

Minutes of the STOP TB Diagnostics Working Group Meeting
Palais de Congres, Paris
Octobre 29, 2004

13:30-17:30

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Agenda

13:30 – 13:40	Welcome and introduction remarks	G Roscigno
13:40 – 13:50	The STOP TB partnership overview	
	and significance of the Working Group (WG)	M Espinal
13:50 – 14:00	The DOTS Expansion WG	
	<i>Priorities and opportunities for collaboration</i>	K Shah
14:00 - 14:10	Becoming a better advocate:	
	<i>Defining and delivering the WGs priority messages</i>	J Carter
14:10 – 14:20	The Global Plan to STOP TB	
	<i>Role of the Diagnostics Working WG</i>	D Maher
14:20 – 14:45	DISCUSSION	
14:45 – 15:00	FIND/TDR Strategic Approach and Workplan	M Perkins
15:00 – 15:30	Coffee Break	
15:30 – 15:40	Laboratory strengthening	F Portaels
15:40 – 17:00	Identifying Gaps and Setting WG Priorities	
	<i>Panel Discussion and WG member participation</i>	
17:00 – 17:10	Identification of Focal Points for Core Team and for Global Plan	
17:10 – 17:25	The Working Group and planning future activities	J Cunnigham
17:25 – 17:30	Closing remarks	G Roscigno

Welcome and introductory comments

Dr. Giorgio Roscigno

FIND is the lead agency of the STOP TB Diagnostics WG and TDR is the secretariat. The WG has met a couple of times the past few years. There are some news that we would like to share and to relaunch new commitments of the WG. The creation of FIND will accelerate the introduction of new technology in the public sector of developing countries.

The program for the day will start with discussions on the STOP TB partnership to put the WG in a context of the partnership. Dr Marcos Espinal will tell us how the WG is important to the partnership. Dr Karma Shah will put the WG in a context of the DOTS Expansion WG. Joanne Carter will tell us how to better advocate new tools and how the Advocacy WG can help the other WG. The second Global Plan to Stop TB will be presented by Dr Dermot Maher. The session will end with a discussion and questions can be raised.

Then Dr Mark Perkins will outline the FIND /TDR work plan. Professor Françoise Portaels will give a short presentation on behalf of the Capacity Strengthening Subgroup of the DOTS Expansion WG.

Following this we will have a brain storming session, trying to identify gaps, how we can move all these things together, how different activities are currently covered, how we can work better as a WG to help the partnership achieve its goal.

After that we will try to identify focal points for each constituency that is represented here so that these focal points will help us recreate a core team that can be more involved in the day to day activities.

Finally Dr Jane Cunningham will tell us about the budget today and the coming up activities of the WG.

Objectives of the meeting:

- To review the history of the STOP TB WG on Diagnostics – progress, setbacks, new developments
- To provide participants with an overview of FIND/TDR strategic agenda and workplan for the development of new TB diagnostic tests, highlighting areas for collaboration and overlap with Working Group member interests
- To identify knowledge, communication and resource gaps that can be addressed in the framework of the Working Group and its Members
- To discuss mechanisms/ strategies to achieve improved and sustainable communication between various stakeholders in diagnostics development and across R&D Working Groups (Diagnostics, Drugs, Vaccines)
- To discuss the role of WG members in advocating for new TB diagnostics and to define the priority messages
- To reconstitute a core Diagnostics Working Group and expand membership to other interested public and private sector groups

The STOP TB partnership overview and significance of WG

Dr. Marcos Espinal

Executive Secretary Stop TB Partnership

- Three Working Groups met at the IUATLD meeting: DOTS expansion, WG on drug development and the Diagnostics WG
- Outside interest on new tool development is increasing
- STOP TB partnership is global, involving approximately 300 institutions, the secretariat is housed at WHO. The partnership responds to a coordinating board, and the board in turn provides guidance to WHO.
- There are 7 WG in the partnership, and the secretariat is the facilitator, “we work for you,”
- STOP TB goals:
 - By 2005
 - 70% Case detection under DOTS
 - 85% Cure rate
 - By 2015: Millennium Development Goals
 - 50% reduction in prevalence and deaths by 2015
 - By 2050: The global incidence of TB disease will be less than 1 per million population

New tools will take us there. Current technology is more than 100 years old. I think we can eliminate TB if we get better tools than the currently available.

