



Federal Ministry
of Education
and Research

Research funding concept **Neglected and poverty-related diseases**



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Neglected and poverty-related diseases



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Summary

The term “neglected and poverty-related diseases” refers to several groups of infectious diseases that put a great burden on developing countries and hamper their economic development. These diseases affect more than a billion people and cause millions of deaths every year. They include malaria, tuberculosis and HIV/AIDS, but also a large number of tropical diseases that are less well known or completely unknown in Germany as well as diseases that predominantly affect children in developing countries.

With the exception of HIV/AIDS, research into these diseases was not a priority for industrialized countries in the past, as it was not profitable for the pharmaceutical industry and government funding tended to focus on diseases that affected the country’s own population. However, there have been significant changes in recent years, initiated by individual industrialized nations, large foundations and the World Health Organization (WHO). Germany too has changed its attitude towards these diseases.

With this concept, the Federal Ministry of Education and Research (BMBF) wants to restructure and continuously expand its support for research into neglected and poverty-related diseases.

This includes four different components:

1. **Many German universities and research institutions already conduct basic, preclinical and clinical research, particularly on malaria, tuberculosis and HIV/AIDS (total BMBF funding: currently about €11 million per year). The funding opportunities for these research activities are being increased, with a special emphasis on diseases that have received less attention in the past. In addition, a German Centre for Infection Research is being established and will also conduct research on the diseases in question.**
2. **In the area of preclinical research, the clinical phase and production, funding for product development partnerships (PDPs) is being introduced, which is completely new in German research funding. PDPs are international non-profit organizations that pursue the goal of developing prevention methods, vaccines, drugs or diagnostic agents/equipment to**
3. **Germany’s participation in the European and Developing Countries Clinical Trials Partnership (EDCTP) already represents the main focus of Germany’s involvement in clinical research on HIV/AIDS, malaria and tuberculosis. This commitment will be increased and expanded in coming years.**
4. **In the past, Germany pursued the goal of improving medical care in Africa through its development cooperation, not through its research funding. The BMBF is currently developing an approach in which African health research systems will be analysed and strengthened through research networks. Important aims of research funding include the participation of local partners and the development and expansion of research capacities in the countries affected. In funding measures such as EDCTP and in junior research groups, a special emphasis is put on the inclusion of researchers from developing countries.**

fight neglected and poverty-related diseases and of bringing these solutions to the market cost-effectively. The new BMBF funding measure will have two disease-related focuses: neglected tropical diseases (infectious diseases as defined by the WHO, including Chagas disease, dengue, bilharzia and elephantiasis) and high-burden diseases that cause high mortality among children in developing countries, for example bacterial pneumonia and meningitis, diarrhoea and malaria. Support will be provided for the development of products that help prevent, diagnose or treat these two groups of diseases. Products developed specifically for children under the age of 5 and/or for pregnant women will be given priority. The basic prerequisite for funding is that no alternatives to the proposed products exist to date.

Overview – Neglected and poverty-related diseases

In what has come to be known as the “90/10 gap“, only 10 per cent of international research funding is used to develop drugs for diseases that account for 90 per cent of the health burden. This is illustrated by the fact that, of the 1,556 new drugs that came onto the market between 1974 and 2004, only 21 were indicated for neglected and poverty-related diseases: eight for malaria, three for tuberculosis and ten for neglected tropical diseases (Source: T. Chirac, Global Framework on Essential Health R&D).

But what are neglected and poverty-related diseases, and what are the challenges when it comes to combating them?

The term “neglected and poverty-related diseases” is not clearly defined. It is generally understood to include diseases that predominantly occur in developing countries, cause a high burden of disease, significantly reduce quality of life or can lead to death, and for which there are no (or no adequate) treatments. Almost all of these diseases are infectious diseases that are either transmitted directly between humans or from animals to humans (zoonoses).

The commitment of the private sector in this area has increased in recent years. However, there are few incentives for the pharmaceutical industry to invest in the development of drugs, prevention methods or diagnostic procedures for these diseases, as those affected are unable to afford (expensive) new products and there are hardly any resources available in the national healthcare or social security systems.

For the purposes of this BMBF funding concept, a broad definition was used, including diseases from the following groups:

- **The “big three” (tuberculosis, malaria and HIV/AIDS) – these diseases are not neglected (any more) in research, but their incidence in developing countries is clearly poverty-related.**
- **“Neglected tropical diseases” as defined by the WHO (17 widespread endemic infectious diseases that are mainly caused by parasites, including African sleeping sickness, elephantiasis, bilharzia, Chagas disease, onchocerciasis and dengue fever).**

- **Diseases that mainly affect children in developing countries, e.g. certain forms of diarrhoea or bacterial meningitis.**

Certain non-communicable diseases that are widespread throughout the world – such as cancer or cardio-vascular diseases – have certain typical manifestations in developing countries. However, this is not the focus of the present concept.

Neglected and poverty-related diseases can also be categorized according to **pathogen** type, which has implications for the treatment options. There are diseases caused by viral pathogens (e.g. HIV/AIDS and dengue fever), bacterial pathogens (e.g. tuberculosis, Buruli ulcer and leprosy), protozoa (e.g. malaria, Chagas disease and African sleeping sickness) and parasitic worms (e.g. lymphatic filariasis and bilharzia).

There are drugs to treat some of the neglected and poverty-related diseases, but many of them are not sufficiently effective or have unpleasant or dangerous side effects, which means that patients often fail to take the drugs as prescribed. This, in turn, promotes the development of drug resistance and reduces the chances of recovery. Other drugs are too expensive or unsuitable for use in tropical environments with bad hygienic conditions, as they are highly perishable or only available in the form of injections. Still others are not suitable for the treatment of children, even though children are particularly affected by neglected and poverty-related diseases. In addition, the quality and applicability of available prevention methods and diagnostic agents are often inadequate.

