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° 12, December 2012

HAT Scientific workshop in Kinshasa DRC

6 December 2012

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Editorial

Dr Kadima Augustin ; HAT Platform Coordinator

As we are nearing the end of the twelth month of 2012, we are happy to provide you with the twelth issue of the regional HAT Platform Newsletter.

In 2012, some of the HAT Platform's specific objectives came to fruition, such as the initiation of the fexinidazole study, the launch of the first rapid diagnostic test for sleeping sickness, and many others which we will discuss in this issue.

By sharing such information, our platform is raising awareness on neglected diseases, and more importantly is helping find new diagnostic and treatment tools for sleeping sickness. If we maintain our collective effort, the day will come, sooner or later, when HAT will no longer be a public health concern.

On behalf of all the members and partners of the HAT Platform, we thank you and wish you the very best for 2013. We must keep working together as the best is yet to come.

The HAT Platform and DNDi would like to thank the following donors for their support since July 2003:

- Department for International Development (DFID) / UNITED KINGDOM
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- A Swiss private foundation and individual donors.

2 SPECIAL FEXINIDAZOLE INITIATION

DNDiFEX004 study finally under way.

ONCE UPON A TIME, THERE WAS DNDIFEX004…

Ignored for a long time, sleeping sickness has generated renewed interest over the past few years. The determination and hard work of DNDi and its network of partners (HAT Platform and other organisations) produced new drugs and new drug regimens. The NECT combination is a good example of the results of such efforts. Although NECT is an effective and better tolerated treatment for sleeping sickness, it requires special training of the medical staff and restricting logistics, both impractical in remote and poorly equipped healthcare facilities, with undertrained staff, so common in the areas with the highest HAT incidence.

DNDi and its partners therefore launched an ambitious program to develop an oral drug for the treatment of sleeping sickness. This type of treatment, as well as diagnostic tools that are superior and easier to use, even in remote areas, have been requested by the national control program of the HAT Platform member countries.
We will not detail here the preclinical development nor phase I studies, and focus rather on the pivotal phase II/III study, registered on the www.clinicaltrials.gov website under the reference DNDI-FEX004.

The study was prepared in three stages:

I. Sites selection

A preliminary selection of potential study sites was performed based on the epidemiological data supplied by the national programmes of the HAT Platform member countries. The final study sites were selected as follows:

a. Visit to the sites from July 2010 to March 2012:

- Bandundu, Vanga, Yasa-Bonga (DRC): July 2011 by a mixed team from the DRC national HAT control programme, DNDi, and Swiss TPH
- Batangafo (CAR): May 2011 by a mixed team from DNDi and MSF-E
- Masi-Manimba (DRC): July 2012 by a mixed team from the DRC national HAT control programme, and Swiss TPH
- Yambio, Lui (RSS): October 2011 by a mixed team from the MoH (RSS), DNDi, Swiss TPH, HAT Platform, and DRC national HAT control programme
- Yei (RSS): April 2012 by a mixed team from DNDi, Swiss TPH, HAT Platform, and DRC national HAT control programme
- Dingila (DRC): September 2012 by a mixed team from DRC national HAT control programme, DNDi, and Swiss TPH

b. Prospection/survey

Prospection/survey in the villages surrounding certain sites to determine whether these sites would be able to include at least 5 patients per month. This stage was completed in the DRC and RSS with the support of the HAT Platform, DRC national HAT control programme and INRB, with funding from DNDi:

- Vanga (DRC): August 2011 by a team from DRC national HAT control programme
- Lui: (RSS): February 2012 by a mixed team from DRC national HAT control programme, HAT Platform, and MoH/RSS
- Yei (RSS): April 2012 by a mixed team from MoH/RSS, DRC national HAT control programme, INRB/DRC and HAT Platform

c. Sites chosen:

- Bandundu (Bandundu HGR in DRC)
- Batangafo (Batangafo Hospital MSF-E in CAR)
- Dingila (Dingila Hospital MSF Switzerland in DRC)
- Dipumba (Dipumba CRT in DRC)
- Masi-Manimba (Masi-Manimba HGR in DRC)
- Vanga (Vanga HE in DRC)

2. Teams training

The site teams were then given a training course on the following themes:

a. Good Clinical Practice, Kinshasa Nganda, October 2011.
The course was led jointly by a team from Swiss TPH and the HAT Platform. All the investigators, all laboratory managers, as well as the head nurses in the chosen sites participated in this course.

b. Update on HAT and standard precautions, Caritas Kinshasa, January 2012.
The course was led jointly by a team from DRC national HAT control programme, Swiss TPH, Ngaliema Hospital, CNPP and MSF (Sylvie Puit).

After a review of the clinical presentation of HAT and standard precautions, the participants were divided into three groups for more targeted training:

- Investigators (physicians)
- Review and demonstration of the physical examination of a normal individual
- Basic cardiology and endocrinology review
- Review and demonstration of neurological examination
- Nurses
- Standard precautions
- Preparation and administration of the NECT combination
- Drug management
- Laboratory technicians
- HAT diagnosis, practical exercises
- Demonstration of the specific study tests (piccolo blood che mistry, count, WBC differential, etc.)
- Standard precautions

c. Investigator meeting
The investigator meeting ended the series of lectures and training courses on the preparation of the fexinidazole study.
It was held in Kinshasa in June 2012 with the investigators and nurses in charge, supported by the sponsor DNDi and teams from Swiss TPH, Cardinal System and Cardiabase.

During this meeting, the investigators were shown how to use the electronic case report form (e-CRF) and exchanged with representatives from Cardinal System, supplier of the e-CRF. They were also shown how to use the portable ECG device CarTouch and exchanged with representatives from Cardiabase, supplier of this tool who will also be responsible for the management of the ECGs attached to the e-CRF.

3. Rehabilitation and Equipment

DNDi was responsible for the rehabilitation and equipment of the hospital buildings, laboratories, incinerators, latrines, water and electricity supply systems in the chosen sites, in compliance with the GCP and international standards. Most sites were located in rural areas. VSATs were installed in three of the six sites which did not have an access to the Internet, to ensure they could use the e-CRFs and remain in almost permanent contact with all those involved in the study.

4. Initiation Visits and inclusion launch

The DNDiFEX004 study was then initiated, with a series of site visits and the inclusion of the first patients. To date, inclusion has been authorised in six sites, the first patient having signed the informed consent form on 07/10/2012 in Vanga (code number 02001).

The DNDiFEX004 study provided an opportunity for DNDi to introduce novelties tantamount to small revolutions in our countries:

- Use of the e-CRF
- Use of the automatic analyser PICCOLO

We wish to express our respect and gratitude to the whole DNDi team in Geneva, Paris, Kinshasa, and in the study sites, as well as to our partner institutions, who worked so hard to bring about this great project to which we wish the best of luck.

Press release

New Oral Drug Candidate for African Sleeping Sickness
Phase II/III Clinical Trial Launched in the Democratic Republic of the Congo and Central African Republic

[Geneva, Switzerland, and Kinshasa, Democratic Republic of the Congo – 6 December 2012]
A new oral-only treatment for sleeping sickness has entered Phase II/III clinical study in patients with late-stage sleeping sickness in the Democratic Republic of the Congo (DRC) and soon in Central African Republic (CAR). The study, initiated by the Drugs for Neglected Diseases initiative (DNDi) and its partners, will test the efficacy and safety of fexinidazole, with once-daily tablets for ten days.