We have DOTS. DOTS is good but the only thing we have and it needs to be supported while we find the new tools. DOTS needs to be improved with new diagnostics, drugs and vaccines.

Challenges

- Additional resources for health and poverty reduction
 - Workforce crisis: more & better human resources
 - Better harmonized and more effective aid
 - Strengthened health systems: primary care
 - Improved performance monitoring
- Consolidate, sustain and advance achievements
 - Mobilise communities, the private sector, and enhance political commitment
 - Accelerate response to HIV/AIDS emergency
 - Invest in research & development to shape the future

The partnership consists of 7 WG. The crosscutting Advocacy WG was recently created. All of us need advocacy and communication. Five years ago you were only hearing about DOTS, but you were not hearing about mobilising communities, bringing corporate sector into TB control and advocacy and communication.

The WGs are:

- DOTS Expansion WG
- DOTS-PLUS MDRTB WG
- New Drugs WG
- TB/HIV WG
- TB Diagnostics WG
- New Vaccines WG
- Communication and Advocacy WG

The partnership holds a forum every 1-2 years. This year Mandela was engaged for the first time. Communication and Advocacy is a key for the partnership.

It is important for the R & D community to keep engaged through the WG because current tools are not sufficient and being away and isolated is not the solution.

MGIT has been available in industrialized countries for 15-20 years. It is a failure of us all that it is not available in the developing world.

Do not create new tools for the sake of it. New tools have to be inserted in the framework of TB control.

Portfolio

- Shared responsibility
 - Novartis donation to GDF – Eli Lilly discount to the GLC
- Networking
 - Learning from others – duplication
- Forum for a common agenda on new tools issues
 - economics, regulatory requirements, trial site register, immunological issues, market introduction, advocacy and communication
- Get new tools into TB control in poor countries
 - Cross fertilization with other WGs
- Global Plan to Stop TB

The Global Plan to Stop TB (and 2003 update)

- Contains the business plan of the partnership including sections on all the activities of each Working Group plus the costs for the activities.
 - DOTS Expansion Working Group:
180 countries implementing DOTS
 - Working Group on TB/HIV:
Policy for TB/HIV collaborative activities

- ▣ Working Group on DOTS-Plus for MDR-TB:
Treatment for MDR-TB in more than 10 countries
- ▣ Working Group on New Diagnostics:
Enabling environment for commercial tool development
- ▣ Working Group on New TB Drugs:
Pipeline of promising compounds
- ▣ Working Group on New Vaccines:
▣ Two vaccine candidates entering phase I clinical trials

The reason that Dermot [Dr Dermot Maher] is here is to explain the Global Plan. We want you to be involved in the development of the plan. We prefer inclusiveness and as said we work for you.

Partnership Governance: Coordinating Board

It is important to be engaged in the partnership because you will need contact with the members including:

- High TB burden countries (4): China, India, Brazil, DR Congo
- Regional representatives (6)
- WHO, World Bank, UNAIDS, GFATM
- Working Group Chairpersons (7)
- Financial donors (4): *CIDA, Japan, Euro (NL), USAID*
- Foundations (1): *Gates Foundation*
- NGOs and technical agencies (3): *IUATLD, CDC, IFRC*
- Communities affected by TB (1): *Under selection*
- Chair of the WHO STAG: *Mexico vice MOH*
- Corporate business sector: *Heineken*

The DOTS Expansion Working Group ***Dr. Karam Shah***

Chair of the DOTS Expansion WG

The number one issue emerging from the DOTS Expansion WG meeting was laboratory strengthening.

- One challenge we have faced for a long time is the laboratory. Laboratory is not only about the tools but also management, operations issues.
- There are >10 new tools available in the market. They are not used in the programs but we are using them in different capacities as consult in tertiary hospitals. BUT no tools have replaced sputum smear microscopy, it is the most

simple, cost effective and specific test and it is simple to manage but still we do not operate smear microscopy comfortably.

- New tools should be patient and program friendly and better than what is available now.
- The need of the day for DOTS Expansion is more coordination and collaboration between the different WG.

Becoming a better advocate

Joanne Carter

Acting Chair of the Communication and Advocacy WG, Legislative Director of a grass root advocacy organisation ["**Results**"] based in the US and 6 other countries.

