AccessNews

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

MEDECINS SANS FRONTIERES

No 13 May 2006 R&D SPECIAL FOR 2006 WORLD HEALTH ASSEMBLY

Why it's High Time to Change the Rules of the Game

The HIV/AIDS pandemic has vividly brought to the world's attention the fact that an increasing percentage of the world's population lives without access to essential medicines. The access crisis is twofold – on the one hand, crucially needed diagnostics, drugs, and vaccines that safely and efficiently respond to diseases affecting the world's poorest do not exist; and on the other, patients living in poverty cannot afford their own treatment, as those medicines that do exist are priced beyond their reach.

Much of this is due to the research and development (R&D) paradigm that exists today. Pharmaceutical companies argue that strong intellectual property protection, backed up by patents and data exclusivity and entrenched in international trade agreements, is necessary to pay for R&D. The rationale of this model is simple: patents provide time-limited exclusivity to the inventors of a product to reap its commercial benefits. This is a way of encouraging companies to invest in innovation, and ultimately benefits society as a whole.

So much for the theory. The reality Médecins Sans Frontières witnesses everyday in its field programmes tells a different story. Firstly, patents create a monopoly for drug companies, and in the absence of competition, firms can price their products in a way that maximises revenue – at the expense of patients. The impact of competition on the prices of HIV/AIDS medicine shows how access to life saving treatments can vastly improve once this monopolistic situation is ended and generic competition can begin (see figure 1).

Secondly, if medical R&D is predominantly funded by the profits generated from marketing products, it follows that companies will naturally seek to invest in research for products that maximise potential returns. When R&D is driven into areas of profitability, the research for treatments which don't hold much promise of profits – because the sufferers of that disease are overwhelmingly poor, for example – simply doesn't take place. Neglected diseases are the most striking example of this failure (see box A). ***Cont on page 2***

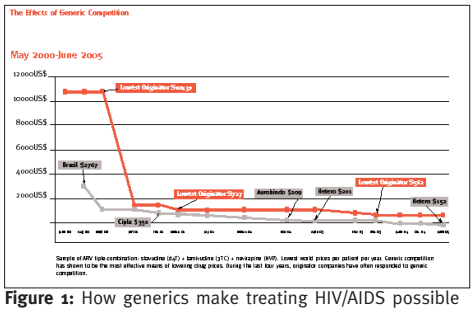


Figure 1: How generics make treating HIV/AIDS possible

Summary

This issue of AccessNews highlights the flaws in the R&D system – and the deadly consequences of those flaws. It also looks at possible solutions being discussed at the 2006 World Health Assembly.

A : *The R&D system is still not delivering on neglected diseases*

■ Between 1975 and 1999, a total of 1,393 new chemical entities were marketed globally. Less than 1% of these were for neglected diseases and tuberculosis – diseases which account for 12% of the total disease burden.

■ Many argue that the situation has changed since then – but the facts disprove them. An article published in the Lancet this month shows how, updated to include the years from 1999 through 2004, of the 1,556 new chemical entities, only 20 new drugs – again, a mere 1% – were for tropical diseases and tuberculosis.

■ Product development partnerships (PDPs) devoted to drug development may have filled their pipelines with compounds that address neglected diseases, but without greater and long-term public funding of these initiatives, these promising candidate drugs will stay where they are – in the pipeline. Today, governments contribute barely 16% of PDPs' funding, whereas philanthropic organisations provide 79%.

AIDS: Helping Develop a Quick and Easy Viral Load Test

MSF Co-operates on Crucial Research and Development Project

Caring for children with HIV/AIDS is charged with obstacles. The struggle begins with doctors not being able to tell whether antibodies found in a small baby's blood are from the mother or whether they suggest the child itself is infected with the virus. Frustrated with the situation, MSF has been cooperating with scientists working on a new technology.

Children are rarely born with HIV in industrialized countries, where transmission of the virus from the mother to the unborn child is usually successfully avoided, and children can be routinely diagnosed and treated. But there are 2.2 million children living with HIV/AIDS in the world. Most of them live – and die – in Africa.

