

Financing neglected disease R&D: principles and options

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Despite the establishment of product development partnerships (PDPs), new commitments from public and private donors, and important new initiatives from pharmaceutical firms and developing countries, funding for scientific and medical innovation for diseases that disproportionately affect the developing world remains inadequate.

Although a comprehensive, sustainable solution to the problem of neglected disease R&D has not yet emerged, governments, experts, and industry have proposed a number of new ideas, including both “push” mechanisms to finance R&D and “pull” incentives to spur private sector investment (see Figure 1). Some of these mechanisms, including the advance market commitment for pneumococcal vaccines and the US FDA’s Priority review voucher, have been launched by donor governments, but it is too soon to evaluate their impact.

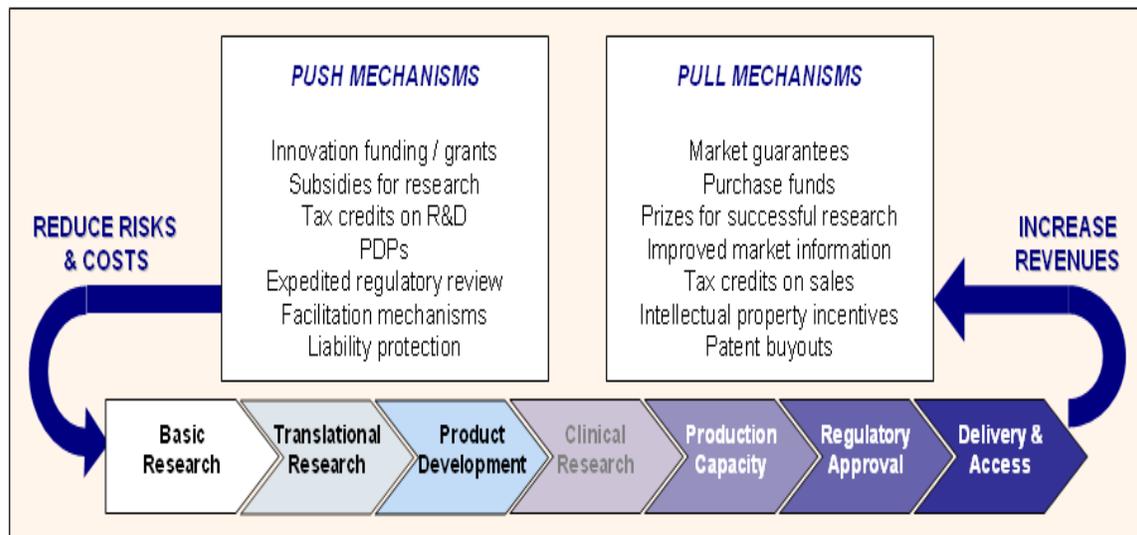


Figure 1: Push and pull mechanisms

¹ This note is based in part on an analysis carried out for DNDi by Paul Wilson of Columbia University, who prepared an initial draft.

WHO Member States are currently considering the report of the Expert Working Group on R&D Financing (EWG) convened to examine financing, coordination and proposals for new and innovative sources of funding to stimulate R&D for Type II and III diseases, and the specific research and development needs of developing countries in relation to Type I diseases, as part of the implementation of the Global Strategy and Plan of Action (GSPA) on Public Health, Innovation and Intellectual Property adopted by the 2008 World Health Assembly.² The EWG's report proposes a framework for assessing R&D incentives and financing mechanisms and recommends several proposals and classes of mechanisms for further consideration.

From its inception, DNDi has advocated for increased resources for R&D for neglected diseases and for new and sustainable mechanisms to support this R&D. Moreover, DNDi is itself an example of a new form of international collaboration in health R&D that has successfully attracted new public and private funding to this field. Both to influence discussions on R&D financing at the WHO and in other fora and to support its own long-term funding strategy, DNDi has conducted an evaluation of existing and proposed R&D incentives and funding mechanisms.

The study has focused substantially but not exclusively on mechanisms that would strengthen the PDP model, either by directly funding PDPs, by filling gaps in the R&D spectrum that PDPs are not well suited to fill, or by creating stronger incentives for private and public sector firms to collaborate with PDPs. DNDi's analysis has naturally focused on mechanisms that might support the development of new treatments for the "most neglected" diseases that are its primary focus, but many of the main conclusions apply to other diseases and product types.

This note will describe the criteria that DNDi has used to assess R&D financing mechanisms and then outline a few mechanisms that DNDi believes could fill important gaps in the current system.

