

MEDICAL INNOVATION FOR NEGLECTED PATIENTS

Important Progress Over Past Ten Years, But “Fatal Imbalance” Persists



South Sudan 2012 © John Stanney/vii

Over the past half century, there have been unprecedented improvements in health outcomes, spurred in part by unparalleled scientific progress in the pharmaceutical sector. Yet access to the benefits of medical progress and scientific advancement has not been equitably shared and many innovation gaps remain.

THREE FUNDAMENTAL PROBLEMS

There are three fundamental problems with medical innovation today.

First, global public health needs are not in the driving seat. Regardless of how great the needs may be, where commercial potential is weak, there is little “pull” to develop new technologies. The innovation cycle is broken, with few or no incentives for the development of effective, safe, quality, suitable and affordable health technologies – leading to needless suffering and death. There are numerous illustrations of the lack of suitable diagnostics, vaccines and medicines (see text boxes). In addition to innovation gaps for Chagas disease, drug-resistant tuberculosis (DR TB), and vaccine-preventable illnesses, other examples include diagnostics and treatments for leishmaniasis and human African trypanosomiasis (sleeping sickness); medical tools such as new diagnostics and appropriately adapted formulations for children with HIV/AIDS and TB; and new antibiotics to address the rise in antimicrobial resistance, which has made treating previously treatable diseases more difficult.

Second, as a result, developing countries must often “make do” with innovation that primarily caters to conditions in developed countries. Medical tools are too often developed first for developed countries and only rolled out in resource-limited settings in a second stage. Newer vaccines against rotavirus, for example, may have the potential to prevent lethal childhood diarrhea in Africa, but they have been developed with resource-rich conditions in mind. Rolling them out in developing countries will pose severe strains because these vaccines are incredibly bulky and come with considerable cold chain capacity requirements.ⁱ These worrisome findings should come as no surprise, however. If new medical tools are developed for and tested in developed countries alone, the needs of populations in developing countries will inevitably be an afterthought.

Third, even when there is enough of a profit incentive to drive innovation – for example when diseases affect both developed and developing countries alike – the resulting products are too often priced out of reach. Developing countries are not the only ones to be hit, as ever higher prices for new medical tools strain the healthcare budgets of developed countries as well, posing access barriers to increasing numbers of people. New drugs to treat HIV or cancer can cost hundreds of times more than a person’s average annual income, and the battle for access increasingly has to be waged drug by drug, country by country, company by company.

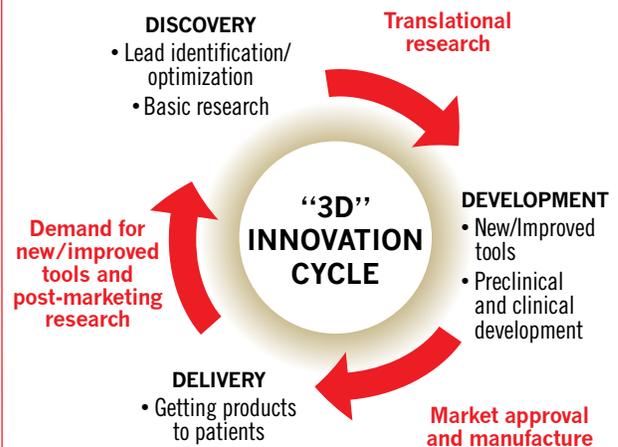
Medical innovation must aim to change practice, for the benefit of patients. But ideas, knowledge and inventions can only benefit patients who have access to the fruits of innovation. What is needed, therefore, is not just innovation – but both innovation and access.

The WHO Commission on Intellectual Property Rights, Innovation and Public Health: The Innovation Cycle

Lack of medical innovation and lack of access to medical tools, particularly as they affect developing countries, were first acknowledged as serious problems by the World Health Organization (WHO) over two decades ago. The need for governments to take concerted action has been clear since the publication of the report of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) in 2006ⁱⁱ.

The report conceived of research and development (R&D) as a cycle, with three major phases feeding into each other: discovery, development and delivery.

Innovation Cycle



The report of the Commission on Intellectual Property Rights, Innovation, and Public Health (2006), WHO.

