REQUEST FOR LETTERS OF INQUIRY

REQUEST FOR LETTERS OF INQUIRY – DEVELOPMENT OF A RAPID IMMUNITY ASSESSMENT TOOL

SUBMISSION DEADLINE: MARCH 27, 2012 10:00 AM PST

BILL & MELINDA GATES *foundation*

OVERVIEW

Document Purpose

The purpose of this Request for Letters of Inquiry ("***RFLOI"***) is to solicit letters from interested parties/recipients *("**Recipient**")* so that the Bill & Melinda Gates Foundation (the "***Foundation***") may identify potential candidates for the development of an easy-to-use tool that rapidly assesses immune status of children against select vaccine-preventable diseases. Inquiries will be welcome that focus on prototype development, and which detail plans for future commercialization possibilities.

About the Bill & Melinda Gates Foundation

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life. Based in Seattle, the Foundation is led by CEO Jeff Raikes and co-chair William H. Gates Sr., under the direction of Bill and Melinda Gates, and Warren Buffett.

Project Background

The Foundation is focused on ensuring that all children in the developing world receive a full complement of available vaccines, protecting them against a range of vaccine-preventable diseases. The Foundation endorses and strives for the goal outlined by the Global Immunization Vision and Strategy (GIVS), of at least 90% vaccination coverage in every country, and at least 80% coverage in every district.

Regular measurement of vaccination coverage across the developing world is important to measure progress against coverage goals, and to identify areas of weakness in delivery systems so that corrective action can be taken. Current tools and processes to measure vaccination coverage have significant limitations, leading to estimates of coverage with questionable precision.

This RFLOI will solicit proposals from organizations to develop a prototype and detail a commercialization plan for an immunity assessment tool that can help more accurately measure vaccination coverage in the developing world.

Existing Tools/Processes and Basis for Contract:

We have summarized some of the main tools and processes *currently* utilized for assessing vaccination coverage in the developing world along with key limitations of each:

- *Administrative coverage reports*. These are reports which are generated by each country, and which are aggregated from administrative data reported at the district level and below. The data are based on a tally of vaccinations given in a defined "catchment"

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

area. Coverage estimates derived from these data are usually inaccurate (at times grossly inaccurate) because of inflation of numbers and the uncertainty in denominator estimates (i.e. the estimated population of surviving infants.)

- *Household surveys*. Periodically, surveys are conducted of households to determine if children in a target age group in the household received the appropriate vaccines. These surveys utilize sampling techniques such as cluster surveys, or lot quality assurance sampling (LQAS). These techniques try to ensure sub-populations are captured in estimates and results may be less affected by inaccurate census data. However, in many low-income countries regions may be inaccessible to survey teams due to political insecurity and/or geographic constraints. Another challenge is that surveys rely on parental recall of the vaccines administered (which are frequently inaccurate) and/or home-based vaccination cards (which are not universally distributed or retained, may not be brought to each immunization visit to be updated, and may not be correctly filled in).

- *Serosurveys*. These surveys consist of collecting blood samples from children in the target age group and testing for the presence of antigen-specific antibodies. This involves transporting the samples using a reverse cold chain to a central laboratory where serum is separated and assayed for the presence of antigen-specific antibodies. For infections such as tetanus and measles, there are data on the antibody concentration which correlates with protection against infection or disease. These tests can determine protection against disease, which can uncover additional information on the performance of a vaccination system (e.g., poor handling of vaccines if seroprevalence is low in areas where coverage is known to be high). However, serosurveys have significant limitations. For infections other than tetanus (for which there is no natural immunity) and hepatitis B (a subunit vaccine), current assays are not able to distinguish between antibodies resulting from vaccination and those resulting from infection, thus the use of antibody assays to validate coverage in areas where infection is prevalent is challenging. The need to collect blood samples can also lead to low participation rates in surveys, and the process to collect the samples and analyze them in a specialized lab is time-consuming and sometimes complex.

The goal of this RFLOI is to significantly improve on these tools and processes in terms of accuracy of results and/or ease of use in the field.