New health tools specifically designed for use in resource-poor settings are direly needed, but they are not developed because industry sees no prospect of profit in addressing the needs of those who live below the poverty line.

This is why MSF has chosen to participate in a research and development project that aims to make detecting HIV in children under 18 months possible. MSF and the Diagnostics Development Unit at Cambridge University, UK, are entering into an agreement to develop a simple, cheap and rapid HIV viral load test for use in resource-poor settings. Headed by Dr. Helen Lee, the team at Cambridge consists of scientists who left industry to be able to develop inexpensive tests for detecting infectious diseases in patients in developing countries.

"If successful, the SAMBA ('Simple Amplification Based Nucleic Acid Test') test would make it possible to diagnose HIV in infants under a year and half while the parents are waiting, a procedure that is currently too complicated to be done at district level in resource-poor settings. Today, this level of diagnosis in infants is limited to specialized laboratories in the capitals," explains Dr. Tido von Schoen-Angerer, Director of R&D with MSF's Campaign for Access to Essential Medicines. Performed with a simple plastic device, the SAMBA test will radically simplify the technology that amplifies the viral RNA, that is, the virus's genetic material, thus making it detectable in the patient's blood.

Having a simpler and cheaper test to measure the amount of the HIV virus in the blood is also important when treating HIV//AIDS because it shows how the immune system is responding to antiretroviral treatment. "The other use of SAMBA would be to check adherence and to determine when exactly to switch patients to more powerful second-line drugs," says Dr. von Schoen-Angerer.

"Even when patients take their treatment very regularly, resistance inevitably ends up developing after a few years. Without viral load testing, problems may be recognized too late, reducing the chances that a second-line combination will be successful," said Dr. Eric Goemaere, head of mission for MSF's AIDS programmes in South Africa, where 16% of patients who have been treated by MSF for four years have needed to be switched to a second-line combination.

In the past months, MSF has been supporting the Cambridge research team in defining the required characteristics for the test to address the specific needs in resource-poor settings. An experts' meeting convened by MSF helped determine cut-off thresholds for adherence monitoring and the "when to switch to second-line" decision. MSF will be involved in field-testing the device.

Getting involved in an R&D project is not a traditional role for a humanitarian organization like MSF. "We are so desperate to have a simple test like this that we decided to step in. It is outrageous that research like this that specifically addresses the needs of resource-poor settings is of no interest to companies and is still not prioritized more and funded by governments," says Dr. von Schoen-Angerer. ■ **Laura Hakokõngäs**

But this is not simply a problem of poverty – rich patients are affected too.

Because of how R&D is rewarded today, it makes more sense in profit terms for a drug manufacturer to develop a drug with no added therapeutic benefit for a particular condition, even if there already is a drug on the market for that same condition. Research activities are therefore wasted on the development of so-called 'me-too' drugs (see box B), when at the same time, vast areas of medical need are not being addressed. The Priority Medicines report published by WHO in 2004 raised these issues convincingly.

That the current global system for supporting innovation in new medicines and other health technologies is inadequate, was clearly reflected in the establishment by WHO in 2003 of the **Commission on Intellectual Property, Innovation and Public Health (CIPIH)**. The Commission was asked to "produce an analysis of intellectual property rights, innovation and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries." The CIPIH published a comprehensive report of its findings in April of this year.

Its conclusions on the impact that patents and international trade agreements have on access to medicines, and on the role that governments should play on this issue, speak for themselves. The report concludes that intellectual property is irrelevant in stimulating innovation for many of the diseases affecting people in developing countries, where patients have limited purchasing power. Further, the report draws attention to the fact that patents can actually hamper innovation, by blocking follow-on research or access to research tools. It also points out that even in regions with strong intellectual property protection, innovation results are declining.