The driving force behind the innovation cycle – the expectation of a high return on investment – has been increasingly recognized as the source of critical failings, particularly for developing countries and neglected people.

2001 – 2012: TEN YEARS ON, WHAT HAS CHANGED?

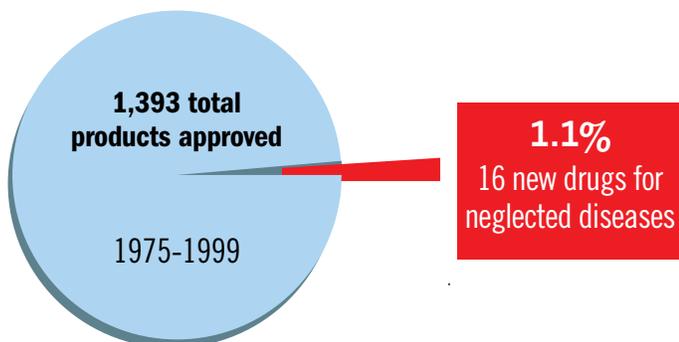
In 2001, Doctors Without Borders/Médecins Sans Frontières (MSF) and the Drugs for Neglected Diseases Working Group – an interdisciplinary think tank that explored alternative models for new drug development, and that subsequently led to the creation of the Drugs for Neglected Diseases *initiative* (DNDi) – released a report on the crisis in neglected disease R&D entitled *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases*.ⁱⁱⁱ

Since then, to what extent have things changed for the majority of neglected patients? The following sections focus on what has – and what has not – happened when it comes to diseases classified as neglected. It is, however, important to acknowledge that for people in developing countries, the burden of disease is shifting, and there is a need for further studies into the R&D needs for non-communicable diseases, or NCDs.

RESEARCH & DEVELOPMENT

In 2001 R&D for neglected diseases at a standstill: In 2001, despite the heavy toll exacted by infectious diseases in the developing world, R&D for drugs to treat infectious diseases in these same areas had ground to a near-standstill.^{iv} From 1975 to 1999, 1,393 new drugs were brought to market globally, but only 16, or 1.1%, were for tropical diseases (including malaria) and TB, despite the fact that these diseases represented 12% of the global disease burden.^v During this same period, 179 (12.8%) new drugs were developed for cardiovascular disease, which represented 11% of the global disease burden.ⁱⁱⁱ Overall, the report highlighted that only 10% of the world’s health R&D was dedicated to illnesses that affect 90% of the global disease burden – a “fatal imbalance” often referred to at the time as the “10/90 gap”^{vi} – and described this state of affairs as a colossal market and public policy failure.

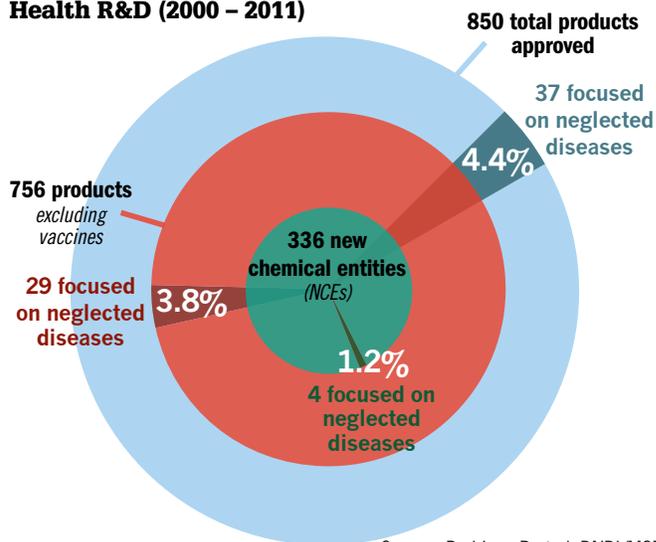
Health R&D (1975 – 1999)



Based on 2004 WHO disability-adjusted life year (DALY) data.

