PLATEFORME REGIONALE DE RECHERCHE CLINIQUE THA
TRYPANOSOMIASE HUMAINE AFRICAINE
HUMAN AFRICAN TRYPANOSOMIASIS
HAT REGIONAL PLATFORM FOR CLINICAL RESEARCH

HAT Platform

REGIONAL PLATFORM FOR CLINICAL RESEARCH

NEWSLETTER N° 19, May 2018

Investigators' meeting for fexinidazole and acoziborole clinical trials, Kinshasa, DRC 5 September 2017

Partners

FIND · MEDECINS SANS FRONTIERES · IRD · DNDi Drugs for Neglected Diseases *initiative* / *Initiative* Médicaments contre les Maladies Négligées · EANETT · Swiss TPH

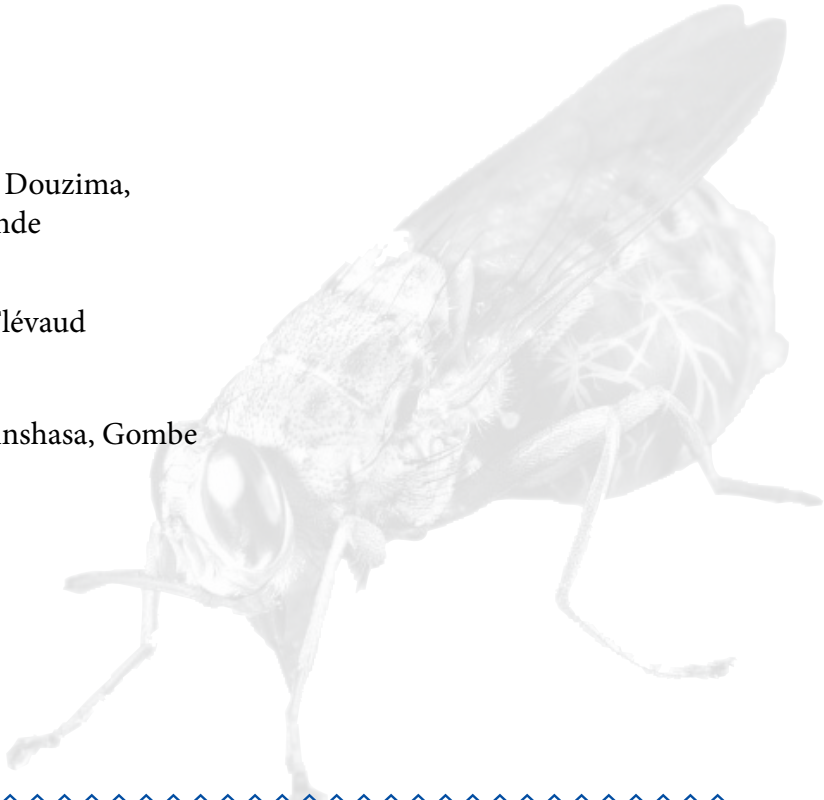
Others partners:
International and national research groups: ITMA, INRB, CDC, TRC-KARI, University of Makerere...

HAT PLATFORM COORDINATION
Avenue Milambo, N° 4, Quartier SOCIMAT Kinshasa, Gombe
Democratic Republic of the Congo

Email:
fmbo@dndi.org

Tel:
00243 81 4313838

Our thanks to Violaine Dallenbach and Louise Burrows for proofreading the newsletter



Contents

Editorial

Dr Florent Mbo
HAT Platform Coordinator

Dear Readers,

In this 19th edition of the Newsletter, you will find a review of the HAT Platform achievements over the 13 years of its existence, as well as of its supporting role to the World Health Organization (WHO) and to all partners involved in research on human African trypanosomiasis (HAT), with the objective of eliminating the disease by 2020.

The mission of the HAT Platform focuses mainly on developing appropriate clinical trial methodologies, resolving the challenges related to administrative and regulatory requirements, building clinical trial capacity (human resources, infrastructure, and equipment), sharing information, and strengthening links between endemic countries.

« The clinical trials and operational studies conducted on human African trypanosomiasis during all these years have helped improve good clinical and laboratory practice »

The clinical trials and operational studies conducted on human African trypanosomiasis during all these years have helped improve clinical and laboratory practices in multipurpose health services, and have strengthened the health system in general in endemic countries. Together with the national HAT control programs, and under the leadership of the WHO, the HAT Platform has provided patients and populations living in remote areas with access to less toxic drugs such as nifurtimox-eflornithine combination therapy (NECT), rapid diagnostic tests, and innovative screening strategies.

Other oral medications such as fexinidazole (for which a file has been submitted by Sanofi to the European Medicines Agency for evaluation) and acoziborole (clinical trials in progress) may further improve the management of HAT and speed up the elimination of this disease.

Happy reading!

Epidemiological profiles of endemic country members of the HAT Platform in 2016

Reports from HAT Platform member countries show a downward trend in new cases in 2016. However, active and passive screening activities dropped due to insufficient resources and security issues in some endemic countries, particularly in South Sudan, the Central African Republic, the Republic of the Congo, and the Democratic Republic of the Congo.

The Central African Republic reported 60 new parasitological cases, over 80% detected through passive screening.

South Sudan reported only 4 new parasitological cases through passive screening due to security problems preventing any active screening in the country. Most people living in endemic areas fled to neighbouring countries, with over 300,000 to the Yumbe health district in northern Uganda.

Guinea reported 107 new parasitological cases, of which 87 in the late stage and 20 in the early stage. The main outbreaks occurred in Boffa and Dubréka. Screening activities resumed after the Ebola epidemic, which disrupted the entire health system.

In Chad 36,090 people were passively and actively examined in 2016, identifying 53 new cases, of which 33 in the late stage, 19 in early first stage, and 1 of undetermined stage.