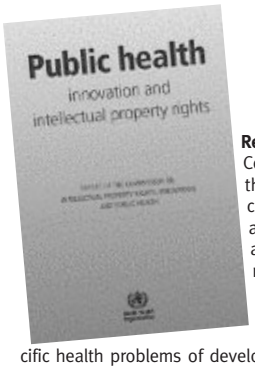
"The CIPIH report clearly signals that innovation is meaningless if the people who need it do not have access to it," said Ellen 't Hoen, Director of Policy and Advocacy at MSF's Campaign for Access to Essential Medicines. "One message that comes through loud and clear from the report is that governments have to be proactive and ensure that health R&D does meet the needs of patients, and that newly developed products are accessible and affordable to those that need them."

B : The R&D system fails patients in rich countries too: the prevalence of 'me-too' drugs

- In Canada, a study published in the British Medical Journal rated barely 5% of all newly-patented drugs approved in the country as 'breakthrough.' Alarmingly, drugs classified as 'me-too', meaning that they have no added therapeutic benefit, were responsible for 80% of the soaring rise in prescription costs experienced in the country. This provides a telling illustration of the waste in a system that rewards innovations that provide little or no therapeutic gain.
- A survey published in April 2005 by La Revue Prescrire, assessing the 3,096 new products approved for the French market between 1981 and 2004, concluded that 68% brought 'nothing new' compared to previously available preparations.
- A breakdown of the 1,035 new drugs approved by the United States Food and Drug Administration (FDA) between 1989 and 2000 revealed that more than three quarters are classed as having no therapeutic benefit over existing products.

Only with comprehensive reform of the current R&D system for essential health tools will that be possible. One immediate way to address these issues is for governments and WHO to promote the proposals made by Kenya and Brazil for a "Global Framework for Essential Health R&D." The proposal, submitted to the WHO Executive Board in January 2006, will be debated at the World Health Assembly in Geneva. It calls on WHO to facilitate talks between interested governments, on establishing new international mechanisms that ensure that medical R&D is driven by health needs, and delivers products that are appropriate, affordable and accessible. Such time-bound discussions are necessary if governments are serious about acting on their responsibility to ensure greater access to medical innovations for all.

James Arkinstall



What does the CIPIH report say?

Ten Selected Recommendations From the Report

Recommendation 2.10
Countries should provide in their legislation powers to use compulsory licensing, in accordance with the TRIPS agreement, where this power might be useful as one of the means available to promote, inter alia, research that is directly relevant to the specific health problems of developing countries.

Recommendation 3.3
WHO should initiate a process to devise mechanisms that ensure the sustainability and effectiveness of public–private partnerships by attracting new donors, both from governments and the private sector, and also to promote wider participation of research institutions from developing countries. However, governments cannot passively rely on what these partnerships could eventually deliver; there is a need for a stronger commitment on their part for an articulated and sustainable effort to address the research gaps identified in this report.

Recommendation 4.10
Governments need to prioritize health care in their national agendas and, given the leverage to determine prices that patents confer, should adopt measures to promote competition and ensure that pricing of medicines is consistent with their public health policies. Access to drugs cannot depend on the decisions of private companies but is also a government responsibility.

Recommendation 4.13
The Doha Declaration clarifies the right of governments to use compulsory licensing as a means of resolving tensions that may arise between public health and intellectual property, and to determine the grounds for using it. Developing countries should provide in their legislation for the use of compulsory licensing provisions, consistent with the TRIPS agreement, as one means to facilitate access to cheaper medicines through import or local production.

Recommendation 4.16
Companies should adopt patent and enforcement policies that facilitate greater access to medicines needed in developing countries. In low income countries, they should avoid filing patents, or enforcing them in ways that might inhibit access. Companies are also encouraged to grant voluntary licences in developing countries, where this will facilitate greater access to medicines, in cases where patents do exist on medicines and other products, and to accompany this with technology transfer activities.

