



Addressing the Crisis in Research and Development for Neglected Diseases

Today, 35,000 people will die from malaria, tuberculosis, HIV/AIDS, sleeping sickness, chagas and kala-azar. Communicable diseases kill almost 15 million people every year.¹

Neglected diseases

Neglected diseases mainly affect people in developing countries. They are the diseases which do not represent a commercially viable market for pharmaceutical companies, because those affected do not have the purchasing power to afford treatment solutions. Companies therefore shirk away from investing into risky and expensive research and development for these conditions.

The *most* neglected diseases are the obscure afflictions which many of us have barely heard of – they include human African trypanosomiasis (or sleeping sickness), South American trypanosomiasis (also known as Chagas disease), Buruli ulcer, dengue fever, leishmaniasis, schistosomiasis, lymphatic filiriasis. These diseases, far removed from our shores, fall outside the scope of the drug industry's R&D efforts.

Other neglected diseases, more familiar because they also hit people in wealthier countries, are still neglected in that the overwhelming majority of those affected throughout the world do not have access to safe and affordable diagnostics, drugs or vaccines. This is true of the “big three” - HIV/AIDS, tuberculosis, and malaria. For these, a reasonably sized commercially viable market does exist – malaria is a health risk for tourists for example – but, crucially, not one for treatments that are adapted for remote or poor settings, where the majority of the patients live.

The lack of safe, appropriate and affordable diagnostics, drugs and vaccines for neglected diseases is striking:

- 60 million people are at risk of contracting sleeping sickness. Diagnosing this fatal disease requires a lumbar puncture which is beyond the capacity of regular health facilities in affected countries. Treatment is based on a highly toxic arsenic derivate in use since 1940s and a former cancer drug from the 1980s.
- Kala-azar kills 60,000 people each year, but antimony treatment developed in the 1930s has remained the mainstay of therapy despite considerable toxicity and the need for injections during the four-week treatment.
- 1,400 children die *every day* of AIDS-related complications, but existing methods to diagnose HIV in infants are too difficult and costly to perform in most poor country settings, and soluble and easy to take children's tablet do not exist although they would be relatively easy to develop.

- TB is responsible for nearly two million deaths each year but treatment takes six months and is difficult to implement, depending on increasingly ineffective drugs dating from the 1950s and 60s. The only test simple enough to be widely implemented is sputum microscopy, developed in 1882 but detecting the disease only in 45-60% of cases.
- 340 million sexually transmitted infections occur every year. Simple, effective treatment exists but many are not getting it because of lack of simple, reliable tests.
- Chagas disease is found on the American continent and claims up to 50,000 lives a year. Due to lack of adequate tests, this chronic disease is usually diagnosed too late for current drugs to be effective. The only two available medicines, nifurtimox and benznidazol, were developed in the 1960-70s.

That these diseases remain neglected is a direct result of the inadequacies of the current profit and patent-driven drug development system which steers R&D into areas of profitability rather than need.

Inadequacies of current systems for health R&D

Global spending on health research has increased dramatically from US\$ 30 billion in 1986 to US\$ 105.9 billion today. This may seem good news. But a closer look shows how 90% of this money is spent on the health problems of less than 10% of the world's population.² This is commonly referred to as the 10/90 gap. The global pharmaceutical market is today worth US\$ 518 billion. 87% of this is made in North America, the European Union and Japan.³

This huge disparity in spending has dramatic consequences for the output of new treatments by pharmaceutical firms. Between 1975 and 2004, of the 1,556 new chemical entities marketed globally, only 20 new drugs - a mere 1.3% - were for tropical diseases and tuberculosis, diseases which account for 12% of the total disease burden.⁴

A breakdown of the 1,035 new drugs approved by the US Federal Drug Administration between 1989 and 2000 revealed that more than three quarters are classed as having no therapeutic benefit over existing products, or so-called 'me too' drugs.⁵ At the same time it was noted that less than 1% addressed diseases that primarily afflict the poor and for which new treatments would have the greatest effect on world healthcare.⁶

Intellectual property rights (IPR) and international trade mechanisms

The current R&D system is profit and patent driven and efforts to increase patent protection also in developing countries had come with the promise of increased innovation benefiting those countries. However, there is consensus, supported by the UK government-sponsored Commission for Intellectual Property Rights, that higher levels of intellectual property protection have **not** resulted in increased drug R&D for global health needs.⁷ Worse, in some cases R&D may actually be hampered by IPR, either through the complexities of dealing with large numbers of patents (some human genes are patented as many as 20 times for example), or because follow-on innovation is rendered impossible. Negotiating with universities and companies for access to knowledge, chemical compounds, and research tools are prohibitively complicated and time-consuming.⁸

The WTO Doha Declaration on TRIPS and Public health recognises the huge burden of pharmaceutical patents and subsequent high drug prices for developing countries and outlines ways for countries to set patents aside when needed.

