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# AccessNews

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES
MEDECINS SANS FRONTIERES

## Access and Innovation: Developing new medicines that people can afford

"Drop the Case!" – such was the rallying cry shouted by a protestor marching in New Delhi earlier this year, angered at Swiss pharmaceutical company Novartis's legal bid to force the Indian government to tighten its patent law.

In Bangkok and elsewhere, the target of demonstrators' ire has been Abbott Laboratories – whose response to Thailand's legal attempts to secure greater access to medicines for its population has been to refuse to register any new products in the country, thereby denying all Thai patients access to all its medicines for the future. Slogans such as these and drastic retaliatory measures like Abbott's are an illustration of how seemingly irreconcilable two positions have become: in one corner, companies needing to secure commercial rewards for investing in research and development for new medicines; opposite them, people in developing countries that can afford neither the high drug prices that come with patents, nor the 20 year wait before patents expire.

At Médecins Sans Frontières (MSF), we experience these problems first hand: we can neither afford the prices of newer essential medicines for patients in our projects, nor do we see enough innovation for many of the diseases that primarily affect people in poor countries.

In February, in China, I saw how one in five people with low immunity in our AIDS treatment programmes suffers from an eye infection known as cytomegalovirus, or CMV. CMV leads to blindness if untreated. The only feasible treatment is patented by Roche – that other Swiss pharma giant – and sold in China at a whopping US$ 9,000 for a treatment.

So can both sides be reconciled? Can we have investment in new, better medicines and have them at affordable prices at the same time?

Continued on page 3


Photo © Sheila Shettle

■ *Protestors in New Delhi show their anger against Novartis.*

## Thailand under fire for trying to provide medicines to its people

Thailand pleasantly surprised the public health community when it took the bold step of issuing a compulsory license to overcome a patent barrier to the AIDS drug *efavirenz* in November 2006. A compulsory license allows a government to produce or import a generic version of a drug patented in a country, for public use. Thailand's AIDS treatment programme had been facing both price and supply problems with *efavirenz*, leading to rationing of the drug in some areas. And discussions with pharmaceutical company Merck, the patent holder in Thailand, had not proven fruitful. Through the terms of the compulsory license, Thailand has imported 66,000 bottles of generic *efavirenz* from India since the beginning of 2007, and the lower cost is allowing an additional 20,000 people to be treated with the drug. Brazil, one of the few other countries that has made universal access a reality, has followed suit and issued a compulsory licence against the same drug in May 2007.

When Thailand issued two more compulsory licenses in January 2007, for the drug *lopinavir/ritonavir* – the cornerstone treatment for AIDS patients who have become resistant to their first set of medications – and on the heart medicine *clopidogrel bisulfate*, the pharmaceutical industry and its advocates were incensed. There have been efforts to consistently misrepresent reality, with portrayals of Thailand's moves as a reckless attack on the intellectual property system that is claimed to foster innovation. Far from being illegal under World Trade Organization rules, Thailand's actions are an entirely legitimate way to increase access to essential medicines, particularly at a time when drugs are becoming patentable everywhere. In an act of clear retaliation, Abbott Laboratories, the company that holds the patent on *lopinavir/ritonavir* in Thailand, announced that it would withdraw its applications for registration of seven new medicines in the country. Among these was the newer version of *lopinavir/ritonavir*, which has a crucial benefit for patients in hot climates because it, unlike the older version, no longer requires refrigeration.

After discussions with WHO Director Margaret Chan, Abbott announced a price reduction from US$2,200 to US$1,000 per patient per year for the drug in middle-income countries. Membership in this lower price club, however, comes with conditions attached: that countries "respect" the company's patents, which is to say that if Thailand does not withdraw its compulsory license on *lopinvair/ritonavir*, it will not be eligible for the reduced price. This kind of action has a word: blackmail. Abbott has further made it clear that it will only resubmit its applications for registration of the seven new drugs if the country backs down on its compulsory licenses. In doing so, it is holding patients hostage. Ironically, in the US, the very same company is demanding a compulsory license on a competitor so that Abbott can produce a hepatitis C test, arguing that public interest would adversely be affected otherwise: double standards abound.

In a new attack on Thailand and its legitimate defence of public health, the United States has announced that it's placing the country on its Priority Watch List – a list of countries drawn up by the US Trade Representative's Office for monitoring of their protection of intellectual property rights which can have consequences in terms of attracting foreign investment among other things. Abbott was one of the companies calling for Washington to place Thailand on the list.