In 2012 Some progress, but pipelines still falling short: In 2012, DNDi and MSF conducted a study to reassess the state of R&D for neglected diseases in the last 12 years.^{vii} Of the 756 new drugs approved between 2000 and 2011, 29 (3.8%) were indicated for neglected diseases, even though the global burden of disease is estimated at 10.5%.¹ Of these, only four were new chemical entities (NCEs), three of which were for malaria, with none for TB or neglected tropical diseases (NTDs). Moreover, as of December 2011, only 1.4% of a total of nearly 150,000 registered clinical trials were focused on neglected diseases, with very few of these trials for NCEs. Looking ahead, estimates from the current pipeline show that an average of 4.7 new products each year (excluding vaccines) could be delivered for neglected diseases through 2018 – a significant improvement, if realized, compared with the 2.4 new products averaged each year for the period 2000-2011 and the 0.6%^v to 1.3%^{viii} new products per year for 1975-1999.

Health R&D (2000 – 2011)



Source: Pedrique B et al, DNDi/MSF forthcoming publication, 2013⁷

These results paint a somewhat mixed picture: important progress has been made, with a greater number of newly approved drug reformulations, repurposed products, and vaccines that have had real patient benefits. But it is far from enough. The overall proportion of NCE approvals for neglected diseases is still insufficient, particularly as compared to other diseases, and highlights the persistence of the “fatal imbalance” between global disease burden and therapeutic product development for neglected diseases.

LANDSCAPE AND FUNDING

In 2001 Few actors in R&D and insufficient funding, public or private: Government and not-for-profit/philanthropic funding for neglected disease R&D totaled only about \$100 million

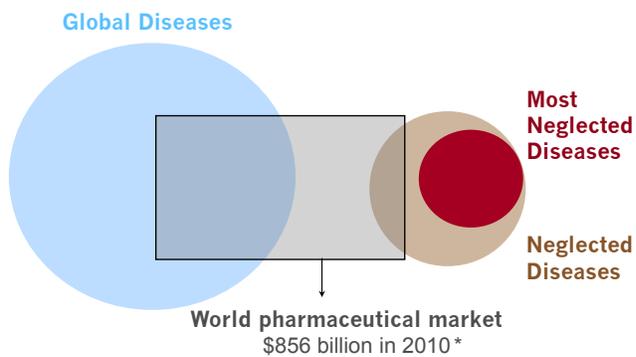
1 Based on 2004 WHO disability-adjusted life year (DALY) data.

DEFINING NEGLECTED DISEASES

A serious, disabling or life-threatening disease can be considered neglected when treatment options are inadequate or don't exist, and when their drug-market potential is insufficient to readily attract a private sector response. Infectious and parasitic diseases that predominantly or exclusively affect people in developing countries are most commonly understood by the term “neglected diseases,” but even within this category a distinction is often made, based roughly on levels of R&D activity, between “neglected” diseases such as HIV/AIDS, malaria, TB, and dengue, for example (where there is more commercial or semi-commercial R&D activity and generally speaking more resources available), and “most neglected” diseases, such as sleeping sickness, leishmaniasis, Chagas disease, Buruli ulcer, and other neglected tropical diseases (where there has typically been little to no R&D activity and few resources). These diseases are distinct from “global diseases,” such as non-communicable diseases, for which both the public health needs and R&D activity are significant, but for which a majority of people affected in developing countries are not of interest for the pharmaceutical market. Innovation is therefore not necessarily adapted to their needs, and technologies that do exist can often be out of reach due to high prices. The shortcomings extend to areas such as antibiotics, where new medicines need to be developed. As low- and middle-income countries now face a double burden of disease, with

both infectious diseases and, increasingly, non-communicable diseases, all areas of market and/or public policy failure – all the instances where the existing system has failed to meet public health needs – must be addressed.