The Republic of the Congo reported 18 new cases out of 16,149 people examined, of which 13 were identified through passive screening and 5 through active screening. The HAT foci visited were located in the districts of NGabé, Makotimpoko and Imboulou.

Angola declared 19 new cases. In the first half of 2017, a screening campaign identified 12 parasitological cases, including 10 cases in the Uíge province alone. A total of 38,964 people were examined, 31,897 through active screening and 7,067 through passive screening.

The Democratic Republic of the Congo (DRC) reported 1,766 new cases out of 2,627,764 people examined. The DRC is the most affected country with more than 85% of all cases reported worldwide, but the number of new cases is decreasing.

Uganda is the only country where both forms of human African trypanosomiasis coexist. In 2016, 14 new cases were reported, of which 5 were *gambiense* cases and 9 were *rhodesiense* cases.

Summary of HAT Platform achievements since 2005

1. Contribution to the development of and access to a new treatment combination

The HAT Platform participated in clinical trials on nifurtimox-eflornithine combination therapy (NECT) and in the Phase IV NECT-Field study. In the 13 most endemic countries, NECT is now used as first-line treatment for all late-stage *gambiense* HAT patients. These clinical trials on NECT helped reduce the number of eflornithine infusions from 54 to 14. NECT combination therapy is now included in the Model List of Essential Medicines of the WHO, who ensures its supply.

2. Participation in four clinical trials

- **Phase III and IV clinical trials on NECT**

  The study objective was to assess the efficacy and safety of the nifurtimox-eflornithine combination therapy (NECT) for late-stage HAT, compared to the standard dosage regimen of eflornithine.

  Number of patients included and treated: 269 in 4 sites (the DRC and Congo)

- **NECT-Field study**

  The study objective was to document NECT's safety profile under field conditions.

  Number of patients included and treated: 629 in six HAT treatment centres in the DRC (Kwamouth, Bandundu, Dipumba, Katanda, Vanga, and Bonga Yassa), including 100 children under 12 years old, 14 pregnant women, and 33 breastfeeding women.

- **Phase II/III clinical trial on fexinidazole (FEX-004, FEX-005, and FEX-006). Start date: December 2012**

  The study objective was to assess the safety and efficacy of an oral regimen of fexinidazole (a 2-substituted 5-nitroimidazole with proven trypanocidal activity) versus nifurtimox-eflornithine combination therapy in patients with late-stage gambiense HAT.

  Results of the studies were published in *The Lancet*[1]

  These results open the possibility of a paradigm shift in the treatment of this deadly disease.

  Between 2012 and 2016, an open-label randomized pivotal Phase II/III clinical trial compared the efficacy and safety of the new treatment, fexinidazole,

1 Kande et al. Oral fexinidazole for late-stage African *Trypanosoma brucei gambiense* trypanosomiasis: a pivotal multicentre, randomised, non-inferiority trial. *Lancet.* 2018 Jan 13;391(10116):144-154. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)32758-7/fulltext

with today's first-line treatment, nifurtimox-eflornithine combination therapy (NECT), in meningo-encephalitic (stage-2) g-HAT patients. 394 patients were recruited across 10 sites in the Democratic Republic of Congo (DRC) and Central African Republic. Treatment success rates of 91.2% were measured for fexinidazole, with 97.6% for NECT, 18 months after the end of treatment. The results show that fexinidazole is effective within a predetermined acceptability margin, set following a survey with practitioners, based on the significant advantages of having a first-line treatment that is oral. There were no major differences in safety. Two additional studies confirmed the efficacy of fexinidazole in haemo-lymphatic (stage-1) and early-stage-2 g-HAT patients (98.7%), and in children (97.6%), 12 months after the end of treatment. 230 adults were recruited as a part of the safety and efficacy trial in stage-1 and early-stage-2 patients, and 125 children for the paediatric trial. Overall, these additional studies did not reveal any new safety signals regarding the use of fexinidazole.

These results have enabled Sanofi, DND*i's* industrial partner for fexinidazole, to proceed with steps towards regulatory approval through the European Medicines Agency (EMA) Article 58 procedure (which allows the EMA to give opinions, in cooperation with WHO, for evaluation of certain medecinal products for human use that are intended exclusively for markets outside of the European Union), with a view to ensuring patient access to fexinidazole in HAT-endemic countries

- **FEX-009 clinical trial.**
  Start date: November 2016

  The study objective of the FEX-009 clinical trial is to collect information on special population groups (including pregnant or lactating women, and patients with poor nutritional status or with chronic diseases) not included in previous fexinidazole trials. Patients are treated either in hospital or at home, and preliminary information is collected on treatment compliance and efficacy in outpatients.

  Number of patients included and treated: 55 in 7 sites in the DRC (Bagata, Bandundu, Dipumba, Kinshasa, Masi Manimba, Mushie, and Roi Baudouin) and one site at Dubreka in Guinea.

- **Acoziborole clinical trial (OXA-002).**
  Start date: September 2016

  The objective of the OXA-002 study is to assess the efficacy of acoziborole as a single-dose treatment in patients with late-stage gambiense HAT. Patients are followed for 18 months after treatment, with a preliminary evaluation at 12 months.

  Number of patients included and treated: 100 in 9 sites in DRC (Katanda, Isangi, Dipumba, Bandundu, Ngandajika, Masi Manimba, Kwamouth, Roi Baudouin, and Bolobo) and another site at Dubreka in Guinea.

The HAT Platform is contributing to these studies by:

- Training of investigators and clinical site staff,
- Facilitating investigator meetings on acoziborole, fexinidazole, NECT and NECT-Field studies,
- Realization of exploratory missions with FIND for studies on HAT rapid diagnostic tests,
- Contacting regulatory authorities and ethics committees.

3. Publication of 18 newsletters in French and English

18 newsletters have been distributed to the HAT platform member countries. Articles on NECT for the treatment of late-stage HAT have also been broadcast on television and radio.