In this context, the WHO distinguishes between “tool ready” and “tool deficient” diseases – in other words, diseases for which prevention methods, diagnostic agents or drugs already exist, meaning that the challenges are „merely“ logistical and social; and diseases that not even modern medicine can cure. The BMBF’s funding focuses on diseases in the latter category, for which there are no suitable prevention, diagnosis or treatment options.

The “big three”

The “big three”: HIV/AIDS, malaria and tuberculosis cause more than four million deaths worldwide every year. Despite the efforts made in recent years, these diseases are still spreading. HIV/tuberculosis co-infections and tuberculosis resistance are a serious problem.

Although there are effective **malaria** drugs on the market, resistance is on the rise and new drugs are urgently needed in order to remain one step ahead of the disease. The development of a vaccine is an ambitious goal, but one that promises immense rewards. As with other zoonotic diseases, vector control¹ is a central aspect: To eradicate malaria, it needs to be possible to fight the carriers of the disease in a way that is environmentally friendly and not hazardous to people’s health. To this end, new prevention methods and environmentally friendly insecticides against which there is no resistance need to be developed.

It is now possible to treat **HIV/AIDS** with antiretroviral therapy, but there are a huge number of people, particularly in Africa, who do not benefit from this treatment. Antiretroviral therapy requires continuous monitoring. What is needed are cost-effective diagnostic agents or diagnostic equipment that enable a reliable diagnosis even under very basic conditions. In addition, the spread of HIV urgently needs to be slowed down. As a rule, women are more at risk of infection than men, but they are often not in a position to negotiate the use of condoms. To enable women to protect themselves, intensive efforts have been made for years now to develop microbicides (vaginal gels and other agents that can be applied externally to prevent or reduce the risk of infection). The development of a vaccine is another ambitious goal that is being pursued with a great deal of dedication around the world.

Treating **tuberculosis** remains a huge problem. The odds of recovery are only 81 per cent even in Germany, and the outlook is much worse in places with an inadequate supply of effective drugs. In addition, multiresistant pathogens are on the rise, which makes treatment much more difficult. HIV/tuberculosis co-infections are a special problem: People who are HIV positive are particularly vulnerable to tuberculosis. At the same time, there are some problematic interactions between the drugs

used to treat the two diseases. It is often very difficult to even reach a clear diagnosis. Current activities therefore focus on the development of new drugs that significantly reduce the duration of treatment and increase the chances of recovery. Efforts also need to be made to develop innovative diagnostic procedures and an effective vaccine.

Neglected tropical diseases as defined by the WHO

The World Health Organization (WHO) uses the term „neglected tropical diseases“ to refer specifically to 17 diseases that are particularly prevalent in tropical countries, especially in very poor areas, remote rural areas, slums and conflict zones. According to the WHO, there are 149 countries and regions in which neglected tropical diseases are endemic, and at least 100 countries in which two or more of these diseases are endemic.

- Buruli ulcer (bacterium related to the tubercle bacterium)
- Chagas disease (protozoan parasites)
- Dengue fever (virus)
- Dracunculiasis (Guinea-worm disease)
- Human African trypanosomiasis (or sleeping sickness; protozoan parasites)
- Leishmaniasis (or Kala-azar; protozoan parasites)
- Leprosy (bacterium related to the tubercle bacterium)
- Lymphatic filariasis (or elephantiasis; worm disease)
- Onchocerciasis (or river blindness; worm disease)
- Schistosomiasis (or bilharzia; worm disease)
- Helminthoses (intestinal worm infections)
- Trachoma (bacterial)
- Treponematoses (bacterial)
- Cysticercosis (tapeworm)
- Echinococcosis (tapeworm)
- Rabies (virus)
- Fascioliasis (flukes)

According to the WHO, more than a billion people suffer from these diseases. Neglected tropical diseases have received particularly little attention in past research activities, as they have lower mortality rates than the “big three” and do not offer lucrative sales markets. Nevertheless, they cause chronic health effects and hamper economic development in the affected regions, as sufferers are often unable to work for months on end, rendering them incapable of providing for themselves or their children. For many of these diseases, there are either no drugs

¹ Vector: An organism that transmits a disease from one host to the next. The term “vector control” refers to efforts to control these carriers.

at all, or the drugs available have severe side effects or are only effective at certain stages of the disease. In addition, the diagnosis of parasitic diseases tends to be very difficult and is often impossible under basic conditions. Reliable, easy-to-use and climate-resistant drugs, diagnostic agents and diagnostic equipment are urgently needed. The development and clinical testing of drugs that are suitable for children has been particularly neglected, despite the fact that children are the worst affected.

Eleven of the diseases on the WHO list are zoonoses (like malaria), meaning that they are transmitted from animals to humans in various different ways. Zoonoses offer a particularly good opportunity for prevention – fighting the animal carriers can stop them from spreading. This is known as vector control, and it plays an important role in the fight against malaria, for example. However, the case of malaria also illustrates how important it is to develop control methods that are suitable, environmentally friendly and not hazardous to people’s health. The large-scale use of the insecticide DDT against mosquitoes in the past led to impressive successes in the fight against malaria, but also caused substantial environmental damage and resistance to this insecticide. Today, more gentle methods are used, such as spraying house walls with new insecticides or the use of long-lasting insecticidal mosquito nets. However, these methods are still not enough to prevent malaria infection reliably.

