

## New Interventions for Global Health: a new Grand Challenge

### Background

Under this new Grand Challenge we seek original and innovative concepts for vaccines, therapeutics and diagnostics **with the potential to be translated into safe, effective, affordable and widely utilized interventions** to protect against the acquisition, progression or transmission of infectious diseases or provide a cure for infectious diseases in resource-limited settings. **This request for proposals will fund full awards that could include grants, [program related investments](#) and/or contracts up to USD \$10,000,000 per awardee for up to four years but must include an industry, biotech or other translational partner. We will also consider funding pilot awards of up to USD \$2,000,000 for up to four years with the anticipation that successful applicants will apply for a full award in subsequent years.**

Vaccines have been a cornerstone of global health campaigns to provide protection against infectious diseases. However, discovery of new vaccines currently relies on a long and costly process of trial and error, and this approach has an uneven record of success. The proliferation of novel antigens, adjuvants, and formulations requires new methods to more reliably select those entities that will elicit protective immune responses.

The global health community also needs new ways to protect against infectious diseases that do not resemble traditional vaccines in seeking to reproduce the immune response to natural infection. Rather, we seek vaccines that induce responses that are either uncommonly induced or not naturally induced by natural encounter with pathogens of global health importance, which include [HIV](#), [malaria](#), [TB](#), and [diarrheal, respiratory](#) and [neglected diseases](#) that fall within the Foundation's priorities. In addition, to vaccines for humans, we seek new [animal vaccines](#) for priority infectious diseases that impact dairy cattle, small ruminants and poultry in developing countries.

To do so, we need new approaches to expand the range of health interventions that protect against infectious diseases. Teams that bridge traditional disciplinary siloes and utilize approaches that increase the application of genomics, proteomics, biophysical analysis, sophisticated cell-based assays, and bioinformatics tools to these problems are likely to provide new opportunities for generating such candidate vaccines. In addition, improved paradigms for rational vaccine design are needed.

Complementing vaccines, antibiotics and anti-viral therapies have been the cornerstone of infectious disease treatment, control programs and elimination campaigns for many diseases. However, the effectiveness of existing treatments for [our priority infectious diseases](#) is increasingly compromised by the evolution of drug-resistant pathogens. We lack an understanding of the key determinants of the evolution of resistance, and the ability to slow the emergence of resistant variants. Most screening approaches in use today produce compounds that are likely to fail over time.

Furthermore, combination therapies currently limit the emergence of resistance to antimicrobial agents, but even then resistance can emerge. While new drug discovery efforts may expand our arsenal of compounds, simply having more drugs does not address the potential emergence of resistance. We need new ways to create drugs that are less likely to be made ineffective by pathogen evolution, which

would enhance the useful lifespan of anti-microbial agents, and reduce the frequency of treatment failures.

Effectively using therapies requires timely and accurate diagnostics. Most diagnostic tests require the invasive acquisition of blood or tissue samples, which contain information-rich markers for specific diseases. Conventional sample collection methods are followed by complex processing, where the processing of samples (e.g. blood or sputum) brings with it complex logistics and time delays given current technologies, standard practices and analytic methods. Unfortunately, this process usually comes at the price of high cost, patient annoyance, product acceptance, and significant training for health workers. As a result, currently available diagnostics are not suitable for most priority global health conditions and settings where low cost, ease of use, and field-rugged solutions are imperative. This topic presents an opportunity to harness inter-disciplinary innovation from engineering, physics, chemistry and biology to create novel, low-cost, easy-to-use diagnostics that could be transformative for resource limited settings.

### **What we are looking for (Vaccines):**

The goal of this challenge is to **identify novel vaccine concepts for generating protective immune responses to global health pathogens of interest— to solicit creative, novel approaches to the identification and generation of protective immune responses in order to move the best vaccine concepts and candidates forward into clinical development.** Unconventional approaches to effectively drive or harness immune responses to protect against infection and disease will be considered.