■ **Sheila Shettle**

## Taken hostage!

### Thai patients bear the brunt of Abbott's refusal to sell new AIDS drug

Somying lives in the slums of Bangkok with her 10 year-old son Amcorn, and daughter Kaew, aged 13. She and her son are among the 580,000 Thais living with HIV. Each day she's forced to buy ice to prevent her medicines from spoiling in the stifling heat because she can't afford a fridge.

*"A man comes by boat at around 10:30 to sell us the ice. I normally buy two to three ice buckets every day. After buying the ice, I have to drain the water out of the icebox. Then I have to remove all the drugs and pour all the water out. Finally I put the new ice back in the box and then the medicines."*

Somying is forced to spend a quarter of her monthly household budget on ice for the medicines she and her son need. Luckily for her the national health system pays for the drugs. And she's doubly lucky because for many others in the country, the drug *lopinavir/ritonavir* is not available at all. But it's still a huge drain on her resources and energy.

*"We need to buy the ice for the drug but it would be much better if we could use that money for other needs."*

What's frustrating is that the company that produces the drugs, Abbott Laboratories, has produced a new version of *lopinavir/ritonavir*, which no longer needs refrigeration. But Abbott has refused to sell the drug in Thailand in order to punish the Thai authorities for issuing a compulsory licence for the drug. Somying and Amcorn are among the 8,000 patients who need *lopinavir/ritonavir* in Thailand, yet only one in ten actually gets it due to its price and not a single patient can get hold of the new heat-stable version. Abbott's manoeuvres are further endangering the lives of Somying, Amcorn and thousands of others like them who need that heat-stable drug now.

■ **Jean-Marc Jacobs**

## Novartis trying to shut down the 'pharmacy of the developing world'

Novartis has taken the Indian government to court, in an attempt to tighten the country's patent law. This would pave the way for many more patents to be granted on newer medicines and severely jeopardise India's ability to produce affordable medicines for millions of patients across the developing world.

Over half the antiretroviral medicines used in the developing world come from India, and such medicines constitute over 80% of those used to treat more than 80,000 patients in MSF AIDS treatment projects. India has been able to produce affordable versions of medicines patented elsewhere because until 2005, the country did not grant pharmaceutical patents.

Novartis says it's taking a stand on a question of principle to protect the whole system of intellectual property rights. But if the company wins, it is patients across the world that will be paying the price.

The story starts in 1998 when Novartis filed a patent application in India for *imatinib mesylate*, a drug used by cancer sufferers which the company markets as Glivec®. The application sat in a 'mail box' of patent applications along with thousands of others until 2005 when India's patent laws were amended to become compliant with international trade rules and patent offices in India began reviewing patent applications.

At this point, a number of Indian patient groups filed a "pre-grant" opposition to the patent application on *imatinib mesylate* because it is simply a salt form of the original invention, imatinib. This process allows any interested party to oppose a patent before it is granted. The important original innovation of imatinib had already been patented in 1993 in other countries, but was too early to be considered under India's amended patent law.

Novartis' patent was rejected by the Chennai patent office in January 2006 on the grounds that the newer version of the drug did not show increased efficacy over a previous version, and therefore did not qualify for a patent according to the definitions set out under section 3(d) of the country's patent law. In May

Continued on back page

## Summary

# There's No Time to Wait: Tuberculosis needs are

***No matter the spin, the facts speak for themselves. Tuberculosis (TB) kills nearly two million people per year. Resistance to existing TB drugs is growing at a rapid pace, with 450,000 new cases of drug-resistance detected each year. And not only is HIV fuelling the TB epidemic in Africa, but with multi-drug-resistant (MDR) and extensively-drug-resistant (XDR) strains of TB appearing, this disease cocktail is becoming ever more deadly. The epidemic simply cannot be stemmed with current diagnostic and treatment tools.***

Photo © Brendan Bannon

■ *Monica Juma is co-infected with MDR-TB and HIV and receives treatment from MSF in Nairobi's Mathare slum*

While roughly one drug for HIV has been developed each year since the start of the epidemic 25 years ago, the latest novel TB drug in today's standard therapy was developed in the 1960s. And none of the tests that exist today are good enough. If we're to stand a chance of detecting TB in poor or remote settings, simple tools that don't require an army of lab technicians with high-tech equipment will have to be developed.

We need new drugs and we need new tests for TB. Getting to a point where our patients can get these will be a long journey.
The first years of this century have seen new efforts in TB R&D – but they are tiny compared to the challenge. A meeting convened by MSF and the Weill Cornell Medical College in New York in January 2007 brought together industry, product development partnerships, WHO, governments, donors, NGOs and research scientists and identified what needs to happen now: if we are to succeed, TB R&D requires massive financial investment, clear leadership, and new approaches to stimulate drug discovery and accelerate clinical development (see box with conference statement). The Treatment Action Group has critically analysed how little support TB R&D is getting and who is providing it and who is not.

