




# COUGH UP FOR TB!

The Underfunding of Research for Tuberculosis  
and Other Neglected Diseases by Germany

CAMPAIGN FOR	 <b>MEDECINS SANS FRONTIERES</b>
<b>ACCESS</b>	
TO	
<b>ESSENTIAL MEDICINES</b>	

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# Abstract

In their work in field projects, MSF staff can only do so much, they frequently lack sufficient treatment possibilities to address diseases that primarily affect people in developing countries. Because research for neglected diseases, including tuberculosis (TB) and malaria, is typically not profitable, drugs, diagnostics and vaccines for these diseases are desperately lacking.

For nearly a decade, MSF has been advocating for more efforts and resources to be invested into research and development for such diseases, and has even been supporting research itself. Last year, MSF contributed 5.8 million euros to fund the non-profit drug development partnership it co-founded in 2003, the Drugs for Neglected Diseases Initiative (DNDi). This is not enough. To secure long-term funding for research into neglected diseases, there needs to be far more public funding than today. This report analyses for the first time how much funding the Federal Republic of Germany is contributing towards research into TB, malaria and other neglected tropical diseases. More than 30 experts have been interviewed for this research, and more than 90 research projects examined.

MSF's analysis reveals that the total funding contribution stands at 20.7 million euros for 2007. This includes both project funding and institutional funding. Of those 20.7 millions, 9.0 million euros went to malaria, 7.5 million euros to TB and 4.3 million to research into neglected tropical diseases such as leishmaniasis, sleeping sickness or worm-related diseases (Fig. 1, p9). Their respective figures were sent before publication to the relevant German funding and research institutions (federal ministries for research, for development and for health, the Bernhard-Nocht-Institut, the Forschungszentrum Borstel, and the Max-Planck-Institut für Infektionsbiologie). Their comments are included in this report.

Our conclusions are clear: the total sum of public research spending in Germany is utterly insufficient to meet the needs. A particularly detailed analysis was conducted for TB, where we looked at the amount of funding Germany should be giving so as to represent a fair contribution, as measured by shares of economic wealth. We found that Germany, even if you include funds spent by the country indirectly via the EU level, spends only 15 percent, - or one seventh - of the amount that could be deemed appropriate (Fig. 6, p18). Robert Koch, who discovered the TB bacillus 130 years ago, would turn over in his grave if he knew how much his home country had given up the fight against this disease, compared to other industrialised countries!

MSF feels that Germany, as the third largest economy in the world, and as a self-proclaimed centre of excellence

for research and development, has an important responsibility to support this essential activity. Germany must use its capacity to address the global need for access to live-saving diagnostics, treatments, and vaccines.

Germany's poor performance becomes especially apparent when one examines the German contribution to international product development partnerships (PDPs). In 2007, EU member states jointly contributed 27.3 million euros to PDPs relevant for diseases discussed in this report. The German contribution towards this new and important model for applied research and development was a shocking zero. MSF urges the German government to massively increase public research funding for TB, malaria and neglected tropical diseases. These funds must be earmarked so that this important research does not compete with projects in other research areas. MSF is pushing for research programmes that specifically address diseases that predominantly affect people in developing countries.

MSF's demands are directed towards all institutions that fund such research, namely the three relevant federal ministries (for research, health and development), as well as the German Research Society (DFG), the Max Planck Society and the federal states (Bundesländer). Other research institutions that so far have not been active in this area at all are also urged to become involved, such as the Helmholtz Society of German Research Centres and the Fraunhofer Society.

MSF urges for an increase in institutional funding for the relevant research institutes, and stronger participation of the German government in the creation of alternative mechanisms to support research and development, such as those currently under discussion at the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property of the World Health Organization.

Germany has to change its strategy in the fight against neglected diseases. The concerned federal ministries for research, health and development have to clarify their respective competencies in this area. The ball is in their court.

Desperately-needed tools must be developed if MSF is to be able to treat its patients, and that these are made affordable. Intellectual property protection should not stand in the way of access to innovations that are critical to people in the developing world. This is especially crucial for tools that are developed with public funding. Governments must ensure that patents do not lead to prices that are higher than production costs.

# Abbreviations

<b>BMBF</b>	German Federal Ministry for Education and Research (Bundesministerium für Bildung und Forschung)
<b>BMG</b>	German Federal Ministry of Health (Bundesministerium für Gesundheit)
<b>BMZ</b>	German Federal Ministry for Economic Cooperation and Development (Bundesministerium für wirtschaftliche Zusammenarbeit und Entwicklung)
<b>BNI</b>	Bernhard Nocht Institute for Tropical Medicine (Hamburg)
<b>DFG</b>	German Research Foundation (Deutsche Forschungsgemeinschaft)
<b>DFID</b>	Department for International Development (United Kingdom)
<b>DZK</b>	German Central Committee for Combatting TB
<b>EDCTP</b>	European and Developing Countries Clinical Trials Partnership
<b>FIND</b>	Foundation for Innovative New Diagnostics
<b>FZB</b>	Research Center Borstel (Forschungszentrum Borstel)
<b>GFATM</b>	Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)
<b>GNP</b>	Gross National Product
<b>HZI</b>	Helmholtz Centre for Infection Research
<b>IGWG</b>	Intergovernmental Working Group on Public Health, Innovation and Intellectual Property
<b>IUATLD</b>	International Union against Tuberculosis and Lung Disease
<b>MDR-TB</b>	multidrug-resistant tuberculosis
<b>MMV</b>	Medicines for Malaria Venture
<b>MPIIB</b>	Max Planck Institute for Infection Biology
<b>MPG</b>	Max Planck Society
<b>MSF</b>	Médecins sans Frontières/ Doctors Without Borders
<b>NGO</b>	Non-Governmental Organisation
<b>ODA</b>	Official Development Assistance
<b>PDP</b>	Product Development Partnership
<b>TAG</b>	Treatment Action Group
<b>TB</b>	Tuberculosis
<b>TDR</b>	Special Programme for Research and Training in Tropical Diseases
<b>VPM</b>	Vaccine Project Management GmbH
<b>WHO</b>	World Health Organisation
<b>XDR-TB</b>	extensively drug-resistant tuberculosis

# Foreword

**Professor Stefan Kaufmann**  
**Max Planck Institute for Infection Biology,**  
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Although they are often described as dealt with, infectious diseases continue to pose a significant threat to humanity worldwide. This shameful state of affairs is exacerbated by the knowledge that many infectious diseases could, in the present day, be successfully treated, indeed prevented. The situation is complicated by the fact that the pipeline for new medicines and vaccines is very nearly dry. The best summary is afforded by the 10/90 rule-of-thumb: merely 10% of expenditure in health is directed towards diseases that affect 90% of the world's population; similarly, only 10% of biomedical research expenditure worldwide is used for the development of medicines for diseases which afflict 90% of humanity.

What diseases are these, for which so little is done, even though they cause so much human suffering? They include, first of all, the most neglected tropical diseases, which draw so little attention because we quite simply have little to fear from them. Numerous helminthic diseases, like bilharzia (schistosomiasis), elephantiasis and river-blindness (onchocerciasis), belong in this category, as do sleeping sickness (Human African Trypanosomiasis), Chagas disease, Kala-Azar (visceral leishmaniasis) and cutaneous leishmaniasis, which are spread by eukaryotes. These diseases do not always lead to death, but they are associated with great human suffering for millions of people.

Other neglected diseases may perhaps be more familiar to us, but we don't take them much more seriously. These include malaria and tuberculosis (TB), which together are responsible for the loss of three million human lives a year. Yet TB is much more widespread in Europe than is commonly believed. And the threat from TB has been greatly amplified, even in Europe, by the advent of multidrug-resistant, and extensively drug-resistant strains of the disease-causing bacteria. These strains are treatable only with extreme difficulty, or not treatable at all.

Although mortality figures are shocking, a far better indicator of the human burden is the years lost to a given disease. Tuberculosis, malaria and the most neglected diseases cause an annual total loss of almost 140 million life-years. Quite apart from the personal suffering of afflicted individuals, these are life-years that are lost to the economy, particularly in poor countries, and this loss handicaps their ability to emerge from poverty.

It is obvious that something must be done. Much could be achieved with existing medical and technical capacities, for example through the provision of sanitation (clean water) and mosquito nets. But such efforts are insufficient, and new interventions are badly needed. These require research and development, and the public sector and industry have equally failed. In the 30 years between 1974 and 2004, 1,556 new medical entities came to market. Of these, eight were for malaria, three for tuberculosis, and ten for all of the most neglected diseases together. Because financial incentives to make medicines for these diseases do not exist, the pharmaceutical industry sees no need to act, and the public sector is little better.

Let us take the example of tuberculosis: each year, only 300 million Euros are spent on TB research and development of new TB medicines globally. That is so clearly inadequate: conservative estimates of what is needed to tackle TB are in the region of 700 million Euros per year.

Just over 125 years ago, Robert Koch discovered the cause of tuberculosis in Berlin. We have had a vaccine for about 90 years and medicines for the treatment of tuberculosis for about 50 years. 1880 to 1970 represents about a century of successful tuberculosis research, with many of these successes coming out of German laboratories. Since then the lines have been dead. We still depend primarily on the diagnostic, therapeutic and preventive tools developed up until 50 years ago - with very worrying consequences: half of all tuberculosis patients are missed using these tools, and remain a source of infection for their families and friends; the vaccine protects children, but not their parents; therapies are barely effective, or completely ineffective against multi-drug- and extensively drug-resistant tuberculosis. New medicines, vaccines, and diagnostics are desperately needed. And we must be clear that the results of research undertaken today will only be available to us five to twenty years from now.

As the following report from Médecins Sans Frontières/Doctors without Borders (MSF) shows, the German state spends only 7.5 million Euros on tuberculosis research. This figure rises to 9.5 million when we include EU subvention. It should not be expected that success stories in tuberculosis would emerge from Germany under these circumstances. It is shameful that a country belonging to the world's largest industrialised nations contributes a mere 2.5% of the global tuberculosis research budget. Our

contribution to malaria and the most neglected tropical diseases is even more shameful. A paltry 0.12%<sup>1</sup> of the German research budget is directed to the neglected diseases examined by MSF, Germany does not even attain the 10:90 rule of thumb. The declaration of Chancellor Angela Merkel during her G8 Presidency, in 2007, of the intention to fight harder against diseases of poverty deserves recognition; now actions must follow words.

**Berlin, April 2008**

**Professor Stefan Kaufmann  
Director, Max Planck Institute for Infection Biology,  
Berlin**

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<sup>1</sup> Basis: Expenditure for Research and Development by Federal and State governments, according to the Report of the Federal Government on Research 2006: 16.8 million Euros.

# 1. Neglected diseases, neglected people

Every day, in the countries in which they help sick people, MSF teams are confronted with the tragic reality that they do not have the necessary tools they need to treat their patients. This situation is particularly dramatic for those diseases that occur predominantly in poor countries. For these, it is frequently the case that new, effective medicines, vaccines or simple-to-use tests simply do not exist. This is because these neglected diseases are much less researched than diseases for which high medicine prices in western industrialised nations can be attained. There is no incentive for the pharmaceutical industry to invest in neglected diseases. Without the prospect for profits, the industry is only interested in

assuming responsibility for development insofar as it advances her public relations profile.

This lack of interest has terrible consequences. Every year a total of three million people die as a consequence of malaria and TB alone; over a billion suffer from neglected tropical diseases.

That a system of development of medicines based solely on patents contributes frequently to the unnecessary death and suffering of affected populations is now beyond dispute. Even governments and the pharmaceutical industry now concur that fundamental changes must be made here<sup>2</sup>.