Neglected Diseases Primarily Affect Developing Countries & Lie Outside the Global Pharmaceutical Market



* Source: IMS Health

There is also significant R&D activity for non-medical “lifestyle” conditions – such as baldness, erectile dysfunction, cellulite reduction, and so forth – for which there are no pressing public health needs. This is represented in the graphic as the white space that falls outside the medical needs circles but within the shaded box representing the pharmaceutical market.

per year for TB, malaria, sleeping sickness, and leishmaniasis combined.ⁱⁱⁱ Findings from a survey of the top pharmaceutical companies showed little private sector investment or activity in the field of neglected diseases. In the five years prior to 2001, no company had brought to market a single drug for sleeping sickness, Chagas disease, leishmaniasis, malaria, TB, or other viral, bacterial, or fungal infections (excluding HIV/AIDS).ⁱⁱⁱ The UNICEF/UNDP/World Bank, WHO Special Programme for Research and Training in Tropical Diseases (TDR) was a major player and had been operational for 25 years; most neglected disease products registered were done so with support from TDR, even though funding remained chronically low.

While certain research institutions such as the US National Institutes of Health have always been major funders of infectious disease R&D, particularly for HIV/AIDS, governments by and large have not filled the vacuum left by industry,

particularly for the “most neglected” diseases. Instead, public sector research was increasingly focused on diseases affecting primarily developed countries, actively pursuing possibilities for commercialization. At this time, philanthropic actors like the Bill & Melinda Gates Foundation, Wellcome Trust, and Rockefeller Foundation were beginning to get involved and started playing an increasingly large role in funding public/private partnerships, leading to concerns that governments were abdicating their responsibility and letting the action of foundations act as an “alibi for government inaction.”ⁱⁱⁱ

In 2012 A broader range of actors and initiatives, but insufficient coordination and sustainable funding: Over the past decade, new R&D initiatives have been launched by a broad range of stakeholders including academic groups and emerging countries, including India, Brazil, and South Korea. A majority of pharmaceutical companies are now engaged

to varying degrees in neglected disease research and new programs from traditional donors, such as the European and Developing Countries Clinical Trials Partnership, have been established. Numerous initiatives have also come from developing countries. The emergence of non-profit product development partnerships (PDPs) like DNDi has also been significant, as such organizations now play a dominant role in neglected disease R&D, managing a large proportion of products in the pipeline and around one third of global grant funding (outside of NIH funding).

Undoubtedly, there have been some individual successes that emerged from this proliferation of global health R&D actors – for example, PDPs were responsible for over 40% of neglected disease products registered between 2000 and 2011, including new TB diagnostics and malaria combination treatments. But these advances do not yet represent the kind of “game-changing” scientific breakthroughs that are needed. PDPs and other *ad hoc* R&D initiatives cannot be considered to be *the* solution to the systemic lack of innovation or *the* sole way to address the needs of patients who have limited purchasing power. There is also a need for coordination to set priorities and avoid duplication.

Today, there is an average of \$3 billion in total funding annually for neglected disease R&D. This includes funding for HIV/AIDS (\$1 billion), TB, and malaria. The public sector plays a key role, providing 64% (\$1.9 billion).^{ix} Even if it represents a major increase compared to the previous period, funding remains inadequate: the estimation of needs by the WHO Consultative Expert Working Group on R&D Financing and Coordination (CEWG) was \$6 billion. And the funding that does exist is from a highly concentrated handful of key players (e.g. Bill & Melinda Gates Foundation and the Wellcome Trust on the private funding side, and the US – with massive NIH funding, primarily for HIV/AIDS research – and a handful of European countries on the public side) and appears to be stagnating. Moreover, with the shift toward greater public sector support for basic research rather than late-stage product development – and with the decrease in philanthropic funding, especially for some of the most neglected diseases such as Chagas disease, leishmaniasis and sleeping sickness – there is a high risk that promising compounds in the pipeline will not make it through the most costly phase of R&D and into the hands of patients.

POLICY AND ENVIRONMENT

In 2001 No enabling policies: The **Fatal Imbalance** report highlighted the failure of governments to adequately intervene and steer R&D toward the greatest needs. It reviewed

CHAGAS DISEASE



Paraguay 2012 © Seamus Murphy/VII

“My message to doctors in other countries, scientists, is not to forget about us. With your help we can improve, we can make progress with our community, with our children, instead of dying before we turn 60 or 70.” – Valveno Machucha, Chagas patient and community leader, Chaco, Paraguay.

