New Diagnostics Working Group

2009 progress report

Giorgio Roscigno & Madhukar Pai
Co-chairs

Andy Ramsay & Martine Guillerm
Secretariat

www.stoptb.org

The Vision of the NDWG

- To develop and introduce cost-effective and appropriate new diagnostic tools that will contribute towards improved control of the global TB epidemic and improve the quality of patient care

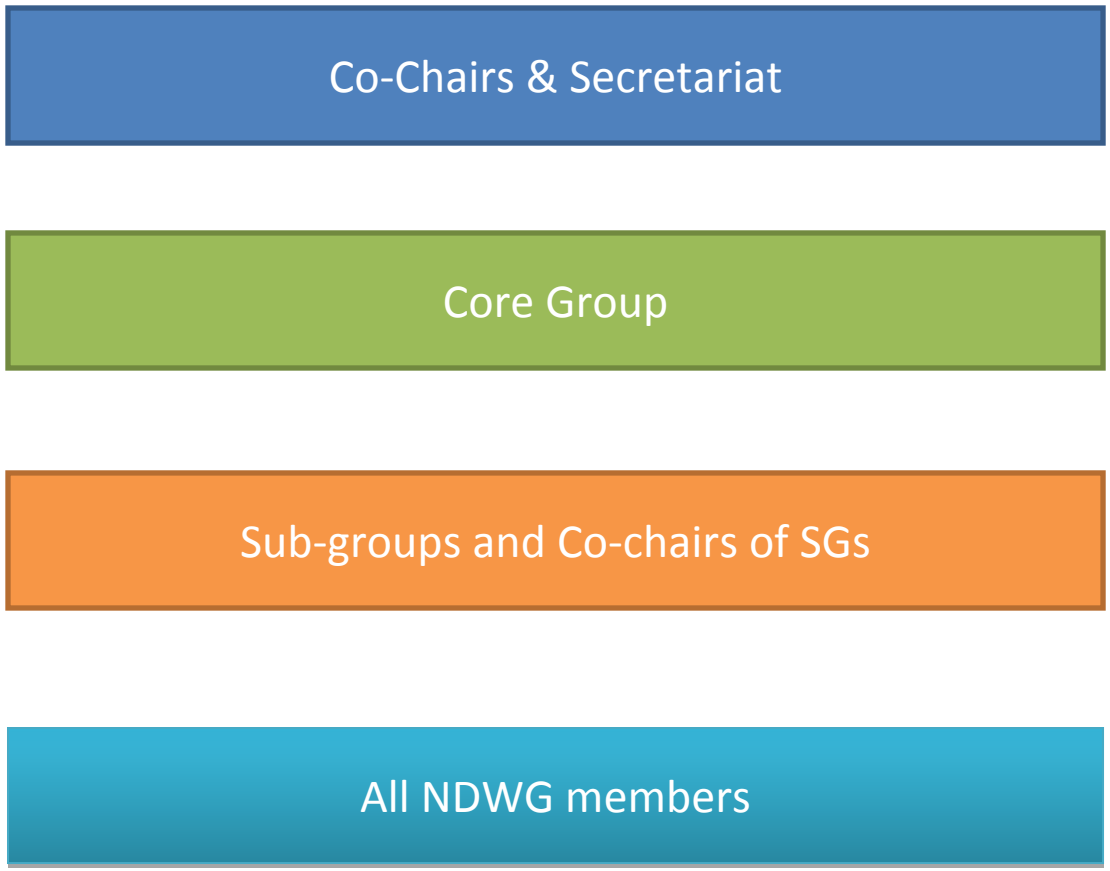
Overall Goals

- To improve TB case detection both through higher sensitivity/specificity and improved accessibility – simple, accurate, cost-effective, same day, near-patient products that perform equally well in HIV-infected persons and children, and improve patient important outcomes

- Rapidly and inexpensively identify drug resistant TB disease in all patients, including people living with HIV infection and children, enabling timely effective patient treatment to reduce both individual morbidity and continuing transmission

- Accurately and reliably identify latent TB infection and define the risk of future progression to active disease enabling rational and targeted use of preventive therapy in appropriate subjects, especially child contacts and people living with HIV/AIDS

NDWG structure



New Diagnostic Working group
Core Group Members

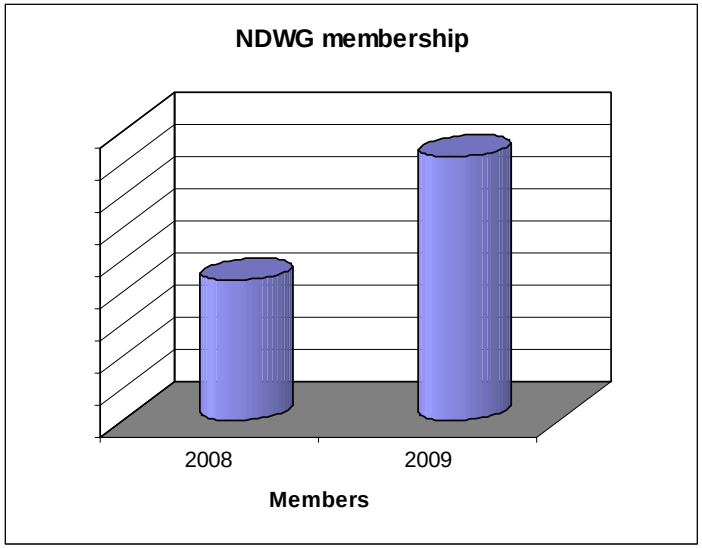
Academia	Arend Kolk, *University of Amsterdam, Netherlands*
Diagnostics manufacturer	Jean-Francois de Lavison, *EDMA, Belgium*
NGOs	Francis Varaine, *MSF, Paris*
NTP	Charles Sandy, *NTP, Zimbabwe*
National TB Reference Laboratory	vacant
Patient community	Savita Luka, *New Delhi, India* Mayowa Joel, *Lagos, Nigeria*
WHO Stop TB Partnership	Christian Lienhardt, Stop TB Partnership, Geneva
Lab Capacity Strengthening Sub-Group	John Ridderhof, *CDC, Atlanta, USA*
Diagnostics developer	Mark Perkins, *FIND, Geneva, Switzerland*
Int. Union against TB and Lung disease	Anne Detjen, *TREAT TB team, NY, USA*