## As brutal and poisonous as chemotherapy

### Treatment of multi-drug-resistant tuberculosis in Uzbekistan

Uzbekistan suffers from one of the world's highest rates of multidrug-resistant tuberculosis (MDR - TB). MDR-TB is diagnosed when the disease-causing bacteria are resistant to the two most important TB medicines, Isoniazid and Rifampicin. In such cases, the already onerous treatment regimen of six months increases to up to two years, initially hospital-based and later ambulant. According to an MSF study in its projects, the MDR-TB rate in newly diagnosed TB patients is globally around 13%. In patients who have previously received treatment against TB, the rate is 40%.

In the autonomous republic of Karakalpakstan in the northwest of the country, where the economic situation is particularly grim and medical treatment faces great obstacles, MSF has supported the state authorities in their battle against TB since 1998. In 2003, the first national programme for treatment of MDR-TB was opened in Nukus, the capital of Karakalpakstan. To date, around 600 MDR-TB patients have started therapy. More than 150 of them have been cured. The majority are still in therapy.

Of the total of 178 patients who have ended treatment, about every eighth suffers from the extensively drug-resistant form of TB (XDR-TB). This means that the TB causing bacteria are resistant to both the first and second line treatments. For these patients, there are almost no treatment options.

In 2007, 265 new patients were admitted to the MSF MDR-TB programme in Nukus.

The newest regularly used TB medicines were developed over 40 years ago. The long treatment

regimens for TB are accompanied by heavy side effects and long periods of isolation.

*“Those who enter therapy must come to terms with the fact that they can no longer go to work, or have sex with their partner, or play with their children as long as they remain infectious. The intensive therapy in hospital lasts at least six months. The patient receives a cocktail of five medicines, which includes a painful daily injection, and a handful of pills both mornings and afternoons. The side effects are not only unpleasant, they are often unbearable. The therapy is as brutal and as poisonous as cancer chemotherapy.”*

Dr. Cathy Hewison, MSF doctor, on MDR-TB therapy

The cure rate for patients with MDR-TB in Nukus is 60%. The rate in Germany is not much better. According to the Robert-Koch Institute, the cure rate in Germany for MDR-TB is 68.2%. For success rates to improve, both new diagnostics and new medicines must urgently be developed: ones that are more effective, have fewer side effects and drastically reduce treatment times.

*“The hardest thing was the side effects of the medicines. I constantly had to vomit, and saw things that weren't there. But I never thought of giving up. I had to live for my little daughters. I cannot tell you how happy I am to be cured.”*

An MSF patient in Nukus.

MSF has observed an increase in TB cases in its projects worldwide. In 2006 TB was present in 203 projects in 40 countries, and over 24,000 people received TB treatment through the organisation.

<sup>2</sup> See for example the Report of the WHO Commission on Intellectual Property, Innovation and Public Health. <http://www.who.int/intellectualproperty/en/>



To date little real action has followed this acknowledgement.

The MSF Campaign for Access to Essential Medicines has taken this intolerable situation as the point of departure to ask how much effort Germany puts into research for neglected diseases. Does the public sector in Germany do enough to prevent the death of millions of people from these infectious diseases? How much money do the federal government and leading research institutions invest into research and development of effective medicines and vaccines for diseases that have been neglected, in some cases, for decades?

## 1.1 Why this Report?

At the global level, the public sector has not assumed its responsibility to close the existing gap in research for neglected diseases. This continues to threaten the life expectancy of many people. Of the 2 billion US dollars (USD) required annually to tackle TB, for example, only 400 million is currently invested globally<sup>3</sup>.

Since 2006, an intergovernmental working group<sup>4</sup> (IGWG) has been negotiating at the World Health Organization (WHO) the question of how to improve the health situation in developing countries through more research and development, and through improved and especially more affordable access to valuable medicines.

The negotiations enter a decisive phase in April 2008 and could be completed by the end of May 2008. At the time of publication of this Report, there is consensus between the more than 100 negotiating states that “the range of measures to promote, coordinate and finance public and private research in both developed and developing countries into Type II and Type III diseases, and into the needs of developing countries in relation to Type I diseases, needs to be substantially enhanced. Greater investment, in both developed and developing countries, is essential.”<sup>5</sup>

In contributing to these efforts, we want to undertake with this report an evaluation of whether Germany fulfils her responsibilities as set out in this IGWG challenge. At the same time, MSF wants to set a basis for evaluating, in the coming years, whether or not the situation of neglected diseases and people has improved.

The federal government claims that much is being done, and for example, in the area of TB, many projects are being supported. In a current report of the Treatment Action Group (TAG), however, Germany places 24th in the ranks of donors for TB research.<sup>6</sup> This is unimpressive for a country that claims to be a world-leader in research and development.

MSF wanted to get to the bottom of these contradictory claims. After extensive research, we present in this report an overview of the German contribution to research for TB, malaria and neglected tropical diseases. We analysed, in total, more than 90 publicly funded research projects and the institutional support of various pertinent active research institutions. In evaluation, 70 individual research projects and research budgets were assessed as relevant and were used in the analysis. Although that sounds like a lot, the results in Euros and cents are in no way impressive. The total sum invested in research into TB, malaria and the neglected tropical diseases is a mere 20.7 million Euros.

This is shocking when one compares the invested resources with the available potential. Germany is not only an impressive research location, but has also historically played a very important role in the area of tropical medicine and infection research, we are told by researchers and pharmaceutical companies. A prominent example is the work of Robert Koch: to the present day, TB diagnosis is based on Robert Koch's methods of sputum-microscopy. Unfortunately this is a diagnostic approach that misses half the cases of infection. Shortly before and after Robert Koch, Emil Adolf von Behring and Paul Ehrlich were also awarded with the Nobel Prize for Medicine. Koch student Bernhard Nocht founded the contemporary Bernhard Nocht Institute for Tropical Medicine (BNI) in Hamburg in 1900.

The federal government has recently launched the 'Germany - Land of Ideas' initiative. This initiative aims, according to official goals, to emphasise Germany's attractions as a location for industry, and to quote the government, underline the “essential characteristics of the German people: ingenuity, creative ardour and visionary thinking”. We think this ingenuity should also benefit poor countries and the poorest patients. Yet Germany currently lags far behind countries like the UK and the Netherlands in this regard.

## 1.2 Underlying assumptions and methods

In compiling the amounts invested in supporting research we proceeded on the following basis:

We did not attempt in this report to evaluate the qualitative merit of the research (which research was good or bad). We assumed that the available financing instruments function in the way that they support research that fulfils desired scientific standards. We then investigated the amounts invested in 2007 in research into TB, malaria and neglected tropical diseases.

We were not interested in what research and

3 TAG 2007. <http://www.treatmentactiongroup.org/publication.aspx?id=2486>

4 WHO Intergovernmental Working Group on Intellectual Property, Innovation and Public Health

5 WHO Document A/PHI/IGWG/2/Conf.Paper No.1 Rev.1

6 TAG is an independent think-tank on AIDS research and policy. An important issue for TAG is HIV-TB co-infection. <http://www.treatmentactiongroup.org/>

development was done in Germany, but in what the public sector financed in research and development in 2007. We compiled project support and institutional resources of the public sector, and not funds from, for example, the Bill and Melinda Gates Foundation.

In many cases, an exact attribution of funds for research was not as easy for us to undertake as we would have liked. This was especially the case for research support through the German Research Foundation (DFG) and the institutional support within research institutions. We therefore approximated these sums, and consulted in doing so with the respective institutions.

In attempting to investigate as thoroughly as possible the figures used, we conducted numerous interviews with experts and requested information from the three implicated ministries, namely, the Federal Ministry for Education and Research (BMBF), the Federal Ministry for Economic Cooperation and Development (BMZ) and the Federal Ministry of Health (BMG) on their budgetary allocations for research into neglected diseases. These figures were compared with budget plans and budgetary accounts, in as far as these were available, and any resulting inconsistencies were then re-evaluated.

We did not include any research projects that did not receive financing from the federal level. For universities, we only included project funding and not the basic institutional funding of the university institutes. We counted, for example, DFG research funds, but not the personnel costs of professors or the operating costs for buildings.

The proportion of costs borne by the States (Bundesländer) included in the report are related to their allocated financial contributions to the institutes of the Leibniz Society.

The figures presented are the result of carefully researched, and from our perspective, appropriate estimates. We rounded all figures to the nearest 100,000 Euros. All figures refer to the year 2007. For multi-annual projects, we distributed the allocated funds equally for the duration of the project.

In addition to summarising the funding resources, this report also sought to highlight structural deficiencies in research support, and potential solutions. It is of primary concern to us that the conditions for the sick people in poor countries improve. For that to occur, the results of research must be products that are affordable.

## 2. Tuberculosis, malaria and neglected tropical diseases

This report deals with TB, malaria and the 14 diseases defined by the WHO as neglected tropical diseases. These selected diseases are a useful pragmatic proxy for analysis of Germany's activity. This does not mean, however, that our recommendations seek to exclude other, often even more neglected diseases.

Around one billion people suffer, according to the WHO, from one or more neglected tropical diseases. Some diseases, especially helminthic (parasitic worm-induced) diseases, are treatable but have lacked effective and safe medicines and diagnostics for years. Three million people die every year as a consequence of TB and malaria alone.

Despite these shockingly high figures, only 21 of the 1,556 new medical entities developed between 1974 and 2004 were for neglected diseases, including malaria and TB.<sup>7</sup>

The imbalance between the degree of suffering of people in developing countries and the global engagement in research and development of new medicines for them in the last thirty years is blatantly obvious.

Policy, research and practice experts, as well as the pharmaceutical industry agree that private research will by default not occur when those who are affected do not constitute a lucrative market for the products and return on investment cannot be assured. In view of this obvious market failure, it is the obligation of the public sector to intervene.

From our research, Germany's public contribution in 2007 to these diseases amounted in total to 20.7 million Euros (as detailed in Figure 1). As we explain later, we consider this sum far from adequate.

In contrast to her attitude to the diseases in this report, Germany takes very seriously the rare and orphan diseases of the industrialised countries. The BMBF reacted to the lack of industry interest in research on rare muscular dystrophies or metabolic disorders by establishing a programme to close the research gap. According to the BMBF, “for the period 2003-2008, 31 million Euros in total is available for ten research networks. In 2007, 6.5 million Euros was made available for nine networks.”

