since DNDi’s creation, the role of neglected disease endemic countries in responding to their public health needs has been a central concern both in the innovative models DNDi has utilized in its functioning and in its advocacy activities. Research capacity in developing countries can be at risk of being directed towards the needs of populations in developed countries, so not only must the capacity be built and maintained, local leadership is also required to ensure that the research is serving the needs of the countries themselves. This is part of a larger need for increased public leadership, which also comprises regulatory and health systems strengthening.

To ensure that DNDi ‘walks its talk’, three areas of work are specifically addressed in the regions as part of the reinforcement of the role of DNDi Regional

‘Walking the Talk’ for Sustainable Capacity in Disease-Endemic Countries
Offices: technology transfer notably to increase suppliers and ensure supply of treatments through local production, data management capacity, clinical trial capacity strengthening, as well as two new initiatives that began to take shape in 2014 for leishmaniasis in Latin America and filariasis in Africa.

Ensuring alternative sources of ASAQ FDC antimalarial – technology transfer to Zenufa

DNDi took up a technology transfer project for the manufacture of ASAQ to a second partner, after Sanofi, in malaria-endemic countries of Africa in 2009. With the support of the pharmaceutical expert group, Office Technique d’Etude et de Coopération Internationale (OTECI), some 100 manufacturing sites in several African countries were reviewed and Zenufa in Tanzania was selected. Zenufa had the advantage of its presence in the Democratic Republic of the Congo (DRC), a country highly plagued by malaria and where ASAQ is the recommended treatment.

A technology transfer contract with Zenufa was signed in March 2011. Zenufa required support from DNDi for technology transfer with a special emphasis on Good Manufacturing Practice (GMP). The partners for the technology transfer were Bertin Pharma (Bordeaux), who had previously partnered with DNDi for the initial ASAQ pharmaceutical development up to the industrial scale-up phase, and AEDES, responsible for the operational and financial management of the project, with support from OTECI. Sanofi also supported the project using its experience of having its ASAQ manufacturing site in Morocco. In October 2014, the Tanzanian Food and Drug Administration granted Zenufa Good Manufacturing (GMP) status, and registration batches were manufactured for which registration as well as WHO pre-qualification dossiers are expected to be filed in 2015.

Clinical trial capacity

RedeLeish network to build expertise for leishmaniasis in Latin America

In order to bring together a collaborative network for the promotion and exchange of information on treatment and diagnosis, and to boost clinical research for leishmaniasis in Latin America, the Network of Investigators and Collaborators was formed in 2013. Initially mainly in Brazil, the network began to extend to researchers and experts from other Latin American countries, notably at a key gathering of some 60 regional experts from seven Latin American countries, hosted in Rio de Janeiro in September 2014.

Data management centre in Africa – aiming for quality excellence

The DNDi Africa Regional Office has been running its own clinical trial Data Centre since 2004. The centre is part and parcel of a clinical trial management group based in the DNDi Africa office and is responsible for data management and analysis to facilitate activities carried out by DNDi and LEAP in Africa. The centre has evolved its capacity to produce data based on international standards, i.e. International Conference on Harmonization (ICH) and Good Clinical Practice (GCP), by using GCP-compliant open source solutions, such as OpenClinica (www.openclinica.com), together with in-house built software for query management to deliver quality data in the region. In 2014, the Data Centre was engaged in a broader process of quality management, which aims at ISO9001 certification in the near future.

Filariasis platform to define future patient needs

In 2014, the filariasis programme aimed at fine-tuning the target product profile for a macrofilaricide as well as determining future patient needs and evolution of the disease epidemiology. Several expert meetings were held, notably with clinical trial investigators from the Democratic Republic of the Congo. In addition, these meetings aimed at refining the clinical development plans for onchocerciasis and lymphatic filariasis. The Joint Action Forum of APOC in Addis Ababa was attended, and the plans for a new DNDi filariasis clinical research platform, to be based on an in-depth stakeholder analysis, began to take shape. The platform structure will be based on the models of other DNDi disease-specific platforms in Africa, notably LEAP and the HAT Platform.