Recommendation 4.20
Developing countries need to decide in the light of their own circumstances, what provisions, consistent with the TRIPS agreement, would benefit public health, weighing the positive effects against the negative effects. A public health justification should be required for data protection rules going beyond what is required by the TRIPS agreement. There is unlikely to be such a justification in markets with a limited ability to pay and little innovative capacity. Thus, developing countries should not impose restrictions for the use of or reliance on such data in ways that would exclude fair competition or impede the use of flexibilities built into TRIPS.

Recommendation 4.21
In bilateral trade negotiations, it is important that governments ensure that ministries of health be properly represented in the negotiation, and that the provisions in the texts respect the principles of the Doha Declaration. Partners should consider carefully any trade-offs they may make in negotiation. Bilateral trade agreements should not seek to incorporate TRIPS-plus protection in ways that may reduce access to medicines in developing countries.

Recommendation 4.23
Developing countries should adopt or effectively implement competition policies and apply the pro-competitive measures allowed under the TRIPS agreement in order to prevent or remedy anti-competitive practices related to the use of medicinal patents.

Recommendation 4.25
Developing countries should adopt or effectively implement competition policies in order to prevent or remedy anti-competitive practices related to the use of medicinal patents, including the use of pro-competitive measures available under intellectual property law.

Recommendation 4.27
Governments should take action to avoid barriers to legitimate competition by considering developing guidelines for patent examiners on how properly to implement patentability criteria and, if appropriate, consider changes to national patent legislation.

The Independent Researcher: Interview with Dr. Helen Lee

The Chinese-American biologist Dr. Helen Lee has spent her career developing diagnostic tools. She began her journey in Paris at the Centre National de Transfusion Sanguine, where she was responsible for developing the first widely used monoclonal blood typing reagents in France. From Paris, she went to Abbott Laboratories in Chicago, where her R&D group developed one of the most successful products at Abbott — the Human T-cell Leukemia virus screening assay for blood banks. She then became the General manager of the Probe Diagnostic Business Unit.

Over the course of her extensive career in the diagnostics industry, Dr. Lee realised that the diagnostic needs of developing countries were not being met in corporate R&D settings. Armed with seed funding of $300,000 from WHO, she left industry in 1995 and moved to the University of Cambridge to start the Diagnostics Development Unit. Subsequent support from the NIH and the Wellcome Trust enabled her group to focus on the development of technologies to improve the performance of rapid tests. The goal of the group is to develop simple, innovative and high performance rapid tests for the detection of infectious diseases in resource-limited settings.

In 2002, Dr. Lee co-founded a spinout company, Diagnostics for the Real World (DRW) based on the technologies developed at Cambridge. MSF is collaborating with Dr. Lee's R&D unit at Cambridge and with DRW for the development of SAMBA, a simple, point-of-care test for HIV detection in babies and for antiretroviral therapy monitoring in resource-poor settings. Crucially, neither of these are currently possible in remoter areas, where the needs are greatest.

You previously worked as a researcher for a large pharmaceutical company. What motivated you to leave industry?
I think my motivation was simply to be useful. It became apparent to me that the diagnostic needs of developing countries could not and would not be met by mainstream industry because there is no profit in it. The raison d'être of Abbott — as is the case with any for-profit corporation — is to generate maximum profit in order to give the shareholders the highest return for their investment. It would be unrealistic and in a way unfair to think that companies, particularly publicly listed companies, could deviate much from this goal. Therefore, I realised that if I really wanted to make diagnostic tests for diseases affecting the developing world, I would have to create a different structure that would allow or even


Photo courtesy of David Sayer

encourage me to take on this activity. Three of my colleagues at Abbott also shared the same objective, so together we formed a nice little nucleus to take on the challenge.

