



HOW A **GLOBAL R&D CONVENTION**

**COULD FILL THE GAPS LEFT BY TODAY'S
MEDICAL INNOVATION SYSTEM**

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“ Today, a growing injustice confronts us. More than 90% of all death and suffering from infectious diseases occurs in the developing world. Some of the reasons that people die from diseases like HIV/AIDS, tuberculosis, sleeping sickness and other tropical diseases is that life saving essential medicines are either too expensive, are not available because they are not seen as financially viable, or because there is virtually no new research and development for priority tropical diseases.

This market failure is our next challenge.

The challenge however, is not ours alone. It is also for governments, international government institutions, the pharmaceutical industry and other NGOs to confront this injustice. What we as a civil society movement demand is change, not charity. ”

Nobel Lecture delivered by Dr. James Orbinski, Médecins Sans Frontières International President 1998-2001, after MSF was awarded the Nobel Peace Prize in 1999.

More than a decade after the international medical humanitarian organisation Médecins Sans Frontières (MSF) accepted the Nobel Peace Prize with these words, our field teams still grapple every day with the fact that the drugs, diagnostics and vaccines needed to treat patients are unavailable, unsuitable or unaffordable.

This is a direct consequence of today's medical innovation system. Building on a decade-long process of analysis and deliberations, experts at the World Health Organization have now recommended that it is time to change the way medical research and development (R&D) is conducted, in order to address the needs of developing countries. Governments now have an opportunity to support this landmark recommendation and start negotiating a binding convention on biomedical R&D that could fill innovation gaps.

Why today's R&D model doesn't work for the needs of developing countries

The current R&D system is driven by market forces, not health needs, and relies overwhelmingly on the patent system to recoup R&D costs by charging high prices for the medical tools that reach the market. This creates two key problems.

Firstly, the needs of people in wealthy countries trump the needs of people in poor countries. When people affected by a given disease are too few or too poor to compete with markets in wealthy countries, medical challenges go unaddressed.¹ Since wealthy country needs drive innovation, tools primarily designed for high-infrastructure, resource-rich environments are only subsequently rolled out for use in resource-limited settings—even if they may not be practical to use or are not designed for the disease burden, or indeed the specific disease strains in developing countries.

Secondly, when medical tools do exist – because the diseases affect rich and poor countries alike and the population of patients in wealthy countries is enough of a market pull – they are often priced out of reach. This holds true for new HIV/AIDS and cancer drugs for example. This has led to bitter disputes as those seeking to enforce patent-protected monopolies collide with those seeking to secure the widest and most affordable access to new medical tools.

Over the past ten years, product development partnerships (PDPs) have been created to fill some of the innovation gaps and new funding from philanthropic foundations and governments has been forthcoming. MSF has tried to play its part in addressing the R&D gaps too. In 2003, MSF co-founded the Drugs for Neglected Diseases initiative—together with several governmental research institutions—and continues to be one of its core funders.² Through our field operations we also participate in product innovation and introduction of new products wherever we can.

These efforts have resulted in some urgently needed improvements. However, on the whole these efforts have been ad hoc, inadequate and are not part of a sustainable system designed to meet today's developing country health challenges.

There is an urgent need for a complementary system to drive and fund innovation for people in developing countries.³ Such a new system needs to speed up the development of vaccines, diagnostics and drugs designed for the medical needs of people in developing countries.

The Wish List: What is Needed

- **Diagnostics:** small, simple-to-use, robust, reliable and inexpensive diagnostics and monitoring tests that can be used at the lowest level of the health care system, as close as possible to the patient's bedside.
- **Drugs:** a well-filled pipeline of new drugs across the disease areas that affect developing countries. We need drugs that are effective, well tolerated, inexpensive and adapted to resource-poor settings (heat-stable, low pill burden, treatment regimen as short as possible). Newer generation drugs need to be ready when resistance develops.
- **Vaccines:** formulations and presentations suited for resource-limited settings – vaccines that are heat-stable, can be administered without an injection and require less doses or have flexible dosing schedules. We need additional, affordable vaccines to target the diseases or specific strains of pathogens that are most common in developing countries.



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Materials are readied for a vaccination campaign in the Democratic Republic of Congo. Additional R&D is needed to produce vaccines not only aimed at the appropriate strains most common in developing countries, but also that do not require refrigeration prior to being administered.

❖❖❖ What could a Convention on health R&D look like?

