TB LAM
Paving the way for next-generation point-of-care testing
TB LAM – Paving the way for next-generation point-of-care testing

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Geneva, Switzerland

Meeting Report

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EXECUTIVE SUMMARY

The “TB LAM – Paving the way for next-generation point-of-care testing” meeting was co-hosted by the Foundation for Innovative New Diagnostics (FIND) and the Stop TB Partnership on 6 February 2020 in Geneva, Switzerland. The meeting brought together a diverse group of stakeholders who share the common goal of improving point-of-care testing in tuberculosis (TB). In addition to representatives from the World Health Organization (WHO), Bill & Melinda Gates Foundation, Global Health Innovative Technology Fund (GHIT) and The Global Fund, the meeting included representatives from the Japanese Ministry of Health, Labour and Welfare, Zimbabwe’s AIDS/TB Programmes, India’s Ministry of Health and Family Welfare, and Cameroon’s Bamenda Center for Health Promotion and Research. The meeting provided a timely update on available and upcoming TB LAM tests, evidence to support their use for clinical decision making, and what needs to be done to bridge critical TB testing and access gaps. The roundtable also explored the potential for TB LAM to be expanded to broader patient groups in the future.

Catharina Boehme, CEO of FIND, opened the meeting by highlighting that diagnosis is still the weakest link in the TB care cascade. Three million cases of TB are still missed each year, and novel tools and strategies for diagnosis will be essential to bridge this gap. While the literature clearly shows that the TB lipoarabinomannan (LAM) test saves lives and is a cost-effective approach in people living with HIV, uptake has been low. Lucica Ditiu, Executive Director of the Stop TB Partnership questioned why progress has been slow in TB, especially as the TB LAM test has been endorsed by WHO since 2015. Lucica called for the community not to lose sight of the goal to end TB by 2030 and asked the community to start using TB LAM and ensure that those in need have access to the test.

The Japanese government has played an important role in catalysing investments for TB research and development, including the development of a novel TB LAM test (for example, SILVAMP TB-LAM (FujiLAM)). Speaking on behalf of the Ministry of Health, Labour and Welfare, Japan, Chiaki Noguchi emphasized the value of the TB LAM test in HIV and TB-endemic countries but pointed out that the societal impact of the test has been limited to date. She noted that the community needs to collaborate, share and use tools like the TB LAM test to meet global goals for TB elimination.

To include important insights from the patient perspective, TB/HIV patient advocate Carol Nawina Nyirenda shared her personal story of battling both TB and HIV. She emphasized the importance of diagnostics in those living with HIV and TB, as the two diseases can worsen one another, and TB remains the most common cause of death for people living with HIV. Carol noted that the TB LAM test could be a real “game changer” as patients can provide a urine sample in private, allowing a degree of privacy compared with the current sputum-based tests. Carol also highlighted the critical role of ongoing education for patients and healthcare workers to drive demand for the TB LAM test from the ground upwards.

In the first of two presentations, Morten Ruhwald, Head of Tuberculosis at FIND, provided an overview of the science behind TB LAM tests, and shared data on the impact of the AlereLAM test in the real-world and the increased sensitivity of the FujiLAM test. Despite the modest sensitivity of current LAM tests, Morten pointed out that they have a unique role in the diagnostic landscape in terms of providing rapid and affordable diagnosis to those who need it most. Alexei Korobitsyn, Global TB Programme, WHO, provided an update on WHO policies for the use of TB LAM tests and the changes implemented in the
recent 2019 guideline. The 2019 WHO guideline has increased the scope and strength of the recommendations for using TB LAM, allowing for better definition of the appropriate patient population for the test. However, it was noted that LAM tests with improved sensitivity and specificity will be required in the future.