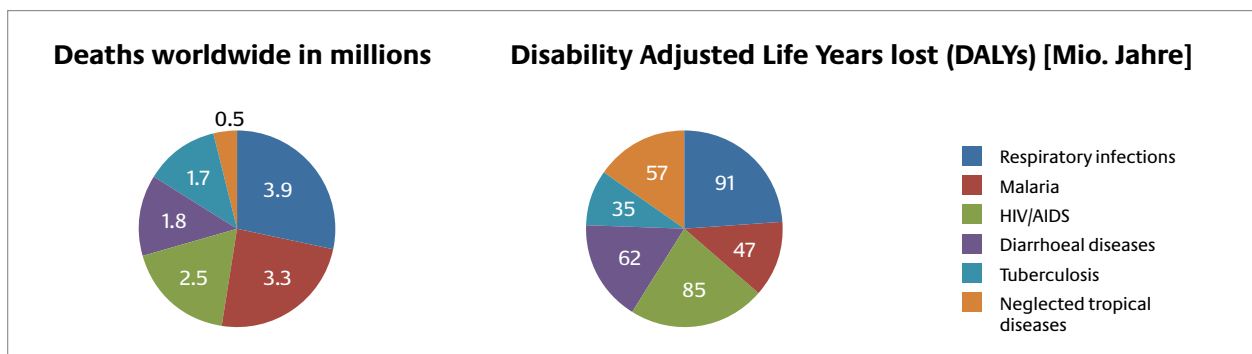
Neglected diseases with high child mortality

In addition to the groups of diseases mentioned above, there are a number of diseases with high child mortality rates in developing countries, for example bacterial pneumonia, meningitis, diarrhoeal diseases and rheumatic fever. This only refers to strains of patho-

gens and aspects of the diseases that specifically affect developing countries. As a result of the inadequate healthcare systems of the countries in question, these diseases are often not diagnosed and treated in time. Vaccines that are suitable for infants would be an effective way of reducing child mortality in the target countries.

Global burden of disease

Mortality statistics alone do not provide a sufficiently detailed statistical measure of a population’s health. DALYs (Disability-Adjusted Life Years lost) are often used to depict the total number of years affected by illness or disability or lost as a result of premature death. The diagram below shows how this changes the impact of different diseases: Neglected tropical diseases cause a relatively low number of deaths, but make up a much larger proportion of DALYs



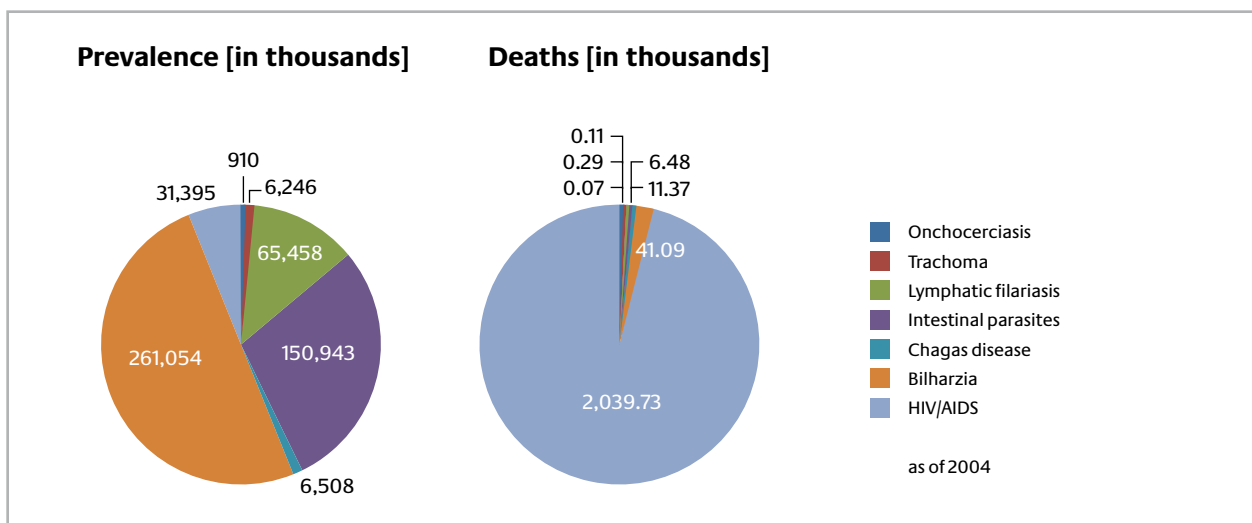
Source: http://www.globalhealth.org/images/pdf/gho/2008_id_understanding.pdf; as of 2004 (different sources put the mortality rate of malaria at between 1.3 and 3 million deaths per year)

The following two diagrams show that some diseases that hardly appear at all in death statistics (but which nevertheless cause great suffering) are extremely wide-spread. This is particularly clear when comparing HIV/AIDS with some of the neglected tropical diseases.

The diagram “Deaths in thousands” (see below) shows how many people died of certain diseases during the period in question (2004). The diagram “Prevalence in thousands” shows how many people suffered from these diseases in 2004. A comparison between the two diagrams shows that the mortality rate is often not proportional to the prevalence of the disease and is therefore not a suitable indicator of the population’s health in any given region. For example, bilharzia (schistosomiasis) is much more prevalent than HIV/AIDS. This disease very rarely leads to death, but it often has a severe impact on the quality of life of those

affected. It can easily be treated using praziquan-
tel, which has few side effects, but if left untreated, bilharzia can cause severe damage to the internal organs.

Another example is lymphatic filariasis, which affects more than 65 million people and can, in its most severe form, lead to elephantiasis – an extreme swelling of the legs or external genitalia caused by lymphatic blockage. While rarely fatal, this disease severely impairs quality of life, as the swellings associated with elephantiasis disfigure sufferers, disable them and often render them unable to work. Elephantiasis can currently not be cured, only alleviated.



