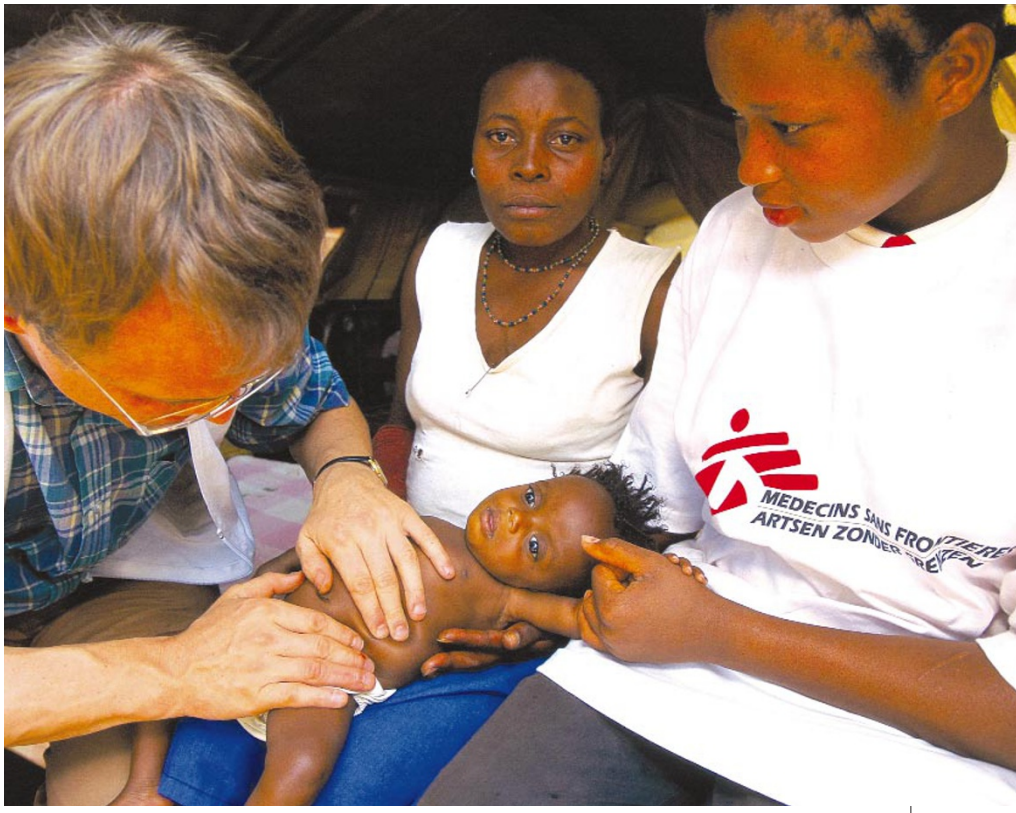
Raiding the medicine cabinet

Many candidate drugs to fight diseases in the developing world have been shelved before approval — until now. Enter a medical charity that made its name by bringing hope to the world's disaster zones. Declan Butler reports.



Bucking the trend: Médecins Sans Frontières aims to beat the neglected diseases of the developing world.

R. JOB/MSF

When James Orbinski, then president of Médecins Sans Frontières (MSF), received the 1999 Nobel Prize for Peace on behalf of the charity, his acceptance speech amounted to a call to arms. "More than 90% of all death and suffering from infectious diseases occurs in the developing world," Orbinski told the assembled great and good. "Some of the reasons are that life-saving essential medicines are either too expensive or are not available because they are not seen as financially viable, or because there is virtually no new research and development for priority tropical diseases. This market failure is our next challenge."

This week, Paris-based MSF makes good on that pledge, by teaming up with a consortium of other organizations to launch a non-profit enterprise dedicated to developing essential drugs and distributing them to the world's poorest. For no more than US$26 million annually, the Drugs for Neglected Diseases initiative (DNDi) aims over the next decade to register six or seven new drugs and to have another eight in the pipeline.