New models are emerging, but more needs to be done

The emergence of public-private models

Today, the lack of R&D for neglected diseases is an increasingly recognized fact. Over the past few years a number of encouraging initiatives have emerged. A number of not-for-profit product development partnerships (PDPs – sometimes called public-private partnerships or PPPs) have been created to develop new drugs, diagnostic tests, and vaccines for neglected diseases. Examples include the International AIDS Vaccine Initiative (IAVI), the Medicines for Malaria Venture (MMV), the Global Alliance for TB Drug Development (GATB), and the Drugs for Neglected Diseases Initiative (DNDi), co-founded by MSF. A recent report by the London School of Economics charting the new landscape of neglected disease R&D estimates that, based on their current drug pipelines and assuming standard attrition rates, PDPs could bring eight or nine new drugs to market in the next five years.⁹

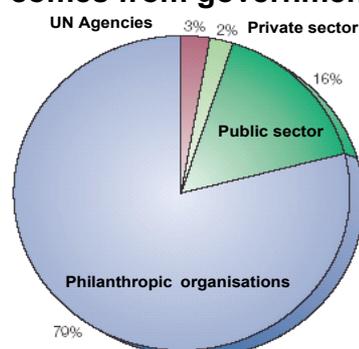
The emergence of PDPs offers an interesting new model: the costs of R&D are paid for directly and no longer financed by a pharmaceutical company, as in the current model, through high drug prices and stringent patenting. This new model will allow the resulting products to be sold at prices close to production cost.

But the success of the PDPs depends on whether they can raise sufficient funds to carry these projects through to fruition. Currently, PDPs have not even secured funding for their existing projects; and as they fill their pipelines and more promising compounds move into clinical trials, their funding needs are increasing significantly. It has been estimated that an additional US\$ 200 million per year is required to fund existing PDPs involved in the development of new drugs.¹⁰ Without this, existing new drug candidates for neglected patients will stay where they are – in the pipeline.

Today, the work of PDPs is essentially driven by philanthropic organisations such as the Bill & Melinda Gates and the Rockefeller Foundation. Governments provide a paltry 16% of their funding. In fact, MSF, a private medical humanitarian organisation, currently contributes more to PDPs engaged in drug development than all EU countries combined. It is particularly unclear where the resources to finance the very expensive later stages of development and clinical trials will come from.

Figure and table 1: Total cumulative PDP funding (as of April 2005, including forward funding committed by that date):¹¹

Only 16% of funding towards PDPs comes from governments



Donor	Total in million US\$	% of total
Philanthropic		
Bill & Melinda Gates Foundation	158.7	58.9
Médecins Sans Frontières	29.7	11
Rockefeller Foundation	20.3	7.5
Wellcome Trust	2.8	1.1
Philanthropic total	211.6	78.5
Governments		
USA	16	5.9
UK	10.9	4.1
Netherlands	10.5	3.9
Switzerland	4.4	1.6
European Commission	1.5	0.6
Governments Sub-total	43.6	16.2

While the work of PDPs is important as a first step in addressing health R&D for the poor, it is far from sufficient. Too often, one solitary research initiative exists for a neglected disease or even for the entire neglected field of diagnostics: would we consider one drug research initiative a sufficient response to cancer, for example, as we do for TB?

No-profit no-loss investment by pharmaceutical firms

In the last few years, alongside the creation of PDPs, some pharmaceutical companies have responded to public pressure about their failure to develop new tools for diseases that predominantly affect people in developing countries by creating special R&D facilities or initiatives. For example, GlaxoSmithKline, Novartis, AstraZeneca and sanofi-aventis have all been involved in R&D for neglected diseases on a 'no-profit-no-loss' basis. Importantly, the firms have stated they will make their products affordable and accessible to patients in developing countries.

These endeavours are not motivated by commercial incentives but by the wish to create a positive corporate image or to secure a strategic position in emerging economies. There is a lesson to be learnt here: the current lack of R&D for neglected diseases will not be resolved through the creation of commercial incentives for multinational drug companies (unless the incentives were colossal). Indeed, companies not currently working on neglected diseases have indicated that even incentives would not attract them into this field of research.¹²

Obstacles to R&D remain, and public sector leadership is needed

Lack of public leadership

No public body has taken steps to define needs and set priorities for neglected disease R&D and the field is left almost entirely to philanthropy. Now, more than ever, the world needs a more efficient, innovative, and needs-driven system for setting priorities and financing R&D supported by real political commitment from governments and new rules of engagement.

