must have been obtained for the donation of the embryo;
6. No financial inducements were provided for the donation of the embryo.

To facilitate research using human embryonic stem cells, the NIH has established a Human Embryonic Stem Cell Registry ("the NIH Registry") that lists the human embryonic stem cells that meet the eligibility criteria. This registry is available at: <http://stemcells.nih.gov/registry/> .

Research involving the derivation of new stem cells from human embryos or the use of human embryonic stem cells that are not listed on the NIH Human Embryonic Stem Cell Registry may not be conducted with Federal funding.

If a particular human embryonic stem cell line has not been required by the Statement of Work, an offeror proposing research involving human embryonic stem cells must cite a human embryonic stem cell line that is listed in the NIH Registry in its proposal.

PART IV, SECTION M, EVALUATION FACTORS FOR AWARD, paragraph 4, TECHNICAL EVALUATION CRITERIA, is revised as follows:

CRITERION 2, is revised to read as follows:

CRITERION 2: COMPREHENSIVE STRATEGIC DIAGNOSTIC DEVICE DEVELOPMENT PLAN	30
<ol style="list-style-type: none"> 1) The suitability and feasibility of the proposed key objectives and milestones for optimizing the HIV POC diagnostic concept. 2) The soundness and feasibility of the proposed qualitative and quantitative criteria for deciding whether and when to proceed to the next phase of the product development process for the HIV POC diagnostic device. 	

<p>3) The soundness, adequacy and feasibility of the proposed steps for development, characterization and qualification of reagents and assays for preclinical research including plans to ensure research is carried out pursuant to NIH policies and guidelines (Department of Health and Human Services (HHS) regulations for the protection of human subjects 45 CFR 46.102(f)(2)).</p> <p>4) The status of patents, intellectual property and licensing issues for the technology that will be used to complete all the contract objectives.</p>	
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CRITERION 5, is revised to read as follows:

<p>CRITERION 5: FACILITIES, EQUIPMENT AND OTHER RESOURCES</p>	<p>15</p>
<p>Documented availability and adequacy of facilities, equipment, and other resources necessary to safely and successfully perform all phases of the proposed project, including:</p> <ul style="list-style-type: none"> A. Adequacy of available facilities for the duration of the contract, including documentation/schematic of the floor plans, and resources to perform validation studies, produce the diagnostic devices under GMP conditions and obtain, add or delete facilities as necessary due to progress or lack thereof during the course of product development. B. Adequacy of plans for compliance with all safety guidelines and regulations, including training and monitoring of personnel for exposure to infectious and other hazardous materials. C. Adequacy of other research support resources (including Information Technology systems) that will be required to effectively complete the Offeror’s proposed Statement of Work. 	

ATTACHMENT 4, BACKGROUND AND INTRODUCTION, and ATTACHMENT 5, RESEARCH AND TECHNICAL OBJECTIVES, are revised to remove restrictions on human subject research and requirements for submitting the device for FDA approval. Please refer to the documents attached.

END OF AMENDMENT #3 to RFP-NIAID-DAIDS-NIHAI2008027

ATTACHMENT 4: BACKGROUND and INTRODUCTION

RAPID HIV POINT-OF-CARE DIAGNOSTIC DEVICE FOR RESOURCE-LIMITED SETTINGS NIAID-DAIDS-BAA-NIHAI2008027

The National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) supports and conducts research that strives to understand, treat and ultimately prevent the myriad infectious, immunologic, and allergic diseases that threaten millions of human lives. NIAID supports extramural research to control and prevent diseases caused by virtually all infectious agents. This includes basic biomedical research, such as studies of microbial physiology and antigenic structure; immunity; applied research, including the development of diagnostic tests; and clinical trials to evaluate experimental drugs and vaccines.

