The Role of Prizes in Developing Low-Cost, Point-of-Care Rapid Diagnostic Tests and Better Drugs for Tuberculosis

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MSF expert meeting on IGWG and R&D for tuberculosis

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Introduction

MSF has thoughtfully convened this timely meeting of experts to address an important question: how to boost R&D for a low-cost, point-of-care rapid diagnostic test and better drugs for tuberculosis?

By posing two different questions, MSF has illuminated the difficulties in considering efficient R&D initiatives directed at discrete targets. The efforts to stimulate development of the diagnostic test present different challenges than do initiatives directed at drug development.

One can imagine a variety of programs involving both “push” funding and “pull” incentives. At the outset, it should be said that any serious effort to stimulate development of either the

diagnostic test or the drugs would have a strong component of push funding, both to ensure that research is undertaken, including in areas where the prospects for commercially successful and appropriable outcomes are low and sustainability of the research effort is important, and to provide a mechanism that lends itself to the broader sharing of information.

My talk will focus on "pull" incentives for research and, in particular, on the potential role for prizes in stimulating R&D for both diagnostic tests and drugs.[1]

Recently KEI published a study on the use of innovation prizes in a diverse number of areas over several hundred years.[2] This study highlights the freedom that one has to design prizes. There are prizes that have *sui generis* specifications of rewarded outcomes and intellectual property rules, and episodic funding, and others that offer a systematic mechanism to reward innovation in a particular area with sustainable systems of finance. There are prizes that reward the "best" performance (the best new marble-sawing machine), the "first" performance of a specific technical achievement (measuring longitude, making Windows run on a Mac), or that reward a class of outcomes (efficiencies in manufacturing costs, preventing deaths, killing enemy solders, etc). The management style of prizes also varies considerably.

In considering the possible role of prizes to stimulate R&D for a low-cost, point-of-care rapid diagnostic test, or better drugs for tuberculosis, one will have to consider both the specific outcomes or achievements to reward, but also the amounts, and the decision-making system that will administer the prize and resolve disputes.

Each prize system also has to consider the practical challenges of administering prizes. Is a prize awarded when the "best" of a class of entrants isn't impressively good? How does one market prizes to potential entrants? Will the offer of a prize powerfully leverage an entire community of competitors, such as the Ansari X-Prize, or so dilute the expectations of winning the prize that potential entrants are discouraged from investing the resources and

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[1] For discussion of innovation prizes, see: Ron Marchant, "Managing Prize Systems: Some Thoughts on the Options," *Knowledge Ecology Studies*, Vol. 2 2008; James Love, "Prizes, not prices, to stimulate antibiotic R&D," *SciDev.Net*, March 26, 2008; Board on Science, Technology and Economic Policy (STEP), *Innovation Inducement Prizes at the National Science Foundation,* National Academies Press, 2007; Thomas C. Erren, "Prizes to solve problems in and beyond medicine, big and small: It can work," *Medical Hypotheses,* 68, 2007, 732–734; Bruce G. Charlton. "Mega-Prizes in Medicine: Big Cash Awards May Stimulate Useful and Rapid Therapeutic Innovation," *Medical Hypotheses,* 68, 2007, 1-3; James Love and Tim Hubbard, "The Big Idea: Prizes to Stimulate R&D for New Medicines," *Chicago-Kent Law Review,* Vol. 82 No. 3, November 2007; Carl Nathan, "Aligning Pharmaceutical Innovation with Medical Need," *Nature Medicine*, March 2007, 13(3):304-8; Joseph Stiglitz, "Scrooge and Intellectual Property Rights: A medical prize fund could improve the financing of drug innovations," *British Medical Journal*, 333, December 23, 2006:1279-80; Gerard Llobet, Hugo Hopenhayn, and Matthew Mitchell, "Rewarding Sequential Innovators: Prizes, Patents and Buyouts," *Journal of Political Economy*, vol. 114(6), December 2006, pages 1041-1068; Juri Saar, "Prizes: The Neglected Innovation Incentive," ESST: The European Inter-University Association on Society, Science and Technology, 2006; Kevin Outterson, "Patent Buy-Outs for Global Disease Innovations for Low and Middle-Income Countries," *American Journal of Law and Medicine*, Vol. 32, 2006; Richard Newell and Nathan Wilson, "Technology Prizes for Climate Change Mitigation," Resources for the Future Discussion Paper, 05-33, 2005; John F. Duffy, "The Marginal Cost Controversy in Intellectual Property," *University of Chicago Law Review*, Vol. 71, No. 1, 2004; Nancy Gallini and Suzanne Scotchmer, "Intellectual Property: When is it the Best Incentive System?," University of California, Berkeley Working Paper E01-303, 2001; Steven Shavell and Tanguy van Ypersele, "Rewards versus Rights," *Journal of Law and Economics,* 44: 525-547, 2001; Michael Kremer, "Patent Buyouts: A Mechanism for Encouraging Innovation," *Quarterly Journal of Economics,* 113: 1137-67, 1998; DF Horrobin, "Glittering Prizes for Research Support," *Nature* 1986; 324:221.

