



Instructions for Responding to the Letter of Intent and Request for Application

Laboratory and Field Evaluations of Advanced Technologies for Diagnostics in Low-Resource Settings

I. Summary of Deadlines

All deadlines are 17:00 Pacific time

Item	Due Date
Request for Letter of Intent (LOI) announcement	February 6, 2009
Questions regarding the request for LOI	March 23, 2009
Responses to questions published	March 30, 2009
Letters of intent due	April 17, 2009
Initial applicants selected	May 8, 2009
Questions on the application	May 22, 2009
Responses to questions (via email and published)	May 29, 2009
Full applications due	June 12, 2009
Selection of final applicants	July 10, 2009
Due diligence and interviews (optional at the GHDx Center's discretion)	July – September 2009
Estimated award date	September 15, 2009

II. Project Background and Purpose of Solicitation

A. Summary

The Center for Point-of-Care Diagnostics for Global Health (GHDx Center) at PATH announces an opportunity for innovators in this field to participate in laboratory and field evaluations of their point-of-care diagnostic tests. The evaluations will assess the suitability of the technologies in low-resource settings (LRS). In particular, the GHDx Center is interested in point-of-care diagnostic tests that are at an advanced stage of development and that target common causes of communicable and noncommunicable disease in LRS.

The GHDx Center is managed by PATH in collaboration with the University of Washington, Departments of Global Health, Laboratory Medicine, and the Division of Infectious Diseases at the School of Medicine. Funding for the GHDx Center is provided by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) (National Institutes of Health [NIH]) as part of

Instructions for Responding to the Letter of Intent and Request for Application

the Point-of-Care Technologies Research Network. *Applications should be made to the GHDx Center.*

Laboratory evaluations. The GHDx Center will organize, manage, and support collaborative laboratory evaluations. Grantees will receive up to US\$25,000 per year for two years to support activities related to laboratory evaluation at PATH. During the evaluation, grantees will receive technical assistance from the GHDx Center and in some cases will be allowed to create new prototypes based on data generated through this process.

Field evaluations. In addition to grantee awards of up to \$25,000 per year, the GHDx Center will provide in-kind support for clinical field studies provided by the Center. The GHDx Center will organize, manage, and financially support clinic-based field evaluations in LRS of promising technologies that have successfully gone through the laboratory evaluation process. Thus, the GHDx Center will provide a comprehensive field evaluation of the grantee's technology. Results of the field evaluation(s) will be shared with grantees to inform their continuing product development efforts. It is anticipated that the value of the field evaluation to be provided by the GHDx Center will be not less than \$125,000.

B. Background

Accurate diagnosis of infectious diseases increases the opportunity for prompt and appropriate treatment of the patient. In LRS, most diseases are managed syndromically through assessment of clinical symptoms. This results in many patients being unnecessarily and incorrectly treated. In addition to poor patient health outcomes, these approaches can accelerate drug resistance and do not provide important information required for surveillance and containment of disease outbreaks. There is an urgent clinical and public health need for point-of-care diagnostics appropriate for uptake in LRS.

The World Health Organization Sexually Transmitted Diseases Diagnostics Initiative (SDI) created the ASSURED criteria to describe ideal diagnostics for LRS. This acronym stands for:

- A - Affordable
- S - Sensitive
- S - Specific
- U - User friendly (requires minimal training)
- R - Rapid and robust
- E - Equipment free
- D - Deliverable to LRS

The majority of diagnostic technologies in use in LRS do not fit the ASSURED criteria and serve only those seeking care in urban or peri-urban clinical settings which have sufficient laboratory infrastructure. The GHDx Center does not expect 100% of the ASSURED criteria to be met by applicants, but this information is provided as a model.

C. Objective

The primary objective of this opportunity is to support laboratory and field-based evaluation of innovative diagnostic technologies that may improve point-of-care diagnosis in LRS. Specifically, we are seeking to support late-stage development of diagnostic assays that target common causes of communicable and non-communicable disease in LRS.

Instructions for Responding to the Letter of Intent and Request for Application

Under this solicitation, we are seeking diagnostic assay technologies that:

- Have data on analytical sensitivity and specificity and/or dynamic ranges of detection for a model, or clinically useful, analyte system.
- Require minimal input for pilot-scale manufacture for preclinical evaluations (hundreds to low thousands of tests).
- Have a viable pathway to commercialization.
- Are not currently available in LRS (but may be available in the developed world).