### ***A few of the many options to be considered include:***

- New approaches to the generation of conventional or common pathways of immune protection.
- Novel vaccine concepts, targets and constructs inspired by new observations or understanding about the nature of the targeted organism or the human response to that organism;
- New vaccine constructs that target specific tissue or cell types for appropriate induction of local and systemic immunity;
- Novel vaccines designed specifically for populations with high disease burden or risk of infection;
- Novel vaccines to protect dairy cattle, small ruminants and poultry from priority infectious diseases;
- Novel approaches to the effective stimulation of protective immune responses;
- Immune system-boosting nutraceuticals (including probiotics) to tackle malnutrition and to improve vaccine effectiveness in vulnerable communities;
- New computational or laboratory-based systems for rapidly testing vaccines and predicting their efficacy;
- Applications of radically new technologies for disease protection, such as production of immunogens using synthetic biology or radical genetic engineering approaches;
- New ways to monitor the human immune responses to vaccines; and
- New approaches that employ multiple interventions in combination.

***We will not consider funding for:***

- Projects focused on discovering targets of a disease prevalent predominately in the developed world;
- Identification of HIV, TB or malaria antigens without the addition of ways to radically and reproducibly improve their effectiveness or efficiency;
- Projects targeting molecular pathways targeted by currently available antigens or adjuvants currently in clinical development;
- Vaccine concepts not based on an explicit hypothesis or rationale for improved performance over those candidates currently in development;
- Approaches that represent incremental improvements to conventional solutions;
- Basic studies of pathogen or human biology without a clear component that tests the potential for translation into specific and practical health solutions

**What we are looking for (Therapeutics):**

With this topic we also seek to explore **new therapeutic approaches** that limit the emergence of resistance -- by limiting evolutionary pressure on drug targets, blocking potential evolutionary paths, or other novel mechanisms. In all cases, proposals must articulate how the emergence of drug resistance would be limited and how the likelihood for emergence of resistance could be tested.

***A few of the many options to be considered include:***

- Novel mechanisms of action, for example targeting critical host components essential to infection and disease with little or no toxic effect on the host;
- Targeting components of the pathogen that are implicated in disease rather than infection, or that are so highly constrained that resistant variants cannot be easily selected;
- New formulations or delivery modalities that improve the in vivo pharmacological characteristics of drugs, where a specific biological rationale exists that these improvements can limit emergence of resistance;
- Altering the inherent capacity for pathogens to evade drug sensitivity;
- Mathematical analysis, modeling and prediction of the evolution, spread and fitness of resistant mutants during drug treatment, both within a single individual and within an epidemiological context. Explicit linkages to the discovery of new drugs must be made apparent.

***We will not consider funding for:***

- Conventional drug discovery approaches (e.g., standard high-throughput screens against pathogens, optimization of known drugs, hybrid-drug approaches, target-based drug development, drug combinations or formulations);
- Identification of new targets or compounds with no biological rationale concerning the emergence of resistance or no clear means of evaluating whether the target, compound, or approach is likely to limit the emergence of resistance;
- Explorations of current hypotheses unless they involve the use of technologies that have not previously been used to study the disease or pathogen;

- Testing compounds against currently drug-resistant pathogens without a clear hypothesis as to why the resultant compound would be less likely to generate resistance;
- Specific targeting of pathogens that cause diseases not on the foundation’s priority disease list;
- Community-based interventions aimed at improving adherence to drug treatment regimens;
- Use of combinations of existing agents without regard to new mechanisms of action or new drug administrations related to drug resistance.

**What we are looking for (Diagnostics):**

In addition to vaccines and therapeutic concepts, **we seek innovative diagnostics** that have the potential to drastically change how we measure a patient’s health condition in developing world settings. Proposals may offer methods to detect disease-causing pathogens as well as biomarkers, indicators of metabolic status, and micronutrients. They may employ existing platform technologies or detection modalities, but they must be accompanied by credible biophysical signatures or biomarkers specific for global health conditions.

