



## Prizes for Global Health Technologies

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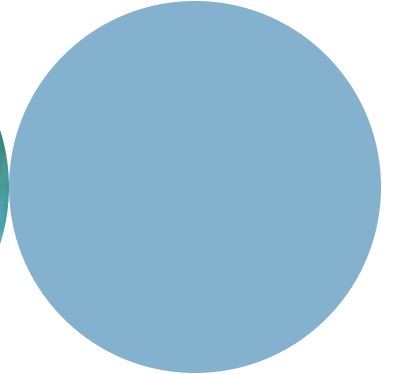
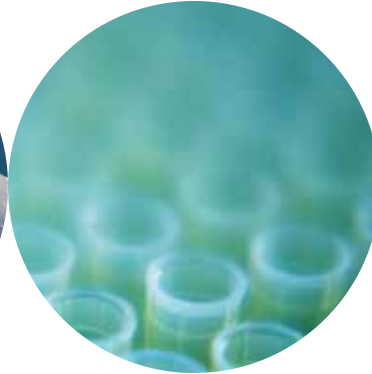
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## List of Abbreviations

ALS	amyotrophic lateral sclerosis
AMC	advance market commitment
BBBS	Bangladesh, Barbados, Bolivia, and Suriname
BVGH	BioVentures for Global Health
FIND	Foundation for Innovative New Diagnostics
IP	intellectual property
IVD	in-vitro diagnostics
KEI	Knowledge Ecology International
MSF	Médecins Sans Frontières
NGO	nongovernmental organization
OECD	Organisation for Economic Co-operation and Development
PDP	product-development partnership
POC	point-of-care
R&D	research and development
R4D	Results for Development Institute
SSM	sputum smear microscopy
TB	tuberculosis
WHO	World Health Organization

## EXECUTIVE SUMMARY



**Prizes are enjoying a resurgence. More and larger prize contests are being launched and prizes of all kinds are attracting attention from scholars, policy-makers, governments, and funders.**

In the health field, several groups have proposed incentive prizes—large cash rewards for achievement of specified objectives—as a way to spur development of needed new health technologies (drugs, vaccines, and diagnostics) for the diseases of the developing world, products that have been largely neglected by a pharmaceutical industry focused on lucrative markets in high-income countries. There is little experience with prizes for health product development, however, and many questions remain about the feasibility of this approach. This study addresses some of these questions, including the relevance of prizes for different kinds of technologies, the willingness of product developers to pursue a prize, the merits of prizes for final products (“end” prizes) as well as important milestones in product development, and the best way to promote affordable access to products developed through prizes. It focuses primarily on the potential of prizes for specific products to motivate research and development (R&D) by for-profit firms.

The study has two main parts: a general analysis of the strengths and weaknesses of prizes as a way to drive product development and access in the developing world and a detailed case study of recent prize proposals for point-of-care (POC) tuberculosis (TB) diagnostics. In addition, it offers a preliminary analysis of prizes for other health products and of the merits of prizes relative to other approaches to financing neglected-disease R&D.

The study relies on a review of previous work on prizes, on interviews with prize and disease experts and with industry executives, and on analysis by the authors.

Prizes, like advance market commitments—and the patent system—promote investment in specified products by increasing the reward for success, in contrast to grants and other so-called “push” mechanisms that reduce the cost or risk to product developers. An important advantage of prizes is that sponsors do not have to choose among candidate products or product developers: they need only define with sufficient precision the desired product (or product-development milestone) and then leave the door open to all comers. Prizes can thus bring new minds and new ideas to difficult problems and are particularly attractive when the way forward is not clear and substantial innovation is required. Since prize sponsors pay only if their conditions are met, R&D funding through prizes can be considered a form of “results-based financing.”

An important disadvantage of prizes relative to grants and contracts is that only researchers and product developers who can bear the risk and raise the necessary funds for R&D upfront can participate. This may exclude valuable contributors.

A prize for a neglected-disease drug, vaccine, or diagnostic test will have failed if the new product does not reach the people who need it. No R&D mechanism can guarantee access, but prize design should at least take access into account. Several ways to promote access to products developed through prizes have been proposed. One approach is to make the prize reward contingent on licensure of relevant intellectual property (IP) to all interested manufacturers. This strategy could be a powerful way to ensure sustainable supply at an affordable price, but only if generic production is feasible, markets are



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sufficient to attract suppliers, and prize specifications steer developers toward appropriate technologies. Moreover, licensing provisions must be acceptable to product developers if a voluntary prize mechanism is to succeed. Other ways to promote access are to include cost provisions in the prize specifications or to require winners to supply the product at an agreed price or at an agreed markup from cost. These approaches may not be as effective as competitive supply in driving down prices and ensuring supply over the long run but may be more practical in many cases.

Tuberculosis claims almost two million lives every year and progress in controlling the disease in developing countries has been slow, especially where HIV prevalence is high, in large part because of inadequate drugs, vaccines, and diagnostics. In particular, there is broad consensus that an improved diagnostic test—one that would be more sensitive and accessible than sputum smear microscopy, the current standard in most poor countries—could save many lives and slow transmission. The primary obstacles to development of the needed point-of-care tests are technological: the two most promising paths are blocked, respectively, by lack of biomarkers and lack of a suitable platform for use in remote areas. The X PRIZE Foundation and a coalition of four countries, Bolivia, Barbados, Bangladesh, and Suriname (BBBS), supported by Knowledge Ecology International and Médecins Sans Frontières, have independently proposed prizes for improved TB tests. Both are end prizes for tests that meet a set of specifications in field trials. Neither is yet funded or launched. We have assessed these proposals in detail, drawing on information provided by the proposal developers, as well as publicly available documents, and interviews with TB experts and diagnostic firms.

The X PRIZE proposal offers \$5–20 million for winning products, depending on performance in several dimensions, while the BBBS proposal offers a \$100 million grand prize to the first winning product plus smaller prizes along the way. We conclude from interviews with diagnostic firms and our own analysis that the X PRIZE purse, while it might cover R&D

costs, is probably too small, given the risks, to spur widespread industry investment. There may be a substantial market for a POC TB test; thus, the prize need not provide the sole return on investment. Yet \$5–10 million is small compared to the expected market, so would probably not change the commercial calculations of firms. The prize amount suggested by BBBS, considered in isolation from other aspects of this proposal, is almost certainly sufficient to interest a wide range of firms.

The two proposals differ as well in their approach to access. BBBS would require that winning product developers license all IP necessary for competitive supply, in the field of use, to a patent pool. They must also meet a manufacturing cost provision or market penetration test. We conclude that licensing provisions for diagnostics would deter some firms from participating. Making prizes large enough to compensate for lost market exclusivity could make licensing acceptable to many firms, but only if an acceptable and enforceable way can be found to handle IP related to technological platforms that can be used for multiple tests. The X PRIZE proposal requires only that contestants submit a manufacturing plan with some cost information—we believe that this provision is unnecessarily weak and that the prize criteria should include a cost ceiling of some kind. Firms consulted for this study had no objection in principle to cost targets.

The two proposals include other features that would increase their appeal to product developers, including subsidized clinical trials and, in the case of the X PRIZE proposal, access to specimen banks and a promise to help aggregate demand. The X PRIZE Foundation's demonstrated capacity to attract media attention could also appeal to industry.

Would a TB diagnostics prize change the behavior of firms and speed development of urgently needed new tests? Discussions with firms, based largely on hypothetical scenarios, cannot provide a definitive answer. But we believe that a prize of the right size and design could make a difference. The class of firms most likely to respond to this kind of incentive is established biotechnology companies, which have

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more flexibility to pursue secondary applications of their technologies than start-ups, are attracted by revenue opportunities too small to interest the largest diagnostic firms, and are more willing to consider new business models. Biotechnology firms are also more likely to provide the type of breakthrough innovation needed and might see a TB prize contest as an opportunity to validate their technologies. But these firms, which have a high cost of capital and may not be able to take a product all the way through clinical trials, would be more interested in a milestone than an end prize. Since the primary obstacles to a POC TB test are technological and the market could probably pull promising candidates through later development, a milestone prize might be the most appropriate design for this product.

Some of the largest diagnostic firms are already investing in TB tests and might find the publicity associated with a global-health prize attractive, but they are less willing than biotechnology firms to consider prizes a viable commercial alternative to market revenues.

More generally, our discussions suggest that milestone prizes are more familiar to most firms, as milestone payments are a common feature of partnerships between firms. End prizes designed to substitute for inadequate markets constitute a more radical departure from established ways of doing business and our interviews suggest that the idea is not always well understood. In theory, prizes that are sufficiently large to offer a return on investment comparable to that promised by alternative uses of resources should be able to compete successfully for R&D investment. Since commercially unattractive markets are characteristic of neglected-disease products—this is, after all, the main reason they are neglected—end prizes should continue to be developed as potential solutions. But milestone prizes may be an easier—and quicker—way to test important features of the prize concept and familiarize industry with this new mechanism. Milestone and end prizes are not incompatible, of course, and some groups are considering incentive structures that include rewards at more than one stage.

To what extent do our conclusions from TB diagnostics hold for other diagnostics and for other drugs and vaccines? We believe that much of our analysis could apply quite broadly. But several features of products and product markets influence the value and design of prizes. First, the potentially considerable market for an improved TB test means that a milestone prize may be sufficient; this will not be the case for many neglected-disease products with much smaller markets, which will require additional subsidy in the form of end prizes or push funding to reach patients. Second, prizes for drugs or vaccines would probably have to be much larger than prizes for diagnostics because of the greater R&D costs and longer development timelines. Third, licensing and competitive supply as a strategy for sustainable access is most suited to small-molecule drugs, for which generic regulatory pathways are well established and patents are the main barrier to competitive supply.

When are prizes a better approach than other R&D financing mechanisms, including grants and subsidies through product-development partnerships? Our study did not focus on this question, but our analysis suggests that prizes are probably most useful where two conditions are met. First, the way forward is not clear and new ideas are needed to overcome scientific or technological barriers; second, the kinds of innovators whose participation is most required are likely to be able to find funding to pursue a prize. Where these conditions are not met—for example, when the necessary R&D is relatively straightforward and product developers with the necessary expertise can be identified—conventional push approaches are probably more appropriate and less costly.

CHAPTER 1  
INTRODUCTION



# 1 New drugs, vaccines, and diagnostic tests that meet the needs of the developing world could save millions of lives.

But despite the enormous potential benefits of these new health technologies, which could include vaccines against malaria, drugs for late-stage Chagas disease, and faster and more sensitive tests for tuberculosis (TB), only a small fraction of global investment in health research and development (R&D) is devoted to them.<sup>1</sup> Although there are often many obstacles to development of particular products, the fundamental cause of this imbalance is the poverty of those who would benefit from them and of their governments. This translates into small and uncertain markets and lack of incentive for investment by the private pharmaceutical industry, which is responsible for most health technology development and manufacturing.

Governments and philanthropic foundations have attempted to substitute for private-sector investment in these products through grants to university researchers and to product-development partnerships (PDPs), among other channels.<sup>2</sup> A variety of alternative approaches to accelerating neglected-disease R&D have been proposed, however, and several have been implemented in recent years.<sup>3</sup> The Center for Global Health R&D Policy Assessment, a project of the Results for Development Institute (R4D), is carrying out in-depth studies of several of

these new ideas, with the aim of helping potential donors, policy-makers, and others to decide whether and in which circumstances these new approaches could be useful.<sup>4</sup>

R4D's work in this area builds on and aims to contribute to an ongoing effort by the World Health Organization (WHO). In 2006, WHO established an intergovernmental working group to address issues of innovation, intellectual property (IP), and public health, which drew on analysis conducted by an earlier WHO commission. R&D incentives and financing were subsequently considered by an expert working group, and a new group is currently being established to revisit these issues.<sup>5</sup> These WHO processes remain an important forum for discussion of how to better align R&D with global public health needs.

Prizes, which have been used for centuries to reward achievement and stimulate innovation, are enjoying a resurgence lately, and governments, foundations, and the private sector are exploring their potential in a variety of contexts, including global health.<sup>6</sup> Advocates have proposed that large cash prizes could spur the development of needed health technologies—drugs, vaccines, and diagnostics—by bringing new ideas to difficult problems, focusing R&D effort on public health needs, and providing

<sup>1</sup> Commission on Health Research for Development, *Health Research: Essential Link to Equity in Development* (New York: Oxford University Press, 1990) and subsequent reports on the “10/90 gap” by the Global Forum for Health Research.

<sup>2</sup> George Institute for International Health, *Neglected Disease Research & Development: New Times, New Trends*, (G-FINDER 2009): accessed 15 Nov 2010, [http://www.policycures.org/downloads/G-FINDER\\_survey\\_of\\_global\\_R&D\\_funding\\_for\\_Neglected\\_diseases\\_2009.pdf](http://www.policycures.org/downloads/G-FINDER_survey_of_global_R&D_funding_for_Neglected_diseases_2009.pdf).

<sup>3</sup> Robert Hecht, Paul Wilson, and Amrita Palriwala, “Improving Health R&D Financing for Developing Countries: A Menu of Innovative Policy Options,” *Health Affairs* 28, no.4 (01 Jul 2009): 974–85.

<sup>4</sup> For more information on the Center for Global Health R&D Policy Assessment, visit <http://healthresearchpolicy.org/>.

<sup>5</sup> The report of the intergovernmental working group led to the adoption by the 61st World Health Assembly of a *Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property*, [http://apps.who.int/gb/ebwha/pdf\\_files/A61/A61\\_R21-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/A61/A61_R21-en.pdf). The executive summary of the expert working group's report can be found at [http://apps.who.int/gb/ebwha/pdf\\_files/EB126/B126\\_6Add1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB126/B126_6Add1-en.pdf).

<sup>6</sup> “And the Winner Is...” *The Economist Online*, (San Francisco, 5 Aug 2010): accessed 05 Nov 2010, <http://www.economist.com/node/16740639>.

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a return to commercial investment in products with small or uncertain markets.

These ideas are attractive, but there has been very little experience so far with prizes as an incentive for pharmaceutical R&D, especially for the expensive later stages of product development.

This report analyzes the potential of prizes for global-health R&D, asking in what contexts—for what kinds of products and for what stages of product development—they might accelerate R&D, and analyzing how they should be structured to achieve the desired ends. As a case study, we consider prizes for TB diagnostics, as several groups are developing proposals in this area. We believe that many of our findings from this in-depth example are relevant to other diagnostics, drugs, and vaccines, although with important caveats.

There are, of course, many kinds of prizes. This study assesses what are sometimes called incentive or inducement prizes—cash awards for the achievement of specified aims—as opposed to recognition prizes such as the Nobel that reward past achievement. More specifically, we focus on prizes for specific new products or for substantial R&D milestones on the path to these products.<sup>7</sup> We do not consider either small inducement prizes for solutions to specific technical or scientific problems or proposals for very large prize funds covering a broad range of products. These multiproduct prize funds proposals are intellectually compelling but involve complex additional issues. These ideas may be considered in a subsequent R4D assessment.

Our assessment looks to answer several questions, in detail for the TB diagnostics prize proposals and in more general terms for prizes for other health products.

- Are the specifications for the product or milestone clear, achievable, and sufficiently ambitious? Would a product that satisfied them meet needs in the field?
- Would the proposed mechanism engage innovators and spur investment in the necessary R&D? Is the reward sufficiently large to shift industry priorities? Which kinds of firms are most likely to be attracted by the prize?
- Does the proposal include workable mechanisms for ensuring that a product that won the prize would reach those who need it? What provisions does it make for sustainable supply at an affordable price?
- More generally, to which types of products and which stages of R&D are prizes best suited and which aspects of prize design are most important in determining success? In particular, in which circumstances are milestone prizes or end prizes (or a combination of the two) the best solution to a particular R&D challenge?

We have addressed these questions through review of the published literature and interviews with prize proponents and experts, TB and diagnostics specialists, and executives and investors from the diagnostics industry, supplemented in places by our own theoretical analysis. Appendix A lists the people interviewed for the study. Our interviews with potential prize competitors focused primarily on for-profit firms, because we believe that participation of industry is critical to the success of prizes aimed at final products or advanced milestones in pharmaceutical product development.<sup>8</sup> Most of the firms and investors that we consulted were based in the United States and Europe: exploration of the potential of prizes for engaging researchers and product developers in developing countries is an important area for further work.

<sup>7</sup> We also do not consider the intriguing idea that prizes could also be used to spur innovation in health product delivery.

<sup>8</sup> Much if not most breakthrough innovation happens at universities. But university scientists are generally not able to translate their ideas into actual products and must have up-front funding in the form of grants. The goal of the interviews with firms was not to elicit the preferences of industry per se, but to understand whether prizes would change investment decisions of firms of different types and how these decisions might be influenced by various aspects of prize design. This information is crucial to an assessment of prizes, since their success requires the voluntary participation of product developers.

## INTRODUCTION

In chapter 2 of this report, we provide an overview of the potential benefits of prizes and address some important aspects of prize design. In chapter 3 we draw on this framework to analyze the TB diagnostics prize proposals. Chapters 4 and 5 consider prizes for other technologies and outline some advantages and disadvantages of prizes relative to other R&D incentives. In chapter 6 we present some broad conclusions and acknowledge some important limitations of our study.

CHAPTER 2  
GENERAL FRAMEWORK





## There is considerable theoretical literature on prizes and similar inducements to innovation.<sup>9</sup>

Although we cannot provide a thorough review of this work here, we present in this chapter an overview of the main potential advantages and disadvantages of prizes as a tool for driving innovation in global health, as well as an analysis of several important elements of prize design. This general framework will inform our detailed assessment of TB diagnostic proposals in chapter 3 and our preliminary look at the potential of prizes for other technologies in chapter 4.

We begin this chapter with a summary of some of the developments which led to the recent interest in prizes as a way to spur development of needed health technologies for the developing world.

### 2.1. Background

Innovation prizes have a long history. The prize offered by the British government in 1774 for determination of longitude at sea (the Longitude Prize) is perhaps the best-known example,<sup>10</sup> but

governments, foundations, and individuals have offered numerous prizes for the achievement of pre-specified objectives in areas as diverse as agriculture, mathematics, aviation, and medicine.<sup>11</sup> Many of these prizes were successful and led to important new technologies.

With the growth of government grant funding for research and increasing reliance on the patent system to spur commercial investment, the use of prizes to drive innovation declined in the twentieth century.<sup>12</sup> But prizes are back in fashion: a recent report from McKinsey & Company found 60 prizes of \$100,000 or more launched since 2000; although this list includes so-called “recognition prizes” honoring past achievement, inducement prizes account for most of this new money for prizes.<sup>13</sup>

There have been few prizes for neglected-disease health technologies, however. In 1994, the Rockefeller Foundation offered a prize of \$1 million for the development of a simple, rapid point-of-care (POC) test for gonorrhea and Chlamydia infection.<sup>14</sup>

<sup>9</sup> Brian D. Wright, “The Economics of Invention Incentives: Patents, Prizes, and Research Contracts,” *The American Economic Review*, 73, no. 4 (1983): 691–707; Suzanne Scotchmer, *Innovation and Incentives*, (Cambridge, MA: MIT Press, 2004); Michael Kremer and Rachel Glennerster, *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, (Princeton: Princeton University Press, 2004); and Steven Shavell and Tanguy van Ypersele, “Rewards versus Intellectual Property Rights,” *Journal of Law and Economics*, 44, no. 2, (2001): 525–547. See also the prizes bibliography developed by Knowledge Ecology International, <http://keionline.org/content/view/82/1>.

<sup>10</sup> Dava Sobel, *The Illustrated Longitude: The True Story of the Lone Genius Who Solved the Greatest Scientific Problem of His Time*, (Walker, 1998).

<sup>11</sup> *Selected Innovation Prizes and Reward Programs*, Knowledge Ecology International, (2008): accessed 15 Nov 2010, [http://www.keionline.org/misc-docs/research\\_notes/kei\\_rn\\_2008\\_1.pdf](http://www.keionline.org/misc-docs/research_notes/kei_rn_2008_1.pdf); William A. Masters and Benoit Delbecq, *Accelerating Innovation with Prize Rewards: History and Typology of Technology Prizes and a New Contest Design for Innovation in African Agriculture*, IFPRI Discussion Paper 00835, (December 2008): accessed 15 Nov 2010, <http://www.ifpri.org/sites/default/files/publications/ifpridp00835.pdf>. See also Lee Davis and Jerome Davis, *How Effective Are Prizes as Incentives to Innovation? Evidence from Three 20th Century Contests*, paper presented at the DRUID Summer Conference on Industrial Dynamics, Innovation, and Development, (Elsinore, Denmark, 2004): accessed 26 Jan 2011, [http://www.druid.dk/uploads/tx\\_picturedb/ds2004-1343.pdf](http://www.druid.dk/uploads/tx_picturedb/ds2004-1343.pdf).

<sup>12</sup> William A. Masters and Benoit Delbecq, *Accelerating Innovation with Prize Rewards: History and Typology of Technology Prizes and a New Contest Design for Innovation in African Agriculture*, IFPRI Discussion Paper 00835, (December 2008): accessed 15 Nov 2010, <http://www.ifpri.org/sites/default/files/publications/ifpridp00835.pdf>.

<sup>13</sup> *And the Winner Is...: Capturing the Promise of Philanthropic Prizes*, McKinsey, (2009): accessed 26 Jan 2011, [http://www.mckinsey.com/App\\_Media/Reports/SSO/And\\_the\\_winner\\_is.pdf](http://www.mckinsey.com/App_Media/Reports/SSO/And_the_winner_is.pdf).

<sup>14</sup> S. Berkley, “Diagnostic Tests for Sexually Transmitted Diseases: A Challenge,” *Lancet*, 343, no. 8899, (19 Mar 1994): 685–6 and David Mabey, Rosanna W. Peeling, and Mark D. Perkins, “Rapid and Simple POC Diagnostics for STIs,” *Sexually Transmitted Infections*, 77, no. 6 (2001): 397.



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This award was never claimed, however, perhaps because the technical requirements were too stringent and the amount too small.<sup>15</sup>

The more recent interest in prizes for global health stems from at least four sources. First, the Center for Global Development's proposal for Advance Market Commitments (AMCs) for new vaccines for the developing world, which arose out of earlier academic work on prizes and AMCs and led to the current pneumococcal vaccine AMC, drew attention to the idea of large rewards for successful product development as an alternative to grants and other conventional forms of support for neglected-disease R&D.<sup>16</sup>

Second, large prize funds covering a broad range of products have been proposed as an alternative to patent-protected monopolies as the primary incentive to commercial medical innovation.<sup>17</sup> These very ambitious proposals, put forward by James Love of Knowledge Ecology International (KEI) and his collaborators and also by Thomas Pogge and Aidan Hollis as the Health Impact Fund, are focused as much on ensuring access to new products at affordable prices as on stimulating new innovation. The concept of an all-encompassing prize fund for medical innovation was embodied in a bill submitted to the US Congress by Senator Sanders of Vermont in 2007.<sup>18</sup> Prizes and prize funds were also discussed by the WHO Intergovernmental Working Group on Public Health, Innovation, and Intellectual

Property. The resulting World Health Assembly Resolution endorsed exploring prizes among other incentive mechanisms.<sup>19</sup>

Third, the success of InnoCentive, an organization specializing in the design and management of prizes for solutions to specific scientific and technological challenges, has attracted the attention of the neglected-disease R&D community.<sup>20</sup> Several product development partnerships have used InnoCentive to launch prize contests. These prizes have generally been small, however, and have typically been aimed at the solution of particular technological problems, not actual product development. For example, the International AIDS Vaccine Initiative posted a \$150,000 challenge on InnoCentive for a way to produce an important viral protein in a particular conformation.<sup>21</sup> Although there were more than 300 responses to the challenge, none met the requirements. But a contest posted by the Global Alliance for TB Drug Development, for simpler and safer ways to synthesize a candidate drug, had two winners.<sup>22</sup>

Finally, the success of the Ansari X PRIZE for private space flight, perhaps the most publicized recent prize contest, has greatly raised the profile of prizes among policy-makers and the general public.<sup>23</sup> Since the space prize, the X PRIZE Foundation has moved into new areas, including biotechnology and medicine, and it is considering launching a prize for TB diagnostics.<sup>24</sup> We assess this proposal in chapter 3.