What do you think is wrong with today's dominant R&D paradigm that is clearly failing the poor?
The answer is really very simple – the poor are failed on many fronts because they are poor. Industry would not spend their resources developing drugs or diagnostics for the poor because there is no money in it. In general, academia cannot develop drugs or diagnostics for the poor because they do not have the necessary product development and clinical trial skills that only really reside in industry. In addition, it is not their raison d'être to develop products but rather to do basic research and publish. Therefore, you have a situation where the institutions with the skill sets do not have the incentives, those that may have the incentives do not have the skills. The situation is further exacerbated by the fact that it is difficult at the best of time to obtain R&D funding. It is even more difficult to obtain funding for product development outside of industry. Except for a few organisations such as the Wellcome Trust or the Gates Foundation, there is a real funding gap in this domain.

What do you see as the main challenges in R&D for diseases that primarily affect people in poor countries?
The answer is funding, funding and funding. Funding for R&D to develop drugs and diagnostics specifically for people living in resource-poor settings. Funding to help set up appropriate manufacturing and distribution systems, to provide technical support, repair and maintenance. Funding to strengthen and maintain healthcare infrastructure so that the essential drugs and diagnostics can be delivered to those who need them the most, particularly in rural settings.

What do you think it will take to overcome these challenges?
Political will and good will. Without political will, a chasm as large as the ones we are facing cannot be bridged. However, despite the power of governmental and institutional interventions, it will take individuals with good will and idealism — albeit rooted in realism by necessity — to do the real work of bridging the gap.

Scientists Support R&D Resolution at WHO: Interview with Dr. Tim Hubbard

Dr. Tim Hubbard heads Human Genome Analysis at the Wellcome Trust Sanger Institute, Cambridge, UK. He has been responsible for the analysis of the human genome at the Wellcome Trust Sanger Institute since 1997. The Institute was responsible for determining a third of the human genome sequence. Recently, Dr. Hubbard has been involved in proposing alternative sustainable economic models for supporting worldwide healthcare R&D, that at the same time address the issue of access to medicines. The views expressed by him in this interview do not necessarily reflect those of the Sanger Institute or the Wellcome Trust.

According to the report of the Commission on Intellectual Property, Innovation and Public Health, the therapeutic significance of pharmaceutical products reaching the market is declining. Does this mean that the research and development system is not working?
Numbers from the U.S. Food and Drug Administration show that over the last ten years, 75% of all new registrations have no new therapeutic benefit. This is largely because the current incentives encourage companies to sell drugs which have large markets. Even if there's a drug already on the market for a particular condition, it makes more sense - in profit terms – to develop a 'me-too' drug for that market. In other words, there's a lot of incentive for companies to develop another drug for the same disease where there's a big market. This kind of model means that some health needs will remain unmet.

What do you think could be done to change this?
It's down to the basic economic model. If you have today's sort of model, you will reward marketing, and your development drive will be in that direction. The kind of model I and others have proposed is that you separate the marketing from the research. That way the research, because it's not connected with selling as much as you can, is more directed toward rewarding innovation. And then you can tailor what you're going to reward, and set a higher benefit on rewarding developments in areas where there are fewer drugs at the moment, or where there are unmet needs. You can tailor your incentive structure to encourage commercial innovators to work on things they wouldn't previously, since in this model they would get a reward.

What would be one way of doing this?
We've seen quite a few examples recently of what we call 'prize models', which provide incentives. Examples for this are the Ansari X-prize recently won for launching a person into space and the US military doing prizes for roving vehicles. Providing an incentive structure that rewards direct innovation seems to be something that can work. It can focus people's minds on trying to work out new ways of treatment, other than from the start worrying about whether there is really a big enough market to guarantee a large return on investment, which is the way things are being driven at the moment. Today, there are innovations that don't reach the market because the marketing people within companies decide it's not a large enough market to continue this research.

What role could governments play in addressing these issues? What steps could they take to improve the research and development system?
I think the biggest thing is the need for governments to recognize that all countries should be contributing to R&D. Even poor countries should be investing some fraction of their GDP in R&D. At the moment this is done through purchasing: when a country purchases medicines, a proportion of the cost goes to the pharmaceutical company, and is reinvested in R&D. But this is not a very efficient process - as we've seen.