We talk ourselves out of the fact that this is exciting. People in the partnership say the “this new tools stuff is exciting but it is so complicated”. It is not that difficult but we haven’t tried. We can easily make it more complicated than it has to be. To make it work we need to do two things:

- Put diagnostics in a context
- Make a decision not to make it complicated

- Outside policy makers and others have no idea that the main tool is 100 years old, how many patients we are missing with the current tool, the difficulties diagnosing HIV/TB and MDRTB.

- It was a good teaching opportunity when 2 US Congressional staff visited a lab in India and got to look in the microscope to see how complex a process it is to diagnose TB.
- People have to understand that it is not that complicated and what new diagnostics could do.
- Whether we like it or not MDRTB and HIV/TB are the most “sexy” areas. We could use the diagnostics for these areas as an entry point to say how this can impact overall treatment success and increase case detection.

- We need to define the needs financially and develop a resource mobilisation plan for new diagnostics. It is not a huge amount that is needed to make a lot happen and a number of things are in the pipeline and they are coming quickly.

- Initially the WG will work with one global subgroup and then subgroups on country level.

- We will help to promote the work the other WG re doing

The Global Plan to STOP TB

Dr. Dermot Maher

Who wants a Global Plan to Stop TB?

- Stop TB Partnership
- Millennium Project (report of working group on TB)
- WHO 2004 Executive Board resolution
- 2005 World Health Assembly resolution

Why do we need a Global Plan to Stop TB?

- As a vision of what we can achieve
- As a roadmap to achieve targets
- As a tool for advocacy and fundraising
- To support long-term national planning
- To stimulate research and development

Global TB control targets

- *2005 (World Health Assembly)*
 - to detect 70% of smear-positive cases
 - to treat successfully 85% of all such cases
- *2015 (Millennium Development Goals)*
 - to halve TB prevalence and deaths (since 2000)
 -

N.B. achievement of the impact targets (prevalence and deaths) depends on sustained achievement of the process targets (case detection and treatment success)

The Global Plan to Stop TB

First global plan: 2000-2005

- described mechanisms, activities and resources needed to accelerate progress towards 2005 targets
- plans of action of 6 Stop TB working groups:
 1. DOTS Expansion
 2. DOTS-Plus
 3. TB/HIV
 4. Drugs
 5. Diagnostics
 6. Vaccines

Second Global Plan to Stop TB, 2006-15

Key features:

- 10 years' timeframe
- builds on first Global Plan and Progress Report
- leads to 2015 Millennium Development Goals (MDGs)
- complementary to MDGs TB working group report (that calls for support for the Global Plan)
- consistent with proposed World Health Assembly resolution in 2005
- responds to country needs for long-term planning and financial sustainability
- develops strategic directions set out by 2nd ad hoc Committee on the TB epidemic

Process for developing the Second Global Plan to Stop TB: 2006-2015

Process is:

- coordinated by Stop TB Partnership secretariat
- guided by steering committee
- informed by feedback from first Global Plan
- based on contributions of the 7 Stop TB Partnership Working Groups (DOTS Expansion, DOTS-Plus, TB/HIV, drugs, diagnostics, vaccines, and advocacy & communications)
- driven by 2015 targets

Members of steering committee

O Adeyi (World Bank)

F Ahmed (Bangladesh Rural Advancement Committee)

N Billo (IUATLD)

J Broekmans (KNCV)

K Castro (CDC, USA)

M Espinal (Stop TB Partnership secretariat)

M Freire (Alliance for TB drug development) *Will represent the R&D WG including Diagnostics in the Steering Committee*

P Hopewell (San Francisco General Hospital, USA)

PR Narayanan (TB Research Centre, Chennai, India)

F Omaswa (Ministry of Health, Uganda)

M Raviglione (WHO Stop TB Department)

K Shah (National TB Programme, Pakistan)

R Tapia (Ministry of Health, Mexico)

Review of progress in developing Global Plan, 2006-2015

- ⇒ May 2004 - WHO Executive Board approved resolution on Global Plan for 2005 World Health Assembly
- ⇒ June 2004 - WHO Strategic and Technical Advisory Group endorsed outline of Global Plan
- ⇒ June 2004 - Outline sent to all partners for feedback
- ⇒ July 2004 - Outline endorsed by Coordinating Board
- ⇒ August 2004 - Steering committee endorsed by Board
- ⇒ September 2004 – work initiated on projections

Contributions of Working Groups (WGs) to development of plan

Rationale

- Successful development of plan depends on contribution of all WGs.
- Process builds the "buy-in" necessary for the implementation of the plan by the WGs.
- WGs stand to gain from a plan with wide support (political and financial).