### 2.1 Tuberculosis

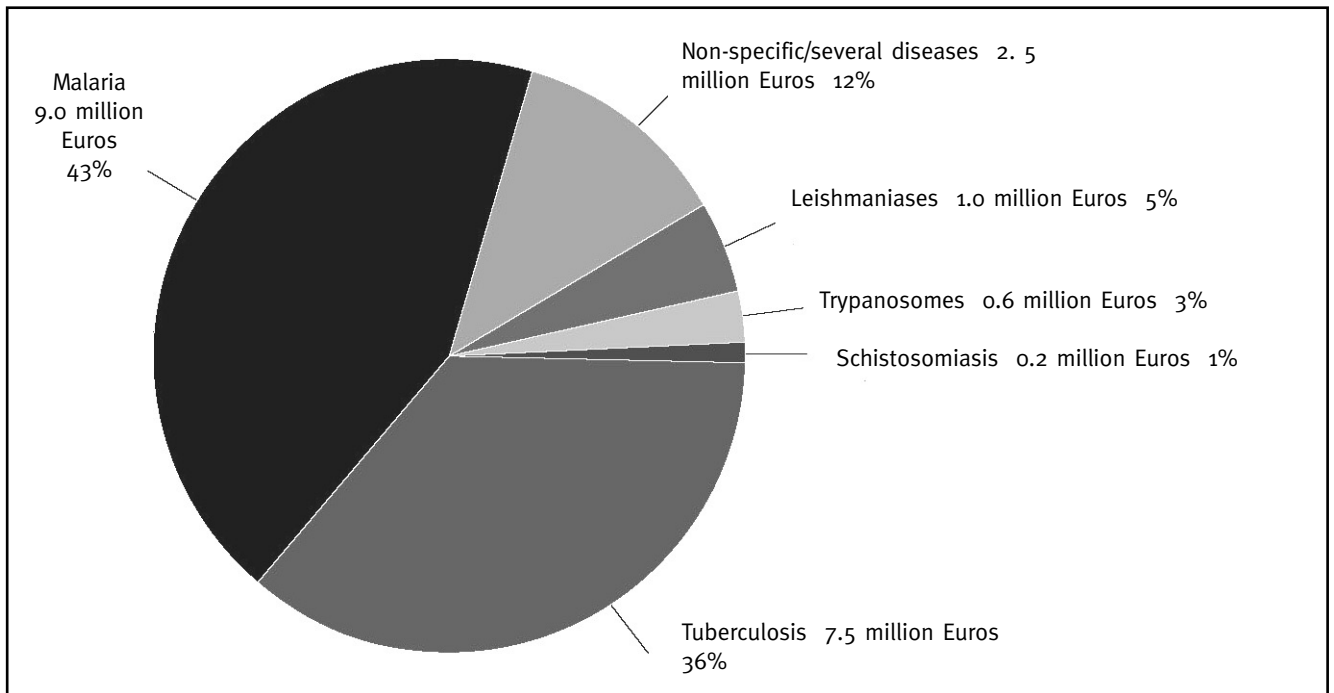
Tuberculosis (TB), which according to the WHO effects nine million new cases a year, has not been researched for decades. As the disease is no longer considered a threat in Germany, research is resting on its laurels, according to the TB expert Dr. Stefan Kaufmann, founder of the Max Planck Institute for Infection Biology (MPIIB). This although, according to the WHO, 1.7 million people die every year from the disease. “The current inability to control TB in a reasonable fashion is the result of the missed opportunities of the last decades,” he asserts. For diagnosis, one continues to depend on the methods developed by Robert Koch over 125 years ago. For a vaccine, we continue to use the Calmette-Guerin Bacterium (BCG) vaccine developed by the Institut Pasteur in the early part of the 20th century. The most effective standard therapies depend on Isoniazid (developed 1952), Rifampicin (1965), Ethambutol (1968), and Pyrazinamide (1970): The equally often used streptomycin was developed in 1944.

The Federal Ministry for Economic Cooperation and Development (BMZ) actually confirms the neglect of TB. In response to a 'Grosse Anfrage', the BMZ responded<sup>8</sup>: “No new medicines for TB have been brought to the market in the last 20 years”. According to the BMZ, the Global Alliance for TB Drug Development has, with the participation of German researchers, developed a number of new approaches for the development of medicines, but the BMZ estimates it will be a number of years before they will have newly developed medicines at hand. This is also true for a TB vaccine for which a number of candidates are in development.

Significant research activity in TB started with the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). The resources available continue to be insufficient, according to experts like Kaufmann or the parliamentarians (and doctors) Wolfgang Wodarg and Karl Addicks, to prevent the fact that a growing number of patients cannot be treated at all.

7 Chirac, P. & Toreele, E. Global framework on essential health R&D. The Lancet, 2006, 367: 1560-1561

8 (written response) quote from the Bundestag documents 1675542 and 16/3209



**Figure 1:** Research support amounts for the various diseases: A total amount of 20.7 million Euros. (As total sums have been rounded to the nearest 100,000 Euros, individual sums, here as in the remaining graphs, do not add up exactly to the total.) Trypanosomes cause Chagas disease and sleeping sickness.

## 2.2 Malaria

The situation for malaria is similar. Drug resistance has developed to a range of medicines used to treat this mosquito-borne disease. The WHO recommends the use of artemisinin-based combination therapies. These are very effective, but one must also confront the development of resistance to these combinations over the long term. All the newer malaria medicines in development are based on the same class of drugs, so if resistance to artemisinin develops, no alternative drugs would be available for malaria treatment. A vaccine is in development, but experts consider that this, which will be available in the coming years, will only have limited effectiveness.

## 2.3 Buruli Ulcer, sleeping sickness and others - unfamiliar but dangerous

The WHO has developed a list of 14 neglected tropical diseases.<sup>9</sup> The majority of these are preventable, curable, or as in the case of Guinea worm, could be eradicated. Children are particularly vulnerable to these diseases. Often only old and dangerous medicines are available for these diseases, which disproportionately affect people in poor countries. They are therefore frequently referred to as diseases of poverty.

The 14 diseases are: Buruli Ulcer, Chagas disease (American Trypanosomiasis), cholera/epidemic diarrhoeal diseases, Dengue Fever, Guinea worm, endemic treponematoses (e.g. endemic syphilis), sleeping sickness (Human African Trypanosomiasis), the leishmaniases (kala-azar or visceral leishmaniasis and cutaneous leishmaniasis), lymphatic filariasis (elephantiasis), onchocerciasis (river-blindness), schistosomiasis (bilharzia), helminthic infections, and trachoma.

<sup>9</sup> [http://www.who.int/neglected\\_diseases/diseases/en/](http://www.who.int/neglected_diseases/diseases/en/)

### 3. The Financing Institutions

A total of 20.7 million Euros of public monies was invested in 2007 in research support for TB, malaria, and the neglected tropical diseases. From Figure 1, it is clear that this was predominantly spent on research into TB and malaria. Figure 2 shows how much each financing institution invested, and this is briefly described below.

#### 3.1 The Federal Ministry for Education and Research (BMBF)

In 2007, the BMBF spent over 354 million Euros for project support in the area of “life sciences with a focus on pharmaceutical research and medical technology”. For 2008, the BMBF has indicated an increase of 46% in funding. The funding support will, according to these reports, increase to 400 million Euros. That is a large amount and the largest single line item allocation of the Ministry’s project funding.

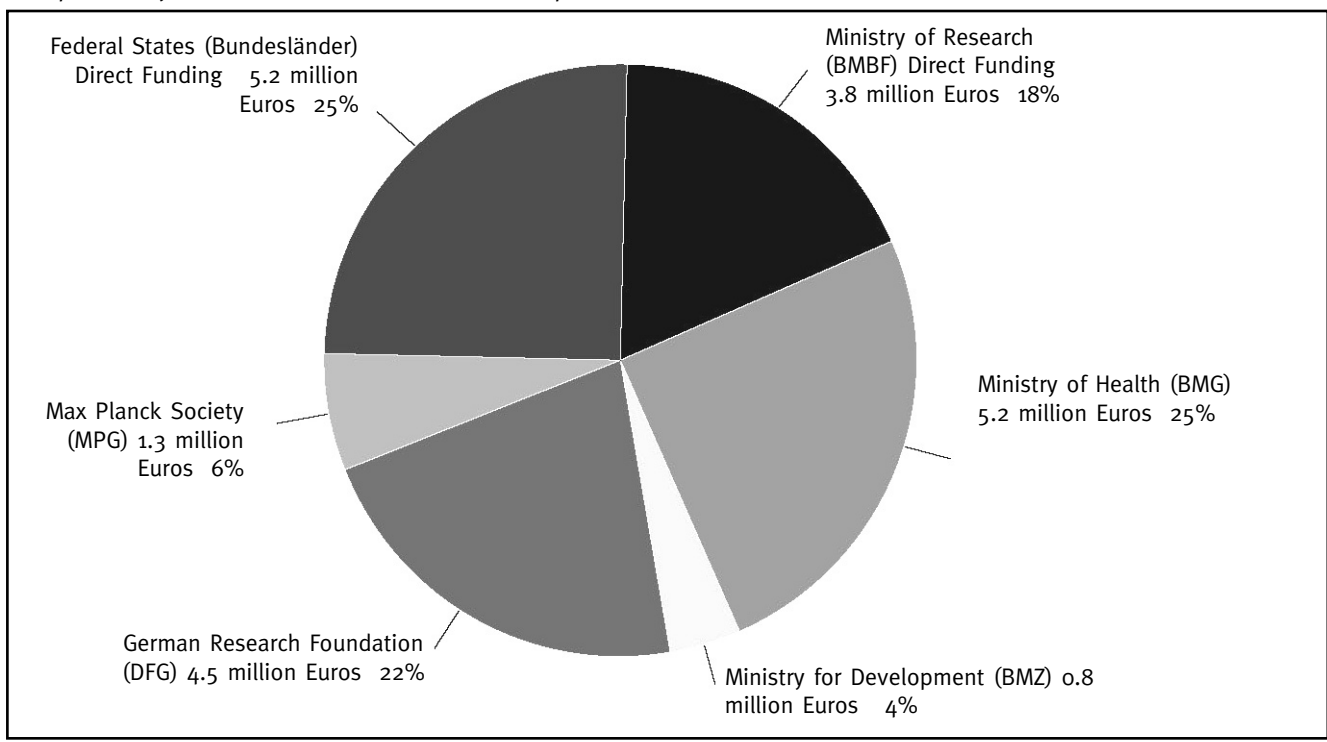
The fraction of this funding allocated to TB, malaria and the neglected tropical diseases is very moderate, in fact almost negligible in proportions: according to the Ministry, 3.8 million Euros of these funds are directly allocated for research into malaria and TB.

With regard to the neglected tropical diseases, the ministerial officer responsible writes, “Beyond TB, malaria and HIV, no projects for the neglected tropical diseases (as defined by the WHO) are funded”. Concrete dedication of funds only followed for the monies earmarked for the Malaria Initiative and for co-financing a project of the European and Developing Countries Clinical Trials Partnership (EDCTP<sup>10</sup>). “Only the resources for the Malaria Initiative and EDCTP were reserved for these diseases; the remaining calls in the area of infectious disease were described more generally,” according to the official.

Within the context of the EDCTP, the BMBF assures us that in 2007 over ten calls for proposals for HIV, TB and malaria were issued.

German researchers are, if successful in their bids for EDCTP financing, co-financed by the BMBF. This funding is already included in the 3.8 million Euros mentioned above. However, according to a study commissioned by the European Commission, the EDCTP is having extreme difficulty in its efforts to establish itself. The funds promised to date by Member States have not been transferred in the amounts promised, and have also not been applied for by research groups.

**Figure 2:** Donor institutions with amounts allocated in 2007. In addition to the amounts explicitly shown here, the BMBF also contributes 50% of the budget of the Max Planck Institute and 58% of the budget of the DFG. They then independently decide how the resources are expended, and this is illustrated here.



<sup>10</sup> The EDCTP (European and Developing Countries Clinical Trials Partnership) is a programme of the EU to conduct clinical trials for medicines and vaccines against HIV/AIDS, TB and malaria.

### **3.2 German Research Foundation (DFG): Almost nothing for neglected tropical diseases**

The situation is just as unsatisfactory with the DFG. For current DFG-funded projects, including four large collaborative projects and special research projects related even in the broadest sense to research for malaria and TB, a total of 3.4 million Euros were allocated in 2007. For the 14 neglected diseases defined by the WHO, the situation was grim. No more than six projects considered one of these diseases. The majority, such as Buruli Ulcer or leprosy, were completely ignored.

In 2007, the DFG established an Africa Programme, with a focus on infectious tropical diseases. The financial resources allocated to this programme are as yet unknown. It is, however, a step in the right direction.