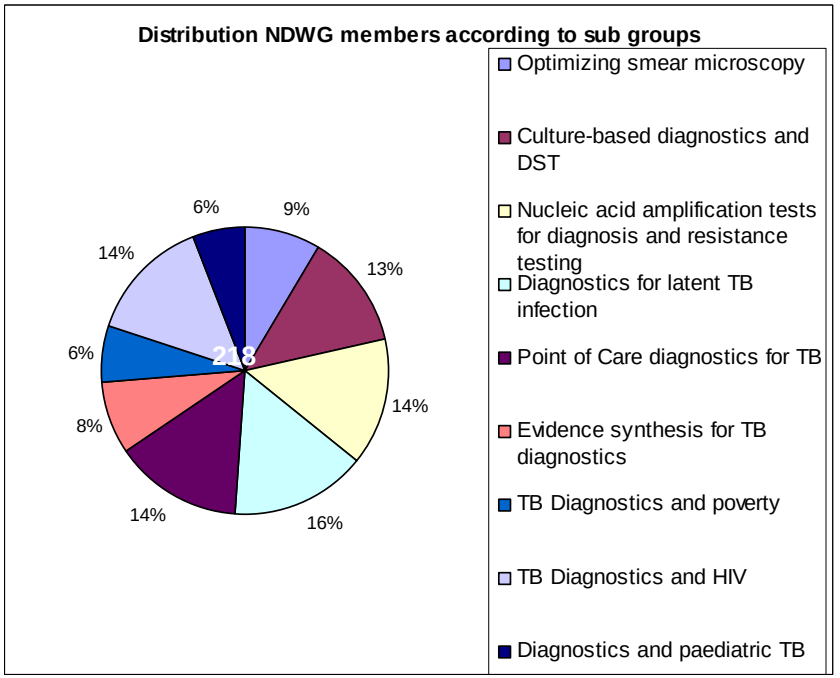
New Diagnostics Working Group
Sub Group Leaders

Rick O'Brien, FIND, Geneva, Switzerland Karen Steingart, University of California, USA	Evidence Synthesis for TB diagnostics
Tom Shinnick, CDC, Atlanta, USA Leen Rigouts, ITM, Antwerp, Belgium	Nucleic-acid amplification techniques for TB, including detection of drug resistance
Bertie Squire, Liverpool School of Tropical Medicine, UK Gillian Mann, Liverpool School of Tropical Medicine, UK	TB Diagnostics and Poverty
Keertan Dheda, University of Cape Town, South Africa Philip Hill, University of Otago, New Zealand	Diagnostics for Latent TB infection
Ruth McNerney, London School of Hygiene and Tropical Medicine, UK Catharina Boehme, FIND, Geneva, Switzerland	Point of Care Tests for TB
David Moore, Universidad Peruana Cayetano Heredia, Lima, Peru Nicolas Durier, Family Health International, Thailand	Culture-based diagnostics for TB, including drug susceptibility testing
Luis Cuevas, Liverpool School of Tropical Medicine, UK Paul Klatser, KIT, Netherlands	Optimizing TB smear microscopy
Colleen Adel Daniels, WHO Stop TB Dept, Geneva, Switzerland Barbara Laughon, NIH, USA	TB Diagnostics and HIV
Anneke C. Hesseling, Stellenbosch University, South Africa Steve Graham, The Royal Children's Hospital, Melbourne, Australia	Diagnostics and paediatric TB