Sleeping sickness – or human African trypanosomiasis – is fatal without treatment. Spread by the bite of a tse-tse fly, the disease threatens the most remote areas of 36 sub-Saharan African countries and, while currently in a period of decline, is known to re-emerge to epidemic levels when surveillance efforts wane. Children below 15 years of age represent nearly a quarter of current patients and DRC alone accounts for the majority of reported cases throughout Africa.

Current treatments for stage 2 of the disease – or late stage, when the parasites cross the blood-brain barrier – are difficult to administer as they require infusions that are only possible within a hospital infrastructure, in addition to the heavy transport necessary to get them there. Patients living far from this type of structure often have to travel for days, even by foot, to access treatment centres.

'This is a major step in research and development for neglected tropical diseases. It shows that it is possible to bring a new chemical entity through the pipeline to offer an entirely new perspective on tackling a disease like sleeping sickness', comments Dr Bernard Pécoul, DNDi's Executive Director. 'It is by connecting all of our partners in the endemic countries and around the world with the support of engaged donors – all with a common goal – that we can and will continue to search for adapted treatments for these diseases', he added.

Fexinidazole is the first success of the extensive compound mining efforts pursued by DNDi within the nitroimidazole project initiated in 2005 to explore new and old nitroimidazole drug leads. The objective is to progress fexinidazole through this pivotal Phase II/III study in order to register the drug as a new treatment for stage 2 sleeping sickness caused by the parasite Trypanosoma brucei (T.b.) gambiense, as well as for stage 1 sleeping sickness and sleeping sickness caused by T.b. rhodesiense.

If ultimately successful, fexinidazole would be the first oral treatment to be used for both stage 1 and stage 2 sleeping sickness, thereby replacing the complicated diagnosis and treatment paradigm, which includes systematic lumbar punctures of every diagnosed patient to determine the stage of the disease before deciding which treatment to administer.

'This new chemical entity gives us hope of a drastically simplified way to care for our patients', said Dr Wilfried Mutombo, National Human African Trypanosomiasis Control Programme , DRC, Investigator and Coordinator of the fexinidazole trial. 'In addition, the investments made into renovating the laboratories and hospital wards, training personnel, and introducing adapted technologies that allow us to report in real time on each patient, has elevated an entire group of dedicated professionals to international clinical research standards', he added.

The study was initiated and is conducted by DNDi in collaboration with the Swiss Tropical and Public Health Institute (Swiss TPH) and the Human African Trypanosomiasis national control programmes of the Democratic Republic of the Congo and Central African Republic, in addition to collaboration with Médecins Sans Frontières (MSF). The French pharmaceutical company Sanofi and DNDi co-develop the drug: DNDi is responsible for preclinical, clinical, and pharmaceutical development, while Sanofi is responsible for the industrial development, registration, and production of the drug at its manufacturing sites.

Recruitment for the study will include 510 patients at five clinical sites in DRC and one site in Central African Republic.

About the fexinidazole study
The efficacy and safety study is a pivotal, non-inferiority, open, multicentric and randomized Phase II/III study. The treatment regimen for fexinidazole will consist of 1 dose of 1800mg (3 pills) once a day for the first 4 days and 1 dose of 1200mg (2 pills) once a day for the following 6 days (10 days in total). The reference treatment, NECT, which will be administered for 10 days as well, with 3 oral administrations per day of nifurtimox for 10 days in combination with 2 intra-venous infusions per day of elfornithine (2-hours long each) for 7 days. Two-thirds of patients will receive fexinidazole, and one-third will receive NECT.

The study will measure the safety and efficacy of fexinidazole, with NECT as the active comparator. NECT is currently the first-line treatment for stage 2 of the disease, which notably has replaced since 2009 the toxic arsenic-based melarsoprol. The protocol for the fexinidazole study was reviewed by an international ethics working group convened by the Société Française et Francophone d'Ethique Médicale (SFFEM) with WHO support, before being approved by the national authorities and the MSF ethics committee.

Support for the study
This project is supported by the Bill & Melinda Gates Foundation, Médecins Sans Frontières, the Spanish Agency for International Development Cooperation (AECID), the British Department for International Development (DFID), the French Ministry of Foreign and European Affairs (MAEE), the GIZ on behalf of the Government of the Federal Republic of Germany, the Dutch Ministry of Foreign Affairs (DGIS), the Swiss Agency for Development and Cooperation (SDC), and other individual donors.

About sleeping sickness
Sleeping sickness (or human African trypanosomiasis, HAT), which threatens millions in 36 countries in sub-Saharan Africa, is fatal if left untreated. The disease is caused by parasites transmitted by the bite of a tse-tse fly and is often asymptomatic for years (stage 1) until the infection reaches stage 2, where it crosses into the central nervous system and brain. Currently, prior to treatment, the stage of the disease must be determined using a diagnostic spinal tap to extract cerebrospinal fluid from the patient.

About DNDi
The Drugs for Neglected Diseases initiative (DNDi) is a not-for-profit research and development organization working to deliver new treatments for neglected diseases, in particular sleeping sickness (human African trypanosomiasis), Chagas disease, leishmaniasis, specific helminth (filarial) infections, malaria, and paediatric HIV. Since its inception in 2003, DNDi has delivered six treatments:
two fixed-dose antimalarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, and a paediatric dosage form of benznidazole for Chagas disease.

DNDi has helped establish three clinical research platforms: Leishmaniasis East Africa Platform (LEAP) in Kenya, Ethiopia, Sudan, and Uganda; the HAT Platform based in Africa for sleeping sickness; and the Chagas Clinical Research Platform in Latin America.
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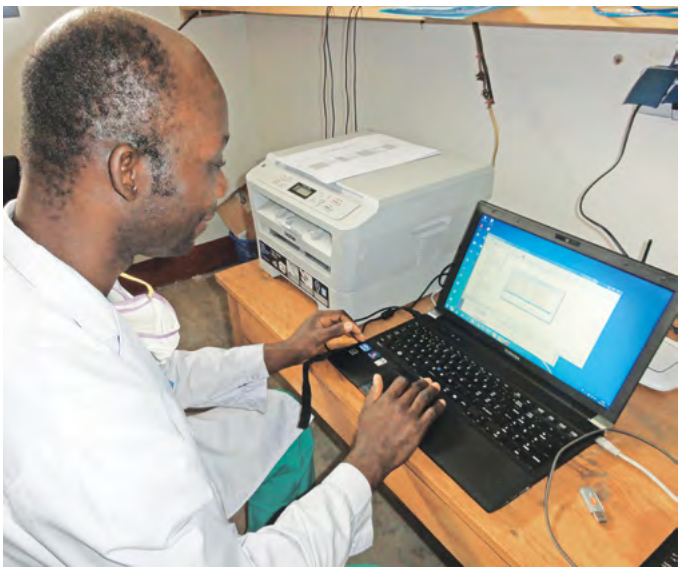

3 LATEST SCIENTIFIC EVENTS AND MISCELLANEOUS INFORMATION

I) Training Course on Good Research and Clinical Practice in Tse-tse and Trypanosomiasis

Juba, South Sudan, 11-13 September 2012

Préambule

A three-day training course was held in Juba, South Sudan, for personnel involved in sleeping sickness research and control (see attached agenda). The main objective was to present the good research and clinical practice to the medical staff of South Sudan. The course was officially opened by the General Director of the National Diseases Control Directorate of the Ministry of Health.