The first panel of the meeting “TB LAM tests: from development to policy uptake and implementation – where do we stand today?” was moderated by Lara Vojnov, Diagnostics Advisor in the HIV and Hepatitis Department at WHO. Alongside discussions on barriers to achieving the most desirable target product profile (TPP) for LAM-based tests, Kathleen England (consultant, Fujifilm) provided an update on ongoing clinical studies of the FujiLAM test, while Duncan Blair (Vice President, Global Health Initiatives, Abbott) cautioned against the “techno-optimism” of waiting for future technology to solve problems, rather than using existing tests. Melissa Sander (Bamenda Center for Health Promotion and Research) shared her experience of using AlereLAM in a hospital setting in Cameroon and Lara Vojnov provided an update on WHO plans to revise guidelines for people with advanced HIV.

The second panel “Bringing POC LAM-based diagnostics to scale – can this bridge deadly TB testing gaps?” was moderated by Isaac Chikwanha of GHIT. The panel focused on access barriers for TB LAM, including regulatory barriers, pricing issues and what needs to be done to overcome these challenges. Key issues that came up were the lack of funding in some regions, lack of alignment between TB and HIV programmes in terms of procurement, and perceptions that the recommendations are or have been unclear. Fujifilm also shared their plans to scale production of the FujiLAM test and address pricing issues.

Closing the meeting, Sergio Carmona, Director of TB, HIV and Hepatitis C at FIND, asked the group to keep in mind Carol’s story and the human impact of their work, in terms of the challenges and complications patients face in getting a TB diagnosis, as well as the risks associated with leaving patients undiagnosed. Sergio stressed that patients and communities can play a role in driving demand for the TB LAM test, and pointed out that people are currently being underserved by existing diagnostics. He noted that in the HIV community, a test like TB LAM would have been picked up without such a delay and questioned whether the test could be bought from the more generous HIV budgets in the future. Stakeholders were urged to ensure regulatory and associated issues are cleared quickly moving forward. Sergio also called for innovation in technology and beyond, in terms of funding allocation, communication with countries and how technical support is provided.
Catharina Boehme, CEO of FIND

Lucica Ditiu, Executive Director of the Stop TB Partnership
KEY POINTS AND NEXT STEPS

1. There is an urgent need for non-sputum-based diagnostics in TB
   - Diagnostics are still the weakest link in the TB care pathway

2. TB LAM based tests are simple, inexpensive and can be used at the point-of-care in low-resource settings

3. Despite modest sensitivity, existing TB LAM tests can be used to provide rapid and accessible diagnosis to the sickest patients with the worst prognosis
   - TB LAM tests are uniquely able to improve TB diagnosis rates in patients living with HIV, and particularly those with advanced HIV
   - AlereLAM has been shown to increase TB diagnosis rates and reduce mortality in patients living with HIV
   - TB LAM tests should be used pragmatically to meet the needs of underserved patients

4. Next-generation TB LAM tests with increased sensitivity are required to meet the TPP
   - The FujiLAM test shows increased sensitivity compared with AlereLAM, meeting the TPP for a non-sputum-based TB diagnostic
   - Future innovation will be valuable to further improve sensitivity and refine the assay
   - Abbott and Fujifilm are both working on innovations for TB LAM technology

5. Ongoing studies will provide evidence for expanding the test to populations beyond those living with HIV
   - Fujifilm are preparing a package of evidence on the use of FujiLAM in different populations for WHO review

6. Concerted efforts are needed to drive demand for and uptake of the test
   - Educating patients about the value of diagnostics can drive demand from the ground upwards
   - Ongoing education for healthcare workers and high-risk communities will be essential to ensure demand for and uptake of the test
   - Guidelines may require clarification on the adoption of such tests at the country level
   - WHO guidance on LAM-based tests will need to be adapted to accommodate tests such as FujiLAM when additional data on its diagnostic accuracy, evidence on feasibility and acceptability from settings of intended use have been generated
   - Further sessions on TB LAM at key meetings would be valuable to highlight the benefits of the test to stakeholders

7. Procurement processes need alignment and simplification
   - Collaboration between stakeholders involved in the procurement process is essential to facilitate the process
   - Alignment is required between TB and HIV programmes in terms of procurement, and the test could be purchased from HIV budgets if needed
   - If required, countries can reprogramme Global Fund grants to procure TB LAM

8. The pricing of TB LAM tests needs to be carefully considered to facilitate procurement and patient access, while enabling sustainability and future investment in the technology
KEY COMMENTS

The area of diagnostics is still the weakest link in TB.