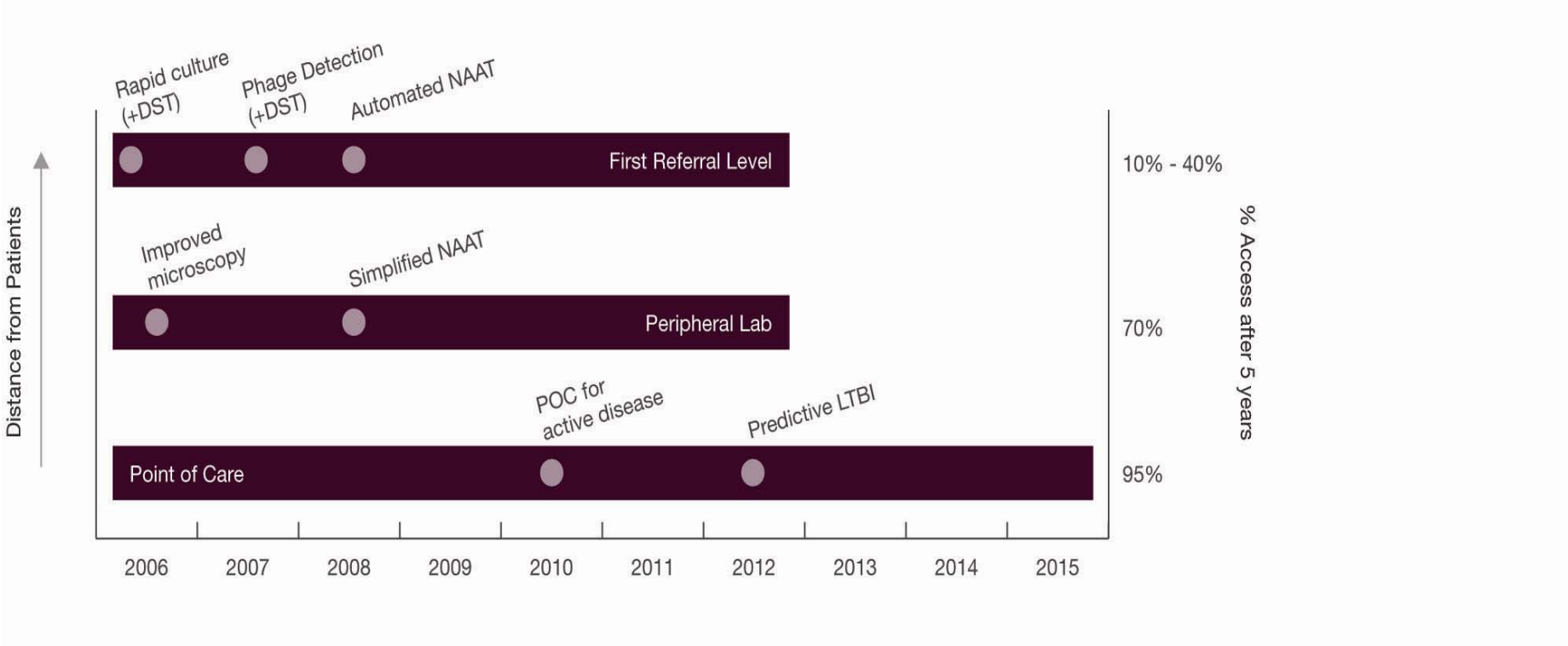
NDWG structure

- New Paediatric TB Subgroup established
- Nomination and election of four new Core Group members and four Subgroup Co-Chairs
- Total membership doubled in the last year (400+ now)





Progress in meeting Global Plan targets



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THE GLOBAL PLAN TO STOP TB 2006-2015

Global Plan: Progress Report 2006 – 2008

Published: November 2009

Table 6: Global Plan Milestones for New Diagnostics

GLOBAL PLAN INDICATOR	TARGET	PROGRESS
REFERRAL LEVEL		
Rapid culture (+DST) for M. tuberculosis and diagnosis of MDR-TB	2006	Endorsed by WHO in 2007
Rapid speciation test for confirming M tuberculosis grown in culture	2008	Endorsed by WHO in 2007
Manual nucleic acid amplification test (NAAT) for detection of M tuberculosis and isoniazid and/or rifampicin resistance	2008	Endorsed by WHO in 2008
Automated NAAT for detection of M tuberculosis and rifampicin resistance	2008	Expected 2010
PERIPHERAL LABORATORY		
Improved microscopy	2006	More sensitive definition of a smear positive case: endorsed by WHO in 2007 Reduced number of smear examinations required: endorsed by WHO in 2007 Light-emitting diode (LED) flurorescene micros-copy - approval by WHO expected in 2009 Front-loaded smear microscopy - approval by WHO expected in 2009
Introduction of simplified NAAT (1)	2008	Expected 2011

[1] http://www.who.int/tdr/

[2] http://www.stoptb.org/retooling/

[3] New laboratory diagnostic tools for tuberculosis control (ISBN 978 92 4 159748), World Health Organization, 2008.

However, not all targets were met; pipeline has grown and right shifted

Summary of technologies			Estimated costs			
Technology	Description	Product	Training[1]	Infrastructure[2]	Equip.[3]	Consumables
WHO-endorsed tools (2006-2008)						
Liquid culture	Commercial broth-based culture systems detect TB bacteria (manual and automated systems are available); can be configured for DST.	BacT/ALERT 3D; MGIT	Extensive (3 weeks)	■■■	High	High
Molecular line probe assay	Strip test simultaneously detects TB bacteria and genetic mutations that indicate isoniazid and/or rifampicin resistance.	GenoType® MTBDR and MTBDRplus; INNO-LiPA Rif.TB	Moderate (3 days)	■■ to ■■■	High	High
Strip speciation	Strip speciation test detects a TB-specific antigen from positive liquid or solid cultures to confirm the presence of TB bacteria in culture samples.	Capilia TB Rapid Diagnostic Test	Minimal (1 day)	■■■	Low	Medium
Tools in late-stage development/evaluation						
Automated detection and MDR screening	Device allows automated sample processing, DNA amplification and detection of *M. tuberculosis* and screening for rifampicin resistance.	Cepheid GeneXpert device and Xpert MTB cartridge	Minimal	■	High	High
Colorimetric redox indicators	Technique detects isoniazid and rifampicin resistance in culture samples after incubation with redox dyes.	Non-commercial method (Resazurin)	Extensive	■■■	Low	Medium
Front-loaded smear microscopy	Based on 2 or 3 specimens but aims to examine specimens on the day that patient presents to the health service (thus identifying 95% of TB cases).	n/a	Minimal	■	Low	Low
Interferon gamma release assay	Blood test detects specific cellular immune responses indicating TB infection.	QuantiFERON®-TB Gold In Tube; T-SPOT.TB®	Moderate	■	Low	High
LED fluorescence microscopy	Robust fluorescence microscopy (FM) systems based on light-emitting diodes (LEDs) that could allow the advantages of FM at levels of the health system where conventional FM would be impractical.	Fraen	Moderate	■	Medium	Low
		LW Scientific	Moderate	■	Medium	Low
		Zeiss	Moderate	■	Medium	Low
Microscopic Observation Drug Susceptibility (MODS)	Manual liquid culture technique uses basic laboratory equipment (incl. an inverted light microscope) and microscopy skills to detect TB bacteria.	Non-commercial method	Extensive	■■ to ■■■	Medium	Medium
New solid culture methods	Solid culture technique measures nitrate reduction to indicate isoniazid and rifampicin resistance.	Non-commercial method (Nitrate reductase assay)	Moderate	■■ to ■■■	Low	Medium
	Solid culture technique simultaneously detects TB bacteria and indicate isoniazid and rifampicin resistance.	Non-commercial method (Thin layer agar culture)	Extensive	■■ to ■■■	Low	Medium