Vaccine Trial Needs

Large scale vaccine test-of-concept clinical trials to assess the potential of an HIV vaccine to elicit protective immunity against HIV-1 are being planned for the near future. Currently, HIV-1 screening and diagnosis is accomplished through the use of rapid tests and/or by serological tests (Enzyme Immunoassay (EIA) and Western Blot (WB)). The complex mixture of HIV-1 epitopes (peptides, proteins, DNA expression plasmids, and recombinant viral vectors) present in the vaccine, can elicit persistent antibody responses in vaccinated volunteers that are detectable by FDA-licensed HIV-1 detection kits. Vaccine-induced antibody responses may result in false assumption of HIV infection or indeterminate reactivity when sera of vaccinated volunteers are tested using existing serological detection assays.

A test that does not rely on detecting patient HIV-specific antibodies, e.g. based on molecular nanotechnology, needs to distinguish between vaccine recipients that test positive by immune responses to vaccine from those that test positive due to HIV-1 infection. In developed countries HIV-1 infection is often confirmed by detecting HIV proviral DNA in infected cells using polymerase chain reaction (PCR), or by quantifying HIV viral RNA in plasma using reverse transcription-PCR (RT-PCR) and other techniques. This is difficult in resource-limited settings due to the high cost of equipment and reagents, the lack of trained staff, and the need for complex laboratory infrastructure to perform these assays. Furthermore, it may take several days to weeks from the time a blood sample is drawn to the time a PCR result is obtained from the laboratory. A quick turn-around time has important implications with regard to volunteer retention and tracking at point-of-care (POC) settings.

Additional Public Health Needs

A rapid viral detection assay could facilitate the identification of acutely-infected persons as well as aid in infant HIV-1 diagnosis. It is well known that seronegative patients acutely infected with HIV are highly viremic and are more likely to transmit virus than patients who have seroconverted. Therefore, identifying acute infections enables the infected individual to access appropriate risk reduction counseling and/or treatment programs and serves as an important public health intervention tool to limit secondary spread of HIV. In addition, rapid POC diagnostic technologies are critically needed to identify HIV-infected infants versus uninfected infants.

The uninfected infants carry maternal HIV antibodies that would react with the current antibody-based rapid tests, making current tests unsuitable for diagnosing their infection status. Early diagnosis of HIV-infected infants and their mothers will facilitate access to treatment programs and provide reassurance to families of uninfected infants. Finally, identifying HIV-infected individuals allows earlier access to treatment regimens and would be an important tool for therapeutics research and programs in resource-limited settings.

Point of Care Diagnostic Device

Many simple POC diagnostic devices exist to monitor host biomarkers for disease, to manage various health parameters and to detect different pathogens. To adapt these technologies for use in the HIV field it would be necessary to: (a) bridge the reagents for specific application to HIV-1; (b) simplify sample preparation and procedures for detecting virus from biological fluids; (c) conduct studies to demonstrate reagent stability over a wider temperature range and in rapid turn-around times; (d) conduct validation studies in laboratory-controlled environments and in field conditions; (e) evaluate positive (M, N and O subtypes) and negative samples from target populations; (f) file for approval; and (g) address technical, manufacturing, commercialization and distribution issues.

The purpose of this BAA is to develop a simple-to-use, rapid HIV POC diagnostic device for use in resource-limited settings that is capable of distinguishing HIV-infected individuals from those who have been vaccinated with candidate vaccine constructs and subsequently developed vaccine-induced seropositivity. Additional technological applications include identifying acutely HIV-infected individuals and HIV-infected infants. The end result will improve the level of care by earlier initiation of treatment, potentially curbing new infections by counseling acutely-infected patients, and reducing the cost and time to obtain laboratory analysis.

Resource-limited settings include the home, rural, urban and outreach community public health care clinics in geographical regions of the world that lack the necessary infrastructure, medical capacity and trained personnel to adequately diagnose HIV-1 infected individuals of that community. POC diagnostics for resource-limited settings are tests that are performed near the patient and at-home/self-tests that require quick turn around time and do not require permanently dedicated space in a clinical laboratory. Examples of research include improved self-collection methodology, single unit swab and fluid processing, non-sterile collection devices with preservation capability, and integrated collection and processing methods for use in home-based test kits and/or for public health-based POC diagnostic testing.

