



Grand Challenges Canada
Grands Défis Canada

Grand Challenges Canada

and the

Grand Challenges in Global Health

Initiative of the Bill & Melinda Gates Foundation

REQUEST FOR PROPOSAL

***To develop technologies that help assess
multiple conditions or pathogens at point-of-care***

Executive Summary

Grand Challenges Canada and the Grand Challenges in Global Health initiative of the Bill & Melinda Gates Foundation are partnering on an initiative, directed primarily at researchers in low- and middle-income countries, that seeks to create a new class of point-of-care (POC) diagnostics that will be easy to use, low cost, multiplexed and able to assess disease stage and provide information on prognosis.

The ultimate aim of these new tools is to achieve significant positive health impacts and rapid uptake in resource-poor settings. The main participants in this Phase I will be Component Builders who will advance the state of the art in component technologies. In a subsequent Request for Proposal (RFP) for Phase II, in addition to Component Builders, the key participants will be System Integrators who will take the best available component technologies and integrate them into viable POC diagnostic platforms. A distinguishing feature in this RFP is its targeting primarily to researchers from, low- and middle-income countries, and the proposed funding of research to understand the biological, social, and environmental factors that affect implementation and scaling up of the POC technologies to achieve sustained health improvements in the “real world.”

In addition to the \$30 million USD announced in December 2009 by the Bill & Melinda Gates Foundation, this RFP adds up to \$12 million Canadian to be awarded over three years in this Phase I. The topic areas are 1) Sample collection, concentration, and preparation; 2) Amplification and detection technologies; 3) Readout and signal transduction; 4) Enabling technologies for diagnostics; and 5) Implementation research for POC diagnostics

Phase I

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1 INTRODUCTION

Grand Challenges Canada and the Grand Challenges in Global Health initiative of the Bill & Melinda Gates Foundation are partnering on an initiative that seeks to create a new class of point-of-care (POC) diagnostics that will be easy to use, low cost and otherwise appropriate so that these new tools achieve significant impact and rapid uptake in resource-poor settings. In December 2009 the Bill & Melinda Gates Foundation announced a request for proposals (RFP) “to develop technologies that help assess multiple conditions or pathogens at point-of-care” (www.grandchallenges.org/diagnostics/Pages/Introduction.aspx).

This is a complementary RFP aimed at investigators from low- and middle-income countries which represents an initial step in the partnership between Grand Challenges Canada and the Bill & Melinda Gates Foundation on point-of-care diagnostics. This new RFP will contain an additional component, namely the opportunity to submit proposals under the new topic area of implementation research for point-of-care diagnostics, as well as additional elements, namely a proposal development grant, workshop, and other measures, aimed to attract and assist applicants from low- and middle-income countries. Grand Challenges Canada and the Bill & Melinda Gates Foundation will foster alignment and collaboration across the two RFPs to create a single community of global investigators on point-of-care diagnostics.

1.1 Grand Challenges Canada (GCC)

In the 2008 Federal Budget, the Government of Canada announced the Development Innovation Fund that will:

...
“support the best minds in the world as they search for breakthroughs in global health and other areas that have the potential to bring about enduring changes in the lives of millions of people in poor countries.”

“For example, new vaccines and cures could save millions of lives lost to tropical diseases. Higher-yield, drought-resistant crops could prevent future famines. And lower-emission energy sources could power industrial development and job creation with a minimal carbon footprint.”

Grand Challenges Canada (GCC), a new Canadian not-for-profit organization, is the vehicle to deliver the Development Innovation Fund, in a consortium with the International Development Research Centre (a Canadian Crown corporation); and the Canadian Institutes of Health Research (a Government of Canada agency). Grand Challenges Canada is hosted by the McLaughlin-Rotman Centre for Global Health (University Health Network and University of Toronto).

The **vision** of Grand Challenges Canada is to develop a consortium of world-leading Canadian and International scientists, research organizations, and leaders from the business sector, to develop breakthrough solutions to global challenges and ensure that these solutions are available to those who need them the most.

Grand Challenges Canada's **mission** is to identify global grand challenges, fund a global community of researchers and related institutions on a competitive basis to address them and support the implementation/commercialization of the solutions that emerge.

Grand Challenges Canada's core **values** include: Scientific Excellence, Collaboration and Partnership, and Accountability for Results.

In this RFP, Grand Challenges Canada and the Bill & Melinda Gates Foundation are continuing the mission set forth in the Grand Challenges in Global Health initiative (www.grandchallenges.org/Pages/default.aspx) and continuing to invest in solutions to Grand Challenge 14: *Develop Technologies that Allow Assessment of Multiple Conditions and Pathogens at Point of Care*. Specifically, we seek to create a new class of point-of-care (POC) diagnostics that will be easy to use, low cost and otherwise appropriate so that these new tools achieve significant impact and rapid uptake in resource-poor settings.

1.2 Background

In the developing world, tools are not available to easily and accurately assess a person's health status, and the risks of various illnesses and treatment options. In addition, little information about the burden of disease is available to guide population health decisions. This severely affects the care that people receive. A solution, according to studies conducted by the Diagnostics Forum¹, is to move toward a common point-of-care (POC) diagnostic platform for global health. POC diagnostics are not only intended to be used in a laboratory or clinic by a trained user. They can also be operated by minimally trained community health workers in settings that have limited infrastructure. The platform we envision will have the ability to assess multiple pathogens and health conditions using a set of common technical, logistical, and medical decision-making approaches. The combination of 1) a point of decision test, and; 2) a common platform, will ultimately result in better health outcomes.