Tools in early phase of development

Tool	Level of health system	Tool	Level of health system
Breathalyser screening test	Community or point-of-care	Sodium hypochlorite (bleach) microscopy	Peripheral laboratory
First-generation loop-mediated isothermal amplification technology platform (LAMP)	Peripheral laboratory	Sputum filtration	Peripheral laboratory
Lipoarabinomannan (LAM) detection in urine	Peripheral laboratory	TB Patch Test	Health post
Phage-based tests	Reference laboratory	Vital fluorescent staining of sputum smears	Peripheral laboratory

[2]Key	Description
■	Basic laboratory[4]; no specialized biosafety equipment.
■■	Biosafety level 2. Specialized biosafety equipment required, such as biosafety cabinet.
■■■	Biosafety level 3. Biosafety cabinet and other primary safety equipment required. Controlled ventilation system that maintains a directional airflow into the laboratory required.

[1]Estimates assume that technicians are already trained in existing TB diagnostic techniques (such as smear microscopy and culturing) and the necessary laboratory safety precautions.
[3]Product prices may vary depending on geographical location and terms of supply. Ranges are indicative only: Low (minimum-2000 US$); Medium (2001-7000 US$); high (7001+ US$).
[4]Detailed information available in the WHO Laboratory Biosafety Manual: http://www.who.int/csr/delibepidemics/WHO_CDS_CSR_LYO_2004_11/en/.

World Health Organization & Stop TB Partnership. New laboratory diagnostic tools for tuberculosis control. World Health Organization, Geneva, 2008

RTF and NDWG

Updating Global Plan to Stop TB

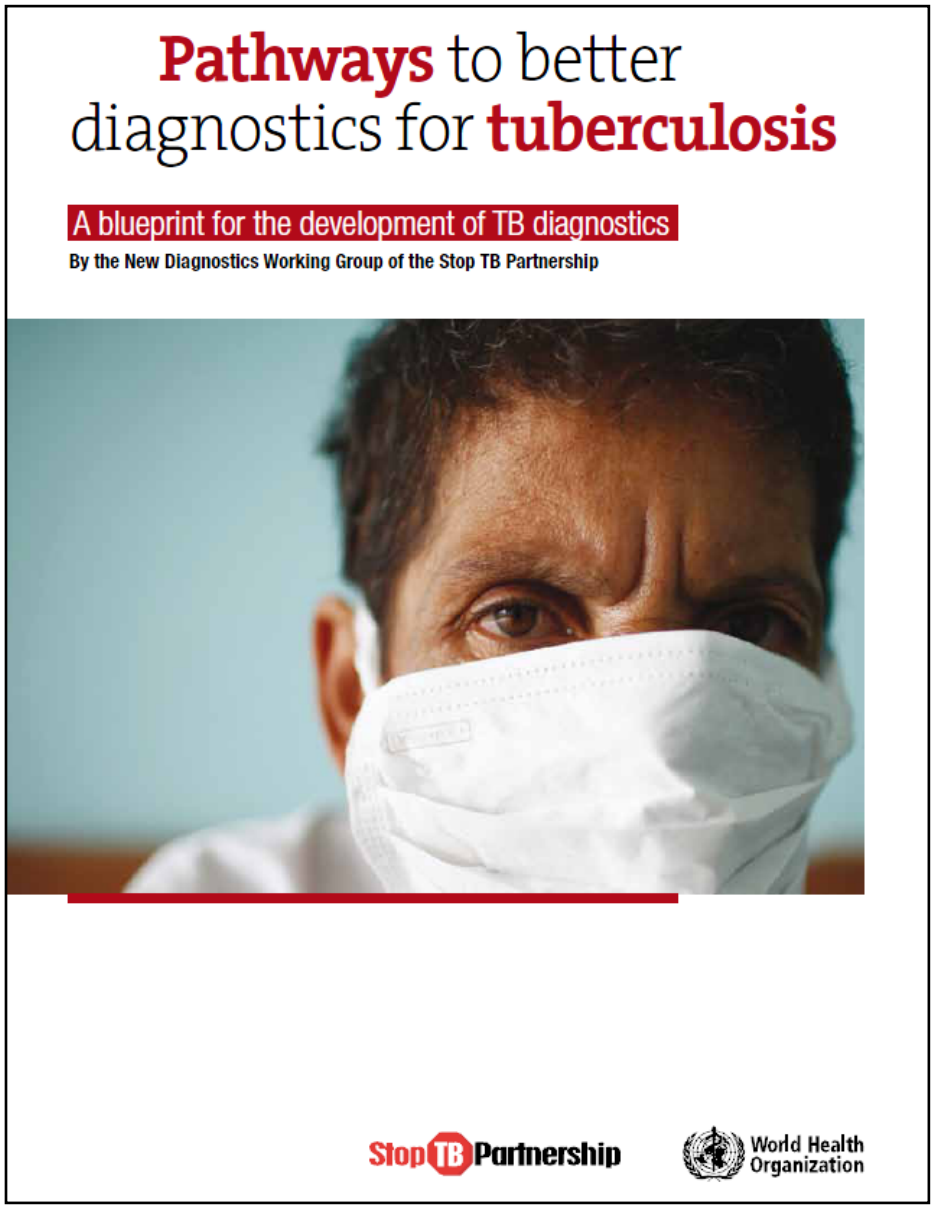
Updating the Research and Development component of the Stop TB Partnership's Global Plan to Stop TB, 2006-2015