Objective of RFLOI:

The purpose of this RFLOI is to solicit inquiries toward the development of a prototype and the detailing of a commercialization plan for a tool that rapidly assesses the immune status of children against selected vaccine- preventable diseases (e.g. tetanus,measles, etc.). The ideal tool would be low cost,easy to use in the field, and on a large scale, by those working in national immunization programs. This tool would be used as an adjunct to current vaccination coverage surveys - to help more accurately determine/validate coverage levels and assess

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

population-level immunity. Letters of inquiry should address how the potential recipient would develop a prototype tool and create a plan for commercialization.

The target parameters are as follows:

- The Foundation expects to invest up to $6 million US toward this project over a three-year period. It is likely that the total amount awarded will be split between a number of grant recipients, with varying award amounts based on project scopes and timing. Ideally, prototype development will be complete by the end of 2013. The commercialization plan should detail how the product could be produced at scale by 2015.

- Key desired characteristics are summarized below. It is important to note that these are ideal characteristics of an immunity assessment tool. Potential recipients will not be excluded if one or more of the characteristics cannot be achieved. In fact, all organizations are encouraged to apply, even if several characteristics cannot be met.

    - Test should sample oral fluid
        - An acceptable alternative would be a test utilizing samples of very small volumes (<100 microliters) of whole blood (obtainable from a quick finger/heel stick sample) to measure antibody levels
    - Sample collection should be rapid (< 1 minute per child)
    - Sample collection should be feasible in young children aged 6 months and above
    - Test collection should be as simple as possible, assuming use by minimally trained personnel
    - Immediate point of care (POC) results are ideal
        - An acceptable alternative would require the transport of samples without a cold chain to a central laboratory within the same country, where assays would be conducted ("sample and send")
    - Sample collection must be feasible in low income countries in a variety of climates, ranging from sub-zero to tropical temperatures
    - As with test collection, the reading and interpretation of results should be simple to understand and not rely on subtle visual cues (e.g. minimal color change) that can be misinterpreted
    - If a device is required along with collection instrument, it should be inexpensive small, durable, and simple to use
    - Test should be safe (i.e., easy to avoid contamination)
        - Designed so additional safety wear is minimal or not required
        - A used kit should be easily identifiable
        - A used test should have clear route for safe disposal
    - Test should assess IgG antibody levels against, at a minimum, tetanus toxoid. Ideally, polio and measles should also be included. The potential to add other antigens, such as *Haemophilus infuenzae* type b and hepatitis B, to this platform should be described in the proposal. All assays should be done from a single sample andutilize one collection device.

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

- Test results should indicate if IgG levels measured are above or below currently accepted standards for protection against infection and disease
- If the test is done on oral fluid, results should be validated against concurrent antibody measurements from serum (to ensure against a false negative result due to insufficient IgG in the oral fluid sample).
- Cost of test should be inexpensive, allowing for procurement and introduction into developing country immunization programs. Applicants should provide estimates of productions costs at different volumes.

The Foundation will invite select applicants to submit full proposals based on a scored review of the letters of inquiry. Proposals will be assessed by a panel of internal and external reviewers according to the criteria laid out in the section entitled "Assessment of Letters of Inquiry" below.

Execution of Agreement and Related Issues:

Funding Modes: Generally, the Foundation funds projects such as this one through grants. In some circumstances, the Foundation may determine that an alternative funding mechanism such as Program Related Investment (PRI) is appropriate.

The funding mode and terms will be determined by the Foundation taking into account various factors including the final partnership model and Foundation/Recipient requirements such as charitable intent, legal requirements and tax requirements.

Data Sharing: Depending on the final funding agreements, we may require confidential access to details of technologies employed as well as production costs, at the time of funding and/or at a future date as a condition of funding.

Assessment of Letters of Inquiry:

Proposals will be evaluated by a **panel of Foundation and non-Foundation staff using the criteria described below:**

1. Potential of the technology
    a. Potential of proposed technology to deliver on target product profile as outlined above and to be utilized within structures and conditions of the developing world

1. Organizational capability and technical capabilities of the proposed team
    a. Experience in developing and using antibody assays
    b. Project team experience with antibody detection technologies

2. Application Quality
    a. Overall quality of application, including recommended approach, insight and recommendations on how to tackle complex issues, including Global Access

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

requirements. Identification of key challenges and their impact on deliverables and results (e.g., feasibility in developing world, regulatory, and manufacturing)