Eliud Wandwalo, Senior Disease Coordinator, TB at the Global Fund

Technology is not only about making it more sensitive, but also simpler to use – imagine if next time we meet there’s a self-test for TB diagnosis such as TB LAM.

Sergio Carmona, Director of TB, HIV and Hepatitis C at FIND

A lot of work has gone into developing TB LAM, so on behalf of affected communities, thank you!

It’s time now that we ensure that this tool is rolled out broadly and has its intended impact...the longer we keep it locked away, people will keep dying.

Carol Nawina Nyirenda, Executive Director, CITAM+

Although current tests have modest sensitivity, they have a unique role in the diagnostic landscape, as they provide rapid and accessible diagnosis to the sickest patients with the worst prognosis...However, we need a next-generation test that has higher sensitivity and we know it’s within reach.

Morten Ruhwald, Head of TB at FIND

Techno-optimism is stopping us implementing tests that have been proven to save lives.

Duncan Blair, Abbott

Note: Comments have been paraphrased and edited for clarity.
Why POC tools matter, Carol Nawina Nyirenda, CITAM+
Carol Nawina Nyirenda, a TB/HIV patient advocate, shared her personal story of battling both TB and HIV and the role that diagnostics played in her journey. Carol stressed the importance of diagnostics in those co-infected with HIV and TB, as the two diseases can worsen one another, and TB remains the most common cause of death for people living with HIV. HIV infection can also affect TB symptoms, sometimes resulting in the absence of a productive cough, which can make common sputum-based diagnosis challenging. Obtaining a TB diagnosis can still be a stigmatizing experience for patients, faced with healthcare professionals in masks and protective wear to reduce the infection risks associated with sputum collection. The TB LAM test could be a real “game changer” as patients can provide a urine sample in private, allowing a degree of privacy compared with the current sputum-based tests. Carol also emphasized the importance of education for patients and healthcare workers. A key issue in the uptake of the test is that there is little understanding of TB in the community, so the value of the test is under-appreciated. However, patients would likely be very keen for a TB LAM test if they understood its value and the consequences of not being diagnosed and treated for TB. In addition, community and healthcare workers shouldn’t be expected to learn everything about a new tool in one session, and ongoing education will be essential. Community mobilization and the ongoing education of patients and healthcare workers was recommended to create demand for the test from the ground upwards.

The promise of TB LAM tests, Morten Ruhwald, FIND; presentation
Morten Ruhwald provided an overview of the science behind urine-based TB LAM tests and the evidence for their value in diagnosing TB. The LAM antigen is an attractive target for a diagnostic test, as a component of mycobacterial cell walls present in high levels in urine. Interestingly, levels of LAM are higher in HIV-positive patients and even higher in patients with advanced HIV compared with people without HIV. The inverse correlation between CD4 count and LAM sensitivity makes LAM a unique and valuable marker for patients with advanced HIV, where standard tests don’t work well. The AlereLAM test is currently the only test on the market, but the FujiLAM test is likely to enter the market this year or early next year. Importantly, the MSD LAM Reference Platform now allows developers to benchmark their tests. In terms of the TPP for non-sputum TB diagnostics, AlereLAM was noted as not quite meeting the TPP given its sensitivity of around 50%. FujiLAM was noted as better fitting the TPP, as it is designed with an amplification step that allows it to detect 10-fold lower levels of LAM (50 pg/mL), driving a higher sensitivity of around 70% in people living with HIV.