A Workshop held in Geneva on 24-25 September 2009

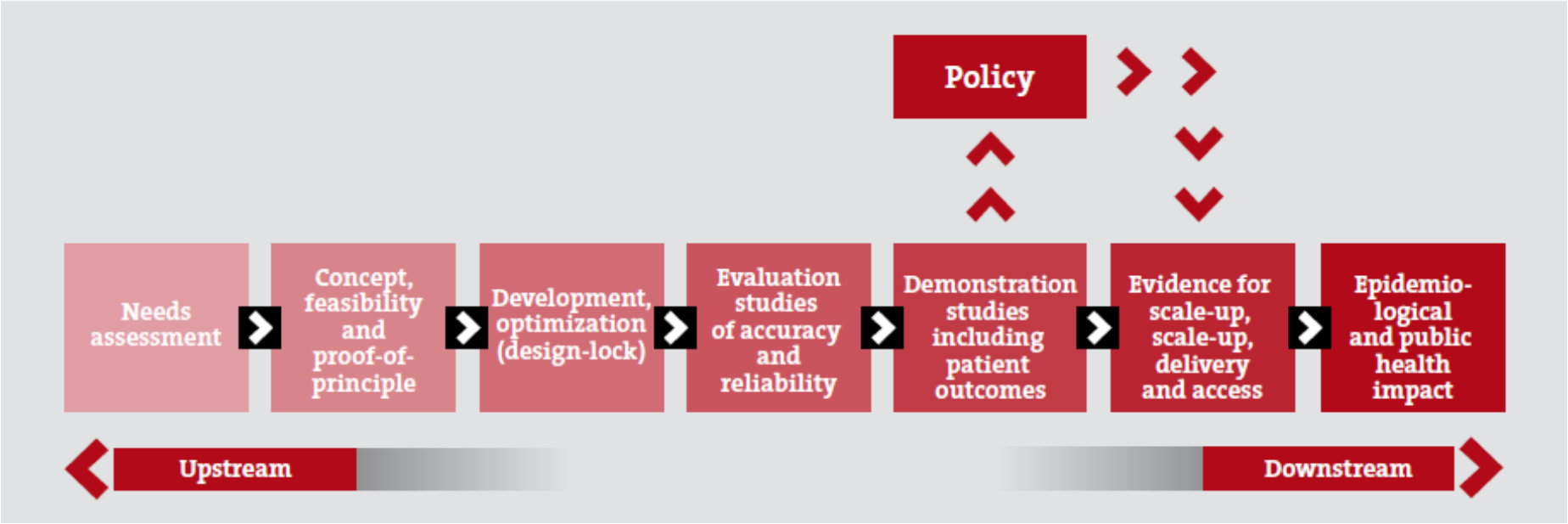
1. To review and update the goal, objectives, major activities, indicators and targets for the new drugs, new diagnostics and new vaccines components of the Global Plan to Stop TB for the period 2010–2015
2. To estimate the funding needed to implement the major components of the research agenda/workplan during the period 2010–2015, including identification of potential funding gaps

New publication

Available on NDWG website:
http://www.stoptb.org/wg/new_diagnostics/



Promoting a standardized pathway to develop TB diagnostics



ANNEXES - see CD in back cover

The principles of current TB diagnostic tools

30+ contributors

Contributors are listed in alphabetical order.

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Bertie Squire, Clinical Tropical Medicine, Liverpool School of Tropical Medicine

Francis Varaine, TB Working Group, Médecins sans Frontières, Geneva, Switzerland

These experts' contributions have undergone a thorough review at all stages, and in addition to several of the contributors themselves, the following are to be thanked for having given their time to ensure this document is an up-to-date and accurate reflection of the subject matter: Heidi Albert, Peter Anderson, Jean-François de Lavison, Peter Kaspar, Sang-Jae Kim, Gerd Michel, CN Param, Richard Urbanczik and Véronique Vincent.

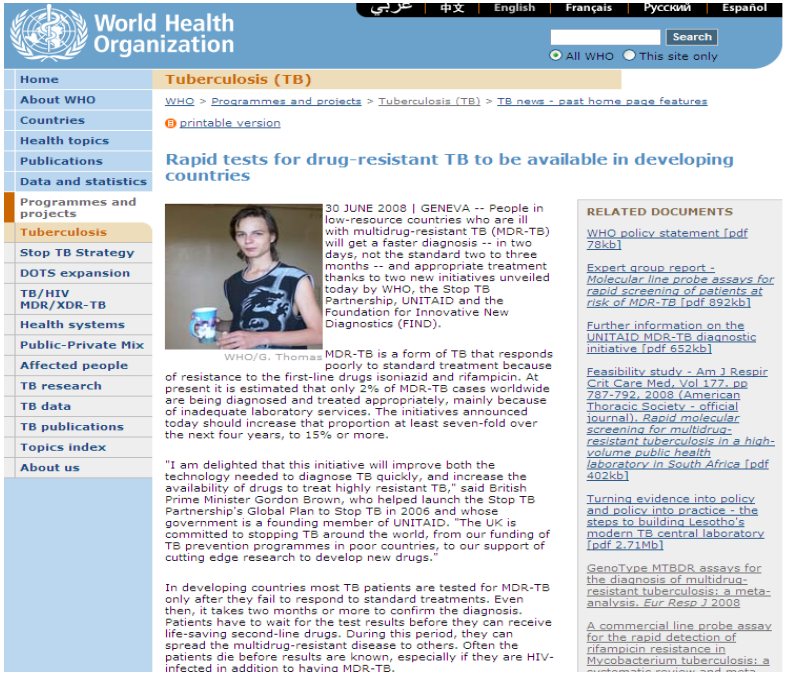
Special thanks to:
Russell Dacombe, Tony Murdoch & Martine Guillerm