Supported by DNDi, the RedeLeish specific objectives are to bring together leishmaniasis experts in Latin America to increase collaboration and maximize existing resources and expertise in areas where serious gaps exist. The network also aims to strengthen institutional capacity for clinical research and to identify priority needs in the development of research projects whilst contributing to the implementation of strategic policies and research priorities. Finally, the network will promote the harmonization of clinical trial methodologies and design in the region.
LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

Founded: 2003 in Khartoum, Sudan
Over 60 individual members, representing over 20 institutions

The LEAP platform aims to strengthen clinical research capacity, which is lacking in part due to the remoteness and geographical spread of the patients, most of whom live in the most impoverished regions of Africa. The platform is also a base for ongoing educational cooperation between the countries in the East African region and standardization of procedures and practices in the region, within the scope of local regulations. LEAP evaluates, validates, and registers new treatments that address regional needs for visceral leishmaniasis.

Treatment and access
A roundtable discussion on Access to SSG&PM in Eastern Africa was held during the first LEAP Scientific Conference in Ethiopia. Pharmacovigilance (PV) Steering Committee meetings to disseminate results of the PV study to stakeholders from Ethiopia and Sudan were held in Ethiopia. Participants included representatives from Ministries of Health, Drug Regulatory Authorities including EFMMACA, WHO, and LEAP members.

Clinical trials
Recruitment into the HIV/VL study to evaluate the efficacy of AmBisome® + miltefosine combination and of a higher-dose AmBisome® monotherapy in Ethiopian patients with HIV/VL co-infection commenced in 2014. The study is being conducted in Gondar and at the MSF Abdurafi site.

Communications
The second and third editions of the LEAP Newsletter were published in April and September 2014.

Capacity building
Good Clinical and Laboratory Practices (GCLP) training in Gondar, Ethiopia, was delivered to 36 laboratory technicians in accordance with the GCLP principles. The HIV/VL LEAP 0511 protocol training and GCLP refresher was carried out in Ethiopia. The Randox International Quality Assessment Scheme RIQAS training was conducted for laboratory technicians to improve their understanding of the RIQAS process. The 20th Principal Investigators (PI) meeting was held in Nairobi (Kenya) to evaluate progress made by LEAP over the last ten years and to plan for the next decade. The 20th and 21st LEAP meetings were held in Kampala (Uganda) and Bahir Dar (Ethiopia).

2014 HIGHLIGHTS
- LEAP ‘Scientific Conference’ held in Ethiopia, with over 130 participants from some 14 countries, provided updates from LEAP activities and engaged a broad range of African researchers in VL and other neglected disease areas
- Results from SSG&PM pharmacovigilance study presented

NUMBER OF SITES IN 2014: 7
In 2014, the LEAP Platform was operational at several clinical trial sites: Gondar and Arba Minch (Ethiopia), Kimetel and Kacheliba (Kenya), Anuata (Uganda), Doka and Kassab (Sudan).

PEOPLE TRAINED IN 2014: 275

PARTNERS: Kenya Medical Research Institute (KEMRI), Kenya; Institute of Endemic Diseases (IEND), University of Khartoum, Sudan; MSF; Leishmaniasis East Africa Platform (LEAP); BaseCon, Denmark; Utrecht University, The Netherlands; Koninklijk Instituut voor de Tropen, The Netherlands
HUMAN AFRICAN TRYPAANOSOMIASIS (HAT) PLATFORM

Founded: 2005 in Kinshasa, Democratic Republic of the Congo
Over 120 individual members, representing over 20 institutions

The HAT platform builds and strengthens treatment methodologies and clinical trial capacity in sleeping sickness-endemic countries, so that new treatments for this fatal disease can be rapidly and effectively evaluated, registered, and made available to patients. After the success of the Nifurtimox-Eflornithine Combination Therapy (NECT), included in the WHO List of Essential Medicines for the treatment of stage 2 HAT for adults and children, and its widespread uptake, the primary goals of the HAT Platform are to develop appropriate clinical trial methodologies for entirely new treatments tested for sleeping sickness, overcome system challenges related to administrative and regulatory requirements, build new and enhance existing clinical trial capacity (human resources, infrastructure, equipment), and share information and strengthen ties among endemic countries.

