

Making drugs accessible to poor populations: a funding model



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According to a recent publication by Mary Moran et al¹, public-private partnerships (PPPs) or product development partnerships (PDPs) involving non-governmental organizations (NGOs), academia and the pharmaceutical/biotech industry have generated a growing early pipeline of new drug therapies for neglected diseases such as malaria, tuberculosis, Dengue and parasitic diseases such as Leishmaniasis, human African trypanosomiasis and Chagas disease. This activity resulted in about 63 projects in

2005¹, several of which are in early clinical testing. A more recent survey is shown in Figure 1.

Despite the high attrition rate it is to be expected that several of these projects will approach full development towards registration with costs of several hundred million US dollars per project. A study by Dalberg, commissioned by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) and Novartis² estimates that US\$ 6–10 billion will be needed for that purpose in the next 10 years.

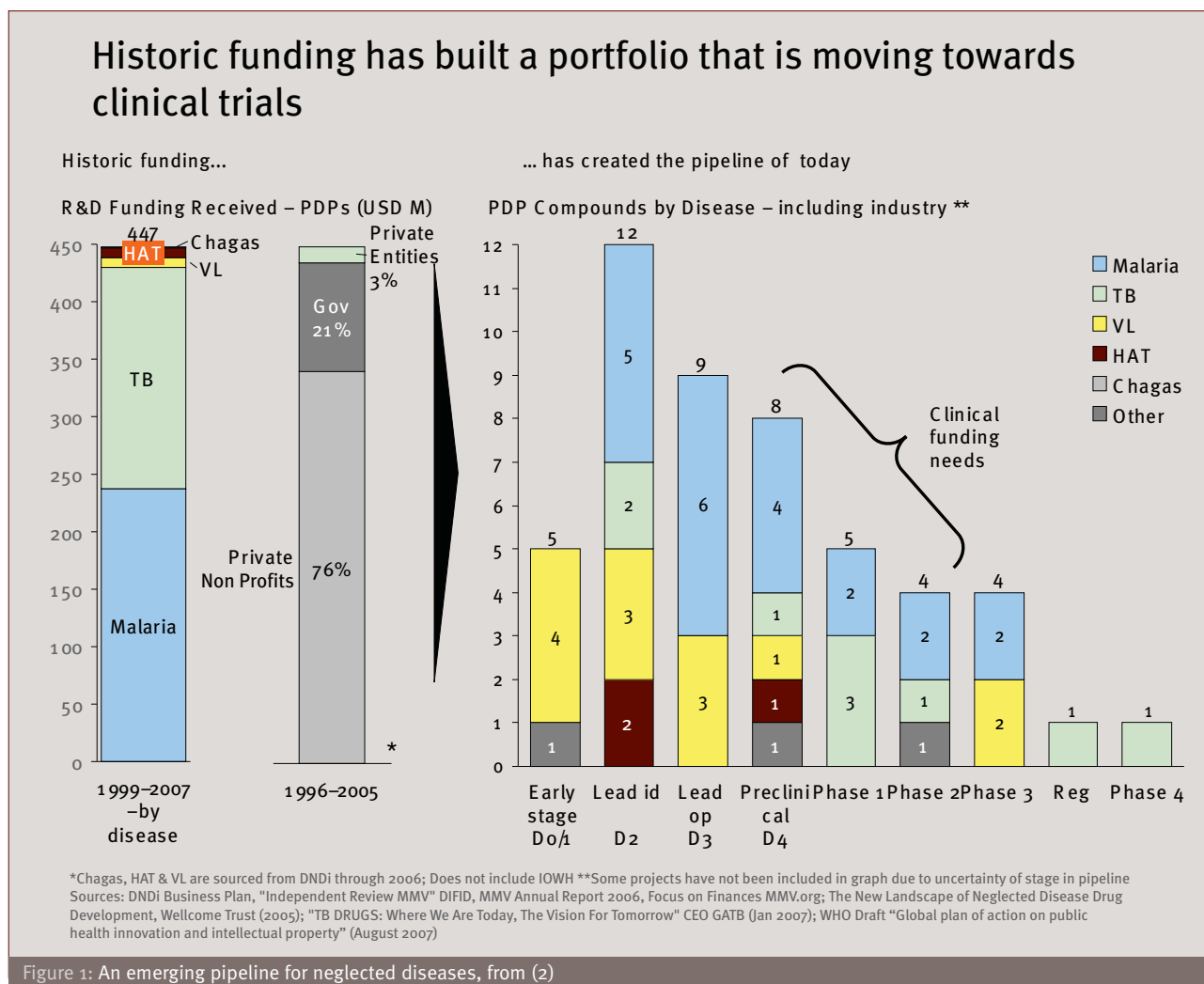
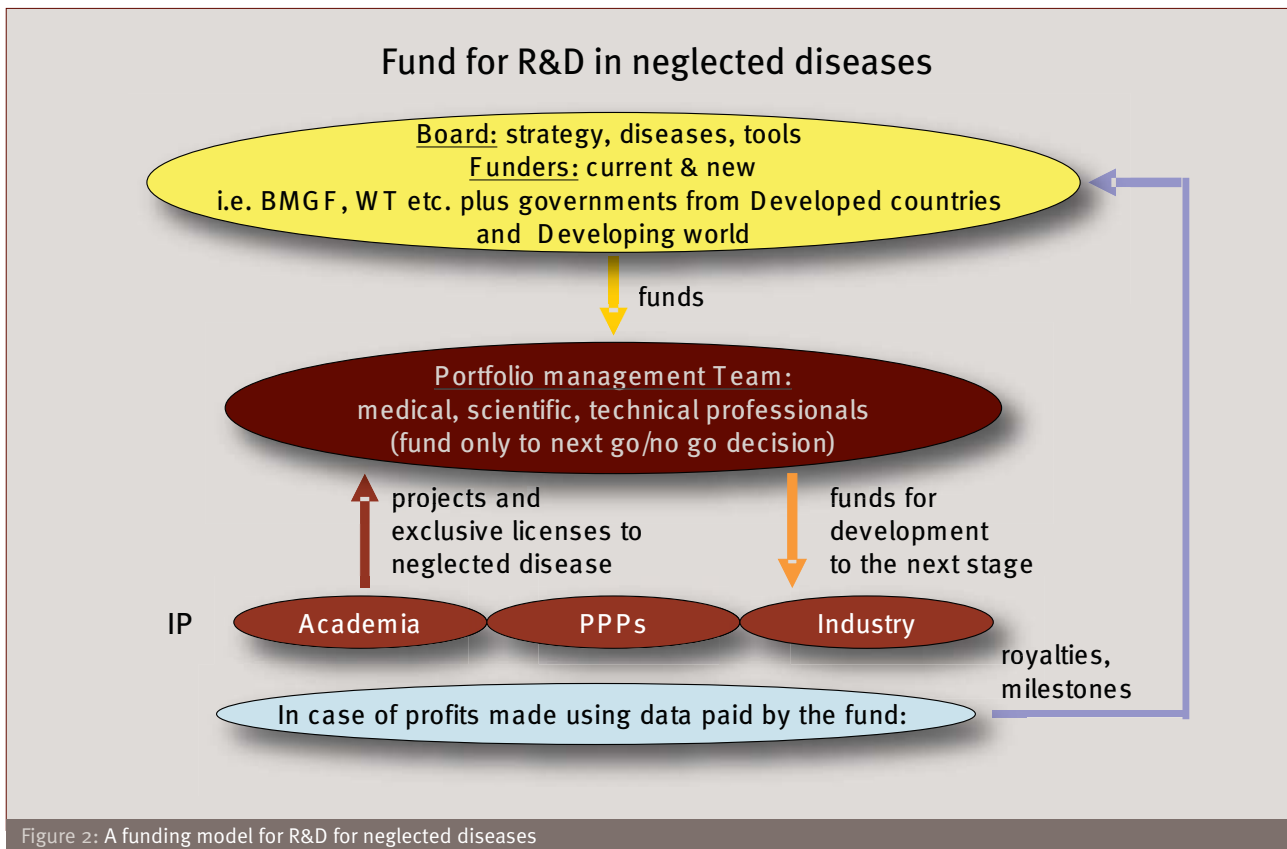