Although the number of cases of sleeping sickness has dropped (WHO reports), South Sudan is one of the three countries still reporting a high incidence of the disease. This training course was thus deemed necessary to build the country's research and control capacity to sustain gains made. The first day was dedicated to an introduction to research on Human African Trypanosomiasis (HAT) and its vector, the tse-tse fly.

The course also examined control options, challenges and new frontiers for vectors in human and animal African trypanosomiasis. Participants were also introduced to bioinformatics concepts and their clinical applications.

The remaining two days were dedicated to lectures and practical sessions covering GCP and international guidelines; roles of investigative and sponsor staff, ethics committee; informed consent, protocols and standard operating procedures; essential documents (theory and practical work); and challenges of conducting clinical trials in disease endemic countries (DECs).
The course was co-sponsored by Drugs for Neglected Diseases Initiative (DNDi) and NIH/Yale University under our current programmes for capacity building.

The course was attended by 21 participants from the Ministry of Health and Juba University and was led by highly experienced facilitators, including Augustin Ebeja, Grace Murilla, Caroline Masiga-Kithinji and Paul Mireji.

Training objectives

1. Introduce research to the Ministry of Health staff
2. Strengthen the capacity of South Sudan for carrying out clinical trials
3. Assist the country in its efforts to establish a functional ethics committee
4. Assist the country in determining the needs for sustaining gains achieved by control programmes

Expected results

1. Creating a highly sensitized community of researchers
2. Well trained staff to support clinical trials

Discussion points and way forward

1. Widespread population movements due to civil war contributed to the spread of sleeping sickness.
2. Data on infesting species and distribution are not known due to the current lack of tse-tse control activities.
3. HAT re-emerged when the sponsors of control activities (mainly international NGOs) left the country. More cases are being reported in the Equatorial Region. AMREF and WHO are planning surveillance activities.
4. The HAT diagnosis is still a problem and the participants felt that capacities ought to be strengthened in this area.
5. There is a need for training on disease mapping, which is very important to plan control programmes.
6. Funding both research and control is a challenge.
7. Staff turnover at the Ministry of Health being high, more staff needs to be trained to replace those who left the HAT programme.
8. Most of the areas reporting HAT are inaccessible, making it difficult to reach patients.
9. Some of the suggested solutions included:

a. Organising refresher courses for working staff including medical doctors
b. Boosting motivation
c. Organising active screening of populations at risk
d. Establishment of partnerships for both research and control
e. Reactivation of tse-tse control in order to break the transmission circle

Other problems needing solutions were mentioned:

Problem	Suggested solution
Inadequate staff	Short-term training for middle level staff
Lack of funds – inadequate government support	Develop grant proposals
Strategy for HAT control	Develop strategy and include vector
HAT managed by clinical officers	Build capacity; at least 2 medics at post-graduate level per year?
HAT centres are found in hospitals where medics are stationed, however the latter are not interested; lack of sensitization	Undertake education and awareness campaigns to sensitize medics

In conclusion, the course was very well received. It was noted that the country lacks the critical manpower in tse-tse and trypanosomiasis (T&T) research to support control programmes.

Treatment failures have been widely reported but no research has yet been done to identify the causes. A new disease (nodding disease) with symptoms similar to sleeping sickness has been identified, but it does not respond to treatment with available drugs.

The country is currently in the process of initiating tse-tse work. Opportunities for collaboration were identified as well as critical areas for capacity building for which TRC was requested to assist, especially in the short skill building courses and postgraduate level research and training. These activities are to be supported by both DNDi and Yale University.

2. HAT Platform Steering Committee meeting in Juba, South Sudan

The second 2012 HAT Platform Steering Committee meeting was held in Juba, South Sudan, in September. The first meeting was held in Ndjamena, Chad, in May at the Star Hotel on 14-15 September 2012.

The participating countries included South Sudan, DRC, CAR and Uganda. Angola, Sudan and Chad were notably absent. The mood at the meeting was significantly dampened by the authorities' refusal to let a representative from Chad (Peka Malaye) enter the country at Juba international airport, even tough the necessary paperwork had been done. Dr Richard Laku, the host/organizer, promised to engage the Ministry officials on this matter. Joseph Ndungu and Olaf Valverde from FIND and DNDi, respectively, were also present, as well as Grace Murilla from EANETT.

The Minister of Health of South Sudan officially opened the meeting. The agenda included reading and adoption of the previous minutes, country presentations, presentations from partners, and the discussions on the way forward.

The minutes of the previous meeting were adopted and the presentations yielded intense discussions. After two days of deliberations, the following recommendations/resolutions were made:

1. The minutes of the meeting held in Ndjamena in May 2012 were adopted with minimum amendments and updates.

2. DRC is the preferred country to register the HAT Platform as a legal entity, since it has the most number of HAT cases.

3. Procedures and checklists for the registration process should be available by the next meeting.

4. The next newsletter will provide space for news from each country.

5. Need for GCP/GLP training for all member countries, especially monitors in CAR.

6. Uganda: COCTU structure, function and new developments (inauguration of the technical committee) to be published in the next newsletter.

7. South Sudan: need for short skills training for middle management and case management training for all healthcare workers.

8. National training courses should have an international component involving neighbouring countries, e.g. Uganda and South Sudan, DRC and Republic of Congo, CAR and Chad.

9. Organize ethics training for SOP implementation for French- and English-speaking countries.

10. Support the development of research guidelines in CAR, South Sudan and Chad.

11. Data from country presentations during this meeting should be considered preliminary.

12. Formalise a system to support young scientists in training for MSc. or PhD, focusing on a way to motivate and retain people already working in the system.

13. Scientific conference to be held in June in Nairobi and each country to send 4 participants (DRC could send more, funding permitting). Explore possibility of smaller sessions for heads of ethics committees of each country or other subjects of interest.

14. Deadline for submission of the abstracts for the scientific conference (Nairobi) extended to end of Feb 2013.

15. Encourage member countries to use CTC and mini-columns (DRC produce mini-columns at INRB).

16. Partners (DNDi, FIND and EANETT) pledge their continued support for HAT Platform activities to achieve the objectives.

17. Next HAT Platform Steering Committee meeting will be held jointly with the Scientific Conference in Nairobi in June 2013, and the second 2013 meeting will be held during the ISCRTC conference.

18. Meeting organization and visa arrangements must be improved to avoid incidents such as the one that happened to one of our members who was refused entry into the country.

The meeting was closed on 15th September 2012, having run without any major problems.