UNITAID project launched in June 2009

- WHO endorsed line probe assays in 2008
- Project to provide rapid diagnostics for MDR-TB in 27 endemic countries
- Collaboration between WHO, Global Laboratory Initiative, FIND and Global Drug Facility

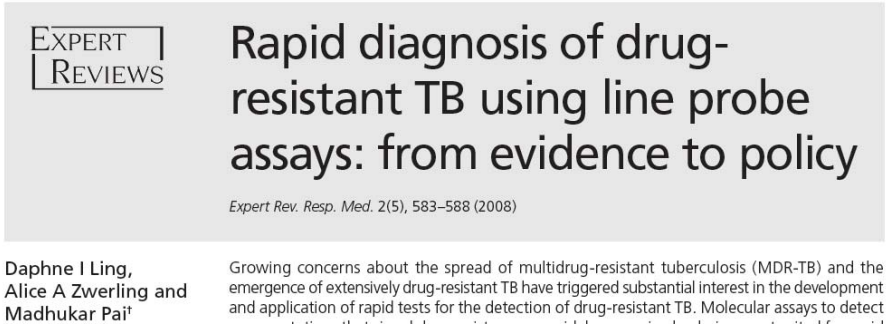
UNITAID TOGETHER TO HEAL

POLICY → ACTION



http://www.who.int/tb/features_archive/mdrtb_rapid_tests/en/index.html

http://www.unitaid.eu

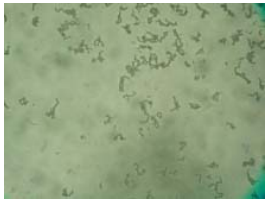


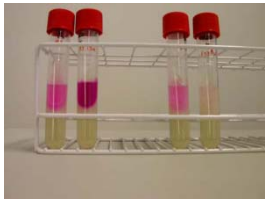
EXPAND-TB supplies MDR-TB diagnostics to high-burden countries. With a new grant of US$ 61 482 085, the project, led by the GLI in close collaboration with FIND and GDF, will be expanded to increase the countries covered from 16 to 27. The overall objective is to jump-start strengthening of laboratories in these countries, through collaboration between a variety of partners.

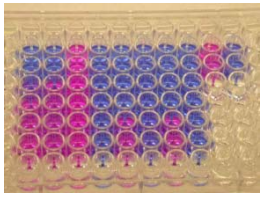
WHO policy reviews in 2009

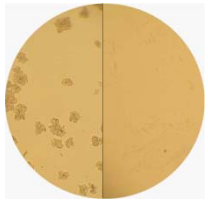
Expert Group meetings in Sept 2009
STAG-TB review in Nov 2009 (recommendations pending)

- Microscopy
  - LED microscopy
  - Sputum processing
  - Front-loaded approaches
- Non-commercial DST and phage-based methods
  - MODS
  - TLA
  - NRA
  - CRI
  - Phage assays









Point-of-care diagnostics Sub-Group organized symposium at ESM 30th annual congress Porto

SYMPOSIUM SPONSORED BY STOP-TB WORKING GROUP ON NEW DIAGNOSTICS, POINT OF CARE SUB GROUP
A SYMPOSIUM ON POINT-OF-CARE TESTS FOR TUBERCULOSIS

Dr. Catharina Boehme, M.D., Foundation for Innovative Diagnostics (FIND) (Geneva, Switzerland)

What is a POC test?

Carol Nawina Nyirenda (Zambia)

Why do we need rapid tests: a patient's perspective?

Prof. Rosanna Peeling, Ph.D., London School of Hygiene & Tropical Medicine (London, UK)

Rapid tests for TB: what is wrong with them?

Dr. Gerd Michel, Ph.D., Foundation for Innovative Diagnostics (FIND) (Geneva, Switzerland)

Biomarker discovery: are we making progress

Dr. Ruth McNerney, Ph.D., London School of Hygiene & Tropical Medicine (London, UK)

Volatile markers for TB: myth or reality?