The ball is now in the InterGovernmental Working Group's (IGWG) court. The IGWG has been charged with drawing up a global strategy and plan of action for public health and innovation. The framework must aim at securing an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries.

With such acute needs, and with the initial steps of a research agenda developed, IGWG delegates should start with TB and ask WHO member states to make binding commitments to support TB R&D.

■ **James Arkinstall**

*"I think that part of what has happened with TB is unfortunately a premature declaration of victory. Because we have had treatment for TB with a six-month interval, which is fairly effective, there has been a tendency to not see the need for the development of newer drugs. There are newer drugs being evaluated and we just need to scale up and accelerate the evaluation and use of these drugs and not take another two decades to accomplish that."*

Dr. Kenneth Castro, Director, Division of TB Elimination, Centers for Disease Control and Prevention

*"I think it's critically important to understand that TB diagnostics is a real research orphan and that with current tools we're only diagnosing less than 40 percent of the TB cases in the world. It's really a diagnostic emergency especially for people and children with HIV. It's not widely understood that children with TB are not diagnosed with the existing tools."*

Mark Harrington
Executive Director, Treatment Action Group

## *The medical needs that must define the TB R&D agenda*

*Dr Tido von Schoen-Angerer, Director of the MSF Access Campaign spells it out:*

■ **What do we really need to improve the situation?**
From a treatment standpoint, we need a new TB therapy that is much shorter than the current six-month treatment. Ideally, we would have a treatment that lasts only a few weeks. It must be active against MDR as well and be possible to take simultaneously with antiretrovirals for HIV. There is consensus on these criteria but is also becoming increasingly clear that we urgently need to improve treatment for MDR-TB, while simultaneously working on a better standard therapy.

■ **Does the current TB drug pipeline offer any hope of achieving this goal?**
MSF recently mapped the TB R&D pipeline in a comprehensive report that was published in October 2006. There are seven drugs in clinical trials right now. We concluded that none of them will bring the absolute breakthrough that we are hoping for, but they could bring some improvements. We need to focus on how to make these drugs available as quickly as possible and find ways to accelerate the development of them. At the same time more needs to be done on the drug discovery side to feed the pipeline with more promising compounds.

■ **Are there any other options?**
Dr. Leonard Sacks of the U.S. Food and Drug Administration and other experts propose to evaluate all the drugs in the pipeline through clinical trials in MDR-TB patients because of the urgent need to find a better answer to MDR-TB and XDR-TB and because it would be easier to show efficacy in this population than in drug-susceptible patients. The current treatment for drug-susceptible patients – although it is long and difficult for patients to take and for health care providers to oversee – still cures 95% of patients with strains of TB that are susceptible to the first-line treatment. That is a high bar of success for any new drug to beat before it is going to replace the existing regimen. But second-line drugs for MDR-TB have poor efficacy, so it is easier to show that a new drug works and this could hopefully improve MDR-TB treatment even before the new drugs are explored for integration into the first-line treatment. The problem is that owners of new compounds – except for one – have not yet agreed to this concept.

■ **Has the recent outbreak of extensively drug-resistant TB (XDR-TB) in South Africa shown us that the problem isn't only with the drugs?**
XDR-TB is the tip of the iceberg of a failing TB strategy. For each case of XDR-TB there are many MDR-TB cases behind it. We have TB patients in the Caucasus where the TB strain developed from MDR-TB to XDR-TB, even under optimised and carefully administered treatment. So XDR-TB is not only a problem of poor programmes but a problem that we are creating due to inadequate drugs. And the diagnostics problem is extremely urgent: most patients co-infected with MDR-TB or XDR-TB will be dead before they can be diagnosed due to difficulties and time delays involved in diagnosing it.

■ **How is the progress in developing better tests for TB?**
The current pipeline for new TB diagnostics is even weaker than the drug pipeline: there are no methods in the pipeline that will be better in detecting TB and be simple enough to be implemented at primary care level. The scientific challenges to develop such a test are enormous and there are simply not enough groups working on this on top of there being very little funding available. While waiting for big breakthroughs, we also see that new, simpler and faster techniques to culture TB and detect resistance, such as the thin-layer agar method, are not receiving sufficient attention, possibly because they are less commercially attractive to companies than selling large machines. Developing better tests and treatments for TB is a challenge for humanity.