4. Organisation of 4 scientific meetings jointly with EANETT

These meetings have been organised in Nairobi in 2010 and 2013, Kinshasa in 2014, Ndjamena in 2015, and Conakry in 2016. Steering committee meetings are held annually and the HAT Platform ensures that its members participate in the biannual meetings of the International Scientific Council on Research and Control of Trypanosomiasis. In addition, the HAT platform coordinator generally gives scientific presentations at scientific congresses.

5. Organisation of 22 training sessions with over 400 people trained

Trainings conducted and number of people trained	Venue and year
Training of ethics committees in ethics review (142)	Kinshasa 2007
	Khartoum 2007
	Kampala 2007
	Luanda 2008
	Juba 2009
	Bangui 2010
Training of physicians in Good Clinical Practice (32)	Nairobi 2006, Kinshasa 2011 & 2012, Juba 2012
Training of physicians on clinical examination of patients (25)	Kinshasa 2007
Training of clinical monitors (13)	Kampala 2008
Participation in ICAT 6&7 (26)	Kinshasa 2014, Kampala 2017
HAT training in Dinamadji health district (30)	Dinamadji 2015
HAT Clinical training in South Sudan (41)	Juba 2015
Training of Guinean physician in the DRC (1)	Kinshasa 2014
Training of laboratory technicians from South Sudan in the DRC (3)	Kinshasa 2016
Waste management training in clinical trial sites	Mushie, Vanga, Bagata, Masi 2016

7th International Course on Human African Trypanosomiasis (ICAT 7)

Francis Louis

7th International Course for African Trypanosomiasis, August 2017

ICAT7, the 7th International Course on human African Trypanosomiasis, was held at the prestigious Makerere University in Kampala, Uganda from 7 to 25 August 2017, with financial and pedagogical support from WHO, DND*i*, and the HAT Platform, as well as the unfailing logistical support of Professor Enock Matovu from Makerere University.

This three-week course, organized by the Association against Trypanosomiasis in Africa (ATA), was particularly intensive. It brought together 20 learners from Uganda, the DRC, Malawi, South Sudan, Chad, Congo, Angola, and Guinea Conakry. Teachers came from France, the United Kingdom, Switzerland (WHO and DND*i*), the DRC, and Uganda.


Practical work: 7th International Course for African Trypanosomiasis. Kampala. August 2017

The focus was on interactivity, practical work (serology, parasitology, entomology), and group work, which the learners particularly appreciated.

This year, the main themes were the elimination of HAT as a public health problem by 2020, and the control and surveillance strategies involved.

The members of the BUSOGA promotion, thus called in memory of the terrible trypanosomiasis epidemic that struck this province of Uganda in the 1920s, soon developed a special bond, which was clearly present at the 34 ISCTRC held in Livingstone (Zambia) from 10 to 15 September 2017.

The evaluations carried out by ATA showed a satisfaction index of 18/20 and an average 5-point progression compared to baseline, which illustrates both the quality of the teaching and the interest of the learners.

Improvements are introduced based on the participants' feedback on the training session. It is gratifying to see that approximately 150 professionals involved in HAT control activities attended the 7 ICAT courses, thereby creating a network of experts throughout African countries affected by sleeping sickness.

It should be noted that the vast majority of these experts remain, in one way or another, involved in the field of trypanosomiasis. This loyalty could be celebrated during the 35th International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) in 2019, which coincides with its 70th anniversary. The organizers of this event are also willing to celebrate ATA's 20th anniversary, to which all trypanauts, learners, and teachers will be invited. DND*i* and the HAT Platform would naturally be present as well.

Practical work: 7th International Course for African Trypanosomiasis. Kampala. August 2017

Clinical and operational research opportunities in Angola: the Viana Centre

Josenando Théophile, Amadeu Dala, Makana Don, Kungatikilu Davin, and Florent Mbo

Angola ICCT office (Institute for Combat and Control of Trypanosomiasis)

The Angolan Ministry of Health decided that the Viana Centre is to become a research centre for parasitic diseases.

This centre includes:

- The administrative ICCT (*Institut de Combat et de Contrôle de la Trypanosomiase*) building, with staff offices and a conference room with a capacity of 40 to 45 people, an overhead projector, and sound equipment,
- Three additional rooms with overhead projectors and a capacity for 40 people to host training sessions, as well as 3 other rooms with overhead projectors for training courses or seminars,
- Buildings for consultations and hospitalization, and treatment rooms,
- 12 air-conditioned rooms for visitors (doctors, nurses, or foreigners),

- A new building that can house clinical studies, with common and private rooms, and offices for investigators and nurses,
- 2 well-appointed laboratory rooms, with a projector in the central one,
- 12 new vehicles from the mobile units, including 7 Land Cruisers and Nissans, as well as ambulances to bring patients to the hospital,
- A catering service for patients and medical staff,
- Internet access,
- A library,
- A pharmacy,
- Access to water,
- Laundry facilities,
- A garage for vehicle repair,
- A hygiene and sanitation service.

The Viana Centre offers optimum conditions for clinical research, as well as a good national road network, so that patients living more than 100 km from the capital Luanda can be brought to the centre.

This centre is directed by:

General Director	Prof Josenando Théophile
Deputy Director in charge of executive services	Dr Amadeu Domingos
Deputy Director in charge of finance	Dr Mogardo Paulo
Head of the laboratory department	Makiadi Felix
Head of technical management	Mafuta Daniel
Head of the clinical department	Dr Makana Don
Consultation coordinator	Dr Kungatikilu Davin

Number of physicians: 5
Number of nurses: 23
Number of laboratory technicians: 14


Meeting room for Investigators, Viana Center


Hospital room, Viana center

Management of sleeping sickness in peripheral health centres

Veerle Lejon, DiTECT-HAT Project Coordinator

The DiTECT-HAT (Diagnostic Tools for Human African Trypanosomiasis Elimination and Clinical Trials) project trained health staff involved in the evaluation of new algorithms for passive HAT detection.

