

DNDi

drugs for neglected
diseases initiative

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PhRMA members spend 81% of R&D in the USA. Of the remaining 19%, 0.2% goes to Africa (\$11m), 0.9% to Asia/Pacific (\$40.3m) and 3% to Latin America (\$140m)

Source: Pharmaceutical Research and Manufacturers of America, Annual Membership Survey, 2002

A New Year Begins

Welcome to 2003. We start the year with the second edition of the DNDi newsletter. This is the year that the initiative will be incorporated as a legal entity and placed firmly in the hands of the Founding Partners. It is also the year that new promising projects will be identified and launched. But before we look into the future let's take stock of the past month...

Meet the Team

Founding Partner Representatives are actively participating in the countdown to incorporation: Bernard Pecoul (MSF), Eloan Dos Santos Pinheiro (Fiocruz), Michele Boccoz (Institut Pasteur), Monique Wasunna (AfricaDNDi), Rob Ridley (TDR), V.Muthuswamy (ICMR), and V.Navaratnam (MOH/ Universiti Sains Malaysia). In addition, an Interim Team is in place and fully functioning. It comprises a group of people working with DNDi full-time, part-time or on secondment, on either coordination or project identification.

Coordination Team:

Yves Champey, a retired medical doctor, with years of experience in the drug development industry, has now taken on the challenge of leading DNDi.

Bruce Mahin, fundraising advisor, was Financial Director of MSF France and gives generously of his time and expertise.

Derrick Wong, strategy and organization advisor is working tirelessly to get the DNDi incorporated by July 2003.

Jaya Banerji, communications expert, striving to make DNDi a household name.

Patricia Martorell, efficient and patient assistant who holds the team together.

Thomas Sagnac, a consultant with Ernst & Young, has been key in developing the DNDi business plan.

Portfolio development team:

Dyann Wirth, professor at the Harvard School of Public Health, is leading the long-term project portfolio team, assisted by **Susan Thomas**.

Els Torreale, co-Chair of the DND-Working Group, is leading the search for short and medium term projects together with **Piero Olliaro**, a member of TDR's Product Research & Development arm.

Upbeat Rio Meeting

In Rio de Janeiro, between 30 November and 3 December 2002, the DNDi core group met, the R & D portfolio teams assessed progress in identification of long and short/medium term projects, and the DND Working Group (DND-WG) held a 2-day forum on creating an enabling environment for R&D for neglected diseases.

The Rio meetings ended with a unanimous confirmation of the belief that there was no time to lose in addressing the fatal imbalance in the R&D of drugs for the diseases that befall the world's poorest people. Scientists and medical professionals from all over the world attended the meeting, which was extensively covered by the Brazilian media. (Copies of the media report as well as the meeting report will be available shortly and can be requested from patricia.martorell@geneva.msf.org)

A Passage to India

Between 7 and 9 January 2003, Yves Champey and Jaya Banerji met with the directors of CDRI (Central Drug Research Institute) Lucknow; Cipla Ltd., Mumbai; and Ranbaxy Laboratories Ltd., Delhi. The primary objective was to urge these institutions and companies to affirm their intent to collaborate with DNDi and confirm access to their R&D expertise and resources/tools. The responses at each meeting were positive and enthusiastic.

CDRI has everything needed for drug discovery from robotic screening, bio- assays, a compound library of 12,000 compounds and over 1,000 scientists. Although 80% per cent of its focus is malaria and TB, it has a good, validated, screening process for leishmaniasis, one of DNDi's three focus diseases. Dr C.M. Gupta, Director CDRI, also agreed to help DNDi develop drugs for developing countries using cheap technology.

Cipla is willing to produce any drug DNDi needs, and sell it at cost. Dr Hamied, MD, also confirmed his willingness to help DNDi on actual projects. The company has agreed to share its expertise in production of actives (APIs).

Ranbaxy's Director-Global Marketing, Dr Purohit, confirmed that the company would be willing to undertake R&D work and share expertise and R&D resources. If targets are identified, they can make the drug.

In addition to these meetings, Yves and Jaya also met Prof Ganguly, Director General of **ICMR**, a Founding Partner of DNDi. Prof Ganguly will attend the Founding Partners meeting on 13-14 March. Dr Vasantha Muthuswamy, Deputy Director, has agreed to be part of an Ethics team put together by James Orbinski and Solomon Benatar, which will present its findings to the Founding Partners in March. She will also write a document on IPR and patent issues, harmonization of regulation between countries, risks to patients, GCP guidelines etc.

A Voyage to the Far East

Bernard Pecoul was in Singapore and Malaysia the week of 20-24 January, presenting DNDi at the Inaugural Symposium of Novartis's new National Institute for Tropical Diseases (NITD). He also met with Dr Mohd. Ismael Merican, Deputy Director General (Research and Technical Support), and the Ministry of

Health, Malaysia, in Kuala Lumpur, to obtain agreement on the DNDi charter. The Malaysian Ministry of Health is a Founding Partner of DNDi.

Nairobi Meetings in the Pipeline

Bernard Pecoul and Els Torreele will present DNDi to the Director of KEMRI, the Kenya Medical Research Institute (KEMRI) on 12-14 February. Dr. Monique Wasunna, KEMRI, is organizing their visit. They also hope to meet with health experts from AMREF and other institutions in Kenya.

This preliminary visit will be followed by another in April when KEMRI and AfricaDNDi will invite scientists, academics, and researchers from Africa to join the move to redress the balance in drug R&D for neglected diseases. This will be the first AfricaDNDi conference.

What exactly are short, medium, and long-term projects?

