DND*i* works closely with partners in disease–endemic countries to strengthen existing clinical research capacity.

STRONG INVOLVEMENT OF ENDEMIC COUNTRIES THROUGH THE CLINICAL PLATFORMS

Since DND*i*'s creation, endemic countries have been involved in its mission to develop treatments that are well-adapted to patients in need. These disease-specific, regional clinical research platforms strengthen and sustain research capacities in the countries where the diseases occur. Their collaborative approaches have resulted in tangible results for patients, healthcare workers, and researchers alike.

These platforms form part of a broader, positive trend of research networks that incorporate North-South and, importantly, South-South collaborations to build and sustain capacity in the countries where the diseases occur. Today there is a growing consensus on the need for, and mobilization to build, such capacity 'from within' endemic regions, for example the European & Developing Countries Clinical Trials Partnership (EDCTP) and the African Medicines Regulatory Harmonization (AMRH) initiatives.

Two new treatments developed

Two new, better-adapted treatments developed and implemented – NECT for sleeping sickness and SSG&PM for visceral leishmaniasis – and a replenished R&D portfolio for Chagas disease: these are among the concrete outcomes of the three DND*i*-supported research platforms, made up of the Leishmaniasis East Africa Platform (LEAP), the Human African Trypanosomiasis (HAT) Platform, and the Chagas Clinical Research Platform (CCRP). Bringing together researchers, clinicians, health workers, representatives of Ministries of Health and of regulatory authorities of endemic countries, industry partners, as well as not-for-profit and civil society members, their activities serve to avoid duplication of research efforts and to share knowledge and know-how. The platforms are part and parcel of key clinical trials that are conducted at the highest international standards.

In 2013, the three platforms focused on progressing clinical studies to their targeted milestones: the HAT platform doubled the number of sites for the Phase II/III clinical study in the Democratic Republic of the Congo in order to accelerate recruitment, and also prepared two studies to complement data on additional study populations; LEAP geared up for the start of a new Phase II study for an oral treatment for visceral leishmaniasis; and the CCRP completed the Phase II E1224 study that provides essential data and methodology for further research on Chagas disease treatment. Last year, communications activities were particularly intense with important meetings taking place for each of the platforms, on the occasion of DND*i*'s 10-year anniversary, and also with information sharing tools: the CCRP Web Forum increased its activity and members, while LEAP launched a newsletter.

Objectives of the platforms

- → **Define and update** patients' needs
- → **Build and strengthen** clinical research capacity and conduct research
- → **Efficiently coordinate** research activities and information sharing
- → **Facilitate** implementation, access, and registration of new treatments

LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

Founded: 2003 in Khartoum, Sudan

Over 60 individual members, representing over 20 institutions

2013 HIGHLIGHTS

- → Completed recruitment of patients (3,164) in the SSG&PM pharmacovigilance study
- → Launched new Phase II proof-of-concept study, evaluating the safety and efficacy of fexinidazole in VL patients in Sudan
- → The 19th LEAP meeting held in Nairobi, in June, with 80 participants from LEAP member countries (Ethiopia, Kenya, Uganda, and Sudan)

Treatments & Access

Following the recommendation of SSG&PM as first-line treatment for VL in East Africa by the WHO Expert Committee on the Control of Leishmaniases (2010), the treatment is now included in the Essential Medicine Lists of Kenya, Uganda, Ethiopia, and Sudan. PM is now registered in Uganda (end 2011) and Kenya (February 2013). New VL treatment guidelines were revised in the four countries and were adopted in Kenya (January 2012), and are awaiting official launch in Uganda, Sudan, and Ethiopia.

Clinical trials

The SSG&PM pharmacovigilance study (started 2011) to monitor safety and effectiveness of SSG&PM combination recruited 3,164 patients in Ethiopia, Sudan, Kenya, and Uganda by end 2013. A new Phase II study to evaluate the efficacy of AmBisome®+miltefosine combination and of a higher-dose AmBisome® monotherapy in Ethiopian patients with HIV-VL co-infection was initiated. Additionally, a Phase II proof-of-concept study evaluating the safety and efficacy of fexinidazole in VL patients in Sudan was initiated at the close of 2013.

Capacity strengthening

Pharmacovigilance (PV) and Good Clinical Practice (GCP) training sessions were delivered to 40 investigators, laboratory technicians, nurses, and pharmacists in Abdurafi, Ethiopia. In Entebbe, Uganda, a Human Subjects Protection (HSP)/GCP Train the Trainers Programme was attended by 5 people (clinical trial manager, trial monitors, and a site investigator). Fifteen laboratory technicians from Ethiopia, Kenya, Uganda, and Sudan participated in the Urine LEISH Antigen Elisa Standardization Training session held in Nairobi, Kenya. A GCP refresher and protocol training was held in Doka, Sudan (13 p.). Fifty-five health workers in Lodwar and Kacheliba, Kenya, received training on the newly launched VL guidelines and on the use of SSG&PM. In addition, LEAP supported 4 graduate students in 2013.