Source: <http://www.who.int/gho/en/>

Burden of disease among children and pregnant women

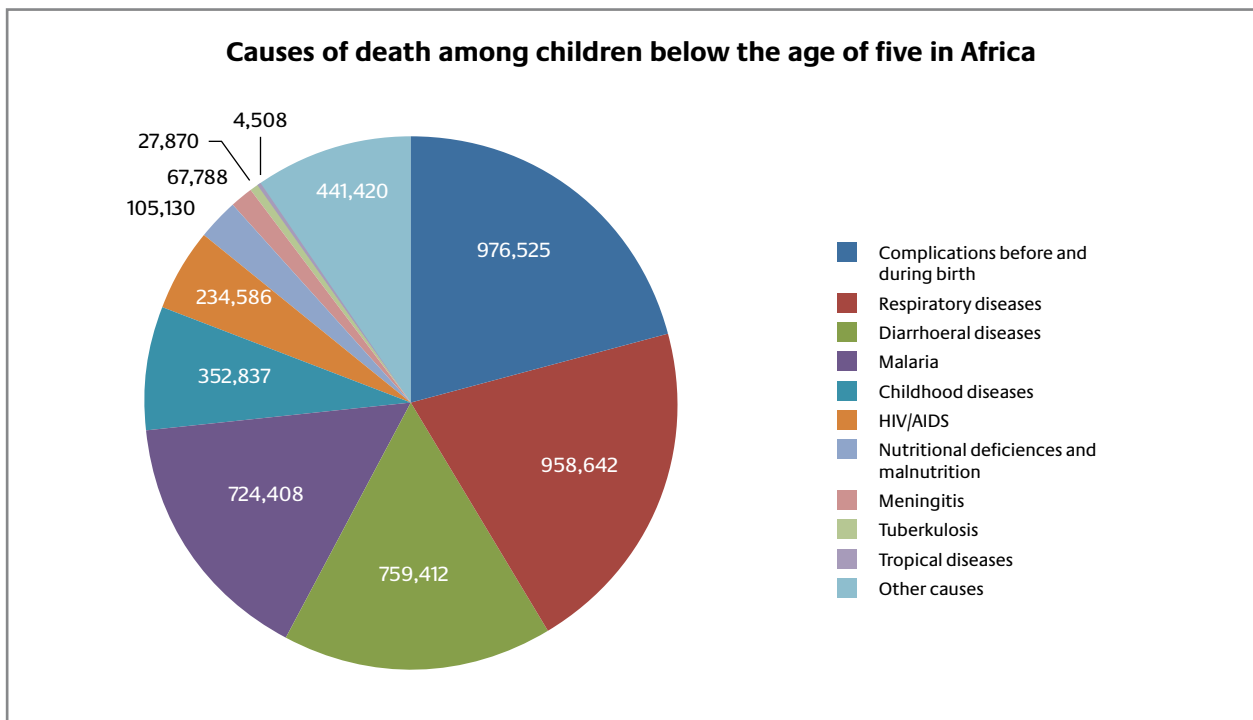
Children under the age of five and pregnant women are particularly affected by neglected diseases. Children are especially vulnerable because their immune systems are not fully developed. According to the WHO, 2.2 million people die of diarrhoeal diseases every year, most of them children under the age of five. The diagram below shows that, in addition to malaria, diarrhea and pneumonia are very common causes of death among young children. This is influenced by local living conditions such as water, sanitary conditions, hygiene and nutrition – about 35 per cent of all deaths among young children in developing countries are associated with malnutrition.

However, non-fatal illnesses such as parasitic diseases can lead to severe impairments, for example growth disturbances and developmental delays that can jeopardize children’s success in school. Although there are suitable treatments, drugs cannot prevent

re-infection. Holistic concepts need to be developed that prevent the transmission of parasites on a long-term basis.

For many diseases, there are no suitable ways of diagnosing sufferers at an early stage. Diseases such as Buruli ulcer are difficult to treat once they have reached the later stages and cause severe deformities among those affected, 70 per cent of whom are children. This disease is so little understood that not even the modes of transmission are entirely clear.

Pregnant women are also at special risk. For example, the course of malaria is more severe than in women who are not pregnant, but treatment is only possible to a limited extent as it can have side effects to the unborn child. That is why new, safe drugs are urgently needed that offer a better outlook for the mother and child. The “big three”, other infectious diseases and complications in childbirth and motherhood lead to almost **250 million Disability-Adjusted Life Years lost (DALYs)** among women in Africa every year.



Source: http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html

The innovation process – From basic research to the successful fight against neglected and poverty-related diseases

The aim of improving health and increasing the quality of life of people in developing countries has been pursued in various ways for many years. From religious missions offering healthcare to disaster relief to research stations in endemic areas funded by industrialized countries – efforts are being made to provide support on a local level. In this context, various problems have arisen that prevent help from being provided in an effective way. One big problem is the limited availability of effective, low-priced drugs and methods for prevention and diagnosis. Another issue is the need to develop and support functional healthcare systems that can provide people with basic healthcare.

The latest report of the WHO's Commission on Macroeconomics and Health, which was published in 2006, highlights the correlation between health and economic growth and calls for investments of at least US\$3 billion per year in research and development to improve the health of the world's poorest people.

This poses two challenges for the BMBF as a **research ministry**: On the one hand, the need to develop adequate prevention methods, diagnostic procedures and drugs; on the other hand, the need to support the development of functional local healthcare systems by establishing the necessary local health research structures.

The BMBF is facing up to both of these challenges. When it comes to research into neglected and poverty-related diseases, the ministry plans to engage in activities in the following areas and the interfaces between them:

1. **Basic research: Basic scientific work with the aim of finding a new target for potential new drugs (mainly in German research institutions, partly in cooperation with partners in developing countries). Basic research identifies new biomarkers for infections, thus paving the way for the development of better and more viable diagnostic procedures. Not least, basic research provides insights on how diseases are transmitted – which is still not entirely clear in the case of some diseases.**
2. **Preclinical research: All targeted research activities that have the aim of finding or testing new active substances or diagnostic procedures, including proof of concept. In addition to the desired effect, important aspects include the basic suitability of the substance as a drug (for example, the potential applications of water-insoluble substances are very limited) and the possibility of producing it cost-effectively in sufficient quantities.**
3. **Clinical phase and production: All clinical phases from the basic testing of an active substance or a diagnostic agent on humans to market maturity and beyond (including clinical trials in Africa). This also includes further steps leading up to the launch of the new drug (particularly finding the most suitable form of administration, production and approval).**
4. **Healthcare- and application-related local research: Not just the care of patients, but particularly local health research that directly affects the viability, quality and sustainability of diagnostics, care and vector control.**



The aim in all these activities is to take a collaborative and inclusive approach with the partners so that the capacities of research institutions in the affected countries are built up in a sustainable way. In Germany, the BMBF has been supporting the first step of the innovation process for various diseases for many years, but this is only true to a limited extent for the second step. The third step has been supported in the case of the “big three”, particularly via Germany’s involvement in the EDCTP (the European and Developing Countries Clinical Trials

Partnership, an initiative of the EU and individual European countries for conducting clinical trials in Africa on HIV/AIDS, tuberculosis and malaria). The second and third step of the innovation process – in other words, preclinical research and the clinical phase including production and approval – are to be supported in a targeted way through product development partnerships starting in 2011. A funding approach on “Local healthcare and research” is currently being planned.