Principles for assessing incentives and financing mechanisms

In evaluating the broad range of possible new mechanisms for financing neglected disease R&D, DNDi has considered seven basic criteria. These criteria overlap to a considerable degree with those applied by the EWG, but place greater emphasis on sustainability, access, and governance.

1. **Effectiveness:** Is the mechanism likely to speed the development of needed and appropriate new drugs, vaccines, and diagnostics? Will it engage the required research and product development expertise in neglected disease R&D? Will it do so as efficiently as alternative approaches?
2. **Contribution to sustainable access:** Would new health technologies developed with the help of the mechanism reach those who need them, particularly the most neglected people? Does the mechanism promote appropriate design, affordability, distribution, and use, even in the absence of a viable market?

² Public hearing on the Report of the World Health Organization Expert Working Group on Research and Development Financing http://www.who.int/phi/publichearing_researchdev/en/index.html

3. **Financing source:** Who would pay for the mechanism? Is the source adequate, sustainable, and fair? Is it new or distinct from current sources of funding for neglected disease R&D?
4. **Political, financial, and institutional feasibility:** Can the mechanism be funded and implemented?
5. **Governance:** Who would set priorities and allocate funds? Would the mechanism be transparent and legitimate as well as technically sound and efficient?
6. **Breadth and sustainability:** Could the approach be expanded or replicated to cover other neglected diseases? Would it establish a stable and predictable source of funding? Would it contribute to a comprehensive and long-term solution to the problem of neglected disease R&D?
7. **Ownership and participation by endemic countries:** Would endemic countries have a substantial role in designing, funding, and governing the mechanism? Would the mechanism support and build capacity among researchers and drug developers in endemic countries?

It is unlikely that any single mechanism will solve the problem of neglected disease R&D financing: a number of measures tailored to particular types of diseases and health technologies and to particular stages of R&D will probably be necessary. The fit of a proposed mechanism to particular circumstances must be considered along with these general criteria.

As existing push and pull mechanisms have not proved sufficient to drive neglected disease R&D on the necessary scale, ideas that would represent a substantial change from the status quo should be considered along with more incremental improvements to the current system. According to DNDi's experience, two types of measures are specifically needed to fill in R&D gaps: new incentives to stimulate early-stage discovery of promising compounds for neglected diseases, and additional sustainable funding to ensure late-stage development of and access to promising compounds.

Promising new mechanisms

1. Milestone prizes to stimulate discovery

Discovery is an important gap in the current neglected disease R&D system. The PDPs have focused to date to a substantial extent on the "low-hanging fruit" of drugs licensed for other indications, shelved product candidates, and new combinations and formulations of existing drugs. But they need to replenish their pipelines to ensure a continued flow of promising candidates into late-stage development.³ Current financing mechanisms, including conventional partnerships with PDPs, are not ideally suited to engaging industry, notably biotech companies, which could bring new powerful tools to neglected disease drug, vaccine, and diagnostic discovery.

³ See Bio Ventures for Global Health (2007). "Closing the Global Health Innovation Gap: A Role for the Biotechnology Industry in Drug Discovery for Neglected Diseases", available at <http://www.bvgh.org/documents/InnovationMap.pdf>

Substantial rewards for attaining specified milestones along the path to a new drug or other health technology could be a useful supplement to grants and other push funding to boost innovation for diseases for which market incentives are deficient and where patents are not an effective incentive. As with other pull mechanisms, prizes have the advantage that sponsors pay only for success. Moreover, they offer a way to support progress toward a clear goal without specifying the particular route that it should take. This is especially appropriate for early-stage R&D, when the best approach may not be known and when the most likely innovators cannot always be identified in advance.

Milestone prizes also promise far earlier pay-outs than advance market commitments, priority review vouchers, or prizes for licensed products, and are thus more likely to attract new actors such as biotechs, which cannot make major investments in pursuit of rewards that may be more than a decade away. At the same time, prizes of this type could be a way to test important features, such as IP management and access provisions, of more ambitious and potentially transformative prize mechanisms, including final product prize funds that would reward innovation in proportion to health benefit.⁴

2. Sustainable funding for product development and access

A substantial funding gap also looms for late-stage product development. PDPs, pharmaceutical firms, and public-sector institutions have now advanced several compounds through discovery and early clinical trials, but financing is not ensured for the upcoming large efficacy trials, manufacturing scale-up, registration, and the various activities required to ensure adoption and equitable access in disease-endemic countries.⁵

The UNITAID airline ticket tax and the “voluntary solidarity contribution” being developed by the Millennium Foundation are promising examples of sustainable funding sources. Taxes on financial transactions, particularly a small tax on currency exchange,⁶ are another potentially promising way to raise long-term funds for neglected health R&D as well as for other development priorities.