Global Access and Intellectual Property

Since the output of this program may lead to innovative technologies and/or products that will result in improved diagnostics for those that need of them most in the developing world, the successful development of these high priority products may require substantial involvement and support of private-sector industries as sub-contractors, and may also involve collaborations with multiple organizations, including academic and/or non-profit research institutions. It is the intent of this program to support the formation of appropriate public-private partnerships that are essential to meet these urgent global health needs. Intellectual property (IP) rights and the management of IP rights are likely to play an important role in achieving the goals of this program. To this end, the foundation requires that, even at the LOI stage, all applicants seriously consider their willingness to submit a full proposal in compliance with the foundation's proposal guidelines, a portion of which asks for certain information and intentions regarding intellectual property and global access concerns. Specifically, the Bill & Melinda Gates Foundation requires that you agree to use good faith efforts to conduct and manage the research, technologies, information and innovations involved in the Project in a manner that enables (a) the knowledge gained during the Project to be promptly and broadly disseminated, and (b) the intended product(s) to be made available and accessible at reasonable cost to the developing countries of the world. The Foundation refers to this as "Global Access."

As part of the foundation's review and evaluation of each full proposal, due diligence will be conducted with respect to each participant's ability and commitment to manage intellectual property in a manner consistent with the stated scientific and charitable goals of the Bill & Melinda Gates Foundation. Due diligence activities may include inquiry into an applicant's:

1) Freedom to operate and ability to freely use and acquire needed background technology;

2) Commitment to share data and technology with other participants to facilitate the development of a common set of technical and business standards regarding tools that rapidly asses the immune status of children against selected vaccine-preventable diseases;

3) Commitment to promote the utilization, commercialization and availability of inventions for public benefit in developing countries; and

4) Business plan for the development and sustainable commercialization of the rapid immune assessment tools developed as part of this program.

In order to facilitate this due diligence process applicants are encouraged to provide information with respect to items 1-4 above in their submission materials.

Applicants and their collaborators will be required to participate in the creation of a Global Access Strategy in an effort to codify their commitment to achieving the stated scientific and

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

charitable goals of the Bill & Melinda Gates Foundation to promote the utilization, commercialization, and availability of inventions for public benefit in developing countries. The Global Access Strategy will include provisions for the management and use of intellectual property, know-how and technologies to facilitate collaboration with other participants in this program with the goal of developing and delivering viable tools that rapidly asses the immune status of children against selected vaccine-preventable diseases.

Applicants are also expected to make new information and materials known to the research and medical communities in a timely manner through publications, web announcements, progress reports to the foundation, and other appropriate mechanisms. These concepts may be discussed at some length with the applicants that are invited to submit full proposals, and will be addressed (to the extent appropriate) within each final grant agreement.

RESPONSE GUIDELINES

Response Instructions

Please adhere to the following instructions when responding to this RFLOI:

- All questions must be answered in order for Recipient to be considered for this RFLOI.
- Recipients or their representatives may not contact anyone else within the Foundation regarding this RFLOI during the application process. All communication relating to the RFLOI, including questions and clarifications, should be submitted via email to the Foundation at gh.immunity@gatesfoundation.org.

RFLOI Response Requirements:

Please refer to the LOI Instructions document for detailed response requirments and instructions for formatting and submitting the LOI.

1. In order to minimize time and cost for Recipients, while allowing for sufficient data for review, letters of inquiry (LOIs) should be not more than five pages in length. Additional information will be requested from respondents who best meet the evaluation criteria.

2. In addition to the LOI, respondents may include materials such as standard company brochures and biographical information/qualifications of 3-5 key project staff.

3. Detailed description of proposed technology to rapidly detect presence of antibodies/antitoxins in human specimens (e.g., oral fluid).

4. Proposed product specifications in the form of a target product profile (see sample).

5. Development plan to achieve these specifications.

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

6. Detailed description of currently available immunity test against which prototype will be compared and process of conducting comparison.

7. Process to determine if product can be effectively utilized within developing country immunization programs, including issues around thermostability.

8. Proposed plan to secure supply of reagents.

9. Outline of commercialization plan, including plan for manufacturing, distribution, licensing, and adoption by key stakeholders.