On another level, you can get impressive developments through public private initiatives, such as DNDi (the Drugs for Neglected Diseases Initiative). They're proving that they can lead to R&D at a much lower cost than things going on in a pharmaceutical company. But these efforts are currently mainly supported through philanthropy, and this is not a sustainable structure. Governments need to be more active here.

I also think that it's possible to construct a global framework, based on countries ensuring a fraction of their GDP is devoted to R&D. This would produce a sort of fair alternative. It would be a new way of structuring a competitive framework for R&D, where countries say that they're going to ensure their country is paying a fraction towards R&D - but it would allow them to choose different ways for paying that. This could be implemented via the "Global framework on essential health research and development" resolution which is being proposed by Kenya and Brazil, and has now been passed to the May 2006 World Health Assembly.

In January, with the Nobel Prize winner John Sulston, you organized a letter signed by more than 290 scientists from 51 countries in support of this resolution. Why do you think there has been such a response from the scientific community to your letter?
I think the scientists would like to see more use made of research. For people who work in medical or biological research, there is a feeling that this should contribute to improvements in health. I think everybody can see that there is somehow a disconnect between what can or has been developed, and whether it's accessible or not. This is a system which has been demonstrated through the AIDS crisis, but it's clear that it affects everybody. We see this in the UK with rationing under the National Health Service, we see it in America where some people are well provided for and lots of people are completely outside the system. Not being able to afford drugs affects everybody. It's a universal problem, and there ought to be a better way of organizing things. I think even as scientists, we see that there should be a better way of doing things.

The Scientists' Letter

Global Framework on Essential Health Research and Development

January 25th, 2006

Dear Members of the WHO Executive Board:

As scientists, many of whom work in fields connected with biomedicine, we are writing to express our support for the resolution submitted by the Republic of Kenya at the 117th meeting of the WHO Executive Board on January 23rd 2006.

Although we have very varied scientific backgrounds, from basic research to specific clinical research, we are all deeply concerned with deficiencies in the way that biomedical research science is supported and translated into treatments that improve health outcomes around the world. In the research setting we see many possibilities to develop drugs to treat neglected diseases, but a lack of sustainable support for the R&D process. In the clinical setting we see the problem of affordable drugs to a greater or lesser extent in health care systems in all countries.

At a time of huge progress in basic research science and more money being spent on biomedical R&D than ever, we are deeply concerned about the ability of existing mechanisms to translate this into a global improvement in public health. We have all felt the impact and promise of the free availability of genome sequence data, notably from the human genome project. At the same time we see research activities increasingly complicated by legal restrictions, such as intellectual property rights, which can interfere with free data exchange and can limit biomedical research progress. We do not see a good balance between medical need and resource allocation in the existing system to support R&D. For example, there is less focus on neglected diseases, vaccines or replacement antibiotics than their potential impact on global health outcomes would justify.

The resolution appears to address all of these issues in a balanced way. For example, it does not seek to eliminate the use of patents to incentivise commercial innovation, but instead allows other incentive systems to be used along side and considered under trade rules. It also proposes long term solutions to sustainable funding, prioritisation and access issues.

We call upon the Executive Board to support this important and timely resolution.

Sincerely,

Sir John Sulston FRS, 2002 Nobel Laureate in Physiology or Medicine,
Former Director of the Wellcome Trust Sanger Institute, Cambridge, UK.

Dr. Tim Hubbard, Head of Human Genome Analysis,
Wellcome Trust Sanger Institute,Cambridge, UK.

This letter has been signed by over 290 scientists from 51 countries.

Tuberculosis Treatment:
Needed Breakthrough Won't Happen Without Much Greater Public Investment


© Giovanni Diffidenti/Gamma

With tuberculosis (TB) killing 1.7 million people and newly infecting nine million each year, this curable disease is far from being curbed. The HIV/AIDS pandemic exacerbates TB's scourge through co-infection, as does the increasing emergence of drug-resistant TB. The standard TB treatment available today is long and complex. It relies on drugs developed over forty years ago and takes six months for patients to complete, and the last four decades have brought nothing in the way of improvement.