Communications

The first edition of the LEAP Newsletter was published in June 2013.

Members

Center for Clinical Research, Kenya Medical Research Institute (KEMRI), Kenya; Ministry of Health, Kenya; Institute of Endemic Diseases, University of Khartoum, Sudan; Federal Ministry of Health, Sudan; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; Federal Bureau of Health, Ethiopia; Makerere University, Uganda; Ministry of Health, Uganda; Médecins Sans Frontières; i+ solutions, The Netherlands; OneWorld Health (OWH/PATH), USA; AMC/KIT/Slotervaart Hospital, The Netherlands; London School of Hygiene & Tropical Medicine (LSHTM), UK.

- → **Over 1,400 patients** enrolled in clinical trials by the end of 2013
- → **Over 4,150 patients** treated outside clinical trials by the end of 2013
- → **Over 3,150 patients** treated in pharmacovigilance Phase IV study (SSG&PM)

HUMAN AFRICAN TRYPANOSOMIASIS (HAT) PLATFORM

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

2013 HIGHLIGHTS

- Opening of five additional sites for fexinidazole study recruitment (increase from 4 to 9)
- Two new protocols for complementary populations in the fexinidazole study submitted for ethical approval (end 2013)
- The 2nd HAT Platform-EANETT conference in June, in Nairobi, with 130 participants

Treatments & Access

In 2013, with the addition of Angola, NECT became first-line treatment for stage 2 sleeping sickness in all eight HAT Platform countries. A total of 99% of stage 2 HAT (*T.b. gambiense*) patients were treated with NECT, in 12 countries. In addition to inclusion (in 2009) in the Essential Medicines List of the WHO, NECT was included as recommended treatment in WHO's Essential Medicines List for Paediatric Use in July 2013.

Clinical trials

Fexinidazole: By the end of 2013, 9 clinical trial sites (5 more than in 2012) had included 206 patients in fexinidazole Phase II/III clinical study in DRC and CAR. The HAT Platform provided support for the submission of two new complementary cohort trials (one for stage 1 and early stage 2 in adults, and another with children between 6 and 14 years of age) to the ethical and regulatory authorities of DRC in December.

Capacity strengthening

Three important international scientific conferences on HAT took place, in June in Nairobi (co-organized by the HAT Platform and EANETT); followed by Kinshasa (6th CIPIP) and Khartoum (32nd ISCTRC). Two national strategic meetings were organized by member countries, with international support, in Brazzaville (Rep. of Congo) and N'djamena (Chad).

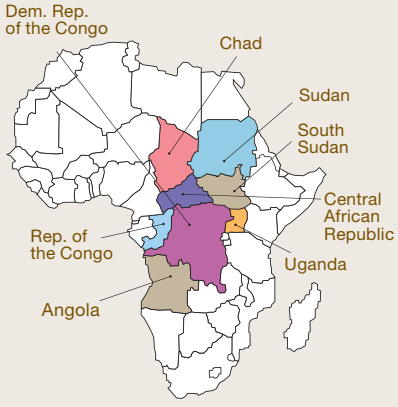
A training session on Good Clinical Practice (GCP) was given to 22 professionals in DRC in August for the opening of new sites. Other training courses took place, including a 'Training of Trainers in GCP' (5 people) in September in Uganda, and a fluorescent microscopy course (14 p.) with FIND in November in DRC. Two meetings were organized to support the development of strategic plans for the national control programmes, one in Rep. of Congo (30 p.), one in Chad (35 p.).

Communications

HAT Platform Newsletters were published in July and December 2013.

Members

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; 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 Trypanosomosis (EANETT); Centre interdisciplinaire de Bioéthique pour l'Afrique Francophone (CIBAF); WHO Department of Neglected Tropical Diseases as observer.