### **3.3 The development cooperation ministry (BMZ) and the health ministry (BMG): Limited responsibility**

The Federal Ministry for Economic Cooperation and Development (BMZ) and the Federal Ministry of Health (BMG) currently consider that they have only limited responsibility for this issue.

In a statement to MSF from the BMZ, the restraint in engagement was so justified: “With regard to research and development of medicines, we abstain, owing to the high costs from investing resources allocated for development cooperation, beyond what is given to TDR<sup>11</sup>. This is also true for participation in the financing of structures to conduct clinical trials in developing countries, because the advancement of innovation systems and research in developing countries is not part of the priorities of German development cooperation. In this area, in the framework of international donor coordination, Canada, the Netherlands and Sweden are particularly active.”

TDR (The Special Programme for Research and Training in Tropical Diseases) received 0.47 million USD (0.38 million Euros) in 2006 from the BMZ. In 2007, the amount increased to 0.75 million Euros. This is still a very modest amount, given that Germany does not conduct its own research into these diseases, and compared with the contributions of many European neighbours (Belgium 2006, 1.01 million USD / 0.8 million Euros; Denmark 2006, 1.71 million USD / 1.37 million Euros).

The BMG told us they do not finance any basic or applied research and development for TB through project funding<sup>12</sup>, despite increased attention to TB, owing to the rapidly increasing number of cases in Eastern Europe. Nevertheless, the BMG supports the German Central

Committee for Combating TB (DZK), as well as German participation in the International Union against Tuberculosis and Lung Disease (IUATLD), despite the fact that research plays only a marginal role at DZK and no role at all at the IUATLD. The work of the DZK is focused on developing the guiding principles for dealing with TB in Germany. The BMG budget includes funding for the Robert Koch Institute. Even so, no meaningful research for the diseases included in this report can be undertaken on those resources made available by the BMG.

The most important contribution of the BMG is its basic institutional funding of 50% of the Research Centre Borstel (FZB) and the Bernhard Nocht Institute (BNI). These institutes are, Germany-wide, the largest recipients of research support in the context of this report. If one considers this institutional funding, the BMG is the largest donor for research for these neglected diseases.

### **3.4 The States: Co-financing of the Leibniz Institutes**

Fifty percent of the institutional support for the Institutes of the Leibniz Society - that is, the Bernhard Nocht Institute (BNI) and the Research Center Borstel (FZB), comes from the budgets of the States (Bundesländer). The lion's share of this 5.2 million Euros is borne by the states of Hamburg and Schleswig-Holstein, the respective homes of these institutions. The States also indirectly finance the Max Planck Society and the German Research Foundation (DFG).

### **3.5 The Max Planck Society (MPG): Coincidence or personal engagement?**

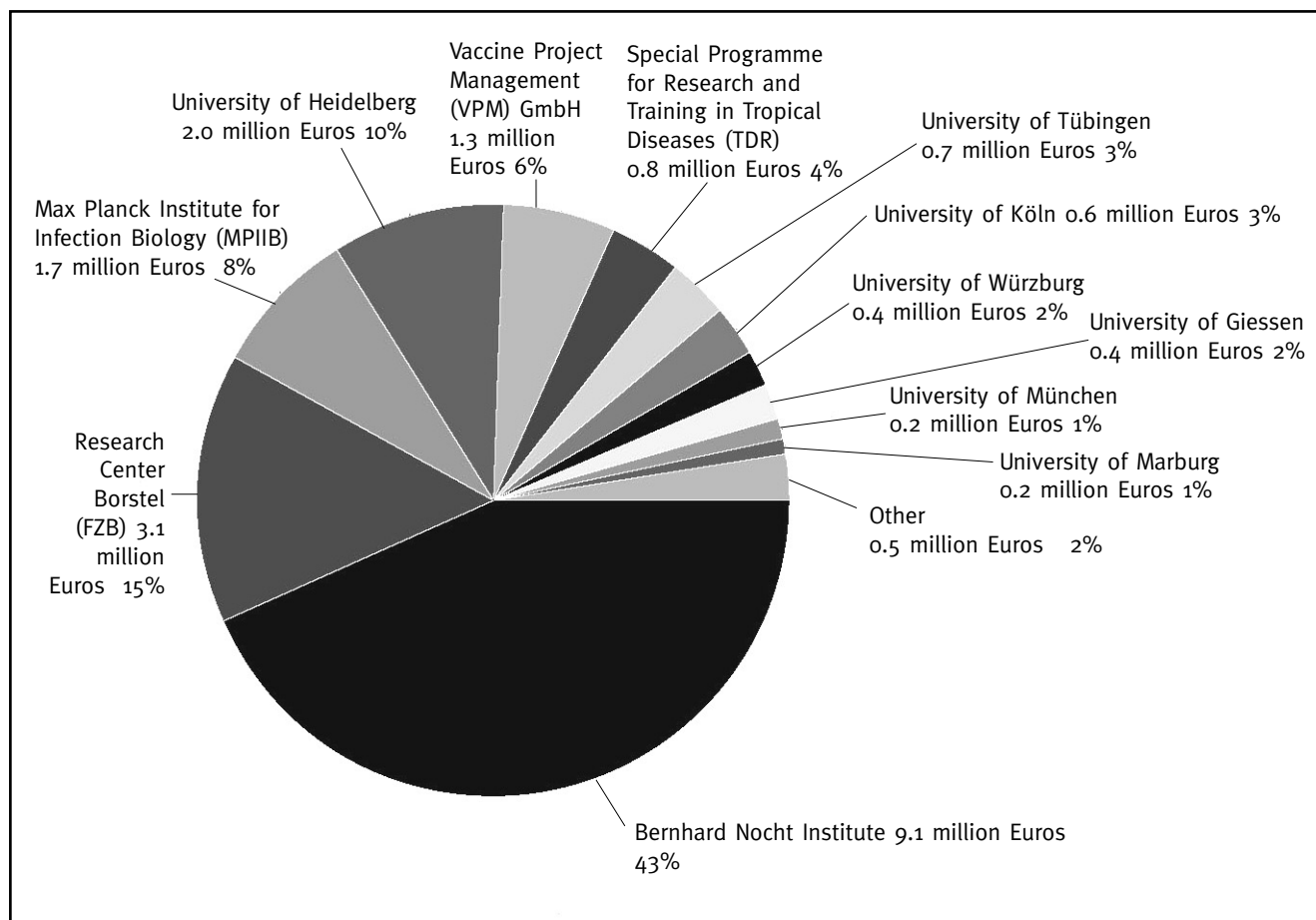
There is no single Max Planck Institute that specialises in research for the diseases covered in this report. The Max Planck Institute for Infection Biology (MPIIB) in Berlin is, however, a current leading global centre for research into TB and has invested around 1.3 million Euros of its internal resources in this research.

This sum, a significant proportion of the German research expenditure for the diseases relevant to this report, could easily fall away if the MPIIB or its director took interest in other research questions. Even the employment of a researcher in an institute abroad could significantly change the situation. There are many examples of this in the German research world.

<sup>11</sup> TDR - Special Programme for Research and Training in Tropical Diseases (TDR), a global scientific collaboration programme, cosponsored by the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the World Bank and the World Health Organization (WHO).

<sup>12</sup> Owing to more recent information received after the publication of the first edition of the Report, we have refined this statement in the second edition; we have also changed the heading and the last sentence of this paragraph in the second edition.

## 4. Research Institutions



**Figure 3:** Institutions receiving public support, with total funding received for the diseases in this Report in the year 2007. Included are all institutions that received over 150,000 Euros in 2007.

### 4.1 Bernhard Nocht Institute for Tropical Medicine (BNI)

The Bernhard Nocht Institute for Tropical Medicine (BNI) in Hamburg is the largest recipient of German public research funds for the diseases covered in this report. A particular research priority is malaria.

The BNI receives external funding from 2 projects of the research ministry (BMBF) and four different projects of the German Research Foundation (DFG). As a Leibniz Institute, the BNI receives additional institutional support from the government, which is paid in equal share by the federal government and the States, in this case especially the state of Hamburg.

If one divides the multi-annual funding received by the BNI from the BMBF equally between the project-years, one arrives at a total annual sum of 0.7 million Euros from the BMBF in the year 2007.

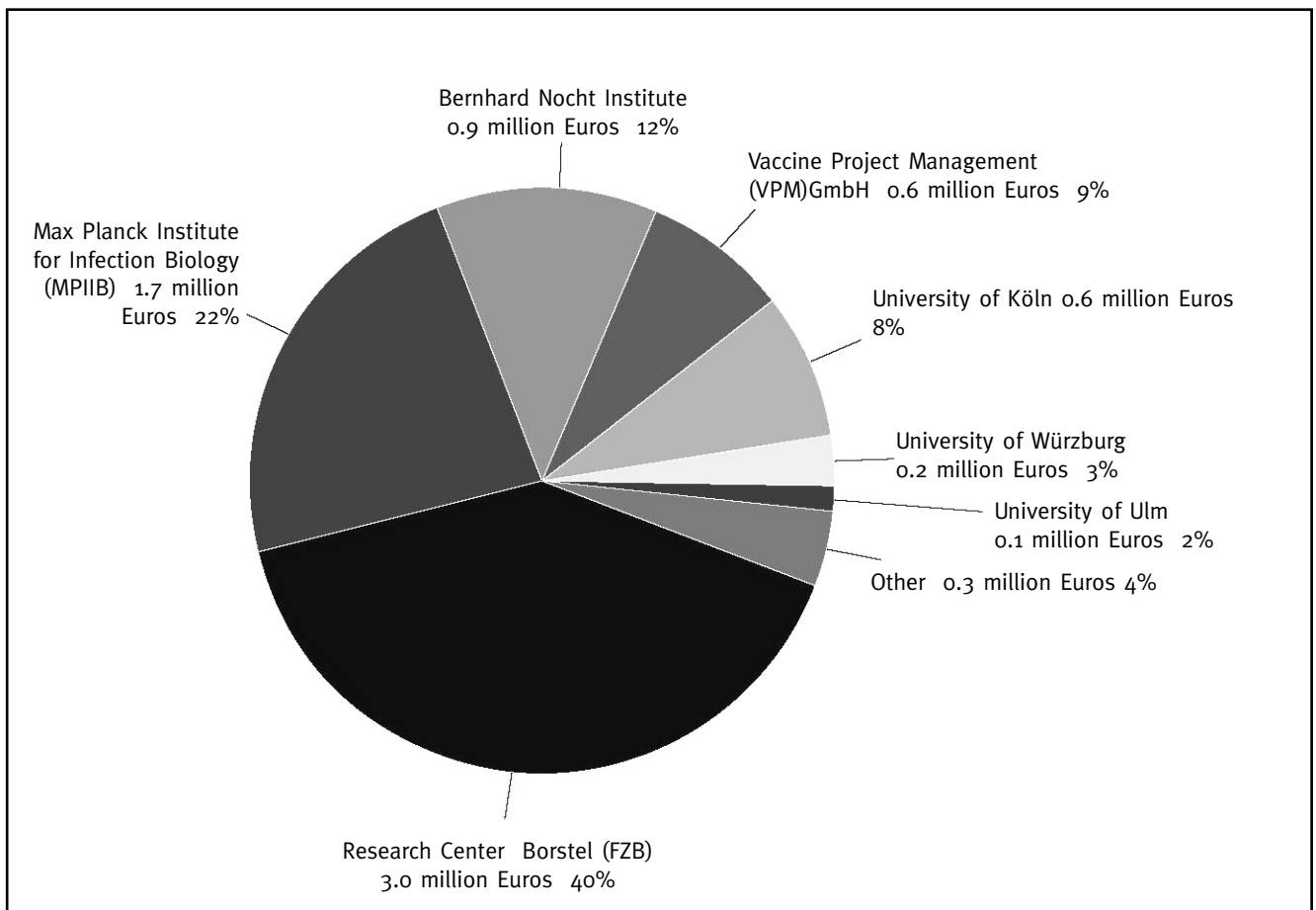
The institutional support in 2007 for the BNI from the federal government amounted to 5.4 million Euros. This

is supplemented by matching funds from the States, bringing the total to 10.8 million Euros. According to the BNI these funds were distributed as follows between the diseases: amoebal diseases: 0.7 million Euros; HIV/AIDS: 0.3 million Euros; viral haemorrhagic fevers (especially Lassa and Ebola): 1.8 million Euros; leishmaniases: 0.6 million Euros; TB: 0.8 million Euros; helminthic infections: 1.2 million Euros; malaria (priority disease): 5.4 million Euros.

