



Submission to the Expert Working Group on Research and Development Financing
Médecins Sans Frontières - Campaign for Access to Essential Medicines
April 2009

EXECUTIVE SUMMARY

Context of the EWG

The vast gaps in research and development into health tools for diseases that disproportionately affect developing countries are evident, and witnessed by MSF field teams every day.

The Expert Working Group does not take place in a vacuum. It is important that it builds on the analysis and directions given by the report of the Commission on Intellectual Property, Innovation and Public Health (CIPIH). The report introduced a re-conceptualised definition of innovation as encompassing discovery, development and delivery, thereby including access as an integral part of innovation. The Expert Group should take as its starting point this broad definition of innovation.

The EWG should assess proposals for alternative mechanisms against the World Health Assembly Resolution WHA60.30's call for the development of proposals that address "**the linkage of the cost of research and development and the price of medicines**". It is vital that the EWG take into account this inherent relationship between cost and price, and the need to overcome it and ensure access to the products of innovation.

Innovative solutions to tackle the problems created by the current dependence on intellectual property (IP) to finance R&D have been suggested in recent years and deserve to be given full attention by the Expert Working Group. They include patent pools, prize funds and proposals for a convention on R&D.

This submission will focus on the development of one alternative mechanism, a prize fund, for one area of particular need, TB diagnostics, in order to illustrate what the Expert Working Group must do to facilitate the development of new ways to finance neglected areas of medical research.

Assessing the different alternative mechanisms

The EWG will receive a number of different proposals suggesting widely varying alternative financing mechanisms for research and development. In order to evaluate their relative strengths and weaknesses with precision, the EWG should develop a set of principles and criteria against which each alternative mechanism should be assessed. These must include:

- **The ability to address identified medical needs**
- **The ability to ensure sustainable access to the fruits of innovation**

Numerous other proposals exist. Bolivia and Barbados have also proposed prize funds for the development of new medicines and diagnostic tools for Chagas disease. Patent pools, such as the one for second-line antiretrovirals medicines currently being examined by international drug agency

UNITAID, have the potential to accelerate access to more affordable medicines and to stimulate the development of innovative products such as fixed-dose combinations. While the UNITAID pool will focus on AIDS medicines initially, the patent pool model should be explored by the EWG to see whether it could also help improve access and boost innovation in other neglected disease areas.

A sustainable policy that tackles the fundamental problem of a monopoly-based innovation and access system is still lacking. Initiatives that can quickly yield results are needed, such as voluntary and compulsory licensing, patent pools, and implementation of pro-access national IP laws. While individual initiatives are important, work must begin on longer-term systemic changes that will provide both health needs-driven R&D and equitable access.

The EWG needs to examine such proposals, including for a biomedical R&D treaty. The Global Strategy called on WHO to *“encourage further exploratory discussions on the utility of possible instruments or mechanisms for essential health and biomedical R&D, including inter alia, an essential health and biomedical R&D treaty.”*

The Expert Working Group must drive forward these proposals ready to report back to governments for the 2010 World Health Assembly. The Group must also determine for each mechanism considered to be promising what concrete steps are necessary in order for the work to advance. These need not wait until its final report. The EWG should recommend to WHO the hosting of meetings prior to its final report, in order to explore promising mechanisms in more detail.

In its final report to governments, the Expert Working Group must not limit its work to a mere survey of proposals. Rather, its final report must be operational and provide an indicative workplan as to how to take forward the proposals identified to boost research and development for diseases that disproportionately affect developing countries, in a way that ensures access to the products thus developed.



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Médecins Sans Frontières (MSF) welcomes the opportunity to make a submission to the Expert Working Group (EWG) on research and development financing.¹

This submission will focus on the development of one alternative mechanism, a prize fund, for one area of particular need, tuberculosis diagnostics, in order to illustrate what the Expert Working Group must do to facilitate the development of new ways to finance neglected areas of medical research.

The context of the EWG's work

The EWG does not take place in a vacuum.

