

# Remarks by Christy Hanson, TB Research Advisor, U.S. Agency for International Development

## Stopping Tuberculosis: The Need For Diagnostics

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### Panel Discussion by The Global Health Council, Aeras Global TB Vaccine Foundation, and the Foundation for Innovative New Diagnostics

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I am going to speak today on behalf of Irene Koek who is both the Chair of the Stop TB Partnership's Coordinating Board and the Chief of Infectious Diseases at USAID. I similarly wear two hats - one from the Stop TB Partnership, and one from USAID, so I hope to offer a broad perspective. I will focus my remarks around three basic points:

1. The problem of diagnosis of TB - and its implications for controlling the epidemic
2. The tremendous opportunities that are now coming forward - and why I think this is a great time for optimism
3. The way forward - and what action is being taken globally and what specifically the USG and USAID are doing

Last November at the IUATLD World Conference on TB and Lung Health, the critical need for improved diagnostics, diagnostic tools and better approaches and the need for improved laboratories was asserted again and again. Mario Raviglione, the Director of the WHO Stop TB Department appropriately referred to diagnosis as the Achilles heel of TB control. Peter Small of the Gates Foundation in his plenary talk on diagnosis and health systems noted that "at its core, the root of the TB epidemic is the failure to diagnose."

Many people who die of TB do so because the infection is never diagnosed, or is diagnosed too late to be cured. New safe, affordable, and easy-to-use diagnostics are desperately needed to accurately screen for and identify active tuberculosis, monitor treatment response, rapidly detect drug resistance, and identify latent infection in those at greatest risk of active TB.

The best approach we have to diagnose TB in resource limited settings is over 100 years old. More troublesome, it is only sensitive about ½ the time and far less so in HIV positive patients where TB is deadliest. Getting a diagnosis for TB can often take anywhere from a few days to several weeks if not longer - during which time a patient with an infectious case of TB could be unwittingly infecting family and other members of the community. Correct diagnosis of TB can take months if it is not found by the test most commonly used - and screening for drug resistant TB often does not happen until the first few months of treatment does not work - or there is treatment failure - and the patient remains ill. All too often, only then, is drug susceptibility testing done - if the facilities are available. Most of the time they are not, but if they are, current tests take months before the results are available.

Some basic functions of health systems must work if we are to give communities access to the rather blunt diagnostic tools we currently use. For diagnosis, first and most critically, there must be laboratories - and well functioning laboratories. There must also be trained health care workers and lab technicians, the means to get samples to labs and the results back again; a process for keeping the lab supplied with slides and reagents. To do drug susceptibility testing, there must be some capacity to culture a sample - safely and accurately. There should also be a functioning laboratory network, where referrals can move smoothly and quickly through the system. A quality assurance system and infection controls must be in place to ensure accurate results and the safety of lab personnel.

Unfortunately, at the country level, such systems often do not exist or are weak at best. Clinics commonly run out of certain drugs and supplies, and health workers may be absent. Patients "shop for services" in the private sector, where often international standards for TB diagnosis and treatment are not followed. The current recommendations

of multiple sputum samples requires patients to return to a lab 2 days in a row, with labs often a day's walk away. In rural areas, results may not be transmitted back for a week or more. In many settings, patients have no realistic alternative source and are in effect denied care.

Recent research efforts led to a change last June in the norms for smear diagnosis and case definitions for smear-positive TB, enabling more cases to be immediately labeled as such. The health and economic effects of inadequate diagnostic tools and practices can be severe. Poor TB patients commonly spend the equivalent of several months salary seeking a diagnosis and will miss a considerable amount of time at work.

For health to improve, we must untangle and resolve the intricate and challenging issues that plague health systems in developing countries. To do this we must remove financial barriers that limit individual access to services; boost support to clinics providing these services; improve training and education; address stewardship, financing, and accounting systems - all weaknesses that conspire against good health. Simultaneously, we need to improve the tools available to bring rapid diagnosis closer to the patients and less labor intensive and safer for health workers and the health system. Civil society can and should play a role in advocating for the resources for health and for access to the services.

There clearly is an enormous challenge before us. However, I believe that now, more than ever before, there are tremendous opportunities and very real reasons to be optimistic that we can make significant progress on accurately and quickly diagnosing patients and putting them on effective treatment. You will hear more of the details and specifics from my colleagues, but I wanted to summarize four reasons for why I and others are feeling optimistic now.

First, as you will hear in greater detail, there are new tools and improved approaches for diagnosis - several are available now, with even more expected within the next several months. Giorgio will talk about the work of FIND and others, but let me just mention some of the new methodologies already being employed. Partners such as TDR and MSF have demonstrated the advantages of enhancements to smear-microscopy, such as adding bleach or centrifugation to the smear preparation process, which increase sensitivity by 10-15%. Using LED microscopes, rather than traditional microscopes, makes the slide staining process simpler and similarly, provides important sensitivity gains. Once cost-prohibitive, LED technology has become affordable thanks to FIND and others. Partners, such as PATH, WHO/PAHO, and MSF are exploring various culture techniques and are adapting culture technologies to reduce biosafety concerns and contamination errors of liquid culture.