New financing models – innovative approaches to research funding

Generally speaking, there are two strategies for supporting research and development on active substances and vaccines to fight neglected and poverty-related diseases: **push** and **pull**. Push strategies involve the direct funding of research and development; pull strategies change the market and create incentives for companies.

Push strategies include project funding, tax incentives, financing for product development partnerships, accelerated approval procedures, liability protection or mechanisms to facilitate research work. **Product development partnerships** (or PDPs), in which pharmaceutical companies, academic laboratories and organizations from civil society work together, are an **example** of a successful push strategy. PDPs have existed since about 2000; the first products are already on the market.

Examples of **pull strategies** are purchase guarantees, purchase funds, improved market information, negative taxes on product sales, patent incentives or patent purchases. An **example** of a pull strategy is an **Advance Market Commitment** (or AMC), which is essentially a purchase guarantee. Such an AMC was agreed for a pneumococcal vaccine in 2007 (volume: €1.5 billion; partners: Bill & Melinda Gates foundation, Canada, Italy, Russia, the UK, Norway). Another example is accelerated consideration by the approval authorities. The waiting time in the approval process for drugs and vaccines against neglected and poverty-related diseases could be shortened compared to “normal” drugs and vaccines for the market in industrialized countries. AMCs are not research funding as such, but are designed to change the economic conditions. For this reason, they do not fall within the responsibilities of a research ministry. Another example of a pull strategy are research awards, which could play an important role in the future.

Basic research, preclinical research and clinical phase – funding in Germany



Infection research can look back on a very long tradition in Germany. Many German universities and non-university research institutions conduct basic and preclinical infection research. German pharmaceutical companies also carry out successful research into new anti-infectives.

The following section will present examples of basic, preclinical and clinical research projects, categorized according to disease, that are funded by the BMBF in Germany. In addition, it will give a short overview of other funding providers and research institutions that focus on neglected and poverty-related diseases. Finally, it will offer an outlook for BMBF funding in this area.

HIV/AIDS

The BMBF supports extensive national and international research projects across all areas of HIV/AIDS research. One of them is biomedical research, including basic and applied clinical research, another is social science research. In recent years, the results have been increasingly used for the development of new strategies and measures. A national patient cohort has been created with the help of numerous HIV/AIDS centres as part of the HIV/AIDS competence network. It currently contains data for more than 8,000 documented patients. The patient cohort is currently made up of patients from 25 treatment centres, including ten clinical outpatient departments and 25 private surgeries across Germany that specialize in HIV/AIDS and continually document clinical and socio-demographic data. The BMBF is providing €18.5 million for the HIV/AIDS competence network between June 2002 and April 2011.

The BMBF's project funding also supports a broad range of urgent research into HIV/AIDS under various funding priorities. For example, a special emphasis is put on vulnerable population groups (e.g. female migrants) within the area of prevention

research. In the "Molecular Diagnostics" funding priority, several working groups are working on the development of new diagnostic procedures, particularly with a view to improving differential diagnosis for different subtypes of the HI virus. Basic research projects under the "Systems Biology" research priority focus on the complex interplay between virus and host cell in order to find new approaches for future diagnostic procedures. Within the "Novel Therapeutic Approaches" and "Go-Bio" funding priorities, a number of outstanding researchers and research groups are working on new approaches that could ultimately lead to a curative treatment of HIV infections. The approaches pursued involve new target molecules in the infected cells that were not at the focus of HIV treatment in the past ("Novel Therapeutic Approaches") and efforts to completely remove the genetic material of the virus from the infected cells using recombinant enzymes ("Go-Bio"). Under the "Clinical Studies" funding priority, the START study on the strategic use of antiretroviral therapy (ART) is being funded for a period of six years. The aim of this multi-centre trial is to study the differences between immediate versus delayed ART intervention (measured according to CD4 titre) in 300 previously untreated patients and, in the process, observe the impact on serious AIDS-defining and non-AIDS-defining diseases.

Other clinical research projects focus on the major role of improved protection against infectious diseases and the important issue of comorbidities (e.g. HIV/AIDS and heart failure), since HIV/AIDS patients often require different treatment options than patients who are not infected with HIV.

In total, the BMBF's ongoing project funding for HIV/AIDS research amounts to about €25 million (as of 2009) with an average annual funding volume of €5-6 million. Approximately €500,000 of this money is spent on research that is directly relevant to developing countries.

Malaria

As part of its project funding, the BMBF supports a large number of different research approaches that pursue the aim of fighting malaria more effectively. In the area of applied genome research (NGFN-Transfer), efforts are being made to identify new anti-malaria compounds, either by targeting special properties of the parasitic pathogen or by disrupting the complex interplay between the pathogen and host cells in the blood and/or the liver. Several research projects ("Go-Bio") deal with other specific properties of the pathogen (movement and mechanisms during penetration into the host cell). In addition, various national research projects are working on the development and clinical trial of malaria vaccines.

The BMBF's project support for malaria-related research activities currently amounts to about €6.5 million, with an average yearly funding volume of approximately €1.2 million. Around €500,000 of this money is available every year for collaborative work with developing countries that are particularly strongly affected.