It is important that it builds on the analysis and directions given by the report of the Commission on Intellectual Property, Innovation and Public Health (CIPIH). The report called attention to the need for changes in the way health R&D is prioritised and financed. It introduced a re-conceptualised definition of innovation as encompassing discovery, development and delivery, thereby including access as an integral part of innovation. The Expert Group should take as its starting point this broad definition of innovation.

The EWG should assess proposals for alternative mechanisms against the World Health Assembly Resolution WHA60.30's call for the development of proposals that address "**the linkage of the cost of research and development and the price of medicines**". It is vital that the EWG take into account this inherent relationship between cost and price, and the need to overcome it and ensure access to the products of innovation.

Here, MSF notes with regret that the call for submissions to feed into the work of the Expert Working Group fails to mention either the need to ensure access to any developed products, or the current problems associated with the lack of access to existing product

The vast gaps in research and development into health tools for diseases that disproportionately affect developing countries are evident. MSF doctors, for example, are unable to provide good care for people with tuberculosis, due to the lack of good diagnostic tools and because drug

¹ The November 2006 submission by MSF to the first IGWG public hearing is available at:
http://www.who.int/phi/public_hearings/first/15Nov06EllentHoenMSF.pdf
The September 2007 submission by MSF to the second IGWG public hearing is available at:
http://www.who.int/phi/public_hearings/second/contributions_section1/Section1_tHoenEllen-MSF.pdf

regimens everyday lose yet more of their effectiveness. Despite the successes of treating HIV in the West, our HIV/AIDS projects are still desperately lacking adapted tools to monitor treatment, for children, and for people infected with both HIV and other diseases, such as tuberculosis, kala azar or malaria.

Current approaches to stimulate R&D into diseases that disproportionately affect developing countries, such as through direct grant funding of researchers or financing product development partnerships (PDPs), are important but cannot provide a complete solution to the R&D needs. MSF continues to support such approaches – whether as co-founder, with a number of governmental research institutions, of the Drugs for Neglected Diseases Initiative (DNDi); or in on-going collaboration with different academic and private actors that respond to market failures and develop simplified CD4 tests and a field-adapted tool for diagnosis of HIV in infants and for monitoring of HIV treatment failure.

PDPs respond to part of the problem but are by no means enough: viewing the response to tuberculosis, for which PDPs exist, and the response to cancer or cardiovascular disease, by comparing the number of potential drugs under development for example, illustrates the shortcomings of relying solely on PDPs. There is increasing documentation that new philanthropic efforts are far from enough to address the crisis. Indeed, PDPs themselves acknowledge that more governmental responsibility is needed,² just as pharmaceutical companies have stated that they cannot respond without an overhaul of the system.³ The Expert Working Group must explore these and additional concerns.

With the adoption of the Global Strategy and Plan of Action for Public Health, Innovation and Intellectual Property in May 2007, there is now also wide recognition of the need for new approaches in order to address those urgent medical needs. The limitations of a ‘more of the same’ strategy focusing exclusively on raising extra financial resources or relying mostly on product development partnerships have become clearer. The creation of the EWG is perhaps the most salient proof of how widely shared is the view that alternative financing mechanisms for medical R&D are necessary.

One area of need: tuberculosis diagnostics

The shortfall in funding for tuberculosis R&D is uncontested. The latest figures given by the Treatment Action Group in their annual survey of tuberculosis R&D funding showed the current levels of investment represent barely one-fourth of the US\$9 billion recommended by the Global Plan to Stop Tuberculosis for the period of 2006 to 2016, and one-tenth of the US\$20 billion that TAG estimates are needed.⁴ Additional research from Médecins Sans Frontières has charted the vastly insufficient contributions to TB research by Germany and the European Commission, with further country studies in preparation.⁵ The funding gaps across many neglected diseases have been well documented including health areas that receive hardly any funding.⁶

² Boosting Innovation for neglected diseases – a call to governments; DNDi Research Appeal, available from www.researchappeal.org

³ Novartis chief in warning on cheap drugs, Financial Times, 30th September 2006, London

⁴ http://www.treatmentactiongroup.org/TB_RD_2009.aspx

⁵ Cough up for TB! The Underfunding of Research and Development for Tuberculosis and Other Neglected Diseases – Germany, MSF 2007; and European Commission, MSF 2008. www.msfaaccess.org

