

PROPOSAL by Bangladesh, Barbados Bolivia, and Suriname

Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis

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Executive Summary

The governments of Bangladesh, Barbados, Bolivia and Suriname are attaching for discussion a proposal for the endowment of a Prize Fund for TB Diagnostics.

The proposal is an example of how a prize fund can be designed to incentivise innovation for a diagnostic test for a single neglected disease.

This proposal is based on an earlier proposal presented by the governments of Barbados & Bolivia in April 2008 during the WHO Intergovernmental Working Group on Public Health, Innovation and Intellectual Property. During that process, several governments expressed support for undertaking further discussions on this proposal.

The Problem

Tuberculosis is a major health problem, associated with 9.27 million incident cases and nearly 1.8 million deaths only in 2007¹. It is particularly deadly for patients who are co-infected with HIV/AIDS, and for patients who are infected with new strains of drug resistant TB, including multi-drug resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). An effective TB-control program requires early diagnosis and immediate initiation of treatment. Any delay in diagnosing TB not only impairs a patient's prognosis, but also increase the risks of transmitting the disease within the community. The laboratory has always played a critical role in diagnosing tuberculosis (TB) and monitoring its treatment. However, there is a dearth of innovation in this area. The current basic diagnostic technology is over 120 years old and involves a specifically equipped laboratory and the use of trained personnel that is capable of examining sputum with microscopes over a period of days. Also inadequate laboratory networks are a hindering progress against diagnosing the disease. Complications stemming from the HIV epidemic and multidrug-resistant TB (MDR-TB) prevent effective TB control that relies entirely on microscopy-based case detection and management. Effective control currently involves access to laboratory services at every level, which requires managing and supporting laboratory networks that provide reliable and consistent decentralized services. Modern techniques such as fluorescence microscopy (FM), use of liquid cultures for isolation and DST, and amplification for detection of and/or for study of drug resistance are expensive, labour-intensive or relatively slow. Under normal conditions, using this diagnostic method to detect the main form of TB, pulmonary TB, can miss about 60-80% of cases.

Although recent efforts to scale up sputum smear microscopy (SSM) capacity at the peripheral level of the health care system, there are still many patients that do not have access to microscopy at their

1 WHO Report 2009: Global Tuberculosis Control: epidemiology, strategy, financing.

nearest health facility. It has been estimated that only a fraction of patients are seen at microscopy-centre level (25%), compared to 60% of patients seen at peripheral health clinics, where there is no adequate lab infrastructure². It is therefore clear that the greatest need for a new test for TB is to be infrastructure-independent to allow its use at the lowest level of the health care system, where the majority of patients are seen, therefore at Point-of-Care (POC) level. Therefore more efforts are needed to develop and implement new technologies.

A new TB test should not only be available at POC, but should also address other fundamental gaps seen such as the overall low performance and inadequacy of existing diagnostics. The latest WHO report on TB control mentions that in the highest-burden countries, less than 44% of all forms of incident TB cases were diagnosed through SSM in 2007. These numbers representing the overall problematic of SSM including, besides poor access and low sensitivity, the inadequacy of SSM to diagnose pulmonary TB in children and in HIV positive individuals, in addition to its failure to detect other forms of the disease like its extra pulmonary form. This inadequacy is highly distressing considering that within the 15 countries with the highest TB incidence rates, 7 countries shows their proportion of incident rates for of HIV-positive TB cases representing more than 66% of the overall TB incident rates. Considering that 14 out of these 15 highest burden-countries are in Africa, where access to health care is very poor and resources are limited, it clearly stresses the urgency of developing a new diagnostic test for TB that would be used at POC level and would be adequate for HIV-positive individuals.

The lack of an inexpensive and easy-to-use rapid diagnostic tool is a major gap in the efforts to manage and treat this disease, particularly in developing countries, where the healthcare infrastructure is poor, resources are limited, and the long delays in testing are particularly problematic and can lead to death even before a patient receives his or her results.

Despite the valuable work supported by grant programs administered by programs such as the Foundation for Innovative New Diagnostics (FIND), there is wide agreement that there is insufficient progress on the development of a new test that meets the need for a rapid, low cost test that can be used at POC level in resource poor settings.

Commercial incentives for investing in such a test are quite low. The biggest targets for the test are low-income persons living in developing countries. By definition, an “inexpensive” diagnostic test will not have a high price. Only a handful of researchers have focused on this problem, and many academic and private sector researchers neglect to share information, materials or technology that may be relevant to this neglected but important R&D problem.

The Basic Proposal – TB Diagnostic Prize Fund

The proposal is to endow a prize fund to support innovations on TB diagnostics. The fund, which would be endowed at \$100 million or more³, would be used to resource several innovation inducement

2 Diagnostics for tuberculosis – Global demand and market potential. WHO/TDR and FIND. 2006

3 Several experts with experience in the field of diagnostics have indicated a prize of \$100 million is more than sufficient to stimulate the development of a qualifying diagnostic test for tuberculosis. The prize incentive will exist in an environment where considerable “push” funding is available from programs or institutions such as FIND or the U.S. NIH to undertake research on new diagnostics for TB. We welcome the work of the EWG and others to provide analysis and evidence that a different figure would be more appropriate. We caution the EWG or others to avoid under-resourcing the TB diagnostic prize, on the grounds that a smaller prize will have less leverage with developers in terms

prizes and to induce the sharing of knowledge, materials and technology.