By creating a binding Convention on health R&D, countries would agree to a sustainable system of medical innovation with adequate and predictable financing, to deliver products that are focused on the priority health needs of developing countries.

The Convention would create norms to ensure that the fruits of innovation and new medical products are accessible and affordable.

How would this work? The detailed terms and conditions would be negotiated by countries in a process led by WHO, as was done for the Framework Convention on Tobacco Control, which was created under article 19 of the WHO Constitution and which now has over 160 country signatories.

The WHO Consultative Expert Working Group on R&D: Financing and Coordination (CEWG) has just submitted its final report concluding that a Convention could bring about several concrete advances.⁴ It could:

❖❖❖ ESTABLISH AN EVIDENCE-BASED, INCLUSIVE PROCESS THAT SETS THE PRIORITIES FOR MEDICAL R&D:

WHO and its partners have already defined the R&D agendas for some diseases. A more comprehensive effort across all medical needs should now be undertaken through the R&D Convention. Why is this needed?

- It could steer innovation towards **developing country needs that commercially driven R&D is failing to address**. In our work in around 65 countries, MSF field doctors bear witness to the many different gaps that exist. Five of the most salient gaps in medical innovation today – suitable vaccines, unmet needs in HIV/AIDS, antibiotic resistance, diagnosis and treatment of neglected tropical diseases (NTDs), and diagnosis and treatment of tuberculosis – are described in this report.
- It could overcome the problem of the fruits of innovation all too often being **ill-suited to address developing country needs**. Today's reality is one where products are developed first and foremost for rich countries and only in a second stage are rolled out in the developing world – without adaptations necessary for resource-poor environments. Developing country medical needs are different – vaccines are a good illustration of this fact. Rotavirus vaccines developed for high-income markets are less targeted to the needs in some sub-Saharan African countries, where different strains of the virus are common. Conditions vary too. Poor health infrastructure means products need to be as simple as possible, to work in remote areas or with minimally qualified health staff. What we need, for example, are measles vaccines that can be administered without a needle. But most vaccines today, across a wide range of diseases, come with constraining cold chain requirements and require us to trace the same child several times because of multiple dosing schedules.

❖❖❖ LINK GLOBAL R&D PRIORITIES WITH ADEQUATE AND SUSTAINABLE FINANCING:

Today there is no link between existing initiatives to determine R&D priorities on the one hand, and initiatives to boost the flow of funding for medical innovation on the other. This means that beyond what advocates can do to draw attention to unmet medical needs, there is no process to stimulate R&D into priority health areas, leaving us reliant on an ad hoc patchwork of insufficient, uncoordinated R&D efforts, with priorities set by philanthropic institutions, donor governments and corporate social responsibility programmes, rather than patient needs.

Medical priorities should be linked with binding financial commitments through the R&D Convention. What could this achieve?

- It would ensure money is driven to an area defined as a medical priority. The research needs and required funding for **tuberculosis**, for example, have been clearly defined by WHO, through a process involving a wide range of partners.⁵ The 2011-2015 Global Plan to Stop TB provides detailed R&D targets for drugs, diagnostics and vaccines, including estimated costs for each area.⁶ However, as this priority setting is not linked to the provision of funding, it is not possible to adequately drive the development of the needed tools. TB research funding is falling far behind the targets set by the Global Plan. In 2010 TB drug development received only 31% of the annual \$740 million Global Plan target and funding for TB diagnostics only reached 14% of the \$340 million target.⁷
- Research priorities have also been set by WHO and UNAIDS for **HIV/AIDS**⁸ but because there is no link between priority setting and funding, there is no way to ensure those priorities are advanced. With HIV, the market alone may be unable to develop long-acting formulations which could enable greater scale-up in developing countries. The same is true for products for children, because paediatric HIV has largely been eliminated in the developed world. A Convention could put in place the financing and appropriate incentives to link developing-world HIV R&D needs with adequate funding.
- It would provide a more secure basis for today's fragile innovation in the field of **neglected tropical diseases**. Severely neglected by the commercial system, R&D for visceral leishmaniasis, sleeping sickness and Chagas disease attracted less than \$150 million in 2010.⁹ As the current system is largely reliant on philanthropy and the largesse of a few donor countries, there is an ever-present risk that certain areas could suddenly be dropped if donor priorities were to change. Products for NTDs currently in the development pipeline need sustainable and predictable financing to make it to the market.