An Option to perform additional studies to further develop the proposed HIV POC diagnostic device so that it can inform treatment decisions may be exercised by the Government. Viral load is not used to monitor HIV-infected patients in most resource-limited settings because assay performance is complex, requires sophisticated equipment and the cost of trained personnel overall exceeds the cost of treatment.

Currently, treatment initiation and switching to salvage therapies is carried out using clinical staging tables without laboratory support, or in some cases with limited CD4 data. Furthermore, recent evidence indicates that HIV-1 viral load predicts disease progression better than CD4 T cell counts. Therefore, a device with a broader range of sensitivity, corresponding to a predetermined higher viral load for use by health care workers, in association with clinical parameters, to assist in making treatment decisions regarding therapy modification for HIV-infected patients is highly desired.

ATTACHMENT 5: RESEARCH AND TECHNICAL OBJECTIVES

RAPID HIV POINT-OF-CARE DIAGNOSTIC DEVICE FOR RESOURCE-LIMITED SETTINGS NIAID-DAIDS-BAA-NIHAI2008027

RESEARCH and TECHNICAL OBJECTIVES

NIAID invites research proposals for product development activities that will lead to simple-to-use, rapid HIV POC diagnostic devices for use in resource-limited settings capable of 1) distinguishing HIV-infected individuals from those who have been vaccinated with candidate vaccine constructs and developed vaccine-induced antibodies in the absence of true HIV-1 infection, and 2) identifying acute HIV-1 infections and HIV-1 infected infants.

The scope of product development activities to be supported includes the following:

- optimize the performance of the diagnostic device
- perform validation testing using archived or prospectively collected clinical specimens in the early phases of development
- perform reagent and device acceptability studies in resource-limited settings to identify critical design features
- preclinical studies
- test HIV-spiked samples in biological fluids (e.g. whole blood or mucosal transudates)
- qualify and validate the assay using appropriate clinical specimens from on-going or completed vaccine studies, and complete a development report
- regulatory support or scale-up Current Good Manufacturing Practices (cGMP) manufacturing to produce kits for testing and clinical trial evaluation of an Investigational Use Only (IUO) device
- assist in the development of a training program on the use of the HIV POC diagnostic device

The Offeror must propose to advance a rapid, HIV POC diagnostic device along a milestone-driven development path to a diagnostic product. Offerors are required to adopt and further develop a previously identified candidate POC diagnostic device for use with HIV and include preliminary data that includes relevant information on sample preparation. The HIV POC diagnostic device may be positioned at any point in the product development pipeline, ranging from the initial transition from basic to translational research through later stages close to final product evaluation. **Plasma or other bodily fluids that require laboratory manipulation prior to use in the HIV POC diagnostic device are not within the scope of this BAA and are not responsive.** The HIV POC diagnostic device should test clinical specimens in parallel with currently available, validated laboratory tests. Clinical specimens can include archived specimens or specimens from an ongoing clinical trial to evaluate the diagnostic device under field conditions.

A mechanism for requesting archived specimens is available through the HIV Vaccine Trials Network at <http://www.HVTN.org>. **The Offeror must provide assurances to the Government that all clinical samples obtained for use in development of the HIV POC diagnostic device are collected pursuant to DHHS regulations and that all proposed research is carried out according to NIH policies and guidelines (Department of Health and Human Services (HHS) regulations for the protection of human subjects 45 CFR 46.102(f)(2)).** The HIV POC diagnostic device must be advanced through the product development process and into assessment with clinical trial specimens by the end of the award period. In addition, the Government may exercise the option within the contract to add new parameters to the diagnostic device that can make it capable of providing treatment decisions.

The HIV POC diagnostic device must demonstrate feasibility for use in resource-limited settings and at the POC without the use of supporting laboratory equipment such as centrifuges, vortexes or pipettes.

Any processing of patient samples for downstream applications must be self-contained within the HIV POC diagnostic device and require limited sample manipulation. The HIV POC diagnostic device must include safe containment of potentially infectious material.