The challenge for these POC diagnostic platforms for global health is to define and achieve the needed performance characteristics of rapid, accurate assessment of individuals' health status, including robust, simple-to-use technologies for achieving parallel, multi-pathogen, reliable and valid clinical measures in developing world settings. High throughput approaches to genomics, proteomics, metabolomics and the measurement of other analytes, coupled with novel technologies of miniaturization and multiplexing create the possibility of radically new ways to detect and diagnose health and disease states in individuals, even in remote or impoverished settings with limited infrastructure. The coupling of new and existing validated biomarker signatures with microfluidic platforms could place effective diagnostics within reach of users with minimal training in the developing world.²

¹See set of call to action papers in Nature Supplemental at <http://www.nature.com/diagnostics>

² *Requirements for high impact diagnostics in the developing world*, Mickey Urdea et al., Nature S1, pp 73-79 (23 November 2006). doi:10.1038/nature05448

Improved diagnostics platforms hold the benefit of potential:

- Unequivocal identification of pathogen type and subtype
- Rapid assessment of susceptibility and immunity to health threats
- Rapid diagnosis of exposure and disease
- Rapid detection of emerging pathogens
- Rapid parallel diagnosis of multiple infectious agents
- Accurate assessment of disease stage and prognosis
- Better detection and management of outbreaks and emerging acute and chronic health threats
- Quantification of disease incidence in endemic countries

1.3 Program Goal

We seek to create point-of-care (POC) diagnostic platforms that share common standards for use, development and integration. This will enable diagnostic devices that are lower cost, easier to use, more readily accepted, more thoroughly disseminated and more appropriate for health care in the developing world.

We hope to achieve the design and initial proof-of-principle for a POC diagnostic platform with a target product profile that includes the following characteristics:

- Quick time-to-answer
- Simple readout
- Low cost
- Good sensitivity and specificity
- Able to be used by minimally trained personnel
- The ability to function above 30 °C and at high humidity
- The ability to be stored for long periods of time without refrigeration
- The ability to conduct tests without the need for local reagents/water and/or specialized laboratory equipment
- The ability to detect multiple pathogens or to distinguish between different pathogens and/or strains and subtypes
- The ability to assess disease stage and provide information on prognosis using host biomarkers

1.4 Key Objectives

In order to create common point-of-care (POC) diagnostic platforms with common performance, training and logistics aspects suitable for low resource settings, it is important to achieve the following objectives:

1. Develop a framework for collaboration by recommending a common set of technical and business standards for the development and integration of POC diagnostics components
2. Advance the state of the art in critical component technologies consistent with the business and technical standards developed under this program

3. Integrate best-in-class component technologies into POC diagnostic platforms under the framework of standards developed in this program
4. Understand the biological, social, and environmental factors that affect implementation and scaling up to achieve sustained health improvements in the “real world.”³

The current Phase of this effort will be focused mainly on achieving Objectives 1 and 2: developing standards related to component integration, user experience and logistics requirements and conducting proof-of-principle investigations into component technologies, and Objective 4: implementation research.

1.5 The Role of Collaboration

There will be three groups working to achieve the objectives of this overall program (i.e. in Phases I and II).

- A Science and Technology Advisory Group (STAG), with representation from low- and middle-income countries (LMICs), will be responsible for developing a framework for collaboration by recommending a common set of technical and business standards for the development and integration of diagnostics components. For a more detailed description of the STAG, please refer to Appendix A.
- Component Builders (CB) who will advance the state of the art in critical component technologies. This will be done consistent with the business and technical standards developed by the STAG.
- Systems Integrators (SI) who collaborate with Component Builders (both from within and outside of this program) to develop new POC diagnostic platforms consistent with the standards developed by the STAG.

This current Phase will include Component Builders (CB) who will advance the state of the art in component technologies. In the latter Phase II, Systems Integrators (SI) will work with Component Builders (CB) to integrate the best-in-class component technologies into viable POC diagnostic platforms. Some organizations may have the capacity to participate at both levels. The STAG will be active through both phases in creating a common set of standards allowing the Component Builders and System Integrators to collaborate on novel platforms. The STAG will operate concurrently with Phase I Component Builders.

Group	Acronym	Function
Science &	STAG	Objective 1 - Provide framework for collaboration by

³ see Temina Madon, Karen J. Hofman, Linda Kupfer, Roger I. Glass. PUBLIC HEALTH: Implementation Science *Science* 14 December 2007: Vol. 318. no. 5857, pp. 1728 - 1729

Technology Advisory Group		creating common set of technical and business standards
Component Builders	CB	Objective 2 - Advance the state of the art in critical component technologies
System Integrators	SI	Objective 3 - Integrate best-in-class component technologies into competing diagnostic platforms

1.6 Advance State of the Art in Critical Component Technologies

One of the assumptions from systems engineering is that it would be possible to disaggregate the complex diagnostics research and development problem into more manageable and focused challenges. This new *Grand Challenges* effort has been structured in such a way that individual research groups can submit proposals that provide best-in-class innovations for each of the key components. Those groups will be encouraged to focus their efforts on significant innovations on the key components that limit performance. This RFP is designed to allow Component Builders to play to their strength(s) in component technologies without having to rush into suboptimal integration of solutions to the POC diagnostic platform. The main goal of the Component Builder will be to show proof-of-principle operation and data for their component technology. As long as the component is optimized while conforming to the standards being defined by the STAG, the technology will be compatible with any future platform built upon this concept. Also, in keeping with the spirit of this program, the Component Builders will be encouraged to collaborate with each other, including both participants funded from this current RFP and the RFP previously announced by the Bill & Melinda Gates Foundation in December 2009.

1.7 Integrate Component Technologies into Platforms

We hope to have a sizable number of component technologies that will operate in a “plug-and-play” fashion, allowing Systems Integrators to work with Component Builders to create optimized platforms based on best-in-class component technologies, but also paying attention to the requirements of forming a target product profile from the platform concept. We are not currently setting a specific cost target; however, the Systems Integrators will have to understand the interplay between the cost of goods for instrumentation, cost per test for consumables, and costs for reagent storage, distribution and disposal. The ease-of-use metric may include automation, lowering the need for trained personnel, easy interpretation of results, and streamlined workflow for batch processing. Goals for minimal infrastructure may include minimizing needs for electricity and water, and little or no supporting lab instrumentation like centrifuges, microscopes, thermocyclers, or autoclaves. By trying to meet all these requirements, we can better ensure the adoption of the POC diagnostic platform for developing world applications.

