03.

Strengthening Existing Capacities

Working Together to Face Research Challenges

Making a solid impact on the ground, DNDi has built partnerships with researchers and health officials in endemic regions that help to strengthen the region's research capacity. Such strengthening relates to both personnel and infrastructure: for example, this laboratory technician working at Dipumba Hospital, in Mbuji-Mayi (DRC), has been trained on HAT diagnostic tools as part of the activities related to the NECT study.

Developing drugs is a long and arduous process that requires skilled and knowledgeable partners throughout all stages of the pipeline and into the field. In order to bridge some of the gaps seen in drug R&D for neglected diseases, DND*i* uses and strengthens existing research capacity in disease-endemic countries.

CLINICAL TRIALS

Conducting clinical trials on neglected diseases often means that research must be conducted in some of the most remote areas where little infrastructure of any kind, yet alone health, exists and where political instability is also frequent. Diagnosis and treatment of patients is difficult in itself, but DND*i* and partners must also ensure that clinical research is carried out at international standards of quality.

NEEDS ASSESSMENT

DNDi has identified several key components to be met:

- Fostering trust and building partnerships with local communities, patients, and healthcare workers. As many local partners have long historical relationships with local populations, they are vital in facilitating the process
- Improving local infrastructure and ensuring that the entire logistical chain in place is compliant with Good Clinical Practices (GCP)
- Recruiting, training, and supporting relevant human resources. Quality healthcare workers at a local level must not only identified but must be maintained and enhanced through training. Such personnel include both the staff conducting the clinical trials (doctors, laboratory technicians, and nurses) as well as those monitoring the trial (clinical monitors and data safety monitoring boards)
- Working with governing and regulatory authorities at local, national, and regional levels. These authorities play a crucial role in evaluating and approving clinical protocols, ensuring drug availability (by registering drugs and by facilitating drug importation, in terms of logistics), and making changes to national treatment guidelines and protocols. National ethics committees also play a critical role
- Ensuring prioritisation and sustainability of clinical research worldwide, through increased public awareness in donor countries and among local communities.

Capacity strengthening can involve the physical upgrading of facilities related to clinical research (such as patient wards and diagnostic laboratories). When research and treatment of visceral leishmaniasis began in Gondar, Ethiopia, it was in a tent.

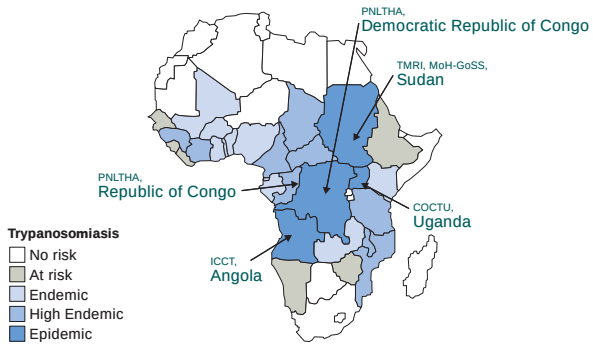
Now, DND*i* and LEAP partners have built and are using a new building which was completed in May 2008.

DNDi'S SYSTEMATIC RESPONSE

DND*i* and partners are tackling each of these issues by adopting strategic and integrated approaches as clinical trials are implemented:

- In partnership with groups and investigators in endemic regions, the regional research platforms of the Human African Trypanosomiasis (HAT) Platform and the Leishmaniasis East Africa Platform (LEAP) aim to ensure that clinical research capacity is strengthened in a coherent regional approach that overcomes system barriers and facilitates the availability of new medicines when they are developed
- The national control programmes of the most affected countries are essential members of both platforms as they play a key role in areas where clinical investigations are taking place
- Acting as transnational support networks, the platforms enable partners to share different experiences, knowledge, and problem-solving techniques. Through sharing of information and expertise at a regional level, fundamental problems at the field level can also be addressed
- Physical upgrading of facilities related to clinical research (such as patient wards and diagnostic laboratories) is undertaken by DND*i* at trial sites so as to ensure they meet GCP standards. These facilities are not owned by DND*i*.

> THE HAT PLATFORM



- Target disease: HAT
- Core partners: STI; national HAT control programmes of most affected endemic countries (see map on left); national and international research groups (eg. ITMA, INRB, CDC, and KARI-TRC); NGOs like MSF; FIND; WHO; TDR; regional networks (eg. EANETT, PABIN, AMANET)
- DNDi contact: Augustin K. Ebeja
- Project start: August 2005; Kinshasa, DRC

- In addition to physical infrastructure, trained staff are needed in order to carry out GCP-compliant trials. Training is important not just at the start of a trial, but is a continuous process which updates existing staff and trains new members. From external consultants to the experienced trial site staff, the sharing of better practice 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 at international standards
- At the final R&D step, there is the challenge to make new treatments available to patients. The post-registration phase requires that all partners actively monitor the safety (pharmacovigilance), efficacy (monitoring of resistance), and field effectiveness of the products in real-life conditions. But, even before doing this, it's imperative to determine how the drug will be made available through a well-defined implementation strategy
- These platforms also have an advocacy role to play at community, national, and international levels. As representatives of countries most affected by neglected diseases, they have the legitimacy to showcase the plight of what patients endure and how best to meet their urgent needs.