⁶ Moran M, Guzman J, Ropars AL, McDonald A, Jameson N, Omune B, Ryan S, Wu L. Neglected disease research and development: how much are we really spending? PLoS Med. 2009 Feb 3;6(2):e30

Funding for tuberculosis diagnostics R&D is even within this context a neglected priority. Barely 9 per cent (US\$42 million) of the US\$284 million invested in TB R&D was allocated to R&D in diagnostics in 2007. Participants at the MSF/TAG/PIH expert meeting last month called for an increase in the funding allocated to TB diagnostics R&D by at least fourfold.

But while increasing the spending attributed to TB R&D through ‘push’ funding and grants is essential, alone it will not be sufficient to deliver a TB point-of-care test. Alternative mechanisms to steer medical innovation towards areas of greatest need, and that also ensure access to the final products, are also necessary.

One potential solution: prize funds

The governments of Bolivia and Barbados, as a part of the Intergovernmental Working Group on Intellectual Property, Innovation and Public Health, supported the establishment a prize fund for a tuberculosis point-of-care diagnostic test. Furthermore, the Bill & Melinda Gates Foundation has provided a planning grant to the X-Prize Foundation to develop a prize reward strategy to find a better diagnostic tool.

In addition, over the past year, various meetings have focused on how to better meet the current gaps in TB diagnosis by promoting new strategies to stimulate R&D for the development of a TB point-of-care test. These meetings have included the TAG-ARASA meeting held in Cambridge on 6-7 April 2008, entitled “The Urgent Need for a Point-of-Care Dipstick Diagnostic Test for Tuberculosis” and the MSF meeting held in Geneva on 11 April 2008 entitled “Financing Medical Innovation Through Alternative Mechanisms”.⁷

This meeting reviewed a number of alternative incentive mechanisms and concluded that the use of prize fund for a TB diagnostic should be explored further.

This submission will focus on the development of one alternative mechanism, a prize fund, for one area of particular need, TB diagnostics in order to illustrate what the Expert Working Group must do to facilitate the development of new ways to finance neglected areas of medical research.

Assessing the different alternative mechanisms

In recent years, a number of innovative solutions to tackle the problems created by the current dependence on intellectual property (IP) to finance R&D have been suggested and deserve to be given full attention by the Expert Working Group. The EWG will receive a number of different proposals suggesting widely varying alternative financing mechanisms for research and development.

In order to evaluate their relative strengths and weaknesses with precision, the EWG should develop a set of principles and criteria against which each alternative mechanism should be assessed. These must include:

1. The ability to address identified medical needs

Medical innovation must be steered so that it can address the medical needs of patients. It is vital for the EWG to assess the ability of proposals for alternative financing for research and development to answer the real medical needs identified by field practitioners, communities and other end-users.

⁷ For a meeting report, please see www.msfacecess.org/

The importance of a firm grounding in medical needs can be illustrated in the field of tuberculosis diagnostics, as the tests current available are severely inadequate, in particular for children, for people living with HIV/AIDS, for people with extra-pulmonary forms of TB.

Determining the medical needs

Sputum smear microscopy, currently the most widely used diagnostic method in the developing world, only detects the disease in less than half the patients who have TB. The best alternative, culture, gives more accurate results but comes with additional serious drawbacks including time to results and complexity. Although techniques that work on analysing the DNA of the mycobacterium can give results in less than 48 hours, they demand highly sophisticated pieces of equipment.

We are still very far from a TB diagnostic tool that can be used at the point-of-care, as close to the patient's bedside as possible. Yet the vast majority of TB patients - an estimated 85 percent - seek care in small clinics and health posts where they either have access to only sputum smear microscopy, or no test at all.⁸

Efforts to research and develop new tuberculosis diagnosis tests must ensure that the new tools make a difference and bring enhanced performance. Any new test must thus be assessed against the medical needs that are identified by field practitioners.