CHAGAS CLINICAL RESEARCH PLATFORM (CCRP)

Founded: 2009 in Uberaba, Brazil

Over 80 institutions represented from 22 countries, bringing together over 200 people

Members

Ministries of Health and National Control Programmes of high-burden endemic countries (Argentina, Bolivia, Brazil, Mexico, Paraguay, Honduras); Pan American Health Organization (PAHO); Department for the Control of Neglected Tropical Diseases, WHO; Médecins Sans Frontières; International Federation of People Affected by Chagas Disease (FINDECHAGAS) and several patient associations

ARGENTINA: Hospital de Niños Ricardo Gutiérrez; Instituto Nacional de Parasitología Dr. M. Fatala Chabén; Hospital de Niños de Jujuy; Hospital Público Materno Infantil – Salta; Centro de Chagas y Patologia Regional, Santiago del Estero; Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); Fundación Mundo Sano, ELEA

BRAZIL: Instituto Oswaldo Cruz; Instituto de Pesquisa Evandro Chagas–Fiocruz; Centro de Pesquisas René Rachou–Fiocruz; LAFEPE

BOLIVIA: Universidad Mayor de San Simón; Platform of Integral Care for Patients with Chagas Disease; CEADES

MEXICO: Instituto Carlos Slim de la Salud

SPAIN: ISGlobal and Barcelona Centre for International Health Research (CRESIB)

USA: Merck; Sabin Vaccine Institute

JAPAN: Eisai Co. Ltd

FRANCE: Institut de Recherche pour le Développement

GERMANY: Bayer

OTHER: researchers from Universities of Colombia, Venezuela, Bolivia, USA, Canada, Brazil, and Paraguay.

2013 HIGHLIGHTS

- **E1224 clinical study results: despite limited sustained efficacy for E1224 as a single medication, this study provided key information for further research and development of Chagas disease treatments (combination treatment and improved benznidazole regimens) and shared with CCRP through an on-line discussion with over 70 active participants**
- **Annual CCRP meeting in Bolivia, in April, as part of the 'Chagas Week', where 18 ongoing clinical and preclinical studies on Chagas disease were presented**

Treatments & Access

Promoting Chagas disease treatment access and advocacy was a key objective in 2013. The CCRP strengthened its engagement with patient associations and the International Federation of Chagas Disease Patients (FINDECHAGAS). It also directly supported scale-up of diagnosis and treatment of Chagas disease, and access to the paediatric dosage form of benznidazole. In 2013, follow-up activities were undertaken for countries' demand forecasting for Chagas treatments, as well as for the dossier submission for inclusion of benznidazole 12.5mg in the WHO Essential Medicines List for Paediatric Use, which was officially granted in July.

Countries highlighted on the map represent Chagas disease-endemic Latin American countries with platform members. Other CCRP members' countries not indicated on this map are listed on the left.

Clinical trials

In 2013, four studies (three that started in 2011 and one in 1999) supported by the CCRP concluded their activities: a population pharmacokinetics (PK) study of the use of benznidazole in children, including the new paediatric dosage form (Argentina); a study to evaluate and optimize the polymerase chain reaction (PCR) method for diagnosis and assessment of therapeutic response in patients with chronic indeterminate Chagas disease (Bolivia); the TRAENA study to assess benznidazole's ability to change the natural evolution of chronic Chagas disease in adult patients (Argentina); and a study to evaluate the safety and efficacy of E1224 (Bolivia).

Capacity strengthening

In 2013, experts and technical meetings were held in Bolivia, Spain, and Switzerland to address: new tools for diagnosis and assessment of patients with Chagas disease (NHEPACHA Network) (17 people); experimental models for Chagas disease (18 p.); lessons learned from the E1224 study (25 p.); and new treatment regimens with benznidazole (23 p.). A technical workshop on drug discovery and development was also offered to 100 CCRP members.