10. Address any major risks, contingencies or partnerships required to achieve goals.

11. Provide estimates of cost per unit of tool once developed and commercialized under a variety of manufacturing and volume assumptions.

In addition to the project scope as described above, Recipient's response should address the following:

- What unique capabilities, technologies or know-how does your firm or organization have that are relevant for this project?
- What experience does Recipient have in working with the Foundation?
- Provide a list of similar technologies developed and/or commercialized by your firm or organization.

Response Delivery Instructions

LOIs must be submitted electronically, using the forms and process described at the following address:https://unison.gatesfoundation.org/Applicant/_layouts/Portal/Applicants/ApplicationForm.aspx?RequestId=b586027d-6b1c-e111-bb06-0019b9f2848b.

All LOIs must be submitted by 10:00 am PT on Tuesday, March 27, 2012. Late submissions may not be considered. If you anticipate difficulty in meeting this deadline, please e-mail: gh.immunity@gatesfoundation.org.

Foundation Contact

Foundation staff will be available to answer questions about this RFLOI until 10:00 am PT on Tuesday, March 27, 2012. Please submit any questions to: gh.immunity@gatesfoundation.org.

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

Timetable

The evaluation and selection process will adhere as closely as possible to the following schedule. However, the Foundation may modify this schedule at its sole discretion.

Event	Timeframe
Response Due Date	Tuesday, March 27, 2012, 10:00 am PST
Follow-up and Notification	Friday, May 11, 2012
Follow-up Consultations	Monday, May 14, 2012 – Friday, June 1, 2012
Proposal Selection	Friday, June 8, 2012

Intent and Disclaimer

This RFLOI is made with the intent to identify a Partner to deliver results as described above and in other areas of this RFLOI. The Foundation will rely on Partner's representations to be truthful and as described. The Foundation assumes it can be confident in Partner's ability to deliver the product(s) and/or service(s) proposed in response to this RFLOI. The response will be incorporated into a future agreement should the Foundation wish to enact the proposed agreement.

This RFLOI is not an offer to invest/partner. The Foundation assumes no responsibility for cost incurred in responding to this RFLOI. All responses shall become the property of the Foundation upon submission.

If the Foundation amends the RFP stemming from the RFLOI, copies of the amendments will be sent to all Recipients selected for this RFP.

Release

Recipient understands that the Foundation has chosen to solicit responses from a number of parties, and that submission of a response does not guarantee that the Foundation will enter into a new agreement with, or continue any current contract(s) with respondents.

Recipient agrees that the Foundation may, in its sole discretion: (1) amend or cancel the RFLOI, in whole or in part, at any time; (2) extend the deadline for submitting responses; (3) determine whether a response does or does not substantially comply with the requirements of the RFLOI; (4) waive any minor irregularity, informality or nonconformance with the provisions or procedures of the RFLOI; (5) negotiate with any and all respondents the Foundation deems acceptable; (6) issue multiple awards; (7) share responses generated by this RFLOI with consultants and experts whom the Foundation may retain to help it evaluate them; and (8) copy the responses. Recipient also agrees that all responses become the property of the Foundation.

In exchange for the opportunity to be awarded a contract, Recipient agrees to not bring a legal challenge of any kind against the Foundation relating to the Foundation's selection and award of this contract, even if Recipient is not awarded a contract.

Recipient represents that it has responded to the RFLOI with complete honesty and accuracy. If facts provided in Recipient's response change, Recipient agrees to supplement its response in

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org

writing with any deletions, additions or changes within ten days of the changes. Recipient will do this, as necessary, throughout the selection process. Recipient understands that any material misrepresentation, including omissions, may disqualify it from consideration for a contract award.

Recipient understands that it may receive proprietary and confidential information from the Foundation during the RFLOI process ("***Confidential Information***"). Recipient agrees to not use Confidential Information for any purpose other than its participation in the RFLOI process and to not reveal Confidential Information directly or indirectly to any other person, entity, or organization without the prior written consent of the Foundation. Recipient further agrees to exercise all reasonable precautions to maintain the proprietary and confidential nature of Confidential Information.

PO Box 23350, Seattle, WA 98102, USA V 206/709.3100 F 206/709.3180 www.gatesfoundation.org