In March 2009, MSF, together with Treatment Action Group (TAG) and Partners In Health (PIH) convened an expert meeting that brought together test developers, clinicians, laboratory experts and representatives of patient communities in order to determine precisely what the priorities of researchers and test developers should be. The objective of the meeting was to identify and prioritise the medical needs that a point-of-care (POC) tuberculosis diagnostic test should address, and establish the minimum criteria to guide test developers.

In preparation for the meeting, a field survey was conducted in order to ensure any definition of the features of POC TB diagnostic test benefited from the involvement of end-users. This expert opinion check, in which 30 participants from 17 countries were interviewed by phone, including TB practitioners involved at all levels of care, professionals in charge of TB programmes at national level or from research institutions, will be made available shortly.⁹

The focus on point-of-care was selected in light of the need for a new TB test to be available where the majority of patients are seen: at the peripheral level of the health care system, defined as the primary health care facility with no on-site access to laboratory testing.

Through these consultations, a strong consensus¹⁰ on the minimal requirements for a point-of-care test for tuberculosis emerged around the following points:

- A new test must give results that are significant and telling enough to allow the

⁸ TDR, FIND. Diagnostics for tuberculosis: global demand and market potential. Geneva: World Health Organization Special Programme for Research and Training in Tropical Diseases and Foundation for Innovative New Diagnostics, 2006. Available at: www.who.int/tdr/publications/tdr-research-publications/diagnostics-tuberculosis-globaldemand/pdf/tbdi.pdf

⁹ Please check www.msfaaccess.org/main/tuberculosis/poc-meeting-march-2009/ for updates.

¹⁰ Report pending. Please check www.msfaaccess.org/main/tuberculosis/poc-meeting-march-2009/ for updates

- clinician to decide upon treatment initiation
- A new TB POC diagnostic test must detect active TB in adults regardless of their HIV status
- A new test must significantly improve the current capacity to diagnose TB in children
- A new test must give results fast: on the same day of sample collection, and within 1-4 hours in order to allow rapid treatment initiation and minimise the loss of patient follow-up
- A new test must be easy to perform in order to allow a health worker to carry it out with minimal training. It must not require sophisticated maintenance or technical support; any instrumentation required must be low-cost so that it can be replaced when broken instead of relying on costly technical support by the manufacturer – such support being unfeasible in many settings.
- Sample collection for a new test must not be invasive

Samples that are more practical and easier to collect than sputum are needed. However, because of concerns around the feasibility of developing a point-of-care test that relies on samples other than sputum, the minimal specifications agreed upon at the MSF-TAG-PIH expert consultation did not include a specific reference to the need for replacing sputum as the sample for testing. However, given that the minimal specifications do include a need for good performance (sensitivity and specificity) in people living with HIV and children, the potential for a sputum-based test to answer those specifications would appear to be severely limited, particularly for paediatric patients.

Further consultation is necessary in order to share the specifications of this expert meeting with the broader tuberculosis community and build on this work, so that medical needs are at the forefront of any drive to develop new tests for tuberculosis.

2. The ability to ensure sustainable access to the fruits of innovation

Research alone will not ensure access to drugs for the poorest people. The stark reality is that even if research does take place, access to the fruits of innovation is far from guaranteed because it depends on pricing or registration policies.

When appropriate tools do exist, MSF all too often struggles to access them – with devastating consequences. Our teams in Asia tell of HIV/AIDS patients going needlessly blind because of a virus – a treatable condition, but one that continues to maim because exorbitant prices keep the best drug out of reach. And nine years after the U.S. Food and Drug Administration (FDA) approved a pneumococcal vaccine able to dramatically reduce the number of children dying, the vaccine remains expensive, is marketed in a highly impracticable form and is not available in the vast majority of least-developed countries where it could reduce unnecessary deaths.

We need medical innovation, but innovation is meaningless if the medicines it produces are not affordable enough for us to access.

It is vital that the EWG, when assessing proposals for R&D financing examines carefully how access to the resulting products will be achieved. New ways to finance essential health R&D in a sustainable matter mean that R&D costs must be separated from the end price of products.

The Expert Working Group should analyse any proposals for their ability to both drive innovation and ensure sustainable access in the long-term.