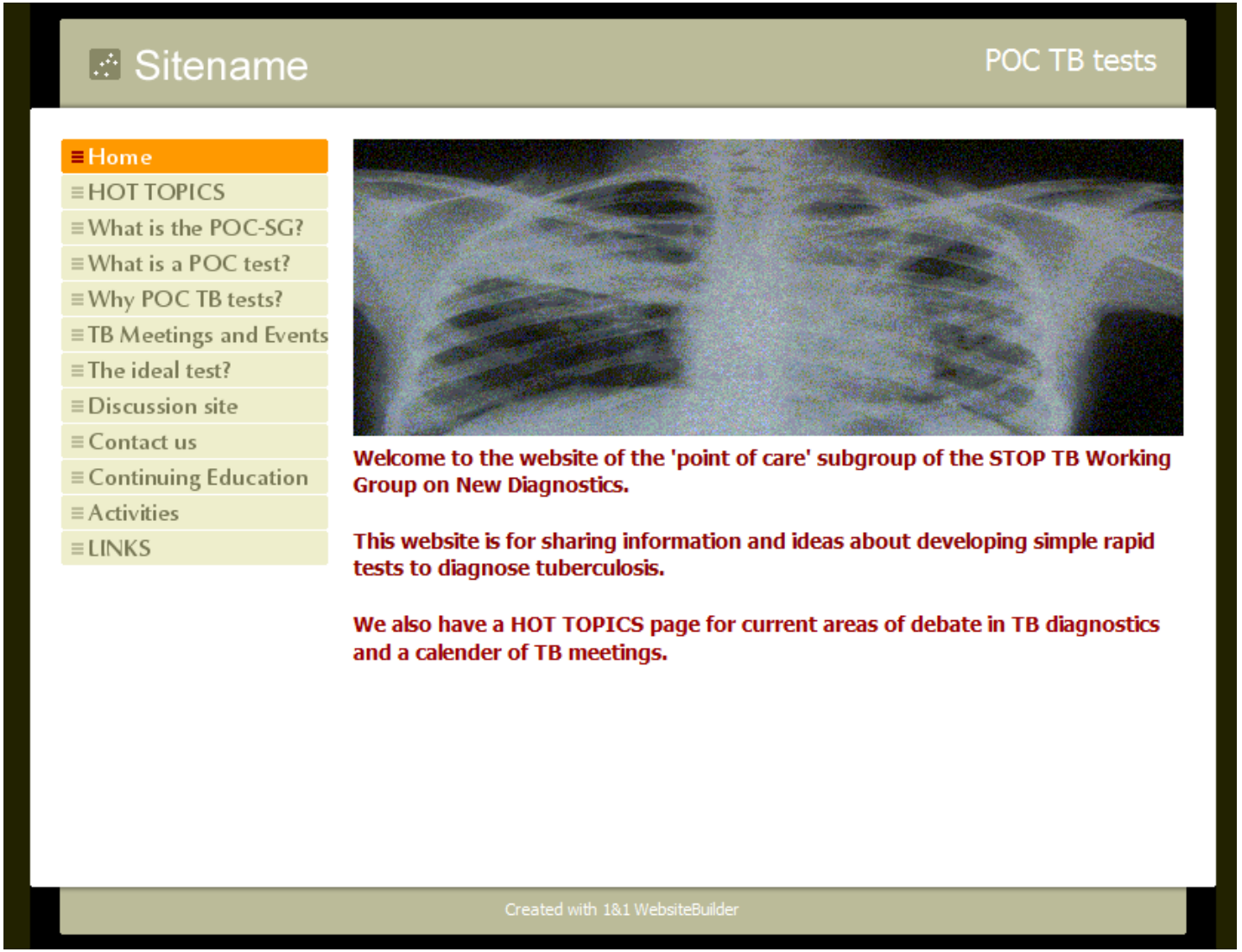
Dr. Amy P Wong, Ph.D., X PRIZE Foundation (California, U.S.A.)

Barriers to TB test development

Discussion: The way forward

Platform and floor

http://www.tbdiagnostics.org/



New Diagnostics Working Group website updated

Stop TB Partnership

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Working Group on New Diagnostics

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News

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Affiliations

FIND

TDR

Royal Tropical Institute

CDC

Médecins Sans Frontières

Merieux Alliance

The International Union of TB and Lung Diseases

McGill University

World Health Organization

Liverpool School of Tropical Medicine

25 November 2009

ANNUAL MEETING NEW DIAGNOSTICS WORKING GROUP

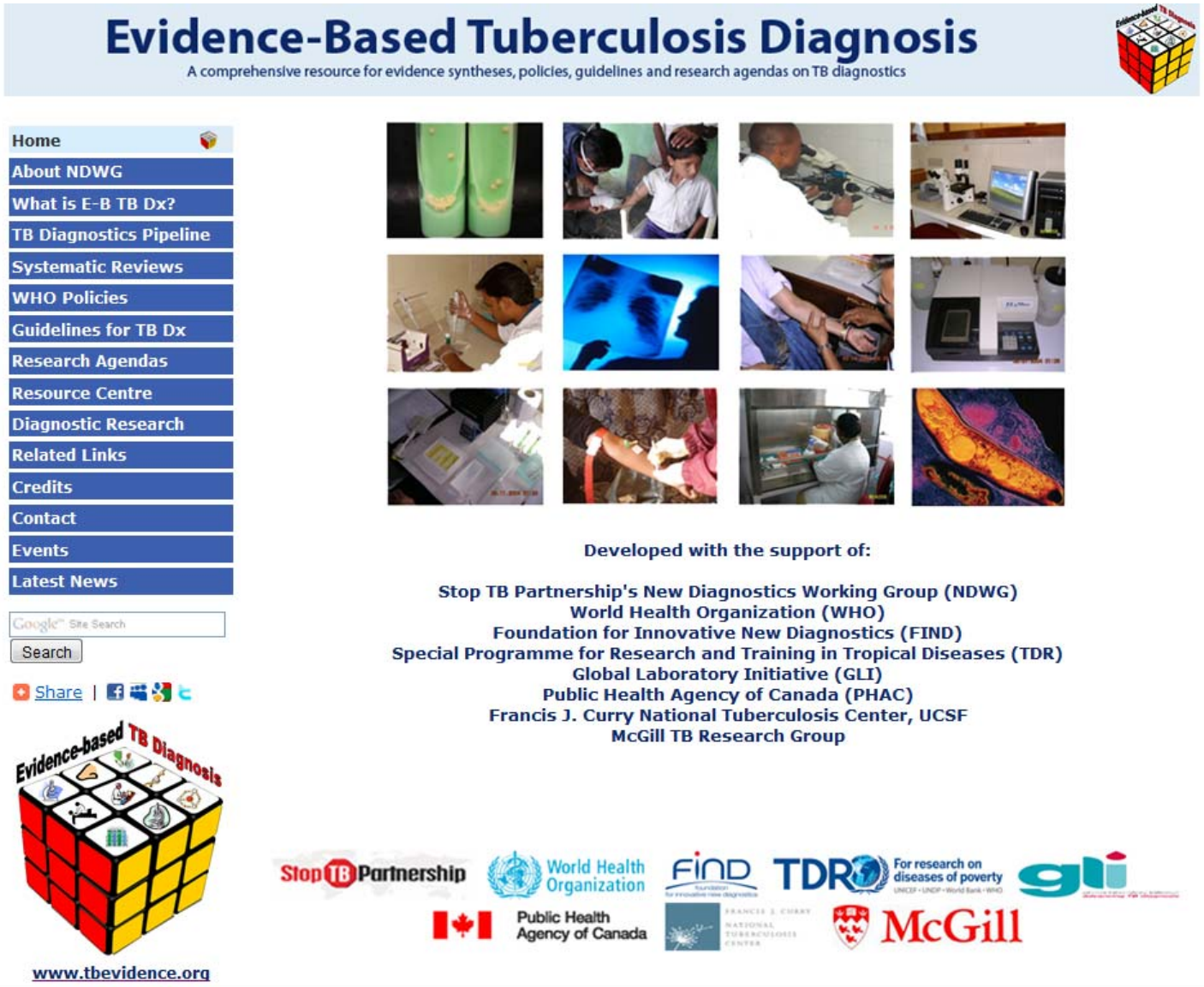
The Stop TB Partnership New Diagnostics Working Group is holding its annual meeting in Cancun, Mexico, in conjunction with the 40th Union World Conference on Lung Health.

