**Project title:** Open Source Fever Diagnostic Project

**Project summary:**

*Low–cost, open source, multiplex point of care (POC) diagnostic test for the differential diagnosis of fever/sepsis*

The project is a multi-government collaboration to fund a low-cost multiplex point of care (POC) diagnostic test for the differential diagnosis of fever/sepsis. The motivation is to improve the diagnosis of patients suffering from fever in low-resource settings, thus enhancing treatment options, and also, reducing inappropriate use of antibiotic drugs. While motivated by the need for tests in resource-poor settings, the innovation will be also useful in non-resource poor settings and high-income countries, increasing the global social value of the innovation.

The project begins with the identification of an innovation need, and then proposes a method of financing investments to achieve the needed diagnostic services. The voluntary plurilateral funding by governments will be used in a combination of push and pull funding mechanisms, implemented with full de-linkage of R&D costs from product prices. The cost of the project is between US$70 million to $200 million, depending upon the level of funding support secured. The value of a successful innovation vastly exceeds the high end of the project funding, and the bulk of the funding would be in the form of obligations to only reward successful innovations, substantially lowering the risks and improving the expected cost benefit of the project to the project’s funders/donors.

The Target Product Profile (TPP) being developed for this test is targeted for use at the minimum in district health settings for patients (neonates, children and adults) presenting with fever syndromes. Because the causative pathogens of fever will differ by clinical setting and geographical region, one key feature of this diagnostic test is the flexibility to integrate epidemiological data of fever pathogens in various settings into the test. The final selection of the pathogens that need to be included in the test should be informed by the particular geographical and clinical setting for which the fever diagnostic test will be used.

In order to meet the needs in resource-limited settings, the specifications are in accordance with previously established WHO ‘assured’ criteria for the test to be ‘affordable, sensitive, specific, user-friendly, rapid, robust, equipment-free and deliverable to end-users.’

**Governance and Administration**

The governance of the project would include an Executive Board, consisting of the project’s funders/donors, high burden countries and representatives from affected communities. Rules to disclose and manage potential conflicts of interest would be created. The work of the Executive Board would be informed by a technical advisory committee within the WHO that would analyse and provide data on causes of fever in different geographic regions; draw on expertise within WHO on quality assurance of medical devices and on standards for interoperability of devices in order to inform and align the work of the Executive Board. The Executive Board would set high-level policies and enter into a contract with one or more entities to manage a portfolio of grants and innovation prizes. We anticipate that the Special Program for Research and Training in Tropical Diseases (TDR), UNITAID or the World Bank would be among the entities that could manage the grants and/or prizes portfolio.
Medical Need

Fever is the most common presentation of infections. Fever without focal signs and symptoms is one of the most common reasons for admission to hospitals in low-income countries. [1,2] While accurate malaria diagnosis is now possible with the availability of a rapid diagnostic test (RDT)[3], there still remains a lack of diagnostic microbiology services for bloodstream infections and other common causes of fever despite efforts in improving laboratory capacity [4, 5, 6]. Because of this, health care workers use an empirical approach to the treatment of fever syndromes, which leads to either inappropriate use of antibacterial drugs and/or missing a critical window for diagnosis of certain diseases, leading to both unfavourable clinical outcomes as well as risking the promotion of antimicrobial resistance[2].

Flexible donor funding of push or pull

The project’s funders will have the opportunity to provide general support for the project, which the Executive Board would allocate to either grants or innovation prizes, or to choose to fund either grants or innovation prizes.

Open licensing of intellectual property rights, data and know-how

The intellectual property rights from the grants and innovation prizes would be conditioned upon the open licensing of intellectual property, data and technology transfer, possibly within a field of use, to ensure open and competitive access to research outcomes.

Grants and contracts

Funding for research grants and contracts will be sought from funders/donors. Grants (or contracts) will be particularly useful to focus research on areas where prizes are considered too costly to manage or where project managers have greater confidence in their ability to identify and manage research projects to achieve research objectives.

Innovation Prize Funds

The program would include four different types of innovation prize funds.

1. Biannual best progress prizes. One set of prizes would be awarded every two years to reward the best progress toward the development of the ‘end point’, which is an open–source, low cost multiplex point of care (POC) diagnostic test for the differential diagnosis of fever/sepsis.

2. Milestone prizes. The Executive Board and the selected administrator of prizes could also provide funding for various milestone prizes, rewarding the successful achievement of specific research objectives considered to be useful in achieving the end point. For example, a milestone might be the identification of a biomarker that distinguishes between bacterial and viral causes of fever.