Treatment and access
In 2014, with the addition of Nigeria, NECT became first-line treatment for stage 2 sleeping sickness in all T.b. gambiense-affected countries, including for children.

Clinical trials
Fexinidazole: By the end of 2014, ten clinical trial sites had included 359 patients in fexinidazole Phase II/III clinical study in DRC and CAR. The two new complementary cohort trials, one for stage 1 and early stage 2 in adults, included 110 patients, and another with children between 6 and 14 years of age included 56 patients. A total of 525 patients have been included in the three trials thus far.

Capacity strengthening
The HAT Platform and EANETT co-organized an international scientific conference on HAT in September. A training on Trypanosomiasis management was co-organized between the national sleeping sickness control programme of Chad and the HAT Platform in May in Bodo (Chad) with the support of DRC national control programme experts and the participation of 22 doctors and nurses. The Platform supported and participated in the 6th International Course on Trypanosomiasis, organized by the association ‘Les Trypanautes’ with the support of WHO and DNDi. The Platform was also involved in the preparation for the investigators’ meeting for the fexinidazole trials in Kinshasa for 30 participants.

Communications
Two HAT Platform Newsletters were published in July and December 2014.

Dr Augustin Kadima Ebeja, HAT Platform Coordinator, moved to a new position with the World Health Organization in November 2014. Dr Ebeja spent eight years of his life building the HAT platform, working tirelessly to inspire his colleagues in HAT endemic countries to ‘keep up the good fight’ against the disease and to maintain the important capacity for clinical trials. We wish to thank Dr Ebeja for his immense service to DNDi and to HAT patients. We are also happy he is still working in the field of neglected diseases with the WHO in the DRC as their NTD focal point.

PARTNERS: National sleeping sickness control programmes, research institutions and national laboratories of public health of the most affected endemic countries: Angola, Central African Republic, Chad, Democratic Republic of the Congo, Republic of Congo, South Sudan, Sudan, Uganda; Drugs for Neglected Diseases Initiative (DNDi), Switzerland; Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Institute of Tropical Medicine-Antwerp, Belgium; Institut National de Recherche Biomédicale (INRB), DRC; University of Makerere, Uganda; Kenya Agricultural Research Institute – Trypanosomiasis Research Centre (KARI-TRC), Kenya; Tropical Medicine Research Institute (TMRI), Sudan; Institut Pasteur Bangui, CAR; Médecins Sans Frontières (MSF); Foundation for Innovative New Diagnostics (FIND), Switzerland; Eastern Africa Network for Trypanosomiasis (EANETT); Centre interdisciplinaire de Biothéque pour l’Afrique Francophone (CIBAF); WHO Department of Neglected Tropical Diseases as observer. Two new members joined in 2014: The National Sleeping Sickness Control Programme of Guinea and the INZI Project of the University of Edinburgh.

2014 HIGHLIGHTS
- Opening of one additional trial site for fexinidazole study recruitment (increase from 9 to 10)
- Three ongoing trials to study fexinidazole in both stages of the disease and in children
- 3rd HAT Platform-EANETT conference in September, in Kinshasa, with 160 participants

NUMBER OF SITES IN 2014: Ten (eight sites actively including patients, with the remaining two doing follow up visits only). In 2014, the HAT platform was operational at ten sites for the fexinidazole study: Four sites were opened in the Democratic Republic of the Congo in 2012 (Bandundu, Vanga, Masi Manimba, and Dipumba), four sites were opened in 2013 (Dinglia, Mushie, Katanda, and Isangi), and one in 2014 (Bagata). The latter site was opened to compensate for two issues: the 2013 trial interruption at the site in Batangafo, Central African Republic, and the steep reduction of cases in Dinglia in DRC, which led to the trial stop there in January 2014. Follow-up of already-included patients is carried out at both sites.