Dr Andrew Edielu

3. NECT pharmacovigilance training workshop for clinicians from Uganda and South Sudan

Arua, Uganda, 5-9 August 2012 by Dr. Charles Wamboga, Manager of the National Sleeping Sickness Control Programme

Introduction

A training workshop on the pharmacovigilance of NECT (Nifurtimox Eflornithine Combination Therapy) for clinicians from South Sudan and Uganda was held from 5 to 9 August

2012, at Hotel Delambience in the Arua district, located in the North Western part of Uganda. It was attended by 15 participants from Adjumani Hospital (3), Moyo Hospital (3), Yumbe Hospital (3) and Omugo Health Centre IV (3), and from treatment centres in South Sudan (3).

Background

In Uganda, NECT was adopted in February 2010 as first-line treatment for late-stage gambiense sleeping sickness in all treatment centres and hospitals in the gambiense focus, following recommendations by the World Health Organisation (WHO).

However, NECT being a new form of therapy, the WHO requires further pharmacovigilance data before it could be validated for the National Control Programme. The National Control Programme could not provide this information on time, mainly because previously trained staff had either been transferred to other healthcare facilities or assigned to different roles/responsibilities.

Therefore, the workshop focused on training more staff in NECT pharmacovigilance, introducing WHO-designed standard data capture forms, and teaching clinicians how to recognise, manage and report Adverse Events (AEs) and Serious Adverse Events (SAEs).

Objectives

Strengthen the capacities of healthcare personnel (clinicians) by:

a. Introducing the NECT kit and its use.

b. Teaching how to detect, manage and report adverse events and serious adverse events related to the use of NECT.

c. Teaching how to produce accurate and timely reports on NECT pharmacovigilance using standard forms.

Methodology

The training course was given over 3 days in Arua (2 days for theory and one day for practical sessions), and included lectures, brainstorming sessions and practical sessions.

Patient forms/charts from the Omugo treatment centre were used during the practical sessions. Each participant used these patient charts to summarise adverse event information before presenting them to the whole group.

Participants discussed with enthusiasm each of the cases presented, and reported that they had learnt a lot.

On the first day, a preliminary test was administered to the participants to determine their level of knowledge on the use and pharmacovigilance of NECT.

The questionnaire administered to the participants after each presentation on AEs showed a general improvement of their knowledge on NECT.

Achievements at the end of the training course

- The participants were up to date on NECT kits.
- They were able to recognise and manage the common Adverse Events (AEs) and Serious Adverse Events (SAEs) associated with NECT.
- They promised to train other medical personnel on the use of NECT, as well as adverse event recognition, management and reporting.
- They pledged to provide timely NECT pharmacovigilance reports.
- After the practical sessions using patient data from Omugo health centre IV, they were very enthusiastic and declared having learnt a lot.
- New participants were brought on board in case management with NECT
- Participants were willing to provide timely data on NECT pharmacovigilance to the programme.

Regrets

Two participants from South Sudan were involved in a road traffic accident on their way to Uganda and missed the training.

Recommendations

Further training courses at the regional level were recommended to share experiences and enhance collaboration.

4. Scientific day on HAT in Kinshasa

A scientific day was held on Thursday 6 December 2012 in the WHO meeting room in Kinshasa, DRC, under the high patronage of the Minister of Public Health of DRC, with funding from FIND. Some fifty participants represented the following HAT Platform member countries:

Angola, Republic of Congo, Central African Republic, and of course DRC, the host country.

The key event was the launching of the first rapid diagnostic test for HAT.

The day started with the national anthem at 9:12. The two highlights of the day included the speeches by the Minister of Public Health, the Director of the national HAT control program and the representatives of FIND, Eiken Chemical, the WHO, and Standard Diagnostics, and the presentation of the study results and discussions.

a. Speech by the Director *ad interim* of the national HAT control programme of DRC

The first speaker was the Director of the national HAT control programme. He started by welcoming those present and highlighted the importance of the scientific day marking the launch of the first rapid diagnostic test (RDT), which is a revolution in HAT control. He asked for the support of the Minister of Public Health to bring this project to fruition. He concluded his address by thanking the various partners of the programme.

b. Speech by the representative of FIND (Joseph Ndungu)

The representative of FIND said that the development of the RDT was made possible by the collaboration between several partners.

He also said that the current test is the fastest and that efforts will be made to generalise its use in all healthcare centres (CS) and mobile units (UM).
Other diagnostic tools will be made available to the national control programmes, such as fluorescence microscopy, LAMP test, and CSF biomarkers. Once validated, they will help improve HAT control.
He ended his speech by thanking the Congolese government for facilitating the work in this vast country.

c. Speech by the representative of Eiken Chemical (Shinichi Kojiya)
He thanked the Minister of Public Health, the WHO and FIND for organising this day. Eiken Chemical is involved in the molecular diagnosis of TB and HAT. He said that the LAMP test is the company's first commercial product for sleeping sickness and that it will contribute to solve this public health concern.

d. Speech by the representative of Standard Diagnostics (Byung Ki Cho)
He thanked all the participants and particularly the Minister of Public Health. Standard Diagnostics has developed other RDTs, e.g. for syphilis, HIV, malaria, and leishmaniasis, the latter being very competitively priced. Standard Diagnostics is represented in 120 countries and has 140 distributors worldwide.

e. Speech by the representative of the WHO (Bazira Leodegal)
He started by saying that the WHO was very honoured to participate in the scientific day on the RDT for HAT. He praised the collaboration between FIND, the biomedical industry and the DRC on the development of the most rapid diagnostic test that will contribute to eliminate HAT.

f. Speech by the Minister of Public Health (Kabange Numbi)
He started by welcoming the participants and said that this day was justified by the fact that DRC is the most affected country with 75% of all reported cases in Africa. He concluded by assuring the audience that the government of DRC is supporting all the clinical studies conducted in the country. He then officially announced the beginning of the scientific day on the launch of the first rapid diagnostic test for HAT.
After the coffee break, the sessions resumed with the presentations of the study results in Angola, DRC and CAR:

- 14,818 people participated in the study on the RDT;
- The sensitivity of the RDT (89.3%) is identical to that of the CATT test with 1/8 dilution (89.3%);
- The specificity of the RDT (95%) is similar to that of the CATT test on whole blood (95%), but slightly lower than that of the CATT test with 1/8 dilution (98.9%);
- A decision was taken to optimise the final product before its launch on the market, to improve its sensitivity without changing its specificity.

After the various interventions, the discussions focused mainly on trypano-tolerance, and the sensitivity and specificity of the RDT compared to the CATT test.
A presentation on HAT confirmation by fluorescence microscopy

outlined the following advantages:

- Very sensitive tool, faster
- Lower energy consumption (solar powered battery)
- Shorter staining time: 3 minutes with acridine orange veterinary surgeons. 45 minutes with Giemsa)
- Higher sensitivity with acridine orange than with Giemsa, but this sensitivity remains lower than that of CTC and mAECT
- Specificity identical to that of the other methods

The HAT epidemiological situation in the Republic of Congo was presented. The number of cases reported in 2012 dropped (24 new cases), but this reduction is due to the poor coverage of the endemic foci.

HAT control is helped by the fact that this disease has been recognised as a public health concern, and by the creation of the national health policy (PNDS).

Several challenges were mentioned, such as insufficient funding and human resources, low population turnout at screening events, and the inaccessibility of some of the foci.