A total of 34 persons in Ivory Coast and 25 in Guinea were trained over two 4-day training sessions in 23 hospitals and health centres in HAT endemic areas of these countries. They learned how to recognize the signs of sleeping sickness and how to correctly obtain patients' informed consent for the study procedures. They also familiarized themselves with the principles of good clinical practice. During the practical workshops, the participants performed various rapid diagnostic tests for sleeping sickness, and they detected trypanosomes using mini-columns and dried blood spots on filter paper for subsequent analysis.

A substantial part of the training was dedicated to the use of tablets to enter electronic data and take pictures and videos of test results for quality control purposes. The health staff has now gained all the knowledge needed for the study, which will start once the national ethical committees have given their approval.

A participant had this to say about the training: "The training was very well received, I learned new things about sleeping sickness and I am now ready to start work in my institution." Koné, a doctoral student, added: "The DiTECT-HAT project is particularly suited to the passive detection of sleeping sickness, which so far has remained a considerable challenge. I think that this project will help improve HAT control and be a real step forward. It will also be useful for other neglected tropical diseases."

The integration of HAT control into a country's healthcare facilities is an essential step towards elimination of the disease. As these health centres often have limited resources, one of the main targets of the DiTECT-HAT project is to validate the performance of diagnostic tools and suggest algorithms for the early and rapid diagnosis of sleeping sickness. The results of this study will be used to produce cost-effective diagnostic algorithms to improve patient management, taking into account the future availability of safer and oral drugs.

DiTECT-HAT is the first project on neglected tropical diseases funded by the European and Developing Countries Clinical Trial Partnership (EDCTP, www.edctp.org). It is a joint initiative of

the Institut de Recherche pour le Développement, PNLTHA of DRC, PNLTHA of Guinea, Institut Pierre Richet in Ivory Coast, Institut National de Recherche Biomédicale in DRC, Centre International de Recherche et Développement sur l'élevage en Zone Subhumide in Burkina Faso, the University of Liverpool in the UK, and the Institute of Tropical Medicine in Belgium.

For further information, please visit www.ditect-hat.eu

Announcement

Dear all,

THE REPUBLIC OF UGANDA
MINISTRY OF HEALTH

UNDER THE PATRONAGE OF HIS EXCELLENCY THE MINISTER OF HEALTH OF UGANDA

5th JOINT HAT PLATFORM-EANETT SCIENTIFIC MEETING

"Research and control activities challenges in keeping HAT below the elimination threshold beyond 2020"
KAMPALA, UGANDA, 3-4 OCTOBER 2018

DEADLINE FOR REGISTRATION AND SUBMISSION OF ABSTRACTS FOR ORAL PRESENTATIONS AND POSTERS IS 31 July 2018

Abstracts to be sent to: fmbo@dndi.org; matovue04@yahoo.com; sokotho@gmail.com

TrypElim Project: innovative tools to accelerate HAT elimination in the DRC

Yves Claes

Even though the number of new cases of human African trypanosomiasis (HAT) fell substantially since 1998, from over 30,000 to 2,353 in 2015, this disease remains a public health problem in the Democratic Republic of the Congo (DRC). Because of this sharp decrease in prevalence, the identification of a single case requires significant efforts. The TrypElim operational research project aims to demonstrate the feasibility of HAT elimination, using innovative approaches in two pilot health areas (Yasa Bonga and Mosango) over a 3-year period (2016-2018).

This project implements several combined approaches to rationalizing HAT control strategies: door-to-door screening with mini-teams, electronic data collection with tablets, active screening planning using the Geographic Information System QGIS, quality control based on pictures and videos, and vector control using next generation traps (tiny targets).

Mini-teams

Conventional mobile units have greatly reduced the number of HAT cases, but this means that it has become much more difficult to identify the last remaining cases. The development of new, more flexible approaches will help accelerate the elimination of HAT. A mini-team includes three scouts and one person to confirm the diagnosis. The screening capability of a mini-team is similar to that of a conventional mobile team. The mini-teams travel by motorcycle to the endemic villages where they perform door-to-door screening. This more flexible approach takes into account the activities of the communities, avoids long queues, and reaches more people in the villages. It is better suited to villages that are sparsely populated and difficult to reach. However, the weakness of the mini-team approach is that the diagnosis of TDR-positive cases is confirmed only a few days after the screening, with the risk of not being able to find those with a positive diagnosis again.

Digitizing

We created an electronic data collection system with Android tablets that synchronizes the data to a central database, which then feeds the Dashboard decision support system, accessible from a website. This system automatically generates epidemiological reports with trends (statistics), monitors the performance of the system (teams), and produces maps with a planning tool for active screening by mini-teams and large conventional teams.

Planning active screening

WHO recommends that mobile units plan their visits to endemic HAT villages (i.e. those with at least 1 case in the last three to five years). If no

cases are detected, these villages should be visited for three consecutive years, and again 5 years later before being considered as non-endemic. We complied with this recommendation when planning the annual screening activities in the pilot areas. Furthermore, we systematically increased the coverage of populations at-risk by adding three mini-teams to the large conventional team, and we included villages within a radius of 5 km of an endemic village. The added value of this approach will be assessed after three years.

Quality control

With the current scarcity of cases in endemic areas, it is becoming increasingly important to guarantee the quality of reading screening and diagnostic test results. Moreover, as the number of cases is dropping, it is increasingly difficult to train healthcare providers and to maintain their diagnostic performance. We introduced a system of taking photos of the screening tests with a tablet and videos of the mobile trypanosomes with a camera attached to the microscope. These images are then sent to the provincial coordination centre where a data manager performs a quality control. These images can also be used for HAT diagnostic training.