However, AlereLAM has been shown to have diagnostic value in people living with HIV, with pooled sensitivity of around 42% overall, increasing to 54% in patients with CD4 cell count <100 cells/µL, but decreasing to around 16% in patients with a CD4 count >200 cells/µL. In a South African study conducted in HIV-positive patients with acute medical admissions to a township hospital, there was a striking improvement in diagnosis with AlereLAM vs standard sputum diagnostics: a 26% increase overall and a 39% increase in patients with CD4 counts <100 cells/µL. It is worth noting that in the 24 hours after admission, only 37% of patients in the study were able to produce a sputum sample compared with 99% of patients who were able to provide a urine sample, demonstrating the value of non-sputum-based
diagnostic tests in this patient population. Evidence on the comparative performance of AlereLAM and FujiLAM in HIV-positive patients supports the improved TPP of the FujiLAM. In a meta-analysis of AlereLAM and FujiLAM’s performance in patients from sub-Saharan Africa, sensitivity was 35% vs 71%, respectively. Sensitivity for AlereLAM vs FujiLAM, respectively, was 56% vs 87% in patients with a CD4 count <100 cells/µL and 11% vs 44% in patients with a CD4 count >200 cells/µL. Performance between inpatient and outpatient settings was comparable for FujiLAM and slightly lower in outpatient settings with AlereLAM.

Critically, LAM-based tests have also been shown to reduce mortality in people living with HIV. In a study of Malawian adults with HIV, patients with low CD4 count randomized to receive AlereLAM (vs standard-of-care diagnostics alone) had a 7.1% adjusted risk reduction in mortality. These findings highlight the substantial impact a diagnostic costing only $3.5 per test can have in a high-risk, highly vulnerable population. A number of studies are currently looking at the performance of TB LAM tests in different patient populations e.g. children, those with extrapulmonary TB, and HIV-negative individuals, with results expected within the next year. Work is also ongoing to improve the TB LAM test profile, in terms of sensitivity (ideally below 10 pg/mL to be able to detect LAM in all patients), better reagents, other antigens, and new assay designs. Morten concluded his presentation by noting that despite modest sensitivity, current LAM assays have a unique role in the diagnostic landscape by providing rapid and cheap diagnosis to the sickest patients with the worst prognosis.

Policy update, Alexei Korobitsyn, WHO; presentation
Alexei Korobitsyn, Global TB Programme, WHO, provided an update on WHO policies for TB LAM and the changes implemented in the recent 2019 guideline. In 2015, WHO issued a guideline on the use of LF-LAM for the diagnosis and screening of active TB in people living with HIV. The 2015 guideline recommended the use of the LF-LAM test for the diagnosis of TB in HIV-positive adult inpatients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/µL, or HIV-positive patients who are seriously ill regardless of CD4 count or with unknown CD4 count. The LF-LAM test was not recommended for other patient populations. The 2019 WHO guideline increased the scope and strength of the recommendations based on the improved quality of evidence available, allowing for better definition of the appropriate patient population for the test. In inpatient settings, WHO now strongly recommends using LF-LAM to assist in the diagnosis of active TB in HIV-positive adults, adolescents and children with signs and symptoms of TB (pulmonary and/or extrapulmonary), or with advanced HIV disease, or who are seriously ill, or irrespective of signs and symptoms of TB and with a CD4 cell count of less than 200 cells/µL. In outpatient settings, WHO suggests using LF-LAM to assist in the diagnosis of active TB in HIV-positive adults, adolescents and children with signs and symptoms of TB (pulmonary and/or extrapulmonary) or seriously ill, and HIV-positive adults, adolescents and children irrespective of signs and symptoms of TB with a CD4 cell count of less than 100 cells/mm³. It is noted that the LF-LAM should be used as an add-on to clinical judgement in combination with other tests and should not be used as a replacement or triage test (see diagnostic algorithm in presentation for further information).

Alexei noted that the AlereLAM test remains the only commercially available urine test that has been shown to reduce mortality in HIV patients with advanced disease, although uptake has been limited to date. Alexei ended his presentation by noting that more accurate LAM tests, in terms of sensitivity and specificity, are needed in the future.
PANEL DISCUSSIONS
Please note that discussions have been paraphrased and edited for clarity.

TB LAM tests: from development to policy uptake and implementation – where do we stand today?
Moderated by Lara Vojnov, Diagnostics Advisor in the HIV and Hepatitis Department, WHO

Q. There is a defined TPP on point-of-care non-sputum biomarker tests. Where do the current urine-based TB LAM tests stand, are they meeting expectations, and what would you say are the barriers in terms of achieving the most desirable TPP?