The Numbers

- 100 million people at risk
- 8-10 million cases, mostly in Latin America
- At least 10,000-12,000 deaths each year, making it the leading parasitic killer in the Americas
- Attacks the heart or digestive tract of one-third of patients, swelling their organs and threatening their lives
- Can be passed from mother to child during pregnancy

Limitations of Current Tools

- Only two drugs available (benznidazole, nifurtimox), both developed half a century ago for other purposes
- Current drugs have undesirable side effects and limited effectiveness in chronic disease
- Current treatments are long, typically lasting 2-3 months
- No treatments available for pregnant women
- No simple test of cure

Urgent Patient Needs and R&D Gaps

- Safe, effective, oral, short-course (less than 30 days) drug for chronic disease (and ideally both acute and chronic stages), that is also affordable and adapted for the field
- A simple test to show the patient has been cured

DRUG RESISTANT TB

“Most of the time I vomit up after taking my tablets, and then I have to take them again...they had so many side effects for me, including actually feeling mentally unstable. I really felt it was like I was losing my mind. I had sore feet, I had cramps on my legs, I had hallucinations at night. I would find myself biting and banging against things. It was really like I was going crazy.”

- Happiness Dlamini, a patient with MSF in Swaziland, on her experiences of living with the treatment for drug-resistant TB.



A 16-year-old MDR-TB patient and her family at home.

The Numbers

- Estimated 8.7 million new cases of TB in 2011
- 1.4 million people died from TB in 2011
- Nearly 4% of all new TB cases are drug resistant.
- 1 in 5 TB patients who have previously received TB treatment are estimated to have drug-resistant TB.
- Barely 1 in 20 TB patients tested for drug resistance

Limitations of Current Tools

- Until very recently, no new TB drugs developed in over half a century.
- Current treatment is very lengthy, taking up to two years, including a daily injection for the first eight months.
- Treatment requires cocktail of up to 20 highly toxic pills

each day, which can produce severe side effects ranging from nausea to deafness to psychosis and even suicide.

- Only 48% of patients on the optimized current treatment will be cured.

Urgent Patient Needs and R&D Gaps

- A safe, effective, oral, short-course of drugs that isn't as toxic and is affordable and adapted for the remote and rural places we work.
- A simple and effective point-of-care test that can be non-sputum-based to diagnose TB swiftly and accurately and improved rapid, accurate and affordable tests to detect drug resistance.
- Pediatric formulations to treat children with drug-resistant TB.

several policy instruments and market-based incentives that governments could enact to induce greater private investment into neglected disease R&D – including “push” mechanisms, such as tax credits, R&D grants, and orphan drug laws; and “pull” mechanisms, such as purchase funds. It also explored the potential of public/private partnerships as part of the solution, and discussed the importance of building research capacity in developing countries as an important strategy to overcome the crisis in neglected disease R&D.

Overall, however, each of these policy instruments was viewed, on its own, as only a partial solution.

In 2012 Still major need for fundamental policy change: Governments, experts, and industry have proposed several policy instruments over the past few years, including both

“push” mechanisms to finance R&D and “pull” incentives to spur investment. Examples often given include the advance market commitment (AMC) for pneumococcal vaccines and the US Food and Drug Administration Priority Review Voucher (PRV) for neglected tropical diseases.

So far, these new incentive schemes have had mixed results and have failed to demonstrate their effectiveness in boosting innovation and engaging new partners. The pilot AMC, for example, was not designed as an incentive for R&D, but rather as a mechanism to scale up the production of an already existing vaccine and accelerate its introduction in developing countries.^x Similarly, the PRV experience, implemented on only one occasion in the US, was awarded for a medicine that had already been available in the developing world for years; no innovation had been spurred by this use of the PRV.^{xi} By contrast,



Mother with child suffering fever in kala azar endemic area, Bihar, India

the WHO Prequalification Programme, while not explicitly designed as an R&D enabling mechanism, has played a major role in facilitating regulatory approval of medicines in developing countries, thereby increasing access – including to adapted formulations for pediatric HIV drugs and fixed dose combinations – for patients most in need. There is a clear need to closely monitor and assess these new mechanisms with regard to their impact both on innovation and access.