PEOPLE TRAINED IN 2014: 235
Training, treatment, and access

In 2014, several meetings and trainings took place in regard to technical discussions and strengthening capacities for research on new treatments and implementation of Chagas treatments including:
- Experts’ meeting about New Treatment Regimens of Benznidazole, Geneva [Switzerland]
- Experts’ Meeting [NHEPACHA Network] Barcelona [Spain]
- Lessons Learned in Clinical Trials and Animal models of Chagas disease, Mexico City [Mexico]
- Congenital Chagas Management, Mexico City [Mexico]

In 2014, the platform had a greater involvement in patient access to treatment issues as a result of a survey conducted among members of the platform and various decision makers. Subsequently, the CCRP was present at all of the Regional Initiatives meetings, convened by PAHO and the National Programmes, where access issues were discussed including: The Andean Countries Initiative [IPAI], Bogota [Colombia] with participants from Colombia, Ecuador, Peru. The Amazonian Countries Initiative, Rio Branco [Brazil]. This meeting was parallel to the Congress of Tropical Medicine in Brazil (MedTrop), and the Southern Cone Countries Initiative, Arequipa [Peru], where the main countries recognized the lack of access to treatment and committed to investing more in R&D.

The CCRP also strongly supports the benznidazole registration process in Mexico and is now encouraging its procurement by state programmes. Surveys were also conducted in order to assess the use of the Demand Forecasting tool. An update of the tool was produced and the CCRP is encouraging its proper use by national programmes.

Clinical trials

In 2014, two studies were supported by members of the CCRP: fexinidazole and benznidazole drug–drug interaction in Argentina [see p. 35] and the fexinidazole study in Bolivia [see p. 35].

Communications

The CCRP Web Forum continued to grow. This online workspace, created in 2011, highlights project milestones, provides clinical trials updates, links up CCRP members, and promotes events.
The overall Chagas (CCRP) and HAT platform budgets remain stable between 2013 and 2014 (respectively EUR 0.2 M and EUR 0.35 M per year per platform). The Leishmaniasis (LEAP) platform costs were multiplied by four (+ EUR 0.6 M) due to the fact that some clinical trial sites have been maintained (mainly the team) even though they were not involved in R&D activities. The costs of these sites (Kimalel and Kacheliba clinical trial sites of Kemri in Kenya, Amudat Hospital with Makerere University in Uganda, Arba Minch Hospital in Ethiopia) were removed from R&D expenditures and allocated toward the strengthening capacities budget. Patients treated outside clinical trials in 2014 in the seven VL clinical trial sites reached 1,533.
2014 KEY FINANCIAL PERFORMANCE INDICATORS

Evolution of clinical sites

PLATFORMS FACILITATED CLINICAL RESEARCH IN RESOURCE-POOR AND RURAL SETTINGS

**CHAGAS CLINICAL RESEARCH PLATFORM**

In 2014, the platform was operational in two sites for Fexinidazole (Bolivia) and one site in Argentina for the Drug-Drug interaction with Benznidazole.

**HAT PLATFORM**

In 2014, the HAT platform was operational in ten sites for the fexinidazole study: four sites were opened in DRC in 2012 (Bandundu, Vanga, Masi Manimba, and Dipumba) and five sites were opened in 2013: Dingila, Mushie, Katanda, and Isangi. A tenth site was opened in October 2014 to compensate for an inclusion stop in Batangafo in CAR where recruitment was suspended in December 2013 due to insecurity, and Dingila in DRC where the steep reduction of cases led to the stop in January 2014, while maintaining follow-up of already-included patients.

**LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)**

In 2013, the LEAP platform was operational in seven DNDi clinical trial sites (the same as 2012 and 2014): Kassab and Doka (Sudan), Amudat (Uganda), Kimalel and Kacheliba (Kenya), and Arba Minch and Gondar (Ethiopia).

Developing research capacities in endemic regions

PEOPLE TRAINED BETWEEN 2013 AND 2014 ALMOST DOUBLED (+98%)

![Graph showing the evolution of clinical sites](image-url)