<sup>15</sup> M. Tam, formerly of PATH and involved in the Rockefeller prize, personal communication to Amrita Palriwala, 19 Jul 2010.

<sup>16</sup> Center for Global Development, *Making Markets for Vaccines*, (2005): accessed 08 Nov 2010, [http://www.cgdev.org/section/initiatives/\\_archive/vaccinedevelopment](http://www.cgdev.org/section/initiatives/_archive/vaccinedevelopment). See also GAVI's website about the AMC, which provides links to many documents, <http://www.vaccineamc.org>.

<sup>17</sup> James Love and Tim Hubbard, "The Big Idea: Prizes to Stimulate R&D for New Medicines," *Chicago-Kent Law Review*, 82, no. 3, (November 2007) and Thomas Pogge and Hollis Aiden, "The Health Impact Fund: Making New Medicines Accessible for All," *Incentives for Global Health*, (2008): accessed 26 Jan 2011, [http://www.yale.edu/macmillan/igh/hif\\_book.pdf](http://www.yale.edu/macmillan/igh/hif_book.pdf).

<sup>18</sup> Medical Innovation Prize Act of 2007, S.2210, 110th Cong. (2007)

<sup>19</sup> WHO, resolution of the 61st World Health Assembly, *Global Strategy and Plan of Action on Public Health, Innovation, and Intellectual Property*, (24 May 2008): accessed 26 Jan 2011, [http://apps.who.int/gb/ebwha/pdf\\_files/A61/A61\\_R21-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/A61/A61_R21-en.pdf).

<sup>20</sup> For more information, visit the InnoCentive website, <http://www2.innocentive.com/>.

<sup>21</sup> "The International AIDS Vaccine Initiative Posts \$150,000 Challenge on InnoCentive in Search of New Approaches to AIDS Vaccine Design," *Medical News Today* (19 Dec 2008), accessed 15 Nov 2010, <http://www.medicalnewstoday.com/articles/133522.php>.

<sup>22</sup> TB Alliance, "A Global Effort to Reduce the Costs of a TB Drug Candidate," (07 Nov 2008): accessed 26 Jan 2011, <http://new.tballiance.org/newscenter/view-brief.php?id=822>.

<sup>23</sup> For more information on the Ansari X PRIZE, visit <http://space.xprize.org/ansari-x-prize>.

<sup>24</sup> "X PRIZE Foundation to Help Fight Tuberculosis Worldwide with Gates Foundation Support," *Medical News Today* (21 Oct 2008): accessed 05 Nov 2010, <http://www.medicalnewstoday.com/articles/126154.php>.

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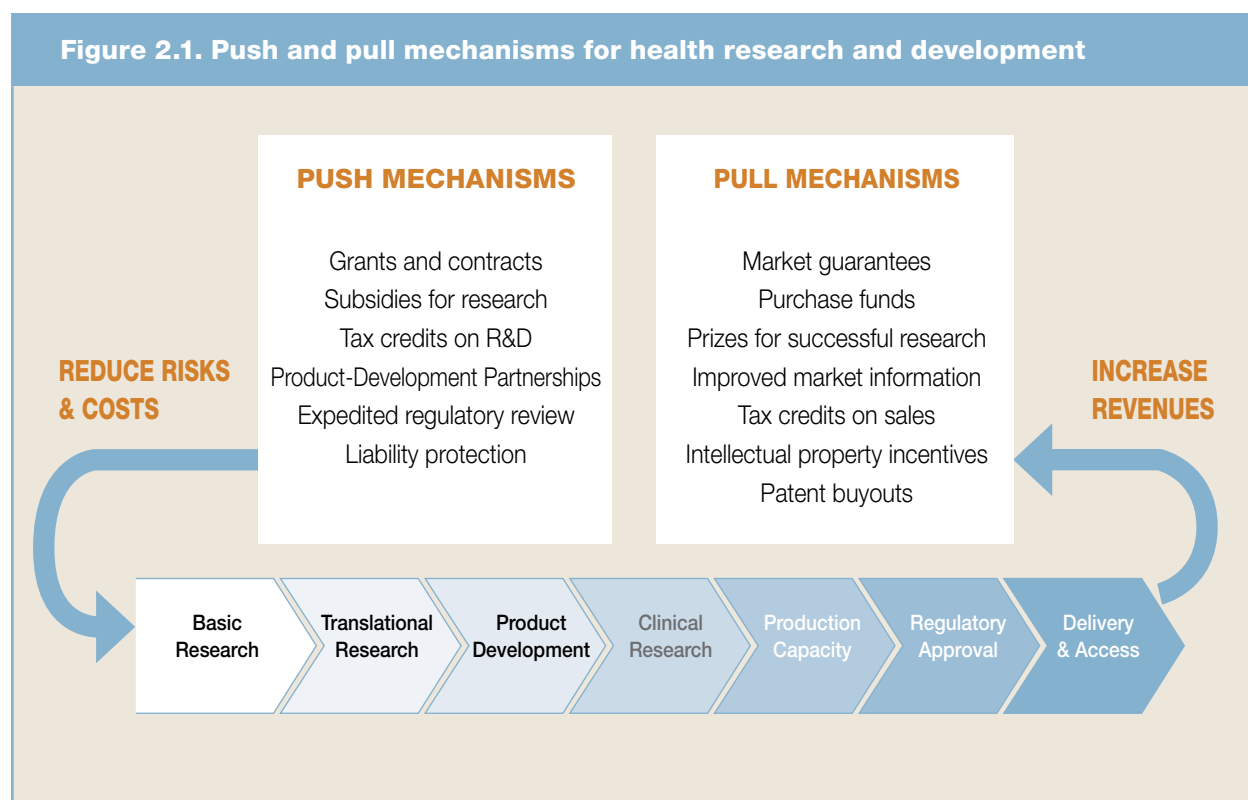
These prize concepts differ greatly in scale, design, and intent—section 2.3 of this chapter addresses some of these differences. But they have converged to make prizes a hot topic among policy experts and funders interested in new health technologies for the developing world. Although the AMC, the big multi-product prize funds, and InnoCentive are beyond the scope of the current assessment, which focuses on prizes for particular products or R&D milestones, we refer to these ideas in several places.

### 2.2. Advantages of prizes

Prizes are an example of a “pull” mechanism for motivating R&D. Incentives of this kind make investment in development of a particular product more attractive by increasing the reward for success, in contrast to

“push” mechanisms that work instead by reducing the risk or cost of R&D—for example, through grants or tax breaks (see figure 2.1). Other examples of pull incentives are advance purchase or market commitments and the US Food and Drug Administration’s Priority Review Voucher, which is essentially a prize with the voucher as the reward instead of a cash payment.<sup>25</sup>

Prizes share two major theoretical advantages with other pull incentives. First, unlike grant funders, who pay whether or not the funded research leads to something useful, prize sponsors pay only for success. (In practice things may not be so clear-cut: sponsors must pay if the product specifications or milestones spelled out in the contest guidelines are met, which may not always mean that the original



Source: Adapted from International AIDS Vaccine Initiative

<sup>25</sup> For an overview, see M. Kremer and R. Glennerster, *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, (Princeton University Press, 2004). On priority review vouchers, see D. B. Ridley, H. G. Grabowski, and J. L. Moe, “Developing Drugs for Developing Countries,” *Health Affairs*, 25, no. 2 (2006): 313–324.

objectives were achieved.) Another way of expressing this is that product developers rather than funders bear the risk of failure. For funders this can be an important selling point.<sup>26</sup>

This advantage of pull incentives is more nuanced than it first appears. Because sponsors must make a prize big enough to compensate product developers for the risk of failure, a prize will cost more than a grant covering one research approach or candidate product. But since many such efforts will fail, the total cost to sponsors of funding enough “shots on goal” to ensure success may be similar to the cost of a prize (if developers’ assessment of risk—and the sponsor’s guess at this assessment—are accurate). This basic equivalence is often misunderstood by advocates of one approach or the other. In the real world, of course, the cost-effectiveness of push and pull mechanisms may well differ for a number of reasons (see chapter 4 and appendix B).

A related advantage of pull mechanisms is an alignment of incentives between sponsors and product developers. Since developers will be paid only if they meet the prize specifications, they are strongly motivated to do so and sponsors do not have to “police effort.” Grant recipients, on the other hand, may be motivated more by the need to perpetuate grant funding than to reach the final objective, and funders must constantly check that their money is being well spent.

Second, prize sponsors only have to specify the desired end—the product or R&D milestone—not the path to this end. In other words, they do not have to “pick winners,” either among competing research approaches or product candidates or among researchers and product developers. Grant funders, of course, must choose whom to fund by evaluating

potential grantees and proposed approaches.

This advantage of pull mechanisms is particularly pronounced when the way forward is not clear to the sponsor or where the best solution to a problem could come from unknown or unexpected sources. (Economists call this an information asymmetry, in that innovators generally know more than R&D funders about their own capacities.) Prizes in this way constitute a more open model for innovation than push funding, in that in theory any researcher can participate and hope to win the reward. The “crowd-sourcing” models of web-based prize mechanisms like InnoCentive take full advantage of this openness, drawing on the expertise and creativity of thousands of potential “solvers” worldwide.<sup>27</sup>

These advantages of prizes apply as well to advance purchase or market commitments, in which the reward for product development takes the form of subsidized or guaranteed product sales. Prizes have an additional advantage relative to these mechanisms, however: they separate or “de-link” reward for innovation from product prices. In other words, they separate markets for R&D from markets for products.<sup>28</sup> Since R&D is expensive and risky, product developers relying on product sales to repay R&D costs must charge more than the cost of producing the product, sometimes much more; this distorts markets and can be an important barrier to access.<sup>29</sup> Love and others have proposed that access to new products could be maximized by paying for R&D through prizes and then allowing prices to fall close to cost through competitive supply. This and other approaches to ensuring access are discussed further in section 2.5 of this chapter and in the TB diagnostics case study.

Another potentially very important advantage of prizes is the ability to attract attention to neglected problems

<sup>26</sup> Curiously, this advantage of prizes can in some circumstances create a budgetary headache for funders. Sponsors pay only if the prize is won, but may have to set money aside for the award. This money may be difficult to reallocate or even lost if the prize is not claimed.

<sup>27</sup> Karim R. Lakhani, *InnoCentive.com (A)*, Harvard Business School Publishing, (October 2009).

<sup>28</sup> James Love and Tim Hubbard, “The Big Idea: Prizes to Stimulate R&D for New Medicines,” *Chicago-Kent Law Review*, 82, no. 3, (November 2007).

<sup>29</sup> Patent protection confers a partial and temporary monopoly, with the attendant economic losses; this drawback of IP is generally accepted by economists. See, for example, Nancy Gallini and Suzanne Scotchmer, *Intellectual Property: When Is It the Best Incentive System?*, UC Berkeley Department of Economics Working Papers, no. E01-303, (2002): accessed 26 Jan 2011, <http://129.3.20.41/eps/le/papers/0201/0201001.pdf>.

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or needs, from a broad public as well as from those who might offer solutions. This attention can lead to new ideas and new effort beyond those associated directly with pursuit of the reward, and perhaps new funding from other sources as well. For prize contestants, it can translate into recognition, interest in their technologies, and good public relations, all which make participation more attractive and may cause them to invest more than could be justified by the prize award itself. Although this benefit of prizes is difficult to quantify, it is often cited by prize enthusiasts and figures prominently in the X PRIZE model, among others. It is worth noting, however, that this “publicity bonus” would presumably be diluted by widespread use of prizes: dozens or hundreds of simultaneous prize contests could not hope to garner as much attention as the Ansari X PRIZE, especially as the novelty of prizes wore off.

A more subtle form of the publicity advantage is the ability of prizes to reshape problems or redefine success in a useful way. Even if a prize does not attract new researchers to a field, it can redirect their efforts or cause them to think about a problem in a new way; if the prize specifications are well chosen, this could put the field on the path to success. For example, the Prize4Life Foundation, which uses prizes to further the search for a cure for amyotrophic lateral sclerosis (ALS or Lou Gehrig’s Disease), hopes to change the way ALS research is done by promoting more rigorous use of animal models and by focusing attention on the need for better markers of disease progression.<sup>30</sup>

Some other potential advantages of prizes are discussed in the McKinsey report.

### Potential risks and challenges

Prizes have potential risks and disadvantages as well, in addition to those mentioned above (see figure 2.2).

Three are particularly important. First, prizes (and pull mechanisms in general) can only work well if the desired result can be defined with clarity and precision and its features captured in practical product or milestone specifications. Bad specifications could discourage R&D altogether, lead researchers in an unproductive direction, limit the range of solutions pursued, or require sponsors to reward development of a useless product. We illustrate some of these risks with specific examples in the case study on TB diagnostics. The challenge of setting good prize specifications—as well as the difficulty of setting the prize amount—is particularly great when research is at an early stage. There is also a risk that prizes may limit the ambitions of innovators and forestall the development of improved products, if there is no incentive to exceed the prize specifications.<sup>31</sup>

Another major risk is that prizes, by pitting researchers against each other, could hinder the collaboration and sharing of information among researchers that PDPs and others have worked so hard to encourage. Prizes can also foster collaboration, as researchers work together in pursuit of the reward, and the design of prizes can be adapted to require or encourage sharing of results, but the mechanism is inherently competitive.<sup>32</sup> To the extent that prizes or other pull mechanisms make investment in certain areas of R&D attractive where it was not before, it is only natural that firms and other researchers who hope to capture some of this new value will be less willing to share what they know with potential rivals.

The competitive dynamic created by prizes is also potentially wasteful in that it can lead to duplication of effort. To the extent that contestants pursue distinct, viable approaches to a solution, the money required to attract many participants may be well spent; but having several developers with equivalent capacities investing in very similar product candidates is probably wasteful. In other words, the benefit of

<sup>30</sup> For more information, visit the Prize4Life website, <http://www.prize4life.org/>.

<sup>31</sup> This problem with prizes can be overcome, at least in theory, by dividing the prize among multiple winners according to measured performance or impact.

<sup>32</sup> For example, InnoCentive has considered introducing features to encourage collaboration within its prize contests. See Karim R. Lakhani, *InnoCentive.com (A)*, Harvard Business School Publishing, (October 2009).



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attracting multiple contestants depends on the diversity of their skills and approaches.

The most important disadvantage of prizes compared to grants and other forms of push funding is that it limits participation to researchers and product developers who can find the resources to fund the necessary R&D upfront. Although if the prize is attractive enough investors may be willing to finance pursuit of the reward, in practice some researchers with promising ideas will be excluded. The seriousness of this drawback depends on the kinds of innovators needed to solve a particular problem and on their capacity to raise the necessary funds.

It should be clear from this discussion that no general conclusion about the value of prizes compared to other ways of funding and motivating R&D is possible: the merits of a prize approach will depend on particular circumstances. But these general considerations provide a useful guide to identifying the cases in which prizes are most promising. We return to this discussion in chapter 5, after analyzing the case of TB diagnostics. Some theoretical aspects of the cost of prizes relative to grants are considered in appendix B.

**Figure 2.2. Potential advantages and disadvantages of prizes for global health technologies**

<b>Potential Advantages</b> 	<b>Potential Disadvantages</b> 
<ul style="list-style-type: none"><li>• Open up innovation: bring wide range of “solvers” to a problem</li><li>• Do not require specifying path to desired end or choosing developers</li><li>• Allow funders to pay only for success</li><li>• Align incentives of developers to those of funder</li><li>• Separate or “de-link” R&amp;D costs from product prices</li><li>• Harness competitive forces</li><li>• Attract attention, add glamour to a problem</li><li>• Redefine a problem in a useful way</li></ul>	<ul style="list-style-type: none"><li>• Exclude researchers or developers unable to fund necessary R&amp;D upfront</li><li>• Require specifying desired product characteristics far in advance</li><li>• May oblige funder to pay for unwanted product</li><li>• Can reduce cooperation</li><li>• May lead to duplication of effort</li><li>• Typically provide no incentive to exceed specified standards</li></ul>

### 2.3. Prize models and design issues

Current models for health-product prizes (both proposed and already launched) vary considerably. At the most basic level, these models differ in their objectives—the problems that they hope to solve—in ways that correspond loosely to the different potential advantages of prizes listed in the previous section. Since these basic differences in objectives are not always clearly articulated or understood, we illustrate the point with some examples (see figure 2.3).




Some prizes aim primarily to solve the problem of inadequate markets for important products—for example, health technologies that are needed most by the poor—by offering alternative sources of return sufficiently large to substitute for the missing markets.<sup>33</sup> The pneumococcal vaccine AMC, although not strictly a prize, falls into this class.

The big prize funds proposed by KEI and the related Health Impact Fund, although they would also correct for small markets, are focused at least as much on another problem: the barrier to access imposed by high prices for new, patented medicines. These proposals hope to remove this barrier by making the prize award conditional on licensure of multiple manufacturers.

Prize4Life and InnoCentive are intended instead to overcome early-stage scientific and technological obstacles by promoting and channeling new innovation. These interventions could be useful even when there might be substantial markets for the desired products, as there would be for a successful treatment for ALS.

The X PRIZE model, for its part, places great emphasis on the ability of prizes to attract attention,

**Figure 2.3. Examples of prize models and objectives**

Prize Model	Objective	Approach
	Augment inadequate markets for new vaccines in poor countries	Create a donor-subsidized market for new vaccines that meet agreed specifications
<b>Medical Innovation Prize Act of 2007</b>	Align medical innovation to public health need; promote access by bringing prices close to costs	Reward new products according to health benefit; enable generic production from regulatory approval
	Overcome scientific barriers to new treatments for ALS; make R&D faster and more efficient	Use milestone prizes to stimulate early-stage innovation and to make trials easier
	“Unlock” a market for point-of-care TB tests in developing countries	Use a prize to overcome technological barriers and attract attention to the field

<sup>33</sup> Diseases that affect few people—sometimes called “orphan diseases”—may also offer inadequate markets for drug developers. Some of the subsidies and other incentives in the Orphan Drug Act therefore resemble measures proposed for diseases of the developing world. The difference, of course, is that a decision to invest less in diseases that impose relatively little burden at the population level may be consistent with public health priorities.



transform thinking about whole fields, and inspire. In general, the X PRIZE Foundation believes that its prizes should not substitute for markets but instead should unlock them, in part by driving development of new technologies for which new markets will naturally materialize and in part by drawing attention to market opportunities that may not have been fully appreciated. These more visionary objectives are difficult to analyze in straightforward economic terms, but they may be powerful nonetheless.

In some circumstances, the main objective of a prize contest could be to reveal information about the capacities of innovators and the real value of technologies, which can then guide the decisions of investors and consumers. By submitting competing technologies to a rigorous test that predicts value in actual use, a prize contest can remove the “information asymmetry” that blocks progress.<sup>34</sup>

In many circumstances, more than one of these objectives may be relevant. But it is important to be clear about what a prize hopes to achieve and to make sure that the design of the incentive is appropriate for the chosen objectives.

Many different prize structures are possible—a full consideration of the relevant issues is beyond the scope of this study. But we address briefly three design issues.

### Winner-take-all versus multiple winners

The most familiar kind of prize is winner-take-all, with the entire prize purse going either to the first candidate to meet the specifications or to the best candidate presented within a specified period. These

designs have the advantages of simplicity and ease of communication. But they also make the contest riskier for potential contestants, which may deter some from participating.<sup>35</sup> In many cases, it may be better to reward several competitors, by giving prizes to all candidates that meet the specifications before an agreed deadline or the first ones up to a set number to do so. Having multiple winners also makes it more likely that multiple products with different characteristics reach the market—in this way the risk to sponsors is also reduced, since the chance that at least one product will have the desired impact is increased.

A further advantage of rewarding multiple winners is that by keeping more firms involved it may help to build a sustainable ecology of global health innovation and product development.

An interesting alternative is to divide the prize purse among contestants according to the estimated benefits of their invention. The prize funds proposed by Love and his coworkers and by the Health Impact Fund would take this approach, relating the size of prize payments for new health technologies to the incremental health benefits that they produce in actual use. A major challenge to this proposal is the difficulty and expense of measuring benefit, especially in developing countries where data are scarce.<sup>36</sup> Similarly, Masters proposes a prize competition for agriculture innovation for developing countries in which the purse would be divided among innovators according to the increases in yield resulting from their inventions.<sup>37</sup>

The main disadvantage of prize designs that reward multiple innovators is that they cost more.<sup>38</sup>

<sup>34</sup> See William A. Masters, “Research Prizes: A Mechanism to Reward Agricultural Innovation in Low-income Regions,” *AgBioForum*, 6 nos. 1 & 2, (2003): 71–74. Information is “asymmetric” because technology developers know more about their capacities than prize sponsors or potential consumers.

<sup>35</sup> Timothy N. Cason, William A. Masters, and Roman M. Sheremata, “Entry into Winner-Take-All and Proportional-Prize Contests: An Experimental Study,” *Journal of Public Economics*, 94 (2010): 604–611.

<sup>36</sup> From the perspective of firms, another disadvantage of payments linked to measured benefits is that they would come later than one-time payments at the time of product registration. Of course revenues in conventional markets are also spread over many years.

<sup>37</sup> William A. Masters, “Research Prizes: A New Kind of Incentive for Innovation in African Agriculture,” *International Journal of Biotechnology*, 7, nos. 1, 2, & 3, (2005): 195–211.

<sup>38</sup> In some prize designs, a fixed purse is divided among all qualifying contestants (although perhaps not equally). But since firms will not participate unless they believe their share will be enough to compensate for costs and risks, there will still be some relationship between the size of the purse and the number of competitors.

### Milestone versus final-product prizes

Another important distinction is between prizes for final products (“end” prizes)—in the case of health technologies, products that have demonstrated their value in clinical trials and are ready for large-scale manufacture—and prizes for the achievement of significant R&D milestones along the way to a product. For health products, possible milestones might be proof of principle in an animal model or (in the case of diagnostics) in rigorous laboratory evaluation, or preliminary demonstration of efficacy in a small clinical trial. A prize contest could include awards at several stages, including ones for final products.

One of the main advantages of milestone prizes, either alone or in conjunction with end prizes, is that they are less costly and risky for contestants, since less investment in R&D is required and the risks of later-stage development are avoided. Milestones can also be reached sooner, which is important if the cost of capital is high. These advantages could be particularly attractive to small firms, which often need to show results quickly and may not have the capacity or resources to carry products all the way through clinical trials and manufacture. Finally, milestone payments are familiar to small firms, as they are often included in product-development deals with other firms. Milestone prizes may be less attractive to big firms, whose expertise is typically in later stages of product development.