Vector control

In one of the two pilot areas (Yasa Bonga health area), screening was combined with a vector control program using next-generation traps (tiny targets), particularly along streams and in areas with a high risk of contact between people and tsetse flies. The effectiveness of tiny targets is similar to that of the larger traps traditionally used by the HAT control program, but tiny targets offer the advantage of a considerably lower unit cost and they can remain in place for a long time without needing maintenance. They can be easily deployed by the community, and an anthropological study is ongoing.

Scaling

In parallel with the pilot project, these innovative approaches are being used throughout the former Bandundu Province, which accounts for over half (60 to 70%) of all cases reported by PNLTHA in the DRC. Fifteen mobile mini-teams will be introduced gradually in endemic health areas, in addition to the thirteen conventional mobile units already in place. Together, these mobile units will screen approximately 2 million people every year.

Innovative approach: Mini-teams

3 screeners and one person to confirm diagnosis

Easy access with motorbike

Door-to-door screening

All materials for screening and diagnosis on a motorbike

HAT activities of the MSF Operational Centre Amsterdam (OCA) in the DRC in 2016-2018

Turid Piening

The MSF mobile human African trypanolysis team (MHAT) is currently conducting active screening in the Maniema, Kasai, and Tanganyika Provinces in collaboration with the national program (PNLTHA). Last year, the project moved to the Kasongo health zone in the Maniema Province, an area known for its HAT transmission. Active and passive screening operations started in March 2016, after setting up a new base and passive screening capacity in the local hospital. Since then, the team has screened 18,156 people, and identified and treated 32 HAT cases.

MSF OCA now plans to extend screening to the Kimbombo and Lusangi health zones.

The MHAT team decided to include the diagnosis and treatment of malaria in their active HAT screening activities. Malaria is the main cause of sickness in the areas where the team has been working; the inclusion of malaria diagnosis and treatment into HAT screening and treatment activities was welcomed by the communities and boosted the acceptance of MSF in the field. In 2016, 15,155 people were screened for malaria, of which more than 80% tested positive.

During its activities designed to better understand the communities and improve coordination and information sharing, the MSF team noticed that radio broadcasts were very popular in the area. This provided a great opportunity to increase community awareness of MSF OCA HAT control activities in Kasongo and in the villages where active screening was planned. A radio program was thus broadcast, featuring a father speaking to his son about the purpose of MSF's activities related to sleeping sickness. It resulted in several people showing up at the hospital for passive screening.

Once its methodology was refined, MHAT screened 8,282 people for HAT and 7,931 for malaria in the first 6 weeks of 2017. These tests identified 28 HAT cases.

A multi-skilled field team and *ad hoc* technical support played a key role in tracking, diagnosing, and treating people with HAT in these remote areas. Well aware of the complexity and importance of laboratory services, the MHAT team started using a camera connected to a microscope, to send videos to the team in Amsterdam who could then provide information and specialist advice.

In order to improve microscopy reading and interpretation of results, laboratory technicians are now sent for training on a regular basis to the ITM in Antwerp, Belgium.

Sleeping sickness remains a neglected tropical disease and MSF OCA is committed to screening and treating people in remote and isolated areas using its MHAT team. In March 2017, the project moved to a new health zone in the Maniema Province. Passive screening started in Kibombo in April, followed by active HAT and malaria screening in selected areas within the health zone.

MSF field activities. 20 August 2016, Maniema province, DRC

Access of displaced populations to sleeping sickness elimination programs

Jennifer Palmer, Okello Robert, and Freddie Kansiime

The Sustainable Development Goals encourage States not to 'forget' populations forcibly displaced by war when conducting development work. This includes internally displaced people as well as refugees who flee their own country. In a programme that allows for equitable integration, displaced populations and host nationals should have equal access to healthcare resources. Per capita spending on both populations should also be equal, with adjustments based on disease prevalence.

The availability of new simple technologies, such as rapid diagnostic tests (RDTs), could potentially promote greater access to sleeping sickness control for many disease-affected populations. However, in Africa, refugee assistance policies vary from country to country and displaced populations do not always have the same basic socio-economic rights, such as access to universal healthcare and inclusion in disease control or elimination activities. Internally displaced populations may also face stigma and other difficulties accessing care. Ensuring real access for displaced populations may therefore require additional operational and governance-related measures.

Based on the governance measures adopted to control sleeping sickness in Uganda, which has accommodated almost 1 million refugees from South Sudan since 2013, we make the following recommendations to help sleeping sickness programmes and donors avoid unwittingly marginalizing displaced populations and maintaining transmission.

Recommendations for national programmes

1. Determine whether displaced populations are at risk of sleeping sickness in areas where your programme can provide services

All 36 African countries endemic for sleeping sickness have taken in populations forcibly displaced by war, and sleeping sickness outbreaks are historically associated with forced migrations. National sleeping sickness programmes should consider whether displaced populations living in their country are at risk of contracting sleeping sickness, either because they have come from or migrated to endemic areas. This may involve working with refugee and humanitarian agencies to locate these displaced populations living in formal or informal settlements. It is important to locate those who are already ill and to determine whether they are living in areas where transmission is possible, even if these areas have been declared disease-free in the past, and to determine whether HAT control services are available in those areas or not.

2. Determine how existing programmes may help reduce the risk of HAT among displaced populations

National disease control programmes may not be formally responsible for the health needs of refugee populations, but refugees may have access to government health services which already collaborate with these national programmes or have the potential to do so. National disease control programmes can identify the government services particularly involved in helping displaced populations. As these services recruit additional staff to respond to humanitarian crises, programmes can intensify training and supervision activities as well as increase supplies. National programmes can also communicate with non-governmental partners involved in humanitarian crises to notify them of sleeping sickness risks, national initiatives, and the possibility of collaborations.