MSF — or Doctors Without Borders — won the Nobel peace prize for putting itself in the firing line, literally. In combat zones judged too dangerous by most aid agencies, its staff have held their ground and delivered medical care to some of the world's most desperate people. No one, therefore, doubts the commitment and courage of MSF's staff. But reinventing the economics of the drug industry presents a different challenge. Can MSF and its partners really succeed where the pharmaceutical giants, and their multi-billion-dollar budgets, have failed?

Yes, claims Bernard Pecoul, who heads MSF's Access to Essential Medicines campaign. "It's an alternative model based on user needs and equitable access rather than profit," he says.

The DNDi's backers argue that drug firms are failing to address many diseases in developing countries because there is no commercial market. In the first instance, the initiative will concentrate on three 'orphan' diseases caused by single-celled parasites: African sleeping sickness, its Latin American relative Chagas' disease and leishmaniasis. Although malaria and tuberculosis are bigger killers, say DNDi officials, public–private partnerships are already striving to develop new treatments for these diseases.

Controlled approach

"We would like to see more diseases covered in the future, but you cannot deal with too many things at the same time," says José Roberto Ferreira, director of international relations with the Brazilian state-owned drug manufacturer Fiocruz, one of the DNDi partners.

In addition to MSF and Fiocruz, the initiative is backed by the Special Programme for Research and Training in Tropical Diseases (TDR) — a Geneva-based initiative sponsored by the United Nations, the World Bank and the World Health Organization — and by the Pasteur Institute in Paris, the Indian Council of Medical Research, the Malaysian health ministry, and the Kenya Medical Research Institute (KEMRI) in Nairobi. Each partner will provide cash or research, and each has considerable experience either with the target diseases or in bringing drugs to the poor at affordable prices. "We know what we are talking about," says Davy Koech, director of KEMRI, which is a world-leader in sleeping-sickness research. Fiocruz, meanwhile, has successfully battled the US government and drug industry to win the right to make cheap copies of patented HIV drugs.

There is certainly a pressing need for new drugs to treat the diseases prioritized by the DNDi. Imagine the outcry in North America or Europe if a drug for, say, congestive heart disease didn't work in one-third of patients, and killed up to 10% of those who took it. Yet those are the shocking statistics for a 50-year-old drug called melarsoprol, used to treat sleeping sickness. The appallingly high rate of fatal reactions is tolerated because the disease otherwise represents a death sentence. But surely it isn't beyond the expertise of today's researchers to develop drugs that are both safer and more effective?

The problem is that the industry's drug-discovery work for such diseases has ground to a halt. Nonetheless, there is hope. DNDi officials say that the R&D portfolios of big drug firms contain candidate drugs for sleeping sickness, and other scourges of the developing world, that never became final products. So to kick off, the DNDi will attempt cheap and fast projects, taking no more than

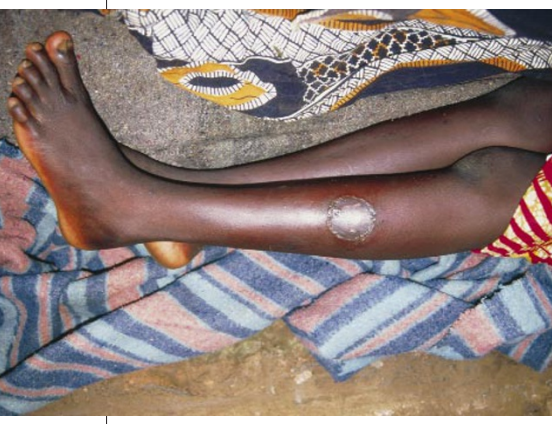
I. COX/MSF

The Kenya Medical Research Institute has extensive expertise in tropical parasitic diseases.

six years, to do the extra research to push such drugs over the regulatory hurdles needed to bring them to market. It will also examine whether the drugs might work better if they are reformulated, or used in different combinations. As an alternative to melarsoprol, for instance, the DNDi is considering a combination of megazol, first synthesized in 1968, but never put through clinical trials, and nifurtimox, which is used to treat Chagas' disease.