Administration

The Prize Fund would be placed in the WHO, following the policies of a TB Diagnostic Prize Fund Committee. This committee would be appointed by the WHO, and include representatives, for example, memberships might be drawn from the following entities:

1. WHO TDR
2. UNITAID
3. The Global Fund to fight AIDS, Tuberculosis and Malaria
4. The Global Alliance for TB Drug Development
5. The Stop TB Partnership
6. A representative of TB patients
7. The Global Health Workforce Alliance

Conflict of interest rules would be put into place. For example, no employees of any organization represented on the committee could win the prizes.

The TB Diagnostic Prize Fund Committee would appoint **expert subcommittees** and staff as necessary to carry out its work, including those with special expertise on **technical issues**, and another to consider **standards for access**.

The TB Diagnostic Prize Fund would be used to support the following prizes:

The TB Diagnostic Grand Prize

The entire \$100 million “TB Diagnostic Grand Prize” would be awarded once an entrant provided a diagnostic test that satisfied, at least, a minimum criterion.

The technical expert subcommittee would review and recommend the appropriate medical and technical criteria for such a test, including such issues as the accuracy of the test and the objectives of the diagnostic test in terms of identifying persons who need treatment, including pediatric patients and patients who are co-infected with HIV and TB. This committee would also consider the field conditions under which the test should be considered, and the acceptable time for results to be available.

Human rights considerations

According to General Comment No. 14 (2000) of the Committee On Economic, Social And Cultural Rights (CESCR), on The Right To The Highest Attainable Standard Of Health, essential health care facilities, goods and services should be available, accessible, affordable, acceptable and of appropriate quality.

of the requirements for licensing intellectual property and ensuring affordable pricing and equitable access to the test.

This means facilities, goods and services must be affordable for all, including for socially disadvantaged groups.

In terms of acceptability, facilities products and services should be respectful of medical ethics and culturally appropriate, i.e. respectful of the culture of individuals, minorities, peoples and communities, sensitive to gender and life-cycle requirements, as well as being designed to respect confidentiality and improve the health status of those concerned.

Health facilities, goods and services must also be scientifically and medically appropriate and of good quality, in light of the realistic options regarding the availability (or lack of availability) of skilled medical personnel, hospital equipment, safe and potable water, and adequate sanitation.

Standards for Sustainable Affordability and Access

The subcommittee would also review and recommend the requirements for affordability and access, including but not limited to the evidence that the diagnostic could be manufactured, distributed and used in the field with acceptable quality and at an affordable price on a sustainable basis.

The standards for affordability and access would focus on pricing ceilings and a market penetration test.

A price ceiling would be established, either as a mandatory requirement, or as an optional requirement, that could be substituted for an alternative market penetration test

A market penetration test would be a requirement that the diagnostic device was actually manufactured, distributed and used by a large enough population to provide evidence that the device would in fact be affordable and acceptable for target populations.

One particularly interesting version of the market penetration test would be where the diagnostic device would be manufactured and sold by one or more third parties without subsidies from the prize applicant, in order to establish the feasibility and sustainability of a competitive supply. Upon reaching sufficient scale of distribution, the standard for affordability and access could be satisfied.

The size of the market penetration test could be smaller for cases where a maximum observed price was met. In cases where a maximum price is not used, the market test would have to be large enough to prove that the actual market price would likely be affordable to the target populations.

More complex would be the case were the prize applicant asserts that device can be manufactured for an affordable price, and even distributes an initial supply of devices, but where there is no assurance that the diagnostic device supply would be sustainable at an affordable price, once the prize money was paid. In such a case, a contestant would be required to provide sufficient assurances, covered by financial guarantees, that the products will be manufactured in sufficient quantities and acceptable quality, at affordable prices.

Evaluation of Contestants

The TB Diagnostic Prize Fund Committee would consider requests to be evaluated for the prize, including preliminary reviews of the diagnostic test feasibility, and for products that pass this initial screen, a clinical evaluation of the efficacy and acceptability of the diagnostic test.

Because the evaluation would involve clinical trials with relatively high fixed costs, but considerably

lower incremental costs of testing additional contestants, the following procedures are recommended.

Upon preliminary evidence that one or more contestant may have qualified for the prize, the prize fund committee would schedule a clinical trial, where all products deemed to have meet the initial screening would be tested. The TB Prize Fund would bear the fixed costs of the clinical studies, which would be undertaken no more than once per year. The contestants would bear the incremental costs of being tested. It is estimated that the fixed cost of such clinical trials would be \$500,000, and the incremental cost for each product being tested would be \$50,000.