Funding

According to the World Health Organization's 2001 Commission on Macroeconomics and Health, at least \$3 billion per year for R&D directed at the health priorities of the world's poor is required.¹³

The large pharmaceutical companies claim that the R&D cost of a commercial drug company per new pharmaceutical product is US\$802 million. If this is the case then very little innovation for neglected diseases can be expected. However the Global Alliance for Tuberculosis Drug Development, a non-profit entity for R&D of tuberculosis drugs, estimated that the total R&D cost for a new tuberculosis drug, including the cost of failure, is between US\$115 million and US\$240 million¹⁴ and cost projections for several PDP compounds are even below US\$100 million.¹⁵ The pharmaceutical industry's estimates are so high particularly because they include opportunity costs.

Regulatory processes

Regulatory authorities in developing countries may lack capacity to assess new drugs developed to treat neglected diseases and that have not been approved elsewhere. However, they alone can assess the risks and benefits of new drugs for diseases endemic in their countries. The European Agency for the Evaluation of Medicinal Products (EMA) recently adopted a regulation that enables it to assess, at the request of WHO, medical products marketed outside the EU. This regulation now needs to be put to test.

Public responsibility – call to governments

Médecins Sans Frontières (MSF) is calling on governments to more urgently address global R&D needs. In the Millennium Development Goals (MDGs) and at the Group of Eight (G8) Summit in Gleneagles, Scotland, in 2005, the wealthiest countries of the world made clear commitments to increase R&D for malaria, tuberculosis, HIV/AIDS, and the most neglected diseases. Countless lives depend on these promises being fulfilled.

Recent examples have shown how political will can ensure international cooperation and the marshalling of tremendous resources for research and development. Unfortunately, the sense of urgency that resulted in swift and efficient responses to the SARS outbreak, the anthrax scare in the United States, and the more recent avian flu threat, is entirely lacking when it comes to R&D for diseases that predominantly affect poor people in developing countries. Despite increased awareness of the problem, governments have not developed viable public policies to ensure needs-driven R&D for new medicines, diagnostics, and vaccines.

Political leadership is needed from all countries to give greater priority to global health R&D and secure long-term funding. Governments all over the world and the WHO have a critical role to play in ensuring that advances in science and medicine will contribute to alleviating suffering and meeting the urgent medical needs of millions of people in the developing world. MSF calls upon governments to support the following:

- **A New Global Framework to Support Needs-Driven Research:** R&D priorities should be defined based on patients' needs to enable countries to direct health R&D accordingly. We ask governments to support the WHO in the development and establishment of a global framework for essential health research and development that would ensure that priority R&D meets patients' need and public interest and designs a system for equitable sharing of the costs of research and development.
- **Increased Public Funding:** Increased public funding is urgently needed to ensure that progress in basic science and biomedicine results in new and affordable drugs, vaccines, and diagnostics for neglected diseases; to support the development phases of R&D; and to secure the use of new products by neglected populations.
- **Access to IP-Protected Knowledge and Tools:** Industry and academia can contribute significantly to R&D for drugs for neglected diseases without foregoing a reasonable profit, by making their wealth of expertise and compound libraries more easily available. We ask policy makers and industry to find innovative ways to make this possible.
- **Regulatory Agency Support:** WHO needs to work with regulatory authorities to allow rapid approval and delivery of drugs to neglected patients. Support of regulatory agencies from agencies, such as the US FDA and the EMEA, is needed to accelerate approval processes for new drugs for neglected diseases. The risks and benefits of each drug or vaccine must be assessed in relation to the needs of patients, the severity of the disease, and available treatments and vaccines. We ask governments to cooperate with the WHO on regulatory approval for drugs for neglected diseases so that essential, life-saving medicines and new health technologies are rapidly available to populations that most need them.
- **Strategies to Strengthen Research Capacity in Disease-Endemic Countries:** Technology transfer and strengthening research capacity in disease-endemic countries should be at the heart of efforts to increase R&D for neglected diseases. For example, significant support is necessary to ensure that there will be sufficient trial capacity in disease-endemic countries.

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⁵ NIHCM 2002

⁶ WHO 2003

⁷ http://www.iprcommission.org/graphic/documents/final_report.htm

⁸ [CIPRGPRI, 2005; and Jensen and Murray 2005]

⁹ *The New Landscape of Neglected Disease Drug Development* LSE/Wellcome Trust, September 2005

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¹⁵ *The New Landscape of Neglected Disease Drug Development* LSE/Wellcome Trust, September 2005

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