3. End Product Prizes. The end product prize would be available to one or more entities that achieve the desired end point, as defined by the Executive Board. If the funding of the end product prizes is sufficiently large, the competition will have a lower threshold to qualify, and be sufficient to induce the development of multiple competing designs that divide the prize money. If the funding of the end product prize is less than $20 million, it will have a higher and more difficult set of qualifying criteria that would be won by the first contestant or set of contestants to qualify during a round of the periodic evaluation of designs seeking to win the end product prize. The end product prizes will be the most expensive element in the project, but also the least risky to the project’s funders/donors, because the money will only be spent if a design achieves the desired end point. We recommend end product prize funding of $20 to $100 million, with the larger amount resulting in a higher probability of success and a more rapid development schedule.
(4) Open source dividend. Between five and ten percent of the end product prize money will be given out to parties not affiliated with the contestant submitting the winning design. In order to qualify for the open source dividend, a potential recipient of the prize money must have provided royalty-free and nondiscriminatory access to knowledge, data, materials or technologies that were considered to have been important in the successful development of the product that wins an end product prize. Recipients of earlier grants or prizes will be eligible for the open source dividend rewards. The process for awarding the open source dividend will be the appointment of a temporary jury of experts who will receive nominations for the open source dividend prizes and allocate the prize money based upon the evidence from the nominations.

Note on grants versus prizes

There is no bright line that separates a target innovation into candidates for grants versus prizes. The flexibility to use either grants and contracts or competitive prize contests is an important aspect of this project.

When does one choose a grant or a prize to finance innovation? This is a difficult question to answer definitively. If one thinks of patent monopolies as a type of a particular type of prize, then it is clear that there is nothing that a patent or a different type of prize could reward that could not also be financed by a grant, including any and all stages of product development. However, the converse is not true. There are tasks that are poor candidates for patents or prizes, including work for which, while useful and perhaps even necessary, are unlikely to rewarded for inventive or stellar performances, or for, where the suppliers are uncomfortable, unable or unwilling to bear the risk of not being paid, or where asymmetric information makes it difficult to assess the risks of success or failure or to evaluate the quality of the effort or output, or any number of practical reasons why creating and managing a competitive contest using cash prizes is an inefficient approach.

The grant system itself can and frequently does lend itself to a certain amount of competition, both in terms of who receives grants from a grant-making agency, and even between grant-making agencies seeking to address common objectives. Indeed, the project could choose to divide its own grant-making portfolio among different grant-making agencies, creating some creative tension, competition and diversity in management of the grants. But prize contests can introduce a degree a competition and a shift in risk bearing that can be beneficial to the party financing the innovation. Among the potential benefits of prizes include the ability to reward unconventional approaches to problems when championed by those who think differently and are willing to bear the risks of failure. The persons who become ‘solvers’ in prize competitions may be a wider cast of characters than the ‘usual suspects’ that are likely to obtain grants. The shifting of risk in prize contests also presents attractive opportunities for a funder/donor to only pay for what works, and not worry about justifying outlays on dead-ends that sometimes turn up despite the most optimistic and promising beginnings.

Note risk bearing, as it relates to grants versus prizes

One of the major differences between grants and prizes, and between different prizes is the distribution of risk bearing between the researcher/developer and the project’s funders/donors. Since failure is not a rare occurrence in product/diagnostic development, the question of who bears the risk is important, as are the consequences. At the risk of some oversimplification, this can be described as follows:

- When grants are used, governments (and other funders/donors) bear all of the risks of failure. When this happens, researchers and product developers are likely to be somewhat lax on due diligence and screening of the projects they pursue.
When milestone, best progress or other interim prizes are used, the risks are divided between the project’s funders/donors and the researcher/product developers. With shared risks, researchers and product developers will be more rigorous and careful in their assessment about what might achieve the milestone, but remain less concerned over whether or not the milestone itself will lead to useful products.

When end product prizes are used, the project’s funders/donors bears little risk, other than the time and costs of administering the prize contest. In such cases, researchers and product managers will exercise a good deal of caution before investing their own money in R&D efforts.

The Ecosystem Approach

This project is designed to create multiple mechanisms to finance development an open source multiplex point of care (POC) diagnostic tests for the differential diagnosis of fever/sepsis. Each of the mechanisms, grants and research contracts, milestone prizes, best progress prizes, end product prizes and the open source dividend, have strong points, but also gaps and weaknesses. The project embraces an ecosystem approach, using multiple mechanisms to advance and acquire development of new technology for fever diagnosis. In this sense, the sum is greater than the individual parts.

*As taken from original proposal template, question 5.*