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A woman in Mumbai, India prepares to take her medicines for drug-resistant TB after receiving her painful daily injection.

Who should pay what?

The level of contributions from each country that is a party to the Convention would be determined through the Convention's negotiation process. This should be based on the principle of fair burden sharing, reflecting an individual country's capacity to pay. The WHO experts' report recommends that *"all countries should commit to spend at least 0.01% of GDP on government-funded R&D devoted to meeting the health needs of developing countries in relation to product development"*.¹⁰

The WHO experts suggest that countries could fulfil their financial commitments in different ways – both by paying directly for medical innovation undertaken to attain the Convention's objectives, and/or by contributing to a pooled fund.¹¹ They suggest that between 20-50% of a country's total funding obligation should go to a pooled funding mechanism.¹²

The report also recommends a number of direct and indirect taxation proposals – including the introduction of a financial transaction tax with a proportion dedicated to health R&D – to raise required funds.¹³

❖ ENSURE MONEY IS USED TO STIMULATE R&D IN THE MOST EFFECTIVE WAY:

With donor funds increasingly scarce, funding should support innovation models that allow limited funds to go further. Today, drug development by the pharmaceutical industry is very expensive raising questions about its effectiveness. Industry even claims R&D cost of \$1.3 billion per drug,¹⁴ although actual costs are likely significantly lower.¹⁵ Relying on alternative models of research and development, and harnessing the lower costs of emerging country manufacturers will therefore be critical.

An R&D Convention could promote more effective R&D.¹⁶ What could this achieve?

- It could harness **collaborative models to deliver R&D** in cost-effective ways. DNDi has delivered new treatments at a fraction of this cost, reporting that 'within nine years and with €120 million [\$158 million], it has developed six new treatments for neglected diseases, which significantly improve upon existing treatment options, and has built a promising pipeline including 11 new chemical entities'.¹⁷ Moreover, DNDi estimates that the cost of fully developing a new chemical entity would cost between \$130-235 million¹⁸ – a fraction of the \$1.3 billion cost claimed by industry.

- It could avoid wasting precious donor resources by **harnessing the capacity of emerging country manufacturers** to produce lower-cost products. Thanks to the lower costs of the Serum Institute of India, for example, the Meningitis Vaccine Project successfully delivered a vaccine for countries across the Meningitis Belt at an affordable price of under \$0.50 per dose. On the other hand, the Advance Market Commitment for pneumococcal vaccines – which provides a \$1.5 billion incentive for manufacturers to sell the vaccines for use in developing countries – mainly benefits multinational companies rather than incentivising new suppliers in emerging markets from investing in development and production of a cheaper product.¹⁹
- It could pull **more actors** into R&D. Grants and funding to product development partnerships are welcome but alternative incentive mechanisms are also needed to entice more actors to get involved. The WHO experts report recommends funding be allocated through prizes.²⁰ Prize funds bring new resources to a given field of research but also, unlike grant funding which is only able to target one potential research group at a time, allow several promising research proposals to be taken forward, by paying out at regular milestones on the achievement of results. This means that several different approaches can be tried. At the same time, prizes only pay for results, so if nothing significant comes forward, resources will not be wasted. One concrete example that MSF has explored is the utility of prizes for developing a point-of-care TB diagnostic.²¹ Discovering and validating biomarkers is a priority research area to advance the development of a simple TB diagnostic,²² a prize could be particularly useful if targeted to this specific area of research. MSF is exploring the feasibility of a prize to incentivise the discovery of new biomarkers to assess parasitological response to treatment of Chagas disease, a first step towards a test-for-cure.

❖ ESTABLISH NORMS TO ENSURE ACCESS TO THE FRUITS OF R&D:

Today's system of medical innovation is one that is predominantly dependent on patent-protected monopolies, and the promise of high prices these bring, to steer R&D. That products are then unaffordable for developing countries is very much an afterthought, leading to repeated battles pitching patents against patients. Initiatives based on the principle of de-linking or separating the cost of R&D from the price of the resulting product are needed so that the cost of R&D is paid for up-front through grants or rewarded by a prize and does not need to be recouped through a high product price.

The R&D Convention could set norms to facilitate access to the fruits of innovation and affordability of the final products. What could such norms achieve?