1.8 Collaborative Framework

In parallel to the funding of the individual technical innovations, we will fund through a separate activity the convening of a group of diagnostics and standards setting experts as a Science and Technology Advisory Group (STAG) to develop a common set of technical and business standards that will guide the Phase II call for proposals. The STAG will recommend common standards of component integration, performance and user experience to help reduce regulatory and business obstacles to collaboration and product uptake. Through this process, we will ensure the groups funded under this initiative (as well as other stakeholders we may identify) agree to common standards for overall performance and interfaces between the components and agree to a common Global Access Strategy that significantly lowers barriers for access to diagnostics in the developing world. These performance standards will allow us to compare how well one approach works against another and will permit investigators attempting to integrate comprehensive platforms to choose from alternative approaches at the component level. The interface standards should also include considerations with regard to the eventual integration with health information systems and automated, mobile communications technologies. The STAG will include members both from high income countries and the developing world where POC diagnostics for global health will find their primary applications.

2 APPROACH

2.1 Program Scope for Phase I

The focus of this request for proposal (RFP) will be exclusively on Phase I. We describe some details regarding Phase II to give applicants insight into how we will likely shape the program in years 4-6. However, due to the changing landscape for technologies, the actual implementation of Phase II may be somewhat different than what we envision today.

Length of Award: It is anticipated, subject to satisfactory attainment of negotiated milestones, that the length of the award to grantees will be three years for Phase I.

Size of Award: The total available funds to support a portfolio of responses to this *Grand Challenge* RFP are the \$30 million USD announced in December 2009 by the Bill & Melinda Gates Foundation, plus an additional up to \$12 million Canadian to be awarded under this RFP over three years in Phase I. Through this RFP, approximately 10-20 proposals will be funded. The value of the 10-20 awards is expected to vary.

Topic Areas

Each Component Builder applicant must classify his or her proposal in one of the following five Topic Areas. In the proposal, applicants must explicitly link their technical goals with a specific set of improvements they plan to achieve for the proposed component. The improvements can be described in the form of new target performance specification or in the form of desired goals. Component builders can submit more than one proposal to different Topic Areas, but each proposal should only address one Topic Area. We recognize that investigators in low- and

middle-income countries (LMICs) might have unique skills, beyond those available in high income countries, to contribute to this initiative.

2.1.1 Topic Area #1: Sample collection, concentration, and preparation (SCCP)

Sample collection, concentration and preparation are critical components for diagnostics development. Challenges in the area of **sample collection** include different protocols for sample volume, sample type (e.g. blood, urine, tissue, sputum, saliva, feces), and waste disposal. Sample volumes for infants and children are frequently limited and therefore new technologies should lower the collection volume required. In the area of **sample concentration**, we will invest in innovative approaches that are simple, require minimal reagents and power (e.g. no centrifuges). In the area of **sample preparation** extraction, separation and cleanup protocols that work across a wide variety of sample types (e.g. blood, urine, tissue, sputum, saliva, feces), require minimal to no reagents and match downstream analysis sub-systems. It is very important for the sample preparation chemistry to be compatible with downstream detection assays. For example, Component Builders should understand that downstream detection assays are potentially prone to interferents like detergents and salts, may have a narrow range of acceptable pH or temperature, need to maintain protein viability (storage), or require a certain level of DNA purity.

2.1.2 Topic Area #2: Amplification and detection technologies

In this topic area, we are looking for detection and amplification methods that advance the state of the art in terms of simplicity, performance and cost. In spite of the expected gains from advances in sample preparation, the copy numbers or concentration of target molecules available for detection will frequently remain low. Therefore, a sensitive molecular detection and analyte or signal amplification stage is likely to be needed for metabolite, nucleic acid and protein markers. One particular area of interest would be amplification methods that eliminate the need for thermal cycling. We also welcome other innovative approaches with superior characteristics such as assay ruggedness, high specificity, quick time-to-answer, reduced cost and complexity, multiplexing, and quantitation capabilities.

2.1.3 Topic Area #3: Readout and signal transduction

In this topic area, we will invest in innovative methods to transduce the recognition of protein markers, biomolecular binding events, or amplification products into detectable readout signals. We are particularly interested in platforms and technologies that enable multiplexed and multi-analyte readouts.

2.1.4 Topic Area #4: Enabling technologies for point-of-care diagnostics

Under this topic area we will invest in additional innovations in critical components including micro-fluidic handling, packaging, power management, reagent handling, waste handling, bioinformatics, and mobile health technologies not captured under the previous three Topic Areas.

2.1.5 Topic Area #5: Implementation research for point-of-care diagnostics

Under this topic area, we will invest in developing and evaluating models (including social innovations and business process innovations or business models) that will help ensure point-of-care (POC) diagnostics reach those who need them. Examples of demand side factors that

might be addressed in the development of such models could include forecasting demand to deal primarily, but not exclusively, with major infectious diseases in the developing world; understanding acceptability to patients, providers and payors; and demonstrating cost-effectiveness of POC diagnostics in specific clinical contexts. The ultimate purpose of this research would be to improve health and patient care.

2.2 Program Structure

This RFP is soliciting proposals from Component Builders from low- and middle-income countries (LMICs) for Phase I. Phase I will run for a total of 3 years with milestones proposed by each of the Component Builders that will demonstrate proof-of-principle for their technology. The Component Builders must specify which Topic Area they will work in and propose how they will improve the state of the art for that component technology. Although the Component Builders within each technical area will work largely independently from one another, they will be required to participate in the standards setting process spearheaded by the Science and Technology Advisory Group (STAG). The STAG will formulate a communications plan to disseminate the details from the standards that are being formed to the Component Builders. In addition, the STAG will offer channels for Component Builders to contribute to the development of the standards.

Near the end of Phase I, we will evaluate the component technologies within each of the technical areas for demonstration of proof-of-principle, potential for compliance to the standards created under the STAG and readiness for integration into a next generation of POC diagnostic platforms. During the course of Phase I, we will also create opportunities for collaboration between the Component Builders. (Applicants from LMICs interested in Topic Area 5 (Implementation research) need not be Component Builders themselves.)