Yet after this standstill, alternative models of drug development have recently emerged and are making inroads into improving TB treatment. Some companies have also re-engaged in this field. But it is questionable whether the efforts currently underway will be enough to provide a revolution in TB treatment that will be needed in the long term to put an end to the toll the disease takes. Dramatically reigning in TB will take much greater investment to ensure that the expanded knowledge of basic TB science is seen through to new drug development.

A Fuller Drug Pipeline – But Will it be Enough?

Thanks to alternative research and development (R&D) models, compared to just five years ago, the TB drug pipeline contains several promising compounds. The TB Alliance, a product development partnership (PDP) funded mainly by the Bill & Melinda Gates Foundation, has played an important role in this, and is associated with roughly half of the drug compounds in the pipeline today.

At the same time, increased public awareness about the lack of R&D for diseases that primarily affect developing countries has prompted some pharmaceutical companies to carry out TB drug R&D on a 'no-profit-no-loss' basis, and three companies are conducting R&D for TB on a commercial basis. Some first steps in the right direction have thus been taken, with hopes that drugs such as moxifloxacin, an existing antibiotic, can provide shortened TB treatment, down from six to four months, by 2010.

Yet although these initiatives are encouraging and have shown that it is possible to make advances on TB drug development, the current efforts are not enough to result in the radical improvements, such as shortening treatment to a few weeks or even days, that will be needed to make TB controllable. First, there are simply not enough promising compounds in the drug pipeline, compared to pipelines for other diseases that predominantly affect wealthy countries. This significantly reduces the likelihood of developing an entirely new treatment combination. Second, many of the compounds in the pipeline today are derivatives of existing ones, or work in a similar way to drugs that are used to treat TB today. While this is the quickest way to bring new drugs to TB, it also increases the risk of cross-resistance problems, thereby rendering drugs ineffective.

Further, PDPs like the TB Alliance face serious funding gaps when it comes to moving candidate compounds into the expensive clinical trial phase. Most of the funding to neglected disease R&D is still philanthropic, with governments only contributing 16% to drug development PDPs in 2005.

Translational Research: From Basic Science to Drugs

Despite movement on various fronts, one crucial problem in the field of TB is that the advanced knowledge about the bacterium that causes the illness is not translated into targets that can be used for screening new potential drug compounds. The major bodies that fund TB research have typically invested in basic research projects and "hypothesis-driven" science, and academic laboratories struggle to find the funds for projects that fall between basic and applied research, creating a critical funding gap.

For diseases that affect wealthy countries, such as cancer or heart disease, drug companies actively scout out advances in basic science with potentially lucrative drug targets in mind. But not so with TB, where most companies are more risk averse, and only embark upon projects once lead compounds have already been identified.

As the TB Alliance has very limited capacity to enter into the realm of this so-called translational research, the academic sector needs to push beyond the "proof of principle" that it traditionally sees as its endpoint. For this to happen, there needs to be focused funding targeted at such translational research projects, seeing basic scientific discoveries through to concrete drug development. This funding needs to come from the public sector. Without this, the PDP model and current industry efforts will not be able to provide the real breakthroughs that are needed, now that all the low-hanging fruit has been picked.

In order for there to be a future with TB treatment as short as a few weeks or even days, governments will have to commit to bridging the gaps between science and drugs and support the necessary clinical development of already identified new compounds.

Sheila Shettle

'Fire in the Veins': Still Injecting Arsenic-derivatives to Treat African Sleeping Sickness
Much More R&D Needed to Make the Disease History

Human African Trypanosomiasis, also known as African Sleeping Sickness, is a fatal and much neglected disease that continues to plague parts of Africa. The drug most commonly used to treat the disease is so toxic that it kills one in 20 patients. While a better drug exists, it is too complex to use in resource-poor settings. In the Democratic Republic of Congo (DRC), sleeping sickness has made a disturbing comeback over the past few decades.