- They could **consolidate best practices into global norms on de-linkage**, technology transfer, and price and supply commitments so they become the benchmark for R&D efforts designed to meet the unmet health needs of developing countries. The Meningitis Vaccine Project (MVP), a partnership between PATH and WHO which resulted in the development of a vaccine against Meningitis A, is an example of what can be achieved when de-linkage is used to ensure that medical needs and affordability concerns are built into the product development process from the outset. The product was designed to meet the specific needs of the Meningitis Belt in sub-Saharan Africa, and used technology transfer to a developing country producer linked with commitments from the producer to a minimum supply at an affordable price. The MVP identified and licensed appropriate technology from the US FDA and reached an agreement with the Serum Institute of India (SII) to develop and produce the new vaccine at an affordable price. In exchange for price and supply commitments, SII benefited from transfer of technology and know-how while PATH funded the clinical trials. The new MenAfriVac vaccine was WHO-prequalified in June 2010 and rolled out, including by MSF, in countries across the Meningitis Belt, and at an affordable price of under \$0.50 per dose.
- They could encourage **openness and sharing of medical research**, overcoming the problem of intellectual property barriers preventing access to the results of **early stage research**. The WHO experts recommend that R&D outcomes be considered as public goods,²⁶ freely available for further research and production. The R&D Convention could therefore set norms that any group obtaining funding through the Convention would need to make its knowledge freely available to others *“to use without legal or contractual restrictions”*.²⁷ The Open Source Drug Discovery consortium in India is an example of advancing R&D through open knowledge.²⁸ The WIPO Re: Search Consortium for Neglected Tropical Diseases provides access to pharmaceutical compounds²⁹ but the norms for access are unacceptably low. Indeed, the Consortium provides royalty-free licences for NTDs, malaria and TB for least-developed countries only, leaving out vulnerable populations in other countries, such as patients with kala azar in India or Chagas disease in Bolivia or Paraguay. The R&D Convention needs to be more ambitious and take the promotion of public health as its starting point. Norms on licensing, should, at a minimum include all endemic countries.

What should the money be used for?

The WHO experts recommend that *“R&D under the Convention should focus on the development of health technologies for Type II²³ and Type III diseases as well as the specific needs of developing countries related to Type I diseases”*.²⁴

“The additional funding generated through fulfilling the 0.01% commitment should be used in particular with the following objectives:

- *To fund R&D in all sectors (public, private and public private partnerships) to address identified health needs of developing countries in relation to the types of R&D defined in our mandate;*
- *To fund all phases of R&D, in particular utilizing open approaches to R&D and prize funds as well as the costs of late-stage development, including clinical trials;*
- *To help build R&D capacity in developing countries and promote technology transfer”*.²⁵

- They could allow **affordability to be built into product development from the outset**. Affordability should be considered for all stages of medical innovation, from basic research through to product development and delivery in order to ensure innovation and access. Innovation is only useful if it is accessible to the patients that need it and yet many new medical products that stand to save lives and reduce illness in developing countries remain unaffordable. Affordability needs to be considered from the very start of a product development process – selecting a low-cost design or low-cost producers for example. A new diagnostic test for TB – the Xpert MTB/RIF – endorsed by WHO in 2010 and an important advance for TB care allowing for quicker results – is expensive to manufacture and expensive to purchase: even at the discounted prices negotiated for 150 low- and middle-income countries, each test still costs close to \$17 – with three tests needed per person – and each machine costs up to \$17,500.³⁰ This prevents making the test widely available in developing countries.
- They could **ensure intellectual property is not a barrier** to newer medical products developed with Convention funding. Competition from multiple producers has been shown to be the most effective in bringing prices down sustainably to affordable levels.³¹ The example of generic competition slashing the price of the first-line HIV regimen by 99% from over \$10,000 in 2000 to under \$100 today³² is illustrative here. However, where patent barriers in key generic-producing countries prevent competition, prices remain high. The lowest price paid for darunavir by any recipient of the Global Fund, for example, is currently \$1,232 for one year’s treatment course;³³ for etravirine, the lowest price paid is \$5,840.³⁴ The Convention should include norms to ensure that any products developed with funding through the Convention should be free of intellectual property barriers, through licensing agreements to multiple manufacturers, so that competition is used to maximum price-reducing effect.
- They could set **supply and price commitments to ensure affordable access even when price-lowering competition is not expected**. Where the market for a product developed through the Convention is too small to support robust competition, for example in the case of treatments for some neglected tropical diseases, affordable access could be ensured by securing price and supply commitments from the developer. Such commitments would need to be agreed at the outset of the R&D process.
- They could harness the potential of lower-cost developing country manufacturers thanks to **technology transfer** as exemplified with the development of the meningitis A vaccine.