After lunch, presentations were made on the on-going studies on:

- fexinidazole (DRC, CAR), and
- LAMP test

The day ended at 16h00.

PRESS RELEASE FIND/ SD

The first rapid test to screen for sleeping sickness is launched 6 December 2012, Kinshasa, Democratic Republic of the Congo

FIND and Standard Diagnostics, Inc. of the Republic of Korea, announced today the launch of the first rapid test to screen for sleeping sickness – a deadly parasitic disease also known as human African trypanosomiasis (HAT). The announcement was made at a workshop hosted by the Ministry of Health in Kinshasa, Democratic Republic of the Congo.

The new test, named SD BIOLINE HAT, has been developed using parasite antigens provided by the Institute of Tropical Medicine in Belgium under a materials transfer agreement with FIND. The test has the potential to dramatically change the way the disease is managed by bringing cheap, easy and rapid testing to HAT patients who often live in remote, rural settings with minimal health infrastructure. Clinical trials have recently been completed in Angola, the Democratic Republic of the Congo and the Central African Republic, where data obtained from more than 14,000 individuals confirmed the excellent performance of the test.

"This important milestone brings us one step closer to elimination of sleeping sickness, as the new rapid test is expected to significantly facilitate diagnosis and therefore speed up identification of patients suffering from this crippling disease", said Philippe Jacon, Chief Executive Officer of FIND.

Sleeping sickness is a deadly, neglected tropical disease transmitted by the bite of the tse-tse fly and affects impoverished rural communities in sub-Saharan Africa. About 70 million people in 36 countries are thought to be at risk. There are no clinical signs that are characteristic of the disease, which makes it difficult to diagnose. If infected people are not treated, they eventually die. Diagnosis of sleeping sickness is done by demonstrating parasites in either blood, cerebrospinal fluid (CSF) or lymph node aspirates using microscopy, which is not easy to perform in screening programmes.

Development of a rapid test for trypanosomiasis that detects antibodies to infection, such as the one launched today, has been hindered by the ability of the parasite to keep changing its surface antigenic coat, which allows it to evade the host's defence mechanisms.

"We urgently need simple and cheap screening tools to detect sleeping sickness, especially in our country, which has the largest proportion of all reported cases in Africa. More practical field-applicable tests that can be used in remote settings will greatly enhance our surveillance and control activities. We are very pleased about the news of this important achievement." commented Dr Félix KabangeNumbiMukwampa, Minister of Health of the Democratic Republic of the Congo.

The new test is an immunochromatographic rapid test that detects antibodies against Trypanosomabruceigambiense, the parasite responsible for more than 90% of sleeping sickness cases. This cheap and very simple-to-use test can be performed by health workers with minimal training, using fresh blood from a finger prick, and the results are obtained after only 15 minutes.

The test is unlike any screening tools in use today, as it is stored at ambient temperature and does not require specialized equipment or electricity, meaning that it can thus be used in very remote settings where most of the infected people are found. This will also be the first ever test for sleeping sickness to be CE marked and to be manufactured by an industrial company following ISO 13485:2003 quality requirements.

"We are committed to continuously develop new rapid tests, always ensuring that neglected tropical diseases such as HAT are amongst our highest priorities. Today, SD is very proud to announce the launch of the first rapid diagnostic test for HAT, which we believe will revolutionize control of the disease. Even though this is a great achievement for us, we look at it as a starting point, as more tests

for HAT and for other neglected tropical diseases are and will continue to be in our pipeline" , said Dr. Byung-Ki Cho, Chief Executive Officer of Standard Diagnostics, Inc.

Development of the rapid test for sleeping sickness has been a joint effort of FIND and numerous partners, among them the Institute of Tropical Medicine (Belgium), MicroCoatBiotechnologie GmbH (Germany), the International Livestock Research Institute (Kenya), the Institute of Tropical Neurology (France), Médecins sans Frontières (Spain), the National HAT Control Programme of the DRC (PNLTHA, Democratic Republic of the Congo), the Centrafrican Institute of Agronomical Research (Central African Republic), the World Health Organization and Standard Diagnostics, Inc. (Republic of Korea). This work is supported mainly by the Bill and Melinda Gates Foundation and the Department for International Development (DFID) of the United Kingdom.

About human African trypanosomiasis, HAT

Sleeping sickness is a deadly, neglected tropical disease that affects impoverished rural communities in sub-Saharan Africa. The clinical signs observed are not characteristic of the disease, which makes it difficult to diagnose, and if infected people are not treated, they eventually die. It progresses from an early or stage 1 disease to a devastating 2nd or late stage form associated with damage to the central nervous system.

During this 2nd stage, patients display a range of psychotic signs that lead to stigmatization by their families and communities. The few drugs that are used to treat patients in this stage are administered over prolonged periods of hospitalization, and are associated with potentially fatal adverse reactions.

About FIND
The Foundation for Innovative New Diagnostics (FIND) is a not-for-profit international organization dedicated to supporting the development of affordable, easy-to-use, cutting edge diagnostic tests that save lives in the poorest areas of the world. From proof of concept to putting new tests into practice, the organization works with multiple and diverse groups, such as academia, industry, donors, partners in the field, Ministries of Health and the World Health Organization. In addition to HAT, FIND also has strong programmes in TB, malaria, leishmaniasis and Chagas disease. Launched in 2003, FIND is ISO certified and financed by both the private and public sectors, including the Bill & Melinda Gates Foundation, the Governments of Germany and of the Netherlands, European Union, UNITAID, UK Department for International Development (DFID), National Institutes of Health (USA), UBS Optimus Foundation, among others.

About Standard Diagnostics
Standard Diagnostics (SD) has developed about 100 different products, including tests for malaria, HIV, dengue fever and syphilis. Since its inception in February 1999, SD has been renowned worldwide for the excellent quality of its rapid point-of-care tests.

This quality relies on in-house developed recombinant antigens and monoclonal antibodies that are the key raw materials used in manufacturing the tests. Through international organizations such as WHO, UNICEF, government procurement and overseas distributors, SD products are supplied to more than 120 countries around the world. Rapid tests for malaria and dengue fever account for 60% of worldwide sales. With a turnover of over 100 million US dollars, SD has evolved into a global pharmaceutical manufacturing company specialized in in vitro diagnostics. As a result of the increasing market demand for SD's new products, additional manufacturing plants are being established in Nigeria and Ethiopia.

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e) International Congress of Tropical Medicine and Malaria (ICTMM)

INTRODUCTION
International forums are particular venues for giving and receiving appointments; then, our HAT platform took this opportunity with the support of DNDi, which financed the participation of two members and a third participant has been funded by the ITM Antwerp.

This 18th Congress of the ICTMM took place from 23 to 27 September 2012 in Rio de Janeiro at the same time as the 48th Congress of the Brazilian society of tropical medicine.

PROGRESS
A total of 1100 participants responded to this forum in the 'ROYAL TULIP' of Rio de Janeiro hotel in Brazil. 63 round tables were organized, 52 conferences and 11 plenary sessions with 405 stakeholders, this scientific program included also 197 abstracts selected for oral presentations divided into 27 parallel sessions.

1620 abstracts were presented in electronic poster format.