Figure 1: An emerging pipeline for neglected diseases, from (2)



In comparison, in the same study the estimated cost of building this early pipeline was around US\$ 0.5 billion, allocated by a variety of private and public donors to PDPs. There is no indication that the current donors could generate sufficient funds for full development of the neglected diseases pipeline. There is a danger that a very unfortunate situation will arise where innovative compounds for neglected diseases in the pipeline that show a promising proof of concept in early human studies will stall in further development for lack of funding.

The model proposed (see Figure 2) describes a possible way to address this situation that attempts to take into account the needs of all stakeholders. It has been discussed with several pharmaceutical companies and representatives of NGOs such as Médecins Sans Frontières, Oxfam and the World Health Organization, who have all indicated that they had no fundamental objections and encouraged us to further develop it. The model is complementary to others such as Advanced Marketing Commitments and Prizes and the differences will be discussed.

A model to fund R&D for neglected diseases (Fund for R&D in Neglected Diseases, FRIND). The model (Figure 3) is designed to apply only to disease areas with large medical need but where no commercial returns can be expected and where normal market mechanisms therefore do not apply and where pharmaceutical and biotech companies can only invest very limited R&D funds. Examples are the 10 diseases on the TDR list³.

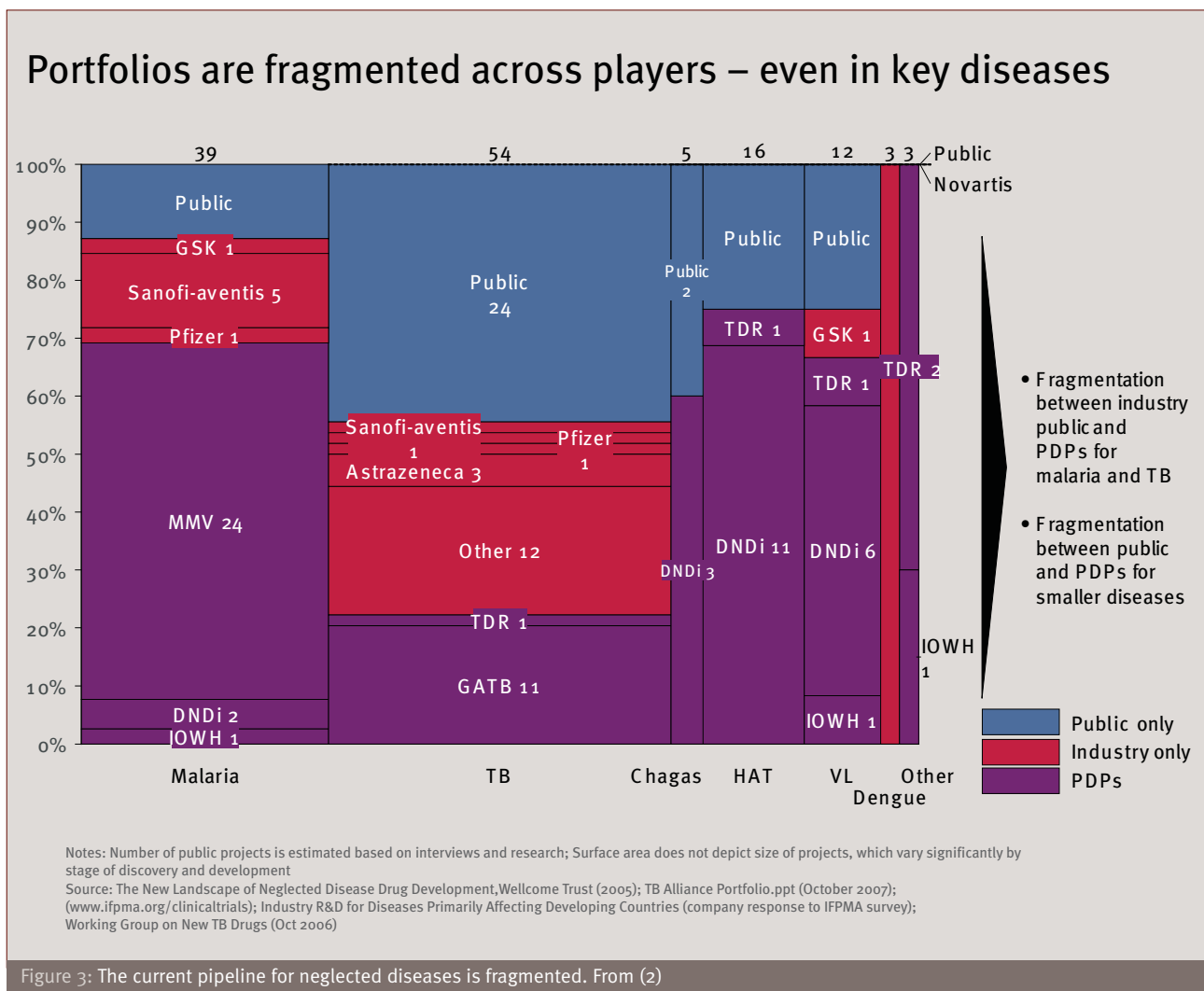
Funding and governance. The fund can be financed by the current donors to PDPs but in view of the magnitude envisaged governments of both developed and developing

nations will have to contribute. Representatives of the donors would constitute the Board of the fund in which the disease scope, product scope (e.g. medicines/vaccines only, or to include diagnostic methods etc.) and the strategy would be defined. The Board would not be involved directly in the portfolio management within the strategy. The mission of the fund must include the obligation to make available the therapies it funds to poor patients in the developing world for free or at an affordable price, or at least at no profit (if a profit can be made, then the normal market mechanisms will be applicable). FRIND would only finance the R&D component and would need partners/other donors for manufacturing and distribution.

Potential applicants. Any entity, academic, biotech/pharmaceutical company or PDP with a therapeutic/diagnostic project fulfilling a medical need for a neglected disease within the scope of FRIND can apply to the fund.