In years 3-6, which will comprise Phase II of this initiative, we will solicit proposals to build integrated point-of-care diagnostic platforms consistent with the standards established during Phase I activities. That subsequent Phase II call for proposals will be open to all the successful awardees from Phase I, but will also be open to any prospective applicants who could deliver superior performance at either a system or component level consistent with the standards set during Phase I. It is through this combination of advancing the key technologies and developing standards under which they can be integrated and continuing innovation can be nurtured that we believe we will be able to meet our objectives for transformational point-of-care diagnostics that will meet the objectives of our development and global health missions.

3 ACTIVITIES & DELIVERABLES

The Component Builders funded under this effort will be expected to engage in the activities and provide the specific deliverables listed below. The overall goal is to deliver scientific and engineering advances on critical components to improve performance, cost, and ease-of-use metrics. In the proposal, the applicants must link their technical goals to specific improvement

in component technology and present a plan to demonstrate those improvements. In addition to engaging in investigative activities related to their component technologies, the Component Builders will be expected to:

- Refine their project plan with a proposed set of critical milestones to achieve technical goals and meet standards set through the Science and Technology Advisory Group (STAG).
- Actively participate in STAG task force for developing standards.
- Develop and commit to a Global Access Strategy consistent with the principles of Global Access described in Section 4.9 below.

The deliverables listed below will help demonstrate the project's progress and success.

- Annual progress report detailing the technical and programmatic achievements (written and site visit)
- A clear proof-of-principle demonstration described in the original proposal and documented as part of the final report. This final report will also provide detailed documentation of the technical work accomplished and success and lessons learned from Phase I projects. Instructions for the annual report and final report will be provided to selected awardees.
- Dissemination of knowledge through publications in peer-reviewed literature, patent applications, etc.

4 RULES AND GUIDELINES

4.1 Program Direction

Grand Challenges Canada and the Bill & Melinda Gates Foundation staff will be substantially involved in shaping this initiative over time. In consultation with independent external experts, our staff will review and select specific projects from among the solicited proposals. The eligibility criteria for funding are as follows:

- a) The Principal Investigator must be from a low- or middle-income country (LMIC), using the World Bank classification⁴ as a guide
- b) Principal Investigators from high-income countries, as defined by the World Bank, are not eligible
- c) It is the overall intention of this RFP to fund both LMIC applicants independently, and collaborations between LMIC and Canadian applicants. We will be developing a parallel program to match Canadian researchers with LMIC researchers. Details of this will be announced in the near future. At the stage of development of full proposals, we will

⁴<http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20421402~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html>

facilitate and encourage, but not require, partnerships between LMICs and Canadian researchers.

- d) It is not the intention of this RFP to exclude existing productive collaborations between researchers in LMICs and those in high income countries other than Canada. If scientifically justified, these collaborations may be part of a proposal. However the LMIC researcher must be the Principal Investigator and the budget would be expected to be primarily used in the LMIC.
- e) Principal Investigators from upper-middle income countries using the World Bank classification (e.g. Brazil and South Africa), as well as from lower middle income countries using the World Bank classification that are part of the G20 (e.g., India and China) will be encouraged to obtain co-funding from their own countries or elsewhere. Evidence of co-funding will be an asset, but not a requirement, at the time of judging the Letter of Intent and full proposals.

Assuming proposals of sufficient scientific merit, the level of funding requested should be adequate to assure completion of the goals in a three-year time frame for Phase I. If this program produces promising interim results, authorization will be sought to move forward with issuing a Phase II RFP prior to the end of Phase I.

Assuming a sufficient number of proposals of sufficient merit, this RFP is expected to fund between 10-20 grants of varying amounts for an aggregate total cost of up to \$12 million Canadian over three years. These grants will be in addition to the grants funded under the RFP on point-of-care diagnostics issued by the Bill & Melinda Gates Foundation in December 2009.

4.2 Application Instructions & Review Process

Full invited applications must propose clear project goal(s), including one (or more) final product(s) during the award period. The applicant must clearly state the interim objectives (proof-of-principle milestones) to be achieved during the project, identify impediments or critical decision points that could require a revision in the work plan or milestones, and provide a detailed scheduled or time line for the attainment of each milestone and/or goal.

This request for proposal (RFP) will make use of a mandatory two-step application process:

Step 1: Submission of a Letter of Inquiry (LOI) to Grand Challenges Canada.

There is a five (5) page limit on the LOI. To submit the LOI, applicants must use the template to be found at www.grandchallenges.ca. Applicant organizations submitting an LOI must fully meet the eligibility criteria listed in sections 4.1 and 4.5. Grand Challenges Canada and the Bill & Melinda Gates Foundation staff, along with external consultants, will evaluate the LOIs, in conjunction with the Canadian Institutes of Health Research, which is a member of the Grand Challenges Canada consortium and responsible for ensuring peer review. Those applicants who are eligible and whose project will have been selected based on the review of their LOI will be contacted directly and will be invited to submit a full proposal.

- LOI must be submitted electronically to Grand Challenges using the forms and process described at the following address: www.grandchallenges.ca
- Each LOI must include in the header of the narrative pages the text “Grand Challenges Canada POC-Dx Program” and “Topic Area (1, 2, 3, 4 or 5).” LOIs can only address one Topic Area.
- Applicants addressing more than one Topic Area must submit a separate LOI for each Topic Area. Multiple LOIs from the same organization is permitted.

Even at the LOI stage, however, it is important to read carefully the full guidelines for applicants given below to make certain that the applicant organization is fully capable of complying with all the requirements and terms of award.

Step 2: If invited based upon a successful LOI, submission of a full proposal to Grand Challenges Canada.

Instructions on the preparation of full proposals will be provided to selected applicants for Phase I. Note that:

- Due to expected high volumes, Grand Challenges Canada will not provide individual critiques or feedback on why an LOI was not selected. Successful applicants at the LOI stage who are invited to go to the full proposal stage will receive constructive feedback on their proposals.
- Grand Challenges Canada will use external reviewers, including experts from low- and middle-income countries (LMICs), to advise on the merit of proposals but final selection decisions will be made by the Board of Directors of Grand Challenges Canada.
- Successful LOIs invited to develop a full proposal will receive assistance in developing their proposals. This will include the award of Proposal Development Grants of \$25,000 Canadian. These grants aim to assist in the writing of the final proposals to meet global standards of excellence and to attend a proposal development workshop. During this workshop, Grand Challenges Canada will assist applicants with understanding effective grant writing techniques including lessons learned from the earlier RFP, technical issues, forming of strategic collaborations, milestones, budget development and general management and administration skills, where needed. In addition, scientists from low- and middle-income countries will be assisted to identify areas where they might wish to partner with Canadian Scientists, and such partnerships will be facilitated and encouraged by Grand Challenges Canada but will not be required.

