

# HAT Platform



## NEWSLETTER N° 10, December, 2011



©Photo W. MUTOMBO

**Training in clinical research and Good Clinical Practice participants;**  
centre Nganda Kinshasa DRC, November 2011

# Contents

1. Editorial .....	<b>P.2</b>	5. Training in clinical research and Good Clinical Practice .....	<b>P.11</b>
2. Report of the regional HATPlatform steering committee meeting, held in Bamako on 11 September 2011 .....	<b>P.3</b>	6. Update on on-going research .....	<b>P.12</b>
3. Salient points of the 31st Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) .....	<b>P.6</b>	7. Floor Given to patients and caregivers .....	<b>P.17</b>
4. 7th European Congress on Tropical Medicine & International Health in Barcelona .....	<b>P.8</b>	8. 2012 scientific meetings and websites of interest .....	<b>P. 19</b>
		9. Recent publications on HAT .....	<b>P. 20</b>



## Editorial

**T**oday, we are publishing our tenth newsletter of the HAT platform, which includes two releases per year. We have been present in major scientific forums which we present in this issue the main lines related to the objectives of our HAT platform.

Updates on current research in the field of diagnosis and treatment of the sleeping sickness are very encouraging, in this bulletin our partners show the main ones, supported with images. A novelty in this bulletin is to give a good place to the testimony of the main beneficiaries of our action, both patients and caregivers. Taking advantage of this time of year, the HAT platform coordination on behalf of all its members have the pleasure and the duty to wish you many good things for the coming Year including a good reading

## Report of the regional HAT Platform steering committee meeting, held in Bamako on 11 September 2011

The steering committee is responsible for the supervision of the HAT Platform operation, and meets at least twice a year. The first meeting this year was held in Bangui, and the second one was held on 11 September 2011, during the 31st Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) in Bamako, Mali.

All the endemic member states, with the exception of Chad, were represented, i.e. the Republic of Angola, the Central African Republic, the Democratic Republic of Congo, the Republic of Congo, the Islamic Republic of Sudan, the Republic of South Sudan, and the Republic of Uganda. Six of our traditional partners were also present at this meeting: DNDi, Suisse-TPH, FIND, CTB, EANETT and MSF.

Some of the topics addressed during the meeting are described below.

### a) Review of the HAT Platform activities over the past five years

The outcome of the training activities organised for researcher and ethics committees is positive. All scheduled training sessions were carried out as planned (except for one session for the ethics committee in Congo Brazzaville not carried out).

In terms of communication, the HAT Platform produced nine newsletters over this period, as well as numerous television and radio broadcasts, meetings, etc.



HATplatform Steering committee members, Bamako/Malie September 2011

©Photo W. MUTOMBO



Workshop steering committee members Bamako/Malie September 2011

©Photo W. MUTOMBO

### Analysis : Strong points / Weak points

STRONG POINTS	WEAK POINTS
<ul style="list-style-type: none"> <li>Regular financial support</li> <li>Training sessions carried out</li> <li>Support of field activities</li> <li>Conferences (scientific or steering committee)</li> <li>Newsletters</li> <li>Setting up/ reinforcing the countries' ethics committees</li> <li>Adoption and implementation of NECT</li> <li>Clinical research on new drugs</li> <li>Collaboration with FIND on improving the diagnosis</li> <li>Joint meeting with EANETT</li> </ul>	<ul style="list-style-type: none"> <li>Little use of trained monitors on a national or regional level</li> <li>Insufficient field visits</li> <li>Termination of the DB289 clinical trial</li> <li>Little or no use of regional experts</li> <li>Lack of interaction with other areas of HAT research (diagnosis, tsetse flies, socio-economic studies, etc.)</li> <li>Little collaboration during meetings with other key actors (OCEAC, etc...)</li> </ul>

## b) Proposed strategic plan for 2012-2014

The HAT Platform has been coming up to speed over its first five years of existence. It is now time to consolidate the sup-

ports and bring in innovations. Consequently, the following main lines of actions have been suggested for 2012-2014.

LINES OF ACTION	Comments
Strengthening the capacities of member states	<ul style="list-style-type: none"> <li>- Training plan with success indicators</li> <li>- Content of the module</li> <li>- Timetable (where, who, etc.)</li> <li>- Document update</li> <li>- Evaluation of the training impact</li> </ul>
Strengthening the capacities of local researchers	<ul style="list-style-type: none"> <li>- Confirm future study sites</li> <li>- Monitoring and use of local monitors</li> <li>- Participation to scientific congresses /conferences</li> <li>- Need to ensure funding for all mentioned activities</li> </ul>
Involvement in current and future studies	<p>Treatment:</p> <ul style="list-style-type: none"> <li>- Implementation of the fexinidazole study</li> <li>- Monitoring of NECT implementation + Pharmacovigilance</li> <li>- Possibility to include within the Platform low-endemic countries (e.g. Gabon, Guinea, Cameroon) as consultants, or for short periods as needed</li> </ul> <p>Diagnosis:</p> <ul style="list-style-type: none"> <li>- Tools to determine the disease stage and follow-up tools</li> <li>- List of initiatives and definition of the added value of each diagnostic tool</li> <li>- Promote the evaluation/validation of new diagnostic tools</li> </ul>
Advocacy and fundraising	<ul style="list-style-type: none"> <li>- Communication/advocacy</li> <li>- Email / teleconference exchanges</li> <li>- Newsletter circulation by email</li> <li>- Increase the use of DNDi website to promote Platform activities</li> <li>- Participation to various meetings</li> <li>- Steering committee</li> <li>- Scientific forum</li> <li>- Annual scientific meeting + EANETT</li> <li>- Organisation of working groups per specific subject</li> <li>- Fundraising</li> <li>- Individual fundraising plans (when, how much, etc...) for each project</li> <li>- Recruitment of fundraising specialists to target donors</li> </ul>

A specific work group has been created to finalise this strategic plan. The novelty is the inclusion of cross-sectoral thematic issues (e.g. role of the Platform in the compilation of clinical research documents, and coordination with the countries' regulatory authorities during research projects).

## c) Contribution of the HAT Platform to on-going studies.

The steering committee discussed the validation and approval process by the countries' ethics committees. The example of

fexinidazole will help strengthen the capacities and encourage exchanges between ethics committees.

A debate was launched on how to improve the fexinidazole study protocol. The question was whether the adjunct treatments are to be given systematically, or only once the diagnosis is confirmed, prior to the inclusion of the patient in the study. Each patient will undergo a 'wash-out period' between the end of this treatment and the beginning of the administration of fexinidazole (the duration of this wash-out period will depend on the half-life of the molecule used). The patient's informed consent and the post-treatment fol-



Workshop steering committee members Bamako/Mali September 2011

©Photo W. MUTOMBO



Workshop steering committee members Bamako/Mali September 2011

©Photo W. MUTOMBO

low-up protocol were examined and proposals were made for their improvement.