Preference will be given to complete assay technologies rather than individual assay components.

Also, for complete assay technologies, applicants must provide relevant information/data on specimen collection and processing, biochemical assay processes, detection, and quality control within each assay run.

D. Description of Selection Process

The application submission and review process is divided into two parts, pre- and post-selection. See section VI. for specific instructions regarding requirements for finalists responding to the full application.

Pre-Selection

1. Announcement of request for LOI: This announcement outlines the process and timeline for the pre-award and post-award activities. PATH reserves the right to modify due dates as deemed appropriate to changes in the overall program. PATH will strive to keep all participants informed of date changes.

2. Questions regarding the request for LOI: All questions regarding the request for LOI must be provided via email by the due date listed above. Questions and answers to all questions will be provided to all respondents.

3. Letter of intent: Interested organizations must submit an LOI by the due date listed above for consideration. Information related to this project, including background on the project and instructions for responding to the request for LOI, can be found at <http://www.path.org/dxcenter/funding-opportunities.php>. The LOI process is competitive. It includes a request for brief descriptions of the technology, capabilities, and a proposed budget.

4. Applicant selection: From the submitted LOIs, the GHDx Center will select up to ten applicants who will be invited to submit full applications. **Full applications will be accepted only from those invited to submit them after successful completion of the LOI process.**

5. Questions regarding the applications: All questions regarding the full applications must be provided via email. Questions and answers to all questions will be provided to all respondents.

Instructions for Responding to the Letter of Intent and Request for Application

6. Full applications: Invited organizations must submit a full application for consideration. Information related to this project, including background on the project and instructions for responding to the request for application, can be found at <http://www.path.org/dxcenter/funding-opportunities.php>. The process is competitive.

Applications must be submitted via email on the application form. Submissions after the due date may not be considered.

7. Application review: The applications of up to ten finalists will be reviewed by GHDX Center staff, and a final group will be selected to proceed to the due diligence process.

8. Due diligence: The GHDX Center will select promising finalist applications to undergo a due diligence review process prior to project selection and initiation of collaborative activities. This process will likely involve an in-person visit by GHDX Center staff to assess organizational capacity and to verify the appropriate maturity of the candidate technology for evaluation purposes. Optional interviews with applicants will be held at the discretion of the GHDX Center.

9. Award notification: Some or all of the applicants undergoing the due diligence will be offered support under this award. Notification of award or non-award will be sent to all applicants.

Post-Selection

Once grantees have been selected, the following activities will occur:

1. Contract negotiation: The GHDX Center and the selected grantee(s) will identify and agree to the obligations of both parties.

2. Strategic planning: Representatives from the GHDX Center and technology grantee(s) will meet to jointly develop an evaluation plan which will include detailed laboratory-based evaluation activities, agreed-upon metrics for quantification of progress towards milestones, and a potential field evaluation.

3. Laboratory evaluation: Selected grantees will provide, at no cost to the GHDX Center, necessary devices, materials, instruments, associated supplies, instructions, and training to carry out the jointly-developed and agreed-upon lab evaluation plan. GHDX Center staff, in conjunction with grantees, will conduct an evaluation of the analytical sensitivity and specificity, reagent and platform stability, and user interface at the PATH laboratory or an affiliated laboratory at no cost to the grantee. The evaluation will allow the grantee to benefit from the resources, skills, knowledge, and background of GHDX Center staff.

The GHDX Center staff will evaluate the technologies using well characterized samples for the target analyte or will select, in collaboration with the grantee, an appropriate gold standard assay for comparison. Additionally, GHDX Center staff may evaluate the technology with samples characteristic of those typically found in LRS and/or the target population(s). Discussions of data and conclusions generated will be conducted in a collaborative and confidential manner.

Instructions for Responding to the Letter of Intent and Request for Application

Based on the data, the GHDx Center's experience evaluating the technology, and the Center's analysis of how the technology will be used in LRS, the GHDx Center will provide constructive, collaborative recommendations on technology improvement (if necessary) to aid in the further development efforts of the technology. In some cases, iterative evaluations may be conducted to advance the best possible prototype technology suited for use in LRS.