4.3 Application Schedule

<i>Key Deadlines</i>	<i>Event</i>
May 3, 2010	Launch of Request for Proposal (RFP)
July 12, 2010	Application deadline for Letter of Intent (LOI) at 11:59 pm EST
August 30, 2010	Invitation for submission for full proposals
October 2010	Proposal development workshop for those invited to submit full

	proposals
November 30, 2010	Application deadline for full proposals
January 30, 2011	Notification of results and beginning of contract negotiations

4.4 Evaluation Criteria

1. **Significance/Topic Responsiveness.** Is the proposal likely to result in - or significantly advance - a component technology (or in the case of topic area # 5 and in some cases #4 an implementation strategy) that will add substantively to our ability to develop a radically new point-of-care diagnostic platform capable of meeting system level performance metrics (e.g. the stated TPP's in the RFP) and be easily implementable.
2. **Technical Merit/Execution Plan.** Is the proposed concept and approach based on sound scientific analysis and technical rigor? Do the applicants provide a clear and defensible description of their approach, evidence indicating the likelihood of success, and a rigorous assessment of risk factors and associated mitigation strategies? Are the proposed time line and interim milestones appropriate, feasible and technically sound?
3. **Level of Innovation.** Is the approach truly novel and a departure from incremental or evolutionary improvements over current technologies? How creative are the described concepts? Do the applicants bring a special expertise that could be beneficial? In order to ensure that investigators with great ideas but with less manufacturing experience do not get overlooked, we will be open to considering small innovations that would add significantly to other components.
4. **Best Value of Effort.** Is the scope of the proposed work and funds requested reasonable and commensurate with the stated deliverables? Proposals that have execution plans which represent particularly thoughtful and efficient use of resources will be preferred over proposals representing comparable efforts that do not represent the same value for the investment. Co-funding of proposals from upper middle income countries using the World Bank classification (e.g. Brazil and South Africa), as well as from lower middle income countries using the World Bank classification that are part of the G20 (e.g., India and China), will be an asset but not a requirement.
5. **Ability to Contribute to Cost and Portability Goals.** Is the component concept consistent with a very low cost design and manufacturing approach? Does it follow - or at least anticipate - the principles of design for manufacturing? Are component concepts proposed consistent with eventual integration into a POC platform suitable for deployment in low-infrastructure environments? Will the proposed component technologies result in lower-complexity, lower power consumption, reduced reagent usage and other improvements suitable for resource constrained locations?
6. **Ease of Integration/Willingness to Collaborate.** Do the proposers state their willingness to work within a collaborative framework? Are there any barriers to collaboration such as

intellectual property or business model? Does the proposal describe how their particular components could be effectively integrated into a system level POC platform? Do the proposers have the ability and desire to work with system integrators (such as in Phase 2)? Do the applicants state their willingness to abide by the Global Access Strategy as conceived by the STAG?

7. *Organizational and Investigator Capability.* Is the research and development team appropriately trained, experienced and well suited to carry out this work? Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers (if any)? Is there strong evidence of substantive organizational capability and commitment? Does the environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environments including partnerships with industry or employ useful collaborative arrangements? Is there adequate evidence of institutional support? Is the institution financially viable?

4.5 Eligibility Criteria

Applicant organizations must be individual non-profit organizations, for-profit companies, or other recognized institutions that can successfully execute the activities in their respective technical area. Grantees awarded projects will be required to actively collaborate with the Science and Technology Advisory Group (STAG) in Phase I and eventually collaborate and engage in technology transfer with System Integrators in Phase II.

4.6 Allowable Costs

Grant funds may be used for the following cost categories: personnel, necessary travel, supplies, contracted services, sub-grants, and consultants. Partial or full support for equipment may be requested subject to the circumstances described below. Please provide budget estimates according to the categories above. In addition, please note:

- Assume that you will need to budget at least a half time of a technical expert to participate in the Science and Technology Advisory Group (STAG).
- Equipment: Use of any equipment purchased with grant funds is limited to charitable purposes for the depreciable life of the equipment.
- Indirect costs: We will provide a limited amount of indirect costs (overheads) based on the nature of the applicant organization, to a maximum of 15% of the amount of the grant.
- Travel funds to participate in meetings twice a year for key members of the team.
- It is not necessary to budget for the participation of a potential Canadian partner in this LOI.

4.7 Privacy Notice

To help us in the evaluation and analysis of projects, all proposals, documents, communications, and associated materials submitted to the Grand Challenges Canada (collectively, “Submission Materials”) will become the property of Grand Challenges Canada and will be shared with other members of the Grand Challenges Canada consortium (International Development Research Centre and Canadian Institutes of Health Research) and the Bill & Melinda Gates Foundation. The proposals will be subject to confidential external review by independent subject matter experts and potential co-funders in addition to analysis by our staff. Please carefully consider the information included in the Submission Materials. If you have any doubts about the wisdom of disclosure of confidential or proprietary information, we recommend you consult with your legal counsel and take any steps you deem necessary to protect your intellectual property. You may wish to consider whether such information is critical for evaluating the submission, and whether more general, non-confidential information may be adequate as an alternative for these purposes.

We respect confidential information we receive. Nonetheless, notwithstanding your characterization of any information as being confidential, we may publicly disclose all information contained in Submission Materials to the extent as may be required by law and as is necessary for potential co-funders and external reviewers, such as government entities, to evaluate them and the manner and scope of potential funding consistent with appropriate regulations and their internal guidelines and policies.

4.8 Warranty

By providing any Submission Materials, the sender warrants Grand Challenges Canada that they have the right to provide the information submitted.