But the choice of milestone versus end prizes also depends on the objective of the incentive. If the main goal is to overcome a technological barrier or to attract new ideas, a prize for a substantial step toward the desired product may be the best choice, since it is in early stages of R&D that a breakthrough is needed. This is particularly true if the market for the product would be sufficient to pull a promising candidate through later stages of development without additional incentives. If the main purpose of a prize is to augment or substitute for too-small markets, however, or to put in place new

mechanisms for product manufacture and access, an end prize is appropriate.

Milestone prizes raise distinct issues, including how to determine the size of the award, how to handle IP to maximize ongoing innovation and protect access, and how to ensure a smooth handover to other product developers if the prize-winner is not willing or able to take the product to market. Milestone and end prizes need not be exclusive, and an incentive structure could include rewards at several points in product discovery and development.

### Management of R&D transitions by prize managers or the market

The question of milestone versus end prizes is tied to the larger issue of how R&D is managed. Pharmaceutical product development is a very complex process, involving a succession of distinct activities requiring quite different skills. In the traditional vertically integrated model, these activities were carried out within a single large company. With the rise of the biotechnology industry and the advent of contract research organizations, R&D now typically involves partnerships among firms and other contributors. Managing these relationships and ensuring efficient handovers between partners entails substantial transaction costs; in purely commercial R&D the task of organizing partnerships is left to the market, and the associated costs are borne by firms. Any mechanism for promoting the development of neglected health technologies must also reckon in one way or another with this feature of modern pharmaceutical R&D. In fact, managing partnerships and handovers are among the most important functions of PDPs and one of the ways that they subsidize neglected-disease R&D. Other existing and proposed neglected-disease R&D incentives and initiatives, including partnering initiatives and patent pools, would also work in part by reducing transaction costs of this kind.

Classic end prizes, like AMCs, leave management of the R&D process to the market: would-be



competitors are free to form partnerships or acquire relevant technology from others.<sup>39</sup> In particular, a pharmaceutical firm interested in pursuing a drug or vaccine prize might look for a promising product candidate developed by a biotechnology firm. For the prize to stimulate innovation by smaller firms that lack the capacity to bring a product all the way through development, these firms must believe that the prize will increase the value of their inventions to big firms. In other words, the incentive must “pull through” from the big companies to participants in earlier stages of the innovation process. The costs and difficulties involved in creating and managing partnerships make this market signal less efficient. Some industry experts interviewed for this report expressed confidence that a sufficiently large prize or market commitment would “pull through” effectively; others were more skeptical.

Milestone prizes offer a way to circumvent this obstacle and reach early-stage innovators directly. The downside of this approach is that milestone-prize sponsors are then left with the responsibility of ensuring that the winning invention is translated into an accessible product, which may entail making relevant IP available to other product developers or even identifying and engaging another firm to carry on the work. More broadly, there seem to be two schools of thought regarding the extent to which prize sponsors should be involved in managing the R&D process. While some prize advocates, especially those who see prizes as substitutes for inadequate markets, believe that industry should be left to organize itself, others argue for a more hands-on approach. InnoCentive, which has until now managed mostly small prize contests, is considering taking on much more ambitious initiatives, for which it will apparently use a phased, managed structure that includes prizes of various types along with other mechanisms.<sup>40</sup> The degree to which prize managers assume responsibility for brokering and overseeing partnerships between

firms will depend in part on whether they have the necessary expertise (see section 2.6).

### 2.4. Prize size

In the broadest terms, prizes should be large enough to motivate a sufficient number of product developers to invest in the required R&D but not larger than the expected benefit of the new product. If this is not possible, another approach to funding product development should be considered (or the new technology simply isn’t worth the cost of developing). But a number of other considerations may be relevant. For example, the prize may need to be big enough to attract media or public attention, if this is important to the prize model.

We will not discuss how to estimate the potential benefit of a new technology—rather we focus on how large an incentive must be to change the behavior of product developers. In considering this issue, it’s important to keep in mind that product developers will have different thresholds for participation. This means that a bigger prize will in general mean more competitors, which in turns means a greater chance of success and possibly success sooner.<sup>41</sup> So while there may be a minimum reward size, below which a prize will not stimulate new activity, increasing the size above this threshold may bring important benefits.

#### Purely commercial considerations

The most basic situation to consider is that of a for-profit product developer considering pursuing a prize on purely commercial grounds, with the prize award the only payoff for its investment. In most situations, of course, a number of other factors will enter into the decision; some of these are considered below. In this context, a firm would weigh the expected investment

<sup>39</sup> The X PRIZE Foundation offers to help participants in its competitions to form teams.

<sup>40</sup> Dwayne Spradlin, InnoCentive, personal communication to authors, 06 Aug 2010.

<sup>41</sup> The relationship between prize size and number of competitors depends on many factors, including the distribution of R&D costs and probabilities of success among potential competitors. If one or a small number of product developers are way ahead of the pack, a prize would probably have to be very large to attract other, less advanced competitors. See appendix B.

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(the cost of the R&D) against the potential reward (the amount of the prize), taking into account four additional considerations:

- **Technological risk:** the chance that it will not be able to develop the specified product or reach the milestone. Most product-development efforts fail.
- **Competitive risk:** the chance that other product developers will win the prize.
- **Cost of capital:** the interest or rate of return that a firm must pay on the funds used for R&D.
- **Opportunity cost:** the potential return from investing scarce resources, including staff, in other projects.

In other words, the risk-adjusted reward must not only exceed the expected costs, but provide a return on the invested capital that compensates for the cost of raising it or (if investment capital is limited) provide a higher return than alternative uses of this capital. In technical terms, these considerations are captured in net present value or internal rate-of-return calculations. In large companies working with well-established technologies, costs and risks can be estimated with some confidence; for start-ups developing new technologies, these calculations necessarily rely to a large extent on educated guesswork and experience.

A critical parameter in these calculations is the cost of capital or the required rate of return (these quantities are in some sense two sides of the same coin: from a firm's perspective, the minimum rate of return that its investors will accept before contributing additional funds represents the cost of capital). The higher the cost of capital, the larger a prize will have to be to represent a viable commercial opportunity. High cost of capital also makes the time to payout critically important. Firms of different classes face different costs of capital. Start-up firms, which rely on venture capital, have a very high cost of capital, as these investors look for a very high return to compensate for the very high risks associated with new firms and new technologies. (This is one of the reasons these firms may prefer milestone prizes over end prizes.) Large firms, on the other hand, can raise

money at much lower rates on stock markets or from commercial banks. These firms may also be able to support R&D from their own revenues, as long as the expected rate of return from the available projects is greater than what they could obtain with other uses of this capital (the opportunity cost). In principle, firms with more promising projects than they can carry out with their existing resources should be able to raise more money and hire more people; in the short run, however, these resources are limited and firms must choose the most promising initiatives.

Most of these considerations are similar to those that govern choices about any R&D project. Technological risk in the case of a prize differs only in that success or failure is determined by the prize specifications (and whatever mechanism is established to judge whether these have been met) rather than by an internal target product profile or the decision of a regulatory body. But the competitive risks that potential participants in a prize contest face are distinct from those that companies face in regular markets, and these risks depend on prize structure. In considering whether to enter a market, firms must decide what share of a market they will be able to capture, given timing, product characteristics, and marketing strength. In pursuing a prize they may face an all-or-nothing outcome. This characteristic of prizes—and the risk to firms—can be mitigated by prize designs that reward multiple winners. Whether this design is more attractive to a potential participant depends of course on how it judges its chances against its competitors.

The relationship among prize size, R&D costs and risks, and the number of competitors is considered in greater detail in appendix B.

### Top-down versus bottom-up approaches to estimating necessary prize size

One approach to estimating how large a prize has to be to attract commercial investment employs the kind of detailed analysis outlined here, using estimates of R&D costs and risks to simulate the calculations of potential contestants. Although this

is the way that firms will assess whether to pursue a prize, at least in principle, this kind of information is often not available to prize designers.<sup>42</sup> Another approach looks instead at the kinds of market opportunities that have typically stimulated investment by firms in a particular industry and assumes that firms would respond to a prize if it offered a similar commercial prospect. Indeed, firms and investors have rules of thumb about thresholds in market size that represent attractive opportunities. Our case study of prizes for TB diagnostics will make use of both approaches to assessing prize size.

### Other considerations

In most circumstances, the prize itself will not be the only return on investment that firms will consider. At least four other types of benefit can be important.

- **Markets for the product.** Although in general markets for the kinds of products considered here are assumed to be too small by themselves to drive the necessary commercial investment—this is in many cases why a prize or other subsidy to R&D is considered necessary—they may be significant nonetheless. Some products may have donor-subsidized markets in the poorest countries or private-sector markets in middle-income countries; some may have small markets in high-income countries. In these cases, a prize only has to be big enough to fill the gap between the market that firms expect and the total reward that would be sufficient to make developing the product attractive. Note that a firm may be able to capture a share of these markets even if its product does not win the prize. An important consideration is whether the product specifications set for the prize would be appropriate for other markets.<sup>43</sup>
- **Market positioning or strategic considerations.** In some cases, even in the absence of a prize,

a firm may choose to invest in a product with relatively small market potential in order to fill out a product line or to stake out a position in a key market. This kind of strategic position is particularly important to large firms with many products. These firms are also particularly interested in establishing themselves in the so-called “emerging markets” such as India, China, and Brazil.

- **Validation of new technologies.** In many cases the technology used in a prize competition may have other more lucrative applications. For example, a technology developed for a new TB test could be used to test for other diseases that are more important in the United States and Europe. A prize competition may offer a firm, especially a start-up, an opportunity to validate a new technology that it hopes to use in larger commercial markets.
- **Public relations and recognition.** A prize may bring positive attention from investors, potential customers, and the general public. For big firms, the positive PR that may come from involvement in a neglected-disease initiative could be quite valuable, while for new firms, recognition may attract money and talent.

While it’s possible to estimate the size of potential markets for products and take this into account in setting the size of a prize, it’s generally difficult to place a value on the other three considerations. They may, however, be quite important in some contexts. Where publicity is the most important attraction to firms, attracting media attention may be the critical consideration in setting the size of the prize.

This analysis assumes that potential participants in a prize contest assess costs and risks realistically. Contestants may overestimate their chances of success and as a result invest more in pursuit of a prize than a rational calculation would suggest. If this is true, prizes can be smaller and still attract the same

<sup>42</sup> Of course firms and their investors often have to make investment decisions without good estimates of the chances of success; in these circumstances formal net present value or return on investment calculations are not very useful.

<sup>43</sup> This will often not be the case. For example, the prize proposals for TB diagnostics emphasize the need for a new test that can be used at peripheral levels of the health systems in poor countries. Although there is a demand for TB testing in developed countries, there is little need for such a POC test.

amount of R&D effort. This phenomenon may explain in part the observation that the teams competing for the Ansari X PRIZE for private space flight spent 10 times more than the total prize purse,<sup>44</sup> although another important factor was probably that contestants factored in important benefits to participation beyond the prize itself, including media attention and validation of their technologies. The two considerations together allow prize sponsors to “leverage” their investment in the prize.

### 2.5. Access issues and treatment of intellectual property

The ultimate goal of a prize for a neglected-disease technology is to reduce disease through the widespread use of a new product. An important risk is that a product will meet the specified criteria and win the prize but never be used, because no one agrees to supply it, because it is unaffordable, or because it is unacceptable in some way to the people it was intended for. A prize cannot guarantee access, but consideration of access in prize design can mitigate some of the risks. In most cases prizes will have to be supplemented by other initiatives focused on getting new health technologies to those who need them.

The risk that a product is unacceptable to patients can be forestalled by careful consultation with prospective users, but planning for supply at an affordable price requires additional elements in the prize design. Three main approaches have been proposed for promoting access to products developed through prizes. It’s important to note that the same issues arise when neglected diseases are supported by other means, and some of the same approaches are available for ensuring access.

#### Cost or price ceilings

One approach is to require that the winning contestant demonstrate in some way that its product can be manufactured at a pre-specified cost. Manufacturing cost then becomes, in essence, another technical requirement. The cost ceiling would be set a level that would make the product affordable to patients, to governments in affected countries, or perhaps to donors willing to subsidize purchase of the product. As with other specifications, this ceiling must be realistic or product developers will not participate.

This approach has two disadvantages. The first is that manufacturing cost is sometimes difficult to define and ascertain independently of information provided by the manufacturer, which may make conformity with this requirement hard to verify. This is apparently the reason the X PRIZE Foundation did not include a cost ceiling in its TB diagnostic prize proposal (see chapter 3). A second disadvantage is that having a product that’s relatively cheap to make doesn’t by itself guarantee that anyone will make it—the developer may not be capable of manufacturing at scale or may not find the market attractive. This risk can be addressed by including in the prize terms an actual supply commitment—an obligation to provide certain quantities of a winning product over a specified period at a specified price—although this may deter some product developers and does not ensure sustainable supply over the long term. Moreover, this approach creates no incentive for manufacturers to make sure their products are used and have the hoped-for impact, only to meet the supply terms.

A related but weaker approach, often used by grant funders of neglected-disease R&D, is to require supply at “cost-plus,” a nominal markup over cost. Although this requirement eliminates most risks for manufacturers, it shares with cost ceilings the problem of verification and does nothing to steer R&D toward products that can be produced at an acceptable cost.

<sup>44</sup> See the X PRIZE Foundation’s description of the Ansari X PRIZE at <http://space.xprize.org/ansari-x-prize>.

### Licensing requirements

A very different approach to access is to require that the winning product developer turn over relevant IP to the organization running the prize contest or grant nonexclusive licenses, either to a licensing pool or directly to interested third parties. In theory this would allow competitive supply of the new product. Since experience with generic drugs, especially HIV drugs, has shown that the competition resulting from generic manufacture drives down prices, this could be a way to achieve sustainable supply at low prices without having to delve into and verify manufacturer's claims about costs. In addition, generic manufacturers, often based in India or China, may have substantially lower costs than originator firms based in the United States or Europe.

This strategy should work well for drugs with high-volume markets (for AIDS, TB, and malaria, for example). But it may not work as well in some other cases. One problem is manufacturing costs: while most (but not all) drugs can be produced cheaply, this is not always the case with vaccines or diagnostics. Unless the licensing provision is accompanied by cost ceilings, the prize sponsor could end up with a product that cannot be produced at an affordable price even by generic manufacturers, and that no one will want to supply because there is no market at a profit-making price. A second problem is that in some cases access to relevant patents is not enough to allow manufacturers to make a product. For many vaccines and some diagnostics, "know-how" is necessary too. The prize agreement can require transfer of this additional knowledge as well, but it is not clear how successful this kind of technology transfer would be when the transferring party is unwilling or at best disinterested. There may be regulatory hurdles as well, especially in the case of vaccines, for which no formal generic regulatory pathway exists. A third drawback to this approach is that in some cases—for example, drugs for sleeping sickness—the market may be too small to interest even one supplier, let alone the multiple suppliers required to drive down prices through competition. In these cases, a purchase subsidy may be needed, which would of course largely defeat the purpose of

competitive supply, although the advantage of de-linking prices from R&D costs would remain.

The idea of linking prizes to IP licensing invites controversy, given the heated controversy over HIV drug patents. Licensing provisions associated with a prize competition would of course be voluntary in the larger sense, as firms could choose whether to participate, and from an economic perspective it should be possible to evaluate a licensing requirement in strictly business terms. If licensing means giving up exclusive control of potentially lucrative markets, the prize will have to be correspondingly larger to compensate firms for what they're losing. On the other hand, if the lost markets would not be profitable, firms should be willing to license without much additional compensation. This calculation depends critically on the restrictions placed on the licensing requirement. In most cases, the licenses would be restricted to the particular application—for example, use of a patented compound as a malaria drug, leaving the firm an exclusive right to exploit the invention for other uses. The license might also be restricted geographically, allowing licensees rights in low- or low- and middle-income countries but not in the United States and Europe. In cases where a product might have significant markets in high-income countries this distinction is crucial and relatively uncontroversial, but it may be difficult to agree on how middle-income countries should be handled.

From the perspective of firms, there are other concerns beyond the loss of exclusive rights to particular markets for the prize-winning product. Some firms may fear that products produced by licensees may leak into high-income markets, although there's not much evidence that this has been a problem. Firms may worry about the quality of products that they do not manufacture themselves. A more complicated concern is that granting licenses for technological platforms or manufacturing know-how with broad application may compromise the firm's most valuable asset and give competitors a leg up in other product areas. Even if license terms in principle don't allow use of the IP for other products, this may be difficult to control.



### Market penetration requirement

A third approach to promoting access is to make part or all of the prize award contingent on a certain level of uptake. Such a condition would not only ensure supply, at least until the requirement is fulfilled, but would make it in the manufacturer's interest to develop an affordable and attractive product and to help with introduction and distribution. Such a requirement would deter innovators who lack the expertise in the relevant markets, however.

A prize with a market penetration test is closely related to an AMC, and AMC advocates argue that by making the reward to product developers conditional on sales in the relevant markets, AMCs solve the access problem while rewarding innovation and paying for R&D.

As this discussion illustrates, there is no perfect way to guarantee that a product developed through a prize contest reaches those who need it. In fact, some might argue that prizes should not be expected to solve the access problem, which is best addressed by other means. But at a minimum, prizes should be designed in such a way that a winning product is likely to be affordable, since R&D decisions have important consequences for manufacturing cost.

These issues are discussed in the context of TB diagnostics in chapter 3.

## 2.6. Governance and management of prize contests

While careful consideration needs to be given to technical aspects of prize design, governance and legal structure are also important. In particular, product developers must believe that the process and the commitment from the sponsor are credible. The issue of credibility is as important to other pull mechanisms as it is to prizes, and one of the important contributions of the vaccine AMC has been to demonstrate that solid contracts between

developers and sponsors are possible.<sup>45</sup> The X PRIZE Foundation also signs contracts with participants in its competitions. While their structures differ, both AMC and X PRIZE Foundation contracts specify technical requirements for the prize (or, in the case of the AMC, access to the subsidized market), define a process to adjudicate whether the requirements have been met, and establish the rules for legal recourse. Legal agreements for prizes must also include any obligations incurred by the winning product developer, including IP, technology transfer, or supply requirements. The challenge is to make contracts sufficiently explicit that donors cannot renege on their commitment when the desired product is developed, but still flexible enough to accommodate unforeseen contingencies. Binding contracts are of course not enough to assure product developers that the prize will be paid: firms must also believe that the entity making the commitment will still exist and have access to the necessary funds when the prize is won.

Since product developers must be able to estimate their chances of winning, the process for determining whether prize criteria have been met must also be clear and credible. It must be clear how product characteristics will be measured and what kinds of data will be used. Typically the responsibility for determining the winner is assigned to an independent technical committee, which may have some authority to modify or waive some technical requirements in some circumstances.

### Technical and prize management expertise

Prize sponsors, such as donor governments, foundations, or individual philanthropists, may not have the necessary expertise in the specific product area or experience with designing and managing prize contests. Sponsors may therefore choose to delegate aspects of prize management to partners with one or the other kind of expertise. For example, a technical organization such as WHO, the US Centers for Disease Control, or a respected

<sup>45</sup> GAVI and International Bank for Reconstruction and Development, offer agreement relating to the AMC for pneumococcal vaccines, (2009): accessed 12 Jan 2011, [http://www.vaccineamc.org/files/amc\\_offer\\_agree.pdf](http://www.vaccineamc.org/files/amc_offer_agree.pdf).

nongovernmental organization (NGO) can be asked to set technical specifications. Prize development and management organizations such as the X PRIZE Foundation or InnoCentive, on the other hand, lack global health knowledge but are well versed in designing prizes and in the operational aspects of contests, including promoting prizes, managing the contestants, and implementing the legal contracts.<sup>46</sup> Prize management organizations of this kind would in general have to rely on expert advisory panels or contracted research organizations to handle the technical aspects of prize design and administration—the credibility of these arrangements will be an important consideration for potential participants and other stakeholders.

### Priority setting and legitimacy

The design and implementation of global-health-technology prizes have implications for resource allocation among competing priorities. For example, in the case of TB diagnostics, countries with high HIV prevalence are likely to need a different test than countries where TB drug resistance is a major problem. Thus, developing countries and patient populations should be consulted on design choices—and of course on the initial choice of health technologies to support with a prize. The extent to which these processes are perceived as legitimate by the countries for which the new technology is intended may affect whether it is quickly adopted and widely used. In the case of the vaccine AMC, the choice of pneumococcal vaccines was made by a broadly representative expert committee. The involvement of WHO in some capacity can lend international legitimacy to a prize and facilitate consultation between developing countries and prize sponsors. Prize governance in this sense is an aspect of the large issue of global health governance.

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<sup>46</sup> A potential drawback of using these organizations is that they have limited flexibility in adapting their prize models to particular products or R&D challenges.





CHAPTER 3  
PRIZES FOR TB DIAGNOSTICS





**In 2009, the governments of Bangladesh, Barbados, Bolivia, and Suriname (BBBS) submitted to the WHO Expert Working Group on R&D Financing a proposal for a prize fund for the development of low-cost, rapid, diagnostic tests for TB.<sup>47</sup>**

This proposal, which is based to a large extent on ideas developed by Knowledge Ecology International (KEI) and Médecins Sans Frontières (MSF), is to date the only public prize proposal in this area. However, the X PRIZE Foundation, which has developed and managed prize competitions in a number of other technology areas, has developed its own TB diagnostics prize proposal with financial support from the Gates Foundation. Although this proposal is not yet public, the X PRIZE Foundation granted us permission to share a summary of this proposal with interviewees and gave us confidential access to more detailed documents. Finally, MSF is continuing work on a TB diagnostics prize and may eventually announce its own proposals. None of these initiatives has yet been funded or launched.

We have devoted considerable attention to these initiatives because these are the most developed prize proposals for global health R&D that we were able to identify and gain access to.<sup>48</sup> The potential of prizes, as well as their design, will vary with product type, market circumstances, and stage of R&D. It is therefore important to go beyond generalities to the details of a particular case in order to illustrate the many factors that could determine success or failure; TB diagnostics offer the most developed example currently available. Moreover, diagnostics in general offer several advantages relative to drugs and vaccines as a testing ground for the prize concept. R&D

costs are lower and product-development timelines shorter than for drugs and vaccines, meaning that a prize can be smaller; diagnostic technology is evolving rapidly, presenting opportunities for radical innovation; and the ability to bring a new product to market is less concentrated in a small number of firms (see chapter 4).

Our case study on TB diagnostics will focus primarily on the X PRIZE proposal, which is more detailed and thus provides more specific material for analysis, but we will address the BBBS proposal as well where it differs from the X PRIZE design in important ways.

After a brief overview of TB diagnostics and the diagnostics industry (section 3.1), we will outline the main features of the prize proposals (section 3.2) and present our analysis (section 3.3). This analysis is based on the theoretical considerations discussed in chapter 2 and extensive interviews with the prize proposal developers, TB diagnostic experts, and current and former executives of large and small diagnostics firms as well as venture capital investors (see appendix A for a list of people interviewed for this study). In our assessment of the TB diagnostic proposals, we cover product scope and technical specifications, prize amount and related determinants of participation in prizes, other prize features and alternative prize designs, access provisions and treatment of IP. We then present our conclusions to the case study.

<sup>47</sup> Full proposal accessed 05 Nov 2010, [http://www.who.int/phi/Bangladesh\\_Barbados\\_Bolivia\\_Suriname\\_TBPrize.pdf](http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_TBPrize.pdf).