Blood samples are tested in Maitikoulou, Silambi, Central African Republic – one of several steps used to determine if a donor is carrying the sleeping sickness parasite. Diagnostics for the most neglected diseases require additional research in order to make them as simple-to-use as possible, ideally even outside of the laboratory.

WHO discussions leading up to the biomedical R&D Convention proposal

In 1996 the World Health Assembly agreed to begin negotiations of the WHO Framework Convention on Tobacco Control (FCTC) under Article 19 of the WHO Constitution. In 2003, the FCTC was adopted as the first treaty under WHO auspices.

In 2006, the report by a WHO-convened Commission on Intellectual Property, Innovation, and Public Health, called on WHO to take the lead and address issues where intellectual property acts as a barrier to innovation and access to medicines.³⁵ An Intergovernmental Working Group on Public Health, Innovation and Intellectual Property was formally established and charged with creating a framework to secure sustainable R&D for the diseases that disproportionately affect developing countries.³⁶

In 2008, after two years of negotiations, countries adopted the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property.³⁷ One of its outcomes was the creation, at the World Health Assembly in 2010, of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG).

The report of the CEWG was published on 5 April 2012. Its central recommendation is that Member States begin a process towards establishing a legally binding convention on R&D for the health needs of developing countries, under Article 19 of the WHO Constitution.³⁸

❖❖❖ Five deadly gaps: why an R&D Convention is needed

Here we highlight five areas where medical innovation is failing, to illustrate in which fields a binding convention for health R&D could bring about change.

1. VACCINES: ILL-ADAPTED PRODUCTS

“ Keeping the cold chain to conserve the vaccines at the right temperature, when it’s 45 degrees Celsius outside is a major challenge. In some rural areas, just maintaining the fridges in working order is hard to guarantee, and we need to produce enough ice packs so that the vaccines are still cold by the time we get to the children. You can imagine how many icepacks are needed, so even getting the vaccines out to the villages is a huge logistical effort in itself. ”

Dr. Michel Quéré, MSF Medical Advisor for programmes in Niger, Chad and DRC

- The current system of R&D has in recent years successfully stimulated development of new vaccines focused on the needs of wealthy countries. Sometimes these products are well suited to epidemiological needs, but sometimes they are not. The two WHO-prequalified vaccines against rotavirus, which causes diarrhoeal disease, target the predominant

rotavirus strains found in the US even though initial research results indicate that the diversity of genotypes found in some sub-Saharan countries may require a refined rotavirus vaccine that is more appropriate for local rotavirus epidemiology.³⁹

- Current R&D has largely failed to produce vaccines that are adapted to the specific logistical needs of developing countries. New technologies that could eliminate the need for cold chain or enable administration without injection are not being sufficiently pursued for developing countries. The Global Polio Eradication Initiative has been able to rely on lay community health workers to vaccinate children in remote villages which has been possible, at least in part, because the vaccine is given orally. More investment is needed into vaccines that can be inhaled, administered orally or through patches or micro-needles.



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27-year-old Emmanuel Misota has brought his 3-year old child Bienvenue for malaria treatment. Improved treatments for malaria will be needed in the future to address growing resistance, and collaborative models for R&D could help deliver them at a fraction of today’s development cost.

- There is a shortage of R&D for diseases that predominantly affect developing countries including TB, cholera, typhoid, dengue, malaria, and other tropical diseases. Beyond philanthropic and sporadic government support there is no model for incentivising the research and development process from discovery to development.

2. HIV: UNMET DEVELOPING COUNTRY NEEDS

“One important antiretroviral drug for children is lopinavir/ritonavir. It exists as syrup which has to be stored at a temperature between two and eight degrees until the moment it is dispensed. After that, it can be stored for only six weeks but only at a temperature less than 25 degrees, so we have to advise families to dig a hole in the ground and keep the medicine in a clay pot in an effort to keep it cool enough. Obviously this is very impractical. The syrup tastes terrible to children and contains more than 40 per cent alcohol, so it really is not optimal to be offering this to a young child. We urgently need another solution.”

