

03.

Strengthening Existing Capacities

Boosting regional networks to meet research challenges

Conducting clinical trials on neglected diseases often means that research must be carried out in some of the most remote areas like here in Amudat, Uganda, areas where little infrastructure of any kind, yet alone health, exists and where political instability is also frequent.



As part of its mission and objectives, DNDi synergises efforts to build sustainable research capacities in disease-endemic countries. The process of strengthening existing capacities, at the individual and institutional level, helps in transferring ownership of the solutions and responsibility to the affected country.



INVESTING IN INFRASTRUCTURE, TRAINING, RESEARCH, AND PARTNERSHIPS

Effective clinical research requires adequate infrastructure, solid partnerships, and leadership of ethical and regulatory authorities to ensure that good clinical practices are observed through the entire process of clinical development. In disease-endemic countries, where many of DNDi clinical trials are taking place, challenges are huge as most of these trials take place in very remote areas.

■ **Building infrastructure, training, and research capacities in the trial sites.** The physical upgrading of facilities related to clinical research (such as patient wards and diagnostics laboratories) is undertaken by DNDi at trial sites so as to ensure they are compliant with Good Clinical Practices (GCP) standards. These facilities are not owned by DNDi. In addition to physical infrastructure, trained staff are needed to carry out GCP-compliant trials. Training is important not just at the start of a trial, but is a continuous process which involves upskilling existing staff and training new members. From external consultants to the experienced trial site staff, the sharing of better practices principles helps to motivate teams working in difficult field conditions. Independent monitors are encouraged to make site visits on a regular basis to ensure that sites are following good clinical and laboratory practices, and standard operating procedures. This monitoring and auditing further educates staff and reinforces the importance of conducting clinical trials to international standards. In

2008-2009, DNDi constructed clinical trials wards in the Dooka clinical trials site, Sudan, and upgraded wards used for the same purpose in two new trials sites – Kimalel centre, Kenya, and Amudat hospital, Uganda. Moreover, DNDi has installed solar panels and repaired the incinerator at the Katanda health centre in the Democratic Republic of the Congo (DRC). More than 164 principle investigators, lab technicians, and monitors have received GCP training and 24 people at-



DNDi has taken a number of steps to help improve local infrastructure.

tended the AmBisome trial initiation. DNDi has also sponsored 16 members of the three platforms to attend different international scientific events. Out of a total of 134 staff involved in the clinical trials and paid by DNDi, 98 are staff at DNDi partners, 5.3 are DNDi core staff, and 30.7 are DNDi associated staff and consultants.

■ **Building sustainable partnerships.** In partnership with scientists and academics in endemic regions, the regional research platforms of the human African trypanosomiasis (HAT) Platform and the Leishmaniasis East Africa Platform (LEAP) aim to strengthen

clinical research capacity in a coherent manner to facilitate the availability of new medicines developed. The national control programmes of the most endemic countries are essential members of both platforms, and they play a key role in areas where clinical investigations are taking place. In order to leverage the biodiversity potential of the Asian region in drug discovery efforts for neglected diseases, the Pan-Asian Network for Neglected Diseases (PAN4ND) aims to translate the discovery of new bioactive molecules from natural, local resources into drugs effective against neglected diseases by sharing screening technologies between institutions. Acting as transnational support networks, these platforms enable partners to share different experiences, knowledge, and problem-solving techniques.

■ **Building transparent working relations with regulatory authorities and national ethics committees at all levels.** In many of the countries where trials could be conducted, the governing and regulatory authorities at local, regional and national levels play a crucial role in evaluating and approving clinical protocols, ensuring drug availability (by registering drugs and facilitating drug importation, in terms of logistics), and making changes to national treatment guidelines and protocols. National ethics committees also play a critical role.

REGIONAL PLATFORMS

LEAP

Leishmaniasis East Africa Platform

- 2003: founded in Khartoum
- 4 endemic countries
- 44 members
- More than 1,000 patients enrolled in clinical trials
- More than 802 patients treated outside the clinical trials in 2008/09

Dr Ahmed Mudawi Musa of the Institute for Endemic Diseases, and LEAP Chair, Sudan: "As important as the effort to find a new drug or a combination



of drugs to treat VL is, LEAP is addressing other critical issues associated with clinical research for neglected populations: capacity-building with excellent training of African scientists and support staff,

and concrete community participation in development and infrastructure strengthening in rural areas. With the help of LEAP and DNDi, we have facilities that allow us to serve unprivileged and marginalised communities with medicines at village level at the Kassab Hospital and Dookah Centre."