Tuberculosis

Research and funding activities in Germany on the subject of tuberculosis cover a broad area, from basic research to clinical research to vaccine development. Various collaborative projects are working on different aspects of tuberculosis research.

One of these activities involves **Vakzine Projekt Management GmbH (VPM)**, a BMBF-funded start-up that organizes and finances the preclinical and clinical development of tuberculosis vaccines. To this end, VPM acquires the property rights to promising vaccine candidates from German laboratories and controls their development until they can be sold on to private-sector partners. Currently, VPM is mainly focusing on bringing the potential tuberculosis vaccine VPM1002 to the clinical trial stage.

In total, the BMBF is providing approximately €10 million for tuberculosis research projects. The BMBF's current annual expenditure on tuberculosis research is about €4 million (as of 2009), of

which approximately €1 million per year is used for vaccine development at VPM. About €400,000 per year are spent on research projects that are directly relevant to developing countries.

Junior research groups working on neglected tropical diseases

The BMBF supports the development of research capacities in the field of neglected and poverty-related diseases by funding junior research groups. A call for proposals was published in 2009 with the aim of expanding research capacities for these infectious diseases on a long-term basis in cooperation with partners from countries which are especially affected by these diseases. Over the next three years, three junior research groups will work on issues related to multiple parasitic infections in Sub-Saharan Africa. In order to make new insights available quickly, significant parts of the research projects are being carried out in the affected regions in cooperation with the African partners. The three junior research groups will have just over €1.5 million at their disposal over the next three years.

Non-BMBF research funding in Germany and Europe

The European Commission's 6th Research Framework Programme provided funding for projects focusing on malaria, HIV/AIDS and tuberculosis. The 7th Research Framework Programme, which runs from 2007 to 2013, is undertaking increased efforts in this area. In addition to a large "Call for Africa" in 2009, there is a thematic priority on neglected and poverty-related diseases under which collaborations with developing countries can receive support, depending on the subject.

The German Research Foundation (DFG) provided approximately €6.1 million in research funding for the "big three" in 2009 (malaria: 2.8; HIV/AIDS: 2.3; tuberculosis: 1.0). The DFG also supports two collaborative research centres that are directly relevant to neglected and poverty-related diseases: SFB 544 ("Control of Tropical Infectious Diseases") at the University of Heidelberg from 1999 to 2011 and SFB 630 ("Recognition, Preparation and Functional Analysis of Agents

against Infectious Diseases”) at the University of Würzburg, which has been conducting research on agents to fight neglected diseases such as leishmaniasis since 2003. There is also a funding priority on infection research in Africa, which supports collaborative projects with African researchers. Here too, the aim is to build up research capacities in Africa.

The Volkswagen Foundation supports young African scientists who want to conduct research on neglected diseases in Africa. In a first call for proposals in 2008, ten fellowships worth a total of €1.34 million were awarded to African scientists.

The Federal Ministry for Economic Cooperation and Development (BMZ) has already supported PDPs in the past. For example, the Drugs for Neglected Diseases initiative (DNDi) and the International Partnership for Microbicides (IPM) received €1 million each in 2008. On a smaller scale, the BMZ (via GIZ and KfW) also supports integrated research activities within health-related capacity building measures, for example research on infectious diseases with a focus on HIV/AIDS in German-African and German-Asian hospital partnerships as part of the ESTHER network (Ensemble pour une Solidarité Thérapeutique Hospitalière En Réseau). The BMZ also contributed financially to the WHO’s „Special Programme for Research and Training in Tropical Diseases” (TDR) in recent years. In addition, German development cooperation includes research-relevant and supporting activities as part of programmes designed to strengthen health systems.

The research support of the Federal Ministry of Health (BMG) in the relevant area focuses on HIV/AIDS and tuberculosis (about €1.5 million in 2009). The Ministry of Health also makes a significant contribution to financing the Bernhard Nocht Institute (BNI) for Tropical Medicine in Hamburg, which forms part of the Leibniz Association. In 2009, the BNI spent about €1.7 million on malaria research, approximately €700,000 on tuberculosis research and about €150,000 on HIV/AIDS projects.

The Federal Ministry of Economics and Technology (BMWi) provides about €300,000 per year (as of 2009) of project funding for the development of malaria vaccines.

The Max Planck Society contributes significant amounts of funding (about €1.3 million in 2009) to the fight against tuberculosis via its Institute for Infection Biology (MPIIB) in Berlin.

The German institutions that focus on researcher exchanges (DAAD, AvH Foundation) have provided smaller amounts of funding specifically to fight the “big three”.

German university and non-university research institutions focusing on neglected and poverty-related diseases

With the exception of HIV/AIDS research, which is directly relevant to the national health system and is therefore undertaken at numerous universities and non-university research institutions, research on neglected and poverty-related diseases is carried out at a relatively small number of institutions in Germany. The Max Planck Institute for Infection Biology in Berlin and the Borstel Research Centre are centres of tuberculosis research. Both institutions conduct a large part of their work in cooperation with partners in affected regions. The Bernhard Nocht Institute for Tropical Medicine in Hamburg and the Institute for Tropical Medicine at the University of Tübingen are internationally well-regarded centres of malaria research. Alongside the centres for tropical medicine and international health at the University of Heidelberg and LMU Munich, these two institutes are the leading centres for the study of neglected diseases in all of Germany. The University of Rostock (tropical medicine), Charité – Universitätsmedizin Berlin (tropical medicine) and the universities of Greifswald and Bielefeld (public health aspects) also work in this area on a smaller scale.

The BMBF is building up a total of six German Centres for Health Research in order to be able to deal more effectively with common diseases that are on the rise. One of these centres is the German Centre for Infection Research (DZI). The decision about the locations of the DZI and the topics and diseases that it will focus on will be taken by an independent, international panel of experts. The DZI will then be established by April 2011. The DZI offers an opportunity to reposition the German research landscape with regard to neglected tropical infectious diseases. The call for proposals

for the DZI explicitly mentioned the possibility of conducting research into neglected and poverty-related infectious diseases and of including international partners specializing in this area.