## What Needs to Happen: New York TB Symposium Statement

### 1. Accelerate drug discovery
■ The public and not-for-profit sector needs to be guaranteed access to professional pharmaceutical services, which mostly exist in the private sector, to develop diagnostics and drugs. Mechanisms must be established to ensure public access to compound libraries and to build appropriate libraries with potential to exhibit anti-TB properties, particularly novel and natural products

### 2. Expand clinical trial capacity and accelerate clinical development
■ Worldwide, only $20 million is spent annually for clinical trials for TB drug compared to around $300 million for HIV drugs in the US alone. Funding bodies should support the creation of a TB clinical trial platform and the massive expansion of clinical trial capacity, particularly in developing countries
■ There is an immediate priority to shorten the time of clinical drug development. Criteria for compassionate use must be established by the WHO and regulatory authorities for important candidate drugs
■ In particular, trials for (M)DR-TB drugs must be prioritized because of the explosive spread of drug resistance and the potential of these trials to show efficacy rapidly
■ Drug trials should seek to integrate studies of potential new diagnostics

### 3. Support new approaches to R&D
■ The lack of TB drug development is a result of the failure of current profit-driven drug research and development model. The TB community must engage in the World Health Organization's Intergovernmental Working Group on Innovation, Intellectual Property and Public Health to establish a global R&D framework to help design new ways of setting R&D priorities and financing.
■ With respect to TB drug development, participants of the New York symposium support current discussion at the WHO for a treaty on essential health R&D that addresses the question of who pays for essential medical R&D and de-links incentives from drug prices, instead rewarding the impact of inventions according to health care outcomes.

### 4. Commit to global TB R&D leadership
■ Strong political leadership is required to improve collaboration among scientists, drug developers, care providers, and affected individuals, in both developed and developing countries, and develop a global priority research agenda for TB

### 5. Increase funding for TB R&D activities
■ There is a critical funding gap for TB R&D. Around $900 million needs to be invested annually in the development of new tools for TB, but only $206 million was invested in 2005, and the funding gap is expected to widen over time. A dramatic funding increase is needed to support drug research and development activities. This is above all a matter of political prioritization.

*"We don't want to take money away from anyone else, but we want TB money to increase. We in the TB community have not learned all the lessons we could learn from the HIV community. There was a tremendous amount of activism in the HIV community. People made a lot of noise and they didn't ask for funding for research-they demanded it. And I think we need to take that approach with TB. We have to demand funding. We have to make some noise and get people to pay attention."*

Dr. Neil Schluger, Chairman of the Steering Committee, Tuberculosis Trials Consortium (TBTC), and Associate Professor, Columbia University

enormous and governments must take action now

# Monica's Two Daily Struggles:

## Fighting MDR-TB and HIV/AIDS in Nairobi's Mathare Slum

***Monica Juma takes more than 20 pills a day. She also receives a very painful injection each morning and has to swallow granules mixed with lemon juice, which upset her stomach. Sundays she gets to take a break. Monica is infected with both HIV and multidrug-resistant tuberculosis (MDR-TB), a more persistent form of the disease that continues to kill nearly two million people every year.***

When Monica started coughing heavily in late 2005, it seemed clear that her TB infection had relapsed for the third time. In less than four years, Monica had been through two full courses of TB treatment, each lasting eight months. If she wanted to stand a chance against MDR-TB, she would now be facing two years of twice daily clinic visits to receive her medicines.

A widowed mother of five, Monica found out she was HIV positive soon after her husband died in 2000. Though he had never been tested, she assumed he died of AIDS, as she watched him become very thin before his death. Monica began taking anti-retroviral (ARVs) medicines in 2003, and does well on them. She receives treatment through the "Blue House," a clinic on the edge of Mathare, one of the more violent slums of Kenya's capital, Nairobi, where Médecins Sans Frontières treats people with TB and HIV.

*"When I started taking ARVs, I felt good and I continued to go to my hometown of Busia near the Ugandan border to buy clothes and shoes to bring back and sell in Nairobi,"* Monica says. *"But then I started coughing up blood again, the chest pains were back and my joints began to hurt. I was getting weaker and I had to stop working."*

Doctors at "Blue House" knew they had to act quickly. It was unclear whether Monica had developed MDR-TB by failing on previous TB treatment and becoming resistant, or whether she had been directly infected by an MDR-TB strain. But as a patient co-infected with HIV, Monica did not have time on her side.

### Starting to tackle MDR-TB

MDR-TB treatment, which ideally requires a place to hospitalize patients that are still in the very contagious early stage of treatment, along with drugs that are extremely expensive and scarce, was unavailable in Kenya until MSF began admitting patients last year. MDR-TB does not respond to the two primary medicines used in standard treatment. What is left is a series of much less potent but much more toxic drugs that have to be taken for a much longer period of time, costing health care providers up to US$ 10,000 a full treatment course.