By definition, amoebal diseases, HIV/AIDS and Ebola are not included in the diseases considered in this report.

### 4.2 Research Center Borstel (FZB)

The largest recipient of public funding for TB research in Germany is the Research Center Borstel (FZB) near Hamburg. Important work for the treatment and diagnosis of TB is undertaken at the FZB. The FZB houses the national reference centre for Mycobacteria, which is recognised by the WHO as a European Reference Laboratory and a Supranational Reference Laboratory.



**Figure 4:** Distribution of public funding for TB research in 2007 between the research institutions

The FZB receives external funding from two BMBF and five different DFG projects. As a Leibniz Institute, the BNI receives additional institutional support from the government, which is paid in equal share by the federal government and the States, in this case especially the state of Schleswig-Holstein, which is home to the Institute.

If one divides the multi-annual funding received by the FZB from the BMBF equally, between the project-years, one arrives at a total annual sum of 0.3 million Euros from BMBF in the year 2007.

The institutional support for the FZB from the federal government amounted to 6.9 million Euros in 2007. This was supplemented by matching funds from the States, bringing the total to 13.8 million Euros. The FZB does not itself publish any accounts of the distribution of institutional resources between the various research projects of the Institute. For the purposes of this report we were obliged to make an estimate of the resource distribution. From our calculations, the FZB allocated 2.3 million Euros to TB research and 38,000 Euros for research into Chagas disease (see Appendix, chapter 8).

### 4.3 The Max Planck Institute for Infection Biology (MPIIB)

The MPIIB in Berlin is an internationally renowned centre for TB research. By its own accounts, it allocated in 2007 approximately 1.3 million Euros of its institutional resources to basic research for TB and the development of improved TB vaccines.

In addition, MPIIB received external funding of approximately 310,000 Euros in 2007 from three BMBF projects, and 70,000 Euros from one DFG project.

The MPIIB receives considerable external funding from a number of other sources, including for example, the Bill and Melinda Gates Foundation. This additional funding is not included in this report, as it does not come from the public purse.



### 4.4 Vaccine Project Management (VPM)

The publicly funded VPM in Hannover performs, according to researchers, an important function in the development of vaccines. An important function of the VPM is to organise clinical trials, including, significantly for this report, the production of a certain amount of vaccines for these trials.

A total amount of 25.6 million Euros over eight years is made available for this project. We have divided this amount equally between the eight years and five projects of the VPM. This results in 0.6 million Euros for TB vaccine production, and the same amount for malaria, for the year 2007.

It is in principle a welcome development that clinical trials here are funded from the public purse. This is precisely the work usually assumed by industry for more profitable diseases, but that is usually ignored for TB, malaria and the neglected tropical diseases.

The VPM, however, is expected to become self-sustaining after the initial start-up funding, and is particularly oriented towards recouping licensing fees

from potentially newly developed vaccines. This means that these new vaccines could become very expensive, particularly for developing countries, as the VPM has no rules to date for particular licensing requirements for developing countries.

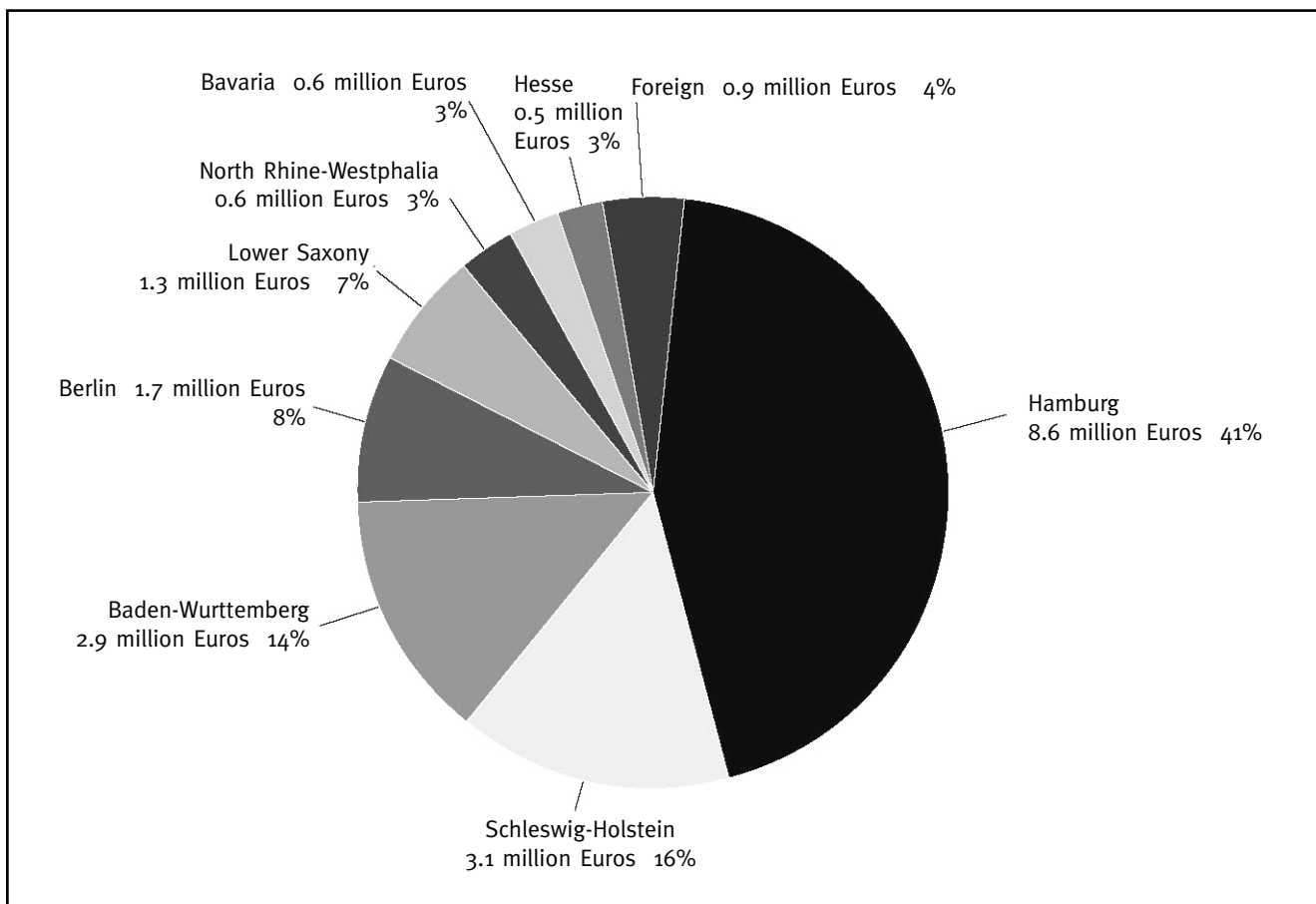
The transfer of know-how developed with public monies into the patent portfolios of a private entity seems to us to be a structurally inadequate way to proceed for neglected diseases

### 4.5 Regional distribution

The distribution of public financing between the various states, especially those states where the institutes are located, is remarkable (see Figure 5).

Two facts emerge from Figure 5: Germany invests only a small sum in research outside Germany, although naturally only a small amount of clinical research could be conducted within Germany for the diseases in this report. In addition, 80% of funding goes to only four states, whereas eight of the sixteen states do not have a single institution supported by public funds.

**Figure 5:** Research support 2007 according to location of the supported institutions



## 5. Structural problems in financial support for research

### 5.1 Absence of earmarked funds

It can only be estimated how much the institutional support for research into neglected diseases actually accomplishes.

A survey of the largest federal- and state- supported relevant research facilities, such as the facilities of the Leibniz Society, the Helmholtz Centres, the Robert Koch Institute and the Fraunhofer Gesellschaft, revealed that relevant research using institutional funding was conducted by the two Leibniz Institutions: the FZB and the BNI.

The Helmholtz Centre for Infection Research in Braunschweig has engaged itself as a champion of infections research within the new 'Roadmap for Health Research Programme of the Federal Government'. A speaker from the Centre fears, however, that research funds for the diseases in this report will, as is to date the case in Germany, remain difficult to come by.

Finally, the MPIIB uses 1.3 million Euros of its institutional support for vaccine research for TB. However, the MPIIB makes clear that the absence of earmarked funds means that the research direction of the Institute can always be influenced by personnel composition. It must also be made clear that the greater part of research funding is not earmarked, meaning that research projects in the area of TB, malaria and neglected tropical diseases must compete with other research areas, which is often to their disadvantage. There are also some built-in systematic disadvantages. Research with the slow-multiplying TB bacteria, for example, is much more time-intensive than research with other disease agents. Even the few large relevant research facilities are therefore very heavily dependent on the research interests of the given residents in the Institutions.

An example shows what this means in practice. The European Molecular Biology Laboratory (EMBL), that receives two-thirds of its financing from member states (including Germany),<sup>13</sup> had made malaria a research priority until recently: with the departure of the General Director, both the entire research group and the focal point for malaria moved to Imperial College, London. The financing to the EMBL for malaria research was lost along with the team.

This means that if the federal government wants to contribute meaningfully to this area, which is so important for poor countries, it needs to set clear strategic goals and make specifically allocated funds available.

### 5.2 A lack of strategies for support and deficient oversight

No such funding strategy is at hand. There is desperate need for it if a bridge is to be built between basic research (disease pathology, candidate cures), clinical research, and the treatment of patients. Ministries and donor institutions must work hand in hand. To this end, the ministries implicated in international public health must also better coordinate their funding policies.

We lack a useful overview of what research is supported in Germany, what is researched where and by whom and what role the various research projects play in themselves and in relation to each other within the masterplan for combating neglected diseases. The development of the overview MSF has attempted in this report was no easy undertaking.

There are no details of funding amounts of the individual financing projects in the DFG-funding database, nor is there any willingness to make these data available.<sup>14</sup> Most of the research institutes we wrote to did their best to give us information about their research expenditures, which, especially in estimating institutional resources, was not easy to do. A great hindrance was the discovery that the large federal research institutes do not publish even summaries of their budgets.

It is very clear that to date, even the federal government has no overview of the research resources for neglected diseases. In the course of our work on this report we heard that the health ministry had compiled data on the funding expenditure in the area of neglected diseases. It would be most welcome if these results were published publicly. They could serve as the basis for the necessary debate on the strategic direction of funding policy in the area of neglected disease.

<sup>13</sup> Additional funding is received from the US Department of Health and diverse private foundations, such as the Wellcome Trust, Swiss Institute of Bioinformatics or the Volkswagen Foundation

<sup>14</sup> On the advice of the statistics department of the DFG we worked with statistical average values. The statistics department informed us that these were 100,000 Euros per year for SFB (partial projects), 65,000 Euros for individual projects (including research groups and SPP), 30,000 Euros per year for scholarships, and 200,000 Euros per year for Emmy Noether groups (note: these are internal DFG reference group codes).