Outlook

The BMBF will continue to expand its support of basic research into neglected and poverty-related diseases. Individual projects are regularly selected under funding measures with a broader thematic context. Research proposals dealing with specific aspects or diseases have to undergo scientific evaluation by international panels of experts. Applications can be submitted in various fields of action under the new Health Research Framework Programme, for example individualized medicine, health industry (biotechnology research), research into common diseases (establishment of the new German Centre for Infection Research, but also future calls providing project funding in the area of infection research) and international cooperation in health research.

These different but coordinated approaches to extend funding for basic and translational research against neglected and poverty-related diseases will lead to a significant increase in the BMBF's spending in this area in coming years – from approximately €11 million in 2010. The first concrete step is a call for product development partnerships with a funding volume of €20 million for the period from 2011 to 2014. In addition, research into neglected and poverty-related diseases can be expected to play a central role at the German Centre for Infection Research, which is being established in 2011. Funding for projects under the EDCTP is very likely to increase in coming years.

Thanks to Germany's increased global commitment, the people who are most in need of help will benefit from national research approaches more quickly and effectively. The close ties at various different levels between the BMBF, the BMG, the BMZ and its implementing organizations, the DFG, the foundations active in this area, the private sector and civil society organizations will lead to more coordinated and targeted activities in future.

Preclinical research, clinical phase and production – Support of product development partnerships



Because people in developing countries do not have much spending power and the health systems are desperately underfunded, there are few incentives for the private sector to develop products specifically for people in these countries. As a result, there is a lack of suitable drugs and vaccines. There is also a need for suitable diagnostic methods: Many neglected tropical and poverty-related diseases cannot be diagnosed accurately under basic conditions. In many other cases too, there are no suitable ways of reaching the correct diagnosis on site quickly. For this reason, the development of robust test methods is another important field of action, as are prevention methods (vaccines, insecticides, microbicides etc). The BMBF has decided to support Product Development Partnerships (PDPs) in order to specifically promote the development of cost-effective prevention methods, diagnostic procedures and drugs.

What are PDPs?

PDPs are non-profit organizations that pursue the aim of developing prevention methods, vaccines, drugs or diagnostic agents/equipment to fight neglected and poverty-related diseases and of bringing these solutions to the market cost-effectively. PDPs usually have a network structure in which different stakeholders work together: academic institutes, public research institutions, pharmaceutical companies and NGOs. PDPs come in very different forms. The five minimum criteria below are also applied by the PDP Funders Group, a loose interest group of countries and organizations that support PDPs:

- a) **The PDP focuses on one or more neglected and poverty-related diseases.**
- b) **The products are specifically tailored to the needs of people in developing countries.**

- c) **The main aim is to improve public health, not to make a profit (not-for-profit organization).**
- d) **The PDP uses management strategies from the private sector (pharmaceutical industry) such as portfolio management and industrial project management.**
- e) **The PDP engages in lobbying to further its own interests and makes efforts to raise awareness of the target disease in question.**

Item c) on the list illustrates the difference between conventional pharmaceutical research, which is (and needs to be) profit-oriented. Item d) highlights the difference between PDPs and academic research: Portfolio management means that multiple projects with the same aim (such as the development of a malaria drug for pregnant women) are pursued at the same time. Promising projects continue to receive funding and less successful projects are stopped. This can only be achieved through professional industrial project management that is not governed by individual interests. In this way, the chances of success can be increased dramatically.

How do PDPs work?

Unlike in research funding, where individual projects have to be as innovative as possible, product development partnerships are not based purely on scientific excellence. Instead, they focus on the needs-based and quick development of prevention methods, diagnostic procedures or drugs. This includes aspects such as low production costs, climate stability and ease of use. Successful examples of products that are already on the market include a malaria dosage prepared especially for children by the Medicines for Malaria Venture (MMV) or various compound drugs for African sleeping sickness and malaria developed by the Drugs for Neglected Diseases initiative (DNDi).

Who finances PDPs?

The George Institute for Global Health, which is headquartered in Australia, has been conducting an annual global survey on the subject of “Research and development funding for neglected and poverty-related diseases” since 2007 on behalf of the Bill and Melinda Gates Foundation. The results are published in G-FINDER, which is the most comprehensive source of information in this area. According to G-FINDER, approximately US\$3 billion were spent on research and development for prevention and diagnostic methods and drugs against neglected and poverty-related diseases in 2008. 73 per cent of this money was spent on research into the “big three” (HIV/AIDS, malaria and tuberculosis). Research into neglected tropical diseases, as defined by the WHO, received 26 per cent of the total volume of funding. Within this group, some diseases received a relatively large amount of funding (for example African sleeping sickness, Chagas disease and dengue fever), while others were given very little attention (for example trachoma, Buruli ulcer and leprosy).

The biggest providers of R&D funding for prevention methods, diagnostic procedures and drugs against neglected and poverty-related diseases (not limited to PDPs) in 2008 were the National Institutes of Health (USA) with US\$1.1 billion and the Bill and Melinda Gates Foundation with more than US\$640 million. Between their establishment and the end of 2008, PDPs received a total of about US\$580 million worldwide.

PDP funding measure of the BMBF

The BMBF plans to launch a new PDP funding measure with a duration of four years (2011-2014) and a funding volume of €20 million in 2011. The BMBF’s first call for proposals for PDPs will have a clear focus in order to highlight and define Germany’s involvement in this field. With this measure, the BMBF wants to make a sustainable contribution to reaching Millennium Development Goals 4 (reducing child mortality) and 5 (reducing maternal mortality).

- **The new BMBF funding measure will have two disease-related focuses: neglected tropical diseases (17 diseases defined by the WHO, including Chagas disease, dengue, bilharzia and elephantiasis) and diseases causing high**

mortality among children in developing countries, for example bacterial pneumonia and meningitis, diarrhoeal diseases, rheumatic fever and malaria.