MSF began treating MDR-TB in Kenya in May of 2006. With four patients enrolled at "Blue House" and three on the shores of Lake Victoria in a town called Homa Bay, MSF remains the only provider of MDR-TB treatment in the country today. Around Nairobi alone, it is estimated there are about 50 cases, but there is no capacity to absorb them. "Blue House" does not have a facility where people with MDR-TB can be hospitalised, so the four patients are seen in a small makeshift isolation area near the back of the clinic. They enter through a special door to avoid contact with other patients, especially those with HIV, who would be prime candidates for developing the disease. A fifth patient is on the way.

*"We had two options: start treatment on an ambulatory basis with good follow-up, or wait until there was an isolation facility, knowing that the first 30 to 40 patients would die,"* says Dr. Liesbet Ohler, MSF's doctor in charge at "Blue House." *"We chose to start treating, but what we have now is only an emergency solution."*

### Cramped quarters

Monica lives roughly four kilometres from "Blue House," in a room she shares with her five children and her four-year-old granddaughter, Joyce. Although tiny, Monica's place at least has two windows to allow for crucial ventilation and sunlight, which both help cut down on the amount of infectious TB bacilli floating in the air. None of her neighbors know she is ill with this aggressive form of TB.

*"Only the children know I'm sick,"* she says. *"I worry about telling the neighbors because of what they might think."* Monica doesn't wear a mask in and around home, but she tries to at night, when she shares her bed with three of her children.

*"I worry about giving MDR to my family, but I have to take care of my children, so I have no choice but to live here with them."*
Monica Juma, MDR-TB and HIV patient

Since Monica has no longer been able to work, her daughter is the sole breadwinner for the family. Working as a household help, she is barely able to earn enough to cover the rent, and Monica takes care of the children in between her trips to the clinic. One of Monica's teenage sons and her grandchild Joyce are suspected of having been infected by her. Joyce in particular spends much of her day with her grandmother.

*"During the day, Joyce plays and enjoys nursery school, but at night she sweats and coughs, and complains of chest pains,"*

*Monica lives in one room with her five children and grandchild*

Photo © Brendan Bannon

Monica says. The doctors at "Blue House" ordered a chest X-ray on Joyce. The white cloudy bits on the x-ray indicate she could have TB.

### An uphill battle

Diagnosing TB is extremely difficult and requires patients to produce sputum samples from within their lungs. To be sure it is a case of MDR-TB, samples must be sent away to labs where the bacilli are grown for up to two months. The wait to be sure about whether a person is infected with "regular" or with MDR-TB can be too long for some, especially those who also have HIV. For children, producing a sputum sample is even more difficult, and requires the expertise of specialists.

*"TB is difficult to diagnose and treat under the best of circumstances,"* says Dr. Ohler. *"But here in these cramped quarters of the slum, where many people don't have windows to bring in a flow of fresh air and sunlight, and where many people are already living with weak immune systems because of HIV/AIDS, the risk of MDR-TB spreading like wildfire is immense."*

TB remains the leading killer of people with HIV/AIDS, who are prone to developing the disease. But diagnosing TB in people with HIV is very difficult and treating both illnesses at the same time can be complex because of drug interactions.

*"I dream of a treatment for standard and MDR-TB that could be as short as several weeks.It's hard not to feel like we're fighting a losing battle with the tools we have today."*
Dr. Liesbet Ohler, (MSF, Nairobi)

Monica, meanwhile, is motivated to take her pills every day. She knows how important it is to stick to her treatment and encourages herself each morning to have the strength to continue.

*"I am feeling quite a bit better, so I can't complain, but I worry about not being able to provide for my kids,"* she says. *"When I complete the treatment, I hope to be able to work again."*

Monica has 21 months of treatment to go. That's 542 more days, and 1,084 more trips to the clinic.

**Sheila Shettle**

*"My only frustration is that everything that we spoke about is still five, ten, fifteen years down the road. I'm returning to Lesotho next week and we need a new drug now. We need newer drugs and diagnostics now. It seems we can't possibly go fast enough and we're in this perpetual race against time when it comes to TB."*

Rachel Cohen,
MSF Head of Mission, Lesotho

Continued from cover

## Access and Innovation: Developing new medicines that people can afford

The pharmaceutical industry claims the answer to the quandary lies in their offers of price discounts to the poorest. Roche has indeed offered a discounted price to the very poorest countries – but with the lower price still topping $1,800 it's not as if anyone can afford this. Roche also excludes so-called middle-income countries such as China from the deal. If you pierce the fog of the public relations hype, piecemeal offers of differential prices fall desperately short of being a solution. Only generic competition – that brought the prices of first line HIV/AIDS treatment down from $12,000 to $130 – has proven effective in bringing sufficient and sustainable price reductions.