Objectives

- Facilitate clinical testing and registration of new treatments for VL in the region (Ethiopia, Kenya, Sudan and Uganda)
- Evaluate, validate, and register improved options that address regional needs for VL
- Provide capacity strengthening for drug evaluation and clinical studies in the region

The DNDi Scientific Advisory Committee (SAC) voted LEAP as 'The Best Partnership of the Year 2009': The selection was based on the following three criteria: quality and effectiveness of the partnership; strengthening capacities in disease-endemic countries; and knowledge gained that can lead to therapeutic innovation.

Recognised as

"Partnership of the Year in 2008"

Partners

- Center for Clinical Research, Kenya Medical Research Institute, Kenya
- Ministry of Health, Kenya

- Institute of Endemic Diseases at University of Khartoum, Sudan
- Federal Ministry of Health, Sudan
- Addis Ababa University, Ethiopia
- Gondar University, Ethiopia
- Federal Bureau of Health, Ethiopia
- University of Makerere, Uganda
- Ministry of Health, Uganda
- Médecins Sans Frontières
- I+ Solutions
- Institute for OneWorld Health
- London School of Hygiene and Tropical Medicine

Financial support

- International Solidarity, Canton of Geneva, Switzerland
 - Ministry of Foreign and European Affairs (MAEE), France
 - Region of Tuscany, Italy
 - Medicor Foundation, Liechtenstein
- In addition, core organisational funding from the following donors has been used by DNDi to support its research efforts with the HAT Platform:
- Department for International Development (DFID), UK
 - Médecins Sans Frontières (MSF)
 - Spanish Agency of International Cooperation for Development (AECID), Spain



HAT PLATFORM

- 2003: Founded in Kinshasa
- 5 endemic countries

"There is limited clinical research activity to assess and/or improve treatments and diagnostics for HAT, in part because patients are usually very spread out, living in remote areas. The national control programmes of the five most affected countries, in collaboration with DNDi, the Swiss Tropical Institute (STI), and a number of other partners, have established this platform for capacity-building in clinical trials for HAT. The overall aim is to build and strengthen clinical trial capacities in these endemic countries so that new and promising inter-



ventions for this fatal disease can be rapidly and effectively evaluated, registered and made available to the patients," said Dr Victor Kande, Director of the HAT National Control Programme of the DRC, member of the HAT Platform.

Objectives

- To strengthen clinical trial capacity for sleeping sickness
- To overcome health system challenges for clinical research
- To share information on HAT research progress
- To improve HAT clinical trial methodologies

Partners

- National HAT control programmes of most affected endemic countries: Democratic Republic of the Congo, Republic of the Congo, Angola, Uganda, and Sudan
- DNDi, Swiss Tropical Institute (STI)
- Research institutes including Institute of Tropical Medicine in Antwerp (ITMA), Institut National de Recherche Biomédicale (INRB), Centers for

Disease Control and Prevention (CDC), Kenya Agricultural Research Institute – Trypanosomiasis Research Centre (KARI-TRC)

- NGOs as MSF, Epicentre
- FIND, WHO
- Regional networks - e.g. Eastern Africa Network for Trypanosomiasis (EANETT), Pan-African Bioethics Initiative (PABIN), The African Malaria Network Trust (AMANET)



PAN4ND

Pan Asian Network for neglected diseases

- 2006, founded in Tokyo, Japan



"This network forms part of a long-term research collaboration between DNDi and the Kitasato Institute, that will make a significant contribution to bringing new treatments to patients suffering

from neglected diseases," says Professor S. Omura, President of the Kitasato Institute.

Objectives

- To link natural products researchers and institutes as a collaborative network
 - To incorporate neglected diseases into our drug candidate screening programmes
 - To standardise network screening methodologies against parasitic targets and other pathogens
- 40.3% of new chemical entities (NCEs) approved by the FDA from 1981 to 2002 were natural products or natural-product derivatives.

DNDi has been acting as a catalyst by supporting the creation and initial steps of the Pan-Asian Screening Network over a three-year period.

Partners

- Central Drug Research Institute (CDRI), India; Eskitis Institute, Australia; Forest Research Institute Malaysia (FRIM); Institut Pasteur Korea (IPK); Kitasato Institute (KI), Japan; Malaysian Institute of Pharmaceuticals and Neutraceuticals (MIPN), Malaysia; Novartis Institute of Tropical Diseases (NITD), Singapore; Shanghai Institute of Materia Medica (SIMM), China.