<sup>48</sup> BioVentures for Global Health, an NGO working to engage the biotechnology industry in global health, is developing proposals for pay-for-success incentives in several areas, including diagnostics. Although these proposals were not ready in time to be included formally in our study, we provide a brief overview of this work in chapter 4.

### 3.1. Background

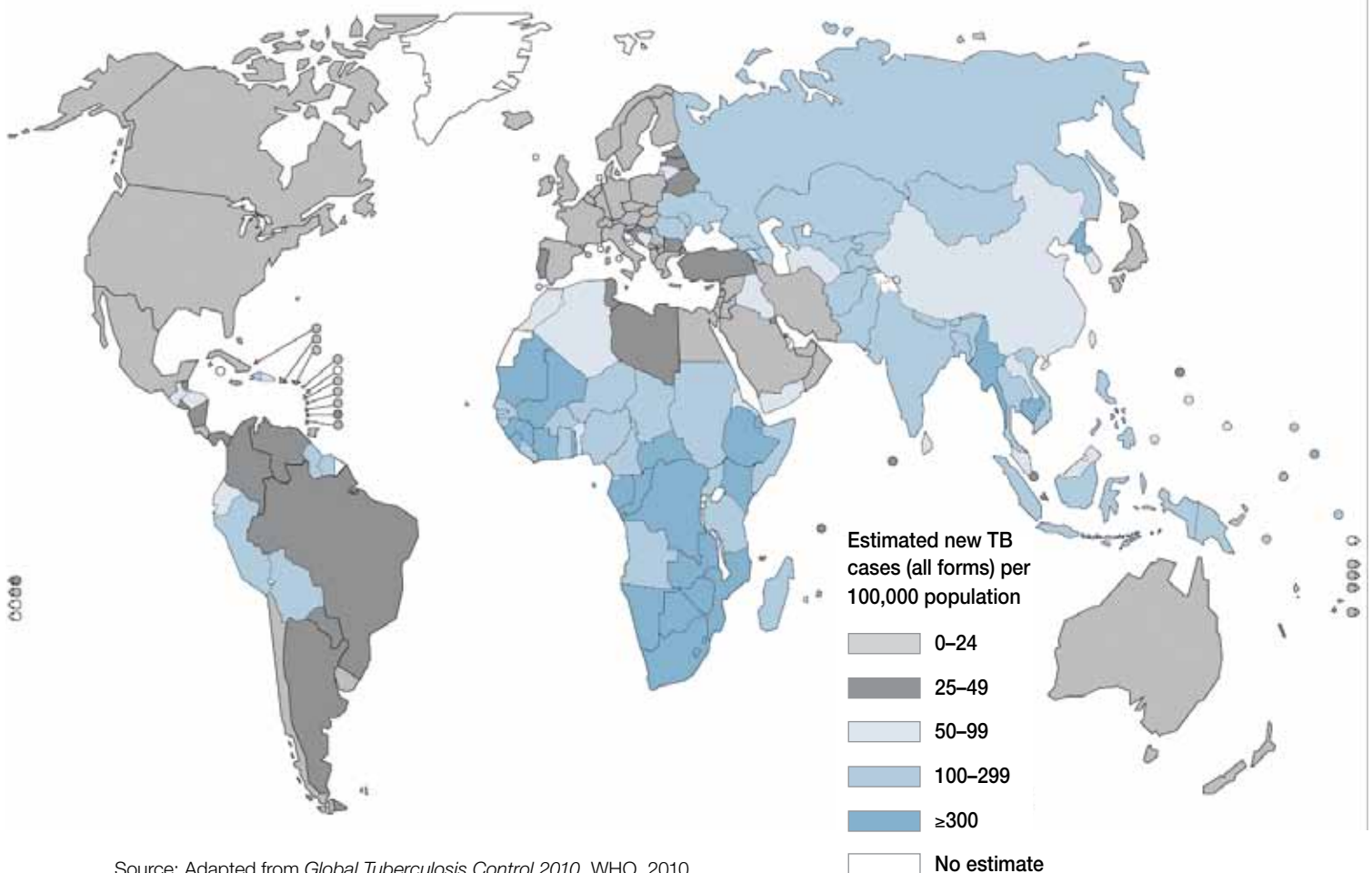
#### Tuberculosis in the developing world and the benefits of better diagnostics

Tuberculosis, a disease largely eliminated from high-income countries decades ago, remains an enormous problem in many parts of the world (see figure 3.1). About 1.7 million people died of TB in 2008, more than of any other infectious disease except AIDS; almost 10 million more developed the disease.<sup>49</sup> Despite broad consensus on a strategy and increased funding, progress in controlling the epidemic has been slow: although per capita

incidence rates may have begun to decline, the annual number of new cases continues to increase.

Many factors have contributed to TB's resurgence, including above all the HIV epidemic, which has dramatically worsened TB rates in areas of high prevalence and now contributes to almost a third of TB deaths. But there is broad agreement that current tools for fighting TB are inadequate. New drugs are needed to shorten treatment and treat cases that are resistant to the standard drugs, and an effective vaccine to replace BCG could make an enormous difference. In addition, however, better diagnostic tests are urgently needed.

Figure 3.1. Estimated TB incidence rates, 2009



Source: Adapted from *Global Tuberculosis Control 2010*, WHO, 2010.

<sup>49</sup> WHO, "Global Tuberculosis Control: A Short Update to the 2009 Report," (2009), [http://www.who.int/tb/publications/global\\_report/2009/update/en/index.html](http://www.who.int/tb/publications/global_report/2009/update/en/index.html).

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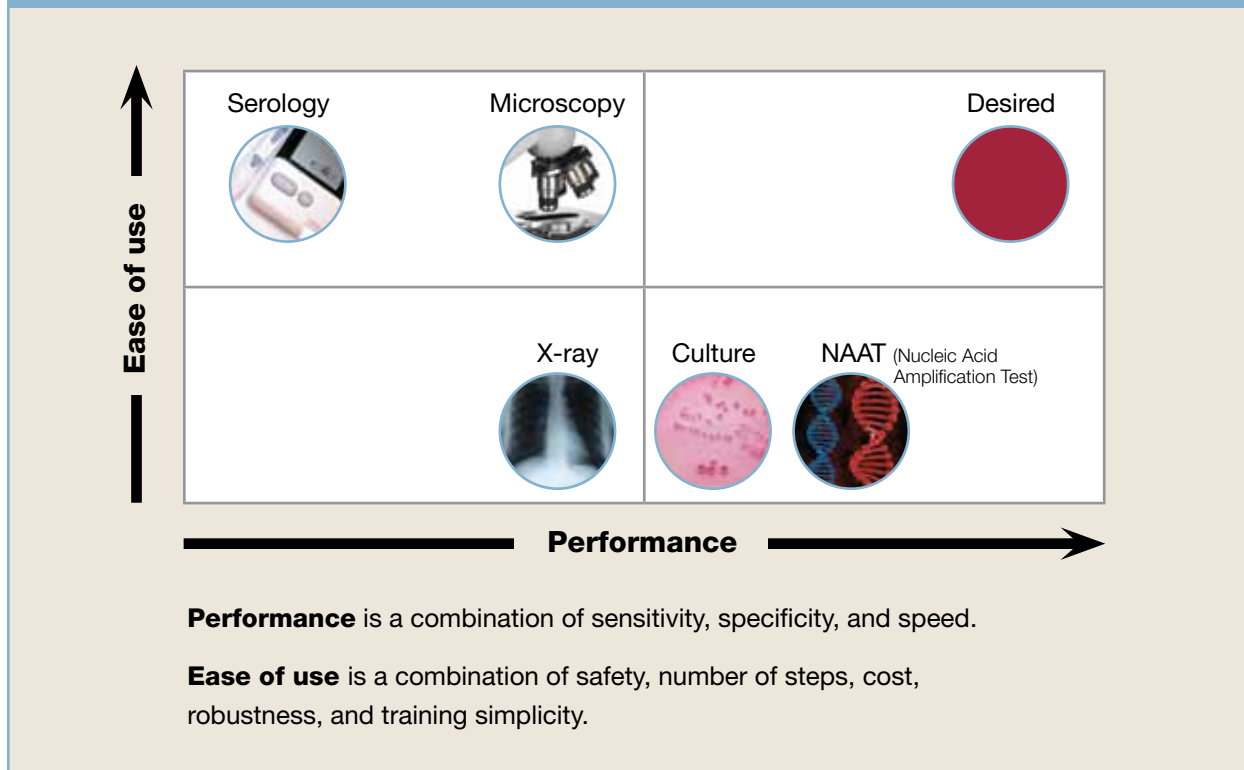
In most developing countries, tuberculosis is diagnosed in the same way it has been for almost one hundred years: by looking for TB bacteria in sputum samples, using microscopes and simple stains. While this method, known as sputum smear microscopy (SSM) is fairly cheap and highly specific (it does a good job of distinguishing TB from other infectious agents), it has a number of crucial drawbacks. It is relatively insensitive, successfully detecting TB in only about half of infected patients; it performs poorly in children (who often cannot provide sputum) and in patients with HIV; and it cannot determine drug susceptibility.<sup>50</sup> Perhaps most importantly, SSM requires at least a simple laboratory with a microscope and a trained technician and typically takes several days to return a result, in part because two

or three samples collected on separate days must be examined. In rural settings, where patients may have to travel long distances to seek diagnosis and treatment, this delay often means that patients with TB do not return for test results and do not begin treatment.

Two other technologies, chest X-ray and sputum culture, are used in some developing country settings to diagnose or confirm TB, but both have serious deficiencies of their own. X-rays are quite unspecific, while culture is very slow and technically challenging. Neither can be used in peripheral settings.

According to a mathematical model of TB diagnosis and treatment in high-burden regions, a new test that was more sensitive, could be used in remote areas where people have little access to health

**Figure 3.2. Advantages and limitations of current technologies for TB diagnosis**



Source: Adapted from WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, 2006

<sup>50</sup> WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006): see in particular pp. 35 and 81, accessed 12 Feb 2011, <http://apps.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-global-demand/pdf/tbdi.pdf>. From a public health perspective, SSM may do better than its overall sensitivity would suggest, as the cases that it can detect contribute disproportionately to transmission.

infrastructure, and returned results quickly could prevent as much as 36% of deaths, saving hundreds of thousands of lives every year.<sup>51</sup> Most of these gains would come from expanding access to testing and reducing loss of follow up. Another modeling study that considered the long-term effect of new tools on TB incidence also found a substantial impact of new diagnostic tests that could reach more people and provide results quickly.<sup>52</sup> New tests to fill other needs—detection of drug resistance, determination of likelihood of reactivation of latent TB, and monitoring of treatment—would also bring significant public health benefits.<sup>53</sup>

There is thus a clear need for improved TB diagnostics and substantial consensus that what is most needed is a rapid, POC test, one that can be used in lower levels of the health system or in the community and gives results while the patient waits. In general, a POC diagnostic test is defined as one that can be used close to where treatment will be provided rather than in a laboratory at a higher level of the health system, but what this should mean in detail for TB tests is not entirely clear. Priorities for POC tests are discussed in more detail below (see “Product scope and specifications” below).

Although SSM, and to a lesser extent X-ray and culture, remain the mainstays of TB diagnosis in low- and middle-income countries, newer technologies relying on amplification and detection of TB-specific nucleic acids (DNA or RNA) are increasingly used in high-income countries. None of the products

currently on the market is yet suitable for use as POC diagnostic in poor countries, however, as all require some degree of laboratory infrastructure and most are quite expensive.<sup>54</sup> Figure 3.2 expresses the advantages and limitations of available technologies for TB diagnosis.

The Gates Foundation and other donors have supported the development of improved diagnostics for important infectious diseases primarily through the Foundation for Innovative New Diagnostics (FIND), a Geneva-based product-development partnership. FIND has in its portfolio several candidate TB diagnostic technologies, ranging from incremental improvements to SSM and culture to radically new approaches.<sup>55</sup> FIND is currently testing a sophisticated device from Cepheid that can provide rapid, sensitive, and specific diagnosis of active TB together with information on drug susceptibility.<sup>56</sup> Although Cepheid’s machine could be very useful in many settings, it is expensive and it is not suited to the most peripheral levels of the health system.<sup>57</sup> FIND’s pipeline includes work on technologies that could result in a POC test, and it is possible that one of these efforts could bear fruit in the next few years even without the added stimulus of a prize, but none of these projects currently seems close to market.

<sup>51</sup> Emmett Keeler et al., “Reducing the Global Burden of Tuberculosis: The Contribution of Improved Diagnostics,” *Nature*, (November 2006). See also the FIND website, <http://www.finddiagnostics.org/programs/tb/need.html>.

<sup>52</sup> Laith J. Abu-Raddada et al., “Epidemiological Benefits of More-Effective Tuberculosis Vaccines, Drugs, and Diagnostics,” *Proceedings of the National Academy of Sciences*, 106 (18 Aug 2009): 13980.

<sup>53</sup> Robert S. Wallis et al., “Biomarkers and Diagnostics for Tuberculosis: Progress, Needs, and Translation into Practice,” *Lancet*, 375, no. 9729, (29 May 2010): 1920–37.

<sup>54</sup> *Ibid.*

<sup>55</sup> One of the most intriguing ideas is that certain animals could be trained to detect TB, much as dogs sniff baggage for drugs and pigs look for buried truffles. Several studies in fact suggest that a species of rat can detect TB in sputum cultures at least as well as conventional microscopy. It remains to be seen, of course, whether this approach would be practical on a large scale. See A. Poling et al., “Using Giant African Pouched Rats to Detect Tuberculosis in Human Sputum Samples: 2009 Findings,” *American Journal of Tropical Medicine and Hygiene*, 83, no. 6, (2010): 1308–1310.

<sup>56</sup> Cepheid press release on FIND website, <http://www.finddiagnostics.org/media/press/090324.html>; M. Perkins, personal communication to authors, 01 Aug 2010. For results of field trials of the Cepheid machine, see Catharina C. Boehme et al., “Rapid Molecular Detection of Tuberculosis and Rifampin Resistance,” *New England Journal of Medicine*, 363, (September 2010): 1005–1015.

<sup>57</sup> Kelly Morris, “Xpert TB Diagnostic Highlights Gap in Point-of-Care Pipeline,” *Lancet Infectious Diseases*, 10, (November 2010).

### Obstacles to development of improved TB diagnostics for developing countries

There is little doubt that lack of need in high-income countries and lack of ability to pay in low- and middle-income countries have historically made TB diagnostics commercially unattractive to product developers. This lack of market was compounded by the divergent needs of rich and poor countries in TB diagnostics and by issues with reimbursement systems in the United States and elsewhere that made POC diagnostics in general commercially unattractive in most cases. But as discussed below, the potential market for a POC TB test in developing countries may actually be quite large now, and industry perceptions may be changing. Thus, lack of market may no longer be as important an obstacle as it has been. However, even if markets in poor countries may be bigger than previously thought, these markets pose other challenges to diagnostics firms, including fragmentation and unfamiliarity (see “The market for TB diagnostics” below).

Beyond commercial considerations, the development of a useful, affordable POC TB diagnostic requires overcoming significant technological barriers, including the identification of appropriate biomarkers and the development of a technological platform for detecting them in difficult environments, where there may be no refrigeration and no reliable running water or electricity, and where highly trained staff are scarce.<sup>58</sup> These problems can probably be solved, but solving them will require substantial investment, much more than the development of a new assay based on known biomarkers and an existing detection platform. Most diagnostic industry experts

interviewed for this study identified technological barriers, in particular the lack of appropriate biomarkers, as the greatest obstacle to development of a POC TB test for developing countries.

The lack of broadly available samples on which to test candidate diagnostics is another important obstacle. Development and testing of a new diagnostic can require thousands of samples, and few if any firms have access to sufficient samples from prospective TB patients.

### The in-vitro diagnostics market and industry

The market for in-vitro diagnostics (IVD), which includes all tests performed outside the body, was estimated to be more than \$28 billion in 2004.<sup>59</sup> Recent projections show the market expanding at an average rate of 6% per year to \$56 billion by 2012.<sup>60</sup> Although the IVD industry consists of hundreds of firms, increasing consolidation over the last five to ten years led to over two-thirds of the market being concentrated in the hands of ten large companies by 2006.<sup>61</sup> Some of these firms (Roche, Abbot, and Chiron) also produce drugs or vaccines, while others specialize in diagnostics and medical devices.

Small firms or start-ups are also important players in the diagnostics industry, and are responsible for much of the recent innovation in the industry. These firms rely, at least initially, on venture capital to support R&D and generally do not have large-scale manufacturing capacity. As in the pharmaceutical industry, it is common for new technologies

<sup>58</sup> Bill Rodriguez of Daktari Diagnostics points out that a POC diagnostic test really requires two quite distinct technologies: one for processing samples and a second for detecting biomarkers in these samples, since it must work without the trained technicians and equipment available for sample preparation in a central laboratory. This is a particular challenge for TB because sputum samples are difficult to work with. B. Rodriguez, comment on draft of this report, <http://healthresearchpolicy.org/assessments/prizes-global-health-technologies-assessment-case-study-tb-diagnostics-3>. Since development of an appropriate platform technology is one of the biggest obstacles to POC diagnostic testing, and since the right platform might be able to run several tests, BioVentures for Global Health believes that a prize for POC diagnostics in the developing world should focus on the development of such multiple-use platforms rather than on a test for a single disease (M. Moree, BVGH, personal communication with authors, 19 May 2010).

<sup>59</sup> WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006): accessed 12 Feb 2011, <http://apps.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-global-demand/pdf/tbdi.pdf>.

<sup>60</sup> Richard Park, “The Year in IVDS, IVD Technology,” (2010): accessed 05 Nov 2010, <http://www.ivdtechnology.com/article/year-ivds-9>.

<sup>61</sup> WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006): accessed 12 Feb 2011, <http://apps.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-global-demand/pdf/tbdi.pdf>.



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developed by small firms to be acquired and commercialized by larger, established companies. The diagnostic industry in emerging economies, particularly India and China, is growing in sophistication, and these firms are capable of manufacturing many types of tests at low cost.

POC testing is broadly defined as “any testing performed outside of the traditional laboratory and conducted close to the site of patient care.”<sup>62</sup> The market for POC tests was estimated at \$11 billion in 2007.<sup>63</sup> Several industry experts stated that challenges with receiving sufficient reimbursement through the US Medicare system and the lack of incentives for doctors to use POC tests have dampened innovation in this area. Recently, the POC market has also suffered from the economic recession as the lack of venture capital and other investment funding has slowed the development of new technologies.

### The market for TB diagnostics

Total global expenditure on TB diagnostic testing is estimated at about \$1 billion/year, more than twice the market for TB therapeutics.<sup>64</sup> But developed countries, despite their low TB burden, account for almost 70% of this spending, the bulk of which is on labor rather than reagents, while the rest of the world, where most TB cases occur, spends much less. Of the \$300 million or so that the WHO estimates is spent in low- and middle-income countries on about 150 million tests, SSM and X-ray account for 80%.<sup>65</sup> Only very small amounts are spent on commercial devices and reagents, including culture and PCR-based systems.

Only three of the ten top IVD companies have TB diagnostics devices or tests in their portfolios.<sup>66</sup> Becton Dickinson, which provides a system for obtaining more rapid results from liquid culture, is the market leader. Biomerieux also has a culture diagnosis system, while Roche has developed a nucleic acid amplification product for TB. Many products using microbiological, nucleic acid, protein detection, or immunoassay technologies are in the pipeline, but few if any of these products would be truly POC in a developing country setting.

Although markets for diagnostic tests and devices in developing countries have traditionally been seen as small despite the great need and potentially high volume, two trends may change this perception. First, rapid economic growth in some middle-income countries, particularly India and China, has spurred rapid growth in markets for pharmaceutical products, especially in the private sector, and created the expectation that these so-called emerging markets will be responsible for much of future growth in global demand for these products. Most of this demand will be for products directed against the same diseases that plague rich countries, such as cardiovascular disease, cancer, and diabetes, but there could be a significant market as well for diseases like tuberculosis where they remain a serious problem, as in India.

The second factor changing perceptions of developing country markets for diagnostics (as well as drugs and vaccines) is the demonstrated willingness of donors to pay non-trivial prices for global health technologies needed by high-burden, low-income countries, especially for AIDS, TB, and malaria. Many countries in Africa, for example, are paying about \$5 for CD4 tests (not counting the cost of the machines),

<sup>62</sup> Ibid.

<sup>63</sup> Atalya Ben-Haim, *The POC Market for Diagnostics of Diabetes, Maternal and Child Health, Tuberculosis, Malaria and Diarrhoeal Diseases in India and the World*, eds. Arijit Sarkar and Namrata Sharma, IKP Centre for Technologies in Public Health, (December 2008).

<sup>64</sup> Gayatri Ramachandran, “Tuberculosis Diagnosis: Attractive Market with a Global Demand,” Frost & Sullivan, (21 Sep 2007); accessed 01 Nov 2010, <http://www.frost.com/prod/servlet/market-insight-top.pag?Src=RSS&docid=107170469>.

<sup>65</sup> WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006); accessed 12 Feb 2011, <http://apps.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-global-demand/pdf/tbdi.pdf>.

<sup>66</sup> Ibid.

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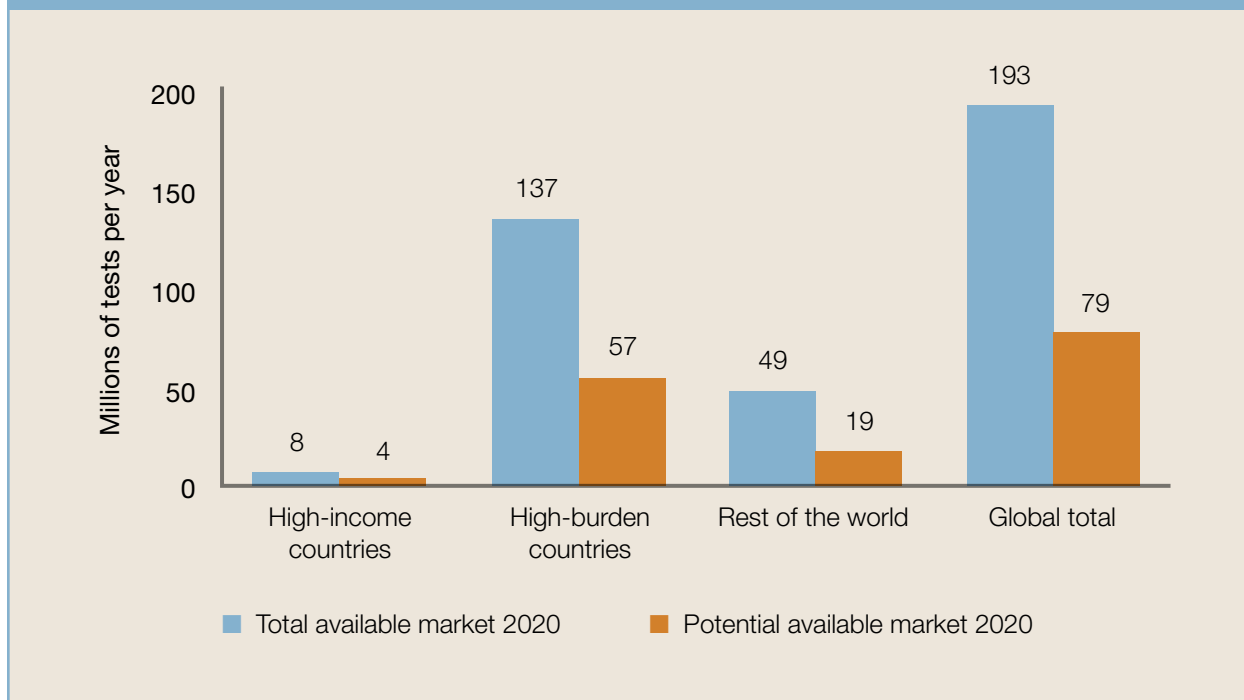
using resources from the Global Fund and the US President's Emergency Plan for AIDS Relief.<sup>67</sup> This experience has changed the perception that to reach people in low-income countries, diagnostic tests have to cost \$1 or less.