[2] *Selected Innovation Prizes and Reward Programs*, KEI Research Note 2008:1, March 20, 2008.

effort necessary to do much?

Without belaboring these points, which are made quite clear by a reading of examples detailed in *Selected Innovation Prizes and Reward Programs,* I will attempt to outline some possible approaches for each of the two tasks set out by MSF.

Intellectual Property, Technology Transfer and Other Issues

Every prize involves a discussion of intellectual property right issues. Unless one is changing domestic law, the prize program will normally consider how the offer of the prize deals with the traditional range of possible decisions by researchers, developers and others to acquire, forgo or license patents, trade secrets and other types of intellectual property. Offers of prizes often (but not always) include requests for some type of licenses to use inventions or know-how, and the existence of patents may determine who can realistically or legally claim all or part of a prize reward. In some areas, the role of the prizes in financing activity can be so important that the offer of the prize includes almost unlimited power to dictate the terms of licensing; in other cases, the prize will have little leverage.

Some prize specifications would work more or less like voluntary or even involuntary patent buy-outs. S.2210, the proposal for a US Medical Innovation Prize Fund, would keep patents, but eliminate the exclusive right to use, make, or sell an invention. Those benefits would be replaced by enormous and costly prizes ($80 billion per year at current income levels).

Most proposals for prizes involving neglected diseases would involve voluntary negotiations for the licenses to use inventions or know-how.

Low-Cost, Point-of-Care Rapid Diagnostic Test for Tuberculosis

Any prize offered to stimulate development of a low-cost, point-of-care rapid diagnostic test is undertaken with an implicit model of the desired outcome and the challenges in achieving that outcome. My assumption is that the public health community is looking for a test that can yield a result with a known degree of accuracy, within a set number of (three?) hours, at a price of less than $5 per test, or some other acceptable number. It is quite helpful to determine early if there is a consensus on these or other metrics (such as the required infrastructure) that will determine whether the desired outcome has been achieved. Strictly speaking, none of this is necessary for some prize designs, but all of it is necessary for other prize designs. Consider, for example, four possible prize contests, using completely stylized parameters:

Diagnostic Test - Contest Number 1

First-to-Succeed Prize. The reward is a prize of $100 million (or a different number). The specification of a successful outcome is a diagnostic test that costs less than $5 to make, tests positive 98 percent of the time a patient has TB, and tests negative 98 percent of the time when patient does not have TB.

How it works. The reward creates an additional inducement to develop such a test. Even if the prize is not sufficient by itself to stimulate development of the test, it can enhance interest in the development of the diagnostic test, encourage groups receiving grants to focus on the most practical and feasible solutions to the problem, and contribute to the overall effort.

What if? What if someone develops a test that meets all of the criteria but one -- it only tests positive when one has TB 95 percent of the time? If a second firm takes everything the first entrant did and improves it just enough to increase the accuracy of the test to 98 percent, should it get all of the prize money, or split it with the unsuccessful 1st entrant?

Possible risk. Motivated by the prize, groups do not share scientific results.

Diagnostic Test - Contest Number 2

Best Progress Prize. The prize simply rewards the best advances in science or engineering that bring you closer to the ultimate goal. The reward is either a fixed amount, like $1 to $10 million, given out every one, two or three years (depending upon how much time you reckon you need to get something useful), or set at some fraction of the "push" grant funding, like 10 percent or 15 percent of all of the push funding.

How it works. To win the prize, you have to be judged by a wider community of researchers to have come up with some results that helped the entire effort move forward. You can't win the reward if you keep your results secret. The prize also may be won by groups that are not part of the established circle of grant recipients, or by groups that use unconventional means to solve problems. You don't know exactly what outcomes will win, but you identify in advance who will decide what was best.

What if? What if there is nothing impressive done during the period?