The specifications required for the diagnostic device to be successfully implemented in the field are summarized in Table 1. These specifications are estimates provided to offerors to assist with proposal preparation and are not meant to be restrictive.

Table 1. Key specifications and ranges for a rapid, HIV POC diagnostic device:

Feature	Specifications	Target requirements
Sample	Type	Non-invasive or Invasive
	Volume (ml)	0.1 -0.2
	Preparation	One to three-step
Assay	LOD (cps/ml blood equivalent)	200 -1000
	Sensitivity (%)	90 -95
	Specificity (%)	99.5 -99.9
	Viral subtypes	M, N, O
Diagnostic	Time to result (minutes)	90 -120
	Shelf life at 37°C (months)	12 -24
	Humidity (%)	70%
	Transportation stress	50°C for 48-72 hours
Controls	Full process negative Internal positive	
Biosafety	Closed, self contained system	Only unprocessed sample transfer
	No biosafety cabinet required	No open handling of material
Instrument	Handheld	Portable
	Power requirements (V)	0 to 9
Cost	Per test result (\$US)	≥12 ≤20
Training	Community health worker (hrs)	≤1
	High school diploma (hrs)	≤8
Reporting	Database interface flexibility	Capture, store & integrate

Activities NOT covered under this BAA:

- Basic research to support the initial development of POC diagnostics
- Phase I, II and III Clinical or field trials

Proposals may be submitted by the same organization for more than one HIV POC diagnostic device but a separate Technical and Business Proposal will be required for each proposed HIV POC diagnostic device.

2) COMPREHENSIVE STRATEGIC DIAGNOSTIC DEVICE DEVELOPMENT PLAN

As part of product development activities for a HIV POC diagnostic device, Offerors must include a Comprehensive Strategic Diagnostic Development Plan in the Technical Proposal (refer to Appendix 6 – Additional Technical Proposal Instructions).

INDEPENDENT EXTERNAL ADVISORY GROUP

Within 3 months of the effective date of the contract, the Contractor shall establish an Independent External Advisory Group to periodically review performance and progress toward achieving defined technical and strategic goals and milestones based on negotiated objectives. The membership of the Independent External Advisory Group shall be proposed by the Contractor after award and agreed to by the Project Officer.

ANNUAL REVIEW MEETINGS

At the end of each year of the base period of performance, the Contractor shall plan and conduct one full day site visit review for NIAID contract and program staff and the Independent External Advisory Group. The Principal Investigator (PI) and all senior Contractor and subcontractor staff shall attend these annual meetings. An update and summary of progress shall be presented.

OPTION

In addition to the objectives outlined above to be provided for in the basic requirement, an Option for additional services under the contract may be exercised at the discretion of the Government and is defined as follows:

When the Contractor has completed the validation phase and developed an HIV POC diagnostic device feasible for use in a clinical trial, the Government reserves the right to exercise the option to provide additional funds for up to 2 years, to perform additional studies to further develop the HIV POC diagnostic device for expanded viral load detection to inform treatment decisions. The diagnostic device must be capable of detecting virus over the limit-of-detection, which, for this purpose is set to 10,000 HIV equivalent copies/ml in blood, as determined by an FDA-approved viral load assay. Therefore, viral loads below 10,000 copies per ml would not react, and would suggest that the treatment is controlling virus replication in the HIV-infected individual. However, a positive reaction would indicate a viral load in excess of 10,000 copies per ml, and suggest loss of virological control, and, in association with other clinical information, provide rationale for switching to salvage therapy.

- a) Perform additional reagent modifications and optimization procedures, as needed, to adapt the design of the HIV POC diagnostic device such that:

Feature	Specifications	Target requirements
Assay	LOD (cps/ml blood equivalent)	≥10,000
	Sensitivity (%)	≥95%
	Specificity (%)	≥98%
Diagnostic	Time to result (minutes)	≤120

Other key specifications and product development activities supported are identical to those defined for the base period.

Propose a Development Plan for this option.