## International Product Development Partnerships (PDPs)

PDPs undertake to advance research into particular diseases. This can, for example, take the shape of the development of a new malaria medicine. PDPs function by funding multiple parallel projects, because the development of medicines is necessarily associated with a relatively high failure rate of many potential candidates during the research stage. PDPs are only seldom involved in conducting research themselves. More often their role is to distribute public and private funds between concrete projects. They also coordinate and integrate the work of industrial academic and public sector partners and in this manner, manage the research portfolios for neglected diseases.

Members of these partnerships can be public research facilities, pharmaceutical companies and NGOs, for example. An example of a successful PDP is the Drugs for Neglected Diseases Initiative (DNDi), which was founded in 2003 by MSF, the Institut Pasteur and public research institutes from Kenya, Brazil, India and Malaysia. DNDi researches and develops medicines for malaria, sleeping sickness, Chagas disease and leishmaniasis and has to date the biggest portfolio for research and development for neglected diseases.

### Open source medicines

In 2007 DNDi produced its first product, the combination therapy ASAQ against malaria. This was done in collaboration with the pharmaceutical company Sanofi-Aventis. ASAQ had an important signalling function as a patent-free 'open source medicine' from the outset. In April 2008, DNDi brought a second combination therapy against malaria to the market: 'ASMQ', particularly suited to the (drug-resistant) situation in Latin America and Asia.

In its goal to develop six to eight new therapeutic options for neglected disease by 2014, DNDi will need an additional 200 million Euros. To date it has secured 74 million Euros from public and private sources. DNDi receives public funding from the EU, the USA and six European governments (the Netherlands, Great Britain, Switzerland, Spain, France, Italy). Additional funding is received from MSF and the Bill and Melinda Gates Foundation.

Four additional PDPs are relevant for the diseases covered in this report: The TB Alliance researches new medicines for the treatment of TB, particularly those that could be used alongside treatment for HIV-infection, and those which shorten therapy. The Foundation for Innovative New Diagnostics (FIND) researches diagnostics for TB, malaria and sleeping

sickness; Aeras is developing new TB vaccines. The Medicines for Malaria Venture (MMV) was founded to develop new effective medicines for malaria.

PDPs have already proven that medicines research can take place outside industry and for much less money<sup>15</sup>. At the same time it is evident that the research and development made possible through PDPs is important, but is alone insufficient to achieve a real breakthrough for neglected diseases.<sup>16</sup>

### Expensive clinical trials

In order to determine that a medicine does not carry unwanted side effects and actually heals or delays a disease, it must successfully pass three clinical trials. This is the most intensive and expensive part of medical research.

It is precisely for this reason that with increasing success, the financial needs of PDPs will steadily increase. To be able to produce real results from the PDP initiatives within a few years, much more money must be invested in them.

Both the pharmaceutical industry and the public sector must assume their responsibilities and invest more in research and development for neglected diseases. Governments cannot depend on the fact that Bill Gates, who with his money assumes the lion's share of the financing for PDPs, will in perpetuity make up the difference, which in reality is the responsibility of public research financing.

To assure continuity and coordination of research for neglected diseases, governments must engage far more actively than at present.

It is also important, in supporting PDPs, to assure that the resulting products are actually accessible to the people who need them. In MSF's experience, this is best achieved when no patent-based monopoly production is allowed, so generic competition is possible from the outset.

### A pill is only effective if it lands in people's mouths

Medicines, vaccines or diagnostics that are developed with public resources must therefore be made immediately available for generic production in developing countries. A pill is only effective if it lands in the mouth of the person who needs it. This is not equally appreciated by all PDPs. Often PDPs also lack a clear and explicit guarantee of this principle.

15 Mary Moran, 2005: The new landscape of neglected disease development. [http://www.lse.ac.uk/collections/pressAndInformationOffice/newsAndEvents/archives/2005/Neglected\\_Diseases.htm](http://www.lse.ac.uk/collections/pressAndInformationOffice/newsAndEvents/archives/2005/Neglected_Diseases.htm)

16 Casenghi M, Cole ST, Nathan CF (2007) New approaches to filling the gap in tuberculosis drug discovery. *PLoS Med* 4(11): e293 doi:10.1371/journal.pmed.0040293

## 6. Will Germany fulfil her responsibility?

Is Germany doing enough? The simple answer is NO. MSF is not alone in considering the contribution to research for neglected diseases insufficient. Researchers, doctors, and politicians with health, development and research portfolios from the German Parliament also consider that more must be done.

Is it possible for the public authorities to do more than they have done, can Germany afford to do more? A few comparative figures show, from MSF's perspective, that doing more to confront the diseases affecting the poorest of the poor - and their children most of all, is not a question of capacity to pay, it is a question of political will.

A look at the German research budget shows plenty of room for change. When one considers the 400 million Euros allocated by the BMBF to project research support in the life sciences, and especially pharmacology and medical technology, it is immediately apparent that the current direct annual support of 3.8 Million Euros for the diseases included here is nowhere near the possible financial limit.

A look abroad is also revealing: the British development co-operation ministry, DFID (Department for International Development), alone planned an investment of 116 million Pounds (148 million Euros) for research projects in the period 2006/2007. DFID considers research into diseases that primarily affect developing countries as development assistance, and spent 29.3 million Euros for research in the area of health<sup>17</sup> in 2007. The expenditure of the British DFID in this area is therefore several times higher than that of the German BMZ, which is only peripherally engaged in this area. DFID has established 15 separate research programmes, in which it cooperates directly with partners in developing countries. DFID states that it intends to further increase its expenditure in this area. DFID, according to a strategy paper it has published<sup>18</sup>, is convinced that research is an engine for development.

The German contribution is also very modest compared to that of private foundations, such as the Bill and Melinda Gates Foundation. This foundation, whose capital has continued in this period to increase incrementally to 60 billion USD, invests a large proportion of its annual budget of 2 billion USD in the area of health research.

MSF is of the view that the German government has an ethical obligation to people in poor countries, and therefore calls for a substantial increase of the German

contribution to research support.

Such research support must also take into account the need to ensure that the results of research represent and deliver advances to the people affected, and these must be affordable. The results of research supported by public expenditure must not be placed out of the reach of people in developing countries by patenting. The BMBF-supported Vaccine Initiative is obliged to calculate licensing fees, such that after eight years of start-up financing the Initiative is self-sustaining. Apparently the protection of intellectual property takes precedence over the advancement of affordable medicines, especially for the poorest. Public research, however, should not be undertaken with the view to create an attractive environment for industry. This has been reaffirmed in our conversations for this report with a variety of researchers.

### 6.1 Tuberculosis - Robert Koch would be turning in his grave

Owing to its significance, we have undertaken a detailed analysis of the situation with tuberculosis. What would a fair contribution of Germany be to the global investment in TB research support, and what does this contribution currently look like? We proceed on the following assumptions:

**1. The global need for TB research funds is 2 billion dollars per year.** The 'Global Plan to Stop TB 2006-2015' (published by the Stop TB Partnership) sees a need for 900 million USD a year. If we consider the basic research and operational research needs not included in this estimate, the need rises to 2 billion USD a year<sup>19</sup>.

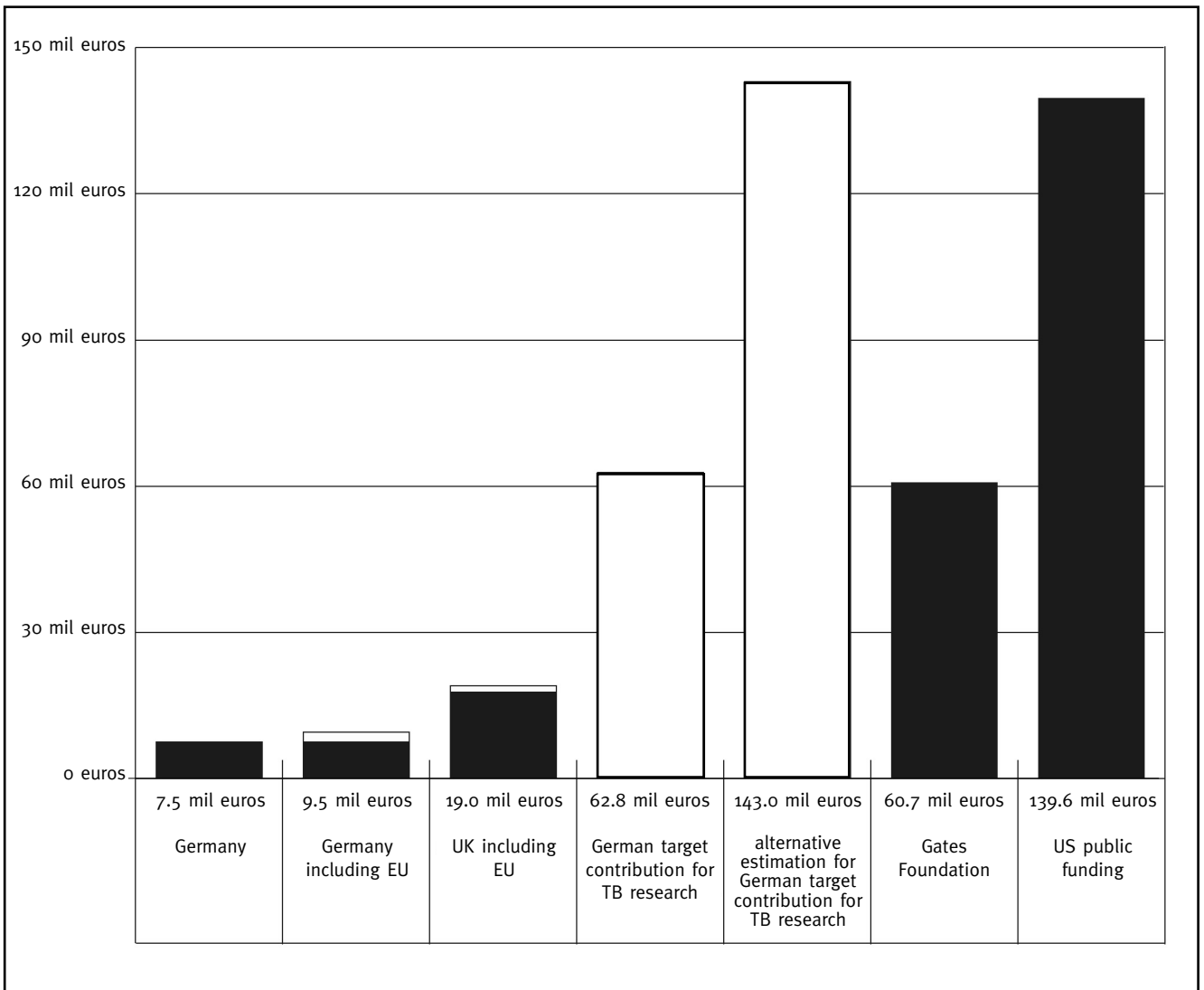
**2. The public contribution to TB research remains at the 2006 level of 59.1%.** This is a conservative estimate. It is likely that foundations cannot increase their contributions at will and industry is not prepared to increase theirs.

**3. The German contribution to research support should be as high as the German proportion of the Gross National Product (GNP) of the OECD States + China, Brazil, India and Russia.** These countries all have domestic research capacity and are therefore included in the calculation. The German proportion of the cumulative GNP of these countries is 7.3%. We therefore assume that the German contribution to the required public expenditure on TB research should also be 7.3%.