What this means for a prize fund for TB diagnostics

Médecins Sans Frontières' experience in charting the reality of access to essential medicines in other disease areas indicates that it is important to address the problem of how the cost of any test will be dealt with - from the outset. While the prize specifications should thus include the need for any diagnostic to be low-cost, there is also a need for mechanisms to be included in the prize design, in order to ensure the sustainability of low prices in the long-term and the ability to scale up production. This is consistent with the concept of a prize fund providing the financial reward through a prize, rather than through high prices based on a market monopoly.

This is a complex issue in relation to diagnostics, and does not just involve questions of IP, but also touches upon questions more concerned with technology transfer and manufacturing capacity. Such mechanisms could include, for example, ensuring that the prize winner licence all patents and know-how to a licensing pool, which would manage the licensing of such rights to third party manufacturers. If competition from different manufacturers of the same product – which has proven to be the most effective way in the field of medicines both as a catalyst for price reductions and to ensure affordable prices in the long-term - is not feasible, then the prize reward should be made dependant on the winner providing guarantees that the products will be of sufficient quantity and quality, and priced at long-term affordable rates in developing countries.

Innovation by itself is of little value to people suffering from TB if the diagnostic tools developed are unavailable though cost or other issues to the people who need them.

In addition, a number of other barriers to the development of such a diagnostic need to be taken into account when developing a prize. The need for collaborative research, for example, is necessary to avoid duplication of effort and to help accelerate scientific progress notably in basic science and discovery of antigens and biomarkers. Any prize must therefore include incentives for open collaboration and access to knowledge and be sufficient to overcome any IP barriers that might surround its development, in addition to inhibiting access to an affordable product. It should also be structured with intermediate prizes to reward solutions to key technical challenges. The inclusion of such intermediate rewards can encourage a wider range of participants and increase the chances of ultimate success.

Conclusions

The Expert Working Group must assess each proposal of alternative financing mechanism according to specific criteria, including: whether it responds to a determined medical need, and whether it allows for sustainable access to developed products.

While we have focused here on tuberculosis and the idea of a prize fund to finance the development of a TB diagnostic, these specific criteria apply to other alternative mechanisms to boost research and development of new tools for other diseases that disproportionately affect developing countries – the Working Group must assess each mechanism in this light.

For numerous other proposals exist. Bolivia and Barbados have also proposed prize funds for the development of new medicines and diagnostic tools for Chagas disease. Patent pools, such as the one for second-line antiretrovirals medicines currently being examined by international drug agency UNITAID, have the potential to accelerate access to more affordable medicines and to stimulate the development of innovative products such as fixed-dose combinations. While the

UNITAID pool will focus on AIDS medicines initially, the patent pool model should be explored by the EWG to see whether it could also help improve access and boost innovation in other neglected disease areas.

A sustainable policy that tackles the fundamental problem of a monopoly-based innovation and access system is still lacking. Initiatives that can quickly yield results are needed, such as voluntary and compulsory licensing, patent pools, and implementation of pro-access national IP laws. While individual initiatives are important, work must begin on longer-term systemic changes that will provide both health needs-driven R&D and equitable access.

The EWG needs to examine such proposals, including for a biomedical R&D treaty. The Global Strategy called on WHO to *“encourage further exploratory discussions on the utility of possible instruments or mechanisms for essential health and biomedical R&D, including inter alia, an essential health and biomedical R&D treaty.”*

The Expert Working Group must drive forward these proposals ready to report back to governments for the 2010 World Health Assembly. It must identify specific proposals that match the criteria required, address medical needs and have the potential to effect change for both innovation and access.

The Group must also determine for each mechanism considered to be promising what concrete steps are necessary in order for the work to advance. These need not wait until its final report. The EWG should recommend to WHO the hosting of meetings prior to its final report, in order to explore promising mechanisms in more detail.

In its final report to governments, the Expert Working Group must not limit its work to a mere survey of proposals. Rather, its final report must be operational and provide an indicative workplan as to how to take forward the proposals identified to boost research and development for diseases that disproportionately affect developing countries, in a way that ensures access to the products thus developed.