3. Identify and address potential communication problems between displaced populations and healthcare providers

All technological innovations, no matter how simple they seem, require communication to ensure they are used properly. The impact of cultural differences between displaced populations (internally or to another country) and healthcare providers in the host country on the use of disease control technologies must not be underestimated, particularly when there are language problems. For instance, when conducting passive screening activities, the healthcare provider will use a RDT for sleeping sickness after a lengthy questioning on symptoms, which becomes difficult if the refugee does not understand the language. Consequently, national programmes trying to integrate displaced populations should take into account any communication problems, and train their staff or use translators to guarantee the quality of the communication between national providers and representatives of the displaced communities.

4. Identify potentially necessary new interventions

If monitoring indicators suggest the programme is delivering fewer outputs than expected in areas serving refugee or internally displaced populations, programmes should consider new interventions that may require external financing. This could include offering 'screening days' in passive screening facilities, organising transport assistance for patients who need to go to a HAT treatment referral centre, or conducting active screening in settlements and refugee reception sites. All new initiatives should also identify and use displaced individuals who have some technical expertise.

Recommendations to sleeping sickness donors

1. Anticipate the needs of displaced people when designing programmes

During negotiations on project contracts, donors could prompt country programmes to integrate at the design stage of their disease elimination programmes the potential needs of displaced populations, both existing and future. Countries could also be offered the option to request an additional budget to integrate activities targeting these populations as humanitarian crises unfold.

2. Support programmes to monitor outcomes in displaced populations

Monitoring equity between displaced populations and host populations is a key priority under the Sustainable Development Goals agenda, which donors of sleeping sickness programmes can promote. Health facilities known to serve high numbers of displaced people, for example, can be closely monitored for their levels of intervention implementation.

Transboundary project to eliminate HAT between the DRC, Congo, and Angola

Simon Kayembe, Joseph Ndungu, and Florent Mbo

Transboundary HAT elimination project's meeting between DRC, Congo, and Angola funded by FIND, Kinshasa, DRC 27 July 2017

A follow-up meeting of the transboundary HAT phase-out project in the DRC, Congo, and Angola was held in Kinshasa from 27 to 28 July 2017, with the participation of actors from the three countries.

The objective of the project is to determine the feasibility of HAT elimination in the Kongo Central cross-border area through intensified passive case detection, using a new diagnostic strategy combining the use of rapid diagnostic tests (RDTs), fluorescence microscopy (LED-FM), and a molecular method called isothermal loop-mediated amplification (LAMP). This approach is complemented by active reactive screening of communities in villages where cases have been

recently identified. The project is implemented in the Kongo Central Province in the Democratic Republic of the Congo, in the Cabinda and Zaire Provinces in Angola, and in the Pool and Bouenza Provinces in Congo.

During the first phase of the project, 600 health centres in Kongo Central examined patients with HAT using RDTs, 23 performed confirmatory microscopy tests on TDR-positive cases, and 5 performed LAMP tests on positive RDT samples. During the second phase of the project, the number of centres testing for HAT was reduced to 141, focusing on areas where cases had been reported in recent years.

In Angola, 50 centres in the Cabinda and Zaire Provinces joined the project with two ILED microscopy centres and two LAMP centres for HAT since December 2016.

In Congo Brazzaville, 54 TDR sites, including two microscopy centres and one LAMP centre in Mandingu and Nkayi, were planned, but 14 TDR sites could not operate due to security issues.

Although the referral rate was low during the first phase of the project, most patients were diagnosed in the early stage. In the second phase, RDT-positive suspects in whom confirmatory tests could not be conducted are being searched for and tested by microscopy in a mobile laboratory.

Other improvements have been or will be made:

1. Integration of HAT screening into the primary health care system,
2. Reduction of distance between TDR centres and confirmation sites by increasing the number of microscopy centres,
3. Health worker training,
4. Introduction of new screening and confirmatory tools.

Transboundary HAT elimination project's meeting between DRC, Congo, and Angola funded by FIND, Kinshasa, DRC 27 July 2017

National HAT Platform meetings in pictures

Angola | Luanda, 20 July 2017

Congo | Brazzaville, 26 September 2017

Guinea | Conakry, 16 December 2017

DRC | Kinshasa, 12 October 2017

Uganda | Kampala, 17 August 2017

Recent scientific publications

Aita Signorell

1. Biéler S, Waltenberger H, Barrett MP, McCulloch R, Mottram JC, Carrington M, Schwaeble W, McKerrow J, Phillips MA, Michels PA, Büscher P, Sanchez JC, Bishop R, Robinson DR, Bangs J, Ferguson M, Nerima B, Albertini A, Michel G, Radwandska M, Ndung'u JM. Evaluation of Antigens for Development of a Serological Test for Human African Trypanosomiasis. *PLoS One*. 2016 Dec 9;11(12):e0168074. doi: 10.1371/journal.pone.0168074.

2. Cheuka PM, Mayoka G, Mutai P, Chibale K. The Role of Natural Products in Drug Discovery and Development against Neglected Tropical Diseases. *Molecules*. 2016 Dec 31;22(1). pii: E58. doi: 10.3390/molecules22010058.

3. de Vries H, Wagelmans AP, Hasker E, Lumbala C, Lutumba P, de Vlas SJ, Klundert JV. Forecasting Human African Trypanosomiasis Prevalences from Population Screening Data Using Continuous Time Models. *PLoS Comput Biol*. 2016 Sep 22;12(9):e1005103. doi: 10.1371/journal.pcbi.1005103.

4. Field MC, Horn D, Fairlamb AH, Ferguson MA, Gray DW, Read KD, De Rycker M, Torrie LS, Wyatt PG, Wyllie S, Gilbert IH. Anti-trypanosomatid drug discovery: an ongoing challenge and a continuing need. *Nat Rev Microbiol*. 2017 Feb 27. doi: 10.1038/nrmicro.2016.193.

5. Haanstra JR, Gerding A, Dolga AM, Sorgdrager FJ, Buist-Homan M, du Toit F, Faber KN, Holzhütter HG, Szöör B, Matthews KR, Snoep JL, Westerhoff HV, Bakker BM. Targeting pathogen metabolism without collateral damage to the host. *Sci Rep*. 2017 Jan 13;7:40406. doi: 10.1038/srep40406.