Growing markets in the emerging economies, coupled with the apparent willingness of donors to pay several dollars a test for important diagnostics in low-income countries, could make diagnostics for TB and some other previously neglected diseases attractive to industry. Volumes could be very high: a 2006 WHO report estimated the "total available market" for a POC TB diagnostic at 193 million tests/year in 2020.<sup>68</sup> This study estimates, however, that only 40% of this total, or about 80 million tests, could be captured by 2020. The majority of this demand would be in high-burden countries (see figure 3.3).

Although the WHO report does not venture a guess at the prices that developers of a POC test would be able to charge in various markets, this analysis clearly suggests that at prices of more than \$1 per test the potential market for a POC TB test could be considerable. Industry and other experts interviewed for this study thought that the WHO estimate of potential sales volume for a new TB test is probably too high; however, they did not dispute that this market could be large.

One challenge for firms considering entering developing country markets for diagnostic tests is the lack of a clear regulatory process. While WHO has established a prequalification process for diagnostic tests analogous to the processes that have provided useful guidance on product quality for vaccines and some drugs, no tests have

**Figure 3.3. Estimates of total available market and potential available market for point-of-care TB tests in 2020**



Source: Adapted from WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, 2006. High-burden countries include both low- and middle-income countries.

<sup>67</sup> M. Murtagh, Clinton Health Access Initiative, personal communication to authors, 16 July 2010.

<sup>68</sup> WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006): accessed 12 Feb 2011, <http://apps.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-global-demand/pdf/tbdi.pdf>.



yet completed the process.<sup>69</sup> In many developing countries, the regulatory process remains quite informal and, to the extent products are subject to government approval at all, no clear standards exist, and authorities typically rely on data from a variety of sources. In fact, many substandard or even useless tests, including for TB and malaria, are on the market in developing countries, according to several diagnostic experts consulted for this study.<sup>70</sup> Such an environment can pose a threat to firms considering investment in products for the developing world. The alternative of seeking US FDA or European Union approval is costly and time-consuming.

### 3.2. TB diagnostic prize proposals

#### The X PRIZE proposal

The X PRIZE Foundation, a nonprofit organization devoted to the development and management of prize contests, has launched prize competitions for private space flight and exploration Ansari X PRIZE and Google Lunar X PRIZE, automobile fuel efficiency Progressive Automotive X PRIZE, and rapid DNA sequencing Archon Genomics X PRIZE, among others. X PRIZE contests for purses of more than \$10 million typically last for three to eight years.<sup>71</sup> The space flight prize was won in 2004 and the fuel efficiency prize was awarded in September 2010.

The X PRIZE Foundation seeks external sponsors to fund the prize competitions that it develops and manages.

The X PRIZE Foundation's philosophy differs from that of some other prize proponents, in that it does not see prizes as a substitute for markets. The foundation's aim is instead to "unlock" latent

or potential markets by motivating innovators to take critical first steps that pave the way for further breakthroughs, and eventually, open up substantial commercial opportunities. An implication of this model is that the prizes themselves need not be the only or even the primary reward to participants. In addition to access to newly opened markets, the X PRIZE Foundation considers publicity and recognition to be important benefits of participation in its prize competitions, and it devotes substantial resources to attracting media attention.

**The TB diagnostics prize.** The X PRIZE Foundation has designed a \$20 million prize competition to create a set of rapid, accurate, POC TB diagnostics for use in peripheral settings in developing countries. Participating teams could win up to four prize purses of \$5 million each if their products were shown in clinical trials to meet all of a set of minimum technical criteria<sup>72</sup> (see figure 3.4) and to perform better than any other qualifying product in one or more of four specific areas. Prizes would be awarded for diagnostics that achieved the highest accuracy, fastest time to result, highest sensitivity in HIV+ patients, or best detection of TB drug resistance. The first two purses would be awarded if at least one team meets the minimum technical specifications, while the latter two would not be awarded unless a product reached the 60% minimum set for performance in these two areas.

The competition would be open to all types of organizations globally; the X PRIZE Foundation expects that many contestants, including small and large diagnostic firms, would choose to register as teams. It is divided into two phases, a laboratory evaluation phase that could last two to four years and a one-year joint clinical study that would test the leading teams' products in two high-burden TB countries

<sup>69</sup> For more information, visit [http://www.who.int/diagnostics\\_laboratory/evaluations/en/](http://www.who.int/diagnostics_laboratory/evaluations/en/).

<sup>70</sup> Kelly Morris, "WHO Recommends Against Inaccurate Tuberculosis Tests," *Lancet*, 377, no. 9769 (08 Jan 2011): 113–114.

<sup>71</sup> The X PRIZE Foundation also conducts competitions called X PRIZE CHALLENGES that address significant technological barriers and are smaller in prize purse, scale, and duration.

<sup>72</sup> These specifications are intended to satisfy the ASSURED criteria (affordable, sensitive, specific, user-friendly, rapid, robust, equipment-free, and delivered) developed by the WHO Sexually Transmitted Diseases Diagnostics Initiative, [http://www.who.int/std\\_diagnostics/about\\_SDI/priorities.htm](http://www.who.int/std_diagnostics/about_SDI/priorities.htm).

**Figure 3.4. X PRIZE technical specifications**

**Minimum criteria**

- Accessible/affordable: can be manufactured to scale and supplied to purchase aggregator in a cost-plus model
- Sensitive: >80% accuracy for TB diagnosis
- Specific: >95% accuracy for diagnosis of non-TB patients
- User-friendly: meet FDA's Clinical Laboratory Improvement Amendments assessment for device usability with a score of  $\leq 12$
- Rapid: total time from sample preparation to result:  $\leq 100$  minutes/test
- Equipment-free: self-contained with no cold chain, electrical, or water supply or climate control needs
- Deliverable: weight <10 kg; size: <30x30x30cm; storage life:  $\geq 12$  months at  $\geq 35$  degrees C and 70% humidity, including transport stress (e.g., 48 hours at 50 degrees C)

**Additional criteria for bonus prizes**

- At least 60% sensitivity in HIV+ patients
- At least 60% success in detecting drug resistance

Source: Adapted from the X PRIZE Foundation

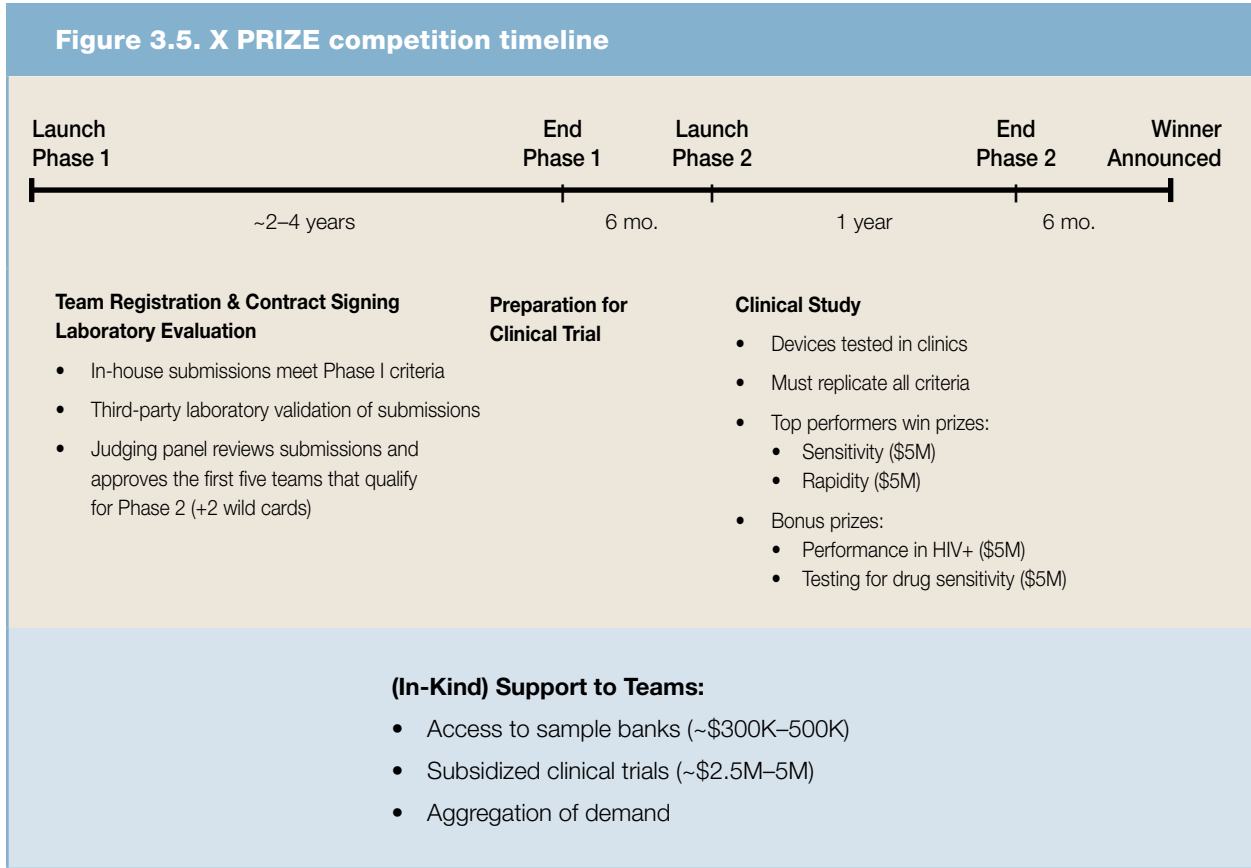
(see figure 3.5). To enter the contest, interested contestants would have to pay a registration fee of \$15,000 or more. The first phase would begin with the signing of a Master Team Agreement, a contract with X PRIZE that spells out the prize guidelines in detail and gives contestants a legal claim on the prize. Teams would submit data from in-house tests of their devices to an independent research organization contracted by the X PRIZE Foundation, which would independently evaluate the devices in its own laboratory (about 100 or so would need to be provided) and validate the team submissions. On the basis of the laboratory evaluations and team submissions, a panel of judges would choose five to seven teams to participate in the clinical studies, suggested to be in South Africa and India. Leading teams would have to be able to provide thousands of devices for these trials. Winners would be announced after the one-year trial and six months of analysis.

During the prize competition, the X PRIZE Foundation would offer competing teams free access to patient

samples (sputum, urine, and blood) from specimen banks. The X PRIZE Foundation estimates that the cost of providing samples could be as much as \$300,000 to \$500,000. In addition, the X PRIZE Foundation will pay for the culminating clinical studies, which are estimated to cost \$2.5 million to \$5 million.

The X PRIZE proposal would allow contestants to retain all IP developed during the competition and includes no licensing provision. Moreover, winning teams are not required to supply their products at a specified price or to demonstrate that they can be produced at an affordable cost. But in order to participate in the clinical trial, teams must submit business plans that explain how their products would be manufactured, describe the status of agreements with “reputable manufacturers,” and provide some information on production costs.

The X PRIZE Foundation is currently seeking a sponsor for the TB diagnostics prize. Although it



Source: Adapted from the X PRIZE Foundation

considers the design process to be complete, the X PRIZE Foundation is open to changes, both in response to the preferences of sponsors and in negotiations with potential competitors preceding the signing of the Master Team Agreement.

It is worth noting that the X PRIZE Foundation has considered the possibility of a TB diagnostic prize focused on India, targeted at Indian researchers and product developers and aimed at spurring the development of tests for the Indian market. We have not assessed this idea—there is as of yet no developed proposal to analyze—but India has a substantial diagnostic industry and growing innovative capacity, as does China. The potential of prizes in these so-called innovative developing countries is an interesting area for further work.

### The BBBS proposal

The proposal submitted by the four countries to the WHO Expert Working Group shares a number of features with the X PRIZE proposal, including the goal of stimulating the development of a POC TB test for use in peripheral settings in developing countries, a two-stage evaluation of candidate products, and subsidy of clinical trial costs by the prize fund.<sup>73</sup> But there are important differences between the two proposals (see figure 3.6).

- A much larger prize purse: a \$100 million “grand prize” for the first contestant to meet the technical criteria, plus a series of small prizes of various types.
- An affordability and access standard, which could be either a pre-specified price ceiling or a market penetration test.

<sup>73</sup> Bangladesh, Barbados, Bolivia, and Suriname, *Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis*, accessed 05 Nov 2010, [http://www.who.int/phi/Bangladesh\\_Barbados\\_Bolivia\\_Suriname\\_TBPrize.pdf](http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_TBPrize.pdf).

Figure 3.6. Summary of TB diagnostic prize proposals

Feature	X PRIZE	Bangladesh, Barbados, Bolivia, and Suriname
Prize amount & structure	\$20M total purse; \$5M prizes for best performance in each of four categories	\$100M “grand prize” for first test that meets criteria; smaller “best contribution” and technical challenge prizes
Technical specifications	Minimum criteria emphasizing sensitivity, speed and low infrastructure requirements	Not defined, emphasis on sensitivity in HIV+ patients implied
Access provisions	No IP licensing requirement, cost ceiling, or supply requirement	Requirement that winner grant licenses for all relevant IP to patent pool to facilitate generic production; cost provisions
Other	Publicity campaigns, access to specimen banks, third-party laboratory evaluation, and paid joint clinical trial	Subsidized clinical trials, features to encourage cooperation and sharing of data

- A requirement that the winner grant licenses on reasonable terms for all patents and know-how needed for competitive supply of the product to a licensing pool.
- Technical specifications: although these are yet to be set, the proposal implies that they would include performance in HIV+ patients. While the X PRIZE proposal would award one of the four prizes for high performance in this group of patients, it does not include it among the minimum criteria to be met by any winning product.
- Governance: the prize competition would be housed at WHO and governed by a committee comprising international organizations, TB NGOs, and a representative of TB patients. In contrast, the X PRIZE would be governed by the X PRIZE Foundation with the help of expert committees.
- Source of funds: the proposal suggests that the prize fund be endowed by governments, including a contribution from developing countries, as well as private donors. X PRIZE contests are typically funded by private individuals or firms, although

the US government is contributing to at least one contest and the X PRIZE is open to other kinds of sponsors, which could include the Gates Foundation and endemic-country governments.

The BBBS proposal also includes several additional awards and incentives, including small inducement prizes for the solution of technical challenges, biannual “best contribution” prizes, and a provision awarding 10% of the grand prize to researchers who contribute to the success of the winners and make their results freely available to all. In addition, it provides a subsidy to encourage participation of researchers and firms in emerging countries.

#### The work of Médecins Sans Frontières on prizes for TB diagnostics

The MSF Campaign for Access to Essential Medicines has made improved TB diagnostics for low-income countries a priority and has been an early advocate of a prize approach.<sup>74</sup> MSF has held several meetings to define the minimum requirements

<sup>74</sup> Visit the MSF Campaign website, <http://www.msfaccess.org/main/tuberculosis/diagnosing-children-with-tb-a-terrible-neglect/>.

for a POC test, focusing on the need for better performance in children and HIV+ patients. The Access Campaign was involved in development of the BBBS proposal and may put forward proposals of its own. MSF is considering both an end prize similar to the BBBS proposal and a milestone prize focused on discovery of new biomarkers.<sup>75</sup>

### 3.3. Analysis of TB proposals

#### Product scope and specifications

**Scope and objectives.** The first question to ask is whether these proposals have correctly identified the most urgent needs for TB diagnostics. Both proposals focus on POC tests. While some TB experts consulted for this study suggested that the importance of a POC test might be overstated and that centralized, high-volume diagnostic laboratories should remain a big part of a diagnostic strategy—South Africa and India are investing heavily in central labs—most agreed that a rapid and accurate TB test that can be used in peripheral settings was a high priority and would have a big impact.

Some interviewees suggested it might be possible to achieve the objectives of increasing access and reducing loss to follow-up by other means. These could include using mobile phones to convey test results to patients or mobile laboratories to reach patients in more remote areas.<sup>76</sup> These ideas highlight the importance of focusing on ultimate goals and illustrate how any set of technical criteria inevitably incorporates assumptions about how the goals should be reached.

In addition to rapidity and accuracy, many have cited a need for greater effectiveness in detecting TB in HIV+ patients and children and detecting TB drug

resistance. While the design of the X PRIZE proposal gives priority to accuracy, rapidity, and POC criteria, it does include prizes for performance in HIV+ patients and detection of resistance. The BBBS proposal does not yet include technical criteria, but the statement of the problem suggests that it would probably give high priority to improved performance in HIV+ people, who make up a large fraction of TB patients in many high-burden countries. MSF also believes that ability to detect TB in HIV+ patients should be a central priority.<sup>77</sup>

**Technical specifications.** According to our interviews with TB experts, there is broad consensus that a POC TB test should be more sensitive and at least as specific as SSM. The X PRIZE proposal's minimum technical specifications of 80% sensitivity and 95% specificity are in line with these general expectations for accuracy. But the appropriate standard depends on how a POC test would be used. Specificity, which determines the rate of false positive results, is particularly important if the test would be used to initiate treatment without a confirmatory test, as TB treatment is long and arduous; SSM is 97–98% specific. In contrast, specificity can be lower if the POC test is going to be used only for screening, to guide referral of patients to health facilities where more definitive testing is available. In this case, however, sensitivity should be as high as possible to avoid missing cases. A screening test that could be used by community health workers might be a way to make active case finding practical.

A test that returns results while the patient waits, perhaps within three hours, is critical to reaping the benefits of POC testing, and the X PRIZE proposal's requirement that results be available within 100 minutes from the time samples are collected seemed reasonable to the experts we consulted.

<sup>75</sup> M. Childs, MSF Access Campaign, personal communication to authors, 15 Nov 2010.

<sup>76</sup> In fact, David Persing of Cepheid suggested that mobile laboratories would be the best way to bring to communities the benefits of his company's GeneXpert technology, which is unlikely to be used in facilities below the district hospital level (personal communication to authors, 8 Nov 2010).

<sup>77</sup> A set of draft specifications developed at a meeting convened by MSF in 2009 proposed that a new POC test should be able to detect 60–80% of culture-positive, smear-negative pulmonary cases, regardless of HIV status. See Jean-Francois Lemaire and Martina Casenghi, "New Diagnostics for Tuberculosis: Fulfilling Patient Needs First," *Journal of the International AIDS Society*, 13, no. 40, (2010).

Some experts thought that the X PRIZE proposal's criterion of an 'equipment-free' test that does not require cold chain, electricity, water supply, or climate control was unrealistic and might be unnecessarily restrictive. A test that can be used in peripheral settings should not need cold chain; however, it is likely that some promising technologies would require rechargeable battery power or water.

In summary, the X PRIZE proposal's technical criteria are broadly consistent with published work on needs in TB diagnostics<sup>78</sup> and most experts that we consulted thought that they were reasonable, sufficiently ambitious to ensure that a new test would have substantial impact, yet attainable. The most commonly voiced concern about the specifications was that they give insufficient weight to performance in HIV+ patients.

Two authorities on diagnostics expressed the view, however, that the criteria as written were not sufficiently detailed to be used to measure performance in a clinical trial and determine winners, especially if very different technologies making use of different sample types were being assessed (see "Implications for prize approach" below). More detailed guidelines could be added at a later stage, but it should be noted that the difficulty of capturing general criteria in sufficiently detailed and rigorous prize guidelines represents a risk to any diagnostic prize proposal.

The X PRIZE Foundation views its technical specifications as evolving until the final prize is launched and expressed a willingness to take these concerns into account.

**Implications for prize approach.** There is always a risk that technical specifications for a prize could rule out certain technologies that might meet the ultimate objectives for which the prize contest was created. In the case of the X PRIZE TB proposal, this point has already been illustrated by the suggestion that creative delivery strategies could make a POC test unnecessary. But such an outcome could also arise for a more technical reason.

The X PRIZE Foundation proposes that the accuracy of candidate products would be assessed against the current gold standard, liquid or solid culture of sputum samples—it is difficult to imagine how this could be done otherwise. But while sputum culture is very accurate in diagnosing pulmonary tuberculosis, the most common presentation, it does not work well in the case of extra-pulmonary tuberculosis, another important clinical problem. In recognition of this constraint, the X PRIZE Foundation acknowledges that its criteria only cover pulmonary disease. But this constraint diminishes the ability of the prize to measure performance in HIV+ people, among whom extra-pulmonary TB is a more common manifestation than in HIV- patients.

But the choice of a gold standard against which to measure tests has implications not only for determining the winner of the prize for diagnosis in HIV+ patients, but also for assessment of technologies using samples other than sputum. A test using urine, for instance, might work equally well in people with TB in or outside the lungs. In an area with high HIV prevalence, such a test might detect a greater fraction of TB cases overall than a test relying on sputum, but still fall below the 80% minimum for sensitivity, as measured by sputum culture. There is probably no easy solution to this problem, as there is no accepted gold standard for diagnosis of TB outside the lungs (or in children, who don't produce sputum easily). But it could well bias the contest against some more innovative technologies, and it illustrates the ways in which the need to be able to measure performance can have implications for prize contests.

### Prize amount

The X PRIZE proposal offers four prizes of \$5 million each, which would be awarded for the products that achieved the highest ratings in particular dimensions (sensitivity, sensitivity in HIV+ patients, detection of drug resistance, and time to result) while scoring above the specified thresholds for

<sup>78</sup> M. Pai et al., "Novel and Improved Technologies for Tuberculosis Diagnosis: Progress and Challenges, *Clinics in Chest Medicine*, 30, no. 4, (December 2009): viii, 16, 701; WHO, *Diagnostics for Tuberculosis: Global Demand and Market Potential*, (2006).



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all so-called minimum criteria. A team could win several or even all four prizes. But since it is unlikely that a particular technology would excel in all these areas, a potential competitor would probably assume a payout of \$5–10 million.<sup>79</sup> Would this amount be sufficient to attract researchers and product developers to enter the competition and invest significant resources in winning the prize?

We conclude from our analysis and from interviews with diagnostic industry executives and venture capitalists that for most firms this amount is probably not enough by itself to drive investment in a new R&D project on purely commercial grounds. In general terms, this conclusion rests both on the fact that \$5–10 million is below the thresholds reported by firms and investors for attractive market opportunities and on back-of-the-envelope analysis of costs, risks, and desired rates of return. But it is useful to consider the circumstances of diagnostic firms of different types (see figure 3.7).

**New start-ups.** One way that a prize could drive new R&D would be by stimulating the formation of new companies with the prize as their primary

commercial objective. But venture capitalists must typically invest \$10–30 million in diagnostic start-ups over several rounds, substantially more if the goal is to bring a product all the way to market.<sup>80</sup> Venture capitalists only make these large investments if they promise a very high potential return—as much as fivefold to tenfold—as most ventures fail. Thus, they look for initiatives that promise a one-time payout of \$100 million or market revenues of at least \$20 million/year. These returns are clearly far more than the X PRIZE purse. Moreover, investors look to get a return on their investment in three years or so: since the X PRIZE competition would take five to seven years, the amount of the prize would have to be even greater.