Governments, for their part, have long agreed that the answer to the problem is to be found with the flexibilities afforded to developing countries by international trade law and the World Trade Organization's (WTO) TRIPS Agreement (Trade-related Aspects of Intellectual Property Rights). The solutions are there, they say, all you have to do is apply them. But when Thailand did go ahead and sought to follow these rules, issuing three compulsory licences including two for antiretroviral drugs, the accusations of foul-play have been deafening, compounded by initial lack of support from the WHO. The move has even landed the country on the US's "priority watch list," reserved for countries that repeatedly violate intellectual property (IP) rules – a somewhat perverse consequence for what, after all, precisely is an application of international IP law.

Other WTO flexibilities, such as a country's right to determine its own patentability criteria, are also under threat. The purpose of Novartis's attack in India is to overturn public health safeguards enshrined in the country's law that exclude patenting of mere changes in known molecules unless they can be shown to significantly improve efficacy. With India's capacity to produce generics of new essential medicines and to export them to the developing world already severely restricted by WTO rules, Novartis's challenge is effectively one more turn of the screw.

Nearly 400,000 people worldwide, including Archbishop Desmond Tutu, authors John le Carré and Naomi Klein, Global Fund Director Michel Kazatchkine, former UN Special Envoy for AIDS in Africa Stephen Lewis, German Development Minister Heidemarie Wieczorek-Zeul, Norwegian Development Minister Erik Solheim, the Indian Health Minister Anbumani Ramadoss, former Swiss President Ruth Dreifuss as well as policy makers from the EU and the US have now joined MSF in demanding that Novartis drop its case. The company has responded that it needs strong patent protection in India if it is to invest in research and development.

We have heard this false promise many times before. Increased patent protection that developing countries like India have now put in place has not led to increased research for new drugs diagnostics or vaccines for diseases that primarily affect people in poor countries. Research and development (R&D) into diseases for which there is little commercial market remains grotesquely insufficient, depending heavily on philanthropic funding. As developing countries have signed away their ability to produce affordable generics, they have won nothing in return. As doctors, we are watching with increasing despair as the tools are taken out of our hands: the current way of stimulating innovation through high drug prices and patent monopolies is failing to deliver.

Take tuberculosis (TB): the resurgence of TB fuelled by the HIV epidemic, and the spread of drug-resistant strains make it increasingly clear that the current tools are not enough to tackle this epidemic. Yet current TB R&D efforts are no match to actual needs with no breakthroughs in sight and colossal funding gaps remaining.

Interestingly, Novartis CEO Daniel Vasella seemed to recognise this himself, when asked last September about how to get affordable new drugs to people in developing countries. *"We have no model which would meet the need for new drugs in a sustainable way" he told the Financial Times. "You can't expect for-profit organisations to do this in a large scale. If you want to establish a system where companies systematically invest in this kind of area you need a different system."*

The only way to do this is by rewarding innovation in a way that doesn't happen at the expense of access to medicines. The pharmaceutical firms justify patents, and the high prices that go with them, on the need to recoup the money spent on R&D.

Continued on back page

# **Research and Development:** Searching for alternative models

***"Are we happy with a system that drives resources to solve the problems of persons with high incomes, and ignores the impact of inventions on outcomes of the poor? Are we happy with a system that raises more than a half trillion dollars per year through drug prices, while delivering only about $50 billion in private sector R&D, most of which is wasted on projects which are either medicinally unimportant or designed for marketing rather than scientific objectives?"***

**James Love, Director of Knowledge Ecology International, voices the anger and frustration of all those working to close the gap between rich and poor in the field of global health care. Who pays and who benefits from the present system of drug development has now risen to top of the agenda and is at the heart of the negotiations underway in the Intergovernmental Working Group set up after last year's World Health Assembly. But if the present system isn't delivering, where else should we look to ensure that drugs are developed for patients in poor countries? Laura McCullagh hears about three proposals for alternative models for R&D aimed at delivering a just solution.**

■ **James Love, director of Knowledge Ecology International has been at the forefront of advocacy efforts to transform the R&D environment and ensure that people in developing countries benefit from innovation in the medical field. He discusses his proposal to set up a Prize Fund to incentivise drug discovery without penalising the patients.**

**How to incentivise innovation in drug development without the customer paying is the driving concern behind the alternative R&D models for R&D now being considered. How would the prize model do this?**
Prizes could be designed in many different ways. The core idea that Tim Hubbard and I proposed in 2002 meetings with Aventis was a prize fund of a fixed size that would reward drug developers on the basis of the evidence of the impact new products had on health care outcomes. Developers would be rewarded for products that improved treatment options.

