# « HAT Platform Newsletter »

**Issue N°1, January 2007**

## Contents



## Editorial

This new information bulletin is designed to improve communication between HAT platform members. It will provide information relevant to the activities of the platform and the contributions received from each member state.
We wish a long life to this newsletter. We hope that after the inevitable teething problems, and with time and our combined efforts, it will become a reference tool for all members of the platform as well as for all researchers working on human African trypanosomiasis.
Each member state will have to contribute to this newsletter with an article on its activities within the platform, or on an interesting subject related to sleeping sickness.
On behalf of the platform's coordination group, and from me, I would like to extend to all of you our best wishes for 2007, which I hope will be seen as a year of genuine achievements for our platform.

*Dr. Kadima Ebeja Augustin, platform coordinator*

Meeting of HAT platform in Nairobi, September 2006

## A silent anniversary

History is being made. The Human African Trypanosomiasis (HAT) platform is not just a passing whim; it is an ambitious project which is now very much alive.
The first strategic meeting on reinforcing the capacities for clinical trials on sleeping sickness was held on August 16-17 2005 in Kinshasa, capital of the Democratic Republic of Congo (DRC). The meeting was organised by DNDi (Drugs for Neglected Diseases initiative), in collaboration with STI (*Institut Tropical Suisse*) and PNLTHA (*Programme National de Lutte contre la Trypanosomiase Humaine Africaine*). The main objectives of this meeting (held as a series of workshops) were to create a network of experts to exchange existing scientific and technical know-how in sub-Saharan Africa on clinical trials on sleeping sickness, and thereby help significantly the clinical trial capacities in the area.

## A silent anniversary *(ctd.)*

The meeting was opened by DRC's Minister of Health (Prof. Bongeli) and General Secretary for Health (Dr Mia Miaka Bilenge Constantin). They said how pleased they were to inaugurate this first workshop in the DRC, in one of the countries worst hit by this terrible disease. The workshop was attended by 54 experts in various fields, including representatives from five countries where the disease is endemic (Angola, DRC, RoC, Uganda and Sudan), as well as representatives from institutions and NGOs involved with sleeping sickness and active in the area (DNDi, STI, ITM, FIND, WHO, CTB, Epicentre, Malteser International, Merlin, TRC-KARI…). The meeting was closed by DNDi executive director, Dr B. Pécoul, and by the General Secretary for Health of the DRC.

Since the platform's creation in Kinshasa, two other meetings have already been held: a meeting of the coordination group in Luanda in Angola (February 13-14, 2006), and a meeting of the platform in Nairobi (September 19-23, 2006) in Kenya.

The platform's action plan, first presented during the meeting in Kinshasa, was adopted during the meeting in Luanda, and a timetable was defined.

Six months later, in August 2006, a big step forward was achieved with the appointment in Kinshasa of the platform's coordinator, Dr Kadima Ebeja Augustin.

In Nairobi, the objectives were to review the platform's achievements to date, secure the joining of a new member (South Sudan) and plan the activities for 2007.

This year, the platform's anniversary was a silent one, without any special celebration. However, in the field, the results of the efforts of all its members prove that the platform is alive and operational. Our wish is to see the platform grow and consolidate its activities before we reach its second anniversary.

Let us keep in touch with the coordination and react on an on-going basis to e-mails and phone calls, so that the second anniversary will mark an even greater success.

This means that we must maintain the momentum and continue to develop this great project. We must strengthen our links with the platform's coordination, as well as contribute and respond to its requests so that we can reach our objectives.

*Dr K. Ebeja Augustin*

**Abbreviations**

ITM: Institute of Tropical Medicine in Antwerp
FIND: Foundation for Innovative New Diagnostics
WHO: World Health Organisation
CTB: Coopération Technique Belge
Merlin: Medical Research Institute International
TRC-KARI: Trypanosomiasis Research Centre, Kenya Agricultural Research

### ACTIVITIES OF THE PLATFORM

- **Training of physicians (DNDi/STI/PNLTHA collaboration):** a training session for the physicians working on research sites will take place from April 16-21 2007 in Kinshasa in the Ngaliema Clinic.
  Three physicians from the RoC and two physicians from Angola will join those from the DRC, bringing the total to 20 participants.
  The objective is to train physicians on the anamnesis and clinical examination of trypanosomiasis patients, in an attempt to standardise the collection of data for future studies.

- **Visit to the platform's member states:** the platform coordinator, Dr. Kadima Ebeja Augustin, is currently visiting Uganda (January 21-26, 2007). The objective of his visit is to consolidate the platform's activities in the various regions. He was in November in South Sudan (Juba) and North Sudan (Khartoum), He will also be travelling in Angola and the RoC to meet the new manager of the HAT programme.

- **A training course for the ethics committee is currently being designed.**

**Progress report on ongoing clinical trials**

An update was presented at the HAT platform meeting in September 2006 in Nairobi, on two ongoing clinical trials on improved treatment options for HAT. The first one is a phase III clinical trial with a new candidate treatment for stage 1 HAT, oral diamidine DB-289 or pafuramidine maleate. The second one is the NECT trial, evaluating the efficacy and safety of a new and simplified stage 2 HAT treatment regimen combining eflornithine and nifurtimox (N+E), compared to the standard 14-day eflornithine treatment. Both trials are progressing smoothly.

**DB-289 trial**
Based on the promising outcome of previous clinical studies, a pivotal phase III confirmatory trial was developed and initiated in the summer 2005 in 4 centers in the DRC (Maluku, Vanga, Kikongo and Bandundu), 1 center in Angola (Uige), and 1 center in South Sudan (Yei). A total of 250 patients, including pregnant and breastfeeding women as well as adolescents, will be randomised in this open-label study to receive DB-289 or the comparator drug pentamidine. The patients will be followed up for two years. So far, more than 200 patients have been enrolled. A safety and efficacy interim analysis will be performed once half of the recruited subjects have undergone the 12-month follow-up examination. Further studies with DB-289 are being planned. The partners involved are currently discussing the possibility of conducting a large-scale, multinational, phase IIIb study, using DB-289 under African field conditions during the drug's registration process. Other studies will examine the safety and efficacy of DB-289 in the treatment of the East African form of trypanosomiasis caused by *T.b. rhodesiense*, as well a new paediatric formulation.

**NECT trial** (a collaborative effort involving Epicentre, DNDi, TDR, STI, PNLTHA DRC, PNLTH RoC, MSF-H, MSF-B, COCTU- Coordination Office for the Control of Trypanosomiasis in Uganda)
Initially started by Epicentre and MSF-H in the RoC, the NECT trial has developed into a multicentre study involving 6 sites in 3 countries. The objective is to assess a new and simplified treatment regimen combining eflornithine and nifurtimox as an alternative first line treatment for stage 2 patients. As of December 2006, a total of 184 patients have been enrolled in 3 sites in the DRC (Isangi, Dipumba and Katanda). Together with the 103 patients enrolled earlier in Nkayi, RoC, and another 45 patients currently enrolled in Uganda, this brings the total number of patients in the study to 332 (way above the minimum number of 280 patients needed to achieve statistical significance). As the follow-up period must be 18 months to establish efficacy, the final results of this study are expected in the second half of 2008. Meanwhile, the preliminary results of the first 103 patients enrolled in Nkayi are nearly finalised (18 month follow-up reached, analysis ongoing) and look very promising. Based on these and on the initial safety results of all the patients, an extension study will be set up during 2007 to further document the efficacy, safety and ease of use of this new N+E combination. More information on this trial can be found in the latest DNDi Newsletter (No. 14, November 2006, see www.dndi.org).

*Dr. Els Torreele, DNDi, and Drs Gabriel Pohlig and Cecile Schmid, STI*

**Diary-Events**

- **HAT internal meetings**:
  - Annual meeting of the platform expected in the second half of 2007 in Khartoum. It will probably be held in November, the steering committee will confirm this date before June.
  - Meeting of the platform's coordination committee postponed until May or June 2007 in Basle (Switzerland). Invitations will be sent two months in advance.

-**International conferences**:
  - 29th meeting of the *Conseil Scientifique International pour la Recherche et la Lutte contre les Trypanosomoses*, Luanda, Angola, 17-21 September 2007.
  - Royal Society of Tropical Medicine and Hygiene – « 100 Years of Tropical Medicine – Meeting of the Millennium Development Goals », London, 13-15 September 2007.
  - 5th European Congress on Trop Med & Intl Health – « Partnerships and Innovation in Global Health », Amsterdam, 25-29 May 2007.

**SYMPOSIUM REPORT**

In October 2006, Dr Kande Betu Kumessu, director of PNLTHA in the Democratic Republic of Congo was designated by DNDi to take part in a symposium held in Giens in France, and organised by a sister platform ***« Rencontres Nationales de Pharmacologie Clinique Giens XXII, 2006 »***.
The subject was: How to carry out clinical research in developing countries? Which recommendations ?
He found the subject very interesting and contributed actively to the group work. He also got some inspiration from the way this platform operates, as some of their objectives are not dissimilar to ours.
The recommendations resulting from this work can be obtained upon request to Dr Kande, director of PNLTHA (*Programme de Lutte contre la Trypanosomiase Humaine Africaine*) from the Democratic Republic of Congo.

## Operational Research and Sleeping Sickness in Angola

Since colonial times, research has always had its place in the structural organisation of the fight against sleeping sickness in Angola. In 1963, year of its creation, the *Missão de Combate as Tripanossomíases-MCT* was giving a lot of importance to research. This anti-trypanosomiasis Angolan organisation included 4 divisions, of which one was created under decree n° 47.657 on April 28 1967 and dedicated to research. At the time, a few studies had already been carried out, particularly therapeutic trials on Novadium and Trypanodium in rats infected experimentally with *Trypanosoma brucei brucei* and *T. b. congolense*, as well as other pharmacodynamic studies.

This research ethos has not been forgotten and the current Angolan anti-trypanosomiasis programme, *Instituto de Combate e Controlo das Tripanossomíases-ICCT*, gives priority to operational research. Over the past ten years, major work has been performed. In collaboration with ITS (*Institut Tropical Suisse*), IENT (*Institut d'Epidémiologie et de Neurologie Tropicale*) from the University of Limoges in France, IHMT (*Institut d'Hygiène et Médecine Tropicale*) of the New University of Lisbon in Portugal, and CIRMF (*Centre International de Recherches Médicales de Franceville*), research has been carried out on the improvement of sleeping sickness diagnosis and treatment. Therapeutic studies have started in Angola, e.g. IMPAMEL I1 project, and studies on the trypanocidal molecule DB-289. IMPAMEL II2 and phase IIb of the study on DB-289 (on-going) are both multinational studies carried out in part in Angola. Other strategic studies have been performed on biological markers to determine the neurological phase in sleeping sickness.

Polysomnographic recordings of sleep-wake disorders associated with sleeping sickness were used to characterise the neurological phase of sleeping sickness. Available results have already been published in communications and scientific journals, such as *Pharmacokinetic investigations in patients from northern Angola refractory to melarsoprol treatment* - Trop Med Int Health 2001; 6: 412-20 - *Efficacy of new, concise schedule for melarsoprol in treatment of Sleeping Sickness caused by Trypanosoma brucei gambiense: a randomized trial* - Lancet 2000; 355: 1419-25 - *Control of human African trypanosomiasis in the Quiçama focus, Angola* - Bull World Health Organ 2002; 80: 738-45 - *Efficacy of 10-day Melarsoprol schedule 2 years after treatment for late-stage gambiense sleeping sickness* - Lancet 2004; 364: 789-90 - *Sleep structure: a new diagnostic tool for stage determination in sleeping sickness* - Acta Tropica 2005; 93: 107-17 - *A link between chemokine levels and disease severity in human African trypanosomiasis* - Int J Parasitol 2006; 36: 1057-6.

In partnership with IRD (*Institut de Recherche pour le Développement*), ICCT inaugurated a few months ago a research project aimed particularly at trypanocidal drug resistance and anti-vector interventions.

*Dr Vatunga Gedeao* (Angola)

[1] IMPAMEL I : Improved application for melarsoprol clinical efficacy
[2] IMPAMEL II: Improved application for melarsoprol effectiveness in the field

## Recent scientific articles

Full articles are available upon request to the coordination. Abstracts can be viewed by clicking on the links below. Please notify the platform coordination of any interesting article.

1) Equivalence Trial of Melarsoprol and Nifurtimox Monotherapy and Combination Therapy for the Treatment of Second-Stage Trypanosoma brucei gambiense Sleeping Sickness.
J Infect Dis. 2007 Feb 1; 195(3):322-329.
Bisser S, N'siesi FX, Lejon V, Preux PM, Van Nieuwenhove S, Miaka Mia Bilenge C, Buscher P.

Combination therapy for sleeping sickness: a wake-up call. J Infect Dis. 2007 Feb 1; 195 (3):311-313.
Pepin J. (related editorial)

2) Three Drug Combinations for Late-Stage Trypanosoma brucei gambiense Sleeping Sickness:
A Randomized Clinical Trial in Uganda. PLoS Clinical Trials. 2006 Dec 8; 1(8): e39
Priotto G, Fogg C, Balasegaram M, Erphas O, Louga A, Checchi F, Ghabri S, Piola P.

3) Melarsoprol versus eflornithine for treating late-stage Gambian trypanosomiasis in the Republic of the Congo.
Bull World Health Organ. 2006 Oct; 84(10):783-791.
Balasegaram M, Harris S, Checchi F, Ghorashian S, Hamel C, Karunakara U.