

NO TIME TO WAIT

Overcoming Gaps in TB Drug Research and Development

January 11-12, 2007 | The Cornell Club, 6 East 44th Street, New York City



A Médecins Sans Frontières/Doctors Without Borders Symposium supported by Howard P. Milstein and Weill Cornell Medical College's Abby and Howard P. Milstein Program in Chemical Biology

DAY 2: Friday January 12, 2007

All sessions and breaks will be conducted in the Ivy Room, 4th Floor, unless otherwise noted.

8:00-9:00 **Coffee and Breakfast**

9:00-12:30 **Working Group Discussions/Workshops**

GROUP 1: Filling the Gap in TB Drug Discovery

Ivy Room, 4th Floor

GROUP 2: Building Clinical Trial Capacity

Library, 3rd Floor

GROUP 3: Accelerating Clinical Development: MDR-TB Trial Design as a Possible Way Forward

Fall Creek Room, 5th Floor

12:30-14:00 **Lunch Break + Time for Moderators to Prepare Breakout Discussions**

14:00-15:30 **Presentation of Working Group Sessions and Discussions**

14:00-14:30 **Presentation of Working Group 1**

14:30-15:00 **Presentation of Working Group 2**

15:00-15:30 **Presentation of Working Group 3**

15:30-15:45 **Concluding Remarks:** Tido von Schoen-Angerer, MD

Director, Campaign for Access to Essential Medicines, Médecins Sans Frontières

Friday January 12, 2007

WORKING GROUP 1: Filling the Gap in TB Drug Discovery (9:00-12:30)

Ivy Room, 4th Floor

Chairs:

Ken Duncan, PhD, *Senior Program Officer, Bill and Melinda Gates Foundation*

Christine Sizemore, PhD, *Chief of TB, Leprosy, and other Mycobacterial Diseases Section, NIAID/NIH*

Short Start-up Presentations (9:00-9:40)

Access to Chemical Genetics Facilities; Access to Compound Libraries

Carl Nathan, MD, *R.A. Rees Pritchett Professor of Microbiology, Professor Microbiology, Immunology, and Medicine, Chairman, Department of Microbiology and Immunology, Weill Cornell Medical College*

Large Consortia as a Possible Way Forward?

Stuart Cole, MD, *Director of the Bacterial Molecular Genetics Unit, Institute Pasteur*

Effective Collaboration Between Academia and Drug Developers – What Can Academia Contribute to the Pharmaceutical Industry?

Federico Gomez de las Heras, PhD, *Research Director of Diseases of the Developing World, GlaxoSmithKline*

Filling the Gap: Phenotypic Screening, TI/TV, or Both?

Koen Andries, DVM PhD, *Distinguished Research Fellow, Tibotec*

Objective:

Identify practical improvements and organizational solutions required to ensure that the public and private sector work in line to boost TB drug discovery initiatives.

Key issues to be addressed:

- Situation analysis: What are the advantages and disadvantages of current initiatives and efforts to fill this gap?
- Needs assessment: What the scientific academic community needs in order to actively contribute to drug discovery?
- Which practical solutions are possible to address the existing needs?
- How to encourage effective collaboration among academia and drug developers?
I.e. definition of criteria that validated target or hit to lead should meet in order to be taken in consideration by pharmaceutical companies
- Effective funding mechanisms
-What funding mechanisms are more suitable for early stage drug discovery projects?
- Intellectual properties issues
-Academic IP policies & neglected diseases
-Handing over innovation to not-for-profit product development

Expected Outcomes:

- Organizational solutions to ensure standardized validation of potential molecular targets.
- Outline organizational solutions to ensure and increase the access to HTS facilities and Medicinal Chemistry expertises.
- Outline strategies to ensure wider access to compound libraries.
- Define the most effective funding strategies to sustain the required new initiatives in the field of drug discovery.
- Identify international and national agencies responsible for implementing the required actions.