Portfolio management team/scientific advisory board. The members of the portfolio management team should have the same profile and skills found in large pharmaceutical companies' portfolio decision teams, i.e. scientific-, medical, technical-R&D, regulatory-, economics- experts familiar both with the therapeutic area and the environment in which the new drugs should be applied (field experts).

Prioritization and allocation principles. The portfolio decisions should be made exclusively on scientific, medical, technical and economic criteria excluding political factors as much as possible. To reduce potential waste of resources it is essential to apply a fund allocation rule where having estimated the totality of funds required for the entire development of the product, the portfolio team would then only allocate the funds



needed to reach the next decision point. At this stage the new results would be evaluated and a new decision to continue funding to the next stage or stop would be made.

Overcoming the fragmentation of the neglected disease portfolio. An analysis of the current neglected disease portfolio² indicates that even within single diseases there are several actors working in parallel and with limited communication between them (Figure 3).

It is expected that the fund under discussion would become the major source of funds for R&D for neglected diseases and one consequence would be that the portfolio management team would eventually see most projects within a disease area which would allow them to compare them, invest in the best ones or combine them.

Intellectual property protection. Intellectual property protection is essential for fostering investments in research for new medicines worldwide and should not be an impediment to access to medicines in the developing world⁴. In the context of FRIND, intellectual property could be handled as follows:

The inventors of the new product to be funded by FRIND (academic institutions, biotech companies, PDPs or pharmaceutical companies) would usually patent their inventions and retain ownership. If any of the entities above apply to FRIND for funding of their project in R or D they in

return would allocate an exclusive licence to the fund for the particular neglected disease within the mission of FRIND. The inventors would retain the rights for all other applications. This is important because nature does not distinguish between diseases of the rich and poor. For instance, a compound developed for Dengue fever, a neglected disease of increasing impact, might very well show useful activity in hepatitis C, an indication with commercial blockbuster potential, because both the Dengue virus and the hepatitis C virus (HCV) are genetically close because both belong to the genus Flaviridae. The inventor might very well want to develop the commercial application (HCV) using their own funds to later sell it with profit where a commercial market exists. If, however, the entity marketing such a therapy uses data that has been elaborated in a FRIND funded activity, royalties and/or milestones should be due to the fund to reimburse their expenses for the data generation.

Discussion

There are several alternative models in discussion to stimulate R&D in neglected diseases, e.g. Advance Market Commitments (AMC)⁵ or Prize mechanisms as proposed by James Love⁶. The current FRIND proposal overcomes a major drawback of the two models discussed above. Any entity that wants to access either AMC or Prize money needs to invest at

risk in the full development of its product for neglected disease and as about 7 out of 10 projects in clinical phase one fail before registration all that investment would be lost. This is a major disincentive not only for pharmaceutical companies but is outright unaffordable for many PDPs, academic institutions or small biotech firms. In addition since many advances in the treatment of disease are incremental, the concept of a “prize” for the first successful product is inappropriate and might be a disincentive to parallel activities. In contrast the current FRIND model would fund the individual R&D phases upfront and would bear the risk. An additional benefit is that through FRIND a portfolio management approach across different players might be established that allows more optimal allocation of (scarce) donor resources to the most promising R&D projects.

The model proposed here and AMCs or Prizes are not mutually exclusive but rather complementary to increase the probability of the creation of urgently needed new therapies for neglected diseases. The brief description of the model in this paper is intended to stimulate discussion and to evaluate its acceptance from the main stakeholders and potential donors. It has already received constructive contributions

from NGOs such as MSF, representatives from WHO, Oxfam and other pharmaceutical companies and is currently being presented to national governments. If sufficient support for this concept can be generated a more detailed model will be elaborated in a second phase. □

Acknowledgements

The author would like to thank Stephanie Meredith, Tido von Schoen-Angerer and Lee Wells for constructive discussions.

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Abbreviations

AMC:	advanced market commitments
BMGF:	Bill & Melinda Gates Foundation
D0:	drug discovery phase 0, target finding
D1:	drug discovery phase 1, high throughput assay formatting
D2:	drug discovery phase 2, high throughput screening, hit finding
D3:	drug discovery phase 3, lead optimization, medicinal chemistry for small molecules
D4:	drug discovery phase 4, late preclinical phase
DNDi:	Drugs for Neglected Diseases Initiative
FRIND:	Funding Model for R&D in Neglected Diseases
GATB:	Global Alliance for Tb Drug Development, Tb Alliance
GSK:	GlaxoSmithKline

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HAT:	human African trypanosomiasis
HCV:	hepatitis virus C
IFPMA:	International Federation of Pharmaceutical Manufacturers & Associations
IOWH:	Institute for One World Health
MMV:	Medicines for Malaria Venture
NGO:	nongovernmental organization
R&D:	research and development
TB:	tuberculosis
TDR:	WHO special programme for research and training in tropical diseases
VL:	Visceral Leishmaniasis
WT:	Wellcome Trust