TOWARD A SUSTAINABLE NEEDS-DRIVEN SYSTEM FOR GLOBAL HEALTH R&D

In 2001, the MSF and Drugs for Neglected Diseases Working Group report concluded with a series of recommendations to policy-makers.ⁱⁱⁱ Many of these – a call for WHO to lead an R&D priority-setting exercise to identify the most pressing gaps; a call to governments to develop comprehensive solutions to the R&D crisis, including possibly through an R&D treaty; a call for increased, reliable and long-term funding for neglected disease R&D; and a call for measures to ensure affordability and equitable access to the fruits of innovation – remain startlingly relevant today.

At the global level, over the past decade, efforts to put the innovation crisis on the international political agenda have been slow-moving. Since the inception of the Commission on Intellectual Property Rights, Innovation and Public Health in

2003,^{xii} a policy process at the WHO level has been underway and culminated in the April 2012 report of the independent WHO Consultative Expert Working Group on R&D Financing and Coordination (CEWG), which provided a blueprint for action. The report recommended that all countries initiate formal negotiations towards a global framework – an R&D Convention – that would strengthen coordination and financing of R&D and ensure the cost of R&D was de-linked from the price of products in order to meet the needs of developing countries.

Despite a clear recognition by all stakeholders that market incentives are failing to generate biomedical innovation that meets the needs of certain patient populations, primarily poor people living in developing countries – and to guarantee access to the fruits of this innovation – the urgent, concerted action needed from

governments to address this situation has not yet materialized.

In November 2012, countries met at the WHO to discuss concrete next steps in relation to the WHO CEWG report. Unfortunately, the only concrete agreement made was in relation to monitoring health R&D through establishing a Global Health R&D Observatory within the WHO. This is an important and necessary first step, but this is nowhere near what is required to address the magnitude of the challenge. Instead of pushing forward with a real plan to address the continued lack of suitable and affordable vaccines, drugs and diagnostics, all countries have really pledged to do is to continue observing the situation. There is a disconnect between the recognition of the scale and urgency of the problem, which is widely shared, and the fact that proposals for transformative change have been pushed back for another four years.

This is unacceptable.

After ten years of debates, international negotiations and the publication of numerous expert reports, the imperative is clear for governments to take concrete action and spur biomedical innovation in areas neglected by the current innovation system. They cannot shirk their responsibility to put in place a sustainable global framework for essential health R&D.

What is needed is public leadership, notably from WHO and

VACCINES

Mali 2012 © Veneta Dearden/MSF

“Unless vaccines are simplified so that they’re better adapted to real-life conditions, we will never get on top of these killer diseases and will always need to respond to outbreaks that we haven’t managed to prevent through effective immunization programs.”

- Florence Fermon, MSF Vaccines Advisor.

The Numbers

- Almost 2 million children under five years old die each year worldwide from vaccine-preventable diseases.
- In 2011, 22.4 million babies – one of every five children born – did not get the basic package of vaccines that can protect them from childhood killers. That number is up from 19 million in 2010.
- 70% of unimmunized children live in ten countries: Afghanistan, Chad, DRC, Ethiopia, India, Indonesia, Nigeria, Pakistan, Philippines and South Africa.
- 4 million people were vaccinated by MSF teams in Democratic Republic of Congo alone during several measles outbreaks in 2010, reflecting the weakness of basic immunization programs in some countries.
- Basic cost of one dose of measles vaccine: 20 cents (US)

Limitations of Current Tools

“Keeping the cold chain to conserve the vaccines at the right temperature, when it’s 45 degrees Celsius outside, is a major challenge. Just maintaining the fridges in working order is hard enough to guarantee.”

- Dr. Michel Quéré, MSF Medical Advisor

- Most vaccines have to be kept at temperatures between two and eight degrees Celsius to remain effective. This requires costly and complicated refrigeration logistics in countries where one cannot count on reliable electricity supplies.
- Children have to be brought to clinics at least five times in their first year of life to get fully immunized against childhood killer diseases; this is a significant burden for caregivers who may live far away.
- Vaccines that use needles for delivery require skilled healthcare workers, who are often in short supply in developing countries.