Background Material:

Carl Nathan, *Nature*, 2004; Pedro Cuatrecasas, *The Journal of Clinical Investigation*, 2006; Development of new drugs for TB chemotherapy, MSF Campaign for Access to Essential Medicines, 2006; Nwaka and Hudson, *Nature Review Drug Discovery*, 2006

WORKING GROUP 2: Building clinical trial capacity (9:00-12:30)

Library, 3rd Floor

Chair:

Richard Chaisson, MD, *Professor of Medicine, Epidemiology and International Health & Director, Center for Tuberculosis Research, Johns Hopkins University*

Short Start-up presentations (9:00-9:40)

Clinical Trial Sites – Global Capability Assessments

Christo van Niekerk, MD FCPaed MFPP, *Clinical Research Scientist, Global Alliance for TB Drug Development*

Ethical and Regulatory Oversight – Bridging the Gap

Alwyn Mwinga, MB ChB MSc Mmed, *Associate director, CDC Zambia*

The Brazilian Experience in Developing Clinical Trials

Renata Guerra, MD, *Hospital Universitário Clementino Fraga Filho, Rio de Janeiro & Center for Tuberculosis Research, Johns Hopkins School of Medicine, Baltimore*

Combating TB Together: The Role of Partnerships and Networks in Capacity Building

Thoma Nyirenda, BSc MB BS MPH, *South-to-South Networking Manager, European and Developing Countries Clinical Trials Partnership (EDCTP)*

Objective:

Discuss the ability of high-burden countries to conduct and monitor clinical studies and outline a plan of action to address shortcomings and build capacity.

Key issues to be addressed:

- What are the global needs for clinical trial capacity given different study needs?
- What short and medium term measures should be adopted to increase human capacity to conduct and monitor trials?
- What are the major challenges in getting studies approved by local regulatory authorities?
- What are possible effective strategies in upgrading lab and infrastructure needs?
- How can partnerships and networks help foster collaboration and build capacity?

Expected Outcomes:

- Outline basic elements of a global framework to increase capacity to conduct and monitor clinical trial in high-burden countries.
- Outline actions that need to be taken in order to build capacity in the following areas:
 - National oversight – IRBs, regulatory reviews
 - Human resources and training
 - Infrastructure and logistics
 - Partnerships and networks
- Assign responsibilities to various international and national agencies in addressing issues.

Background Material:

Excerpts from *The Global Plan to Stop TB 2006 – 2015*; Ebi Kimanani, *Clinical Trial Capacity in East Africa: A Pilot Survey, Drug Information Journal*; The TB Trials Consortium: A Model for Clinical Trials Collaborations, 2001, *Public Health Reports*

WORKING GROUP 3: Accelerating Clinical Development: MDR-TB Trial Design as a Possible Way Forward

Fall Creek Room, 5th Floor

Chairs:

Kenneth Castro, MD, *Director, Division of TB Elimination, Centers for Disease Control and Prevention*
Mark Harrington, *Executive Director, Treatment Action Group*

Short start-up presentations (9:00-9:40)

David McNeeley, *Director Global Clinical Development, Tibotec*
Karel De Beule, *PharMD, MBA, Compound Development Team Leader Tibotec*
Leonard Sacks, MD, *Office of New Drugs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration*
William Burman, MD, *Study Chair, TBTC, Denver Health and Hospitals*
Carole Mitnick, Sc.D., *Department of Social Medicine, Harvard Medical School*

Objective:

Proposals for MDR-TB study design taking into account advantages, disadvantages, and major challenges in implementing.

Key issues to be discussed (9:45-10:45)

- How can preclinical studies in animal models for MDR-TB contribute to clinical studies?
- Risk of giving the new drug as a monotherapy/Difficulties on identification of an optimized background in MDR-TB trials. Is this a concern?
- Efficacy of an MDR-TB regimen: How to do design MDR-TB studies? Which endpoints to choose?
- Possible role of “compassionate use” or open-label trials for MDR and XDR-TB including data obtainable on drug safety and efficacy?
- What trials are needed in order to maximize efforts? Which clinical studies need to be run in order to solve some critical open questions (i.e evaluation of surrogate markers and endpoints, pharmacokinetics studies to evaluate drug interaction)
- What clinical parameters may be important in establishing inclusion/exclusion criteria, and in stratifying the analysis of patients in an MDR-TB trial? Are there multi-pronged approaches that should be used in MDR-TB trials—different populations, different endpoints etc?
- How do we move from MDR-TB to drug sensitive TB, or how should studies for both indications be harmonized or coordinated?
- What organisms and funding bodies should take an active role in boosting clinical research activities?

Break-Out Session (10:45:11:45)

Two separate groups will break-out to propose a trial design for MDR-TB and other complementary compassionate use programs.

Expected outcomes:

1. Basic elements of a study design for MDR-TB that can be implemented to test new compounds when they will be ready for efficacy trials
2. Priority list of necessary clinical studies that need to be performed to feed critical information into developing an optimal trial design for MDR-TB
3. Criteria for clinical trial sites in order to be suitable for MDR-TB trials

Background material:

Minutes, TB Alliance Meeting, November 10, 2006
Clinical Trials of MDR-TB, Charles R. Horsburgh, December 2006