**Who would fund the prize and how would you get international agreement on this?**
Prizes should be funded by governments and or employers – the same entities that pay for health insurance or public health programs now. At some point, a shift from prices to prizes would require new thinking about the trade framework, moving from agreements about IPR to agreements about funding R&D, including but not limited to prizes.

**How would the mechanism work, for instance how would it reward research into antimalarials better than say into developing another anti-obesity drug?**
A prize fund could be designed to apply to everything, or to only some diseases. Obesity is a serious health problem. So is malaria. Not every country has the same health problems or needs. The U.S. might create a prize fund that rewards every disease, and provides extra incentives for public health priorities, like global health problems, like malaria. A developing country that was setting up a prize fund might decide to give all of its money to inventions that were neglected.

**The pharmaceutical industry remains unconvinced by this proposal. They say it would require upfront investment with very uncertain promise of sufficient returns comparable to those they get at the moment through functioning markets.**
The big drug companies, "big pharma", started off being quite hostile to prizes, because they correctly saw it as a challenge to their claim that monopolies are the only feasible reward system that stimulates R&D. However, in 2007, several big companies, including Novartis, Pfizer and GSK, have indicated more flexibility on prizes, if the prizes reward inventions for diseases that primarily impact poor people living in poor countries – where the system of marketing monopolies is clearly not working.

**The Prize Fund approach would require a new global trade framework to deal with issue of sharing the global burden of the R&D costs. This is a huge project?**
We already have such a global agreement. It is called the TRIPS. It requires countries to issue 20 year patents on medicines. This approach is the wrong one. You should have an agreement that allows countries to use all sorts of different mechanisms to stimulate R&D, including not only patents, but prizes, open source R&D projects, etc. I think we can move in this direction. We are taking the first step this year in the WHO IGWG negotiations.

■ **Paul Herrling, Head of Corporate Research at Novartis has come up with a proposal that he hopes will bring together pharmaceutical companies with other partners to create a new international mechanism for R&D. He explains how it would work and who would fund it:**

The idea is simply to do just what the pharma companies do anyway minus the commercial part, that is the money would not come from sales but the money would come from those people who have up until now funded or SHOULD fund these activities – that's of course the charities like Gates and Wellcome and others but also of course governments – both the richer countries with development programmes and the European Community but also very prominently the governments of the countries who have the patients.

**Your proposals still include using intellectual property rights as a way to incentivise the discovery process?**
Some of the drugs we now have for neglected diseases were developed for other indications of the developed world and turn out to also be effective in neglected diseases. The opposite can happen too – what you develop for neglected diseases might be commercially viable in other areas so the idea is that the person who applies to this fund, patent their inventions as they normally would, but the moment they get the money from the fund they would give an exclusive license for the neglected indication to the fund. Now for the other diseases which are not part of this neglected aim, the drug could be licensed to other, commercial people who could develop it. BUT and that's the one twist to it, if the drug given to the fund for TB happens to work, say, in hospital infection and I make money on this, but part of the data I used to do this would have been paid by the fund then I owe a certain license or royalty back into the fund and this is kind of a refinancing of the initial money that went in.

**Working on tropical diseases is a new arena for pharma companies and brings new challenges in terms of developing drugs at very low cost and which are adapted to difficult conditions. Novartis has set up an Institute for Tropical Diseases in Singapore to address these challenges?**
Yes, we even established a small clinical research station in Indonesia because Singapore is the exception in the region, it's a rich spot and those patients are mostly in poor environments so in order to have access to those typical patients we went to Indonesia. What we also learnt with our big malaria project is that even if you have a drug that works at 95% efficacy, you haven't yet solved the problem. You still have to get the drug to the patients.

**How far does the Institute go in realising in concrete form some of the proposals that you've put forward?**
The mission of the institute is probably to go all the way to proof of concept in man – but then for the full development we were looking for partners and so we tried to design agreements that will be both agreeable to the funders and to us the originator and that goes exactly along the lines of what I've been describing so I know already that it's acceptable both for pharma and for funders whose mission is not for profit.

■ **ASAQ is a new fixed-dose combination antimalarial drug which will dramatically improve malaria treatment for patients in poor countries. It's the first fruit from the Drugs for Neglected Diseases initiative (DNDi) set up in 2003 by five public research institutes and MSF. DNDi's Director, Dr. Bernard Pécoul, outlines what can be learned from his experience of developing ASAQ about alternative ways to develop drugs for neglected diseases.**

**You drew on the expertise of many different partners from the public and private sector, from developing and developed countries. Was it easy to work with so many different organisations?**
As soon as we entered into collaboration with a partner whether academic or a biotech company or the private sector – Sanofi-Aventis in this case – we have already defined clearly the principles so it helps a lot when you have it clearly stated where you want to go right at the beginning of the process. Later difficulties were linked to the management of different groups in different places with different timings.