**d) The involvement of HAT Platform partners**

During this meeting, the various partners provided information on their on-going projects:

- Swiss-TPH: presentation of the different areas of research and explanations on the termination of the DB289 study;
- MSF: presentation of the HAT mobile team (MSF-Holland), its objectives, activities, etc.;
- FIND: presentation of its on-going studies, including RDT SD-Bioline, I-led, Molecular LAMP, Biomarkers CSF;
- EANETT: presentation of its platform and main activities;
- Research group on tsetse flies, human and animal trypanosomiasis;

- Pharmacokinetics;
- Evaluation of diagnostic tools for the detection of the parasite in animals

**e) Preparation of the 2012 annual scientific meeting, held jointly by EANETT and the HAT Platform**

The Committee confirmed its decision to organise this scientific forum in Juba, Republic of South Sudan, in September 2012.

A scientific and logistics committee was created to organise this major meeting. A special effort must be made to attract young African researchers, possibly with funding to help them attend and present their work.

**Laurence Flévaud** (reporter),  
**Augustin Kadima Ebeja** (coordinator)



Workshop steering committee members Bamako/Mali September 2011

©Photo W. MUTOMBO



Workshop steering committee members Bamako/Mali September 2011

©Photo W. MUTOMBO

## Salient points of the 31st Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC)



HATplatform delegates to the ISCTRC meeting Bamako/Mali September 2011

©Photo W. MUTOMBO



HATplatform delegates to the ISCTRC meeting Bamako/Mali September 2011

©Photo W. MUTOMBO

The conference was held in Bamako on 12-16 September 2011, in the large room of the Bamako International Conference Centre (CICB), under the high patronage of the Her Excellency Mrs. Cissé Mariam Kaïdama Sidibé, Prime Minister, Head of Government, with the collaboration of the African Union, and coordinated by the Inter-African Bureau for Animal Resources.

Over 340 participants attended this scientific meeting, representing 36 African countries and 10 Western countries. All the HAT Platform member countries were present and over thirty of their representatives were funded by DNDi

The meeting was organised in several sessions:

- Reports from international organisations
- Reports from the countries affected by the disease (national) and PATTEC
- Presentation of articles on HAT and animal African Trypanosomiasis (AAT)
- Discussion on the posters
- Final recommendations

### 1. REPORTS FROM INTERNATIONAL ORGANISATIONS

During the meeting, chaired by Dr. Baba Soumare with Dr. José Ramon Franco acting as reporter, several international organisations presented their reports. These organisations included the World Health Organisation (WHO), the Food and Agriculture Organisation (FAO), the Programme Against African Trypanosomiasis (PAAT), the Agence Internationale

de l'Énergie Atomique (IAEA), the Global Alliance for Livestock Veterinary Medicines (GALVmed), the Eastern Africa Network for Trypanosomiasis (EANETT), the Centre International de Physiologie et d'Écologie des Insectes (ICIPE), the Centre International de Recherche-Développement en Zone Subhumide (CIRDES), the International Livestock Research Institute (IRLI), Drug for Neglected Diseases initiative (DNDi), etc.

Overall, progress has been achieved over the past few years in HAT research and control. The money invested by international organisations helped reduce the number of HAT cases in previously endemic areas.

### 2. REPORTS FROM THE COUNTRIES AFFECTED BY HAT AND AAT

The heads of national HAT and AAT control programmes presented the activity reports for their respective countries. They all reported a continuing control and reduction in the number of cases following the collaboration with international and regional organisations.

### 3. PRESENTATIONS OF ARTICLES ON HAT AND AAT

All 78 presentations focused on a single theme, i.e. approaching research and control of tsetse flies and trypanosomiasis as a development program:

- Human African trypanosomiasis: epidemiology, diagnosis, and chemotherapy



HATplatform delegates to the ISCTRC meeting Bamako/Mali September 2011

©Photo W. MUTOMBO



Others ISCTRC meeting participants Bamako/Mali September 2011

©Photo W. MUTOMBO

- Animal African trypanosomiasis: chemotherapy, chemoresistance, and epidemiology
- Glossina biology, control, and eradication
- Use of land, environment, and socio-economy

#### 4. POSTER DISCUSSION

The Chairperson for this session, Dr. Ahmed H.A reminded the participants that posters are not a second-class method, but instead are true scientific documents designed to help young scientists publish their work and get exposure to the international scientific community.

The poster of our HAT Platform was one of the 37 posters accepted by the Council out of 58 applicants.

#### 5. COUNCIL RECOMMENDATIONS

Various recommendations were made for each of the represented structures and organisations, of which some are listed below:

##### 1. For the WHO:

- Continue to help the activities of HAT control, transmission and identification of isolated regions in endemic countries, to break the chain of transmission of the disease;
- Develop an innovating system based on monitoring and taking into account different epidemiological situations;
- Complete the HAT Atlas and supply the countries with materials.

##### 2. For the FAO:

- Maintain technical assistance in endemic countries;
- Continue the cooperation with partners in the field, especially PATTEC;

- Reinforce management and data analysis capacities;
- Contribute to the control and quality assurance of projects being set up, focusing on monitoring and evaluation.

##### 3. For PAAT:

- Circulate the strategy plan;
- Rebuild PAAT structures;
- Reinforce collaboration and exchanges between PAAT and PATTEC;
- Reinforce the capacities of various training programmes;
- Continue to publish scientific and technical newsletters.

##### 4. For national HAT programs, DNDi, and other partners:

- Resources must continue to be allocated to HAT control, even in countries that have reached the elimination stage, and thereby avoid enormous expenditures in the event of a resurgence.
- The risk estimation model should also include HAT due to T.b. rhodesiense.
- Find ways to reduce the post-treatment follow-up period by using new biomarkers, such as neopterin. Other sources of antigens should be examined to provide other options for HAT screening tests, such as TDR.
- Further tests are required for fexinidazole and SCYX-7158 (oxaborole) in phase I and II trials, to determine their usefulness as new and safe trypanocides, potentially able to eliminate the need for lumbar taps, a procedure which limits the efficacy of control efforts.

**Dr. Digas NGOLO,  
Dr. Pathou NGANZOBO,  
and Dr. Kadima Ebeja Augustin**

## 7th European Congress on Tropical Medicine & International Health in Barcelona



HATplatform poster exhibition, Barcelona October 2011



Oral presentation of the HATplatform by Dr A.Ebeja

The 7th European Congress on Tropical Medicine & International Health was held in Barcelona, Spain, on 3-6 October 2011.

“Sawubona Barcelona”, the official greeting of our congress, means “We see you” in Zulu: we chose it not only because it is a beautiful way of welcoming each other, but for its strength as a shared ethical commitment.

This scientific meeting was attended by 1350 participants and 335 speakers. Oral communications were divided into four main groups:

- Infectious diseases and neglected diseases
- Mother and child health
- Chronic diseases and environmental health
- Healthcare systems and resources

During the HAT session held on 5 October 2011, the WHO described the current situation of the disease (disease burden) and its geographical distribution. The University of Verona (Italy) presented the neurological aspects of sleeping sickness, and DNDi presented the multicentre NECT-Field study, in which our HAT Platform play a prominent role.

A study comparing the long and short pentamidine regimens (10 days versus 7 days) was also presented. Its conclusion was that the efficacy of the 10-day regimen was superior to that of the 7-day regimen.

Our Platform presented two posters and gave one oral presentation. One of the posters was on the health research policy in South Sudan, and the other on the three platforms initiated by DNDi (LEAP, CHAGAS and HAT), and dedica-

ted to finding solutions to these neglected diseases based on their specific parameters.