6. Hamill L, Picozzi K, Fyfe J, von Wissmann B, Wastling S, Wardrop N, Selby R, Acup CA, Bardosh KL, Muhanguzi D, Kabasa JD, Waiswa C, Welburn SC. Evaluating the impact of targeting livestock for the prevention of human and animal trypanosomiasis, at village level, in districts newly affected with *T. b. rhodesiense* in Uganda. *Infect Dis Poverty*. 2017 Feb 6;6(1):16. doi: 10.1186/s40249-016-0224-8.

7. Koffi M, N'Djetchi M, Ilboudo H, Kaba D, Coulibaly B, N'Gouan E, Kouakou L, Bucheton B, Solano P, Courtin F, Ehrhardt S, Jamonneau V. A targeted door-to-door strategy for

sleeping sickness detection in low-prevalence settings in Côte d'Ivoire. *Parasite*. 2016;23:51.

8. Picado A, Ndung'u J. Elimination of sleeping sickness in Uganda could be jeopardised by conflict in South Sudan. *Lancet Glob Health*. 2017 Jan;5(1):e28-e29. doi: 10.1016/S2214-109X(16)30288-1.

9. Rock KS, Torr SJ, Lumbala C, Keeling MJ. Predicting the Impact of Intervention Strategies for Sleeping Sickness in Two High-Endemicity Health Zones of the Democratic Republic of Congo. *PLoS Negl Trop Dis*. 2017 Jan 5;11(1):e0005162. doi: 10.1371/journal.pntd.0005162.

10. Russell S, Rahmani R, Jones AJ, Newson HL, Neilde K, Cotillo I, Rahmani Khajouei M, Ferrins L, Qureishi S, Nguyen N, Martinez-Martinez MS, Weaver DF, Kaiser M, Riley J, Thomas J, De Rycker M, Read KD, Flematti GR, Ryan E, Tanghe S, Rodriguez A, Charman SA, Kessler A, Avery VM, Baell JB, Piggott MJ. Hit-to-Lead Optimization of a Novel Class of Potent, Broad-Spectrum Trypanosomacides. *J Med Chem*. 2016 Nov 10;59(21):9686-9720.

11. Shereni W, Anderson NE, Nyakupinda L, Cecchi G. Spatial distribution and trypanosome infection of tsetse flies in the sleeping sickness focus of Zimbabwe in Hurungwe District. *Parasites & Vectors*. 2016 Nov 25;9(1):605.

12. Lestrade-Carluer De Kyvon MA, Maakaroun-Vermesse Z, Lanotte P, et al. Congenital trypanosomiasis in child born in France to African mother. *Em Inf Dis* 2016; 22: 935–7.

13. Franco JR, Cecchi G, Priotto G, et al. Monitoring the elimination of human African trypanosomiasis: update to 2014. *PLoS Negl Trop Dis* 2017; 11: e0005585.

International meetings in 2017 and 2018

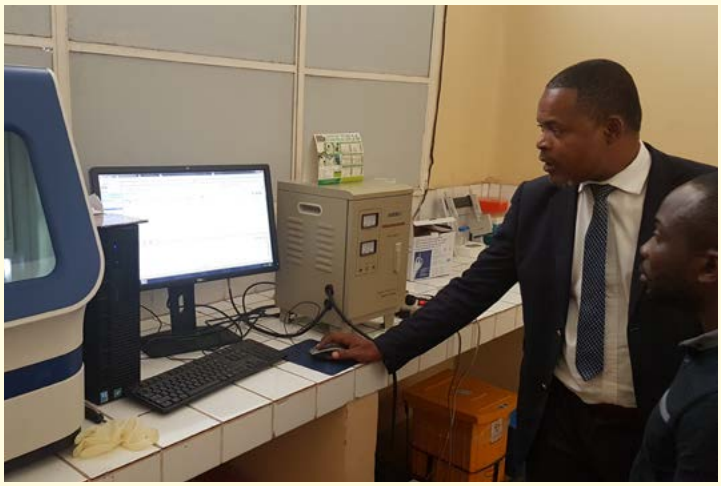
1. 11-15 September 2017: 34th International Scientific Committee for Trypanosomiasis Research and Control, Lusaka, Zambia
2. 16-20 October 2017: 10th European Congress on Tropical Medicine and International Health (ECTMIH), Antwerp, Belgium
3. 5-9 November 2017: 66th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH), Baltimore, USA
4. 30 November 2017: 27th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria
5. 3-4 October 2018: 5th Joint HAT Platform-EANETT Annual Scientific Meeting to be held in Kampala, Uganda

Visits and meetings

Presence of the HAT Platform delegation at the funeral of Dr. Stéphane Ngampo, former director of PNLTHA Congo and Congo HAT platform focal point. Brazzaville, 6 January 2017.

Working visit of the HAT Platform Coordinator in Angola in January and July 2017: Visit of Angola ICCT field activities in Mbanza Kongo, Kwanza Norte, Uige, and Bengo provinces.

Coordinator's visit to Uganda: participation in the HAT Platform meeting in Uganda and field visit to northern Uganda in Arua, Yumbe, and Kiboko districts, September 2017.



Coordinator's visit to Brazzaville from 26 to 27 September 2017 to attend the Congo HAT Platform meeting and visit of the PNLTHA Congo and the National Public Health Laboratory.


Attendance at the clinical investigator meeting on acoziborole and fexinidazole, 6 September 2017, Kinshasa.


Participation in the 34th International Scientific Council conference on Trypanosomosis Research and Control, 10-15 September 2017 in Livingstone, Zambia.