Dr. Marianne Gale, MSF Medical Advisor for paediatric tuberculosis & HIV

- Although HIV treatment in developing countries has benefitted from the development of highly effective treatment with reduced side effects and alternative treatment options when treatment failure occurs, the innovation needs for developing countries are still acute. There is real potential for transforming treatment through the development of long-acting formulations – ideal for decentralising care as they do not have to be taken every day – and low-cost synthesis routes that could lead to significant price decreases.⁴⁰ However, it is doubtful that pharmaceutical companies will find it profitable enough to take this forward and so these much needed advances may never come, unless specific action is taken.
- The needs of children living with HIV have been consistently overlooked. This is because the ‘market’ of children living with HIV is considered to be too small to incentivise commercial investment. There are some 3.4 million HIV-infected children, but almost all of them live in the developing world making childhood HIV a neglected disease.⁴¹ WHO recommends immediate antiretroviral therapy for all HIV-infected children less than two years of age but the safety and appropriate dosing of some key antiretroviral agents used in adults have not yet been established in children and appropriate formulations simply do not exist.
- Viral load is increasingly recognised as a critical tool to monitor patients on ART. As far back as 2003, WHO guidelines recognised the importance of viral load and at that time expressed hope that increasingly affordable methods of determining viral load would become available to support treatment monitoring.⁴² The latest WHO guidelines recommend countries begin to phase in viral load. However, a decade later, there is still no simple, adapted and affordable tool available that would allow governments in resource-limited settings to be able to routinely offer viral load monitoring, although there are a few promising devices in the pipeline.

3. ANTIBIOTIC RESISTANCE: MEDICAL INNOVATION HAS STALLED

“A number of previously treatable diseases – including major childhood killers in Africa – are becoming far more difficult and expensive to treat because of antibiotic resistance. In practice, this may mean that many of these diseases may not be treated at all.”

Nathan Ford, Medical Coordinator, MSF Access Campaign

- Antibiotic resistance in poor and conflict-affected settings threatens the gains made in treating life-threatening bacterial infections, such as sepsis, pneumonia, dysentery and hospital-acquired infections. MSF has documented resistance across a broad range of pathogens and settings.⁴³ The cost of these drug-resistant infections will be borne by already highly vulnerable patients, including malnourished children, people living with HIV/AIDS and hospitalised patients.
- Among other strategies, addressing antibiotic resistance requires the development of new classes of antibiotics and adapted, point-of-care diagnostics which can guide the appropriate use of antibiotics and reduce overuse (for example by distinguishing between viral and bacterial infections). Within the current R&D system, the development of new antibiotics has been neglected. Companies have deemed them unattractive markets because health professionals would necessarily try to reserve and restrict the use of new antibiotics – which would therefore keep sales low. Short treatment courses for acute conditions are also less profitable than chronic conditions which require long-term treatment. Incentives are needed to stimulate R&D into new antibiotics and point-of-care diagnostics; in return product developers would need to sell at low prices and offer licenses to other manufacturers.⁴⁴

4. NEGLECTED TROPICAL DISEASES: MINIMAL INVESTMENT

“Routinely our doctors have to perform lumbar punctures to diagnose people with advanced stage sleeping sickness. Performing a spinal tap under field conditions is painful and risky. When I was in charge of MSF’s sleeping sickness programmes in the Republic of Congo, even the prospect of the test was sometimes too much and people suspected of having the disease took to their heels rather than undergo the procedure.”

Dr. Unni Karunakara, MSF International President

- For over 20 years MSF has run specific case management and control programmes for three NTDs that are fatal if not treated: Chagas disease, kala azar (or visceral leishmaniasis) and sleeping sickness. Most of the diagnostics and treatments available are largely unsuitable, as they require specially trained staff and strong logistical support. For example, the diagnostic tree for sleeping sickness encompasses at least three different tests, including a lumbar puncture to collect cerebro-spinal fluid for microscopic examination. In practice, only expert teams can fully diagnose patients in the African remote settings where sleeping sickness thrives. Treatment of adults with chronic Chagas disease has limited efficacy and numerous possible side effects. Because of these drawbacks, many clinicians in Latin America dare not provide anti-parasitic treatment to patients with Chagas disease older than 15.