**DNDi is also committed to raising capacity in R&D in those countries most affected by neglected diseases. What role was played by developing country researchers in developing ASAQ?**
In this project, we had two important partners, one for the clinical trials in Burkina Faso in the national centre for research on malaria, and the second important partner was in Malaysia and Thailand where we did all the studies on bioavailability. Firstly we developed the methodology because there wasn't a comparable methodology for this kind of project and we then implemented the studies in Thailand and Malaysia which was a great contribution to the project.

**There's no patent on the drug and local companies are encouraged to compete to produce the drugs and in this case the partners have all also waived profits. Will this be the same for all future projects?**
Yes, I think so but we can never say that all projects will be exactly the same. Affordability is a major issue for us in addressing the needs of neglected populations. But what I really believe is important is the aspect of "easy to use". If we develop good treatment that is not adapted to the field conditions it will be useless. So if we have to develop something a little more expensive but which will help to reach the most neglected populations, then we have to find the mechanism to finance the product. I think in terms of priority, the adaptability to the needs of the patient comes first.

**Where does funding come from and how reliable is it?**
We had a plan in terms of fundraising consisting of 50% from governments and the rest either from funding partners, MSF on one side or private donors or foundations. So now for the first time, we have reached our objective and the question is to have some sustainability. Today the subject is fairly popular so that's why governments are ready to put some money in but there is not a sustainable mechanism to ensure the funding will still be present after 2010 and if you want to commit yourself in this field of R&D, you cannot question your funding every two years, it's impossible.

**Continued from page 3** **Access and Innovation: Developing new medicines that people can afford**

Perhaps if we stop pitching innovation against access, we can bring about a system whereby patents don't kill patients.

The right ideas are already emerging. New, additional mechanisms to separate the cost of research and development from the price of drugs have been proposed, most lately in a landmark 2006 World Health Organization (WHO) report on public health, innovation and intellectual property rights and the WHO has established an Intergovernmental Working Group (IGWG) to build on the report's conclusions - to look at both access and innovation. Proposals include priority-setting mechanisms to ensure that health research is steered to respond to the greatest medical needs, and not to the appetites for greatest financial gain. They include financing ideas such as taxes and prize funds to reward pharmaceutical R&D, instead of monopolies. Recognising that some governments invest heavily in health research through public institutes or universities, whilst other governments do nothing, they include proposals for more equitable sharing of the costs.

A number of developing countries have called for a global R&D framework treaty to ensure that all governments contribute equitably to medical innovation while ensuring the availability of affordable health products. The G8 in Germany this year should give support to new ideas to stimulate innovation and not only promote intellectual property as the only possible incentive.

The IGWG should target some concrete goal to show it has teeth and develop and support an international TB R&D strategy as a pilot activity under a global R&D framework. As there is wide agreement that better tools for TB are a global priority, all WHO member countries should make binding commitments to support TB R&D. With research priorities, current R&D efforts and further needs already defined and identified, immediate actions can now be taken.

Ultimately, pharmaceutical companies will also need to decide where they stand: are they ready to explore new ways to be rewarded for their investments into R&D, that don't automatically shut out the world's poor? Or will they continue to prescribe more of the same, and persist in seeking to protect narrow commercial interests regardless of their devastating side effects?

**■ Dr. Tido von Schoen-Angerer is the Director of Médecins Sans Frontières' Campaign for Access to Essential Medicines**

**Continued from cover** **Novartis trying to shut down the 'pharmacy of the developing world'**

2006, Novartis filed a case against the Indian government, seeking both to overturn the rejection of its patent and also to attack the section of India's law that formed the basis for the rejection. Section 3(d) is one of the fundamental public health safeguards enshrined in India's patent law that aims to ensure that patents are not granted as widely as they are in wealthy countries. The hearings in Chennai concluded in April, and the ruling is expected to occur in early summer.

Novartis's actions have provoked outrage among patient groups, politicians and activists around the world, and recall the actions taken by 39 pharmaceutical companies – including Novartis – in South Africa in 1998. Companies at that point tried to block access to cheaper generic medicines by taking the South African government to court, but an international outcry forced the companies to finally back down and drop their case in 2001.

In December 2006, MSF launched a petition calling on Novartis to drop its case. So far, nearly 400,000 signatures have been collected and many eminent individuals have joined their voices to the chorus crying shame on Novartis.

**■ Laura McCullagh**