Possible risk. Many of the people who know enough to judge the prize may themselves be engaged in work that could win the prize, or have ties to people who do. Managing conflicts of interest will be important, to avoid favoritism or self-dealing (real or perceived).

Diagnostic Test - Contest Number 3

Supporting cast prize. As a modification of Contest Number 1, some of the prize money (1 to 10 percent), is set aside to reward unaffiliated scientists or engineers whose published and open-source research is found have been most useful in providing the pathway for the winner of Contest Number 1.

How it works. Even 1 percent of 100 million is a lot of money. Scientists who write about topics relevant to this challenge (in open journals) could become big winners. It encourages scientists to share information, and to think about this problem.

Risks. Creates hard feelings among colleagues when decisions are perceived to be unfair or based upon connections.

Diagnostic Test - Contest Number 4

Solve small problems. A prize fund is created with 10 percent of the push funding from grants from donors. Each of grant recipients is allowed to set specific technical challenges that have rewards attached. The grant recipient and its affiliated parties are not eligible to win the prize. One or more independent committees evaluate the prizes, or management is outsourced to groups like InnoCentive or the new X-Prize life sciences division.

How it works. Lots of moonlighting scientists or small firms work on specific challenges in a major "crowd sourcing" effort.

Risks. The quality of the submissions is not high, and it is expensive and controversial to evaluate entries.

Recommendation for Diagnostic Test Prize Design

I like all four approaches, and recommend each be used together, as a package, in combination with push funding.

The management issues for such a system of prizes would include both the sustainable sources of finance and the decision-making bodies that would implement the prizes. Prizes that include "juries," panels or systems of voting to evaluate "best of" or "supporting contributions or technical achievements, require some thought about who would be deciding/voting, how they are selected and replaced over time, and what controls are put into place to address conflicts of interest.

Better Drugs for TB

In some respects, prizes for drug development can be easier to design than a diagnostic test. While requiring evidence from the field, the measure of the value of some drugs can, in theory, be measured by improvements in health outcomes, measured by QALYs or DALYs, or at least estimated based upon clinical evidence of drug efficacy, combined with data on utilization.

One challenges for doing this for TB only is that there is a narrow set of targets, and this particular target may be difficult to achieve, making it hard to evaluate the efficacy of the prize. For example, in the area of Alzheimer's disease, the prospect of billions of dollars in profits from the lucrative US, European and Japanese markets has yet to yield a successful drug. In some cases, the science is not good enough for successful drug development, and even huge pull incentives are not sufficient to solve problems.

If prizes for the successful development of a drug are aimed at a larger set of targets, it is more likely to succeed somewhere.

Prizes for Final Products

In a prize for a final product, the reward for the successful development of a product is cash paid directly to the drug developer, and not the reimbursement or purchase price of the product itself. How do you set the prize? This is an area of some controversy. In general, you look at exactly the same data and evidence that one uses to evaluate reimbursements. But you have more freedom in terms of how outcomes are rewarded.

Given, however, the freedom to design prizes in interesting ways, there are disputes about several important issues. Some have proposed fixed prizes for each QALY or DALY, giving prize managers the task of estimating the right prize per DALY/QALY, and effectively unlimited liability for prize payments, as well as strong incentives to limit access in order to limit outlays on prizes. KEI strongly rejects this approach. In the Hubbard/Love exercise with Aventis in 2002, we proposed what I think many now recognize as a superior approach. With a reward fund of a size that is fixed in dollar terms, or as a percentage of the health or

drug budget, firms compete for prizes, dividing up a fixed pie, on the basis of the relative merits of the projects. This is the approach taken in S.2210, the Medical Innovation Prize Fund, and it is also the approach that Aidan Hollis has used.

This is also the approach we have proposed in terms of creating a system of rewards that would be based upon a share of Global Fund drug purchases, possibly tied to licensing of products to a patent pool, in order enable generic competition.

Tim and I have recently sketched some of nuances in this approach in our paper, "The Big Idea," including making the case that rewards need not be strictly proportional to QALYs or DALYs, given the nature of high fixed drug development costs, and the stochastic nature of the innovation process.[3]

KEI has recommended also that the prizes be designed to reward the incremental impact of inventions over existing products, and that products that create new approaches receive prize money, even when market shares fall to zero, as follow-on products enter the market, with small but important improvements.

To value the products, Tim Hubbard and I support the approach reflected in S.2210, which involves evaluating data once a year for 10 years, and making 10 separate payments, each based upon what you know at the time, given the available evidence. This gives the drug developer a relatively fast payoff, but also gives the managers of the prize quite a bit of information.