<sup>17</sup> Research supported by DFID includes more than just the diseases named in our report. DFID was unable to give us exact figures for the amount allocated to these diseases. Nevertheless, it is clear that, even considering exclusively the diseases in terms of our report, a much higher sum must be allocated than the amount expended by the BMZ.

<sup>18</sup> Source DFID

<sup>19</sup> TAG report 2007



**Figure 6:** Expenditures on tuberculosis research. (Sources: Real contribution of Germany and fair target contribution of Germany: Analysis by MSF. Remaining figures: TAG report; the TAG figures refer to the year 2006)

From these assumptions, the targeted German contribution to TB research funds should be 62.8 million Euros a year (comparison Fig. 6). According to our calculations, however, Germany expended only 7.5 million Euros in 2007 on TB research. If we include her contributions to the EU, the amount rises to 9.5 million Euros<sup>20</sup>. As such, Germany meets only 15%, or one-seventh of what could be considered her adequate contribution to TB research.

This is a deliberately conservative estimate. Other organisations use different methods. If we consider, for example, the methods used in the calculations of the Aktionsbündnis gegen AIDS (German Action Coalition against AIDS)<sup>21</sup>, one comes to a much higher sum. If one considers, in addition to this higher figure of Germany's fair contribution to public investment in TB research,

that the private investment in TB research does not increase, and as a consequence, the public sector has to cover all of the current shortfall, then the German contribution would have to be 143 million Euros (see Fig. 6). The German contribution in this case would have to increase 15-fold!

When one makes a comparison with what other countries are already doing, then one sees that Germany's current contribution is not worthy of the biggest and richest European nation. Britain, for example, invests twice as much as Germany in TB research, although the German economy, based on GNP, is 26% higher than Britain's. The USA in turn, with 139.6 million Euros expenditure per year<sup>22</sup>, spends around 15-times as much as Germany, although her economic power is not even five times as high.

<sup>20</sup> Here we have added to the amounts determined in this report 19.7% of the amounts determined in the TAG report as EU financing for TB research. The 19.7% is the German contribution to financing of the EU.

<sup>21</sup> The Aktionsbündnis gegen AIDS comes, in calculating the targeted German contribution to combating HIV/AIDS, to the conclusion that Germany should contribute 10.74% of the necessary funds to fight AIDS. They arrive at this conclusion by assuming that the 15 traditional EU donor countries should contribute at least 50% of the total required sum to tackle HIV, as they do for development assistance. The German proportion of the total GNP of the EU-15 is 21.48%. Half of this sum is 10.74%. For details see, e.g. [www.aids-kampagne.de/l8mimages/g8positionspapieraga\\_mai.pdf](http://www.aids-kampagne.de/l8mimages/g8positionspapieraga_mai.pdf)

<sup>22</sup> Source: Research support TAG 2007, the figure refers to the year 2006. The GNP figures are from [www.worldbank.org](http://www.worldbank.org)

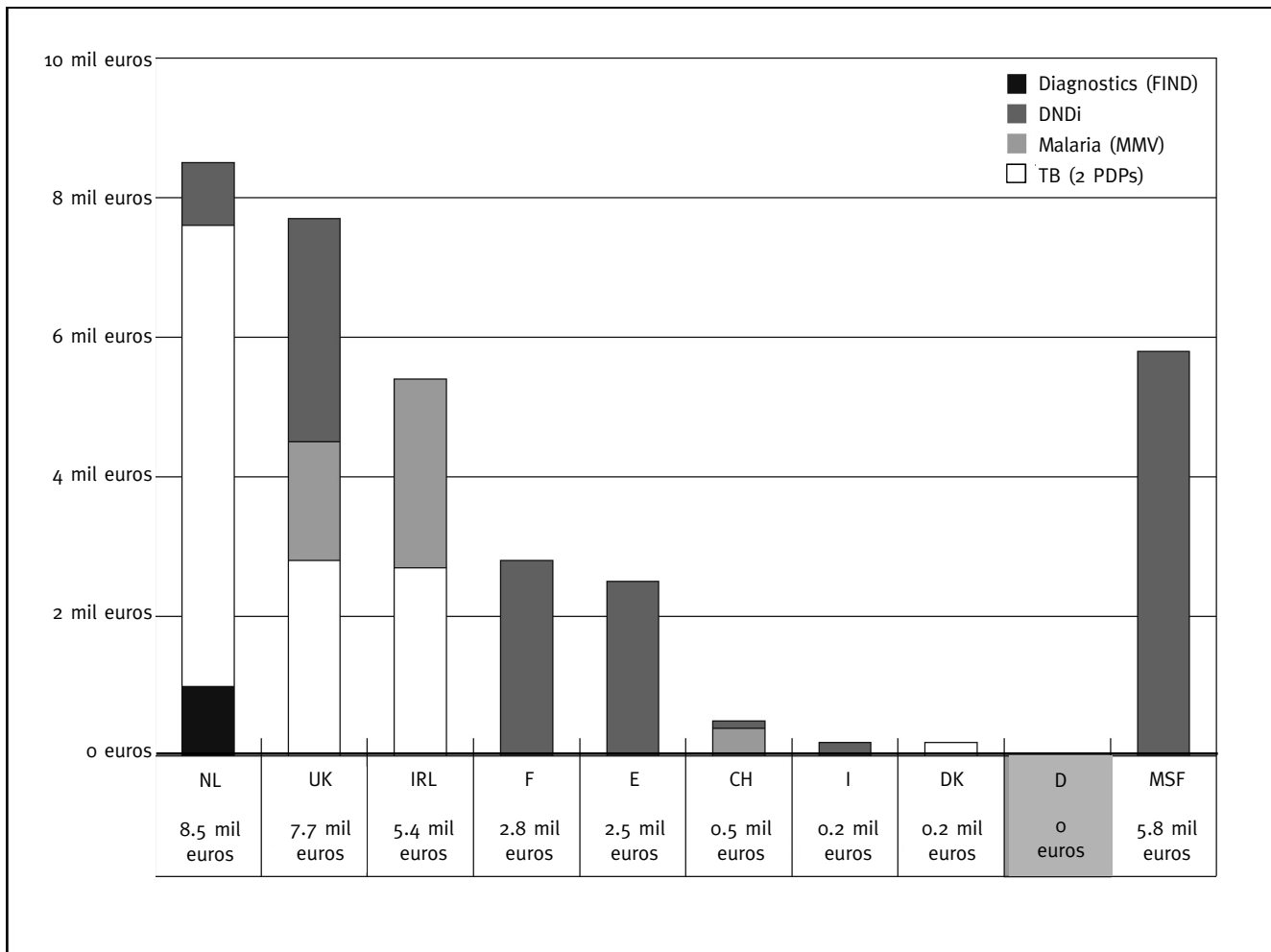


Figure 7: Subsidies from EU-member states to the PDPs relevant for this report, adjusted to the year 2007

## 6.2 International Product Development Partnerships (PDPs)

In the box on page 18, we explain why PDPs play an important role in research and development to combat neglected diseases.

Some governments are already engaged in this battle through their contribution to PDPs. The EU-member states alone have, in the year 2007, contributed a joint total of 27.3 million Euros to support PDPs (see Figure 7).

The government of the Netherlands has in recent years provided support to all five PDPs considered. Ireland and the United Kingdom are particularly active in the battle to develop new treatment options for malaria and TB. The USA, Switzerland, France and Denmark assume responsibility for research into neglected diseases. Spain made known in March 2008 that she would give a further 5 million Euros over two years to DNDi; Italy also supports this initiative.

Germany shows up here in a particularly negative light: to date she has given absolutely nothing to any of these PDPs<sup>23</sup>. The BMZ has nevertheless made a verbal commitment to support DNDi in 2008 to the tune of one million Euros.

This particularly lamentable performance with regard to PDPs appears to be founded on a lack of clarity between the three implicated Federal Ministries who hold this responsibility:

- The Research Ministry (BMBF) is in our estimation unwilling to support research conducted outside Germany, although it is a central tenet of PDPs to work on various projects in various locations.
- The Development Ministry (BMZ) does not consider itself responsible for research.
- The Health Ministry (BMG) does not consider itself responsible for developing countries.

It is wholly unacceptable, from MSF's perspective, that such important instruments as PDPs are hampered, and indeed fall through the cracks, as a result of bureaucratic

<sup>23</sup> The BMZ allocates 1 million Euros a year to the financing of the international Partnership for Microbicides, which is working on a vaccine to prevent HIV. As HIV is not included in this report, this contribution is not counted.

obscurity concerning areas of ministerial competence. The implicated ministries must come to an agreement between themselves on who assumes responsibility in this area. If they cannot, then the Federal Parliament or even the Chancellor must intervene to untie this Gordian knot.

### 6.3 And the European Union (EU)?

The invariable response from the public authorities to criticism of Germany's meagre contribution to research support is to go to the European Commission (EC), where apparently much more is done. We do have data for malaria and TB, which clearly contradict the notion that the EC does more for neglected diseases than individual member states.

According to the Treatment Action Group, the EC Research Directorate spent 12.8 million Euros in 2006 on research for TB. If we calculate the German proportion from her contributions to the EC<sup>24</sup>, this would be 2.0 million Euros. Using the same methods for malaria, according to the Malaria Research Report<sup>25</sup> 2004, Germany contributed 0.9 million Euros of the total EC contribution. These sums are not to be ignored, but are not sufficient to prove a different level of commitment.

Surprisingly, in the debate on research support, the false notion is repeatedly advanced that the Global Fund to Fight AIDS, TB and Malaria (GFATM or Global Fund in short) finances research. This is not the case. The Global Fund sees its role as supporting treatment and spends, at the outside, minimal amounts on 'Operational Research'.

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<sup>24</sup> According to the EU Budget of 2007, Germany contributes 19.7% of the EU budget

<sup>25</sup> [www.malariaalliance.org](http://www.malariaalliance.org)

## 7. New directions for research support

The various correspondents with whom MSF spoke for this report made a wide range of suggestions for strategic reorientation, improved cooperation and innovative research financing.

Karl Addicks, a free-democratic party (FDP) member of Parliament, is the lead initiator of a multi-party group 'health in developing countries' in the German Parliament (Bundestag), and despite dismissal from the ruling coalition parties, is determined that ultimately a subcommittee on these issues will be established on this question.

His social-democrat (SPD) colleague, Wolfgang Wodarg, has called for the establishment of an inter-ministerial committee, in which the experts from the responsible ministries would come together. This committee should be borne by the conviction that one wants to do something. One should not only feel responsible for product development and policies to attract industry to Germany, says Wodarg. "We have a responsibility that goes beyond the current market-incentive systems," he elaborates, in describing the objectives of meaningful work with respect to poor countries. Wodarg also sees a need for the establishment of an international research fund.

### 7.1 MSF's Recommendations

For MSF, the figures presented show clearly that Germany is not meeting her responsibilities. As we have shown above, we consider that for TB, for example, a reasonable investment would be 7 to 15 times higher than at present. How can this target be met? In principle there are several options. As a medical humanitarian organisation MSF will not stipulate the best method for research investment. What is important for us and for our patients are the following three points:

- **Public research investment must radically increase.** In view of our analysis, it is clear that this cannot succeed through the established channels, such as financing of the DFG. Germany must make available far more dedicated, earmarked funds for research into neglected diseases.
- Increased financing of research must be part of far stronger participation of the federal government in **the creation of alternative mechanisms for research and development**, such as being currently discussed by the WHO Intergovernmental Working Group on Intellectual Property, Innovation and Public Health (WHO IGWG).