Roles of the Working Groups and secretariats

- Each Working Group needs to develop its workplan in contribution to the Global Plan.
- The secretariat in each case should facilitate each Working Group's contribution.

Developing the road map to reach the 2015 global TB control targets

1. Construction of possible scenarios for how the regions individually and the world overall can reach the targets, i.e. development of epidemiological and costing projections.
2. Each WG to use the projections as the basis for developing their own long-term workplan in contribution to achieving the targets:
 - milestones and timelines for expected progress
 - Budget
3. Inter-active planning exercise between WGs and team developing projections (each WG needs to identify a focal point).

FIND/TDR Strategic Approach and Workplan

Dr. Mark Perkins

A year and a half ago at a presentation for the STOP TB coordinating board the different WGs presented what they were doing. It was clear that some of the WG that were hosted at WHO, were performing work that was part of WHO's core function. Other WG specifically the tools WGs was held elsewhere and were not funded to hold meetings and to get specific pieces of technological work done. A number of partners were working on TB diagnostics but there was no coordinated strategy for tool directed research, no coordination of field site strengthening, no diagnostics trial registration and standardization and no consensus on what should be done. Beyond this there was no funding.

What's missing?

- Coordinated strategy for tool-directed research
- Coordination of field site strengthening
- Diagnostic trial registration and standardization
- Consensus on phase IV research priorities

Designated funding needed for these activities

DOTS expansion has not improved case detection rates hence, there is a clear need to enhance case detection to attain global TB control targets

The inefficiency of global TB case detection (2004) is illustrated by the following figures:

- 16% of TB cases are AFB+ and detected
- 28% of TB cases are AFB+ but undetected
- 56% of TB cases are AFB-

The recent history of public sector TB diagnostic development is characterized by:

- Years of denial: 1975 to 1996 *“Microscopy is all we need”*
- Years of waiting: 1997 to 2003 *“Facilitating industry will provide the tools”*
- Years of action: 2004 to 2009 *“Medical need – evidence – partnership”*

FIND will drive diagnostics development from concept to delivery in the health system

FIND will work between discovery/research and market access/distribution. FIND will pick up products that need development, evaluation and/or demonstration. Policy makers should be included in the demonstration projects.

An enabling infrastructure for diagnostics development, evaluation and demonstration has been developed and is still under development. Much of the work is performed by TDR

Development

- Specimen Bank
- Strain Bank
- Market Analysis
- Mathematical modelling

Evaluation

- Specimen/strain Bank
- Trial site support
- Standardized protocols
- Regulatory harmonization

Demonstration

- Technical support to NTPs
- Usage Guidelines
- Access assistance
- Operational research

Top 3 Priorities for Tool Development are all within the area of improving case detection.:

1. Detect pulmonary TB with high bacterial load (SS+)
2. Detect pulmonary TB with low bacterial load (SS -, Cx +)
3. Detect extra-pulmonary and pediatric TB

Further down on the priority list comes drug susceptibility testing and detection of latent TB infection.

Segmentation - diagnostic question vs. health system level

The questions asked and the needs depend on which level of the health system you look at.

In health clinics the key question is detection, a test more sensitive than AFB smear is needed -

- dedicated point of care (POC) devices
- minimal skill requirements

In district labs better resolution is needed, a test that is faster than culture to resolve unclear cases and to test resistance.

- easy & robust lab procedures
- support for multiple health problems
- universal platforms

FIND and TDR have a two-phase approach for tool development

One short term that gives significant incremental improvements over existing tools and one long term that will revolutionize patient care and disease control.

Improving sputum microscopy

Microscopy networks exist, people are used to diagnosing by microscopy, the whole case detection framework is written around microscopy. TDR is funding a number of projects aimed at improving it.

New techniques that could be applied on TB diagnosis

- A number of companies work on tests that could be used in POC. FIND is exploring which techniques are most likely to be successful.
- Molecular techniques are likely to be used in district labs but tests that could be used in POC may emerge
- FIND have agreements with two companies working on tests for district labs: Biotec and Salubris.

TK media (Salubris)

The red media changes to yellow by mycobacteria and to green by contaminants. Almost as fast as Bactec.