The central theme of this Congress has been "neglected tropical diseases: a new challenge for the 21th Century " Although malaria, AmericanTrypanosomiasis (the Chagas disease), leishmaniasis have occupied a prominent place at this forum, sleeping sickness (HAT) was aslo on the agenda.
During the session on the main actions of the World Health Organization (WHO) for the control of neglected diseases chaired by Professor Pedro Tauil; presented by Jorge Alvar of WHO; Sleeping sickness has been one of the examples of public involvement of the WHO with both private partners to find diagnostic and treatment tools.

The second session where sleeping sickness has been discussed was organized by MSF and funding aspects of research and development in neglected diseases were presented by Michelle Childs (from Switzerland) and Julien Potet (from France). Here, the advocacy showed that we need to make available more resources for research in sleeping sickness and leishmaniasis.

A round table on the epidemiology, diagnosis and control of the sleeping sickness chaired by Dr. François Chappuis (University of Geneva) and Stijn Deborggraeve (Belgium) has made some updates on the three points mentioned above. Professor Phillip Buscher (Belgium) presented the current situation of sleeping sickness and the prospects for the near future. Dr. François Chappuis on basis of the MSF experience presented the current approaches to diagnosis and treatment.

Professor Dieudonné Mumba has presented a new approach of post-treatment follow-up that reduces the duration to 12 months and selects already at 6 months likely relapse (to treatment).
In connection with the progress of the new chemical entities in clinical development for the treatment of the neglected diseases, there were presentations on the Chagas disease, leishmaniasis and sleeping sickness.

SCYX-7158, which is a molecule of the oxaborole group was introduced by Antoine Tarral (DNDi). This molecule is in phase one clinical trials for the treatment of the sleeping sickness, stage two (advanced stage).

The last session on sleeping sickness has addressed aspects of research on: antigenic variation of the parasite, the possibility of finding a vaccine (the model DNA Vaccine investigational Immunotherapeutic efficacy outcome). The evaluation of trypanocidaldiamines, and ferrocenyldiamines activity against Trypanosomabr genes was presented.

Presentation of estimation (research) of therapeutic oral doses of Fexinidazole, food effect on the pharmacokinetics of a single dose in healthy volunteers of sub-Saharan African origin was made by Antoine. Safety and pharmacokinetic study of Fexinidazole multiple doses supplying fat in healthy volunteers of sub-Saharan African origin.

In the specific context of our HAT platform, we distributed our Newsletters number 8, 9,10 and 11 (a total of roughly 500 copies). We presented a poster showing our achievements at the stand of DNDi. We took part of the panel of experts in the discussion organized by MSF and other parallel meetings of sharing experience. For more details see the site http://ictmm2012


Salão
Quartzo A
PLATAFORMA
HAT
NEWSLETTER

4 UPDATE ON ON-GOING RESEARCH

a. Rapid Diagnostic Test (FIND / Joseph)

FIND and Standard Diagnostics (Republic of Korea) completed the development of a lateral flow rapid test for T.b. gambiense HAT that is cheap and easy to use to screen populations (Figure 1). The tests are individually packaged and are stable at 40°C for at least 2 years; they are performed on fresh blood obtained from a finger prick, and no instrument or electricity is required.

The rapid test detects host antibodies to T.b. gambiense in populations that are at risk, or in individuals with suspected HAT. If the RDT is positive, routine parasitology tests are performed to confirm the HAT diagnosis. This new test provides an alternative to the card agglutination test for trypanosomiasis (CATT), the primary screening tool used by control programmes in areas where T.b. gambiense HAT is endemic.

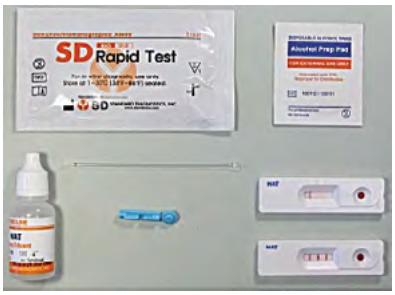


Figure 1: Photo of the new rapid test and its accessories, developed by FIND and Standard Diagnostics. Procedure: place 20 µl fresh blood from a finger prick into the well of the test, and add 4 drops of diluent. The results can be read after 15 minutes. A positive sample produces 2 or 3 red bands, and a negative test produces one band.

Earlier in 2012, clinical trials were completed in Angola, DRC and the Central African Republic, where data obtained from more than 14,000 individuals confirmed the test's excellent performance (Figures 2 to 5).

Figure 2. Collecting finger-prick blood from participants in the Central African Republic during development studies on the new rapid test for HAT

Figure 3

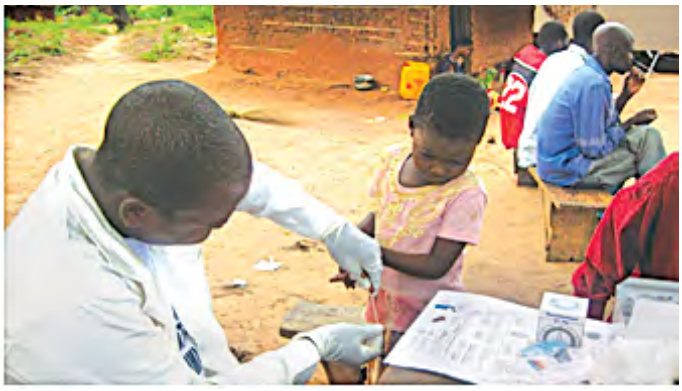


Figure 4

Figures 3 to 5 Collecting finger-prick blood from participants in the DRC during development studies on the new rapid test for HAT

Based on these findings, the design of the product was locked and the test registered (Korean FDA and CE-marking). This very first rapid test for HAT was officially launched at a workshop hosted by the Minister of Public Health in Kinshasa, DRC, on 6 December 2012 (add some pictures).

Studies to further evaluate the rapid test will be initiated in early 2013 at multiple sites in several endemic countries. The objectives of these studies will be to confirm the accuracy of the test, and

determine the costs associated with its use, the cost-effectiveness of diagnostic strategies using the rapid test, and also its ease of use, compared to other methods.
In parallel, FIND and its partners will continue to work on the development of a second-generation rapid test based on recombinant antigens.
The current first-generation test uses native antigens generated from pathogenic trypanosomes, and is not suitable for T.b. rhodesiense HAT. Efforts are therefore being made to develop a second generation rapid test using recombinant antigens, which would be easier and cheaper to manufacture.

b. LAMP (FIND/ Joseph)

Evaluation of the HAT LAMP kit progresses smoothly in the DRC and Uganda

The clinical evaluation of a highly sensitive and specific molecular test for HAT diagnosis is progressing smoothly in Uganda and the Democratic Republic of the Congo (DRC). The test detects parasite DNA, using the loop-mediated isothermal amplification (LAMP) technology developed by Eiken Chemical, Japan.

The test is carried out at a constant temperature, meaning that it can be performed with minimal equipment (Figure 1) by basic laboratories, such as those commonly seen in HAT endemic countries. Furthermore, positive samples are identified visually by colour change or fluorescence (Figure 2). LAMP can be performed by staff with minimal experience in molecular biology, and could also be useful to confirm cure in treatment follow-up.