The oral presentation provided us with another opportunity to review the history of the HAT Platform, its objectives, its main achievements, and the lessons learned. We handed out a large number of the Platform Newsletters n°8 and 9.

Among the many cross-sectional sessions, the one entitled « Science of Elimination » was particularly interesting.

A panel of scientists, chaired by Prof. Marcel Tanner (Director of Swiss Tropical and the Public Health Institute), participated in the discussion: Dr. Bernard Pécoul (DNDi executive director), Prof. Pedro Alonso (Director of the Barcelona Institute for Global Health ISGlobal and of the Barcelona Centre for International Health Research CRE-SIB), Prof. Rose Leke (President of the African Regional Certification Commission), and Dr. Jean Jannin (WHO / NTD).

Prof. Tanner stressed the importance of an accurate definition of elimination and eradication, as policy makers may decide to opt for one or the other. However, this is a question for scientists because the decision must be based on the type of condition and other feasibility aspects. He gave the following definitions:

- Control: reduction of the disease burden
- Elimination: elimination of local transmission (in a given region, country)
- Eradication: complete elimination of the parasite worldwide

Dr. Jean Jannin explained that, based on his own personal experience as the WHO does not have a clear-cut posi-



Scientific Panel chaired by Professor Marcel Tanner

©Photo W. MUTOMBO

tion on these distinctions, the most important factors when talking of elimination are the criteria and indicators showing a reduction in the burden of the disease.

Eradication occurs when there is concrete evidence of the absence of the disease.

Several diseases have been eliminated in the past (e.g. HAT), but eventually resurgences occur. This shows that the concept of elimination is closely linked to how long it lasts. The lack of means to maintain an effective control on the disease is the cause of such failures. The challenge is thus to ensure that elimination lasts.

The WHO lists some eradication programs, such as:

- Poliomyelitis
- Guinea worm disease (eradicated expected by 2015)
- Lymphatic filariasis (eradicated expected by 2020)
- HAT, onchocerciasis, rabies, etc.

Prof. Rose, as an immunologist, described the polio eradication program in India, where the annual number of cases has dropped by 99%. The problem seems to be the availability of means and mobilisation of populations.

Elimination must come from the countries or the regions, because, as seen with malaria, elimination may be pronounced on a global level, when in fact certain areas of Africa are still trying to maintain a lasting control.

Dr. Bernard Pécoul considers that as long as politicians do not admit the extent of the problem, elimination or eradication will remain empty words. However, as a scientist, he does also admit that current tools are not effective enough to ensure the elimination of neglected diseases, such as human African trypanosomiasis, leishmaniasis, and lymphatic filariasis.

Diagnostic and treatment tools for these diseases are complicated and require a functional cold chain. Although the example of NECT showed that the care of patients can be improved with a less toxic product, the determination of the stage of the disease (lumbar tap), and the administration of DFMO infusions remain a problem. Consequently, patients cannot be treated in their villages.

Research is therefore needed to find simple diagnostic tools

and a treatment effective on both stages of sleeping sickness. An appropriate strategy for leishmaniasis is also needed.

The treatment of patients with lymphatic filariasis with microfilaricides can induce serious side effects in patients co-infected with *Loa loa*. A more appropriate strategy would be to find a macrofilaricide (which kills only adult filariae) to treat lymphatic filariasis.

As the development of diagnostic and treatment tools takes 5 to 10 years, the elimination of these diseases is still not within reach.

In his closing address, Prof. Manuel Corachán explained that tropical medicine and global health research play a central role in the Millennium Development Goals (MDGs). However, the objectives are far from being met and those related to health are the least likely to be achieved. It is for researchers to produce evidence-based data for policy makers. They must also monitor and evaluate progress, based on quantitative and qualitative results, and suggest solutions to improve the efficiency of policies.

Prof. Corachán made a series of recommendations for infectious and neglected diseases, some of which are detailed below.

**a. Malaria:**

- Still responsible for approximately 800,000 deaths every year, which is unacceptable.
- The pathophysiology of severe malaria has yet to be clarified.
- Rapid diagnostic tests (RDTs) provided a breakthrough in diagnosis.
- A fever is no longer systematically caused by malaria.
- New drugs are in the pipeline, but it will take time before they can be used.
- The availability of vaccines is closer than ever.
- Pyrethroid resistance is spreading.
- Eradication is a global goal, but unrealistic expectations must be avoided.



DNDi and MSF stand at the 7th European Congress on Tropical Medicine & International Health in Barcelona

©Photo W. MUTOMBO



Prof. Marleen Boelaert of IMT, Anvers

©Photo W. MUTOMBO



Dr. François Chappuis of Geneva University

©Photo W. MUTOMBO

**b. Leishmaniasis**

- More research is needed in vector control methods.
- Affected communities still have limited access to drugs.

**c. Vector-borne diseases**

- The global spread of mosquito vectors raises the threat of outbreaks of chikungunya, dengue fever, and West Nile fever in Europe.
- Increasing people movements due to migration, trade and travels are an added risk factor.
- New vaccines and new control strategies are necessary.

**d. Chagas disease (American trypanosomiasis)**

- Clinical trials are needed to evaluate new drugs for the chronic stages, including promising azole derivatives.
- A new presentation of benznidazole for children will be available shortly.
- A solution to drug stock-outs must be found urgently.

**e. HIV infection**

- The recent success of pre-exposure prophylaxis to prevent HIV infection has led to the discovery of new tools: microbicide gels, vaginal rings and oral tablets.

- Research on HIV vaccine is benefitting from data generated by previous trials and by fundamental research.
- Reinforcement of capacities remains a priority in low-resource countries, where HIV prevalence is high, and where trials are being conducted.
- Innovative approaches in HIV testing, including a self-administered test, have been developed for migrant populations.
- The future challenges related to HIV management in heterogeneous migrant groups in Europe are under discussion.

**f. Tuberculosis**

- New tools for TB diagnosis, treatment, and vaccines are needed.
- The relevance of screening for active and latent TB in migrants is under discussion.

Prof. Manuel Corachán ended his closing address by reiterating the need to endorse the Verona Declaration, which emphasizes the right to health as a fundamental human right for all the people, irrespective of origin, ethnicity, and legal status.

Further details on the other recommendations can be viewed on [www.ectmhbarcelona2011.org/doc/](http://www.ectmhbarcelona2011.org/doc/)

**Dr. Kadima Ebeja Augustin,**  
HAT Platform Coordinator

## Training in clinical research and Good Clinical Practice



©Photo W. MUTOMBO

Training in clinical research and Good Clinical Practice participants; centre Nganda Kinshasa DRC, November 2011

**A**s part of the program to reinforce clinical research capacities, the HAT Platform organised a training session jointly with DNDi and Swiss TPH, on 25-28 November 2011 in Kinshasa, DRC, on the basics of clinical research and good clinical practice.

This training session was part of the preparation of the fexinidazole study sites.

A total of 22 delegates (physicians, nurses, and laboratory technicians) from the Central African Republic (CAR) and the Democratic Republic of Congo (DRC) participated in the session, officially opened by Dr. Kande (physician, director of DRC's national HAT control program, PNLTHA).