Phage replication assay for detection or DST (Biotec Laboratories)

Phage infect mycobacteria in processed sputum. The sputum is plated on lawns of rapid growing *M. smegmatis* after adding virucide. Plaques can be counted the next day. Sensitivity is presently 75-85%. Specificity is high.

FIND will pick up existing technologies at any stage from development and carry them through to demonstration.

Laboratory strengthening

Prof. Francoise Portaels

Head Capacity strengthening and Laboratory strengthening subgroup under DOTS
Expansion WG

Objectives of the Lab Strengthening Subgroup are to:

- Improve performance of smear microscopy , culture and DST at all levels of the TB Lab network
- Develop and implement QC including supervision on SmM, culture and DST
- Improve managerial skills of senior lab staff and technical skills of lab staff
- Improve biosafety
- Develop operational research capacity

A number of countries have been assessed:

- Kenya
- Pakistan
- Uganda
- Bangladesh
- Romania

Missions are planned to:

- Russia
- Indonesia
- Egypt

Main findings:

- Smear microscopy, culture and DST is deficient in availability, capacity and reliability in all countries.
- Lack of communication between national reference lab and NTP in three countries
- Lack and weak input in reference laboratory in planning, budgeting and implementing activities in four countries
- QC supervision rarely or never implemented in all countries
- Training does not often respond to national needs and does not follow international standard in four countries
- Biosafety weak
- Insufficient human resources

The subgroup participated in program review in:

- Indonesia
- Vietnam
- Thailand
- Bangladesh
- Myanmar

Summary of Activities

- TB Lab Assessment
- Development of global strategy to improve the capacity of TB diagnostic services
- Revision of lab assessment tools
- Review and repackaging of available international and national training material
- Participation in the national TB program reviews in collaboration with partners
- Translation of the external QA and smear microscopy guidelines into French
- Organization of lab management training for managers of national labs in EMRO
- Organization of annual subgroup meeting in Paris

Planned activities

- Continue lab assessment in ISAC region and TB high burden countries
- Organize consortium meeting for improving smear microscopy
- Organize two training sessions for the lab management training for managers of national reference labs
- Finalize development of Standard Operating Procedures (SOP) guidelines
- Finalize development of standardized training curricula for AFB smear microscopy and quality assurance
- Development of standardized training curricula for culture, DST and lab management

There are several weak points as far as the lab activities are concerned. It is the time to emphasize that the subgroup has a strong collaboration with the other subgroups and also with the Diagnostics WG.

Identifying Gaps and Setting WG Priorities Discussion

Panel Discussion and WG member participation

Q = question

A = answer

C = comment

S= suggestion

Q, "An electronic nose is very useful but Mark didn't mention it"

A, Mark Perkins (MP) – Time didn't allow comments on all techniques, it is certainly useful, TDR is funding some projects on aerosol detection.

Q, "Can MTB strains be resistant to phage due to co-infectious or genetic reasons?"

A, MP – Occasionally some strains have been found that are not particularly susceptible to phage but almost all strains are infectable. Smear positive patients that show negative results with phage test become phage test positive after culturing those the bacteria so it doesn't seem to be a problem with the strain itself.

Q, Not Audible

A, MP – 1) FIND should not be involved in sequencing the MTB genome. Upstream research is funded by others.

2) FIND's job is to pick up technologies that seem promising to become products. The selection of projects is based on where priority medical needs are. The medical needs are merged to what technologies are available.

3) FIND is interested in DST. A number of new methods are attractive – there are **automated liquid culture systems**, which are much faster than traditional LJ. The important issue is how to implement these cost effectively in settings where they are, **TK culture media** can be made into DST, **phage method** has been introduced as a DST for rifampin resistance, we need to start thinking how to implement rifampin resistance screening in the most effective way.

C, Giorigio Roscigno (GR) – The phage test is the first test to come out of the FIND/TDR collaboration together with Biotech. It will be put in evaluation and demonstration projects in public health sector countries before we will use it in national programs.

Q, Ruth McNerney , LSHTM- "Suggest to create a website were results from testing ideas and tests that did not work could be shared so that others could learn from this. Journals are not interested."

A, MP – One may learn something from high quality trials but negative results from small trials with a limited number of patients might not teach us anything.

C, , Jane Cunningham (JC) – Part of the idea of this discussion is to get comments on what is missing and what other activities are needed to branch out and incorporate into the Global Plan to Stop TB.