Identification of appropriate and viable R&D projects is DNDi's raison d'être. The initiative hopes to develop a balanced pipeline of projects taking into account the fact that some might need to be terminated or "dropped out" at any stage of the drug development process. The project portfolio will contain a mix of 3 project categories: existing drugs, existing compounds, and new targets and lead compounds.

Short and medium term projects

Part of these projects aim at making better use of existing drugs, e.g. via extension of indication to DNDi's target diseases, reformulation to better address local needs, improved regimens, or combination treatments. DNDi will also identify existing compound opportunities, which are candidate drugs that have been partially developed but never finalized or registered. Projects that fall into this category are likely to

be acquired in the first few years of operation, i.e. the medium term. The three pilot IDDPs are examples of these types of short-term projects.

Long-term projects

These projects will focus exclusively on screening new targets and lead compounds and on lead optimization and are unlikely to be acquired before 2004. As these projects will start from the early stage of the R&D process, few results can be expected in the short term.

An Interview with Dr Susan Thomas, Member of the Long-term Project Portfolio Team

Dr Susan Thomas, at the Harvard School of Public Health, has been working on the identification of targets and lead compounds for the DNDi long-term portfolio together with Prof Dyann Wirth and Dr Yves Champey. Her interview reveals that the long-term portfolio team hopes to have a comprehensive list of promising targets and lead compounds to present at the Founding Partners meeting in July.

JB: *What will be the benefits of your work to patients suffering from neglected diseases?*

ST: At DNDi we are all working towards one goal - to support innovative strategies to develop drugs for neglected diseases endemic in impoverished countries so that affordable medicines can be made available to patients who most need them.

JB: *What is the objective of a long-term project?*

ST: To identify potential targets and lead compounds. Unlike short and medium term projects that are working with existing drugs and compounds, a long-term project will identify early lead compounds effective against leishmaniasis, trypanosomiasis, and Chagas disease, our focus diseases, and then take them through the entire R&D process. We are

working from scratch, searching for new chemical compounds to kill the parasite. Basically, we must identify the weak point in an organism/ parasite that can be attacked by a chemical compound, as well as a chemical compound that will kill the parasite and has the potential to be developed into a drug.

JB: *How do you identify lead compounds?*

ST: We look for information available in the public domain by using scientific literature searches and by proactively approaching scientists who have reported studies on compounds they have recently tested. There is a lot of information out there - the literature searches are intensive and we have already identified several groups working in this area.

JB: *How long will this process take?*

ST: Identification of potential lead compounds should be completed shortly. We have already begun to compile a preliminary list. What will take time is the process that follows - testing the compounds against the parasite, and for toxicity, and taking them through the path of drug discovery and development.

JB: *What challenges do you foresee?*

ST: Attrition, for one. This happens when a lead compound is tested against a parasite and seems to kill it, but at the trials in animals, toxic side effects appear and the compound either has to be dropped, or modified and then tested again. Drop-outs happen often and this makes the process enormously time-consuming.

Another challenge will be to work with groups of scientists that are in different geographic locations - we will need to develop mechanisms to share information, access, and progress, and to decide the next steps.

JB: *What kind of collaborations would be most useful in your work?*

ST: We hope to be working with senior scientists from the pharmaceutical industry,

leaders in the academic scientific community, and leaders in the public health community. After we have a list of targets and lead compounds, we will present the most promising ones to a panel of experts, who will help us decide which of these are the most viable. This is crucial assistance.

JB: *What has been the progress so far?*

ST: We have compiled a list of potential targets and lead compounds, which is updated as new information becomes available. At present we have identified around 5 potentially promising targets and lead compounds for leishmaniasis, 10-15 for Chagas, and over 15 for trypanosomiasis. We should have a reasonably comprehensive list by July.

DNDi's credibility is already quite high and growing. Many scientists I have approached have expressed a great deal of interest in DNDi's work. I am getting lots of positive feedback and calls from them. But much work remains to be done.

IDDP Update

The three pilot Immediate Drug Development Pilot Projects (IDDPs) based on existing drugs and compounds continue apace.

At the University of Bordeaux II, France, and Far Manguinhos, Brazil, work is currently focused on the refinement of formulations for the **two artesunate-based fixed dose combinations (ACTs)** for chloroquine-resistant malaria. In addition, toxicology studies are well underway and assay methodologies have been developed at the University of Malaysia. This know-how is being transferred to other partner institutions.

In India, **Paromomycin** trials have begun under the initiative of TDR, ICMR, and IOWH. The results will hopefully help DNDi register the

drug in African countries as a treatment for leishmaniasis.

topics, please write to jaya.banerji@geneva.msf.org

Ranbaxy Laboratories, India, recently informed DNDi that it has the capability to manufacture Paromomycin. This will need to be further explored.

Your suggestions are welcome.

Communications Round up

A **DNDi database** is in the process of being created and proposals are in from vendors for a **DNDi website**. The domain name has yet to be finalized.

Documents: *DNDi: An Innovative Solution*, a 10-paged document, is complete. (Copies of this document can be requested from patricia.martorell@geneva.msf.org)

DNDi Events in 2003

- Founding Partners Meeting: 13-14 March, Institut Pasteur, Paris
- AfricaDNDi conference: April, Nairobi
- Incorporation of DNDi: July, Geneva
- DNDi Asia Conference: October-November, Malaysia (to be confirmed)

Opportunities to Spread the Word

- Campaign Bi-annual Meeting: April, Geneva
- Tropical Communicable Disease Workshop: 28 Apr-1 May, Rio de Janeiro
- Culmination of Flytrap Exhibition: mid-May, Washington
- G8 Summit: June, Evians-les-Bains, France
- TDR Annual Meeting: 23-25 June, Delhi
- BIO (Biotech Industry Organisation): 22-25 June, Washington

Contact us

If you wish to contribute to the newsletter or would like to comment on any of the above