Secondly, we now have a clear strategy for laboratory strengthening from the laboratory subworking group of the Stop TB Partnership. Labs are the backbone of diagnosis. The Global Laboratory Initiative is a comprehensive strategy - designed to develop integrated laboratory and quality systems and cross cutting disease control mechanisms. While the key pieces needed for TB diagnosis are the initial focus of this network, it also is designed to lay the foundation for future laboratory needs for TB and other disease areas--it is not designed solely for TB diagnostics. The strategy includes components on global policy guidance, advocacy and resource mobilization, laboratory capacity development and coordination, quality assurance, coordination of technical assistance and effective knowledge sharing. The Global Laboratory Initiative is mapping the needs to strengthen lab capacity for TB diagnostics worldwide, and is unifying a network of partners to respond to the needs. The first strategic plan of the Initiative, that takes into account the current tools as well as the use of potential future tools, will be discussed in April.

Thirdly, recent outbreaks of MDR and XDR have focused attention on the urgent need to develop more accurate and rapid diagnostics for TB, both susceptible and resistant strains, to ensure appropriate treatment and mitigate transmission. This attention by the public and the press has also galvanized the support of political institutions and policy makers for both the science of new technologies and the means to pilot test and implement them. This, in turn, has translated into increased recognition of the need for key investments in health system infrastructure, including quality assured laboratory management systems, essential to identifying patients requiring treatment and ensuring that they are able to successfully complete a full course. Consequently, there has been a groundswell of voices calling for increased attention to diagnostics and laboratory strengthening - including very clear and loud cries for more investment in research - even from the non-research community.

Governments are increasing political commitment and working to secure sustainable financing. In Europe last fall, health ministers endorsed the Berlin Declaration on Tuberculosis that calls for the full adoption of the STOP TB Strategy, addressing TB/HIV and MDR/XDR-TB, integrating TB care into general health services, empowering affected communities and promoting research. USAID received additional funding for TB in FY 2008, thanks to strong support and hard work from Congress and a number of people in this room today.

Fourth, there is a clear and strong partnership working with countries to aggressively scale up and roll out the tools we have - and lay the foundation for the future.

Let me now turn to what is currently going on. The Stop TB Partnership, which brings together implementers, researchers, product development specialists, donors, country TB program managers and policy makers has not only tried to push forward the development of diagnostics through the work of the diagnostics working group, but is currently bringing the different parts of the partnership together to lay the foundation for rapid uptake of new diagnostics as we get them. The "retooling task force" of the Partnership was established two years ago to facilitate this critically important work. The task force has developed a framework for the introduction of new tools that defines the global and country-level sequence of policy and programmatic steps to efficiently bring new tools into country programmes.

The retooling group met last week to identify key actions for the coming months related to some of the exciting new tools that have been recently developed or are soon to be released. Members of the task force from developing countries described the scene at country-level. Programs are desperate for new tools and product developers from around the globe present new tools that promise highly sensitive/specific results. While most of these tools have not been promoted through international policy, the countries don't have a way to evaluate them. Together with the diagnostics working group and WHO, the retooling task force will articulate a process for standardized evaluations of new tools that allows for comparisons across technologies and leads to evidence-based policy recommendations, empowering countries to make sound decisions on the tools to adopt. Members of the task force from developing countries also underscored the need to identify and explicitly articulate, for each new tool, the human resource and training, storage and procurement needs. As a result, the task force will work with product developers to ensure that product profiles are modified to include these programmatic requirements - in addition to the technical specifics for a particular tool. The retooling task force, together with partners such as WHO and FIND, will be working with countries that are preparing to introduce new technologies or to adopt the revised diagnostic protocols from WHO, to ensure an efficient process and to document experiences for global use.

As you will hear in more detail from Giorgio, the path before us is clear. As part of the Global Plan to Stop TB, clear benchmarks and targets have been identified as part of the work on new diagnostics- leading to the ultimate introduction of a rapid, field appropriate diagnostic tool.

In FY 2008, USAID received additional funding from Congress for TB activities. We intend to use these monies to expand activities in some of our high priority countries and work with the international community to successfully implement the Global Plan to Stop TB. Specifically with respect to diagnostics, we will aggressively move forward to build a foundation to introduce new diagnostic technologies; upgrade laboratory infrastructure, including improved smear microscopy and lab quality assurance, and expanded culture and drug susceptibility testing; provide support to strengthen and expand supranational reference laboratories; and work with WHO and other partners to conduct drug resistance surveys and surveillance.

In PEPFAR focus countries, USAID, CDC and others are working together to strengthen diagnosis/referral systems so that co-infected patients are accurately diagnosed and put on treatment as quickly as possible, which is particularly difficult in individuals who are immunocompromised due to diseases such as HIV/AIDS. PEPFAR is also supporting the GLI and regional training to build lab capacity.

USAID is also working closely with WHO, CDC, in country partners and others to conduct drug resistance surveys - and make sure we have accurate data on the extent and spread of multiple drug resist and extensively drug resistant strains of TB. We are also working with these partners to build drug susceptibility testing capacity as quickly as possible in a number of countries. This includes expanding culture capacity as well as introducing some of the new technologies that we expect to be approved within the next year, which should substantially improve our ability to identify tuberculosis and mitigate its transmission.

The path ahead is clear. Not only is the time for action upon us, it is beginning.