Vaccine supplies at an MSF project in Mali.

- Vaccines are often bulky, increasing refrigeration storage and transport costs.
- Some vaccines developed for wealthy countries fail to address developing country disease epidemiology.
- New vaccines are expensive: two new vaccines for rotavirus and pneumococcal disease alone now make up 75% of the total cost of the basic package of childhood vaccines.

“With an oral vaccine – such as that used for polio – almost anyone can take the droppers to households, and give the two drops to all children aged under five. Having an easy-to-deliver vaccine has made a massive difference to the fight against this disease.”

- Dr. Manica Balasegaram, Executive Director, MSF Access Campaign

What Patients, Health Workers and Health Systems Need

- Vaccines that don’t require refrigeration
- Vaccines that can be given orally or delivered by other non-needle technologies
- Vaccines that can be administered without complex dosing schedules and that can be given in a single dose, preferably as combined vaccines
- Vaccines targeted at developing country disease epidemiology
- Vaccines that are affordable
- Vaccines that induce strong, durable immunity in children living in low- and middle-income countries

endemic countries, to effectively channel the efforts of all actors towards clearly defined goals for needs-driven innovation and equitable access. We need to move towards a new framework for R&D that considers the specific needs of patients in developing countries upfront, at the start of the innovation process; breaks the link between the cost of R&D and the price of products; ensures that the fruits of innovation are accessible and affordable; integrates the interlinked functions of global health R&D monitoring, coordination and financing; and moves beyond the *ad hoc* patchwork of limited efforts seen so far, transforming these individual successes into a sustainable R&D framework based on clear needs and agreed priorities.



An MSF staff member at a sleeping sickness program in South Sudan.

As the blueprint set out by the CEWG report makes clear, this will require mechanisms to *monitor* R&D resource flows, R&D activities of different actors, and R&D pipelines; *coordinate* global health R&D by identifying evidence-based needs and gaps, establishing clear R&D priorities and target product profiles based on patients' needs,² and enhancing efficiencies in the R&D process through more collaborative building of networks and greater sharing of research-knowledge; and *finance* R&D in a sustainable manner, addressing specific R&D gaps, including through new contributions from all countries – moving away from an overreliance on “traditional” donors – as well as new incentives that will ensure both innovation and access.

The overarching framework could serve as an “umbrella” for the functions described above and should be based on minimum standards, or core principles, laid out below that will drive the innovation cycle and guarantee equitable access for patients:

² For example, disease-specific target product profiles (TPPs) drive all of DNDi's R&D project activities. The TPP is a succinct description of the ideal specifications needed for a treatment in order to best respond to the needs of patients. TPPs are developed with leading experts from endemic countries, researchers, clinicians, disease control program managers, patient associations, WHO, and others, and generally include the target indication, population, clinical efficacy requirements, safety and tolerability profile, stability needs, route of administration, and cost. TPPs are reviewed, and if necessary updated, annually in order to keep pace with the latest available scientific and clinical evidence.

- Global health R&D should be **driven by patients' needs**
- Global health R&D should be considered a **shared public responsibility** and the fruits of this innovation should be considered **public goods**
- **Affordability** should be ensured through **de-linking** R&D costs from product pricing
- **Norms** that encourage both innovation and **access** should be encouraged, for example, where there are IP barriers, through open licensing of patent rights and equitable management of intellectual property
- Innovation regulatory **pathways** are needed to expedite research and access
- R&D outputs should be strengthened through more open approaches and greater **knowledge sharing**
- **Research capacity** in low- and middle-income countries should be utilized and strengthened to improve sustainability of R&D efforts
- **Transparency** of funding flows and clinical data

It is time to stop the fatal neglect. After decades of the international R&D system failing to deliver on clear global health needs, a new paradigm is urgently needed. Governments must put in place an R&D framework that monitors, coordinates, and finances medical innovation for neglected populations. Millions of lives hang in the balance.