C, Arend Kolk – We should encourage nanotechnologists to join the TB efforts.

C, Stefan Svenson – Agrees that a website for publishing negative results would be beneficial.

C, MP – Clinical research is not coordinated, difficult to interpret results even from evaluations of the same test in different settings due to different trial conditions. One way to help this is to develop standards for the evaluation of diagnostics. DEEP (Diagnostics Expert Evaluation Panel) has been put together in collaboration with WHO and TDR to develop generic guidelines and disease specific guidelines for the evaluation of diagnostics.

C, Michael ? ,University of Munich – "We lose 30% of antigen in frozen urine compared to fresh when running our ELISA".

C, Dick Menzies, McGill, Montreal – "Create guidelines for when frozen specimens could be used and to even register holdings of specimens that one is willing to share with others".

C, Salman Siddiqi – The problem with almost all new test is that they are all add on tests, you have to do all other testing along with the new test. Our focus should be to find a test that is a replacement not an add-on which is also an add-on to economy.

C, Feldman, Munich – No techniques discussed is available in the field. We should also focus on developing methods to preserve specimens to send them to specialized centers where testing could be done.

A, (GR)– Sending samples does not serve the purpose of capacity building and sustainable efforts in developing countries. The health sector needs to be developed and sustained. It might be good in some circumstances to ship specimens to central labs because it centralizes the health system and takes the patients far from where the public health system works.

C, Peter Wrighton-Smith Oxford Immunotec – 1)Obtaining samples from confirmed TB+ patients is a real problem
2)Technologies used for sputum smear are crude technologies, to solve the problem more innovative techniques will need to be used and they will tend to be more advanced. We can either find low-tech solutions or augment the capacity of developing world labs so that they can also use more technically advanced methods.

Q, Tony Catanzaro, UCSD – Is there a way to increase collaboration? FIND will pick up the best technologies and move them to products. This will increase competition and not foster collaboration.

A, MP – Can we demonstrate that a number of technologies are needed to solve the different problems in different setting and demonstrate what those settings are and what the markets are in the settings. It is important for the industry whether FIND is involved or not. Picking technologies from different places and putting them together might be appropriate for technologies with a simple platform and complicated reagents but not for technologies with complicated platforms.

A, GR – One should not only look at FIND. That is the purpose of this WG. The WG should create alternative ways for new ideas that might not fit into the FIND strategy. New ideas should be put in a context of the global plan where also funding might be available. A website could also be helpful to create a consortium of people that can share ideas and projects.

A, JC – The SARS epidemic is a good example that things can happen quickly if everybody is working together. Web-based communication was important for its success.

Q, Dick Menzies, McGill, Montreal – Is technician time and unit cost included in the DEEP analysis?

A, MP – All operational characteristics need to be included.

C, Stefan Svenson - Could you comment on the fact that for the patients 100% sensitivity and specificity is needed but for public health purposes 80% might be enough. How should that be explained to donors?

A, GR – The public sector is the fundamental issue for FIND. In all contracts and agreements with commercial partners FIND insists that the money invested are leveraged against the availability of the product in the public sector. No country will use a new technology in the public sector unless WHO has cleared it and added it to the guidelines. The private sector is a completely different story. There are no regulations on diagnostics in the private sector in developing countries. The industry also wants rules. TDR and FIND are working to set up guidelines on characteristics of diagnostics together with FDA, EMA and regulatory agencies from high burden countries.

Q, Vladimir Koulchin – What does it cost to diagnose a patient? In Russia it is impossible to get answers to this question.

A, JC – The market analysis that will be published soon and contains data on costs of diagnosis in different countries.

C, MP –

- 1) This is the most thorough evaluation of the TB diagnostics market.
- 2) The reason for setting up a Specimen Bank was that
 - all specimens will be collected in the same way at all collection sites and
 - there will be no doubts as to who owns the specimens, who should have access to them, and all patients have signed consent forms etc.
- 3) Which topics should be addressed by the WG? There has only been a few suggestion until now.

S, Stefan Svenson – The WG should work for common ethical rules for the whole of EU.

C/Q, GR – Can the WG influence EU to harmonize ethical rules and if yes, how should that be done?