Financial support

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- Other private foundations and individual donors who wish to remain anonymous

Achievements

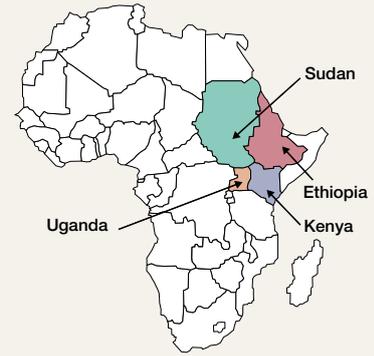
Capacity-building infrastructure

- Building and opening leishmaniasis research and treatment centres in Ethiopia: Arba Minch 2006; Gondar 2008
- Upgrading infrastructure at Amudat Hospital and initiating it as a clinical trial site
- Treatment centre opened in Kimalel, Kenya in January 2009 and treatment centre / laboratory training centre is planned to open in Dooka (late 2009)

- Ongoing improvements to data centre in Nairobi to set up a GCP-compliant data-management system using open source software

Capacity building – training

- Training of clinical monitors, Data and Safety Monitoring Board (DSMB) members, and investigators in good clinical practice (GCP)
- Providing career development training on a case-by-case basis for key members of the LEAP group / trial site teams
- Capacity strengthening of parasite classification research through technology transfer and training



Clinical trials

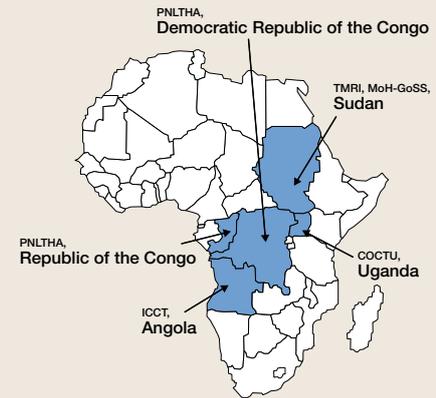
- Development and conduct of the LEAP 0104 paromomycin multi-centre clinical trial comparing paromomycin, sodium stibogluconate (SSG), and combination of paromomycin and SSG for treatment of VL (expected to be completed in Q4 2009. see page 25)
- Adoption by LEAP of phase II study AMBI 0106 to determine the minimum effective single dose of AmBisome
- Development of phase II clinical trial to assess safety and efficacy of miltefosine alone, AmBisome + miltefosine and AmBisome + SSG

Financial support

- European Union FP6
 - Ministry of Foreign and European Affairs (MAEE), France
- In addition, core organisational funding from the following donors has been used by DNDi to support its research efforts with the HAT Platform:
- Department for International Development (DFID), UK
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 - Spanish Agency of International Cooperation for Development (AECID), Spain
 - Other private foundations and individual donors who wish to remain anonymous

Achievements

- **Training:** Members - training on Good Clinical Practice (GCP), ethics, and clinical monitoring General practitioners - a programme on how to examine patients with HAT
- **Communications:** four platform newsletters published in English and French; presentations at various scientific congresses
- **Meetings:** launch in August 2005, and annual platform meetings (Nairobi, 2006; Khartoum, 2007; Brazzaville, 2008); seven steering committee meetings held - in conjunction with annual meetings as well as in Basel (June 2007), and Kampala (June 2008).
- **Clinical trials:** Support to the NECT Phase III and to the ongoing NECT-Field Studies



Achievements

- **Training:** Drug screening workshop at CDRI, Lucknow (February 2007); drug metabolism, pharmacokinetics, toxicology workshop at NITD, Singapore (February 2008); and a training programme in Kuala Lumpur December 2008 which covered natural product extraction and purification together with a seminar series on structure elucidation.
- **Strengthening capacities:** three training visits of platform scientists to reference screening centres (Kitasato Institute, Swiss Tropical Institute, University of Antwerp) between June and December 2007
- **Communications:** Development of manual on drug screening for kinetoplastid diseases

in collaboration with LSHTM, STI, and CDRI; organisation of five regional scientific events: four annual meetings (Tokyo, May 2006; Shanghai, June 2007; and Tokyo, June 2008; Kuala Lumpur, December 2008) and two natural substances drug discovery and development meetings (Kuala Lumpur, November 2006 and 2007). Development of a website dedicated to PAN4ND: www.pan4nd.org