A preliminary test was conducted to evaluate the knowledge of the participants on clinical research and good clinical practice, after which the following modules were administered by the Swiss TPH facilitators:

1. Ethics in research
2. Good clinical practice
3. Informed consent
4. Drug development
5. Clinical study design
6. Clinical study management
7. Clinical study implementation
8. Quality management and SOP
9. Study documents
10. Monitoring
11. Audit
12. Clinical data recording and management
13. Adverse event reporting

The sessions started with theory, followed by role-playing sessions and practical exercises to help the participants assimilate the data and maintain focus. This method was appreciated by all and promoted interaction with the facilitators as well as with other participants experienced in clinical studies.

Exchanges on informed consent, and on the role of investigators and sponsors were particularly intense.

This training session was made special by the presence of the main actors of the fexinidazole project. It was led by the people who will be in charge of monitoring the fexinidazole sites, as well as the medical manager of the DNDi HAT project (sponsor of the fexinidazole project).

The future investigators and site personnel were also present. This contact and the exchanges that took place will play an important role in the success of the implementation of the fexinidazole project.

This training session was a success and the assignment of Swiss TPH has been accomplished.

The network of people with clinical expertise within the HAT Platform is getting stronger and broader.



©Photo W. MUTOMBO

Working group during the training

The ball is now in our court, and it is up to us to meet the challenge. We will start by conducting one of the rare phase II studies in DRC and CAR, then maintain our commitment through the rest of the process, so that late-stage patients with trypanosomiasis can be treated as easily as early-stage patients (oral treatment).

**Dr. Wilfried Mutombo,**  
participant.

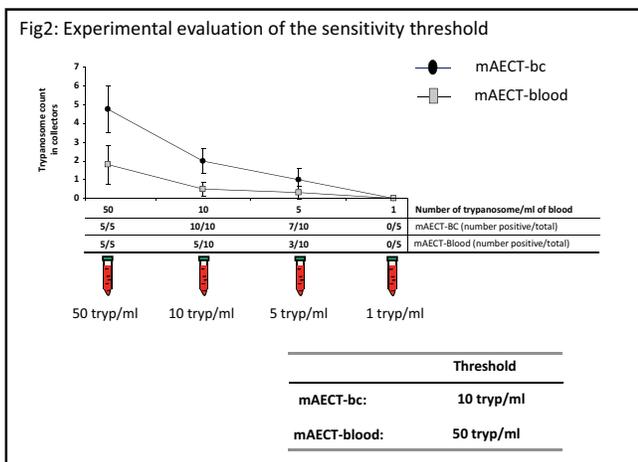
## Update on on-going research

### Sleeping Sickness diagnosis: use of buffy coats improves the sensitivity of the mini anion exchange centrifugation test.

In Bamako, we listened to a presentation on a very useful diagnostic method which can detect smaller quantities of trypanosomes than the most sensitive method currently available. Below is the official summary of this presentation. Camara Oumou1, Camara Mamadou1, Ilboudo Hamidou2, Sakande Hassan2, Kaboré Jacques2, Jamonneau Vincent2,3 et Bucheton Bruno2,3

1 Programme National de Lutte contre la Trypanosomose Humaine Africaine, BP 851, Conakry, Guinée ; 2 Centre International de Recherche-Développement sur l'Élevage en zone Subhumide (CIRDES), 01 BP 454 Bobo-Dioulasso, Burkina Faso ; 3 Institut de Recherche pour le Développement, Unité Mixte de Recherche IRD-CIRAD 177, Laboratoire de Recherche et de Coordination sur les Trypanosomoses. IRD-CIRAD, TA A-17/G, Campus International de Baillarguet, F-34398 Montpellier, France

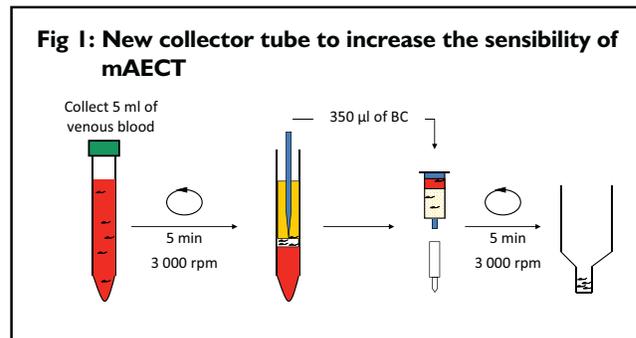
\* Adresser toute correspondance à : Bruno Bucheton, Tél : +226 20 97 62 15 e-mail: bruno.bucheton@ird.fr



The objective of this study was to evaluate a modification of the mini anion exchange centrifugation test (mAECT) for the diagnosis of *Trypanosoma brucei gambiense* human African trypanosomiasis (HAT), in which 350 µl of buffy coat withdrawn from five ml of blood are used instead of blood, in order to increase the sensitivity of the test.

The new protocol was first tested experimentally on serial dilution of trypanosomes and was then further evaluated in the field condition on 57 HAT patients diagnosed during a medical survey carried out in Guinea. Experimentally, the use of buffy coats improved mAECT sensitivity by at least five fold, and enabled to consistently detect parasites in blood at a concentration of 10 trypanosomes/ml.

During the field evaluation, more patients were found positive with mAECT-bc (96.5%) than with mAECT-blood (78.9%,  $\chi^2=6.93$ ,  $p=0.008$ ) and lymph juice examination (77.2%,  $\chi^2=7.67$ ,  $p=0.005$ ). Furthermore the number of parasites per collectors was significantly higher (7.2 vs 2.6,  $p=0.001$ ) when buffy coats were used instead of blood. The use of the mAECT-bc protocol thus enables a significant improvement of HAT parasitological diagnosis in Guinea, without any additional costs and would deserve to be tested in other T.b. gambiense endemic areas.



**Key words:** Human African trypanosomiasis, diagnosis, buffy coat, mAECT

### Development of a screening test for sleeping sickness enters a new phase

The Bill & Melinda Gates Foundation (BMGF) recently renewed its funding to FIND for the development of a rapid diagnostic test (RDT) for human African trypanosomiasis (HAT). The new grant will enable FIND and partners to complete the development, evaluation and introduction of a simple, low-cost lateral flow test that health workers without much training will be able to use in the most remote settings.

Evaluation of the performance of the prototype RDT has now been initiated in Angola, DRC and the Central African Republic. The target is to have the test introduced for diagnosis of HAT by 2013.

©Photo FIND



The new prototype screening test for HAT and accessories being developed by FIND and SD. Procedure: 20µl fresh blood from a finger prick is placed into the test well, followed by 4 drops of diluent. Results are read after 15 mins. A positive sample has 2 or 3 red bands, and a negative test only one red band.

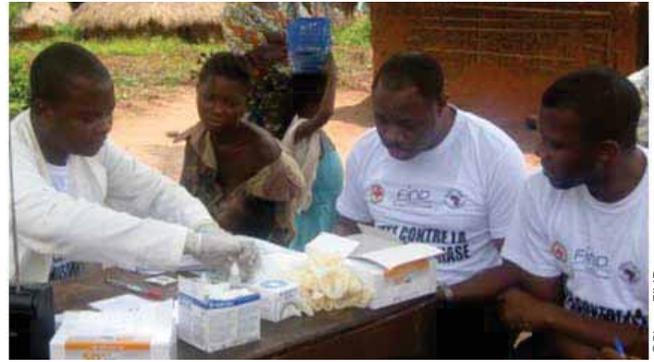
The RDT will make it possible to dramatically increase the population screened, by mobile teams and at remote health posts in endemic areas.

Accelerated screening and control of the disease will be critical to support global elimination efforts. This complements other HAT projects at FIND, including the development of simple tests to confirm diagnosis, to determine the stage of the disease, and to confirm cure after a patient has been treated.



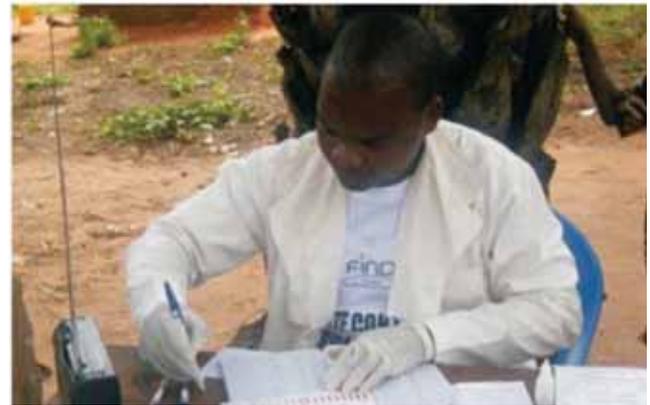
Enrolment of study participants in a village in the DRC

©Photo FIND



©Photo FIND

Dr. Crispin Lumbala, the principal investigator (right) and Dr. Augustin Ebeja, the study monitor, observe a technician (Dieudonné Tshibangu) in the National Sleeping Sickness Programme of the DRC performing the test on a participant's blood during on-going performance evaluation studies.



©Photo FIND

Reading results of the prototype test against a colour scale in the DRC.

### **FIND and partners make major breakthrough in molecular diagnosis of HAT**

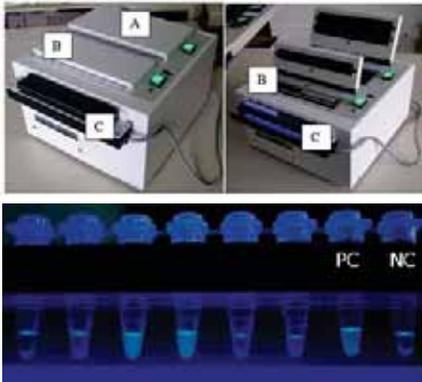
The Foundation for Innovative New Diagnostics (FIND) in Geneva and Eiken Chemical Co. Ltd have made impressive progress towards the development of a simple molecular method for diagnosis of HAT.

The test, which is called LAMP, detects tiny fragments of parasite DNA in the blood of infected people. In September 2011, FIND and Eiken announced at the ISCTRC Conference in Bamako, Mali, that development of the test and its evaluation in experimental settings had been completed. During the same occasion, Prof. Enock Matovu of Makerere University in Uganda gave a comprehensive account of the studies they have been carrying out, that confirm the potential of this test. Clinical evaluation of the test is going on in both Uganda and the Democratic Republic of the Congo (DRC).



©Photo FIND

Trainees using an LED light source to read HAT LAMP results



The Loopamp™ LF-160 incubator used to perform the HAT LAMP reaction. After extraction of DNA, the LAMP reaction is carried out in the reaction block (B), which is calibrated to maintain a constant temperature of 65°C, and to stop the reaction in 40 minutes. The results are visualized under fluorescent light emitted from LEDs (C). Positive samples appear green. PC: positive control, NC: negative control.

The LAMP test is unique because it is highly sensitive and specific, and does not require a sophisticated laboratory infrastructure or storage conditions. Blood can either be used when fresh, or from ordinary filter papers after collection and storage at room temperature.

The procedures for processing samples before they are tested are also quite simple. Blood from suspects who are identified using a screening test is simply heated for 10 minutes, then introduced into the test. The test is performed at 65°C for 40 minutes. Positive samples emit fluorescence, which is observed under a simple LED light.

Introduction of LAMP in the diagnosis of HAT could contribute significantly to the accelerated control and elimination of the disease.

## The NIDIAG study in the Democratic Republic of Congo

(for the HAT Platform Newsletter n°10)

### Introduction: project overview

Globally an estimated 1.2 billion people are affected by one or more neglected infectious diseases (NID). This group of diseases thrives among impoverished populations of developing countries, in remote rural areas, urban slums and conflict zones (WHO & Carter Center 2008).

They include a range of chronic disabling infections, such as Buruli ulcer, Chagas disease, cysticercosis, dracunculiasis, endemic treponematoses, human African trypanosomiasis (HAT), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, trachoma, food-borne trematodiasis but also more acute infections such as brucellosis, enteric fever, melioidosis, cholera, dengue and rabies.

NID cause an estimated 500,000 deaths each year and inflict severe physical disabilities, jeopardizing child growth and pregnancy outcomes.

The aggregate disability-adjusted life year (DALY) tally for NID is 56.6 million, which exceeds the tally of malaria (46 million DALY) or tuberculosis (TB) (35 million DALY) (Hotz et al. 2007).

A major challenge in the clinical management of NID is the weakness of health systems of disease-endemic countries (DEC). People affected by NID mostly present to primary health care centres - be it often late in their therapeutic itinerary (Kibadi et al. 2009; Robays et al. 2007).

Many health workers are unfamiliar with the clinical management of NID. Misdiagnosis is frequent, as the clinical presentation of many NID is non-specific and may be confounded with that of other common conditions (Lejon et al. 2003; Swai et al. 2006).

Current NID-related diagnostic algorithms in most countries are mostly empirical, rarely take into account local prevalence data of NID, do not adequately represent the spectrum of patients and differential diagnosis at the primary care level and usually have not been validated in the field. The disease-specific focus of several 'vertical' NID control programmes has led to fragmentation and severe gaps in patient management.

In response to the HEALTH.2010.2.3.4-2 FP7 call, the NIDIAG ( for "Neglected Infectious Diseases Diagnosis") consortium sets out to develop an improved system for delivering primary health care in resource poor settings and proposes an integrated approach to this challenge. The

consortium is coordinated by the Institute of Tropical Medicine (ITM, Pr. Marleen Boelaert, Antwerp, Belgium) and brings together 13 complementary partners from 4 European States, 4 countries in Asia and 3 countries in Africa, including DRC (see Figure).

### **NIDIAG objectives**

The aim of the NIDIAG project is to improve the early diagnosis and management of NID (and other morbidities) at the primary health care level in resource-poor settings, by developing and validating integrated diagnostic guidelines for several clinical syndromes.

The strategy relies on two pillars: first, a patient-centered approach starting from three major challenging syndromes, namely the persistent fever syndrome, the neurological syndrome, and the intestinal syndrome, which capture most NIDs in Africa and Asia, as well as other major morbidity such as malaria, HIV/AIDS or tuberculosis; second, the development of new point-of-care “rapid diagnostic tests (RDTs) that specifically address the needs of resource-limited settings.

The main outcome of this research will be the “proof-of-concept” elaboration of new clinical guidelines for low-income settings, updated with recent epidemiological evidence and upgraded with a panel of RDTs used alone or in combination.

### **NIDIAG in DRC**

The Democratic Republic of Congo is one of the countries where this research project will take place, through the “Institut National de Recherche Biomédicale” (IRNB), Kinshasa. In DRC, human African trypanosomiasis (HAT) is the NID which will be targeted in priority, because of its prevalence in several rural regions of the country and the difficulty to early diagnose it at the primary care level.

Two syndromes, the persistent fever and the neurological disorders, will be specifically investigated in DRC because HAT may present with any of these clinical features. Other “severe and treatable” conditions causing persistent fever or neurological disturbances will be investigated as well (such as malaria, tuberculosis, HIV infection, typhoid fever), in order to go beyond the classic vertical approach.

The NIDIAG study is initially planned in the “Hôpitaux Généraux de Référence” of Mosango and Yasa-Bonga, located in the HAT-endemic province of Bandundu.

Patients presenting at one of these hospitals with neurological symptoms and/or persistent fever (more than one week) will be offered to participate to the study and enrolled after informed consent.

They will be submitted to diagnostic reference testing

(parasitology, bacterial/mycological cultures, serological or molecular assays), either on study sites or in the INRB. A panel of RDTs, already validated or in clinical development, will be systematically performed on sites in order to estimate their field diagnostic performances (phase 3 diagnostic study for new RDTs targeting HAT, tuberculosis, cryptococcal infection,...).

The study should start early 2012 and last for two years. About 500 patients should be included for each studied syndrome. New clinical guidelines for the two targeted syndromes should be available within 2-3 years. Whenever possible, complementarities and synergies with other ongoing or planned studies in the same area (e.g. DNDI therapeutic trials for HAT) are most welcome.

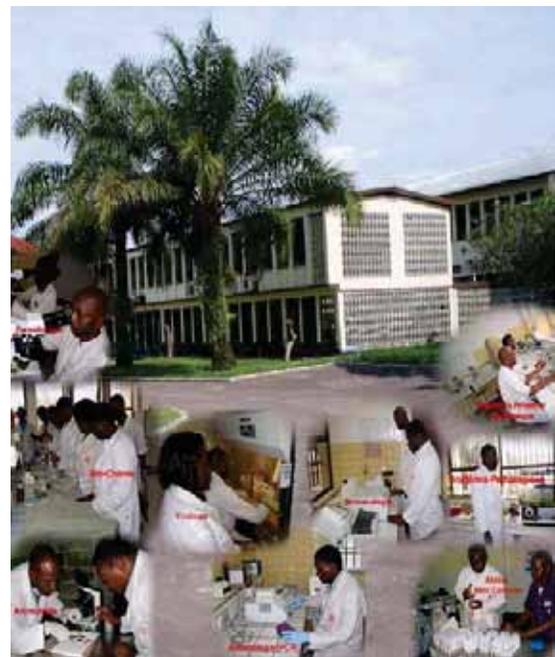
Dr Bottieau Emmanuel, Coordinating Investigator, Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium

Pr. Pascal Lutumba, Country Principal Investigator, INRB, Kinshasa, DRC

Pr. Marleen Boelaert, NIDIAG coordinator, Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium



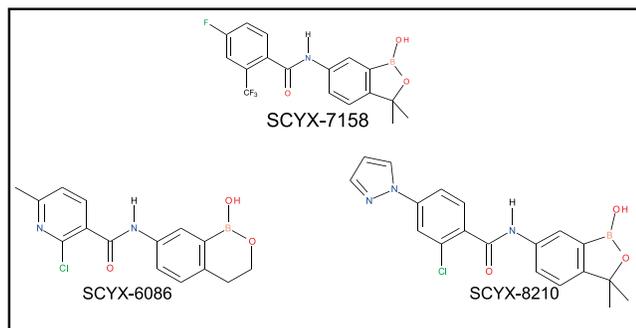
**Institut National de Recherche Biomédicale**



*Joyeux Noël & Bonne Année 2012  
Merry Christmas and Happy New year 2012*

## Novel oxaborole enters clinical development stage for the treatment of HAT

DNDi (Drugs for Neglected Diseases initiative) and its partners, Anacor Pharmaceutical Inc., Scynexis Inc., and Pace University, USA, developed a new class of candidate drugs for the treatment of HAT.



SCYX7158 is a benzoxaborole molecule for oral administration. It has demonstrated *in vitro* activity against strains of *Trypanosoma brucei*, including *T.b. rhodesiense* and *T.b. gambiense*. In murine *in vivo* models, SCYX7158 was effective against both stages of the disease. Preclinical studies in rodents and non-rodents have shown that the compound is well distributed throughout the body, including the brain, and is well tolerated.

Given these promising preclinical results, SCYX7158 will enter its clinical phase development in humans in 2012.

The HAT Platform is able to offer assistance in terms of infrastructure and local experience, as it is accumulating data from its own studies (DB289, NECT, NECT-Field, and soon fexinidazole clinical phase II / III).

Dr. Antoine Tarral, Head of HAT Clinical Program, DNDi

## NECT-FIELD

The first results of this study were presented in our Newsletter N°8 in December 2010 (pages 16-17). Dr. Olaf Valverde from DNDi gave a more detailed presentation during the 7th European Congress on Tropical Medicine & International Health in Barcelona, Spain.

The objective of this study was to evaluate the clinical tolerance, feasibility in the field and efficacy of nifurtimox-eflornithine co-administration in adults, children, and pregnant or breastfeeding women for the treatment of late-stage sleeping sickness (*T.b. gambiense*).

The study was carried out in six sites in DRC, and included 630 patients with late-stage HAT. They were given eflornithine IV 400mg/kg/day for 7 days, and nifurtimox orally 15mg/kg/day for 10 days. The median duration of hospital stay was 16 days (range: 5-46).

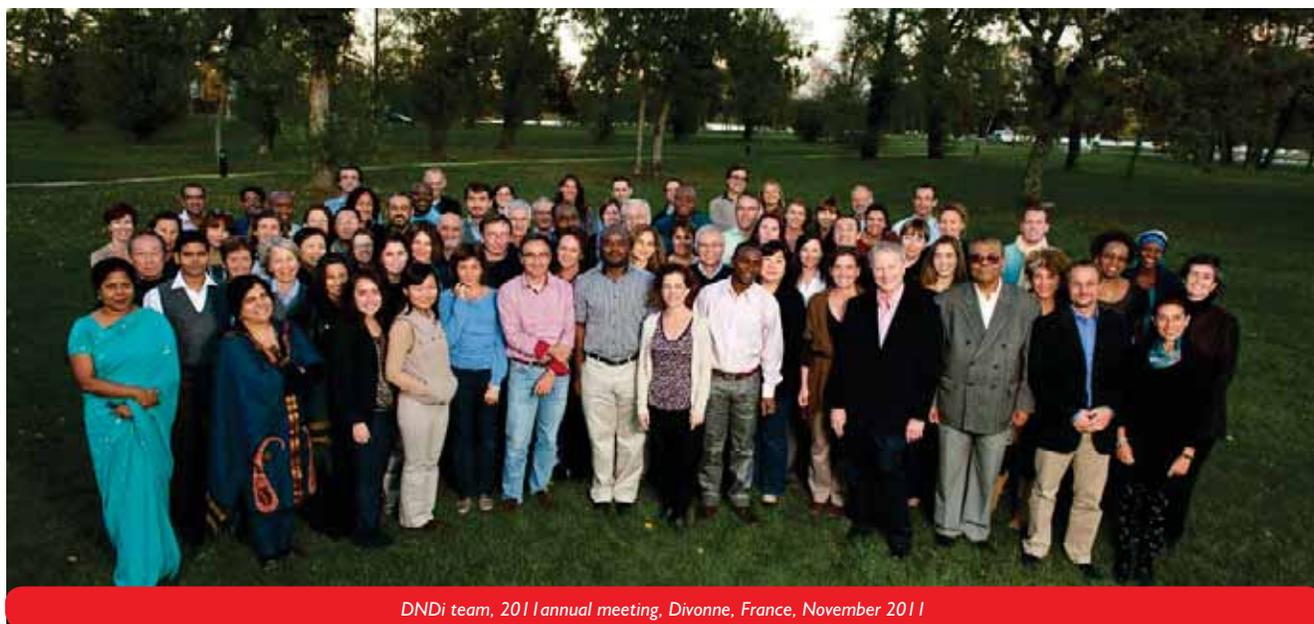
The results of the intention-to-treat population (i.e. all patients who started the treatment) were analysed. This population included 629 patients: 100 children under 12 years old (median 6), 13 pregnant women, and 33 breastfeeding women.

Overall, the symptoms were similar in children and in adults, with the exception of more frequent fever and less frequent headaches in the former. All the children completed their treatment and were discharged from hospital alive. The Karnofsky score was improved after the treatment. Clinical signs and symptoms were reduced (lymphadenopathy, neurological).

Similar improvements were also noticed in pregnant and breastfeeding women.

The use of NECT in this population (children as well as pregnant and breastfeeding women) seems to be safe, but the national programs will continue to monitor these patients very closely before changing their treatment policy.

Dr. Kadima Ebeja Augustin, HAT Platform Coordinator



DNDi team, 2011 annual meeting, Divonne, France, November 2011

©Photo DNDi

## Floor Given to patients and caregivers

### Testimony of patients treated with NECT



©Photo M. ILUNGA

a. My name is Kazadi Kalala. I am 33, married, and I have four children, the youngest being born after I was treated for sleeping sickness. I am a former political and administrative sciences student at the University of Lubumbashi. In 1997, I became a child-soldier, or kadogo, with the revolutionary army supporting the late President Laurent Désiré Kabila. I was sent to Mbuji-mayi.

In 2001, following the death of Laurent Désiré Kabila, I chose to leave the army, and went to work in the diamond mine of Bakwa Nsumpi. I think that it is there that I caught sleeping sickness.

I was diagnosed as carrying trypanosomes in 2008 at the Muya Hospital in Mbuji-mayi and transferred to the Dipumba Hospital for treatment.

I had heard about sleeping sickness before, and I knew that the treatment was difficult, especially with a drug called Arsobal. Many patients were no longer cured with this drug. I am pleased with this new treatment, which consisted on one IV infusion in the morning and one in the evening for one week, in addition to a few tablets. I now feel cured. During my stay in hospital, I met Muyoyi who behaved as a madman, and Kabeya who was totally stricken by the disease. When we were discharged, we were all markedly better. I was very happy to see Kabeya again at the 6-month follow-up visit, fully recovered. »

b. I was diagnosed with sleeping sickness in February 2008 in Kamaleka, about 30 km from Mbuji-mayi. It is probably in the village of Bakwa Nsumpi that I caught the disease while working in corn fields. My husband also got it in 2004 and he had been treated with Arsobal. Six months after his treatment, he was still not cured. He had to be treated again with the same Arsobal, associated this time with a second drug called Lampit in tablet form. It is only in 2006, after a two-year medical follow-up that he was declared cured. In our village, somebody else had also taken Arsobal and he



©Photo M. ILUNGA

was left mentally disturbed. In fact he became mad. Arsobal is a drug which causes a lot of reactions.

With this new treatment based on IV infusions and yellow tablets (NECT), I vomited once the first day of the treatment. After that, I suffered no ill effects which could have prevented me from completing the treatment.

There were four of us in the hospital, two adults, one 2-year old child, and a 12-year old girl, all receiving the same treatment. We were all much better when we were discharged from the hospital.

Doctor! Can you order a vaccine so that we become invulnerable to tsetse fly bites?

c. My daughter was born in Mbuji-Mayi and she is now 15 years old. She was diagnosed with sleeping sickness at the Kamaleka Healthcare Centre in 2009, in the territory of Lupatapata in East Kasai.



©Photo M. ILUNGA

We live with her in Bakwa Mulumba Bakwa Iba, where I converted to agriculture having been a craftsman in Mbuji-

Mayi. It is hence in Bakwa Mulumba that she caught sleeping sickness.

I know this disease because I had it in 1999 and was treated in Dipumba with Arsobal for almost a month. I was given three sets of injections in the vein for three consecutive days, with a seven-day gap between each set.

With the new treatment (NECT), IV infusions are given along with tablets for 10 days. It is very good because my daughter is now cured. Like me, she was mentally disturbed during the disease, but she thinks very clearly now, and she can even help me with my small business. She makes no mistakes when doing calculations. She was in fourth grade when she got ill. She is waiting to be completely cured so that she can go back to school and eventually become a nurse. The new treatment is shorter and does not seem too complicated.

The only problem she had was seizures on the first day of treatment. The seizures were quickly controlled with the administration of two other drugs, and the rest of the treatment was easy.

### Main questions asked at each interview:

- How long have you had sleeping sickness for?
- Where did you get it?
- Were you familiar with this disease before? What did people say about it?
- How was sleeping sickness treated in the old days?
- What would you like to say about the current treatment that you were given?
- What problems did you encounter during the treatment?

Interviews conducted by  
**Dr. Ilunga Wa Kyhi Medard**,  
under the coordination of  
**Dr. Kadima Ebeja Augustin**

### HAT, a truly neglected disease

Civil wars, crimes, unemployment, accidents, floods, various crises, and diseases, such as AIDS, malaria and tuberculosis make headlines, but it is very rare that trypanosomiasis victims are mentioned on the news, even in highly endemic countries, such as DRC.

Although the number of reported cases is dropping, HAT continues to kill. Whether in Africa or elsewhere, HAT affects almost exclusively the poorest populations. According to the WHO, HAT victims have the lowest access to health-



Doctor Pathou Nganzobo, NECT-FIELD Investigator during a training in Kinshasa

©Photo W. MUTOMBO

care services, are the least able to adopt prophylactic measures, and live far from disease control centres.

Even healthcare personnel and carers consider that HAT is a strange disease that only experts can understand. Clinicians seeing patients in their consultation box do not immediately think of HAT.

In DRC for example, HAT is poorly taught to medical students. A newly qualified doctor is hardly able to define the disease, as it is not a priority for the examiners and teachers. Furthermore, there are very few medical theses on this subject.

The main questions are which of the aforementioned factors contribute to maintaining HAT as a neglected disease, and if even experts do not promote control efforts, who will?

It is first for the actors involved in HAT control to initiate change, inform and train new actors on a large-scale, and not limit their action to a reduction in the number of reported cases, but moving instead towards an eradication of the disease, which must no longer be viewed as impossible.

Consequently, partners such as the national control programs, the HAT Platform, DNDi and the others must be encouraged. Furthermore, their actions in the field must be supported, to take full advantage of the considerable efforts and means made available to the investigators of various clinical studies and all actors involved in HAT control.

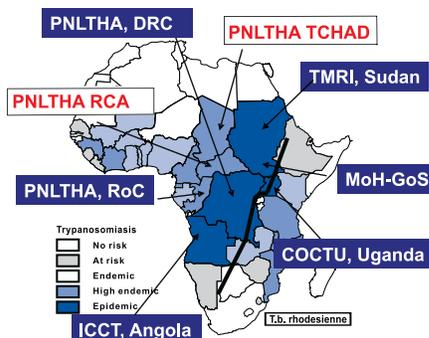
**Dr. NGANZOBO Pathou**, NECT-FIELD Investigator, Bandundu-ville

## 2012 scientific meetings and websites of interest

Date	Location	Event
11/14 March	Atlanta, USA	<b>International Conference on Emerging Infectious Diseases.</b>
31 March /3 April	London, UK	<b>22nd European Congress of Clinical Microbiology and Infectious Diseases.</b>
3/5 April	Glasgow, UK	<b>BSP spring meeting - 50 years of Parasitology in the UK-2012</b>
18/20 April	Geneva, Switzerland	Geneva Health Forum
23/27 April	Addis Ababa, Ethiopia	13th World Congress on Public Health <a href="http://www.etpha.org/2012/">http://www.etpha.org/2012/</a>
24/26 April	Cape Town, South	Forum 2012 (COHRED/Global Forum for Health Research) <a href="http://www.forum2012.org/">http://www.forum2012.org/</a>
8/11 May	Thessaloniki, Greece	30th Annual Meeting of the European Society for Paediatric Infectious Diseases
13/16 June	Bangkok, Thailand	15th International Congress on Infectious Diseases
16/18 June	Washington, USA	Global Health Council Annual Conference

### HATPLATFORM

National HAT control programs in the most affected endemic countries



DNDi  
Swiss TPH

Other partners:  
National and international research groups: ITMA, INRB, CDC, TRC-KARI, etc.

- NGOs operational in HAT control
- FIND
- WHO
- EANETT, PABIN, AMANET...

### Extract of the mission of HATP platform :

The HAT Platform is a regional network, scientific and technical, dedicated to the Human African Trypanosomiasis (HAT), more commonly called "sleeping sickness". Its main objective is to set up a pool of highly qualified regional skills through relevant training in order to facilitate clinical trial and develop new diagnostics and treatment tools against the disease.

## Recent publications on HAT

**Aksoy, S.** "Sleeping sickness elimination in sight: time to celebrate and reflect, but not relax." *PLoS Negl Trop Dis* 2011, 5(2): e1008.

**Barrett, M. P., I. M. Vincent, et al.** "Drug resistance in human African trypanosomiasis." *Future Microbiol* 2011, 6(9): 1037-47.

**Blum, J. A., A. L. Neumayr, et al.** "Human African trypanosomiasis in endemic populations and travellers." *Eur J Clin Microbiol Infect Dis.* 2011, Sep7.

**Bucheton, B., A. MacLeod, et al.** "Human host determinants influencing the outcome of *Trypanosoma brucei* gambiense infections." *Parasite Immunol* 2011, 33(8): 438-47.

**Checchi, F., F. Chappuis, et al.** "Accuracy of five algorithms to diagnose gambiense human African trypanosomiasis." *PLoS Negl Trop Dis* 2011, 5(7): e1233.

**Corbel, V. and M. C. Henry** "Prevention and control of malaria and sleeping sickness in Africa: where are we and where are we going?" *Parasit Vectors* 4: 37.

**Jacobs, R. T., J. J. Plattner, et al.** "Benzoxaboroles: a new class of potential drugs for human African trypanosomiasis." *Future Med Chem* 2011, 3(10): 1259-78.

**Kagira, J. M., N. Maina, et al.** "Prevalence and types of coinfections in sleeping sickness patients in Kenya (2000/2009)." *J Trop Med* 2011: 248914.

**Mumba, D., E. Bohorquez, et al.** "Prevalence of human African trypanosomiasis in the Democratic Republic of the Congo." *PLoS Negl Trop Dis* 2011, 5(8): e1246.

**Simarro, P. P., A. Diarra, et al.** "The human African trypanosomiasis control and surveillance programme of the World Health Organization 2000-2009: the way forward." *PLoS Negl Trop Dis* 2011, 5(2): e1007.

**Tong, J., O. Valverde, et al.** "Challenges of controlling sleeping sickness in areas of violent conflict: experience in the Democratic Republic of Congo." *Confl Health* 2011, 5: 7.

**Wastling, S. L. and S. C. Welburn** "Diagnosis of human sleeping sickness: sense and sensitivity." *Trends Parasitol* 2011, 27(9): 394-402.

**Lorna M. Maclean ; Martin Odiit et al** « Focus Specific Clinical profiles in Human African Trypanosomiasis caused by *Trypanosoma brucei rhodesiense* » *PLoS Negl Trop Dis* 2010, 4(12) e906

**Andreas K.Lindner, Gerardo Priotto** "The unknown risk of vertical transmission in sleeping sickness-A Literature review" *PLoS Negl Trop Dis* 2010, 4(12) e783

**Mamadou Camara, Oumou Camara et al** "Sleeping sickness diagnosis : use of buffy coats improves the sensitivity of the mini anion exchange centrifugation test" *Trop Med Int Health*, 2010 .00(4)00

### 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
- Dutch Ministry of Foreign Affairs (DGIS) / THE NETHERLANDS
- European Union - Framework Programme 6
- Médecins Sans Frontières (Doctors without Borders) / INTERNATIONAL
- Medicor Foundation / LIECHTENSTEIN
- Ministry of Foreign and European Affairs (MAEE) / FRANCE
- Republic and Canton of Geneva, Institution Department, International Solidarity / SWITZERLAND
- Spanish Agency for International Development Cooperation (AECID) / SPAIN
- Swiss Agency for Development and Cooperation (SDC) / SWITZERLAND
- A Swiss private foundation and individual donors.

#### Editorial committee:

**Chairman:** Augustin Kadima Ebeja

**Members:** Olaf Valverde ; Charles Wamboga ; Sylvestre Mbadingai ; Gédéon Vatunga ; Richard Laku ; Victor Kande and Nicolas Mbongo

**Advisers:** José Ramon, Cecilia Schmid and Laurence Flévaud.

#### HAT Platform coordination address

4 Avenue Révolution, quartier SOCIMAT  
Kinshasa, Gombe  
Democratic Republic of Congo  
Email: aebeja@dndi.org  
Tel: 00243 81 081 22 38