Visit to His Excellency the Minister of public Health of the DRC, Dr Oly Ilunga by the head of FIND, Prof. Joseph Ndungu together with delegations from PNLTHA Congo & the DRC and Angola ICCT during the evaluation meeting of the cross-border HAT elimination project, 6 September 2017, Kinshasa.



Participation in the 10th European Congress on Tropical Medicine and International Health 16 to 20 October 2017 in Antwerp, during which the results of the clinical trials on fexinidazole (the first oral treatment for HAT) and a HAT Platform poster were presented.


Participation in the workshop on parasitological techniques used in onchocerciasis on 21-22 September 2017 in Accra, Ghana, where a consensus was reached by experts on the parasitological techniques to be used in clinical trials on filariasis / onchocerciasis.

Participation in the first meeting of the Guinea HAT Platform and Guinea steering committee meeting, 17 to 21 December 2018.

News from the DND*i* filariasis program

Belen Pedrique and Florent Mbo

Second exploratory visit of the DND*i* Geneva filariasis team to the Tshopo and South-Uele provinces in the Democratic Republic of the Congo

In anticipation of future clinical trials on filariasis, the DND*i* Geneva filariasis team conducted a preliminary prospection from March 13 to 23, 2017. At the same time, the DND*i* New York communication team and journalists from The Huffington Post and El Pais travelled there from 13 to 26 March 2017 to prepare a story on onchocerciasis and human African trypanosomiasis. During these missions, working meetings were organized with the National Program for Neglected Tropical Diseases with Preventive Chemotherapy of the DRC, the DRC HAT Control Program, and research institutions (INRB). Visits were carried out in hospitals in Kinshasa and in the Tshopo and South-Uele Provinces, as well as among the population in endemic villages.

Consultation meeting at the national program of neglected tropical diseases with preventive chemotherapy, Kinshasa 14 March 2017.

Badagulu Village is endemic for onchocerciasis: Population affected by blindness.

Visit to the onchocerciasis and ophthalmological clinical case management center, Kisangani DRC, March 2017.

Evaluation visit of a phase 1b onchocerciasis clinical trial site in Ghana by a joint team of the Geneva DND*i* filariasis program and the DRC DND*i* office

The Geneva DND*i* filariasis program team conducted a joint mission with the DND*i* DRC team in Ghana to assess the future study site. During this visit, working meetings were held with the staff of the University of Health and Allied Sciences (UHAS) of Ho, the staff of the clinical trial site at Hohoe, and the National Program for Neglected Tropical Diseases with Preventive Chemotherapy. Some experts were contacted at the University of Ghana and the Noguchi Medical research Institute. The intensive care unit of the Ho Hospital was also visited.

Onchocerciasis clinical trial site visit, Hohoe, Ghana, May 2017.

Onchocerciasis clinical trial site visit, Hohoe, Ghana, May 2017.

Presentation of the new PNLTHA DRC team

On behalf of its members, the HAT PLATFORM steering committee wishes success to the new team

Dr Eric MWAMBA MIAKA, Director of PNLTHA DRC

Dr Vianney SELEMANI, Deputy director of PNLTHA DRC

Mrs Jacqueline DAGU, Head of administrative and financial division of PNLTHA DRC

Obituary

Dr Stéphane Ngampo

In 2016, the HAT Platform lost one of its members, Dr Stéphane Ngampo, former Director of the National HAT Control Programme and former focal point of the Republic of the Congo.

Testimony of Dr Augustin Ebeja

I met Old Stéphane, as we called him, in 2007 during our duties with the HAT Platform.

As Coordinator of the HAT Platform, I was in close contact with all my focal points from the different member countries. Dr Stéphane Ngampo, who often spoke to me in Lingala, formed with Dr Nicolas Mbongo and Prof Joseph Parrha the joyful Congolese trio around which our Platform gravitated. They worked in a friendly atmosphere, laughing and pretending to scold each other, but in the end they always produced results "in the Congolese way", in the good sense of the term.

Dr Stéphane was truly a man of the field: his scientific presentations always included photographs of him digging his car out of the sand, travelling down the river in a canoe loaded with equipment to perform active screening with his team, or in casual dress talking with the village chief over a glass of palm wine.

When we were caught in lengthy discussions during our scientific meetings, he often asked us what was the impact or added value for "us, the men in the field".

I would be missing something if I didn't say how attached he was to his family, often blaming me for sending him far away from them.

I will end by saying that Dr Stéphane Ngampo was a discreet man, that none of us could claim to have known really well, and that I have described here only a very small facet of his personality.

May his soul rest in peace.

Birth announcements

Gratien Benoit Ilunga Mukendi, born 28 February 2017, son of Melchias Mukendi, TDR R&D Fellow, DRC

Iris NUSBAUMER, born 22 December 2016 daughter of Morgane Nusbaumer, Clinical Research Associate, Swiss TPH, Switzerland

The HAT Platform and DND*i* wish to express their gratitude to the following donors for their support since 2003:

- Department for International Development (DFID) / UK
- Dutch Ministry of Foreign Affairs (DGIS) / THE NETHERLANDS
- European Union - Framework Programme 6
- Federal Ministry of Education and Research (BMBF) through KfW / GERMANY
- French Development Agency (AFD) / FRANCE
- Médecins Sans Frontières International
- Medicor Foundation / LIECHTENSTEIN
- Ministry for Europe and Foreign Affairs (MEAE) / FRANCE
- Norwegian Agency for Development Cooperation (Norad) / NORWAY
- Republic and Canton of Geneva / SWITZERLAND
- Spanish Agency for International Development Cooperation (AECID) / SPAIN
- Swiss Agency for International Development and Cooperation (SDC) / SWITZERLAND
- A private Swiss foundation and Other Private Donors

Contact: **Dr. Florent Mbo**
HAT Platform Coordination
Milambo street N° 4 Q/Socimat, Gombe, Kinshasa,
Democratic Republic of the Congo
Email: fmbo@dndi.org
Tel: 00243 81 081 22 38