**Start-up or small firms with other primary products or intended markets.** A more realistic goal for a prize would be to persuade a small firm that is developing a technology for an application other than TB diagnostics to invest in applying this platform to TB. In this case, the prize would not have to cover the entire cost of establishing the company and developing the technology. The prize would still have to cover the risk-adjusted additional investment, which might

**Figure 3.7. Factors influencing prize participation, by type of firm**

Type of Firm	Technological competence	Revenue threshold for conventional markets	Total prize amount	Prize structure	Other benefits
New start-ups	Developing relevant platform or biomarkers	\$20M/year	\$5–10M too small	Strong preference for milestone	Recognition, technology validation
Established small to mid-size firms	Have relevant platform or biomarker	\$20M/year, maybe less if costs are low	\$5–10M might be attractive in some situations	Strong preference for milestone	Recognition
Large firms	Have relevant platform	\$50–\$100M/year	\$5–10M too small to be commercially interesting	Perhaps prefer end prize if public relations benefits are stronger	Positive publicity from global health initiative

<sup>79</sup> The technologies required to meet the different objectives would probably have to be different. Drug resistance in particular will be difficult to detect with most plausible POC technologies. Nucleic-acid amplification technologies such as that used in the Cepheid machine can detect major forms of drug resistance quite rapidly; it is unlikely, however, that these technologies could meet the X PRIZE proposal's equipment-free and ease-of-use requirements. Lateral flow and similar technologies, which look for proteins or antibodies, are the easiest to make POC but are not currently able to detect drug resistance.

<sup>80</sup> This and other figures presented in this section are derived from about a dozen interviews with diagnostic entrepreneurs and venture capitalists. Although accounts of the economics of diagnostic start-ups varied in detail, there was considerable consensus on the general description presented here.



include the cost of adapting the firm's technology platform. The cost of the R&D required to develop a new TB test is difficult to estimate, as it depends on whether the necessary platform is already in hand and appropriate biomarkers are available.<sup>81</sup> Developing a new test for an established platform could cost as little as \$1 million, while developing a new platform would require at least \$25 million and possibly much more. POC platforms impose additional engineering constraints and therefore can be more expensive to develop. Most small diagnostic firms work with a single platform and would only pursue the TB prize if they believed that this platform, perhaps with some modification, might allow them to meet the contest criteria. In this case, if appropriate biomarkers become available, R&D costs could be relatively modest and the \$5–10 X PRIZE proposal amount might in some circumstances be attractive.

A prize is probably a better fit for more established firms than start-ups, because they have more capacity to pursue more than one objective at the same time—investors in start-ups may worry about diversion of time and resources from the primary objective. More established firms, especially those that have gone public and have products on the market, will also have a lower cost of capital than venture-capital-dependent start-ups.

**Large firms.** Large diagnostic firms have a quite different set of circumstances. On one hand, they have a much lower cost of capital than small firms and have diversified product lines employing multiple technological platforms. Like small firms, they may be able to develop a new test for an existing platform relatively cheaply, if biomarkers are available. But their market thresholds are in general much higher, as much as \$50–100 million/year, especially if substantial investment is required. In most cases a prize of \$5–10 million is too small to get their

attention on purely commercial grounds, although considerations other than the prize reward itself may be particularly important for this class of firms (see “Other determinants of participation” below).

We conclude from this analysis that a \$5–10 million prize might in some cases be enough to cover the costs of developing a new TB test, but for most firms would not be sufficient to compensate for the associated risks, both technical and competitive, and the cost of capital. Moreover, the amount is not large enough to justify investment in a new enterprise or a major new project at an established company, although it might suffice if all that was required was to add a test, using established biomarkers, to an existing platform. As this analysis illustrates, the necessary prize size should not be thought of as a simple threshold: in general a larger prize has the potential to attract firms of more types and to stimulate more ambitious, expensive R&D.

But firms deciding whether to invest in a POC diagnostic test would consider not only the prize offered by the X PRIZE Foundation, but potential markets for the product. The two sources of return together would be weighed against R&D costs and risks. The Foundation believes that the market for a potential POC TB test might in fact be very large, as much as \$1–3 billion/year.<sup>82</sup> We believe on the basis of our consultations that this estimate is probably too high, but that the market for a POC TB test could indeed be quite substantial. Our consultations suggest that this view is shared by industry.

The large potential market for a new TB test means that a prize does not have to be as big as it would otherwise have to be to attract competitors. However, if the market is anywhere near as large as the X PRIZE Foundation estimates, the obvious question is not whether the proposed prize purse is large enough, but why a prize should be necessary at all.

<sup>81</sup> In general terms, a “platform” is the technology used in a diagnostic test—for example, an amplification and detection technology to detect pathogen-specific nucleic acid sequences or a lateral-flow format to detect antigens. More specifically, the term can apply to the actual machine used to run the test, which in many cases can be used or adapted to run many different tests—for example, in conjunction with disposable cartridges specific for particular tests.

<sup>82</sup> The X PRIZE proposal estimate assumes 200M tests/year at a price of \$5–10/test. The 200M figure comes from the 2006 WHO market study, which puts the “total available market” for a POC test at 193M. This study estimates, however, that only 40% of this total, or about 80M tests, could be captured by 2020.

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If firms believe that a POC TB test is feasible with the technology they have at hand, a market of even \$100 million/year, a blockbuster in the diagnostic industry, should provide more than enough incentive and a prize of \$5–10 million would add little to the potential return on investment.

If this reasoning is correct, why hasn't a POC test been developed? There are several possible explanations for this paradox. One is that firms have only recently come to appreciate that TB diagnostics for the developing world represent a potentially lucrative opportunity. In fact, several interviewees suggested that industry's interest has been growing. If this is the case, investment in new TB tests may increase whether or not a prize is offered. A second explanation is that firms agree that a substantial market might materialize, but see this market as uncertain, unfamiliar, and difficult to enter. Many large diagnostic firms know little about markets in developing countries—although the so-called emerging markets are a growing focus of attention—and many are daunted by the prospect of winning regulatory approval and negotiating contracts with a large number of unfamiliar governments. The problem may be less the size of the market than its uncertainty, what might be called “market fog.”

It is possible that a modest prize, in conjunction with the potentially large but uncertain market, could tip the balance for some firms that were already considering developing a POC TB test. The prize itself might be a less important attraction than some other forms of support that the X PRIZE proposal offers (access to samples and subsidized clinical trials) and the promise to work with international agencies to aggregate demand (see “Other features of the prize proposals” below). Such a scenario would align well with the X PRIZE Foundation's primary objective for a prize: to “unlock” a market by drawing attention to unappreciated opportunities and inspiring innovation.

Another possible explanation, however, is that firms may be deterred primarily by technological difficulty,

rather than by inadequate market prospects. This view was expressed by several interviewees associated with large diagnostic companies, one of whom revealed that the interviewee's firm had made a considerable investment in developing a POC TB diagnostic suited for developing countries. This effort had so far been unsuccessful because of the lack of appropriate biomarkers.

In conclusion, the reward offered in the X PRIZE proposal would probably be too small in most cases to drive new investment in TB tests by many diagnostic firms, although it could be sufficient for a firm that believes it could build a qualifying test on an established platform, using existing biomarkers. The potential for a large market for a POC TB test means that many firms may already be considering entering this field—a \$5–10 million prize is so small relative to the potential market that it would only make a difference on the margin. The other elements of the X PRIZE proposal could make it attractive.

A prize of \$100 million, as suggested by the BBBS proposal, would almost certainly be big enough to attract investment by a range of diagnostic firms, if they were not put off by the licensing requirements or other features of the mechanism.<sup>83</sup> But a prize purse of this size would be much more difficult to raise. OECD governments or large foundations would almost certainly have to be involved, as anticipated by the proposal developers, as this amount would be beyond the reach of all but a few individuals and most endemic-country governments.

### Other determinants of participation

The preceding section considers whether the prize amounts suggested by the X PRIZE and BBBS proposals would be sufficient to motivate firms of different types to make new investments in TB diagnostics. But, as discussed in chapter 2, other considerations may be quite important in determining whether firms participate in a prize contest. Our interviews confirmed that for small firms, the recognition

<sup>83</sup> \$100M might be enough to compensate firms for the loss of exclusive rights in some markets, but our consultations reached no definitive conclusions on this point.

for a new technology that winning a prize could bring could be quite valuable, although in general this would probably make a difference only at the margin. For some of the big diagnostics firms, the good publicity associated with a high-profile initiative devoted to global health could be quite attractive, and might persuade a firm to participate even if the expected rate of return were well below what it would expect from a purely commercial venture. In fact, one leading firm stated that public relations considerations would probably be the main reason for participating in a TB diagnostics prize contest. But this was not a unanimous view: some executives told us that it is not as important to diagnostics firms to be seen as contributing to global health as it might be to pharmaceutical companies, who have suffered from more negative publicity in recent years. Working on products like TB diagnostics that promise great public health benefits would probably be attractive to scientists and other staff at most companies, and thus good for morale.

More broadly, our interviews revealed that many industry executives simply do not see prizes as a viable alternative to commercial markets. This resistance seemed to be based less on prize amount than on a perception that prizes were a “crapshoot,” that they involved risks or uncertainties that were somehow of a different order than those that firms face in normal markets.<sup>84</sup> This perception may stem in part from the assumption that any prize would be winner-take-all, or that winners would not be determined in an orderly, legitimate way that would allow firms to judge their chances relative to competitors. It was not possible, given the time available for these interviews, to assess whether these perceptions could change with more information and greater familiarity with the prize concept.<sup>85</sup> Moreover, almost all industry

executives interviewed tended to weigh even quite large prizes against other measures with “global health” objectives rather than against “commercial” projects aimed at markets in the United States or Europe.<sup>86</sup> This attitude may not prevent these firms from participating in prize contests, but it may be a significant barrier to prize models intended primarily to substitute for inadequate markets, rather than to promote innovation, attract attention, or bring other benefits to participants.

Reluctance to consider the radical departure from conventional business models that a prize would represent was particularly pronounced among larger firms. This probably reflects in part greater conservatism and in part an understanding that the ability to evaluate and exploit markets—built on manufacturing, marketing, and distribution capacity and regulatory expertise—is a core strength of their businesses. Smaller firms seemed more willing to consider prizes as viable alternatives to other revenue sources, perhaps in part because their business models may already include the possibility of milestone payments or even outright sale of the company to larger firms.

### Other features of the prize proposals

Beyond the prize amount, there are additional features to the prize proposals we assessed—access to sample banks, subsidized clinical trials, and aggregation of demand—which could be quite valuable to firms and could influence decisions on participation. Some of these features can be considered a form of push funding that could complement the pull of the prize. Some of these additional measures could also help to remove significant nonfinancial barriers for firms.

<sup>84</sup> Objections to prizes were sometimes couched in terms that would seem to apply to all “pull” mechanisms, which require up-front investment in pursuit of an uncertain return. But markets themselves are of course a pure pull mechanism in this sense.

<sup>85</sup> This reaction to the prize concept may stem in part from the word “prizes” itself: this is why some proponents of pull incentives, including BVGH, prefer other terms. Another explanation is probably that they are hearing about prizes in the context of global health priorities. It is also possible that some firms who are aware of recent debates over prizes—for example, during the WHO IGWG process—may associate prizes with calls for reduced IP protection. Opposition to prizes therefore may stem in part from concern over changes to the current IP regime.

<sup>86</sup> This difference in how prizes are perceived by proponents—and economists—and by industry can be seen in the history of the vaccine AMC as well. While the group that originally proposed the AMC intended that firms see it as a commercial alternative to rich-world markets, vaccine firms have tended to cast their participation as part of their global access work.

**Access to sample banks.** The X PRIZE proposal would offer firms access to sputum, urine, or blood samples from high-burden regions through a sample bank. These samples can be very difficult to access and could pose an important obstacle for firms, particularly start-ups and smaller firms, in their development of TB diagnostics. We learned from one of the big diagnostic firms in the United States that it had made significant investments to import sputum samples from Mexico and other countries. It is not clear how the X PRIZE Foundation would obtain or grant access to the needed samples.

The provision of samples or other key reagents can be seen as a way to reduce the up-front costs of pursuing a prize and thus lower barriers to entry. As another example, the Prize4Life Foundation provided the expensive genetically engineered mice used by participants in its ALS treatment contest.

**Subsidized clinical trials.** The BBBS and the X PRIZE proposals both include subsidies for the clinical trials. The X PRIZE Foundation would pay for a one-year joint clinical trial for the top five teams that progress to this stage—its current proposal suggests that these trials would be conducted in South Africa and India. The cost of the joint clinical trial is estimated to be \$2.5 to \$5 million. Similarly, the BBBS TB prize fund would bear the fixed costs of the clinical studies, although contestants would bear the incremental costs of testing additional products. The BBBS proposal gives a much lower estimate of the cost of these trials: \$500,000 plus \$50,000 for each product.

Running a joint clinical trial has three potential advantages: 1) more accurate comparison of competing products; 2) overall cost savings since the trials are not repeated for each individual product; and 3) cost savings and other advantages to participating firms, which may not have expertise in conducting clinical trials in developing countries. A disadvantage is that contestants who reach this stage of development first would have to wait until competing products were ready to be tested.

In our interviews, firms agreed that clinical trials are a substantial cost and difficult to conduct in-country, especially where they currently do not have a presence. In addition, well-designed clinical trials could serve as an important step toward regulatory approval in the countries where the trial was conducted and elsewhere.

**Aggregation of demand.** The X PRIZE Foundation proposes to help aggregate demand for TB diagnostics in developing countries by working with organizations such as the Global Fund to Fight AIDS, TB and Malaria or the Global Drug Facility, which already buys TB drugs for developing countries. Firms that we consulted agreed that pooled procurement would help to realize the market potential for TB tests. Making progress in this area may be challenging for the X PRIZE Foundation, however, since the organization has no experience with global health and global health institutions.

There is little doubt, then, that these ancillary benefits would be attractive features of a TB diagnostic prize. More generally, both the X PRIZE Foundation and the Prize4Life Foundation believe that reducing costs and risks to firms with measures of this kind can in some circumstances be as important as the prize award itself. But if this is the case, why is a prize necessary at all, since these forms of assistance could be offered on their own or in conjunction with push funding? A prize mechanism may still be the best way forward, but the case must rest on advantages intrinsic to prizes—for example, the potential to attract innovation from unidentified sources. This discussion illustrates the challenges of evaluating incentive proposals that constitute a bundle of distinct elements.

**Other features of the BBBS proposal.** This proposal includes several elements in addition to the \$100 million “grand prize” for a new TB diagnostic. These include small prizes for solutions of technical challenges, annual “best contribution” prizes, a set-aside for developing-country researchers, and an incentive for collaboration and openness. We did not

specifically assess these ideas, but they are reasonable responses to some of the potential drawbacks of simple winner-take-all prize designs. A risk of adding additional elements to the prize structure is that they may make the competition more complex to administer and more difficult for potential participants to assess.

### Alternative designs: milestone prizes

Neither the X PRIZE nor the BBBS proposal currently offers milestone prizes, although the BBBS proposal would include “technical challenge” prizes for solutions for technological problems and “best contribution” prizes for progress short of the final product. MSF is currently considering a prize focused on discovery of new biomarkers and the X PRIZE Foundation would be open to including milestone awards in a revised design.

Small firms interviewed for this study were unanimous in preferring a milestone prize to a final product prize, for the reasons discussed in chapter 2: shorter time to payoff, reduced risk, and better fit with company capacity. Small firms are also more familiar with the milestone payment concept, which is common in development partnerships between firms. Since the existing proposals did not include these elements, we were not able to explore the details of a milestone-based structure, but firms indicated that a prize of \$5 million or less for an appropriate laboratory milestone would be attractive. Some interviewees with large diagnostic firms also indicated that a milestone structure would be more attractive than an end prize by itself; it was not clear whether they would prefer a structure that included both milestone and final product prizes or milestone prizes only.

The preference for milestone prizes was one of the most consistent findings from our discussions with

firms, suggesting that developers of diagnostic prizes should seriously consider this kind of design, especially when markets are big enough to pull a product to market once the technological barriers are overcome. It's important to remember, however, that milestone prizes have important disadvantages as well, including the need for mechanisms to ensure that product development is completed, the risk of limiting the range of solutions, and the additional challenges of managing IP.<sup>87</sup> Milestone prizes, like end prizes, should consider the implications for access, by rewarding technologies that can be manufactured at an affordable price and by including price ceilings, IP requirements, or both. But these access provisions may be more complicated to implement in milestone prizes than in end prizes because they may have to carry over from the prize winner to another product developer who would bring the winning technology to market. Prize contests focused on milestones, which tend to be more technical in nature and less compelling to the general public, might also be less of a good fit for organizations like the X PRIZE Foundation, which considers the ability to generate widespread publicity an important part of its model.<sup>88</sup>

### Implications for access

The X PRIZE and BBBS proposals take very different approaches to promoting access to prize-winning products. The BBBS proposal would rely primarily on competition to ensure supply at an affordable price, requiring the prize winner to grant to a licensing pool “reasonable and non-discriminatory licenses to all patents and know-how needed for competitive supply of the technologies, in the relevant field of use.”<sup>89</sup> The X PRIZE proposal, in contrast, includes no IP provisions, allowing competing teams to retain exclusive rights to their products.

<sup>87</sup> Ideally, the inventions that enable a milestone to be reached would be available to other product developers to maximize the chance of success, especially if the winner of the milestone prize is unwilling or unable to continue development. But requiring this sharing may deter some potential participants.

<sup>88</sup> The X PRIZE Foundation told us that a TB diagnostics prize focused on a milestone would probably be considered an “X CHALLENGE,” a less expensive and lower-profile class of contest, rather than an X PRIZE.

<sup>89</sup> It should be noted that the BBBS proposal would also offer an alternative if open licensing of the technology and competitive supply is not feasible, whereby the winner would have to provide sufficient assurances that the products would be manufactured in sufficient quantities and with acceptable quality, at affordable prices.



## PRIZES FOR TB DIAGNOSTICS

The X PRIZE proposal would require teams to submit business or manufacturing plans that would describe the status of agreements with a “reputable manufacturer” and provide some preliminary information on likely production costs at scale. But the X PRIZE Foundation considers an “affordable” cost criterion a disincentive to potential competing firms and believes that it would be difficult to define a cost ceiling and objectively audit a cost estimate.<sup>90</sup> On the other hand, the BBBS proposal considers access provisions a central element of the prize design. It requires contestants to demonstrate that a product can be manufactured to scale at “affordable prices on a sustainable basis” either by meeting a price ceiling or a market penetration test.<sup>91</sup>

**IP provisions.** Our interviews with venture capitalists and product developers revealed a mixed view on the issue of licensing requirements associated with incentives for development of products for developing countries. While some interviewees expressed a blanket opposition to any IP provisions in R&D financing mechanisms, others would consider a restrictive licensing approach whereby they would grant licenses for certain markets or regions (for example, low- and middle-income countries) and for specific applications (for example, TB diagnosis), at low cost if these markets were small or at higher cost if real opportunities were foregone.

Such a licensing structure could have important public health benefits if it is possible for low-cost firms in countries such as India and China to manufacture TB tests cheaply without having access to know-how. Several industry experts that we consulted thought that this would be possible. If substantial proprietary know-how is also required to make production by low-cost suppliers possible, reliance on competitive supply becomes more complicated.

However, nearly all firms we interviewed expressed concern about sharing IP for technological platforms,

as this information could be very valuable for future product development and could be diverted to other uses. For example, one large diagnostic company told us that they decided not to participate in the CD4 Initiative, a milestone-based push funding initiative to develop low-cost CD4 tests for resource-poor settings,<sup>92</sup> because it required participants to grant access to all IP, including for platforms, if they are unable or unwilling to supply the product. Nonetheless, two diagnostic companies did participate in the initiative, implying that the IP provisions were not insuperable obstacles to all firms. One solution to the problem of platform IP, suggested by a former executive at a large diagnostic company, is to withhold IP on a critical component and require firms that license the remaining patents to procure this component from an approved source, thus allowing the patent-holder to track how the platform is being used. The problem of platform IP would have to be solved to make a licensing approach feasible for diagnostics.

**Cost provisions.** All firms consulted were willing to work with a cost ceiling for manufacturing to scale and did not view such a provision as a deterrent to participation. Interviewees pointed out that some kind of price target is already a fundamental element of target product profiles for all markets. Moreover, most experts told us that it is in general possible to estimate production costs with reasonable accuracy, at least when there is some experience with the relevant technology. While further investigation is required to determine an appropriate price ceiling for a POC TB test, one possible standard of comparison is the price of current CD4 diagnostics available in Africa, about \$5–10 a test for reagents.

We conclude that the access provisions currently included in the X PRIZE proposal are unnecessarily vague and could result in a winning product that cannot be produced at an affordable cost. A cost

<sup>90</sup> The X PRIZE Foundation considered including a cost provision for consumables only.

<sup>91</sup> The BBBS proposal identifies several ways that competing firms could meet a market penetration test—for example, by showing that the diagnostic device be manufactured, distributed and used by a large enough population or that it be manufactured and sold by one or more third parties without subsidies from the prize applicant.

<sup>92</sup> For more information, visit the CD4 Initiative website, <http://www3.imperial.ac.uk/cd4>.

ceiling of some kind is clearly acceptable to industry (if a level can be agreed). Although we acknowledge the difficulty of verifying claims about cost, we believe these challenges can be overcome. The licensing provisions proposed by BBBS are clearly more contentious, and would probably deter some firms on principle. But our consultations suggest that if these provisions were carefully designed they could be accepted by many product developers. The critical point is that if firms are to give up exclusive rights in potentially profitable markets such as India, China, or Brazil, the prize amount will have to be correspondingly larger to compensate for this loss.

Whether an approach that relies on licensing and competition or on cost ceilings is the best for a particular technology depends on a number of factors, including the feasibility of generic production, the attractiveness of the market to suppliers, and the ability to restrict the use of licensed technology to the product in question.

### Potential sponsors for a TB diagnostic prize

Neither of the proposed TB diagnostic prizes has yet been funded. A prize of the size proposed by the X PRIZE Foundation could in principle be funded by an individual philanthropist, a foundation, a firm, or a national government—in fact, donors of each type have sponsored or cosponsored previous X PRIZES. A larger prize, such as that proposed by the four countries to the WHO working group, would probably require the involvement of governments or large foundations. Accommodating prizes within the legal and budgetary frameworks of government agencies can pose challenges, but these challenges can be overcome, as the vaccine AMC demonstrated. Governments have often used prizes as an instrument of innovation policy in the past, and the US Congress recently passed legislation that provides federal agencies with broad authority to sponsor prizes.<sup>93</sup>

We have not, as part of this study, assessed the interest of governments or other potential funders in sponsoring prizes.

### Competing prizes

The fact that at least two groups are actively working on prizes for TB diagnostics (it is unlikely that the BBBS and MSF proposals would both go forward independently) raises the issue of competing prizes for the same or related technologies. In some ways this would be undesirable, as it might send conflicting signals to product developers about product characteristics and create conflicting IP and access conditions. On the other hand, two prizes could attract more attention and resources than one and increase the total reward to developers whose products met both sets of criteria. What is more, separate prizes might be a way to promote the development of multiple products that met distinct needs.