Funding of this kind would insulate neglected disease product development from shifts in donor circumstances and priorities and would provide the predictability required for long-term planning clinical development. Neglected disease product development needs to draw on new, predictable, and sustainable sources of funds, rather than on grants from the

⁴ Proposal from Bangladesh, Barbados, Bolivia and Suriname on a Chagas Disease Prize Fund for the Development of New Treatments, Diagnostics and Vaccines.
http://www.who.int/phi/mspublichearing_rdf/en/index.html

⁵ A report commissioned by Novartis and the IFPMA estimated that \$3.7-5.9 billion will be needed over the next 10 years for neglected disease drug development alone. Dalberg Development Advisors (2008). “A Feasibility Study for a Fund for R&D for Neglected Diseases.” Commissioned by the International Federation of Pharmaceutical Manufacturers and Associations.

⁶ A 0.005% tax could bring in \$33-60 billion/year while having very little effect on productive economic activity. See Rodney Schmidt (2007), “The Currency Transaction Tax: Rate and Revenue Estimates”, North-South Institute, <http://www.nsi-ins.ca>; and Stephen Spratt (2006), “A Sterling Solution”, a report for Stamp Out Poverty, <http://www.stampoutpoverty.org/?lid=9889>.

small number of industrialized countries and foundations which already provide most neglected disease R&D funding, including for the PDPs.⁷

In addition, sustainable funding is also needed to support a comprehensive access strategy for products once they are developed. In the field of neglected diseases, and particularly the most neglected diseases such as sleeping sickness or visceral leishmaniasis, the existence of a stable, subsidized market is crucial to enlisting a manufacturer and to sustaining adequate supply of a new product at the lowest possible costs.⁸

For vaccines, GAVI is the logical source of funds for purchase. For drugs and diagnostics for AIDS, TB, and malaria, the Global Fund and UNITAID provide this assurance, including crucial interaction with the WHO Prequalification Programme. For other diseases, an extension of the mandates of these organizations or others, including the PAHO revolving fund, could be one solution.

Although UNITAID does not currently fund R&D, late-stage product development and activities related to delivery would be a logical expansion of its mandate, enabling it to fill gaps in the portfolio of products that it supports, to influence product design and cost, and to integrate support for registration, introduction, purchase, and delivery.

Towards a public health & equitable access-oriented framework for R&D

Any mechanisms pushed forward by the international community to finance neglected disease R&D should include the fundamental elements of the WHO Global Strategy on Public health, innovation and IP. In particular, it should promote R&D according to public health needs; build and improve innovative capacity in developing countries, including through transfer of technology; ensure delivery and access to populations in need; and manage IP in a manner consistent with all these objectives.

Such a mechanism should ensure a central role to WHO and its member states in defining public health R&D priorities, consistent with global public health needs.

Endemic countries will also need to have a strong voice in defining priorities, as the main recipients of new neglected disease technologies but also as potential new funders and R&D partners.

Finally, the difficult challenges associated with the provision of and access to medicines in developing countries, particularly in the case of neglected diseases, require that access be addressed as a fundamental goal of any mechanism. A comprehensive access strategy should ensure that new products, developed as public goods as much as possible, will be

⁷ The three proposals related to a new R&D fund which were considered by the WHO working group would rely on conventional government and philanthropic grants, albeit perhaps from new donors.

⁸ In the field of neglected diseases, affordability can only be ensured through delinking the cost of R&D from the price of the final product. In cases where the market is too small to stimulate competition⁸, ND products will need to be supplied at cost, or at a price corresponding to a small margin above the lowest manufacturing costs to ensure sustainability of production.

manufactured at the lowest possible costs in accordance with quality standards, but should also support registration in all endemic countries and ensure sustainable supply in the necessary volumes.

The urgency of providing the necessary health tools to address the global neglected diseases burden requires an expeditious and efficient response from the international community. In considering innovative financing mechanisms for health R&D, we should build upon the successes of existing international organizations and mechanisms that are already addressing market and public policy failures, such as UNITAID, the Global Fund, GAVI or the WHO Prequalification system.