FOUNDED IN 2003 TO ADDRESS THE NEEDS OF PATIENTS WITH MOST NEGLECTED DISEASES, DNDi IS A COLLABORATIVE, PATIENTS’ NEEDS-DRIVEN, VIRTUAL, NOT-FOR-PROFIT DRUG R&D ORGANISATION.
Developing Treatments for the Most Neglected

A patients’ needs-driven R&D model built on South-South and North-South collaboration

Despite revolutionary advances in drug development in recent decades, essential medicines to treat many diseases that affect the world’s poor are either too expensive, no longer produced, highly toxic, or ineffective. Recognising these issues from its field experience, Médecins Sans Frontières committed its 1999 Nobel Peace Prize funds to develop an alternative model for the research and development (R&D) of new drugs for neglected diseases.

As a result, in 2003, seven organisations from around the world joined forces to establish DNDi as an independent, needs-driven, not-for-profit organization to research and develop drugs for people suffering from the most neglected diseases. Acting in the public interest, DNDi bridges the existing R&D gaps in essential drugs for these diseases by initiating and coordinating drug R&D projects in collaboration with the international research community, the public sector, the pharmaceutical industry, and other relevant partners.

DNDi’s primary focus is the development of drugs for the most neglected diseases, such as sleeping sickness (human African trypanosomiasis, HAT), kala-azar (visceral leishmaniasis), and Chagas disease; and it will also consider engaging R&D projects on other neglected diseases. In pursuing these goals, DNDi manages R&D networks built on South-South and North-South collaborations. While using and supporting existing capacity in countries where the diseases are endemic, DNDi helps to strengthen additional capacity in a sustainable manner through technology transfer in the field of drug research and development for neglected diseases.

The primary objective of DNDi is to deliver six to eight new treatments by 2014 for leishmaniasis, sleeping sickness, Chagas disease, & malaria, and to establish a strong R&D portfolio that addresses patient needs for treatment. DNDi aims to establish a robust pipeline that delivers new treatments for all three primary diseases, four lead optimisation projects
Within its vision, DNDi also has two other objectives:

→ To use and strengthen existing capacities in disease-endemic countries and for project implementation;
→ To raise awareness about the need to develop new drugs for neglected diseases and advocate for increased public responsibility.
Why are some diseases more neglected than others?

Market Failure: Drug development in the R&D-based pharmaceutical industry has largely been confined to the R&D sector, with only a small market niche for neglected diseases. The industry's primary incentive is to focus on lucrative markets where it can recover research costs and generate profits. However, neglected diseases, which primarily affect the poor, often lack the financial incentives necessary for drug development.

Public Policy Failure: Over the past thirty years, global health has transformed at an unprecedented rate, but it has not been effective in providing important health tools for populations in industrialized countries, leaving cancer or cardiology research to two or more entities. Policymakers would not be satisfied with a single organization to focus on a given neglected disease or category of neglected diseases. In the case of laboratory equipment, the Institute of Tropical Diseases (NITD) in China, the Foundation for Innovative Diagnostics (FIND), the Global Alliance for TB Drug Development (GTA), the International AIDS Vaccine Initiative (IAVI), the Institute for One World Health (iOWH), and the MMV Institute of Tropical Diseases (NITD) have all sought to foster R&D for neglected diseases by building partnerships based on pragmatic synergies and collaborations.

Addressing the 10/90 Gap

Only 21 new drugs, 1.3% of the 1,556 new drugs registered between 1975 and 2004, were directed toward neglected diseases. In contrast, over 12% of all drug R&D efforts are spent on the development of antibiotics and vaccines for neglected diseases. This imbalance in drug R&D expenditure is a result of the global burden of disease in developing countries, which account for 90% of the population worldwide. Over the past thirty years, global health has transformed at an unprecedented rate, but it has not been effective in providing important health tools for populations in industrialized countries, leaving cancer or cardiology research to two or more entities. Policymakers would not be satisfied with a single organization to focus on a given neglected disease or category of neglected diseases. In the case of laboratory equipment, the Institute of Tropical Diseases (NITD) in China, the Foundation for Innovative Diagnostics (FIND), the Global Alliance for TB Drug Development (GTA), the International AIDS Vaccine Initiative (IAVI), the Institute for One World Health (iOWH), and the MMV Institute of Tropical Diseases (NITD) have all sought to foster R&D for neglected diseases by building partnerships based on pragmatic synergies and collaborations.
A Needs-Driven Approach:

<table>
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<tr>
<th>DISEASE</th>
<th>HUMAN AFRICAN TRYPANOSOMIASIS (HAT)</th>
<th>VISCERAL LEISHMANIASIS</th>
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<td>DESCRIPTION</td>
<td>HAT, also known as sleeping sickness, threatens people in 36 countries in sub-Saharan Africa and occurs in 2 stages: • 1st stage includes headaches and bouts of fever; • 2nd stage, known as neurological phase, occurs when parasite enters central nervous system and is fatal if left untreated.</td>
<td>Visceral leishmaniasis, fatal if left untreated, is characterized by prolonged fever, enlarged spleen &amp; liver, substantial weight loss, progressive anemia, and is complicated by co-infection with other diseases like malaria and HIV. 90% of cases reported in 5 countries (Bangladesh, Brazil, India, Nepal, and Sudan).</td>
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<td>TREATMENT LIMITATIONS</td>
<td>Few in number that are: • Old, toxic; • Difficult to administer and have lost efficacy in several regions; • Stage-specific, with more toxic and difficult-to-administer treatments for stage 2. • Stage 1 – Pentamidine (1940): 7-10 day injections; only works for Stage 1; – Suramin (1920s): used primarily for Stage 1 T.b. rhodesiense HAT. • Stage 2 – Melarsoprol (1949): 10 daily IV injections; painful &amp; highly toxic (5% treatment-related mortality); increasingly ineffective (with treatment failure up to 30% in some regions); – Eflornithine (1981): 4 infusions per day for 14 days; difficult administration mainly used as 2nd line for T.b. gambiense HAT.</td>
<td>Number of treatments has increased in past decade, but there are drawbacks: • Difficult to administer; • Long treatment course (21 to 28 days); • Toxic; • Expensive, limiting use in most disease-endemic countries; • Pentavalent antimonials: toxic, 30-day, hospital-based parenteral treatment with increasing drug resistance; • Amphotericin B: dose-limiting toxicity, 15-20 day, hospital-based IV treatment; • Liposomal Amphotericin B: excellent, but expensive; • Paromomycin: now registered in India (Sept. 2006), but efficacy in Africa not yet determined; • Miltefosine: first orally available drug now registered in India, but expensive and teratogenic in women of child-bearing age.</td>
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<td>PATIENT TREATMENT NEED</td>
<td>• A safe, effective, and practical stage 2 HAT drug to replace current first-line treatments, and to improve and simplify current case management. The aim is to develop one drug that is effective against both stages 1 and 2 of HAT. • A simple stage 1 treatment, to be used at the local health centre level, which could represent a great improvement by increasing access to treatment and coverage of HAT.</td>
<td>• An oral, safe, effective, low-cost, and short-course (10-day) treatment that could replace current treatments, improve and simplify current case management.</td>
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DNDi OBJECTIVES BY 2014

→ 1 new drug registered
→ 1 co-administration recommended

→ 1 new drug registered
→ 2 geographical extensions in endemic regions outside India by 2014
→ 2 co-administrations recommended

50 MILLION AT RISK, WITH AN ESTIMATED 50,000 – 150,000 INFECTED

500,000 NEW CASES REPORTED EACH YEAR
Patient Needs and DNDi Objectives

CHAGAS

~8 MILLION INFECTED, 100 MILLION AT RISK IN THE AMERICAS

Chagas disease, or human American trypanosomiasis, occurs in three disease stages: acute (in which 5% of children die), indeterminate, and chronic. Acute illness often spontaneously resolves in 4 to 6 weeks, at which time patients enter an asymptomatic, ‘indeterminate’ phase that can last 10 years to life. Chronic stage develops in 10 to 30% of infected persons and usually results in death from cardiac arrhythmia or congestive heart failure.

- Benznidazole, nifurtimox are for primary acute & early indeterminate: long treatment period (30-60 days), dose-dependent toxicity, high rate of patient non-compliance.
- No treatment for indeterminate and chronic disease.

MALARIA

1 MILLION CHILDREN DIE EACH YEAR

Malaria, one of the three most deadly diseases in Africa, is present in over 100 countries and threatens half of world population. Every year, 350 to 500 million cases of malaria occur worldwide, with a child dying every 30 seconds.

Treatments exist but:
- Widespread drug resistance (parasitic resistance to chloroquine is over 90% in many parts of Africa);
- Existing combination therapies can be expensive and have complicated treatment regimens;
- No paediatric-strength, fixed-dose combinations.

- Drugs for acute and chronic disease.
- Safer and more effective drugs adapted to patient needs – i.e., pediatric formulation.

→ 1 new drug registered

- A fixed-dose Artemisinin Combination Therapy (ACT) as a response to increasing levels of resistance to antimalarial medicines, as recommended by the World Health Organization (WHO) since 2001.

→ 2 new drugs registered in 2007 ensure utilisation and access