While having two prize contests for the same technology would not necessarily be a bad thing, there are clearly benefits from coordination among prize developers, including avoiding wasteful duplication of consultations with stakeholders and minimizing the incompatibility of prize criteria.

### 3.4. Conclusions on prizes for TB diagnostics

We conclude from this analysis that a prize could help to accelerate development of the improved TB tests badly needed in high-burden countries.

It is difficult to gauge the extent to which a TB diagnostic prize would persuade firms that are not already working in this area to invest in new R&D. There is no doubt that the prize model is unfamiliar to industry and that some firms, especially large ones, would be unwilling to consider such a different business model. Other firms, especially small ones, would have trouble

<sup>93</sup> Tom Khalil and Robynn Sturm, "Congress Grants Broad Prize Authority to All Federal Agencies," White House Open Government Blog, posted 21 Dec 2010, <http://www.whitehouse.gov/blog/2010/12/21/congress-grants-broad-prize-authority-all-federal-agencies>.



## PRIZES FOR TB DIAGNOSTICS

finding the necessary resources upfront.<sup>94</sup> But we believe that a well-designed and sufficiently large prize would stimulate new investment and focus it on the specific needs of high-burden countries. Some large firms would be attracted by the good publicity associated with participation in the contest, and small firms might see it as an opportunity to validate and gain recognition for their technologies.

We believe that a prize focused on a substantial milestone in test development—for example, demonstration that the specified criteria were met in a rigorous laboratory evaluation—might be more useful than an end prize for a fully developed and tested product. This conclusion, which might not apply to other products, rests on two arguments.

First, the potential market for a POC TB test for developing countries appears to be quite substantial, given the demonstrated recent willingness of donors to subsidize the purchase of critical new diagnostics. The diagnostics industry seems to recognize the commercial potential of this market. Thus, a prize may not be necessary to drive later stages of test development.

Second, the major barriers to development of the needed POC test are technological: the lack of antigen or antibody biomarkers suitable for conventional, inexpensive POC platforms and the lack of a platform that would make nucleic-acid-based tests truly POC. Thus, the main goal of a TB diagnostic prize should be to encourage innovation by bringing in new ideas and new types of innovators. These innovators, especially small firms, are more likely to be able to participate in a milestone prize contest.

We believe that the \$5–20 million prize purse proposed by the X PRIZE Foundation as an end prize is probably too small to change the decisions of most firms. Although it might be enough to cover the costs of R&D, it is insufficient to cover risks and to compete with alternative uses of resources. The X PRIZE

Foundation argues that its prizes are not intended to substitute for markets; but if there is already a large market for POC TB tests, a \$5–10 million prize would do little to change commercial calculations. A prize of this size, or even somewhat smaller, would probably be more than sufficient for a milestone award, however. A \$100 million end prize, as proposed by BBBS, would almost certainly be big enough to attract substantial commercial interest and might even be larger than necessary, given the potentially large market. Figure 3.8 summarizes our assessment of both proposals.

We believe that in-kind support such as access to specimen banks and clinical trials organized by the prize sponsor would also encourage participation in a prize, as these measures could help address important barriers to entry.

A prize for TB diagnostics should include mechanisms to ensure that a winning product would be affordable. In our view, a prize should include a manufacturing cost ceiling among the criteria. Requiring that winners grant nonexclusive licenses for relevant IP, restricted by geography and field-of-use, could be a way to drive down prices and ensure sustainable supply. Such a requirement would undoubtedly deter some firms from participating, however, and a satisfactory solution to the problem of IP associated with platform technologies would have to be found to make this approach work for diagnostics.

Our case study of prizes for TB diagnostics illustrates the importance of careful analysis of context, including challenges to product development and market prospects, to understand whether a prize would help to accelerate development of a particular product.

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<sup>94</sup> We did not explore in detail the impact of a prize on academic researchers. Although many would surely be inspired by a prize, their participation would depend on their ability to obtain funding for their research, either from grants or through partnerships with industry. University research is critical to development of all new health technologies, but it is not clear that prizes should directly target academic scientists.

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**Figure 3.8. Assessment of TB diagnostics prize proposals**

Feature	X PRIZE	Bangladesh, Barbados, Bolivia, and Suriname
Prize amount & structure	\$5–10M too small for most firms; most firms prefer milestone structure	\$100M sufficient for firms, but much more challenging to raise; most firms prefer milestone structure
Technical specifications	Reasonable, fairly ambitious	Not yet developed
Access provisions	Too vague; should include cost criterion	Cost or market penetration criteria useful; IP licensing could be contentious, especially for platforms
Other	PR attractive; access to specimen banks, paid joint trial, aggregation of demand, and reduction of barriers to market entry advantageous	Subsidized clinical trials attractive

CHAPTER 4  
PRIZES FOR OTHER GLOBAL  
HEALTH TECHNOLOGIES



## 4

## In the previous chapter we analyzed in detail the potential of prizes for TB diagnostics. To what extent do our conclusions from this analysis apply to prizes for other diagnostics needed in low- and middle-income countries and, more broadly, to prizes for drugs and vaccines?

The answer, not surprisingly, is that it depends: we believe that each case must be analyzed separately, as the value of prizes relative to other instruments depends on the specific circumstances. But it should be possible to delineate some of the features of particular technologies that are most important to understanding whether a prize would be useful.

In this chapter we describe briefly some current prize contests or proposals in other health areas. We then examine how relevant features of other needed global health technologies might differ from the example of TB tests and what implications these differences might have for prizes.

### 4.1. Other prizes and prize proposals

Although more work has been done on prizes for TB tests than for any other global health product, prizes have been proposed or are being developed for other needed health technologies.

#### Other BBBS proposals

The four countries that submitted the proposal for the TB diagnostics prize fund to the WHO working group also put forward two other prize proposals. One outlines a prize fund for new drugs, vaccines, and diagnostics for Chagas disease.<sup>95</sup> Although this

proposal shares many features of the TB diagnostics proposal, it is substantially more ambitious and it incorporates several of the innovative elements of the comprehensive multiproduct prize funds proposed by KEI and others. In particular, rather than awarding a large prize of fixed size to the first product to meet a set of technical specifications, it would reward all new licensed medicines and vaccines for Chagas disease according to their incremental impact on health outcomes, with products receiving payments for up to 12 years. To be eligible, product developers would have to license all necessary patents and know-how to a new Chagas-disease patent pool. New diagnostics would also be eligible for rewards, although the details of how this would work are not specified (it is more difficult to estimate the incremental health benefit of new tests than new drugs or vaccines).

Another BBBS proposal links prizes and patent pools to donor funding for the purchase of medicines, for example through the Global Fund.<sup>96</sup> It suggests that donors contribute a fraction, perhaps 10%, of their spending on drugs for developing countries to a new prize fund that would be used to reward new medicines for the included diseases. These rewards would again be linked to the incremental health benefit of the new products, and would go only to product developers who agreed to submit the relevant IP to a patent pool. In theory, donors (and developing

<sup>95</sup> BBBS Chagas Prize Fund submission to WHO EWG, [http://www.who.int/phi/Bangladesh\\_Barbados\\_Bolivia\\_Suriname\\_ChagasPrize.pdf](http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_ChagasPrize.pdf).

<sup>96</sup> BBBS Donor Prize Fund submission to WHO EWG, [http://www.who.int/phi/Bangladesh\\_Barbados\\_Bolivia\\_Suriname\\_DonorPrize.pdf](http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf).

countries not receiving donor subsidies) would benefit from the lower prices that would come with competitive supply of the new medicines.

Finally, Bolivia, Suriname, and Bangladesh submitted a proposal for prize funds at the national level for new cancer treatments, highlighting the growing importance of noncommunicable diseases in developing countries and extending the prize fund concept into the more controversial domain of products with primary markets in high-income countries.<sup>97</sup>

### BioVentures for Global Health

BVGH is developing one or more proposals for pay-for-success incentives for health technologies needed in developing countries.<sup>98</sup> Although this work is not yet public, BVGH has shared some features of the emerging proposals with us.

- The incentives will be milestone-based, with rewards at one or more development milestones and perhaps also for the end product.
- The primary target of the incentives will be biotechnology firms.
- One proposal will focus on diagnostics. The targeted product may be a platform capable of diagnosing several diseases—for example, a test that could distinguish several common causes of childhood fevers.

### Prize4Life

As mentioned in chapter 2, the Prize4Life Foundation is using prizes to accelerate development of new treatments for ALS. It has conducted two prize contests, one for new biomarkers of disease progression and one for new treatments that demonstrate efficacy in a specified animal model.<sup>99</sup> The \$1 million biomarker prize was recently awarded.<sup>100</sup> Although the focus on a disease with a large market in the

United States puts it beyond the scope of this study, the Prize4Life initiative is an interesting example of the use of prizes to overcome scientific and technological obstacles to the development of new health technologies. It also illustrates the way that prizes can focus attention on critical needs that may not be receiving sufficient attention, in this case markers of progression and rigorous animal models.

## 4.2. Prizes for other diagnostic tests

We believe that much of our analysis of prizes for TB diagnostics would apply to other diagnostics for the developing world. Our findings on the costs, expectations, and attitudes toward incentives held by diagnostic firms of various kinds should be broadly applicable. Three features of TB diagnostics may differentiate this product from many others, however. The first is the relatively large potential market for a successful POC TB test. Although this market is far from certain—especially given the more pessimistic recent outlook for donor funding for global health—many firms seem to find such a product commercially attractive. Important new diagnostics for HIV—for example, a POC CD4 test—might also have enough of a market to interest industry. But tests for many other diseases would be much less commercially attractive, either because they would have to be very cheap to displace existing tests, because the needed volume would be much smaller, or because there would be no meaningful private market and no donor channel for substantial subsidy. Diagnostics for sleeping sickness might be an example of a badly needed product with a very small market.

The main implications of small market size for prizes is that the prize either has to be for the end product and large enough to substitute for the missing market, or, if the prize is for a milestone, be coupled to another mechanism (push funding or a purchase

<sup>97</sup> Bangladesh, Bolivia, and Suriname Cancer Prize Fund submission to WHO EWG, [http://www.who.int/phi/Bangladesh\\_Bolivia\\_Suriname\\_CancerPrize.pdf](http://www.who.int/phi/Bangladesh_Bolivia_Suriname_CancerPrize.pdf).

<sup>98</sup> BVGH prefers not to use the term “prizes.”

<sup>99</sup> For more information, visit the Prize4Life website, <http://www.prize4life.org/page/prizes>.

<sup>100</sup> Bina Venkataraman, “\$1 Million to Inventor of Tracker for A.L.S.,” *New York Times*, 03 Feb 2011.

commitment) to bring the product the rest of the way to market. Where substantial markets exist, milestone prizes may make the most sense, since the market should suffice to pull a promising product through to licensure once technological and other barriers are removed. Access provisions of some kind are still needed, however, since a product intended primarily for private sector or donor-subsidized markets in developing countries must still reach others who need it.

The second important feature of POC TB diagnostics for prize design is technological difficulty. On one hand, the magnitude of the challenge means that the prize will have to be relatively large to compensate for the risk. On the other hand, the need for new ideas and new innovators makes problems like these a good fit for prizes, especially early-stage prizes. Other needed tests are probably easier to develop: the lack of interest by industry in the diseases of developing countries means that there is almost certainly low-hanging fruit to be found, and the necessary tests can in many cases be developed on the basis of existing technological platforms, using known or relatively easily discovered biomarkers. In these cases, prizes of relatively modest size might have an effect, but more conventional approaches might work just as well or better. The meningitis A conjugate vaccine developed by PATH's Meningitis Vaccine Project is an example from outside the diagnostics field of an important product whose development required no scientific or technological breakthrough and which could be pushed to a successful conclusion (with affordable access guaranteed) through a relatively simple partnership structure with foundation funding.

The third distinguishing feature of TB diagnostics is, ironically, that the urgent need for better tests is now quite broadly appreciated, thanks in part to the efforts of MSF. As a consequence, the value of a prize in mobilizing attention and resources and in bringing the problem to the attention of potential solvers is less than it might have been a decade ago, and less

than it would be for other needed diagnostics—for example, for Chagas disease.

### 4.3. Prizes for drugs and vaccines

The considerations discussed in the previous chapter apply to prizes for drugs and vaccines as well: market size, technological difficulty and the need for breakthrough innovation, and level of awareness matter in the same way. But drugs, vaccines, and diagnostics differ in important ways that have implications for prizes. We cannot attempt a systematic analysis here, but will outline a few potentially important differences.

Most importantly, drug and vaccine development is considerably more expensive and time-consuming than in-vitro diagnostic development, largely because of the long and expensive clinical trials required to demonstrate safety and efficacy. An often-cited study estimated the average risk-adjusted cost of developing a new drug at \$800 million.<sup>101</sup> Although some have argued that this figure is inflated, it is clear that R&D costs can be tenfold greater for drugs and vaccines than for diagnostics. This means that prizes for drugs or vaccines, or at least end-prizes for these products, would in general have to be much larger than for diagnostics, probably at least in the many hundreds of millions of dollars, if not billions. The long time it takes to bring a new drug or vaccine to market—typically a decade or more—increases the challenge, especially if the prize is aimed at innovators with a high cost of capital. While diagnostic prizes could be funded by a wide range of sponsors, including individuals, one consequence of the high cost of drug and vaccine prizes is to limit the range of potential sponsors to governments and large foundations and to make governance issues more important.

It's important to keep in mind that these challenges apply not just to prizes but to other incentives for drug and vaccine development: if the real costs are

<sup>101</sup> Joseph DiMasi et al., "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics*, 22, (2003): 151–185.

greater, any mechanism for accelerating development of these products will be more expensive. But the relatively low cost and short development timelines make diagnostics an attractive testing ground for prizes.

The industries are also different. The vaccine industry in particular is highly concentrated, with five multinational firms accounting for 85% of global sales in 2008.<sup>102</sup> Not only sales, but also the capacity to bring new products through trials and the demanding regulatory process, is concentrated in a few firms, although a number of companies in the emerging-market economies can manufacture all but the most sophisticated vaccines and have growing innovative capacity. This means that an end prize aimed at development of a new vaccine, especially a challenging one, would probably have to be designed to interest the handful of multinational vaccine firms. But these firms may be the least likely to consider such a departure from their usual way of doing business, even if they find the publicity associated with participating in a neglected-disease initiative appealing. Moreover, if it is clear that the needed innovation must come from one of a small number of firms, a prize might not be the most efficient way to purchase this innovation. Milestone prizes aimed at smaller companies and perhaps university laboratories might be a useful alternative, with the possibility of handing over to a developing country manufacturer.

Some other differences relate to IP and to the prospects for generic production. For drugs, or at least small-molecule drugs, the regulatory approval process for generic products is well established.<sup>103</sup> Given the sophistication of generic manufacturers, in most cases it should be possible for multiple manufacturers to produce and win regulatory approval for their versions of a licensed drug, as long as patent and other IP barriers are removed. This means that the strategy of linking prizes to licensing and competitive supply could work, as long as the requirement does not deter participation

and the markets are sufficient to support multiple suppliers. Moreover, the problem of platforms with multiple uses is much less relevant to drugs than to diagnostics. But it may be that drug companies would be more resistant to any IP licensing requirement, precisely because patents in many cases represent the only barrier to other suppliers and are thus perceived as indispensable to the industry's business model. For vaccines, as for diagnostics, there is no formal generic regulatory pathway—each new manufacturer must independently demonstrate safety and efficacy, since no two vaccines can be considered identical—although in practice “follow-on” vaccines often have an easier and cheaper path to market. Know-how, especially in manufacturing, is also much more important for vaccines than for drugs. Together these two considerations mean that a licensing and competitive-supply approach to promoting access is much more challenging for vaccines.

<sup>102</sup> C. Sheridan, “Vaccine Market Boosters,” *Nature Biotechnology*, 27, no.6 (2009): 499–501.

<sup>103</sup> Biological drugs, which are increasingly important, face many of the same issues in manufacturing and regulatory approval that vaccines face.





CHAPTER 5  
PRIZES COMPARED  
TO OTHER INCENTIVES



**5 In many circumstances, the most pertinent question, especially to neglected-disease R&D funders, may not be whether a prize could help to drive development of a needed technology, but which approach would be the best way to achieve that objective—the most likely to succeed or the most efficient.**

Would a prize be better than a conventional grant to a university laboratory or an industry partnership brokered by a PDP? This study was not designed to address this question systematically—our approach was not explicitly comparative. Moreover, we believe that there is almost certainly no general answer to the question, which is therefore best answered in the context of a particular product or class of products. We will, however, put forward in this section some additional notes on the relative merits of prizes and grants or contracts, building on the general analysis in chapter 2 and drawing on the interviews with industry executives.

The first point to be made is that prizes and grants or, more generally, push and pull mechanisms, are not mutually exclusive. Different approaches could be used to drive different stages of R&D for the same product, with prizes or market commitments succeeding grant funding of early stages—as in the current system of publicly funded basic research and market-driven product development—or PDP-managed development following a discovery prize. Smaller prizes can be used to solve technical problems at any R&D stage within a large frame of either grant-funded or market-driven R&D, as InnoCentive has shown. Moreover, push components can be added to prizes in order to alleviate some of the problems with pull mechanisms, in particular the danger of excluding innovators with little access to capital. Nonetheless, R&D funders will not in general want simultaneously to fund in full the efforts of product

developers and offer a large product development prize designed to drive private investment in the same R&D. Thus, funders will want to understand the relative merits of the two approaches for addressing particular product development challenges.

### 5.1. Relative cost of grants and prizes

A funder might well want to know whether a product development prize would be more or less expensive than using grants or contracts to achieve the same objective. The following discussion focuses on for-profit firms and substantial, expensive discovery or product development objectives, for which a conventional economic analysis provides an essential, if incomplete framework. For other kinds of prizes aimed at other classes of innovators, the considerations could be quite different. The conclusions presented here are underpinned by a simple algebraic analysis, which is presented in appendix B.

The starting point for thinking about the cost of prizes for product development is the assumption that firms will decide whether to invest in R&D in pursuit of a prize based on a comparison on expected costs and returns from the prize and other sources, taking into account technical and competitive risks, cost of capital, and ancillary benefits such as publicity and technology validation (see chapter 2). Since a prize must offer a return larger than the expected incremental costs, to compensate for the risk of failure

## PRIZES COMPARED TO OTHER INCENTIVES

and the cost of capital it will in general have to be larger than a grant to the same firm for the same R&D. But since the sponsor will not have to pay the prize award unless the R&D is successful, the *expected* cost to the sponsor will approximate the cost of the grant, in the simplest analysis.<sup>104</sup> The same conclusion holds when the prize is made large enough to attract several firms: the expected cost to the sponsor resembles the cost of grants to the participating firms. Thus, to a first and very crude approximation, the costs of push and pull approaches are equivalent.

This simple conclusion omits a number of important considerations, some of which may make prizes more expensive relative to grants while some work in the opposite direction.

### Differences in cost of capital

Prizes must take into account the cost of capital to potential competitors, which can be very high. The fact that prize sponsors (for example, governments or foundations) can in general borrow at much lower rates would appear to make push funding substantially cheaper. As long as capital markets are functioning reasonably well, this difference probably does not reflect real differences in the cost to society of the two approaches to funding product development: the risks that make capital expensive to small firms are real, whether or not they are borne by public or commercial investors. But from a purely financial perspective, this effect may indeed make prizes more expensive to sponsors.

### Windfalls to better-positioned contestants

In most circumstances, some firms will have more applicable technologies or more advanced product candidates than others. In order to attract multiple competitors, a prize must be large enough to represent an attractive proposition not only to the best-placed firm but also to others with a lower chance of winning. This means that the prize will be

larger than would have been necessary to entice the leading firm or firms, and that the expected cost to sponsors (other things being equal) will be higher than that of grants to each firm (for details, see appendix B). The additional cost to sponsors could be substantial. The point is most obvious in the situation where a single firm has a promising product in late-stage development: a prize big enough to attract other firms with much less-advanced candidates would have to be wastefully large, and another approach to bringing the lead product to market is more appropriate.

### Overestimation of chances of success

To the extent that firms or other competitors are too optimistic about their chances of success, they will pursue a prize even when a rational calculation would argue that they should not. This would in turn allow prize sponsors to stimulate more R&D with a prize of a given size, and make prizes cheaper than grants.

### Additional benefits and motivations

The prize award is rarely the only reason competitors decide to pursue a prize: publicity, recognition, and competitiveness all may play a role. Together these factors could make the impact of a prize greater than a simple economic calculation would suggest, allowing sponsors to “leverage” their investment. While these effects are undoubtedly important in some circumstances, we think it is unrealistic to expect that in the realm of health technology development, firms, especially established biotech or pharmaceutical firms, will consistently invest many times what they can reasonably expect to win from a prize, as contestants in the Ansari X PRIZE apparently did. Moreover, firms can obtain some of these ancillary benefits in other ways, including through neglected-disease R&D conducted through well-publicized partnerships with PDPs.

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<sup>104</sup> This is because the same risk of failure that creates the need for a larger prize award reduces the chance that the sponsor will have to pay.

### Incentives

Firms pursuing a prize or market with their own money may work harder or more efficiently than they would with grant or contract funding. This incentive effect could help to make pull mechanisms a better value.

### Lack of information about potential solvers

As this report has emphasized throughout, the main advantages of prizes may be in those circumstances in which the sponsor is unsure which approaches or innovators offer the best chance of success. To the extent that potential prize competitors have a better sense of their own chances than funders, a prize will result in a better distribution of funding among approaches and product developers than the sponsor could achieve. This “allocative efficiency” will in turn make prizes more economically efficient in these contexts.

This analysis of relative cost therefore reinforces some of this report’s central conclusions: the advantages of prizes are greatest when the sponsor does not know which approach or product developer to fund; prizes are least appropriate when there is one or a small number of leading product candidates.

considerations are represented in figure 5.1, which builds on a similar graphic presented in the McKinsey prizes report.<sup>105</sup> Examples of products in some of the categories are provided for illustration. For example, the meningitis A vaccine was a good candidate for push funding, since the path to a vaccine was relatively straightforward: vaccines of this type had already been developed and no major scientific or technological breakthrough was required. AIDS vaccines—and perhaps TB diagnostics—require technological breakthroughs, which could come from a wide range of innovators but would have respectable markets. They are therefore good candidates for milestone prizes. New drugs or diagnostics for sleeping sickness, which also face substantial technological obstacles, would have very small markets. Milestone prizes would be insufficient and would have to be supplemented by end prizes or push funding.