- **Support is provided for the development of products that help prevent, diagnose or treat diseases in these two groups. Products developed specifically for children under the age of five and/or for pregnant women will be given priority.**
- **In order to receive funding, the research must focus on health problems for which there is no suitable prevention, diagnosis or treatment method.**

Aims and criteria

The funds invested should help as many people as possible. To this end, BMBF funding will only be provided if the following conditions are met:

The organizational form of the PDP must either be that of a legal entity or a contractual partnership.

The organization/partnership must work on a non-profit basis and apply methods and mechanisms of project management and portfolio management similar to those used in the private sector.

When submitting an application, PDPs have to have been active in their current organizational form for at least two years and have achieved their first operative successes.

PDPs submitting an application must be able to ensure that the funds will only be used for work on diseases and products mentioned above.

At least 50 per cent of the funds needed for product development must be obtained from other sources (proof to be furnished as part of the application).

The PDP must set itself guidelines on how to deal with partners in research and development and, in particular, on how to handle patent rights. The aim is to keep the product price as low as possible in the target country. This can be achieved through equitable licensing concepts, for example. Wherever possible, the PDP’s patent policies should allow

for market competition through the production of generic drugs, which has been shown to lead to low market prices.

The PDP needs to have established mechanisms for identifying and solving conflicts of interests.

Aspects of development cooperation and efforts to strengthen health systems are not at the focus of the BMBF's funding, but are strongly welcomed. Capacity building measures in the target countries should be pursued wherever possible (e.g. training medical personnel and researchers or building up infrastructure when carrying out clinical trials). Technology and knowledge transfer should take place in a suitable way. If possible, local producers should be given priority.

It must be ensured that newly introduced drugs and vaccines are monitored on a long-term basis (pharmacovigilance), if necessary by investing in and conducting training measures for an improved local quality infrastructure.

In addition to the safety and effectiveness of the new products, the local conditions and the impact on the target country need to be taken into account – the aim of market introduction must always be to reduce the burden of disease in the target country.

Ideally, data collected by the PDPs in the target country should be analysed locally with the help of local experts. At the very least, the data should be made available to the local health systems.

Instead of awarding short-term contracts, the goal should be to build up long-term partnerships with researchers and companies in the target country. This also has the aim of strengthening local institutions.

Clinical-phase research on HIV/AIDS, Malaria and Tuberculosis – Support for the EDCTP



In addition to research itself, efforts to build up clinical research capacities are very important when it comes to developing solutions to the big health problems in developing countries. That is why the BMBF has been acting as Germany's representative in the EDCTP (European and Developing Countries Clinical Trials Partnership) since 2003. The EDCTP is a joint initiative of the European Union, 16 European countries and 47 countries in Sub-Saharan Africa. It is dedicated to fighting the three biggest infectious diseases (HIV/AIDS, malaria and tuberculosis), also known as the „big three“. The focus of the initiative is on phase II and III clinical trials and on capacity-building measures, taking into account the local needs in Africa in an exemplary way and engaging in an equal partnership with African countries. This has made the EDCTP an internationally successful model.

The BMBF supports a total of 9 large international research consortia (two HIV/AIDS, five malaria, two tuberculosis) under the EDCTP (as of October 2010). Funding for six further consortia (three HIV/

AIDS, three tuberculosis) will start in the next few months. Funding is provided for vaccine development (HIV/AIDS, malaria, tuberculosis), research on improved diagnostic agents (tuberculosis) and consortia to introduce new drug treatments (HIV/AIDS, malaria, tuberculosis). Some of the projects funded are explicitly geared towards the particularly vulnerable group of newborns, small children (malaria, tuberculosis) and pregnant women (malaria). A total of €2 million have already been earmarked for projects designed to develop drugs and vaccines from 2010.

The first EDCTP programme phase with a total volume of about €600 million will gradually end starting in 2011. Planning for the second programme phase has already started. Thanks to progress made in research on the „big three“, it will include more phase III clinical trials, which are particularly expensive. The BMBF plans to intensify its involvement in this second programme phase in cooperation with its European and African partners.

Healthcare – Health and Healthcare research in Africa to improve healthcare systems



So far, work under the Health Research Programme has been limited to disease-specific activities with a strong focus on neglected and poverty-related diseases, for example in connection with the European and Developing Countries Clinical Trials Partnership (EDCTP) or the junior researcher programme on neglected tropical diseases. Systematic approaches that also address health policy or operational challenges in developing countries have not been pursued to date.

In the G8 dialogue process, the African partners have identified two fields in which they think further action is needed:

1. **Increasing the networking of existing structures under African leadership, particularly in the areas of maternal, newborn and child health.**
2. **Analysing and strengthening national health research systems in Africa.**

The BMBF wants to become involved in this area – possibly by supporting research networks in Africa. Preliminary work to develop a concept is currently being carried out with the help of the German National Academy of Sciences (Leopoldina). Subsequently, the BMBF plans to carry out a situation analysis during an exploratory phase, with the aim of developing approaches for a BMBF concept that offers noticeable added value compared to previous initiatives of other stakeholders. If possible, the exploratory phase will build on existing reports, statistics etc. drafted by the African Union, the African regions, the WHO, UN organizations (UNESCO, UNECA and others) or the World Bank and take into account the experiences of many years of German development cooperation in the areas of capacity development and strengthening health systems. The partner countries are to be involved in the process of identifying needs, and existing research infrastructures are to be built on wherever possible. The

exploratory phase (preparatory measures, fact finding missions etc.) is to be financed from the budget of the Directorate-General for European and International Cooperation in Education and Research (approx. €200,000; expected start: 2012).

In addition, the BMBF and the BMZ are planning to publish a joint call for proposals together with the French ministries MESR (Education and Research) and MAEE (Foreign and European Affairs) in order to fund Africa-related preparatory measures on subjects including health. The aim is to create the basis for trilateral (German-French-African) initiatives. Projects can receive up to €40,000 of funding.

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