- **The results of research must be accessible to the poorest.** Even the best results are meaningless if they cannot be applied. This means, for MSF, that clear rules must be in place that allow the lowest prices in developing countries. This also means that from the outset, guarantees must be in place that patents will not lead to prices higher than those warranted to cover the necessary production costs. The costs of research and development must be decoupled from the price of the product for developing countries, as advocated by the World Health Organization.<sup>26</sup>

Within this framework, there are a number of options to improve German research support. MSF would like to open discussions on the following recommendations for usefully applying the additional resources made available:

- The **Research Ministry (BMBF)** could establish its own dedicated research programme with a volume of over 20 million Euros per year, for research into TB, malaria and neglected tropical diseases.
- The **Health Ministry (BMG) and the States (Bundesländer)** could increase their support to the Leibniz Society, Bernard Nocht Institute and Research Center Borstel.
- The **States (Bundesländer) and the universities** could establish professorships (chairs) for TB, malaria and neglected tropical diseases.
- The **Federal Government** must decide which ministry will carry the responsibility for supporting PDPs. In a pan-European comparison, Germany's contribution, based on her economic power, would be five to six million Euros annually.
- The **German Research Foundation (DFG)** could establish its own programme for research into TB, malaria and neglected tropical diseases. This could be established as a priority programme of the DFG.
- The predominantly publicly owned **Vaccine Programme Management (VPM GmbH)** should establish clear and binding rules on patents, which guarantee that patents do not constitute an obstacle to generics production in developing countries.
- The **European Molecular Biology Laboratory**, and the **Helmholtz Centre for Infection Research (HZI)** in Braunschweig should undertake research in neglected diseases.



- The **Helmholtz Foundation** could establish a special programme to support research into diseases of particular significance for developing countries.
- The **Fraunhofer Institute** could play an especially important role in the important area of development of new diagnostic technologies.
- The **Max Planck Institute** could become more actively involved. Conceivable would be the establishment of a new institute or a new MPI-Directorship with the corresponding profile.

## Alternative mechanisms for financing research

So far we have laid out traditional methods for financing research. Especially within the framework of the WHO IGWG, other approaches are being discussed. Of particular interest among these are the ideas of prize funds that are being advanced by, for example, the Nobel Prize winner for Economics Professor Joseph Stiglitz. Under these proposals, a firm or research entity that developed a new medicine or vaccine would receive a substantial (in the factor of hundreds of millions Euros) sum and in return the discovery would become immediately available, at least to people in developing countries.

In the German context, this could mean for example the establishment of a **Robert Koch Prize for TB Research**. Whoever developed a new medicine for TB that was as effective as Rifampicin, but worked against MDR-TB, would receive a substantial prize from the federal government. The patent rights would be satisfied and ceded with this prize, at least for developing countries, so that immediate access could be guaranteed through generic production.

The advantage of such a prize would include the fact that payment would be made only for successful outcomes.

It is also important for MSF that increased financial support for research is part of an explicit long-term political strategy, based on the outcomes of the WHO IGWG process, that guarantee innovation and access. Germany must be much more strongly engaged, even within the IGWG process, and actively support the establishment of alternative financing mechanisms.

In the end, it is critical from the perspective of our patients to **strengthen both innovation and access to lifesaving medicines**.

## 8. Appendix

This appendix details the sources of information for the report. Further information about the individual research projects that were used for our calculations can be found, alongside the full report, on our website at <http://www.msfacecess.org/>

In the report we have had to convert the various currencies, for consistency and clarity, and to reflect their relative value. For the year 2006, we therefore used a conversion rate of 1 EURO = 1.25 USD, and for the year 2007 a conversion rate of 1 EURO = 1.375 USD. Both values reflect the median conversion rate in the respective years. The British Pound is converted at the rate of 1GBP = 1.2728 EURO throughout.

### 8.1 Sources

All the sources and quotes used in the report are derived from independently verifiable sources. The numbers used were sent to the respectively implicated Institutions (BMBF, BMZ, BNI, FZB, VPM, MPIIB<sup>27</sup>) for commentary. All commentaries received were integrated into the report. Further information used in the report came from

1. Official websites of the identified institutions
2. Official studies of the identified institutions
3. Official emails and letters

#### Correspondents:

##### Ministries and Federal Agencies:

BMBF: Federal Ministry for Education and Research, (Dr. Gabriele Hausdorf, Dr. Claudia Herok), [www.bmbf.bund.de](http://www.bmbf.bund.de)

BMG: Federal Ministry of Health (Dagmar Reitenbach, Dagmar Kaiser), [www.bmg.bund.de](http://www.bmg.bund.de)

BMZ: Federal Ministry for Economic Co-operation and Development (Dr. Jochen Böhmer, Doris Brauer), [www.bmz.de](http://www.bmz.de)

DFG: German Research Foundation (Dr. Jürgen Güdler, Dr. Andreas Strecker), [www.dfg.de](http://www.dfg.de)

##### Research Institutions:

Bernhard Nocht Institute (Dr. Barbara Ebert, Prof. Rolf Horstmann), [www.bni-hamburg.de](http://www.bni-hamburg.de)

European Molecular Biology Laboratory (Anna-Lyn Wegener, Dr. Matthias Wilmanns)

Paul Ehrlich Institute (Brigitte Morgenroth), [www.pei.de](http://www.pei.de)

FZB: Research Centre Borstel (Dr. Sabine Rüscher-Gerdes, Dr. Bettina Brand), [www.fz-borstel.de](http://www.fz-borstel.de)

HZI: Helmholtz Centre for Infection Research, (formerly Society for Biotechnological Research (GBF), (Dr. Jürgen Wehland), [www.helmholtz-hzi.de](http://www.helmholtz-hzi.de)

MPIIB: Max Planck Institute for Infection Biology, (Prof. Stefan Kaufmann, Dr. Robert Golinski, Dr. Sabine English), [www.mpiib-berlin.mpg.de/research/immunology.htm](http://www.mpiib-berlin.mpg.de/research/immunology.htm)

#### Universities:

Institute for Tropical Medicine of the Eberhard-Karls University, Tübingen (Prof. Jürgen Knobloch), [www.medizin.uni-tuebingen.de/tropenmedizin/](http://www.medizin.uni-tuebingen.de/tropenmedizin/)

Tropical Institute of the Ludwig-Maximilians University, Munich, (Dr. Thomas Löscher, Dr. Gisela Bretzel), [www.tropinst.med.uni-muenchen.de/index.html](http://www.tropinst.med.uni-muenchen.de/index.html)

Institute for Social Medicine, Epidemiology and Health Economics at the Charité University Medical Centre, Berlin (Dr. Peter Tinnemann), [www.charite.de/epidemiologie/german/index.htm](http://www.charite.de/epidemiologie/german/index.htm)

#### Parliamentarians:

Dr. Wolfgang Wodarg (SPD - Social Democratic Party), member of the German Parliament

Dr. Karl Addicks (FDP - Free Democratic Party), member of the German Parliament

#### Other:

Department for International Development (Charles Clift), [www.dfid.gov.uk/](http://www.dfid.gov.uk/)

Koch-Metschnikow Forum (Dr. Timo Ulrichs), [www.kmforum.eu/](http://www.kmforum.eu/)

VPM GmbH: Vaccine Project Management (Dr. Bernd Eisele), [www.vakzine-manager.de/](http://www.vakzine-manager.de/)

#### Written Sources:

Federal Budget 2007, Individual budget items 15, 30, and 23.

Project databank of the DFG (German Research Foundation), [www.dfg.de/gepris](http://www.dfg.de/gepris)

<sup>27</sup> Please note that the abbreviations used here are the official German language abbreviations for these institutions. These abbreviations are kept in German throughout, although for ease of reading the expounded English titles are used. E.g. BMG is the abbreviation for Bundesministerium für Gesundheit - in English, this is the Federal Ministry of Health

## 8.2 Which basic research was included?

In light of the fact that German research support for the diseases considered is overwhelmingly invested in basic research, we decided as a basic principle to consider this in our data analysis. The deciding factor for including a particular project was whether the funding was specifically allocated to one of the diseases considered. So for example, a project researching protein synthesis in *Mycobacterium Tuberculosis* was included, whilst a project researching protein synthesis in Gram-negative bacteria in general was not.

## 8.3 Institutional Support

The following institutions have invested a portion of their institutional financial support in the research of neglected diseases as defined in this report. For these, we have calculated and used that proportion of institutional support that falls within the criteria defined for this study. The institutions are:

- a. MPIIB: The Max Planck Institute for Infection Biology
- b. FZB: The Research Center Borstel
- c. Bernhard Nocht Institute
- d. Robert Koch Institute (owing to the relatively low sum invested of 60,000 EURO, the Robert Koch Institute is included in the graphs under the rubric 'other')

MPIIB and BNI have given rounded figures of the invested monies. The Robert Koch Institute informed us that one researcher is dedicated full-time to TB, which we have calculated at an investment of 60,000 EURO.

Because the FZB does not make exact breakdowns of how much of their institutional resources are spent for on each individual research area, we have for the purposes of this report, used estimates derived as follows:

In the FZB annual report 2005/2006, it is stated that 65% of staff work in research, and we therefore assume that 65% of the institutional support of the FZB flows into research (8.9 million Euros). Besides TB, the FZB also conducts research on numerous other diseases, such as lung cancer. In order to establish how much goes into which disease, we used the website of the FZB to ascertain how many staff belong to each working group and also which working group worked, to which extent, on which disease. Staff who had a coordination role within a unit were assigned according to the number of positions in their unit. Research that was not directly related to, for example, TB or *Mycobacterium Tuberculosis*, but was not disease-specific, belongs by definition outside the scope of this report.

On this basis, we calculated that, from the staff identified on the website, 25.8% work on TB and 0.4% on Chagas disease. Under the assumption that the institutional resources are distributed on this basis, we came to an investment of 2.3 million Euros for TB research and 37,000 Euros for Chagas research at the FZB.

## 8.4 Multinational Institutions

We included the investment of the Special Programme for Research and Training in Tropical Diseases (TDR), a global scientific collaboration programme, co-sponsored by the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the World Bank and the World Health Organization (WHO), dedicated to combating the most threatening diseases of poor countries.

We would have included other international institutions, for example, the product development partnerships (PDPs), if Germany had made any contribution to these.





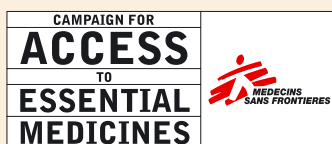
# COUGH UP FOR TB!

Every day the medical teams of Médecins Sans Frontières are faced with the lack of adequate or effective tools needed to treat, detect or prevent disease – especially those diseases that predominantly occur in poor countries, such as tuberculosis, malaria or other neglected diseases. In the case of tuberculosis, the standard medicines – developed over 40 years ago – are now largely ineffective against emerging drug-resistant strains of the disease. Medical tools to treat patients co-infected with HIV are also not up to the task. The result is that 1.7 million people continue to die each year of tuberculosis.

Although governments have repeatedly recognised this disastrous state of affairs, the financial commitments for much needed research and development of drugs, diagnostics and vaccines lag far behind the political rhetoric – raising questions about the seriousness of the international community's response to this crisis in health.

Germany has the financial resources, the scientific expertise and the research infrastructure which could allow it to play a significant role in the fight against tuberculosis, malaria and other neglected diseases. Over a century ago, Robert Koch, professor at the University of Berlin and one of the founders of microbiology, was able to dramatically advance our knowledge of TB and other diseases.

This report for the first time analyses how much funding Germany is today contributing towards research into tuberculosis, malaria and other neglected diseases – and if today's "heirs of Robert Koch" live up to their responsibilities.



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