The Secretariat and Co-Chairs of the Working Group are very pleased to invite all members and non-members to attend the open session on the 3rd of December, 2009 from 13.00 to 17.00h. This meeting will be a great opportunity to obtain information on the latest topics in global TB diagnostics and to become involved in the New Diagnostics Working Group activities. Also, the Working Group will present its latest production:

Pathways to better diagnostics for tuberculosis: A blueprint for the development of TB diagnostics.

For more details and the agenda of the annual meeting, please click here to see the Meeting Flyer.

Evidenced-based TB Diagnosis Website: www.tbevidence.org



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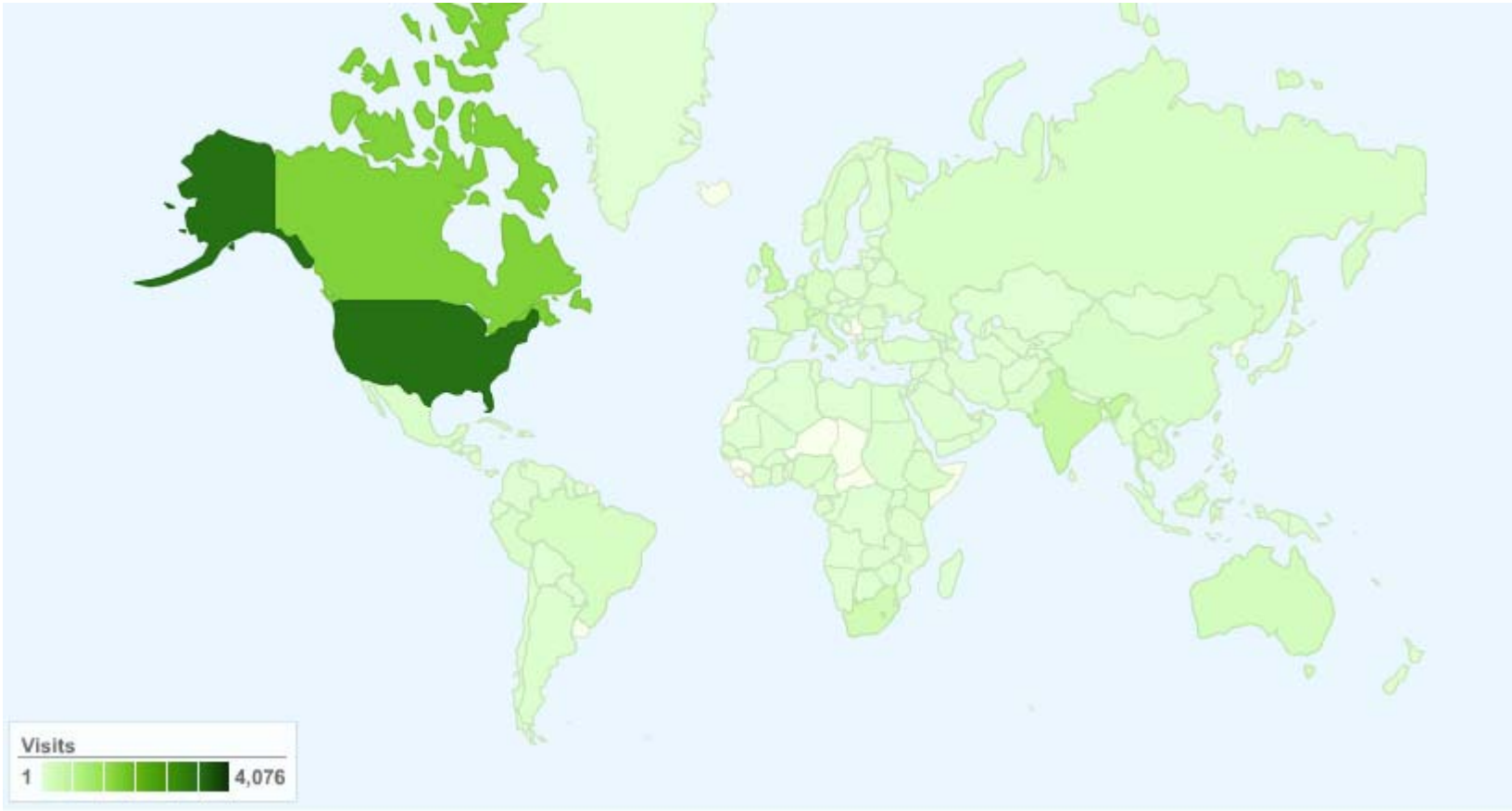

www.ndwgchildsubgroup.org

Collaboration with

- To map the landscape and quality of TB diagnostic research
- To support the development of a Global TB Research Agenda

Acknowledgements

- Secretariat & TDR:
  - Andy Ramsay
  - Martine Guillerm
  - Sanne van Kampen
- FIND, Geneva
- We thank all Core Group and Sub-Group members for their support and contributions
- Marcos Espinal, Executive Secretary, STP