There are special problems when you have products like antibiotics or stockpiled medicines for a pandemic, where the products are more valuable if they are not used right away. For antibiotics, you can use sophisticated inventory, depletion or options models from economics and business, with lots of data, assumptions and modeling, to value products you aren't consuming. Or, you can create simpler prize valuations based upon the prizes earned by drugs in other classes of use, which are similar enough to be used as proxies. This is an area for more research, and it is important, given the huge and growing number of deaths from antibiotic-resistant infections in hospitals.

There is now a re-evaluation of the basic approach of S.2210 in terms of rewarding drug development, in light of further discussion and debate, and there are two general areas for possible changes in the legislative proposal. One is for allocating some of the rewards to developers that meet certain early benchmarks, such as the completion of a successful phase II trial. The second is to address the relationship between prizes (and patents) and secrecy.

Prizes for Early Benchmarks

It is actually quite a bit more challenging to value an early benchmark than a final product. What is the value of completing a Phase II test, when that same product will, more often than not, fail later in the pipeline, or turn out to be a mediocre drug? You just don't know that much at Phase II.

[3] In a recent prize workshop in Washington, DC at George Washington University Law School, Michael Abramowicz made the suggestion that because of the uncertain nature of the innovation process, the prize criteria could be relatively arbitrary, secret or changing, so long as in the aggregate the prizes were large, and drug developers could rely upon the capital markets to diversify the risks.

Some have tried to develop clever models for valuing the Phase II type benchmarks. KEI recommends consideration of a much different approach. Rather than seek consensus on how to value the Phase II type benchmarks, create a method of funding competing intermediaries to make those decisions for you. Resource the intermediaries, let them develop their own methods of rewarding Phase II benchmarks, and then evaluate the intermediaries on an objective criteria for performance: how well did their early rewards pay off, in terms of backing projects that actually did succeed?

Prizes for Small Problems

As for the diagnostic test, one could imagine a system of managing prizes to address a number of smaller programs involving science or engineering. If funded by donors, it would be useful to require as much openness as possible in terms of the licensing. Again, such prizes could be administered and evaluated by one or more independent committees, or the management can be outsourced to groups like InnoCentive or the new X-Prize life sciences division.

Supporting Cast Prize

Like the TB Diagnostic Test, there is considerable value in having a share of the total prize money set aside for rewards for the researchers whose open-source publications and databases contributed the most to the products that actually worked. In terms of S.2210, one suggestion is to make this 1 percent of the total, or about $800 million per year, a huge incentive for researchers to share data.

Recommendation for Drug Development Prize Design

As outlined in some detail in "The Big Idea" and other papers, the reform of the pull mechanism for drug development is an extremely important issue, for several reasons.

1. Governments can use prizes to redirect incentives to areas of the greatest need.

2. Prizes can be structured as more efficient and flexible systems to reward a greater range of outcomes and activities, including, for example, to reward the sharing or transfer of technology and know-how, to reward unpatentable innovations, including those requiring significant investments, to reward products that have a value separate from the value in immediate consumption, and to reward incremental rather than average values.

3. If implemented as an alternative to an IPR-enforced monopoly, prizes are consistent with marginal cost of products, and prizes can also reward products that are cheap to manufacture and are distributed at the lowest cost.

A program of prizes for the development of better drugs for TB could usefully combine all of the approaches discussed above – prizes for small programs, prizes for final products, prizes for the supporting cast, and prizes for meeting early benchmarks, all in combination with programs of grants.

Sustainable Financing

The funding for prizes for products could be part of the existing donor program of

subsidizing drug development. This would be particularly appropriate for prizes for solving small problems or meeting early benchmarks.

It could also become part of the donor programs for delivering treatment. We have recommended in submissions to the WHO IGWG that programs like the Global Fund or UNITAID set aside a fraction of the budgets for a prize fund that is available only to drug developers that license inventions to a patent pool, to enable generic competition for products. For example, by placing 10 percent of the total outlays into a prize fund, all successful drug developers who licensed to the pool would compete for shares of the prize fund on the basis of their relative success in improving health outcomes. The prizes would be available even for firms that did not patent in the relevant geographic area.

There are two more possibilities that are quite important in the context of the WHO IGWG. One is to include commitments to fund R&D as part of a global biomedical treaty; a topic the IGWG has agreed will receive further attention.

The second proposal is to include in the WTO a new schedule for the supply of global public goods, and to use this schedule for binding commitments to fund research in this area.