***A few of the many options to be considered include:***

- Radically new and improved approaches to traditional immune and molecular assay approaches;
- Biochemical amplification or analysis of non-invasive samples such as urine, saliva, sweat or other excreted fluids;
- Fast scanning of retina or capillaries near a body surface for evidence of disease;
- Complex signature analysis for pneumonia, TB and similar diseases via breath acoustics;
- Detection of molecular analytes from breath;
- Measurement of metabolites that indicate nutrient or metabolic status;
- Measurements relevant to maternal and neonatal health.

***We will not consider funding for:***

- The development of a technical improvement of a diagnostic with little apparent relevance or impact to a global health problem;
- Diagnostics of cancer, non-infectious chronic diseases such as asthma, diabetes, allergies;
- Improvements solely in microfluidics architecture or detection signal transduction or other elements of platform technologies without a clear path to a product of relevance to one or more of our priority global health diseases.

In all cases, we seek proposals that are “off the beaten track,” significantly radical in conception, and daring in premise.

**Who we will fund:**

**Full awards up to \$10M and up to four years:** Under this new Grand Challenge we accept applications for **full awards**, each of which could include a grant, program related investment and/or contract up to USD \$10,000,000 and up to four years to accelerate the translation of novel concepts. **Full awards must**

**include an industry, biotech or other translational partner** either leading or participating in the application. We reserve the right to determine eligibility for **full awards** for this call based on these characteristics.

**Pilot awards up to \$2M and up to four years:** Under this new Grand Challenge we will also consider applications for pilot awards of up to USD \$2,000,000 and up to four years to explore novel concepts that require additional investigation with the anticipation that successful applicants will apply for a full award in subsequent years. **Pilot awards** do not include a requirement for a biotech or translation partner but such partnerships would still be welcome.

### **Characteristics of successful proposals**

We seek proposals that clearly demonstrate the attributes below.

- **Innovation**, including creativity of the project’s approach and clear differentiation from existing approaches
- **Scientific and technical excellence**, including a clear and rigorous conceptual framework for research activities
- Potential to lead to prevention and treatment solutions with substantial **impact**
- Unique project **resources**, including investigator and organization capabilities and potential for collaboration
- **Value** in terms of appropriateness of the budget and timeline relative to project complexity, risk, and potential impact

### **Grand Challenges**

#### Definition

Grand Challenges is a family of initiatives fostering innovation to solve key problems in global health and development for those most in need. It seeks to establish a portfolio of projects with complementary approaches that encompass multiple types of innovation, including innovation in biological research, medical health technology and product development, service delivery, and behavior change. Grand Challenges initiatives therefore seek to:

- Engage diverse investigators, including those outside of the areas that might traditionally be associated with the initiative
- Encourage partnerships that bring together investigators from diverse organizations, including for-profit institutions, non-governmental organizations, academic and health research institutions, foundations, and civil society groups

#### History

Today, a variety of funding partners use “Grand Challenges” to accelerate research, creating an expanding network of funding and research partnerships spanning diverse topics. Below are some key examples highlighting how the Grand Challenges family has grown over time:

- In 2003, the Bill & Melinda Gates Foundation launched [Grand Challenges in Global Health](#), a US\$450-million research initiative that came to include multiple funding partners and, in 2007, it

launched [Grand Challenges Explorations](#) (GCE), an accelerated program providing small, initial grants for exploratory research.

- In 2010, the Canadian government funded [Grand Challenges Canada](#) to support global health researchers in low- and middle-income countries and in Canada through multiple grant programs.
- In 2011, USAID launched [Grand Challenges for Development](#), an initiative that brought the Grand Challenges approach to diverse new areas, including agriculture and child reading, through multiple grant programs.
- In 2012, the Gates Foundation and the Brazilian government established [Grand Challenges Brazil](#), a partnership to fund researchers in Brazil through GCE and, to date, the grant program [Reducing the Burden of Preterm Birth](#).
- In 2013, the Gates Foundation and the Indian government launched [Grand Challenges India](#), a partnership to fund researchers in India through GCE and, to date, the grant programs [Achieving Healthy Growth through Agriculture and Nutrition](#) and [Reinvent the Toilet Challenge – India](#).