Over the past year, the DNDi's backers have e-mailed and telephoned across academia and industry, and organized brainstorming sessions worldwide. This effort, combined with an extensive literature search, has turned up 15 lead compounds that might be used to treat African sleeping sickness, 11 for Chagas' disease, and seven for leishmaniasis, says Pecoul. Some of these leads will be selected for more costly and risky projects, operating over a decade or so, to develop completely new drugs. In March, the DNDi and TDR also launched a call for research proposals, generating 71 responses. About half a dozen will be approved in September by the DNDi's scientific advisory committee, to be appointed at a meeting in Geneva on 3 July.

A. CRUMP, TDR, WHO/SPL



Bitten: a telltale lesion shows that this Ugandan teenager has been infected with sleeping sickness.

Good will hunting

How achievable are the DNDi's goals? An annual budget of US$26 million is peanuts compared with the billions that companies spend on developing drugs for the rich world's diseases, and raising even that sum will require considerable effort. MSF plans to commit up to US$7.5 million per year of its own funds to the DNDi over the next five years, and will engage its well-honed public-relations machine to raise money.

DNDi director Yves Champey, a former vice-president of R&D at the French drug firm Rhône-Poulenc Rorer, says that the budget will go far, because a lot of the help will be in kind. Champey is working for free, drug companies will give free access to their libraries of chemicals, and academic labs will dovetail projects funded from other sources to fit with the DNDi's goals. Clinical trials, usually the most expensive part of bringing a drug to market, will be performed cheaply at centres in developing countries where the diseases are endemic, Champey points out.

Champey's upbeat view is shared by the French arm of the business consultancy Ernst & Young, which helped to draft a feasibility study and business plan for the initiative. "The people around the DNDi table are exceptional," says Thomas Saugnac, a consultant for the firm. "If this group can't pull it off, then who can?"

But promising drug leads often fall by the wayside before reaching the clinic because of toxicity, or because they don't work as well as was hoped. If the DNDi backs too many losers, its budget will soon disappear. With little margin for error, acting ruthlessly to kill projects that are going nowhere will be key to survival. And that will mean attracting individuals with relevant industry experience — no easy task, given that the DNDi does not offer fat-cat salaries.

Other experts worry that the DNDi's distributed network of partners could degenerate into a bureaucratic quagmire. "With such a disparate group of independent people and many divergent interests, I would predict that the feasibility of DNDi will not be very high," cautions Paul Herrling, head of corporate research at the drug firm Novartis in Geneva. There are also complaints from some quarters that the DNDi has not sought to bring in the drug giants and biomedical research agencies from rich industrialized countries as full partners.

Champey defends the initial choice of developing-country partners, but says that the DNDi intends to invite other organizations on board as the initiative gathers steam. Some observers wonder whether MSF's ethos may make this difficult. Used to operating under very difficult conditions, MSF has something of a guerrilla mindset and has been highly critical of drug companies. "This attitude is unnecessarily antagonistic, and could be counterproductive," warns Tony Holder, head of parasitology at the UK Medical Research Council's National Institute for Medical Research in London. The DNDi should be working more closely with drug companies, he argues.

Champey concedes that MSF has been reluctant to involve industry directly, but says that the DNDi is counting on such companies taking part and has already had fruitful private discussions with major players including Jean-Pierre Garnier, chief executive of GlaxoSmithKline. Danielle Drew, a spokeswoman for the company, confirms that the DNDi is welcome to review GlaxoSmithKline's library of compounds "to identify any projects or molecules that were not progressed for technical or commercial reasons".

For every sceptic, another expert is willing MSF and its partners to succeed. "It's great that organizations such as MSF, who are confronted with diseases in very difficult countries, should take this up," says Ok Pannenborg, senior adviser for health nutrition and population at the World Bank. ■

Declan Butler is *Nature*'s European correspondent.

www.accessmed-msf.org/dnd/dndi.asp