C/A, Peter Wrighton-Smith Oxford –

- 1) It is extremely difficult to get funding from EU. Perhaps we could go through an independent body to streamline grant funding for initiatives like this.
- 2) Industry can come up with tools but cannot make public sector use them. The WG should have an independent group of experts setting up draft guidelines for the use of new tools and lobby governments around the world to implement the guidelines.

C, GR – This is the difference between FIND and other organizations. FIND will perform demonstration projects. The partnership and other policy makers will be involved in the demonstration to shorten the time between generating knowledge and changing policies.

Q, Afranio Kritzki, Brazil – Can FIND assist in educating personnel in the public sector, technicians, nurses etc to understand research (demonstration projects) because they don't understand it now and the new tools we are to develop are going to be used by them.

A, GR – There will be education when running the demonstration projects. The WG should work together with the lab strengthening subgroup. If we don't strengthen the capacity of the labs there is no sense in bringing new technology. {Poses question to public laboratory representatives in the meeting} What would be the obstacle in the national programs when introducing new technology in the program?

c, Zhao Yanlin, Director National Tuberculosis Reference Laboratory, China.
– The largest problem in China for the moment is QA. Many patients remain undetected with microscope.

C, Adalbert Laszlo – We are looking at including GLP in the training packages we are giving. We are looking at what is needed in a training package for personnel that do not have PhD or MD and who will perform operational research.

C, GR – Maybe lab capacity strengthening should be included in the new diagnostics WG. How can we strengthen the education of lab personnel and how can we raise more funding for this activity ?

C, Michael . Munich – My experience from Tanzania is that they will only do demonstration projects if it is in collaboration with WHO.

Q, GR – Is there a need for more evaluation sites? TDR and FIND have sites but do we need more and is this an activity that the WG should deal with?

C, Peter Wrighton-Smith Oxford –comment ...not audible

C, Lucia Barrera, Argentina – Our main problem is that we must buy the cheapest test because we do not have enough money.

C, GR summarizes what Peter Wrighton-Smith just suggested – Capacity to perform demonstration projects should be developed in developing countries. The industry should have access to the sites to perform projects by paying for the service. Please comment on this.

C, Aziz – 1) We do need more sites to evaluate tests because a specific test will work differently in different settings. 2) It is good for everyone to build lab capacity starting from reference labs and go down

C, Tony Catanzaro, UCSD – The diagnosis of TB is clinical and therefore the tools that are developed must be put in a clinical setting. Detaching the samples from the patient

will require a test with 100% sensitivity and specificity. A larger effort should be made to integrate diagnostic tests in certain clinical settings.

C, MP – We need to do operational research to figure out how tests fit in to diagnostic algorithms. I propose that the website contains information on where the clinical trial sites are. People who have capacity should announce that on the website.

C, Man US accent – Believes that one very important objective of all projects run by TDR or FIND or the WG should be to foster the trial sites in research.

C, Peter Wrighton-Smith Oxford – 1) Academics do not want to do all the work it takes to develop new tests, for example QA and QC testing which is very boring. 2) When a number of labs (commercial and non commercial) collaborate a critical mass will be reached and it will make sense to set up a good lab infrastructure in the trial sites. 3) The critical mass will allow the employment of a nurse to follow up patients and have the lab run in a good way. Nothing unethical will be done. The patients will probably have the best diagnosing, treatment and F/U in the country.

C, Ruth McNerney– Have tested a number of tests in Zambia. One actually works but it is to expensive. Suggests putting more effort in finding funds to finance the use of expensive tests that exist until there is a new cheap test.

S, Stefan Svenson – The WG should go to EDCTP and push for diagnostics.

A, GR – FIND did talk to them and they only have drug and vaccines in their priorities. There may be changes but work has to be put in to that. Diagnostics should not be put as a subgroup to drugs as they have tried to.

Q, MP – Would you contribute to a website listing trial sites? Do you think the site will add info to the website.

C, Probably Ruth McNerney – Non-audible comment

General support for adding trial site information to the website

Identification of Focal Points for Core Team and for Global Plan

C, GR – We need to identify focal points on the different areas.