Applicants with questions concerning the contents of their Submission Materials may contact Grand Challenges Canada at: www.grandchallenges.ca

4.9 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 products may require involvement and support of the private sector, 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. Grand Challenges Canada's Global Access Strategy will guide our approach to IP, and we urge all applicants, even at the letter of intent (LOI) stage, (LOI) stage to consider their willingness to submit a full proposal in compliance with the Grand Challenges Canada Global Access Strategy, the guiding principles of which are as follows:

1. Breakthrough solutions to global challenges are made accessible to those in need, particularly in the developing world. Accessibility relates to both price and availability.
2. Knowledge gained through discovery is broadly, and as promptly as possible, distributed between related projects and to the global scientific community.
3. Commercialization of resulting outputs is encouraged, as long as the first two principles are achieved.

Grantees will be required to develop and sign a Global Access Agreement with Grand Challenges Canada in line with the Guiding Principles. For further information, please refer to Grand Challenges Canada's intellectual property policy at www.grandchallenges.ca.

5 RESEARCH ASSURANCES

It is the policy of Grand Challenges Canada that research involving human subjects, research with animals, and research subject to additional regulatory requirements must be conducted in accordance with the highest internationally recognized ethical standards. In order to receive funds from Grand Challenges Canada, initially and throughout the course of a research project, researchers must affirm and document compliance with the guiding ethical principles and standards outlined below.

1. Research involving human participants must be conducted in a manner that demonstrates, protects and preserves respect for persons, concern for the welfare of individuals, families and communities, and justice.⁵
2. Research involving animals must be conducted in a manner that ensures their humane care and treatment.
3. Certain research endeavors, including but not limited to research with recombinant DNA, biohazards, and genetically modified organisms, may be subject to enhanced regulation and oversight.

⁵ Modified from the core principles articulated in the draft second edition of TCPS (<http://pre.ethics.gc.ca/eng/policy-politique/initiatives/revised-reviser/chapter1-chapitre1/#toc01-1b>)

While not necessary for the letter of intent (LOI), and as applicable to the individual project, Grand Challenges Canada will require that for each venue in which any part of the project is conducted (either by your organization or a subgrantee or subcontractor) all legal and regulatory approvals for the activities being conducted will be obtained in advance of commencing the regulated activity. We will further require you to agree that no funds will be expended to enroll human subjects until the necessary regulatory and ethical bodies' approvals are obtained. For further details, please see the Grand Challenges Canada Ethics policy at www.grandchallenges.ca.

APPENDIX A: STAG WHITE PAPER

1.0 Goal

We want to create a new class of point-of-care (POC) diagnostics that will be broadly applicable in supporting our global health objectives and in particular will be easy to use, low cost and otherwise appropriate to ensure that these new tools will achieve significant impact and rapid uptake in resource poor settings. A POC diagnostic platform for Global Health has the ability to assess multiple pathogens and health conditions using a common set of technical, logistical, and medical decision-making paradigms. The results of the test should allow a minimally trained community health worker or other user to decide if a course of treatment is needed. A science and technology advisory group (STAG) will be created to advise Grand Challenges Canada and the Bill & Melinda Gates Foundation on the particulars of our POC diagnostics platform strategy, facilitate collaboration among the grantees from this RFP, and to set common technical and business standards for POC diagnostics platforms in developing world settings.

2.0 Background and Objectives

In order to bring about common diagnostic platforms suitable for low resource settings, it is important that they have the characteristics of being low cost, requiring minimal infrastructure to operate, short time-to-answer, minimal training to use, moderate to high performance, and simplified storage and distribution requirements. The recommitment to this Grand Challenge was designed to achieve the following objectives:

1. Develop a framework for collaboration by recommending a common set of technical and business standards for the development and integration of diagnostics components
2. Advance the state of the art in critical component technologies consistent with the business and technical standards developed under this program
3. Integrate best-in-class component technologies into diagnostic platforms under the framework of standards developed in this program

There will be three groups of players responsible for carrying out the main objectives. The main participants in this Phase I will be Component Builders who will advance the state of the art in component technologies. In a subsequent RFP that will aim to fund phase II, in addition to Component Builders, the key participants will be System Integrators who will take the best available component technologies (both developed during Phase I and from other potential partners) and integrate them into viable POC diagnostic platforms. The STAG will be responsible for drafting and recommending a common set of standards allowing the Component Builders and System Integrators to collaborate on novel platforms, in addition to advising on POC platform issues and facilitating collaboration. Analogous to the micro-electronics industry, we anticipate that such a framework of standards for diagnostic platforms could provide opportunities for continued innovations in specific components that could be integrated into an

extended value chain of future platforms creating opportunities for improvements beyond the horizon of our investment. In addition, the standards would specify certain performance aspects that would simplify and harmonize logistics and use. Creation of such standards is not only beneficial to future efforts in diagnostics research but also to the general diagnostics industry serving the developing world.

The design and limited proof-of-principle for a POC platform with a target product profile includes characteristics like:

- Quick time-to-answer,
- Simple readout,
- Low cost,
- Good sensitivity and specificity,
- Able to be used by minimally trained personnel,
- The ability to function above 30 °C and at high humidity,
- The ability to be stored for long periods of time without refrigeration,
- The ability to conduct the test without the need for local reagents/water and/or specialized laboratory equipment, and
- The ability to detect multiple pathogens or to distinguish between different pathogens and/or strains and subtypes.

The STAG is critical to the success of this program. In addition to advising Grand Challenges Canada and the Bill & Melinda Gates Foundation on the particulars of our POC platform strategy, STAG will facilitate collaboration among the Diagnostics grantees, and will set common technical and business standards for diagnostics in developing world settings.

3.0 STAG Structure

The structure of the STAG is shown in **Error! Reference source not found.** Teams with separate but distinct functions will work together to carry out the most crucial functions of the STAG. These teams are described in the following sections.

3.1 STAG Executive Committee

The STAG Executive Committee will be formed with advisors and leaders from industry, academia, public-private partnerships, and other organizations engaged in global health work. As the POC platform standards take shape, these leaders will advise us on the quality of the standards and how they will be received by the larger diagnostic community. They will serve as advocates to promote the agreed upon standards to the greater diagnostic community.