A final report of the laboratory evaluation will be released to the grantee and NIBIB/NIH. **Technologies that are found to have acceptable laboratory performance as agreed upon in the strategic planning stage and that are most suitable for use in LRS will be considered for further evaluation in the field.**

4. Field evaluation: Prior to field testing, there is a requirement for Institutional Review Board, NIBIB/NIH, and State Department approval of the use of human subjects in the clinical evaluation of the technology in a clinical field site in the developing world. The GHDx Center will obtain all required permissions to conduct the field evaluation.

The GHDx Center, in collaboration with grantees, will develop and manage a clinical evaluation of technology(ies) in a clinical field site in the developing world. Funding for the implementation and management of this study will be provided by the GHDx Center. Grantees will be required to provide device prototypes and instrumentation for use in this study at no cost to the GHDx Center.

The GHDx Center will identify clinical sites in LRS that have the capacity and competency to carry out reference testing for the target analyte(s) in question along with the test under evaluation and that serve populations with an adequate prevalence of the disease outcome of interest. The GHDx Center will, in consultation with grantees, write the field evaluation protocol. The protocol will include a rationale for recruitment of study participants that allows for a statistically valid comparison of the technology performance against reference tests along with collection of qualitative and quantitative data focused on the user interface. Prior to initiating the study, the GHDx Center will secure institutional and local ethical review and other approvals as necessary. Once the study has started, GHDx Center staff will manage all data collection and data analysis activities. A written report of the study findings will be submitted to grantees and the NIBIB/NIH and is intended to stimulate dialogue on possible next steps for product development and commercialization.

No publication of any results will occur without the agreement of both the grantee and the GHDx Center; however, public disseminations in a timely fashion of both lab and field results that are deemed appropriate by both parties are a desirable outcome to the GHDx Center and NIBIB/NIH.

III. Mechanism of Support

A. Mechanism of Support for the Grantee Institution/Technology

The GHDx Center will support the development of selected technologies as follows:

1. Laboratory evaluation of the technology, including analysis and verification of technology performance, reagent stability, and the user interface of the device. This work will be conducted by GHDx Center staff at no direct cost to the grantee organization. However, as mentioned above, grantees will be expected to provide devices, materials,

Instructions for Responding to the Letter of Intent and Request for Application

instruments, associated supplies, instructions, and training to use the technology at no cost to the GHDx Center.

2. Contingent upon successful laboratory evaluation, the GHDx Center will design, implement, and manage a field evaluation conducted in collaboration with the grantee organization. Funding for the field evaluation will be made to a third-party subcontractor, not directly to the grantee. The level of funding available for this work is dependent upon the specific requirements and scope of the work envisioned, and on the number of technologies selected for evaluation. It is anticipated that the value of the field evaluation will be more than \$125,000.
3. Direct financial support to each grantee organization will not exceed \$50,000 over a two-year period. This funding includes both direct and indirect costs. Funds will be awarded based on mutually agreed-upon milestones, as negotiated with the grantee prior to award. The GHDx Center reserves the option of accepting partial components of an application if appropriate. The GHDx Center reserves the right to discontinue funding at specified performance milestones. Grant funds may be used to support personnel and travel and purchase equipment, supplies, and services directly related to the project.

IV. Eligibility

A. Eligible Institutions

- Applications may originate from for-profit and nonprofit organizations; or from public and private institutions, such as universities, colleges, and laboratories; domestic (US) or non-domestic (non-US) entities (foreign organizations); eligible agencies of the federal government; faith-based or community-based organizations; or others within the eligibility guidelines of the NIH.
- Institutions must be willing to and demonstrate the capacity to meet NIH funding requirements. See <http://grants.nih.gov/grants/policy/nihgps%5F2003/>

B. Eligible Project Directors/Principal Investigators (PD/PI)

- Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution to develop an application. Individuals from under-represented racial and ethnic groups as well as individuals with disabilities are encouraged to apply.

V. Application Evaluation Criteria

Applications that are complete and responsive to the solicitation will be evaluated for scientific and technical merit by GHDx Center staff. Please **do not** contact NIBIB/NIH regarding this solicitation or evaluation. Applications will be scored according to the criteria defined below.