National Reference Laboratories – Fadéla Boulahbal

Industry – Peter Wrighton-Smith, David Laconi, BD, Biotec, Salubris,

Public Research Inst – Tom Shinnick, Stefan(??SVENSON ??),

Academia – Peter Godfrey-Faussett and Ruth McNerney, LSHTM

The Working Group and planning future activities

Dr. Jane Cunningham

M I S S I O N

- To implement research, advocacy and/or operational activities in pursuit of the Group's specific area of interest and of the aims of the Partnership.
- To collaborate with other elements of the Partnership so as to create synergy and value added to actions taken in pursuit of the aims of the Partnership

Terms of Reference

- Map, to the extent possible, the range of TB diagnostic R&D activities underway globally
- Identify inadequacies in materials, knowledge, funding, advocacy or policy that inhibit test development
- Plan, implement and monitor coordinated action to overcome these inadequacies
- Develop means of communication that ensure frank exchange between diagnostic developers and diagnostic end-users
- Expand membership as required to support activities, promoting active participation from disease endemic countries.
- Report to the Stop TB Coordinating Board and Partnership Forum
- Coordinate with other Stop TB partners and Working Groups

Membership

- Open to institutions and expert individuals involved in the development and implementation of accurate, robust and affordable diagnostics for tuberculosis.
 - Academia (9)
 - International Organizations (4)
 - Industry (12)
 - NGO's (3)
 - National TB Programs/Reference Laboratories (16)
 - Donors
 - Public research institutes (6)

Organizational Structure

- A chair (Rosigno) and secretariat (Cunningham)
- A core team with the focal points for the different areas
- A number of subgroups, four suggested
 - Discovery Research
 - Diagnostics Trials
 - Market-Entry
 - Advocacy (may not be a subgroup but needs focal points for the larger WG)

Budget

\$75,000 – \$35,000 has been spent on this meeting. \$40,000 remains.

Planned Activities	Budget
Annual Meeting WG Members Meeting of Core Group +/- subgroups	\$40,000
Global Plan to STOP TB II <i>WG Workplan; Focal Point</i>	\$18,000
Compile and publish inventory of members TB Diagnostic Activities and clinical trial sites	\$3,000
Website: <i>inventories; strategic agenda; meetings; guidelines for appropriate timelines; IVD regulatory policies; discussion forums; Posting results of lab based evaluations or other results</i>	\$9,000
Develop and publish advocacy materials	\$5,000

Monitoring Progress

- Quarterly member update
- Annual report to members and STOP TB Coordinating Board

Discussion

C, GR – No one is dedicated to work only on the WG so the executive secretary in the partnership will be needed to move the work forward in an effective way.

C, JC – We have to spend the money we have been given and spend it well in order to attract new money

C, GR – Meeting Wrap-up...have we met meeting objectives ?

To review the history of the STOP TB WG on Diagnostics – progress, setbacks, new developments.

Mark reviewed the history of the WG

- *To provide participants with an overview of FIND/TDR strategic agenda and workplan for the development of new TB diagnostic tests, highlighting areas for collaboration and overlap with Working Group member interests*

This has also been done, areas for collaboration and overlap with Working Group member interests is still an open dialog.

- *To identify knowledge, communication and resource gaps that can be addressed in the framework of the Working Group and its Members*

We have come up with a challenging list that can be addressed. Minutes of the meeting will be circulated to all.

- *To discuss mechanisms/ strategies to achieve improved and sustainable communication between various stakeholders in diagnostics development and across R&D Working Groups (Diagnostics, Drugs, Vaccines)*

The idea of the website is a fascinating idea. With work and money dedicated to it, it can keep the information flowing between the partners.

- *To discuss the role of WG members in advocating for new TB diagnostics and to define the priority messages*

Not much was discussed. There might be a subgroup. We need to come back to advocacy.

- *To reconstitute a core Diagnostics Working Group and expand membership to other interested public and private sector groups*

A strong group has been reconstituted. Through the focal points the WG can be expanded. Each focal point can invite new members in their constituency.

Closing remarks, Marcos Espinal – I am pleased to see so many volunteers. There are many new global initiatives but many of them will go down. STOP TB is very well placed because it is under one umbrella.

My quest is to find money for you, not for me. I try to keep the TB issues in the minds of the public, the policy makers, the politicians. In the end that is where the money comes from. I am pretty confident that we need these new tools. The discussion today is a good start. TDR/FIND will be the brokers here for you. The ultimate message is that this working group is a consensus building body. A final decision must be made on what is best for TB control to advise the partnership. If we get new tools we will try to get those into the framework.

If you do well I'll try to get more money. A good report from this meeting will allow me to go out and describe the work that the WG is doing.