3.2 GCC and BMGF representation

This team will consist of stakeholders from various parts of both Grand Challenges Canada and the Bill & Melinda Gates Foundation. The exact membership will be determined as this program matures. We initially envision that the key members of this team will consist of experts from Grand Challenges Canada's Scientific Advisory Board and from the Bill & Melinda Gates Foundation's Global Health Discovery team working in diagnostics and biomarkers. They will

work to align the STAG's overall direction with the strategic needs of Grand Challenges Canada and the Bill & Melinda Gates Foundation.

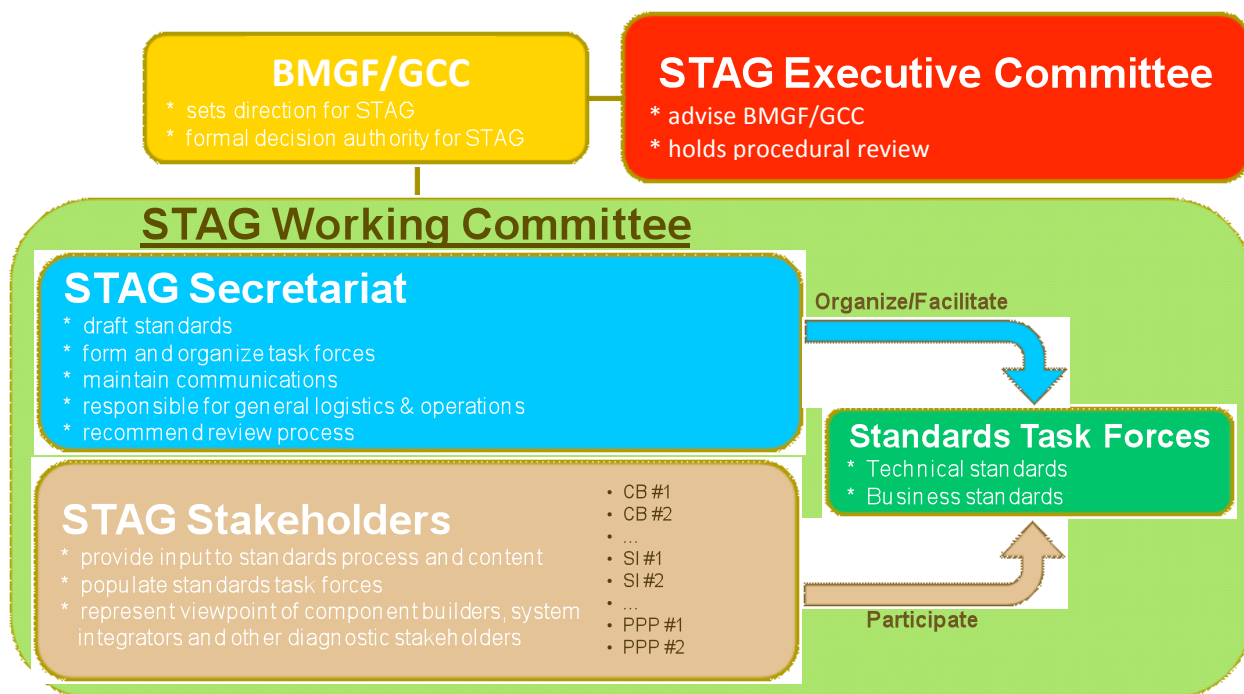


Figure 1 STAG structure

3.3 STAG Secretariat

In parallel to the funding of grants to individual Component Builders from this request for proposal (RFP), we will seek proposals for a STAG Secretariat that will coordinate the STAG Working Committee, the Stakeholders, and the Executive Committee and with Grand Challenges Canada and the Bill & Melinda Gates Foundation. Their mission will be to coordinate the Component Builders' activities in Phase I and make sure they align with the interests of Phase II System Integrators and the overall goals for POC platforms. The STAG Secretariat will take the lead in forming task forces that draft specific standards, facilitate communications, and encourage collaboration by ensuring smooth operation of the overall STAG.

3.4 STAG stakeholders

The STAG stakeholders will consist of participants from Phase I Component Builders and potential Phase II System Integrators. The Component Builders will each be allowed to send representative(s) to work in task forces and also to present their organization's viewpoint. They will be asked to add an estimate for at least one half-time personnel to participate in the STAG as part of their Phase I grant proposal. Each potential System Integrator can also choose to send one volunteer to represent the viewpoints of diagnostic manufacturers. We also plan to include representatives from public private partnerships (PPPs) which have been long-time partners for developing diagnostic tools for global health diseases in developing world settings.

Consideration will also be given to include other stakeholders, end-users, and health practitioners into the general STAG membership if the need exists. We intend that there will be strong representation of low- and middle-income country scientists in STAG.

3.5 STAG Working Committee

The STAG Working Committee will consist of various task forces formed to address each of the standards areas on a needed basis. The members and leaders for these task forces will be drawn from the STAG stakeholders. The Secretariat may actively participate in the day-to-day operations of specific task forces, but will ultimately be responsible for consolidating the outputs from each task force into a set of written standards.

4.0 Developing Standards

A notional process for developing standards is represented by the diagram in Figure 2. One can start with developing world needs and some generalized notion about what specifications are needed for diagnostic platforms to fulfill those needs. The STAG Secretariat (blue team) will consolidate those ideas and form task forces to address those issues. The entire family of task forces together with staff from the STAG Secretariat makes up the STAG Working Committee (green team). An initial set of task forces can potentially be formed around the technical areas from this diagnostics RFP. There should be standards in the areas of sample preparation, recognition and transduction, readout technologies, a cross sectional task force focused on technical integration, and task forces focusing on collaboration and business integration. Other more specialized task forces can be formed as needed. Although we don't envision any barriers to the stakeholders from joining any of these task forces, we expect that the participants will come from Component Builders within that technical area. Each time the task force drafts a set of standards, the Secretariat will ensure that it is disseminated to the entire Working Committee (green team) for review. A more formal procedural review will be held by Grand Challenges Canada and the Bill & Melinda Gates Foundation (gold team) and the Executive Committee (red team). A standard is formalized only if it passes all these stages of review and acceptance. We expect this process to be refined and updated by the Secretariat once it has been convened.