Figure 1: LoopampTM LF-160 incubator used to perform the HAT LAMP reaction. After extraction of DNA, the LAMP reaction is carried out in the reaction block (A), which is calibrated to maintain a constant temperature of 65°C, and to stop the reaction after 40 minutes. Results are visualized under LED light (B).

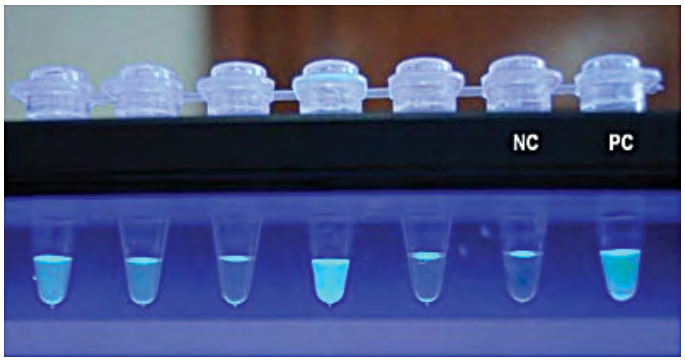


Figure 2: Positive samples emit green fluorescence. PC: positive control, NC: negative control (Photo courtesy of Dr. Enock Matovu)

The HAT LAMP kit has been developed jointly by FIND and Eiken Chemical in a partnership that started in 2008. The LAMP test reagents are dried on the inside part of the cap of the reaction tube, which can be stored at room temperature for up to 12 months. Prototype LAMP tests for HAT developed by Eiken Chemical were evaluated using blood samples from experimentally infected rodents at Makerere University in Uganda (Figure 3).
This work included the optimization of various methods of sample collection.

Figure 3. Optimization of sample preparation for LAMP at Makerere University

The LAMP test for HAT can be performed on blood samples freshly collected, and dried on microscopy slides or ordinary filter papers. The sensitivity of the test is greatly enhanced by initially lysing samples with SDS, and by using the buffy coat in the reaction. The LAMP kit for HAT was launched at the ISCTRC conference in Bamako, Mali, in September 2011.

Further optimization of sample preparation and clinical evaluation of the kit at multiple sites in the DRC and Uganda is at an advanced stage (Figure 4).

Figure 4. A technician displays the results of the LAMP test for HAT at Dipumba hospital in the on-going evaluation studies

At some of the sites in the DRC, the energy required for the entire process of preparing samples and performing the LAMP test is provided by solar panels (Figures 5 to 8).

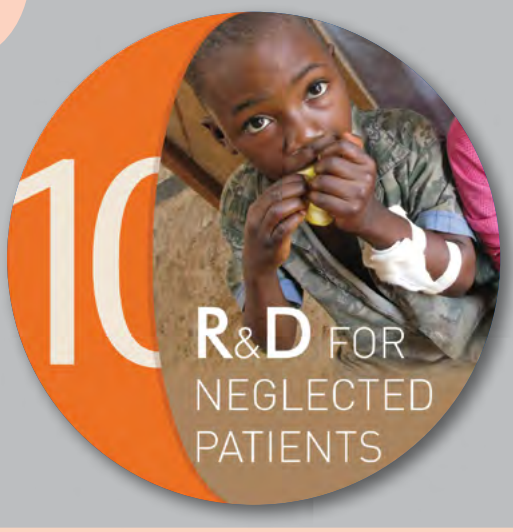
Figure 5. Performing the LAMP test for HAT at Katanda hospital in the East Kasaï province, DRC, during on-going evaluation studies. All equipment for preparing samples and performing the LAMP reaction are solar powered.

Figure 6. Solar panels installed on the roof of Bangumi hospital in North Bandundu province of the DRC. The power generated is used to operate the equipment necessary to prepare the samples in the on-going evaluation of the LAMP kit for HAT

Figure 7. The solar assembly at Bangumi hospital in North Bandundu province of the DRC.

Figure 8. A technician at Bangumi hospital applies blood on a filter paper from a person suspected of having HAT, during the on-going evaluation of LAMP for HAT. After the sample dries, it is put in a plastic pouch and sent by motorcycle to the Bandundu LAMP centre about 35 km away, where the test is performed.

So far, we can confirm that the test is easy to perform in a basic laboratory, by staff with no training in molecular biology, and its performance may be superior to that of any other HAT test in clinical use.



In 2013, DNDi marks 10 years of R&D and concrete achievements

5 LISTENING TO HAT PATIENTS AND HEALTH WORKERS

You read the accounts of patients from East Kasaï in Newsletter n°10, and from South Sudan in Newsletter n°11, and we are now giving you the stories of two patients from the Bandundu Province:

We met Monique on 4 December 2012 in the village of BOKO, which lies 2 hours upstream from Bandundu on the river Kwango.
This 13-year old girl is the third of a family of five children. Her mother was diagnosed and treated for sleeping sickness when Monique was two. In July 2003, when Monique was 4 years old, her father brought her to the Ngila healthcare centre because she was crying all the time but she had no fever and showed no other signs. A lumbar puncture confirmed that Monique was suffering from late-stage sleeping sickness.

She was treated for one month with Arsobal (nine injections divided into three series of three injections at one week interval).
When the mobile team came to her village for active HAT screening, Monique came with her father to be examined like everybody else. We realised then that she had not been checked since her treatment. She was clinically in good health, and her father confirmed that she had been well since her treatment.
Luckily, Monique responded well to this toxic treatment, and her story is typical as many patients do not to come to post-treatment follow-up for fear of the many lumbar punctures it involves.

Angèle, subsistence farmer, village of Musenge, Masi Manimba, Democratic Republic of the Congo

Angèle is barely 20 years old. She is married and has three children. She and her husband work in the fields as subsistence farmers to collect enough food for their family. In July of this year, the mobile unit screening for sleeping sickness visited her village. Angèle was diagnosed with late-stage sleeping sickness. As her husband was ill with measles, Angèle came to the hospital with her mother. Even though she was ill, she had to walk 60 km in two days to get to the hospital. There, she was told she was pregnant with her fourth child, and that she should come back in two months time, i.e. in the second quarter of her pregnancy, to receive the NECT combination. 'I had had terrible headaches and chills every night for 6 months' she said. 'When the mobile team came in my village, I finally discovered what the problem was. Many people have sleeping sickness in my village. My grandmother had it, and my father as well. Both were treated and are now cured', she added.

When Angèle was four months pregnant, she set off again for the two-day journey to the referral hospital in Masi Manimba. She was given the NECT treatment and felt better very quickly. 'I have almost reached the end of my treatment and I feel an enormous difference. My headaches have almost gone and I no longer have chills during the night', she said. Angèle will soon go back to her family, in a village fortunately covered by a mobile unit doing active screening for sleeping sickness. Like Angèle, patients who live far away from referral hospitals typically do not seek treatment unless a clear diagnosis has been made in their village.

Dr Florent Mbo Kuikumbi, provincial coordinating physician of North Bandundu for the National Human African Trypanosomiasis Control Programme (DRC)

Sleeping sickness has several facets. We have to cover all of the endemic areas with surveillance efforts, otherwise there will always be pockets than can later lead to epidemics. Today, for example, in Bandundu Province in the DRC, we can only say we are controlling the disease, not eliminating it. We have to be able to cover all of the disease pockets and follow them for some time.