CLINICAL RESEARCH PLATFORM ACHIEVEMENTS INTO 2008

HAT Platform

- **Training:** for members on Good Clinical Practice (GCP) training, ethics, and clinical monitoring; for general practitioners, a programme on how to examine patient with HAT
- **Communications:** 3 platform newsletters published, presentations at various scientific congresses
- **Meetings:** launch in August 2005, and annual platform meetings (Nairobi, 2006; Khartoum, 2007); 6 steering committee meetings held as well – both in conjunction with annual meetings as well as in Basel (June 2007), and Kampala (June 2008).

LEAP

- **Training:** Good Clinical Practice (GCP), pharmacovigilance, and ethics sessions for clinical monitors, Data and Safety Monitoring Board (DSMB) members, Ethics Committees, and investigators
- **Strengthening capacities:** 6 clinical trial sites established in Ethiopia (2), in Sudan (2), in Kenya (1), and in Uganda (1); the building and opening of leishmaniasis research and treatment centres in Arba Minch, Ethiopia, and Gondar, Ethiopia; treatment centre and laboratory training site under construction in Dooka, Sudan (opening in 2008)
- **Communications:** a newsletter, biannual meetings, and presentations at various scientific congresses.

> LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

- Target disease: VL
- Core partners: KEMRI, Kenya; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; Drug Administration & Control Authority, Ethiopia; Institute of Endemic Diseases, University of Khartoum, Sudan; Makarere University, Uganda; MSF; WHO; TDR; Ministries of Health in Kenya, Ethiopia, Sudan, and Uganda.
- DNDi contact: Monique Wasunna
- Project start: August, 2003; Khartoum, Sudan

Skilled and appropriately trained staff are needed in order the best research and treatment to be delivered at all stages of the R&D pipeline, as shown above. On the left, clinical monitors visit a principal investigator at the LEAP clinical trial site in Kassab, Sudan; on the right, a training workshop on trypanosomiasis screening is being held as part of PAN4ND activities.

SCREENING NETWORK

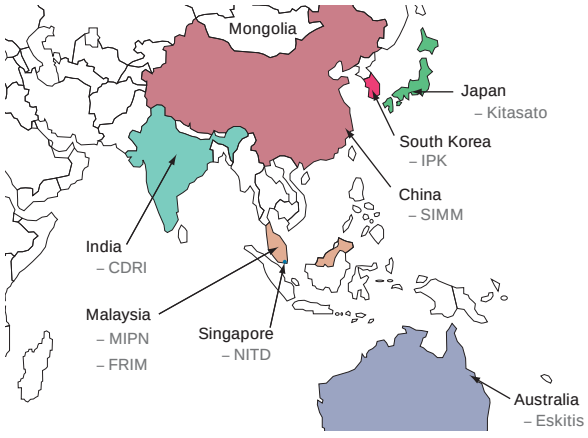
With the objectives to leverage the biodiversity potential of the Asian region in drug discovery efforts for neglected diseases, the Pan-Asian Network for Neglected Diseases (PAN4ND) brings together scientists from research institutions across Asia and the Pacific region (see below). The network, which first formed as Pan-Asian Screening Network (PASN), aims to translate the discovery of new bioactive molecules from natural local resources into drugs against neglected diseases by sharing screening technologies between institutions. To fulfill its objectives, PASN interacts with a Natural Products Working Group, representing several institutions involved in the purification and identification of chemicals from plant, soil, and marine organisms in the region.

There is a strong rationale to explore natural resources in the search for new antiprotozoal medicines, as several anti-infective drugs, including ones targeting parasitic diseases, are from natural origin or derived from it. Two striking examples, first identified by Asian researchers, are artemisinin, for the treatment of malaria, and ivermectin, as a cure for river blindness.

PAN4ND ACHIEVEMENTS INTO 2008

- **Training:** Drug screening workshop at CDRI, Lucknow (February 2007); drug metabolism, pharmacokinetics, and toxicology workshop at NITD, Singapore (February 2008)
- **Strengthening capacities:** 3 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 antiprotozoal drug screening in collaboration with LSHTM, STI, and CDRI; organisation of 5 regional scientific events: 3 annual meetings (Tokyo, May 2006; Shanghai, June 2007; and Tokyo, June 2008) and 2 Natural Substances Drug Discovery and Development meetings (Kuala Lumpur, November 2006 and 2007).

> DISCOVERY RESEARCH PAN-ASIAN NETWORK FOR NEGLECTED DISEASES (PAN4ND) NATURAL SUBSTANCES SCREENING



- Target disease:
  HAT, VL, Chagas
- Core 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.
- DNDi contact: Jean-Robert Ioset
- Project start:
  May 2006; Tokyo, Japan