The fixed costs for clinical trials would be financed by the earnings of the prize fund. Because the clinical trials would not be done more than once a year, the expected maximum cost of such trials would be \$4 million over an eight year period. However, because of the difficulty of overcoming a preliminary review of the feasibility of the diagnostic device, and the significant (estimated at \$50,000) cost of the application to be tested, it is anticipated that there will in fact be no applicants for clinical trials in some if not several years, lowering the overall costs to the Prize Fund of evaluating contestants.

Period of Prize Offer

The relationship between the period of the prize offer and the rules for the offer would be as follows:

1. The prize would be initially offered for eight years, period deemed sufficient for contestants to consider investing in the development of such a diagnostic test.
2. If a prize offer ends without a winner of the TB Diagnostic Grand Prize, the reward could be withdrawn, or offered with a different level of funding and/or terms of reference.
3. Supplementary funding could be offered for the existing term of an offer.
4. At any point, the prize offer could be extended.
5. Different levels of funding or other terms of reference could be offered for the extended term.

Interim Prizes

Until the TB Diagnostic Grand Prize is claimed, the prize amount will be invested in income-generating securities. The income will be used to fund the following prize programs to advance science and technology relevant to the TB Diagnostic test:

Technical Challenge Prizes

Part of the money from investment earnings will be spent on innovation inducement prizes that focus on solving technical challenges, such as the type of prize competitions now being offered by firms like the Lilly-launched start-up company, InnoCentive. These prize competitions could be done in-house, or outsourced to firms or non-profit organizations with expertise in managing such innovation prizes.

Biannual “Best Contributions” Prizes

The other type of prize would be a biannual prize competition for the “best contributions” to the scientific and engineering know-how needed to develop new TB Diagnostic test. The “best contribution” prizes, given every two years, would feature up to three prizes, if entrants were

considered sufficiently good. No prizes would be given if there were no impressive entrants, and the money would be reinvested and re-allocated to the next round of prizes.

Developing Country Researcher Set-Aside

At least half of the rest of the “best contributions” prize money would be a set-aside for research teams working in developing countries.

Intellectual Property Rights for TB Diagnostic Prize Fund

A licensing pool would be created under the name the TB Licensing Agency (TBLA) in order to acquire and manage the needed rights in the relevant patents and know-how for the new TB diagnostic tests. In order to make claims on any of the prizes, the winner must grant reasonable and non-discriminatory licenses to all patents and know how needed for competitive supply of the technologies, in the relevant field of use .

If open licensing of the technology and competitive generic supply is not feasible, the Prize Fund Committee may agree that as an alternative contestant provide sufficient assurances, covered by financial guarantees, that the products will be manufactured in sufficient quantities and acceptable quality, at affordable prices.

Incentives for Collaboration and Access to Knowledge

In order to ensure there are incentives for openness and sharing among researchers, the TB Diagnostic Grand Prize money would be divided as follows: the winning entrant would get 90 percent of the prize money; the remaining 10 percent of the prize money would be given to unaffiliated and uncompensated (by the winning entrant) scientists and engineers that openly published and shared research, data materials and technology, on the basis of who provided the most useful external contributions to achieving the end result⁴. This would include research, data, materials and technology that were either placed in the public domain, or subject to open, non-remunerated licenses.

To qualify for the “best contributions” prizes, published research findings would have to be freely available on the Internet in full text, and with appropriate access to relevant materials and research. As an incentive to journals to make articles available to the public for free, 10 percent of the “best contributions” prize given for a published article would be available to a peer-reviewed journal that published the article, on the condition that the journal made the article available for free immediately upon publication.

Funding

Governments and private donors would contribute to the prize. The WHO should consider possible funding mechanisms for the prize that can be reasonably implemented in both developed and developing countries.

One possible norm for funding the prize would be that participating developed countries would be

⁴ The division of the prize between 90%/10 % is a suggestion that seems an appropriate division to start a discussion on incentives for collaboration and access to knowledge.

expected to contribute 90 percent of the funds, while developing countries would collectively contribute 10 percent.

Developed Country Contributions

For participating developed countries, consideration should be given to contributions in proportion to their GDP.

For example, based upon data before the current economic crisis, if there was participation by the US, Japan, the richest 15 members of Europe, and 13 other high-income countries, the United States contribution would be \$33 million, the richest 15 members of Europe (by per capita income) would collectively contribute \$34 million, Japan would contribute \$11 million, and a group of other developed countries would collectively contribute \$12 million, based upon relevant income shares. For developed countries, these obligations are quite small given the great benefits of the test, and the fact that the test would have utility within health systems everywhere.

Developing Country Contributions

For developing countries, consideration should be given to basing contributions to the prize fund on a formula based upon developing country budgets for the treatment of tuberculosis. This approach will require larger contributions from developing countries that will benefit more from the development of the diagnostic device.

WHO/PAHO Meetings on this Proposal

The WHO should hold meetings in September of 2009 to consider this proposal. PAHO should organize a preliminary regional meeting in May/ June 2009 on the proposal.