We can treat the patients at the level of the community, but the vector – the tse tse fly – that transmits the parasites from an infected person to a healthy one is still out there and will continue to transmit the disease as long as people are carrying the parasite. We have noticed in certain areas where we have treated all the patients we found, the disease re-emerges within a year or two. We have to cover all the pockets with screening – active and passive screening. We have to diagnose and treat all those with the disease.

Today we are hearing alarm bells as the Belgian Technical Cooperation project – which currently finances up to 75% of the control programme – is coming to a close in June of the 2013. If the majority of the activities of the mobile teams and the programme stop, we are looking at a situation that we have already seen in the past: surveillance decreases, and the disease re-emerges even to epidemic proportions. You go to a village and people everywhere are sick, entire villages in a slumber. That is the risk.

Here in Bandundu Province, we will clearly go beyond the entire number of reported cases for the year 2011, and this before the close of year. In 2011 over the entire year, we recorded 1437 new cases only in the northern section of the province, but in the first semester 2012 we are already at 1025 cases so we may see double the amount of cases by the end of the year. So if, in the month of June 2013, the control programme activities cease due to lack of financing, there will be zones that are not visited, vector control will cease, active screening will cease.

As the disease touches the poorest of the poor, the victims do not and can not come to health centres on their own. We see them in the villages, and the mobile teams are their only means to accessing healthcare. By the time they do come to the health centres, the disease is often already at the advanced stage. This is a real problem. Advocacy must continue so that we can ensure a transition period in which we engage with new partners to avoid reverting to situations of stark re-emergence of the disease.

We have already begun to integrate the HAT programme activities into the health system more 'horizontally', but much more needs to be done for before we get there and cover all the needs. Better diagnostics, an oral treatment for both stages of the disease, continued surveillance, and sustainable financing are all part of what it will take to truly tackle the disease. We are clearly not at the brink of elimination.

6 RECENT HAT PUBLICATIONS

1. Checchi F, Cox AP, Chappuis F, Priotto G, Chandramohan D, Haydon DT. Prevalence and under-detection of gambiense human African trypanosomiasis during mass screening sessions in Uganda and Sudan. Parasit Vectors 2012 Aug 7;5(1):157.

2. Priotto G, Chappuis F, Bastard M, Flevaud L, Etard JF. Early prediction of treatment efficacy in second-stage gambiense human African trypanosomiasis. PLoS NTD 2012; 6(6): e1656.

3. Franco JR, Simarro PP, Diarra A, Ruiz Postigo JA, Samo M et Jannin J. Monitoring the use of Nifurtimox eflornithine combination therapy (NECT) in the treatment of second stage gambiense human African trypanosomiasis. Res Rep Trop Med 2012:3 (1):93-101.

4. Alirol E, Schrumpf D, Amici Heradi J, Riedel A, de Patoul C, Quere M, et al. Nifurtimox-Eflornithine Combination Therapy for Second-Stage Gambiense Human African Trypanosomiasis: Medecins Sans Frontieres Experience in the Democratic Republic of the Congo. Clin Infect Dis. 2012 Nov 9. PubMed PMID: 23074318.

5. Schmid C, Kuemmerle A, Blum J, Ghabri S, Kande V, Mutombo M, et al. In-hospital safety in field conditions of nifurtimox eflornithine combination therapy (NECT) for T. b. gambiense sleeping sickness. PLoS Negl Trop Dis. 2012;6(11):e1920.

6. Simarro PP, Cecchi G, Franco JR, Paone M, Diarra A, Ruiz-Postigo JA, et al. Estimating and Mapping the Population at Risk of Sleeping Sickness. PLoS Negl Trop Dis. 2012; 6(10): e1859.

7. Natalia Tiberti, Alexandre Hainard, Veerle Lejon, Bertrand Courtioux, Enock Matovu et al. Cerebrospinal Fluid Neopterin as Marker of the Meningo-Encephalitic Stage of Trypanosoma brucei gambiense Sleeping Sickness. PLoS One 2012 7(7): e40909. doi:10.1371/journal.pone.0040909

8. Kuepfer I, Schmid C, Allan M, Edielu A, Haary EP, et al. (2012) Safety and Efficacy of the 10-Day Melarsoprol Schedule for the Treatment of Second Stage Rhodesiense Sleeping Sickness. PLoS Negl Trop Dis 6(8): e1695. doi:10.1371/journal.pntd.0001695

9. Bouteille B, Buguet A. The detection and treatment of human African trypanosomiasis. Research and Reports in Tropical Medicine 2012 June (3) :35 – 45 DOI: http://dx.doi.org/10.2147/RRTM.S24751

10. Jamonneau V, Ilboudo H, Kabore´ J, Kaba D, Koffi M, et al. Untreated Human Infections by Trypanosoma brucei gambiense are not 100% Fatal. PLoS Negl Trop Dis 20126(6): e1691. doi:10.1371/journal.pntd.0001691

11. Ruiz-Postigo JA, Franco JR, Lado M, Simarro PP. Human African Trypanosomiasis in South Sudan: How Can We Prevent a New Epidemic?. PLoS Negl Trop Dis 20126(5): e1541. doi:10.1371/journal.pntd.0001541.

12. Tweats D, Bourdin Trunz B and Torreele E. Genotoxicity profile of fexinidazole—a drug candidate in clinical development for human African trypanomiasis (sleeping sickness). doi:10.1093/mutage/ges015

13. Wolburg H, Mogk S, Acker S, Frey C, Meinert M, et al. Late Stage Infection in Sleeping Sickness. PLoS ONE 2012 7(3): e34304. doi:10.1371/journal.pone.0034304

7 SCIENTIFIC EVENTS IN 2013

- International Meeting on Emerging Diseases and Surveillance http://imed.isid.org/ VIENNA, AUSTRIA 15-18 FEBRUARY 2013

- Third Annual Encouraging Development of Therapeutics for Neglected Diseases healthtech.com/ngl PHILADELPHIA, PA (USA) 4-5 APRIL 2013

- GLOBAL HEALTH: INNOVATION | IMPLEMENTATION | IMPACT http://2013globalhealth.org/ WASHINGTON D.C. 14-16 MARCH 2013

- 23rd European Congress of Clinical Microbiology and Infectious Diseases http://www.congrex.ch/eccmid2013.html BERLIN, GERMANY, 27- 30 APRIL 2013

- 31st Annual Meeting of the European Society for Paediatric Infectious Diseases http://www.kenes.com/espid2013/ MILAN, ITALY, 28 MAY-01 JUNE 2013

- European Congress on Tropical Medicine and International Health http://www.ectmih2013.dk/ COPENHAGEN, DENMARK 10-13 SEPTEMBER 2013

- ASTMH http://www.astmh.org//home.htm WASHINGTON US 13-17 NOVEMBER 2013

- 8th World Congress on Pediatric Infectious Diseases in Cape Town, South Africa http://www2.kenes.com/wspid/Pages/home.aspx 19-22 NOVEMBER 2013