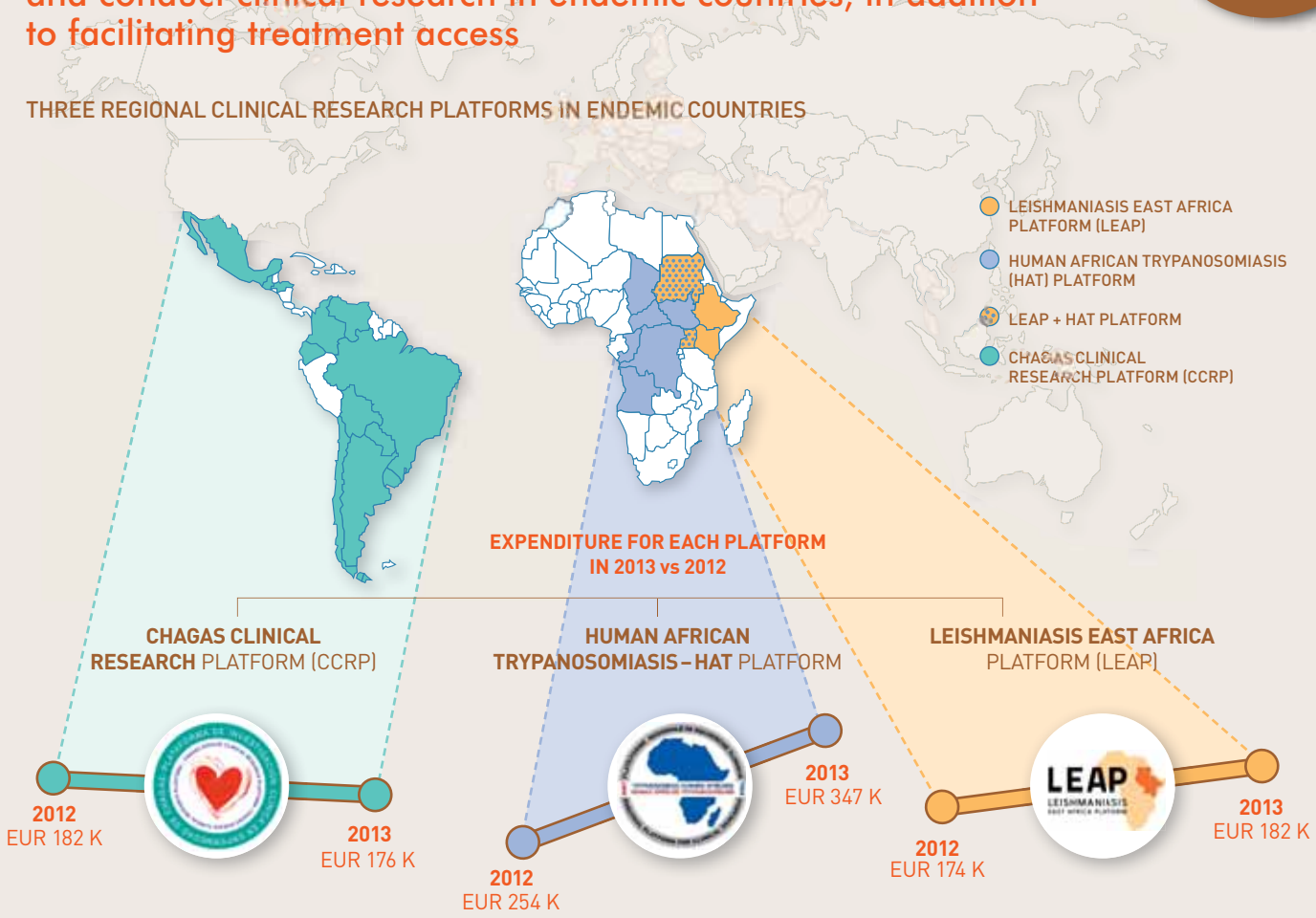
Communications

In 2013, the CCRP Web Forum, an online workspace for discussion, networking, and information sharing – mainly on R&D and treatment access issues – increased its activity and members. The CCRP also published its third newsletter in April.

2013 KEY FINANCIAL PERFORMANCE INDICATORS

Regional disease-specific networks of excellence build capacity and conduct clinical research in endemic countries, in addition to facilitating treatment access

THREE REGIONAL CLINICAL RESEARCH PLATFORMS IN ENDEMIC COUNTRIES



The overall Chagas disease (CCRP) and leishmaniasis (LEAP) platform budgets remain stable between 2012 and 2013 (EUR 0.2 M per year per platform). The HAT Platform costs increased by 37% (+ EUR 0.1 M) due to the second HAT Platform–EANETT conference in June 2013 in Nairobi on the occasion of DND*i*'s 10-year anniversary event, gathering an extended group of 130 experts.

8 Clinical sites in 2013

CHAGAS CLINICAL RESEARCH PLATFORM

In 2013, the platform was operational at 3 sites for the E1224 and the PCR studies (Bolivia) and 5 sites (4 recruiting + 1 back-up) for Paediatric Benznidazole Population PK study (Argentina).

9 Clinical sites in 2013

HAT PLATFORM

In 2013, the HAT platform was operational at 9 sites for the Fexinidazole study: 4 sites were opened in the Democratic Republic of the Congo in 2012 (Bandundu, Vanga, Masi Manimba, and Dipumba) and 5 new sites were opened in 2013: Dingila, Mushie, Katanda, and Isangi, in addition to Batangafo in CAR (where recruitment was suspended in December 2013 due to insecurity, while maintaining follow-up of already-included patients).

7 Clinical sites in 2013

LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

In 2013, the LEAP platform was operational at 7 clinical trial sites (same as 2012): Kassab and Doka (Sudan), Amudat (Uganda), Kimalel and Kacheliba (Kenya), and Arba Minch and Gondar (Ethiopia).

DEVELOPING RESEARCH CAPACITIES IN ENDEMIC REGIONS

An increase of 18% of professionals trained between 2012 and 2013