The overall application score will be based on review and merit of the individual components as well as the merit of the application taken as a whole. All areas will be considered to have equal importance in the review process. Application components will be evaluated on the following basis:

Instructions for Responding to the Letter of Intent and Request for Application

General:

- Completeness of response to the solicitation.
- Consistency with the objective described in this solicitation.
- Technologies that meet a need in LRS.
- Strength of the team to successfully complete the proposed scope of work.

Technical merit and feasibility of the technology will be determined by the following:

- Analytical sensitivities, specificities, or dynamic ranges of detection for a model analyte system should have been already determined on existing prototypes.
- Technologies should have a viable pathway to commercialization, but not be currently available in LRS (may be available in the developed world).
- Applicants should have the ability to manufacture devices for evaluation (hundreds up to low-thousands).
- Appropriateness/specifications of expected final technology to LRS:
 - Expected infrastructure requirements such as water, power, and refrigeration.
 - Expected training requirements for the targeted end users.
 - Instrument maintenance requirements, if any.
 - Improvement of diagnostic result turnaround time for the health care provider, if applicable.
 - Reduction of current testing costs.
 - Applicable to more than one disease or pathogen target of high clinical priority in LRS.
- Other factors that may be considered are:
 - Co-funding or leveraging opportunities of current activities.
 - Direct or indirect involvement and engagement of stakeholders in LRS.
 - Cost to manufacture and perceived future affordability.

VI. Instructions for Responding to the Full Application

A. GHDx Center Contacts

Technical/Program Contact: Matthew Steele PhD, MPH, Program Officer, PATH
Email address: dxcenter@path.org

B. Applicants

Applications will be accepted only from those invited to submit them after successful completion of the LOI process.

C. Fact-Finding Questions

Review the application form and read this solicitation document in its entirety. Questions on this solicitation from those completing a full application will be accepted via email to the contact listed above through the due date listed in I. Summary of Deadlines above. Questions and answers to all questions will be provided to applicants by email. Additionally, questions and answers will be posted on the DxCenter web site under the frequently asked questions section.

Instructions for Responding to the Letter of Intent and Request for Application

Please note that responses will **not** be confidential except in cases where proprietary information is involved. Inquiries received after the due date cannot be accommodated.

Send any questions to dxcenter@path.org.

D. Forms and Format

Application form:

Complete the application form and respond to all information requested.

Budget form:

Attach the completed budget form with a brief budget narrative. Provide itemized costs for the total scope of work proposed. Budgets should include itemized costs for key elements of the scope of work in the following categories:

- **Personnel.** Include the salary rates of key staff and level of effort on the project for each, expressed in percentage of full-time effort.
- **Fringe Benefits.** Explain what is included in your fringe benefit costs. Note that leave should be included in personnel costs.
- **Equipment.** Describe costs and the purpose of equipment required to carry out the scope of work.
- **Supplies.**
- **Travel.** Itemize all anticipated travel (number of trips, travel costs per trip, per diem costs per trip (days x per diem rate), and estimated associated costs.
- **Other Expenses.** Itemize all other expenses not listed in the categories above.
- **Indirect Costs.** Provide the basis for any indirect cost rate, such as summary financial basis or a negotiated indirect cost agreement with a cognizant US agency, if available. Indirect rates are subject to verification prior to award.

Note:

Subcontracts by the grantee to a second party are not allowable under this award. With the exception of the American University of Beirut and the World Health Organization, full facilities and administrative (F&A) costs will not be allowed for non-US grantees. However, NIH provides limited F&A costs (8% of total direct costs less equipment) to foreign institutions and international organizations to support the cost of compliance with NIH requirements including but not limited to protection of human subjects, animal welfare, and research misconduct. NIH will not support the acquisition of, or provide depreciation on, any capital expenditures or support the normal, general operations of foreign and international institutions.

E. Attachments to Application Form

- Reference list.
- Budget form and budget narrative.
- Letter of support from leading institution.
- Curriculum vitae of all key staff (including the principal investigator) from the applicant institution.

Instructions for Responding to the Letter of Intent and Request for Application

The GHDx Center will not consider attachments other than those specifically requested in the solicitation. Elaborate materials, artwork, or other information not directly related to the scope of work are discouraged.

F. Full Applications Due: June 12, 2009

Submit the completed application form, with supporting materials and attachments electronically in a Microsoft document or as a PDF file to dxcenter@path.org by May 29, 2009.