ENDNOTES

- i Isanaka S, Elder G, Schaefer M, Vasset B, Baron E, Grais RF. Bridging the gap from knowledge to delivery in the control of childhood diarrhea. *Bulletin of the World Health Organization* 2012;90:635-635A.
- ii World Health Organization. Public Health Innovation and Intellectual Property Rights. Report of the Commission on Intellectual Property Rights, Innovation and Public Health. 2006. <http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf>
- iii Médecins Sans Frontières. Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases. 2001. http://www.doctorswithoutborders.org/publications/reports/2001/fatal_imbalance_short.pdf
- iv Pécoul B, Chirac P, Trouiller P, Pinel J. Access to essential drugs in poor countries: a lost battle? *JAMA* 1999;281:361-7.
- v Trouiller P, Olliaro P, Torreele E, Orbinski J, Laing R, Ford N. Drug development for neglected diseases: a deficient market and a public-health policy failure. *Lancet* 2002;359:2188-94.
- vi Global Forum for Health Research. The 10/90 Report on Health Research. 2000. http://announcementsfiles.cohred.org/gfhr_pub/assoc/s14791e/s14791e.pdf
- vii Pedrique B, Strub-Wourgaft N, Olliaro P, Trouiller P, Ford N, Some C, Pécoul B, Bradol J-H. The drug and vaccine pipeline for neglected diseases, 2000-2011: a systematic assessment. Forthcoming publication, 2013.
- viii Cohen J, Dibner MS, Wilson A. Development of and access to products for neglected diseases. *PLOS ONE* 2010;5: e10610.
- ix Policy Cures. Neglected Disease Research and Development: A Five Year Review. G-FINDER 2012. <http://www.policycures.org/g-finder2012.html>
- x Médecins Sans Frontières Access Campaign. Spotlight on Advance Market Commitment. <http://www.msfacecess.org/spotlight-on/advance-market-commitment>
- xi Médecins Sans Frontières Access Campaign. The U.S. FDA Priority Review Voucher: The right mechanism to develop drugs for neglected diseases...or corporate welfare in disguise? <http://www.msfacecess.org/our-work/overcoming-barriers-access/article/1300>
- xii World Health Organization. Intellectual property rights, innovation and public health. Resolution WHA56.27, Agenda item 14.9. Fifty-Sixth World Health Assembly. 28 May 2003. http://apps.who.int/gb/archive/pdf_files/WHA56/ea56r27.pdf

ABOUT DOCTORS WITHOUT BORDERS/MÉDECINS SANS FRONTIERS (MSF)

MSF is an international independent medical humanitarian organization that delivers emergency aid to people affected by armed conflict, epidemics, malnutrition, natural disasters, and exclusion from health care in more than 60 countries. On any one day, more than 27,000 individuals representing dozens of nationalities can be found providing assistance to people caught in crises around the world. They are doctors, nurses, logistics experts, administrators, epidemiologists, laboratory technicians, mental health professionals, and others who work together in accordance with MSF's guiding principles of humanitarian action and medical ethics. MSF received the Nobel Peace Prize in 1999.

www.doctorswithoutborders.org

ABOUT DRUGS FOR NEGLECTED DISEASES INITIATIVE (DNDi)

DNDi is a not-for-profit research and development (R&D) organization working to deliver new treatments for the most neglected diseases, in particular sleeping sickness (human African trypanosomiasis), Chagas disease, leishmaniasis, specific helminth (filarial) infections, and pediatric HIV. Since its inception in 2003, DNDi has delivered six treatments: two fixed-dose antimalarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, and a pediatric dosage form of benznidazole for Chagas disease. DNDi has also helped establish three clinical research platforms in neglected disease-endemic countries: Leishmaniasis East Africa Platform (LEAP) in Kenya, Ethiopia, Sudan, and Uganda; the Human African Trypanosomiasis (HAT) Platform based in Democratic Republic of Congo for sleeping sickness; and the Chagas Clinical Research Platform in Latin America.

www.dndi.org

Photos

Cover: Kala azar patients at an MSF treatment center in South Sudan.

Back cover: (Top) National control program mobile team screening villagers for sleeping sickness, Mpata, Democratic Republic of Congo. (Bottom) Patients in the waiting area at Koutiala Hospital in Mali.

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