Three years ago, Isidor's village, lost in the remote territory of Isangi in the Eastern province of the Democratic Republic of Congo, was hit by a mysterious disease. Villagers had begun losing sleep at night while being overcome by an irrepressible fatigue during the day. Some would wander incoherently, sometimes becoming violent; others slipped into a deep coma and died. "People became tired, apathetic. They would go to hospital but could not be diagnosed. Superstition replaced medical knowledge and people started thinking it had something to do with their neighbours, child witches and so on. Even the older generation had forgotten the symptoms and thought it was a new disease," Isidor, a patient with MSF, recalls.

Yet the strange illness was in fact not new to the area. Transmitted by the bite of an infected tse tse fly, sleeping sickness, also known as trypanosomiasis, had long plagued the country while it was still a Belgian colony. Faced with waves of epidemics that ravaged entire villages and destroyed its precious workforce, the colonial administration launched huge campaigns to combat the disease. These efforts were largely successful and, by the end of the 1960s, sleeping sickness had been brought under control.

But years of civil war combined with poor public health management were to ruin health infrastructures and trypanosomiasis came back with a vengeance. When in 2003 MSF set up an exploratory mission in Isangi in conjunction with the DRC's Ministry of Health, they found the area was suffering from an extremely high incidence of the disease.

MSF opened a programme in August 2004 to try to bring prevalence rates from an alarming peak of 14% to less than 1%, largely through an extensive active screening campaign. But in DRC, the most commonly available treatment today has serious drawbacks. The national protocol continues to use melarsoprol, an arsenic derivative that is over fifty years old, for the advanced stage of the disease. Described as "fire in the veins" the drug is injected and excruciatingly painful. Its side effects can be lethal and around 5% of those treated die from complications. In some areas, treatment failure with melarsoprol has greatly increased, reaching up to 30% of cases.

A better drug does exist. Eflornithine, dubbed the "resurrection" drug for spectacularly waking patients from a coma, has demonstrated its effectiveness in many of the places where MSF has used it. It is far less toxic than melarsoprol.

But for many countries, including DRC, eflornithine remains extremely difficult to implement. "It requires significant human resources with four infusions per day for fourteen days. You need nurses 24 hours a day. It is a lot of fluid; you need catheters, not to mention the transport of all the materials to often very remote areas. All this represents a cost that national programmes are often unable to afford even if they are given the drug for free," explains Els Torreele, project manager for DNDi (Drugs for Neglected Diseases initiative), a product development partnership set up by a number of organisations including MSF. MSF and its partners have raised these issues with WHO and the drug's manufacturer, Sanofi-Aventis.

Current developments do give some reason to be hopeful: on the one hand, MSF is encouraging Sanofi-Aventis and WHO to make "eflornithine kits," that include ready-to-use equipment, available to national programmes. A kit is a response to some of the problems that make eflornithine a difficult option for national programmes. "We hope that this will convince national programmes to use eflornithine as it will be much easier to implement," explains Unni Karunakara, medical director at MSF's Campaign for Access to Essential Medicines. In a parallel development, MSF and several partner organisations, including DNDi, Epicentre the WHO/TDR, are conducting clinical trials to establish the efficacy of using eflornithine in combination with another drug, nifurtimox. If successful, this simplified protocol will be much easier for national programmes to implement, as it only requires two infusions of eflornithine per day for seven days. Another big advantage is that using eflornithine in combination will lessen the danger of resistance developing.

But significantly more research and development will be needed to make sleeping sickness history. "Eflornithine is much better than melarsoprol, but it remains a temporary solution. It also has side effects and remains complicated to administer. What would really make a difference is a simple means of diagnosis and a new drug that is easy to use," points out Torreele. "What we need to fight trypanosomiasis efficiently is more R&D and subsequent investment by governments, donors and the international community to find a fully effective, easy-to-use and sustainable drug." – An ambition that the Kenyan and Brazilian Resolution on R&D discussed at the World Health Assembly can help make real.

Véronique Terrasse