• Samuel Schumacher (FIND): High-priority TPP for a biomarker-based test is one that would apply to all patients and one that would be accessible and simple to use. Sensitivity is also critical and current tests fall short, especially outside of people living with HIV. In terms of the science, we also need a better understanding of LAM, e.g. what drives variability between patients. In terms of product development, we need better reagents and need to increase the sensitivity of the test. We also need other formats of assays to increase sensitivity or make the test simpler to use and keep costs at a level where the test can be scaled up.

Q. The global health community is excited about the FujiLAM test, although prospective studies are needed to confirm the initial findings, quantify FujiLAM’s effect on clinical outcomes, establish performance in HIV-negative people and children, and assess the feasibility for point-of-care implementation in a variety of clinical settings. Can you tell us where you stand today with the clinical trials and what have you learnt from the clinical trials so far?

• Kathleen England (Fujifilm): Fujifilm are currently undertaking a number of studies of the FujiLAM test to prepare a data package for the WHO’s review process (further details here). The focus is still on those living with HIV, but we hope to expand to other indications as well. Fujifilm are
currently reviewing various research proposals from partners and investigators. There is a rich evidence base supporting the sensitivity and specificity of the FujiLAM test. We’re currently manufacturing the test on a small scale for research purposes only. However, this will change as we get a better idea of need, and with higher-volume production, we will be able to lower the price of the test. In terms of implementation readiness, everything is on my agenda and currently ongoing in terms of aspects such as registration with countries and validation.

Q. Abbott has been in the HIV market for a long time now. One of the things we’ve seen in the market is that new technologies take a few iterations to get going. While these technologies are very hopeful, we’ve also seen delays in uptake, with countries/donors deciding to wait and use current assays that are procurable, with the hope that things in the future might better. What is your perspective? Has it impacted country uptake?

- Duncan Blair (Abbott): I’m very pro-innovation; however, I think that techno-optimism is a barrier to access and people getting the tests and treatment they need. No other assay has been proven to save lives in TB. Despite that, I’ve had to push for not discontinuing the AlereLAM test, as despite our best efforts, it only provides a small amount of revenue for the company. The Fuji assay sounds exciting and has shown clear improvements in sensitivity and specificity, but it’s not on market yet and has not yet been through the recommendation process. We are currently working to improve AlereLAM, applying the experience we have in malaria. A couple of years ago, we undertook a project to make some significant changes to our lateral flow technology to drive sensitivity down to much lower levels of analyte detection. Some of that technology has been applied to the TB LAM assay in very early-stage research and development, but the intention is to keep the format identical, i.e. no preconcentration step. As mentioned, development pipelines very “leaky”, and only one or two things make it through to market. Consequently, techno-optimism is stopping us implementing tests that have been proven to save lives.

Q. As a TB REACH grantee, you have done a lot of work in the area of TB LAM. Could you describe to us the studies you undertook and what have you learnt so far?

- Melissa Sander (Bamenda Center for Health Promotion and Research): I’m based in Cameroon and have experience of using AlereLAM as part of a study in a hospital setting, where we systematically tested everyone admitted to hospital. 36% of individuals in the study had bacterially confirmed TB and the urine LAM was useful, particularly in those unable to produce sputum. The doctors were surprised, as patients without typical symptoms, such as weight loss, and cough, were testing positive for TB. We were concerned that doctors would use TB LAM as a roll-out test, given that sensitivity is limited, but that didn’t happen. Doctors were just happy to have an additional test to use, especially when sputum couldn’t be produced. The doctors learned that they need to think about TB more. We plan to scale up the systematic testing of hospitalized patients with HIV and we’re hoping to expand to broader patient groups. One challenge is the procurement, as it took a long time to get test and I’m glad to hear that this should be quicker in the future.
Q. This opens up questions around performance vs access. If a patient can’t generate sputum, should we be more flexible about performance standards in that setting?

- