**Invest in R&D to deliver improved treatments**

One of the objectives of the Drugs for Neglected Diseases initiative (DNDi) is to develop improved and new treatments for Chagas disease. DNDi is currently building its Chagas portfolio, which includes projects that yield near-term benefit to paediatric patients as well as long-term projects that will potentially benefit a large population of chronic-phase patients.

Although the disease was discovered more than 100 years ago by the Brazilian physician Carlos Chagas, very little investment has been made in research and development for an effective treatment. Currently available treatments are not effective and poorly tolerated. To address this serious unmet medical need, DNDi has raised funds from public and private donors, and formed R&D partnerships with a number of key institutions to develop Chagas treatments.

**CHAGAS DISEASE IN SHORT**

Chagas disease is caused by the parasite Trypanosoma cruzi (T. cruzi), transmitted primarily by insects known as “kissing bugs”. The disease occurs in two phases.

- The first, acute stage is often asymptomatic or unrecognised due to non-specific symptoms such as fever, malaise, generalised lymphadenopathy (affecting the lymph nodes), and hepatosplenomegaly (enlargement of the liver and the spleen), which spontaneously resolve within weeks.
- The chronic phase may affect the heart and the gastrointestinal tract and, if left untreated, can lead to death. Over 8 million people across Central and South America are infected with Chagas disease. Chagas disease kills more people in this region than any other parasite-borne disease, including malaria.

Through migration, Chagas has spread to Australia, North America, Japan, and Europe.

**Filling gaps in the pipeline**

DNDi has adopted a balanced approach to build a Chagas disease portfolio and works to improve existing treatments through the development of new formulations that are better adapted to patients’ needs. To address the short- and mid-term needs of patients, DNDi aims to find alternative drugs through therapeutic switching. In the long term, new chemical entities have to be developed that fit the product profile. DNDi works with various investigators to overcome methodological constraints that limit the accurate diagnosis and clinical evaluation of responses to new treatments in the pipeline. Additionally, DNDi is involved in strengthening existing clinical research capacities through a regional platform of experts that supports high-standard clinical trials.

**Drug discovery**

Key elements in DNDi’s drug discovery process include:

- **Focused approach to compounds sourcing**: DNDi has access to various chemical compounds, focused drug classes, and classes of existing antiparasitic agents.

**Wild-type T. cruzi**. This technology offers the possibility of more rapid identification of a hit and chemical series of interest to be progressed as drug candidates. The technology has already been successfully developed for the screening of compounds against the intracellular Leishmania parasite by DNDi at IPK.

- **Series to optimise** (from screening to drug candidate): at the end of 2008, a lead optimisation consortium was established to engage in a critical, interactive, and iterative process
- **Lead Optimisation** - allowing a rapid turn-around and with the goal of optimising the antiparasitic efficacy of lead compounds while addressing their distribution metabolism pharmacokinetics (DMPK) properties and improving their safety. This consortium consists of teams of analytical and medicinal chemists, pharmacologists, and parasitologists and includes institutions in Austria [Epichem, Murdoch, and Menash Universities] and in Brazil, the Universidade Federal de Ouro Preto (UFOP).

Target Product Profile for Chagas disease

- **A new treatment for adults and children for acute and chronic disease**
  - priority is a paediatric formulation
  - useful against parasite species in all regions
- **Better safety profile** than existing drugs
  - ideally requiring little or no monitoring
- **Equal or better efficacy profile** than existing drugs
- **Easy-to-use treatment**
  - ideally less than 30 days
  - preferably once-a-day treatment, ideally outpatient
- **Affordable**
  - Stable in tropical climates

* sprinkled on the most neglected and understudied diseases worldwide. Of the US$ 139 million used in 2008 to fund research and development (R&D) of kinetoplastid diseases, 41.5% was for leishmaniasis, 24.8% for sleeping sickness, and only 11.2% for Chagas*. Due to a lack of funding, millions of people infected do not have access to adequate treatment.

It is time to take urgent measures to scale up diagnosis, treatment, and patient access to medical care and to boost research and development. It is time for policy makers and donors to grant Chagas the attention it deserves. In 2009, DNDi and its partners launched a campaign called “Wake up! Time to Treat Chagas Disease!” with the following goals:

- to raise awareness
- to break the silence surrounding the disease
- to boost R&D of new tools for the disease

As part of this campaign, DNDi, Médecins Sans Frontières, and the University of California Los Angeles (UCLA) Program in Global Health convened a one-day symposium on Chagas disease in Los Angeles in October 2009. Participants agreed that urgent measures and concrete solutions are greatly needed. That same month, the Pan American Health Organization (PAHO) adopted a resolution for the elimination of neglected diseases, including Chagas. This is an important step, but needs to be reinforced with measures such as adopting a resolution on Chagas disease at the World Health Assembly in May 2010 in Geneva, and including funding for Chagas programmes in the U.S. Government’s Global Health Initiative.

Good efforts are undoubtedly underway. However, a lot more needs to be done for patients to finally have access to affordable, safe, and effective treatment. ♦

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**Treat Chagas now!**

Chagas disease is a silent killer. Every year it takes the lives of an estimated 14,000 people, many of whom did not even know that they were suffering from the disease. In the endemic countries of South and Central America, 8 to 15 million people are infected, primarily adults. As a result, Chagas has a significant socioeconomic impact. It is the most prevalent parasitic disease in the Americas.

The Brazilian physician Carlos Chagas first described the disease more than 100 years ago, and although much progress has been made in medical research since, there is still no effective treatment for Chagas. It ranks one of the most neglected and understudied diseases worldwide. The US$ 139 million used in 2008 to fund research and development (R&D) of kinetoplastid diseases, 41.5% was for leishmaniasis, 24.8% for sleeping sickness, and only 11.2% for Chagas*. Due to a lack of funding, millions of people infected do not have access to adequate treatment.

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* Neglected Disease Research and Development: New Times, New York (G-feeback 2009), The George Institute for International Health
To treat Chagas disease there are currently two drugs available – benznidazole and nifurtimox – which have limitations. There is a void of treatment options especially when it comes to treating the chronic stage of the disease. Existing antifungal drugs have shown promising activity against the Chagas pathogen. DNDi has been in negotiation with pharmaceutical companies to bring about change and hope for patients in need as quickly as possible. In recent years, the marketed antifungal drug posaconazole (Noxafil®, Schering-Plough) was one of the most remarkable azoles. It has been shown to induce parasitological cure in mice with acute and chronic infections, including benznidazole-resistant strains. It is considered the leading azole candidate for proof-of-concept evaluation. The main drawbacks, however, are the complex nature of the molecule, with an expensive synthesis and formulation, as well as its current price. DNDi has been in negotiation with Schering Plough since 2006. Unfortunately, no agreement has been reached. Two other triazole derivatives, however, ravuconazole (with the pharmaceutical company Eisai, see page 3) and TAK-187 (with pharmaceutical company Takeda) have also shown encouraging in vitro and in vivo results. Both products have completed Phase I testing and are good candidates for further assessment as potential treatments.
What are the symptoms of Chagas?

The disease has two clinical stages:

- **Acute stage**: often remains unrecognized because it manifests through non-specific symptoms such as fever, malaise, generalized lymphadenopathy (affecting the lymph nodes), and hepatosplenomegaly (enlarged spleen and liver). These symptoms usually resolve in four to six weeks. In this stage, the disease is especially dangerous for children; 2% to 8% of infected children die.

- **Indeterminate phase**: during which patients can transmit the parasite to others (e.g. through blood transfusion, mother-to-child transmission) while showing no signs of the disease. This stage may last for decades after the infection has taken place. The chronic symptomatic phase affects 10% to 30% of these patients, who go on to develop heart or gastrointestinal complications.

What is the impact of Chagas?

Chagas disease is a leading cause of infectious cardiomyopathy worldwide, killing more people in Latin America each year than any other parasitic-borne disease, including malaria. It affects mostly poor people living in rural areas or on the outskirts of larger urban centers.

What are the current treatments and their limitations?

Two treatments are currently available: nifurtimox and benznidazole. Both were discovered decades ago and have limited efficacy in the chronic phase of the disease, and a poor tolerability profile in adults. The development of a new treatment that is effective in the chronic phase of the disease is an urgent need. Often, chronic patients will require pacemakers, implantable defibrillators and, in some cases, heart transplants. Many patients also die suddenly, sometimes without ever realizing that they have been infected with Chagas disease. According to WHO, the number of diagnosed cases has been increasing over recent years. This is due to increasing migration. Chagas today surfaces in countries and regions classified as non-endemic, such as Australia, Canada, Europe, Japan, and the United States. In these countries, there is a high risk of transmission of the disease through blood transfusion, congenital infection, and organ transplantation.

DNDi and Eisai are developing the first new compound in nearly 40 years to treat Chagas disease.

Ravuconazole has a very long half life, which will allow dosing once a week. The initial proof-of-concept trial will aim to achieve maximum clearance of the parasite in chronic cases, in which current drugs are effective in 60-70% of cases. DNDi anticipates initiating the first clinical trials in 2010, with confirmation of activity by early 2011. Regulatory approval could come as early as 2014.
Bolivia: Breaking the Silence

By Paulo Gadelha, President of Fiocruz & Tania Araujo-Jorge, Director of the Instituto Oswaldo Cruz.

Since its discovery in 1909, progress in fighting Chagas disease has been made. But many challenges still lie ahead.

In Brazil, an estimated four million people living in one of the affected countries live in poverty or in rural areas, but, through disease is most frequent among those who live in poverty or in rural areas, but, through.

- **The outcome of MSF’s field experience in two Chagas programmes in Bolivia demonstrates the feasibility of implementing Chagas disease diagnosis and treatment programmes in poor, remote, rural areas, as well as urban areas.** While side effects were frequent, only three children required hospital stays to manage these, and there were no deaths due to side effects.

**Treat backing the complex disease**

**Brazil: tackling a complex disease**

By Paulo Gadelha, President of Fiocruz & Tania Araujo-Jorge, Director of the Institute Oswaldo Cruz.

Since its discovery in 1909, progress in fighting Chagas disease has been made. But many challenges still lie ahead.

In Brazil, an estimated four million people living in poverty or in rural areas, but, through disease is most frequent among those who live in poverty or in rural areas, but, through. But he only came to know about it when the disease began to affect his heart about a decade ago. As a result of serious complications, he has recently undergone surgery to implant his sixth pacemaker. He is leading a patients’ association that was formed in 1989 in a local Chagas disease clinic of the Oswaldo Cruz University Hospital (HUOC) at the University of Paraná, Curitiba. The association offers legal, social and psychological assistance to more than 2,800 Chagas patients. The work is conducted with help from volunteers and receives very little assistance from the government, the medical community, the public, or the press. Most of the association’s resources come from donations, which allows it to distribute food assistance and medication that is not available through the public healthcare system. More info: www.chagas.org.br e-mail: chagas.icfc@chagas.org.br

fessional, and patients. Yet undoubtedly the biggest gap concerns the development of new drugs. Brazil remains as committed to playing a central role and leading role as Carlos Chagas and his collaborators did in the first decade of the 20th century.

The challenges are vast: how to explain to people who seem healthy that they have a deadly disease and need to take a drug that makes them feel unwell for 60 days? How to encourage health workers to prescribe a treatment that they are scared to use? MSF, in collaboration with partners at government, municipal, and community levels, is developing and researching innovative approaches related to prevention, diagnosis, and treat- ment - approaches that are appropriate and potentially sustainable in the socioeconomic and cultural contexts where the disease is most common.

While in 2006 the National Chagas Programme started diagnosing and treating patients under 15 years of age, various parts of the country, access to treatment remains unavailable for the great majority. Moreover, the lack of effective, rapid diagnostic tests...
Argentina: More Action Needed

By Hector Freilij, paediatrician, Children’s hospital Ricardo Gutierrez, Buenos Aires.

The Gran Chaco covers an eco-region of 1.3 million km², extending over Argentina, Bolivia, and Paraguay. Chagas disease is prevalent in this region, with incidences rising since 2001 especially in Argentina, despite major control efforts. Currently, it is believed that 1.5 to 2 million Argentines carry the disease. Every week, 15,000 Argentines die of Chagas disease. Most of the infected live in the provinces of Santiago del Estero, Chaco, Formosa, and Tucuman, and northern Santa Fe.

Actions taken to address Chagas disease in the region have largely been limited to vector control. Little has been done in providing treatment and healthcare to infected children, adolescents, and young adults. Nevertheless some progress is being made. The implementation of active screening and treatment campaign for children has just started in schools in Argentina and neighbouring countries, and advances have also been made in training doctors to better detect the disease.

Treatment of adults and children

According to a 1998 WHO/PAHO technical report, treatment of any infected individual may receive treatment, regardless of age – adults can therefore receive etiological treatment. Furthermore, the study clearly demonstrates that fatal Chagas disease may have lower incidence of cardiacopathy. Fortunately, the definition of the indeterminate – or chronic asymptomatic – phase has changed.

In regard to children, doctors and investigators have demonstrated that 9 out of 10 children infected with Chagas disease receiving treatment are completely cured. Furthermore, the adult hospital in the rural area of South-eastern Bolivia has shown that if a child begins treatment before the age of one, the likelihood of cure is almost 100%. The centre about a third of children with indeterminate disease may have lower incidence of cardiacopathy. Unfortunately, the definition of the indeterminate – or chronic asymptomatic – phase has changed.

For more information on the Chagas campaign please consult: www.chagas-break-the-silence.com www.treatchagas.com

TREATMENT IS A PRIORITY

Fausto Torrico, Professor of Parasitology and Infectiology, Universidad Mayor de San Simon, Cochabamba, Bolivia and member of the Scientific Advisory Committee of DNDI; “In Bolivia, where one million (12%) of the total population is infected with T. cruzi, the need for an effective treatment is now a priority. Until the year 2000, more than 60% of the country was virtually infected with visceralis (Kissing bug). In several places, we found that up to 100% of the adult population was infected. Since 2000, the national Chagas control programme has carried out systematic and comprehensive vector control programmes in the six Chagas-endemic departments. Today the risk of infection is low in 50% of the municipalities, but there are still areas of resistance, where infection is higher than 20%. Many challenges lie ahead, but the results are promising. The actions were made possible by grants received from the Inter-American Development Bank (IADB). Unfortunately, the funding finished in 2007 and currently there is a transfer of roles and responsibilities from the central level of the Ministry of Health to local municipalities, whose contributions differ depending on their circumstances – which explains, in part, the difference in our response activities to the disease at the municipal level.”

A PLATEFORM OF EXPERTS TO SUPPORT DEVELOPMENT OF NEW TREATMENTS

The Chagas Clinical Research Platform was launched in 2009 at Uberaba in Brazil, and brings together partners, experts, and stakeholders in a network, which will provide support to the successful evaluation and development of new treatments for Chagas disease. The main objectives of the platform are to facilitate clinical research by creating a forum for technical discussions, to develop a critical mass of expertise and to strengthen institutional research capacities. In addition, the platform will support research that works towards standardisation of methodology to assess drugs efficacy to treat T. cruzi infection, review alternatives for using current drugs approved (new schemes, doses, combination), special scenarios (resistance), and link investigators and groups of experts on Chagas disease in a collaborative network.

Three clinical trials are planned to start in the first semester of 2010. The first is a population pharmacokinetics study of paediatric benznidazole and will be conducted in Argentina and Paraguay as well as in the north of the country where the disease is highly prevalent. The second one is an evaluation of the polymerase chain reaction (PCR) blood test or assessment of therapeutic response in patients with chronic indeterminate Chagas disease, and the third study, conducted in Bolivia, is to evaluate the safety and efficacy of E1224, a new drug of ravuconazole.

The Chagas Platform will meet for the first time in early 2010 to review the target product profile for Chagas disease, to update DNDI’s strategy for the disease, and to provide training for investigators involved in the planned clinical trials.

FIELD OF TREATMENT NEEDS TO BE REINVENTED

Sergio Sosa-Estani, Chief of Epidemiological Service at the National Centre for Research in Endemic Diseases of the Ministry of Health (Argentina) says about Chagas: “Research into the disease is so dated and so oriented towards prevention that the field of treatment has to be practically reinvented. The clinical trials for a new compound E1224, a prodrug of ravuconazole, will help to reinvigorate the field. The traditional method of monitoring treatment measures antibodies to T. cruzi. Although useful, this method is not very accurate, and antibodies can persist for years after the parasite has been eradicated. Researchers have developed two standardised polymerase chain reaction tests that detect T. cruzi in blood with qualitative or quantitative results. It can be used to identify infection in individual patients. The quantitative test will help give a better understanding of the course and staging of the disease and response to treatment. Evidence indicates an association between T. cruzi levels, inflammation, and organ damage. That test is in the process of being validated.”

Extract from http://www.bmj.com/cgi/content/full/339/oct06_1/b4084

TREATMENT IS ALSO PREVENTION

Treating children with Chagas has several advantages: it can avoid the development of cardiac and gastrointestinal diseases later in life; treating little girls now can avoid the transmission of Chagas during pregnancy in their adult life, thus avoiding congenital Chagas disease. Furthermore, it allows for a greater number of blood and organ donors.

As Chagas affects a poor region – it does not reach Buenos Aires – there is little economic interest for big pharmas and others who could make a real difference, and so the disease remains neglected. We know that it can be treated and cured – but knowing is not enough…what we need is action.
U.S.: Increasing Prevalence, Continued Neglect

Chagas disease has traditionally been characterised as a Latin American phenomenon, endemic only to the 21 countries south of the United States border. However, recent studies have shown that the prevalence of Chagas disease outside of Latin America is increasing, in large part due to population flows, and Chagas disease is becoming an important global health issue. (1) Caryn Bern and Sue Montgomery of Centres for Disease Control (CDC) estimate that in 2005 there were 300,167 individuals infected with Chagas disease living in the U.S. (2) This is more than six times the estimated prevalence of Chagas in Spain (47,743) (3) – the country with the next highest population of Latin American immigrants.

**Modes of transmission in the U.S.** According to Bern and Montgomery, “the U.S. cannot be classified as an area of non-endemicity for Chagas in the same sense as Europe or Asia” due to the fact that eleven Chagas-carrying triatomine species live in the U.S. Although the likelihood of vector-borne transmission is rare, due to modern housing conditions and lower efficiency of vectors, there have been seven reported cases of autochthonous Chagas disease in the U.S. (4)

In January 2007, the U.S. began routinely screening blood donations for Chagas disease, and organ donation screening has now begun in some areas. According to the American Red Cross, 1 in 30,000 blood donations nationwide – and roughly 1 in 300 donations from Latin Americans in Southern California – continue to test positive for Chagas disease, even though donations from individuals with a known history of Chagas disease are not accepted. (6)

**A case of neglect** CDC estimates of the prevalence of Chagas disease is based on demographic data, not actual diagnoses. This raises the question: of the 300,000 plus people who are estimated to be infected with Chagas disease in the U.S., how many have been – or will be – diagnosed? Testing for Chagas disease is not routine in the U.S., and the populations most at risk often do not have access to healthcare.

**Health practitioners unfamiliar with Chagas disease** Even when patients are diagnosed, healthcare givers in the U.S. are largely unaware of Chagas disease and are unfamiliar with treatment protocols. Dr Meymandi, director of the Centre of Excellence for Chagas Disease, regularly sees patients who have been referred to her from around the country because of a lack of knowledge in the wider medical community.

In 2007, CDC published practical recommendations for the evaluation and treatment of Chagas disease in the U.S. (7) in an effort to address the lack of knowledge and standardisation in this area, but more education and training in the healthcare community is needed to ensure adequate surveillance, diagnosis and treatment of Chagas disease in the U.S. Bern and Montgomery also estimate that every year, 63 to 315 babies may be born with Chagas disease. Despite the fact that these levels are in the range of other congenital conditions that appear in the American College of Genetics’ recommended newborn screening panel, screening for congenital transmission of Chagas disease is rarely conducted, suggesting a lack of awareness among obstetricians and gynaecologists. To date, no congenital cases have been recorded in the U.S.

Furthermore, Bern and Montgomery conservatively project that up to 45,000 cases of heart disease could be attributed to the disease – in many cases, without the patients or their healthcare providers ever realising the cause. (8) The healthcare community’s lack of awareness may contribute to an increased burden on the healthcare system from patients with serious heart complications caused by Chagas, who may require aggressive treatment, such as defibrillators or heart transplants. These complications are, in large part, preventable if the disease is treated early.

**U.S. global health policies neglect Chagas** Though more than 100 million people are at risk from Chagas in the Americas, the disease is often neglected in U.S. global health and neglected disease policies and programmes for disease control. For example, neglected disease programmes such as the President’s NTD Initiative and the Food and Drugs Administration’s priority review voucher system do not include Chagas. In 2007, less than US$ 2.5 million of the federal budget was spent on research and development (R&D) for new Chagas drugs and diagnostics – a negligible amount for a disease affecting more than 8 million people. (9)

President Obama’s five-year Global Health Initiative could change this by including Chagas disease programmes in its efforts to control NTDs, including: support for increased surveillance, diagnosis, and treatment programmes; investment in R&D for new drugs and diagnostics; regulatory agency support, and measures to strengthen research capacity in disease-endemic countries. Increased attention is also needed to improve screening for those living with Chagas disease in the U.S. Public leadership is needed to ensure Chagas disease is appropriately addressed in international policies (i.e. WHO and PAHO), which should reflect the urgent needs for prevention, treatment, and development of new diagnostics and medicines. Over the long term, the emphasis must be on working with our Latin American neighbours to control the disease.

With the Chagas disease burden concentrated in marginalised populations, Chagas patients do not have the political clout necessary to move this silent disease out of the shadows. DNDi’s Chagas campaign aims to raise awareness about this important public health issue, push for policy changes, and encourage R&D investments that will make a difference for Chagas patients in the future.

**Raise awareness with prominent support: “We’re shadows”** Dr. Sheba Meymandi, director of the Centre of Excellence for Chagas Disease, a former actress from Argentina and is supporting DNDi’s mobile outreach clinic to screen for Chagas disease in Los Angeles.

**Voices from the field**

Dr. Sheba Meymandi, Director of the Centre of Excellence for Chagas Disease

“An actress from Argentina and I’ve always been eager to be part of a project that could make a difference for Chagas patients in the future. I know from having volunteered in the United States that many patients do not have the political clout needed to move this silent disease out of the shadows. DNDi’s Chagas campaign aims to raise awareness about this important public health issue, push for policy changes, and encourage R&D investments that will make a difference for Chagas patients in the future.”

**In the U.S., nitifuranim aqueous is available to physicians through special Centres for Disease Control (CDC) protocols, but benznidazole is more difficult to obtain and is rarely used. According to Dr. Sheba Meymandi, director of the Centre of Excellence for Chagas Disease, “We can get [benznidazole], but it is a very laborious process through the FDA. Hopefully the CDC will have access to benznidazole soon.” Dr. Meymandi adds, “The difference, in terms of the treatments, is that benznidazole is a shorter course – two months – with a better side effect profile. Nitifuramin, which we have easier access to in the U.S., is a three-month course, and the side effect profile is pretty abysmal. It is like giving chemotherapy. Major side effects are nausea, vomiting, memory loss, neuropathies, and the list goes on.”**

**Michelle French, Former Regional Communications Manager, DNDi North America**

**Catherine Lalonde, Consultant CHC**
Chagas Disease: an emerging health problem in Europe

Dr. François Chapuis, Assistant Physician from the International and Humanitarian Medicine Division of the Geneva University Hospitals, describes the current situation in regards to Chagas in the U.S. and Europe: “There has been a sharp increase in the number of patients diagnosed with Chagas disease in non-endemic countries. The U.S. and Europe are now hosts to the disease. In Geneva, 50% of Latin American undocumented migrants are Bolivians from Santa Cruz and Cochabamba, which are the most endemic and poor regions of their country. Over the past five years, we have noticed an increase in the number of patients diagnosed with the chronic (or indeterminate) phase of the disease or with cardiac complications, and we have recorded two cases of congenital Chagas. In 2008, the Geneva University Hospitals, in partnership with the WHO, set up a large study in the local Latin American community: out of the 1,012 individuals tested, 130 were diagnosed with Chagas. Among Bolivians, 26% carried the parasite. These results have prompted us to expand Chagas screening programmes and to improve case management.”

A Call for Action

Chagas disease remains the leading parasitic killer in the Americas. Considering the unmet needs of millions, it is time for a variety of actors to mobilise to push forward urgent measures and concrete solutions. This could include, for example, implementation of the recently adopted resolution for elimination of neglected diseases, including Chagas, by the Pan American Health Organization (PAHO) Directing Council; adopting a resolution on Chagas disease at the World Health Assembly (WHA) in 2010; and including funding for Chagas programmes in the U.S. government’s Global Health Initiative.

Participants of the Los Angeles symposium called on governments, intergovernmental agencies, researchers, drug and diagnostic developers, nongovernmental organisations, patient groups, and funders to take action in two key areas:

1. Scale up diagnosis, treatment, and patient access to care

   Millions of people infected with Chagas are not tested and do not receive treatment in both endemic and non-endemic countries. Urgent actions and measures to increase the medical response to Chagas must be taken to:
   - Implement routine testing, diagnosis, and treatment of Chagas in health care systems, treating all children and offering treatment to adults.
   - Obtain regulatory approval of benznidazole and nifurtimox as well as the future new paediatric formulation of benznidazole, in both endemic countries and non-endemic countries. This will require coordination and harmonisation of regional regulatory efforts and the inclusion of neglected tropical diseases, specifically Chagas, in the WHO/PAHO prequalification process.
   - Secure availability of benznidazole and nifurtimox as well as diagnostic tests by:
     - reinforcing diagnostics and drug procurement systems, forecasting needs, and supply chains
     - implementing the Strategic Fund (revolving fund) to secure long-term affordability of existing drugs in endemic countries rather than relying on a system based on donations
     - exploring approaches, like differential pricing systems, for non-endemic countries

2. Boost research and development for new tools

   Existing tools available to health staff and national programmes are lacking or inadequate, while research and development (R&D) for Chagas is virtually non-existent.

   - ensuring access and affordability of future new formulations, including paediatric benznidazole.
   - Formalise and promote international clinical guidelines for the use of the existing drugs for all stages of the disease.
   - Ensure monitoring and evaluation systems for better epidemiologic data collection to determine the prevalence of Chagas disease.
   - Support research into appropriate models for the delivery of prevention, diagnosis, and treatment of Chagas within health systems in endemic settings.
   - Increase political commitments, funding, and human resources for Chagas patient care programmes.

A recent study showed that less than 0.5% (US$10M) of all worldwide neglected disease R&D funds was devoted to Chagas disease in 2007, and even half was spent on basic research. There is an urgent need to develop new treatments and diagnostics that are safer, more effective, affordable, and adapted to patient needs. Actions and measures to boost and sustain innovation must be taken to:

   - Foster innovation for new tools for Chagas disease that include:
     - continued development of new treatment regimens or combinations that shorten treatment duration
     - developing new diagnostic tools, including a definitive test for cure and a better rapid diagnostic test
     - facilitating access to knowledge for new classes of compounds and existing drugs marketed for other indications
     - increase capacity for clinical research to evaluate and guide the development of new tools and facilitate their use.
   - Support new approaches for the regulation and approval of new treatment tools, including fast-track mechanisms and use of existing biomarkers, to speed up access to new discoveries.
   - Increase public and private funding for Chagas-related R&D including:
     - push mechanisms that include investments for all stages of R&D for new diagnostics and drugs in both the public and private sectors, including in endemic countries
     - pull mechanisms like securing the market through the Strategic Fund (revolving fund) for endemic countries and differential pricing for developed countries, and exploring innovative incentives to catalyse R&D (e.g. price funds, FDA priority review vouchers, etc.)
   - Commit political leadership
     - Adopt a WHO resolution on Chagas disease that addresses the need of more R&D
     - Implement PAHO resolution for elimination of neglected diseases and other poverty related infections.

Recent Scientific Publications on Chagas Disease


Wake Up! Join the Campaign!

By Eric Stobbaerts, Head of DNDi Latin America

In July 2009, DNDi launched its campaign to increase research & development (R&D) for Chagas disease, aimed at finding new and better treatments for patients. The launch of the campaign – with the theme: ‘Wake up now: time to treat Chagas disease’ – took place at the International Symposium organised by Oswaldo Cruz Foundation (Fiocruz) in Rio de Janeiro to mark the 100th anniversary of the discovery of Chagas disease. At a public event on Copacabana beach, researchers and students attending the symposium and Chagas disease patients’ associations pledged their support to the campaign. Brazilian actress, Vera Holtz, volunteered to join the cause as goodwill ambassador for Chagas.

After the launch event in Rio de Janeiro, the campaign gained an international dimension with a series of events in Amsterdam, Buenos Aires, London, Los Angeles, Mexico City and other cities. More information about the campaign can be found at: www.treatchagas.org.
**Sleeping Sickness: WHO has made an improved treatment**

NECT (Nifurtimox-Eflornithine Combination Therapy), has recently been made available to patients and is the first new treatment against human African trypanosomiasis (HAT) or sleeping sickness in 25 years. NECT combination therapy consists of a simplified co-administration of oral nifurtimox and intravenous eflornithine. Developed by DNDi, Epicentre, Médicins Sans Frontières (MSF), the Swiss Tropical and Public Health Institute, and the National Trypanosomiasis Control Programmes of the Republic of Congo and the Democratic Republic of the Congo (IDRC), NECT cuts the cost of treatment by half, reduces the total number of infusions of eflornithine from 56 to 14, and shortens hospitalisation from 14 days to 10. This makes the treatment more convenient for patients.

NECT only requires two infusions a day administered during daytime, which puts less burden on the health staff and makes the treatment far more suitable for remote and resource-poor settings where HAT is being treated. Endemic countries have now begun with the process of ordering the new combination treatment through the World Health Organization (WHO). Until February 2010, the Democratic Republic of Congo, Central African Republic, Chad, Uganda, and South Sudan have accepted NECT as a treatment against HAT in their territories. DRC has received their first 1,000 treatments. More information on www.dndi.org.

**New compound in development for sleeping sickness**

Development of a new compound by DNDi, which has the potential to simplify treatment of human African trypanosomiasis, was announced at the 58th annual meeting of the American Society of Tropical Medicine and Hygiene in Washington DC in November 2009. The drug candidate was developed from chemical technology for new anti-infective drugs licensed by DNDi from the San Diego-based biotechnology company, Anacor, in 2007. This novel technology has been the focus of a DNDi-sponsored drug discovery team at Scynexis Inc. in North Carolina and Pace University in New York and has culminated in the production of the new clinical candidate, SCYX-7158, which will undergo pre-clinical safety testing during 2010. It is anticipated that SCYX-7158 will enter clinical trials as a short-course, oral treatment for second stage sleeping sickness in early 2011.

**Pfizer and DNDi advance international research efforts in the fight against neglected tropical diseases**

Pfizer Inc. and Drugs for Neglected Diseases initiative (DNDi) have signed an agreement that is designed to facilitate advancements in the battle against human African trypanosomiasis (HAT), visceral leishmaniasis (VL) and Chagas disease, which afflict vulnerable populations in the developing world. Under the agreement, Pfizer will have access to the Pfizer library of novel chemical entities in order to screen it for compounds that have the potential to be developed into new treatments. The screening will be undertaken at the Ekinis Institute for Cell and Molecular Therapies, Griffith University in Brisbane, Australia for HAT and the Institut Pasteur Korea, for VL and Chagas disease. Press release on www.dndi.org.

**India and Brazil are among the Top 5 of government funders for neglected diseases**

Key findings of the second G-FINDER report show that nearly US$ 3 billion was spent on making new products for neglected diseases in 2008, but less than 5% was spent on kinetoplastid diseases. Brazil and India ranked in the Top 5 government funders globally, investing US$ 36.8M and US$ 32.5M (1.7%) respectively. The U.S. was the largest government funder (US$ 1.3bn), followed by the European Commission (US$ 129.9M) and the UK (US$ 103.3M). Although this spending almost came to a standstill in 2008, with funding cuts or stagnation everywhere, significant contributions led to a net increase of US$ 105.1m (3.9%). More information on www.thegfnderstitute.org.

**ASTMH 2009 in Washington DC, U.S.**

In November 2009 DNDi attended the American Society of Tropical Medicine and Hygiene (ASTMH) meeting in Washington DC. A joint symposium with sanofi-aventis took place on pharmacovigilance of new anti-malarial treatments. Furthermore DNDi organised a symposium on ASMQ, the fixed-dose combination treatment of artesunate and mefloquine for malaria, and was highly represented in the Kinetoplastida session with several presentations and Isabella Ribeiro, DNDi Senior Project Manager, co-chairing the session. More details on www.dndi.org.

**On the Calendar**

- **31 March - 2 April 2010**
  - 4th East African Health Sciences Congress (EAHSC), Nairobi, Kenya
- **14-18 June 2010**
  - 37th Annual International Conference on Global Health (Global Health Council), Washington, DC, USA
  - www.globalhealth.org/conference_2010/
- **15-20 August 2010**
  - XIIth International Congress of Parasitology (ICOPAH), Melbourne, Australia
  - www.icopah.org/
- **3-7 November 2010**
  - 59th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH), Atlanta, GA, USA
  - www.astmh.org
- **3 December 2010**
  - DNDi Stakeholder Meeting, New Delhi, India

**NEW people at DNDi**

**Scientific Advisory Committee**

- Dr. Federico Gómez de las Heras, retired, former Research Director and Director of Diseases of the Developing World Drug Discovery at GlaxoSmithKline, Madrid, Spain
- Dr. Faustino Terrico, Professor of Parasitology and Infectiology, Universidad Mayor de San Simon, Cochabamba, Bolivia

**Board of Directors**

- **Patient representative:** Prof. Md. Abul Faiz, Professor of Medicine at Sir Salimullah Medical College Mitford, Dhaka, Bangladesh