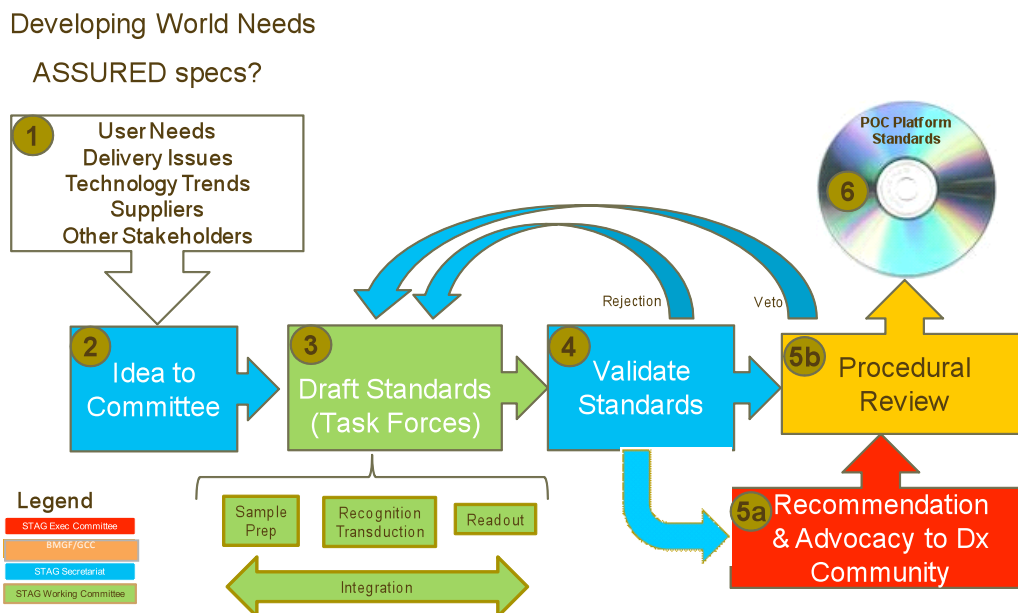


Figure 2 Process for developing standards

5.0 Potential Standards Categories

The final standards document provides guidelines for general POC platform interface design and materials selection that can reduce redundant engineering effort and lead to improved design, manufacturability, operation and lowered costs. The goal is to enable devices from different vendors to interconnect via an open architecture and have common performance and usability features. The specification is intended as an enhanced capability to the state-of-the-art technologies incorporating a combination of electronics and fluidics. It will provide device researchers adequate room for product versatility and market differentiation without the burden of carrying obsolete interfaces, losing compatibility, and choice. Some of the top level standards categories are listed below. They generally refer to:

- Performance – How does the device or system perform, and what limits does it need to operate within?
- Reliability – How long will the device or system achieve its stated purpose under the expected operating conditions?
- Quality – How well must the device or system be made so that it can achieve its stated purpose. An example is interfacial dimensional requirements
- Process – How is the device or system created, and what are the constraints on the fabrication process that limit device variation
- Test – Test, measurement, and methodological standards
- Design Requirements – Interfacial constraints, dimensional constraints, materials performance constraints, etc.
- Logistics
- Internal interfaces & system integration

- User friendliness, ease of use, lower training threshold
- Business standards, IP and information sharing

6.0 STAG Organization

During the second quarter of 2010, we expect to identify a team or organization to carry out the responsibilities of the STAG Secretariat. The STAG Secretariat will put forward a cogent plan on how they expect to achieve the overall mission based on their experience in performing similar activities. Below are some of the elements that will be included in the detailed description of the Secretariat of the STAG:

- Group charter: the STAG Secretariat will need to draft and finalize a version of their charter, which will establish a common understanding regarding STAG membership and governance. A specific example of governance issue is that the STAG needs to clarify the process on what it means to “pass a standard.”
- Framework and plan for communications: communications between the major players in this initiative should be transparent and timely. The STAG Secretariat needs to work with the Stakeholders to agree on how much information will be communicated in a virtual fashion through email or website portal and how often the membership will meet.
- Standards development plan: the STAG Secretariat will be expected to layout the general framework for how to develop technical and business standards. They can form task forces to specialize on a subset of the standards if necessary. As the gap between the POC platform specifications and the component technologies future potential is understood, we expect a better defined and solidified task force structure to emerge.
- Analysis of fit for large scale manufacturing: the STAG Working Committees will need to perform an analysis of the component technologies and standards being advocated in Phase I of this diagnostics program and determine whether they are amenable to large scale manufacturing processes that will be required for eventual delivery of the final product to large numbers of potential end-users in the developing world.
- Broad agreement on concepts and specifications: toward the end of Phase I, the STAG Secretariat should be leading the effort to finalize a set of standards that enable innovation and integration of component technologies into POC platforms for the developing world. There should be broad consensus from current and future participants of this diagnostics program that these standards will enable breakthrough platforms not only for Phase II System Integrators, but also for other stakeholders in the extended diagnostics community serving the developing world.
- Project Plan: the STAG Secretariat will need to define a project plan that specifies what resources they need and the timing of the individual activities needed to accomplish its mission. This project plan will need to be updated on a quarterly basis.

- Clear Definition of the Deliverables from the STAG Secretariat: which must at a minimum include:
 - i) A specific set of Target Product Profiles (TPPs) for the POC platform;
 - ii) Architecture for the technical integration of components into a platform meeting the TPPs defined in i);
 - iii) A specific set of TPPs for each component in the defined architecture of ii). as well as other TPPs for elements of the systems where appropriate; and
 - iv) Clearly defined business and collaboration standards including an approach to the management of Intellectual Property (IP) that ensures that the IP generated with these investments as well as any background technology needed is available to ensure that any POC platform developed under this program is broadly available to meet global health needs in the developing world while at the same maximizing the value of these innovations in the developed world.