- The field of NTD research is particularly neglected. According to an MSF study, only 18 of the 1,556 new drugs developed between 1975 and 2004 were for tropical diseases – and eight of those were for malaria⁴⁵. Advances to date have come from repurposing existing drugs, establishing new combinations of existing drugs and developing paediatric formulations. DNDi, for example, has facilitated the development and implementation of six improved treatments.⁴⁶ These represent benefit for people afflicted by the diseases but are not the scientific breakthroughs on the scale that is needed. There are now a limited number of promising new chemical entities entering clinical trials. Increased investments are needed to support a full replenishment of pipelines and the implementation of clinical trials for all the compounds that have passed the first stages of discovery. But the model for securing innovation for NTD is fragile and largely based on philanthropy and the largesse of a few donor countries. Only \$148 million was spent on R&D for leishmaniasis, sleeping sickness and Chagas disease in 2010.⁴⁷
- The most widely available diagnostic method, microscopy, detects less than half of cases. MSF has advocated for the development of a simple to use and accurate point-of-care diagnostic test for TB. Together with experts, MSF defined the needed specifications of such a test and drew up a roadmap towards its development.⁵⁰ Despite wide agreement on the need, a point-of-care test is still far off and is still not attracting the necessary investment.
- A new diagnostic test for TB – the Xpert MTB/RIF – was endorsed by WHO in 2010 and has been implemented by MSF in 15 countries. The arrival of this test onto the market was an important advance for TB care allowing for quicker results. However, as it requires a relatively stable, uninterrupted electric supply and a low temperature to function, it will be difficult to roll out the machine in peripheral settings. It is also still a sputum-based test meaning that for people co-infected with HIV and for children it remains of limited use, and is not the simple, point-of-care test our field teams need. This shows the limitations of relying solely on adaptation to fulfil developing country needs.

5. TUBERCULOSIS: DECADES OF NEGLECT

“Most of the time, where we work, you have to just make a decision based on your clinical observation – ‘should I or should I not treat this child for TB?’ And making that decision when you’re talking about the life of a child is really challenging. If we could have a point-of-care test for TB that could say yes or no to TB in just fifteen minutes and could be used in the most remote kind places where we work, it could transform our work and so many children’s lives.”

Dr. Bern-Thomas Nyang’wa, MSF Advisor for tuberculosis

- Although three product development partnerships were established to develop new drugs, diagnostics and vaccines for TB and although some drug companies have restarted limited investment into drug development – often as a goodwill gesture – the depth of investment has been insufficient to ensure the necessary breakthroughs.
- No new TB drugs have come to market since the 1960s. The drug pipeline for tuberculosis, without further improvement in the number and quality of compounds, will not be able to produce the number of new drugs needed in the coming years to support the rational selection and development of new drug regimens needed to eliminate tuberculosis.⁴⁸ TB continues to be an unattractive market for companies, with only thirteen drugs in clinical testing, eight of which are new chemical entities.⁴⁹
- There are also rising numbers of children who are infected with drug-resistant forms of TB, who are very difficult to diagnose and have no paediatric formulations of the drugs required to treat them.
- The existing vaccine can only reduce severe complications in children, it cannot prevent infection.

••• Conclusions and Recommendations

“On balance we consider that the time has come for Member States to begin a process leading to the negotiation of a binding agreement on R&D relevant to the health needs of developing countries. This would also be in order to put on a secure footing the implementation of the GSPA-PHI [Global Strategy and Plan of Action on Public Health Innovation and Intellectual Property] which Member States agreed in 2008, and in particular the sustainable financing of R&D⁵¹”

The WHO Consultative Expert Working Group on R&D: Financing and Coordination

The time to act is now. Member States must not allow the momentum to be lost, and should seize this opportunity to consolidate and build on the fragile gains that have been made over the past ten years.

By entering into intergovernmental negotiations to agree a set of norms to guide biomedical R&D relevant to the health needs of developing countries, Member States have the opportunity to ensure that the R&D needs of developing

countries are no longer overlooked. Governments have the opportunity to foster the development of vaccines, diagnostics and drugs that are designed for the developing world, not merely adapted from the rich world; to consider the specific needs of patients in developing countries upfront at the start of the innovation process; to break the link between the cost of R&D and the price of products; to ensure that the fruits of such innovation are accessible and affordable and to move beyond the ad hoc patchwork of limited efforts we have found so far, to a sustainable R&D framework based on agreed priorities.

Following the recommendation of the CEWG report, at the upcoming World Health Assembly in May, Member States should agree to begin a process leading to the negotiation, under Article 19 of the WHO Constitution, of a binding agreement on R&D relevant to the health needs of developing countries.



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MSF integrated Chagas screening and treatment into its primary healthcare services in Colombia in 2009. Chagas disease is endemic in most Latin American countries, yet available treatment has only limited efficacy in chronic cases and there is no diagnostic test of cure.

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