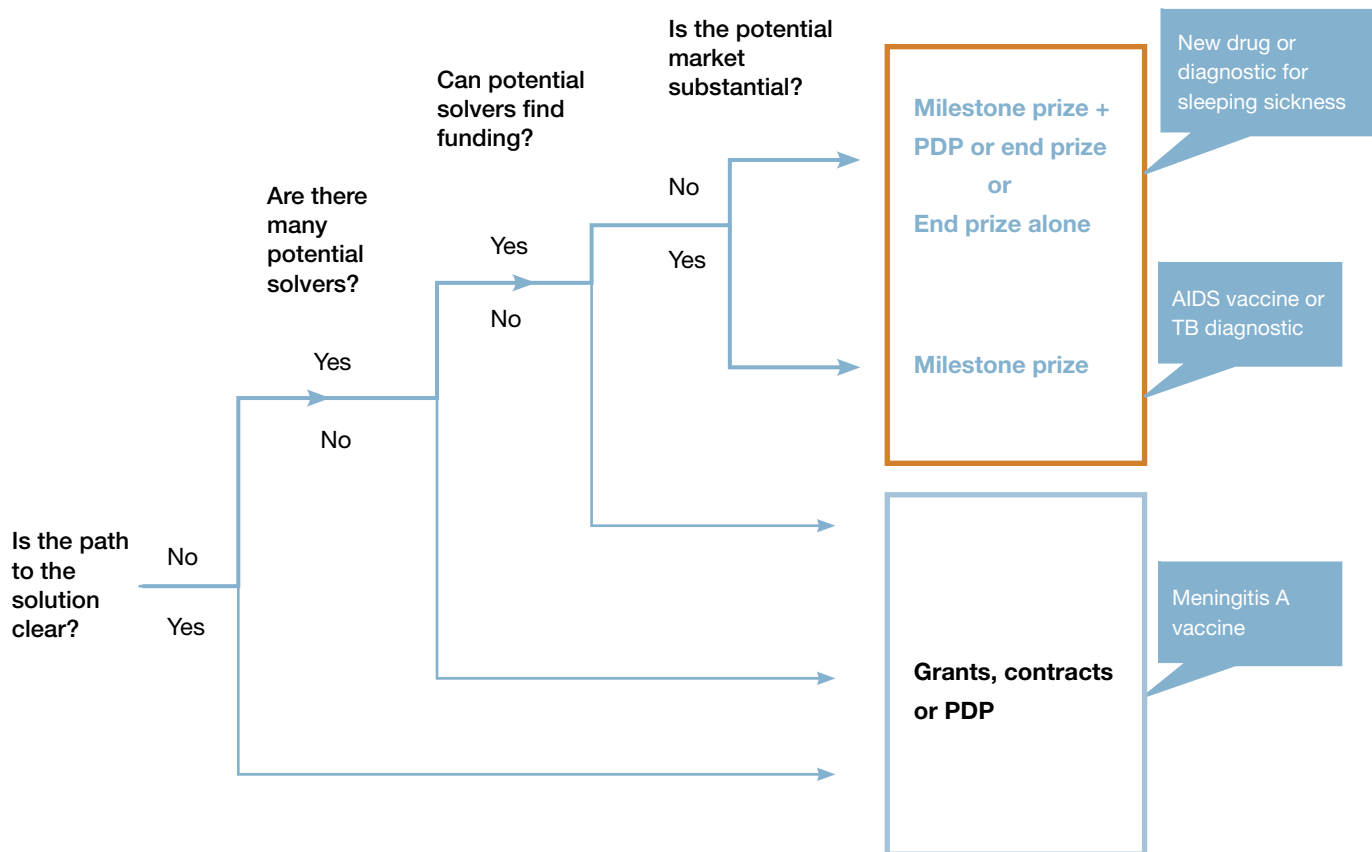
This simple graphic cannot of course accommodate all the factors that should be taken into account in deciding whether to use a prize rather than another approach in a particular context. For example, it omits consideration of the degree to which a prize could attract attention (and new resources) to a particular field, or of some of the factors (discussed in the previous section) which could make a prize very expensive in some contexts.

## 5.2. When to use prizes: a decision tree

We conclude that prizes for health-technology product development are most promising when the path to a product is unclear, when there are a relatively large number of researchers or product developers who might be able to find solutions to the key problems, and when these solvers would be able to find funding to pursue a prize. Moreover, when the market is large enough to bring a product to market if the major technological obstacles were removed, a milestone prize might be the best design, while if the market is very small, either an end prize, an AMC, or further push funding will be necessary. These

<sup>105</sup> *And the Winner Is ...: Capturing the Promise of Philanthropic Prizes*, McKinsey, (2009): accessed 26 Jan 2011, [http://www.mckinsey.com/App\\_Media/Reports/SSO/And\\_the\\_winner\\_is.pdf](http://www.mckinsey.com/App_Media/Reports/SSO/And_the_winner_is.pdf).

**Figure 5.1. Decision tree for prizes for health product development**







CHAPTER 6  
CONCLUSIONS AND  
LIMITATIONS OF STUDY





## Incentive prizes are an intriguing alternative to grants and other forms of push funding as a way to spur the development of needed health technologies for developing countries.

Their greatest potential advantage is that they do not require the sponsor to choose either the most promising path to the desired product or particular product developers. They are thus most likely to be useful when the way forward is not clear and new ideas—and new innovators—are needed. It follows that prizes are not the most efficient mechanism when the needed R&D is relatively straightforward.

An important disadvantage of prizes (and other pull mechanisms) is that they exclude researchers and product developers who are not able to fund the necessary R&D upfront.

Prizes could be used both to overcome scientific or technological obstacles or, like AMCs, to augment or substitute for commercially unattractive markets. But the two uses of prizes focus on different kinds of participants and require different designs.

Milestone prizes, either free-standing or as a part of a structure that includes final-product prizes as well, are particularly attractive in circumstances where the primary obstacles to development of the needed product are at early stages. Prizes of this kind are attractive to biotechnology companies, which have a shorter time horizon than large firms. But milestone prizes must be accompanied by mechanisms to ensure that candidate products are taken all the way to market and will be available to those who need them at an affordable price.

Final-product or end prizes would be most appropriate where the primary obstacle is lack of market, as will often but not always be the case for the products needed by the poor. Prizes of this kind also offer

an opportunity to de-link product prices from R&D costs through IP licensing and competitive supply. In situations where generic production is feasible—and other elements of the prize have guided developers toward low-cost technologies—this approach could be a way to promote sustainable supply at affordable prices. But the viability of end prizes depends on their attractiveness to the typically large firms with the capacity to bring new products all the way to market.

In the case of TB diagnostics, we believe a prize could help to overcome the challenges to develop the POC test needed in many high-burden countries. Since the primary obstacles are technological (notably the lack of biomarkers suitable for conventional POC platforms) and since the market for a good test is probably sufficient to attract developers and suppliers once the obstacles are removed, we believe that a milestone prize might be sufficient, although milestone rewards could be coupled to a final-product prize.

Firms consulted for this project had a mixed reaction to the idea of prizes. Many biotechnology firms suggested that a sufficiently large prize, especially for a milestone that they could reach on their own, could be an attractive alternative to other kinds of return on R&D investment. Established firms were more likely to be able to pursue a prize than start-ups. Large firms, with their business models centered on production, distribution, and pursuit of market share, were in general less willing to consider prizes as an alternative return on investment, suggesting that even large prizes might have trouble changing the priorities of these firms. Some large firms might be

## CONCLUSIONS AND LIMITATIONS OF STUDY

drawn to make modest investments in prize contests by the positive publicity. Not surprisingly, most firms expressed a preference for upfront and risk-free funding in the form of grants over prizes. This preference does not invalidate the advantages of prizes in cases where the funder does not know which firms to fund.

Some but not all firms said that IP licensing requirements could deter them from pursuing a prize.

There are limits to how much can be learned from industry consultations, however. In the absence of a concrete initiative with money behind it, many firms have not devoted much time to the concept and have not reached definitive positions. Although these conversations are necessary, and can provide crucial insights into the needs and priorities of firms of various types, ultimately the only way to know who would participate will be to launch a prize. We believe that some questions will only be answered by experimentation, and that the case for prizes for global health technologies is strong enough to justify investing in one or more carefully chosen initiatives. The great need for better TB tests, together with the modest R&D costs and relatively short development timelines of diagnostics, could make TB diagnostics a good testing ground for prizes.

### Limitations and further work

We outline here a number of important limitations of our assessment. We also suggest areas where additional consultations and analysis would be valuable.

- Our assessment relies on one in-depth case study—prizes for TB diagnostics. At the time we began our analysis, relatively few prize proposals that met our criteria were available to assess. Additional detailed case studies would undoubtedly add important insights and might alter some of our general conclusions.
- Our assessment focused primarily on the potential of prizes as an independent mechanism to accelerate global health R&D. This is largely because the larger R4D project—Center for Global Health R&D Policy Assessment—is structured as a series of assessments of specific policy proposals. As a result, we gave less attention to the relative merits of or interactions between prizes and other mechanisms such as prizes and PDPs. For example, our case study asks whether a prize might be a promising approach for TB diagnostics, but does not address potential synergies among R&D incentives or ways in which prizes might hinder the effectiveness of other mechanisms.
- Our conclusions rest to a substantial extent on our interpretation of one-hour interviews with experts and firms, supplemented by theoretical analysis. But interviews of this kind are often too short to adequately brief interviewees on a complex and often unfamiliar topic, with the results that responses are not always fully informed. Although we hoped to cross-check some of what we heard in interviews against data from other sources—for example, on costs, timelines, and expected returns in the diagnostics industry—we found very little of this kind of information in the published literature. Moreover, it is impossible in a realistic number of interviews to cover the full range of types of firms, especially when the goal of a prize may be to attract participants who are new to a field.
- Due to limited time and resources, most of the product developers and investors whom we interviewed were based in the United States and Europe. It would have been interesting to have more conversations with firms in developing countries. These firms might be more motivated to participate in a prize contest for a disease important to their own countries, and they might have lower costs or different perceptions of risk than firms in high-income countries. (Some interviewees suggested that these firms might actually be *more* risk-averse.) The Center for Global Health R&D Policy Assessment expects to engage firms in emerging-market countries in subsequent assessments.
- We also had few conversations with university scientists, since the TB diagnostic proposals that we assessed were for final products, which

## CONCLUSIONS AND LIMITATIONS OF STUDY

university labs are ill-equipped to develop. Also, academic scientists must in general have grants to pursue R&D, whether or not a prize is offered. However, these researchers might be able to reach a milestone prize, and a prize might motivate them to apply for grants in new areas. It would be interesting to explore further the role of universities, as well as public-sector and other nonprofit research institutions, in the response to prizes, especially milestone prizes.

APPENDICES





## Participants in interviews

Organization	Name	Title
Aberdare Ventures	Paul Klingenstein	Managing Partner
Advanced Medical Technology Association	Ralph Ives	Executive Vice President
Advanced Medical Technology Association	Sarah Smiley	Vice President of Strategy
Ahimsa Partners	Jean Francois de Lavison	President
Alloy Ventures	J. Leighton Read	Partner and Board Member of BVGH
Aviir	Doug Harrington	Chief Executive Officer
Bayer Diagnostics	Rolf Classon	Former CEO
Becton Dickinson	Vani Manja	Sr. Market Segment Director
Becton Dickinson	Gloria Young	Vice President of Global HIV/AIDs Initiative
Becton Dickinson	Krista Thompson	Vice President/General Manager Global Health
BioVentures for Global Health	Andrew Robertson	Chief Policy Officer
BioVentures for Global Health	Elizabeth Aden	Consultant
Catalysis Foundation	Richard Thayer	Chief Executive Officer
CD4 Initiative	Hans-Georg Batz	Director
Cepheid	David Persing	Executive Vice President and Chief Medical and Technology Officer
Cepheid	Ellen Jo Baron	Director of Medical Affairs
Claros Diagnostics, Inc.	David Steinmiller	Founder & COO
Clinton Health Access Initiative	Maurine Murtagh	Director of Diagnostic Services
Clinton Health Access Initiative	Trevor Peter	Scientist
Clinton Health Access Initiative	Amy Wong	Program Manager
Columbia University	Sam Sia	Assistant Professor of Biomedical Engineering
Columbia University, Earth Institute	Yanis Ben Amor	Associate Research Scientist

## APPENDIX A. PARTICIPANTS IN INTERVIEWS

Organization	Name	Title
Daktari	William R. Rodriguez	Chief Executive Officer
Foundation for Innovative New Diagnostics	Mark Perkins	Chief Scientific Officer
Foundation for Innovative New Diagnostics	Lakshmi Sundaram	Advocacy Officer
International AIDS Vaccine Initiative	David Cook	Executive Vice President and Chief Operating Officer
International AIDS Vaccine Initiative	Wilson Lee	Director of Policy and Advocacy
InnoCentive	Dwayne Spradlin	President and Chief Executive Officer
Integrated Diagnostics	Albert Luderer	Chief Executive Officer and Former CEO of BioMerieux US
Knowledge Ecology International	James Love	Director
Knowledge Ecology International	Judit Rius Sanjuan	Attorney
LabCorp	Paul Billings	Former CMO
MIT, X PRIZE Foundation Lab	Erika Wagner	Executive Director
McGill University	Madhukar Pai	Assistant Professor & Canadian Institutes of Health Research New Investigator
Médecins Sans Frontières	Katy Athersuch	Medical Innovation & Access Policy Adviser
Médecins Sans Frontières	Michelle Childs	Director of Policy and Advocacy
PATH	Milton Tam	Former Technical Director
Prize4Life Foundation	Melanie Leitner	Chief Operating Officer and Chief Scientific Officer
ReaMetrix Inc	Bala Manian	Chief Executive Officer
Tethys Bioscience	Mickey Urdea	President of the Board
Tufts University	William Masters	Professor of Food Policy and Economist
USAID	Wendy Taylor	Senior Advisor on Innovative Finance and Public Private Partnerships
Vivacta	Neil Butler	Former CEO
White House Office of Science and Technology Policy	Robynn Sturm	Advisor to the Deputy Director, Open Innovation
X PRIZE Foundation	Eileen Bartholomew	Senior Director
X PRIZE Foundation	Francis Beland	Vice President of Prize Development





# B

## Prize size and cost relative to grant funding

This appendix considers in more detail some of the factors that can be expected to influence the decisions of firms regarding investment in prize contests, and analyzes the cost of prizes relative to grants. The analysis focuses on situations in which the necessary investment is considerable and the prize award is the main benefit that firms hope to obtain from this investment. In some cases other considerations—notably publicity and access to substantial markets—will be important and prizes can be correspondingly smaller than the analysis outlined here would suggest. But much of the logic of these calculations still holds.

As explained in chapter 2, if a prize (or a priority review voucher or a share of an AMC) is the only potential source of return on investment in development of a particular product, the attractiveness of the investment depends on the size of the prize, the chance of winning it, and the cost of R&D, including the cost of capital. A firm with ready access to capital and other resources will decide to participate if  $A \cdot P_w > C$ , where  $A$  is the size of the prize award,  $P_w$  is the chance of winning, and  $C$  is R&D cost (including cost of capital).<sup>106</sup>

If only one firm has a chance to win the prize, then  $P_w$  is the chance of technical success  $P_t$  (the probability that the R&D investment will yield a product that meets the prize criteria).<sup>107</sup> In this simplest of cases, the risk-adjusted minimum expected cost of a prize to the funder ( $A \cdot P_s = C$ ) is the same as the cost of grant that just covers R&D costs, since the chance of having to award the prize ( $P_s$ ) is equal to  $P_w$  as long

as the firm's estimate of its chances is correct and known to the sponsor.

If more than one firm may enter the contest, each must also take into account competitive as well as technical risks and reduce its estimate of expected revenues correspondingly. The prize award will then have to be correspondingly larger to entice firms to participate. (Another way of looking at the same relationship is that larger prizes will attract more firms.) For example, if two firms with equal but independent chances of success participate in a winner-take-all contest, and the chance of technical success for each is 20% ( $P_{t1} = P_{t2} = .2$ ), the probability that a particular firm wins the prize equals the chance that its efforts succeed while those of its rival fail ( $P_{t1} \cdot (1 - P_{t2}) = .16$ ) plus the chance that both succeed and the firm in question is lucky enough to get to the finish line first ( $P_{t1} \cdot P_{t2} / 2 = .2$ ), or 18% in total. Thus, with two potential competitors, the prize has to be about 10% larger than with only a single firm in the running, to compensate firms for the somewhat lower chance of winning. With identical competitors,  $P_w$  is more generally the chance that at least one firm succeeds ( $P_s$ ) divided by the number of competitors ( $N$ ). Since the chance that all fail is  $(1 - P_t)^N$ ,  $P_s = 1 - (1 - P_t)^N$ . With three firms and a 20% technical probability,  $P_w$  is about 16%; with five firms the chance of a particular one winning falls to about 13%.

As the number of identical competitors becomes large relative to the risk of failure ( $N \gg 1/P_t$ ), someone is likely to win the prize and the odds of success for a particular firm converge on  $1/N$ .

<sup>106</sup> Throughout this appendix, an asterisk (\*) is used to indicate multiplication.

<sup>107</sup> The overall chance of technical success can be further broken down as the product of a series of “transition probabilities”—chances of success in each phase of R&D.

## APPENDIX B. PRIZE SIZE AND COST RELATIVE TO GRANT FUNDING

As long as firms have an equal chance of success and estimate this probability sensibly, the costs of a prize and an equivalent set of grants remain the same. The expected cost of the prize is  $P_s * A = P_s * C / P_w$ . But since  $P_w = P_s / N$ , this is  $N * C$ , or the cost of grants to all the participants.

This equivalence breaks down in a number of ways when real-world complexities are introduced. Consider first what happens when firms have differing chances of developing the product. In this case, in order to attract multiple firms, a prize has to be bigger than it would have to be to interest the best-positioned firms. For example, if there are two firms with probabilities of success  $P_{w1} > P_{w2}$ , the expected cost of a prize that brings in both is  $P_s * A = (P_{w1} + P_{w2}) * A = (P_{w1} + P_{w2}) * C / P_{w2}$ . Since  $P_{w1} > P_{w2}$ , this is larger than  $2C$  and a prize costs more than giving grants to both firms. For example, if one firm has a 40% technical chance of success and the other 20%,  $P_{w1} = 36\%$ ,  $P_{w2} = 16\%$ ,  $P_s = 52\%$ , and the expected cost of the prize will be  $.52 * C / .16$  or more than  $3C$ . Thus, it can be expensive to attract more competitors (and thus increase the overall probability of success) if the chances of potential participants fall off quickly. Considering contestants with different R&D costs leads to the same conclusion. For example, if three firms all have a 20% technical chance of success, but expected R&D costs of \$10 million, \$20 million, and \$40 million, a prize would have to be almost \$240 million to attract all three, and the expected payout (about \$120 million) would be 70% more than the cost of grants to all three firms.

One way of thinking about this effect is that in order to make a prize big enough to attract firms with lower chances of success or higher costs, one must pay a kind of rent to better placed firms, who would have been willing to participate with a smaller prize. In contrast, no rent is paid when all firms are engaged through grants or contracts that just cover their costs.

This problem is particularly clear when firms have candidate products at different stages of development. If a firm has a vaccine candidate ready to enter Phase 3 trials, for example, it will respond to a prize

big enough to cover the cost of the trial adjusted for the risk of failure in this last phase of development. But the prize must be much larger to bring in a second firm whose candidate is only in Phase 1, not only because of the much greater risk that this candidate will fail but also because of the risk (to the second firm) that the first firm will walk off with the prize. This larger prize represents, in a sense, a wind-fall to the better-placed firm that could be avoided by giving grants to each. This and similar considerations bedeviled designers of the pneumococcal AMC, who wanted to ensure that two and perhaps more firms would participate but knew that the firms had quite different costs as well as probabilities of success.

Another important consideration is imperfect information: the analysis so far has assumed that firms correctly estimate not only their own chances of success but those of their potential competitors, and that prize funders base the size of the prize award on good information about firms. If these assumptions do not hold, the equivalence of prizes and grants again breaks down. For example, if firms overestimate their chances of success, they may be willing to invest in pursuit of a smaller prize; if prize sponsors are aware of this, they may be able to buy more R&D in this way than they could through grants. On the other hand, if sponsors are too pessimistic (or build in a large margin of safety), they will pay more than necessary to entice firms, and (if firms are rational) more than an equivalent set of grants.

Prizes will also have to be larger if firms are not sure that the sponsor will follow through on the prize commitment, since this increases the perceived risk. (Of course if the sponsor in fact does not intend to pay, the expected costs are very low indeed!)

Considering cost of capital introduces another potentially important difference between push and pull funding. From a firm's perspective, a prize must be big enough to compensate not only for the out-of-pocket cost of R&D, but the cost of raising the money to fund this work up front. Similarly, the sponsor will discount the expected cost of awarding the prize at some rate. If the discount rates of competitors and sponsors are the same, everything again

## APPENDIX B. PRIZE SIZE AND COST RELATIVE TO GRANT FUNDING

comes out in the wash and push and pull approaches are equivalent. But this is unlikely to be the case, since the private sector cost of capital, especially for small firms, can be very high, while governments and large foundations use low discount rates, and can in fact typically borrow at relatively low rates. This would suggest that push funding, which does not require the sponsor to cover firms' cost of capital, will in general be cheaper than pull approaches. This effect could be quite large. For example, if the sponsor can borrow money for grants at 5% while firms must pay 10% and product development is expected to be take five years, a prize will be 26% more expensive than grants; if the cost of capital to firms is 20%, pull is almost twice as expensive as push.

This difference is partly an illusion. The high cost of capital to small firms reflects in part risks that are not captured in the purely technical probability of success, such as the risk that a firm will fail before the project is completed, that are also relevant to grant funding. Although these risks are not reflected in the cost of capital to the sponsor (who does not rely on the success of funded projects to repay loans), they reflect real, socially relevant costs. If the high cost of capital to firms results primarily from high opportunity costs (profitable alternative uses of capital), it could be argued that sponsors should also be using a high discount rate in evaluating projects for grant funding. These are rather theoretical arguments, however: in practice, the need to compensate firms for very high costs of capital may indeed make a prize approach more costly than grants from a purely financial, as opposed to a social, perspective.

But this analysis neglects many of the considerations that make prizes attractive in the first place. The equivalence of prizes and grants (or the greater cost of prizes) assumes that the same firms participate in each case, and that they work with the same efficiency. But prizes make the most sense precisely in those situations where sponsors do not know which product developers are likely to succeed, and therefore which to fund. To the extent that potential competitors know more about their candidates than sponsors, they will make better informed decisions about whether to pursue a prize than the sponsor

would make in awarding grants. The result will be a greater overall chance of success (since the more promising projects will be funded) or, equivalently, a lower cost for the same overall chance of developing the product (since more grants will have to be given to firms with less promising candidates). Incentive effects could also make prizes cheaper, if the financial stake that firms have in success translates into higher-quality R&D or greater efficiency.

Finally, this analysis omits all the additional considerations that may cause firms to invest in pursuit of a prize, including market profits, public relations benefits, and validation of new technologies. In theory some of these benefits could allow sponsors to reduce the size of grants as well as prizes—for example, by subsidizing only partially the development costs of products with some market in high-income countries or in cases where firms expect other benefits. In fact, the good publicity associated with working on neglected diseases has almost certainly contributed to the willingness of some firms to collaborate with PDPs without receiving full compensation for their costs. But a high-profile prize promising widespread publicity for participants could well buy a sponsor more R&D than a corresponding set of grants.

There is therefore no general answer to the question whether prizes are likely to be more or less costly than grant funding of neglected-disease R&D. In a world of perfect information, grants or contracts would be cheaper, as funders could choose the most promising projects and pay only what a product developer would require, whereas a prize would “overpay” firms with the best candidates. Moreover, grant funders benefit from a lower cost of capital. But when sponsors cannot know which developers have the best ideas or candidate products, and may not even know who the potential developers are, these effects may be dwarfed by the greater allocative efficiency of prizes. Thus, this analysis of relative costs reinforces the conclusion that prizes make the most sense when the R&D path—and the capacities of product developers—are uncertain.





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