The subject line of the email should read: "GHDx Application (name of applicant)." We advise that you send files in commonly recognized Microsoft formats or as PDF files. We will not accept responsibility for resolving technical transmission problems associated with applications. Applications received after this due date may not be accepted.

G. Due Diligence Process

As part of the overall selection process, the GHDx Center reserves the option to discuss specific details with those applicants who are finalists for awards. The GHDx Center will select promising finalist applications to undergo a due diligence review process prior to project selection and initiation of collaborative activities. This process will likely involve an in-person visit by GHDx Center staff to assess organizational capacity and to verify the appropriate maturity of the candidate technology for evaluation purposes. Optional interviews with applicants will be held at the discretion of the GHDx Center.

H. Conclusion of Process

The anticipated date that applicants will be notified of the GHDx Center's decision is listed in the Summary of Deadlines section above. The final award is subject to the terms and conditions included in this solicitation, as well as successful final negotiations of all applicable terms and conditions affecting this work.

I. Application Checklist

- Complete the application form. Do not leave any requests for information blank.
- Attach a description of the technology (6 pages, including figures and tables).
- Submit a list of references as cited in the detailed technology description.
- Complete the budget form and provide a budget narrative for each line item and the indirect costs.
- Submit a letter of support from the leading institution or directorship of the private entity.
- Submit curriculum vitae of all key staff (including the principal investigator) from the applicant institution.

Note: All text should be in 11-point type.

Instructions for Responding to the Letter of Intent and Request for Application

VII. PATH Statement of Business

PATH is an international, nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being.

Headquartered in Seattle, Washington, PATH has 34 offices in 19 countries. PATH currently works in more than 70 countries in the areas of health technologies, maternal and child health, reproductive health, vaccines and immunization, and emerging and epidemic diseases.

For more information, please visit www.path.org.

VIII. Terms and Conditions of the Solicitation

As the managing body of the GHDx Center, PATH has set forth the following terms and conditions:

A. Notice of Nonbinding Solicitation

PATH reserves the right to reject any and all applications received in response to this solicitation and is in no way bound to accept any application. We additionally reserve the right to negotiate the substance of the finalists' proposals, as well as the option of accepting partial components of a proposal if appropriate.

B. Confidentiality

All information provided as part of this solicitation must be treated as confidential. In the event that any information is inappropriately released, PATH will seek appropriate remedies as allowed.

Applications, discussions, and all information received in response to this solicitation will be held as strictly confidential, except as otherwise noted.

All full applications will be reviewed by the GHDx Center's scientific subcommittee. The final two applications will be selected for funding and will be subject to review and approvals by the NIBIB Point-of-Care Centers' Steering Committee.

C. Communication

All communications regarding this solicitation shall be directed to appropriate parties at PATH. Contacting third parties involved in the project, the review panel, or any other party may be considered a conflict of interest and could result in disqualification of the application.

D. Acceptance

Award of an application does not imply acceptance of its terms and conditions. PATH reserves the option to negotiate on the final terms and conditions. We additionally reserve the right to

Instructions for Responding to the Letter of Intent and Request for Application

negotiate the substance of the finalists' applications, as well as the option of accepting partial components of an application if appropriate.

E. Right to Final Negotiations

PATH reserves the option to negotiate the final costs and final scope of work and also reserves the option to limit or include third parties at PATH's sole and full discretion in such negotiations. PATH reserves the option of accepting partial components of an application if appropriate. PATH reserves the right to discontinue funding at negotiated performance milestones.

F. Third-Party Limitations

PATH does not represent, warrant, or act as an agent for any third party as a result of this solicitation. This solicitation does not authorize any third party to bind or commit PATH in any way without our express written consent.

G. NIH Terms of Agreement, Regulations, Assurances, and Guidelines

All awards are subject to NIH terms of agreement, regulations, assurances, and guidelines.

For NIH terms of agreement please review:

<http://grants.nih.gov/grants/policy/nihgps%5F2003>

For NIH requirements involving research using human subjects please review:

<http://grants.nih.gov/grants/policy/hs/index.htm>

For NIH requirements involving the use of vertebrate animals in research please review:

<http://grants.nih.gov/grants/olaw/olaw.htm>

For NIH guidelines involving the use of recombinant DNA for research purposes please review:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html>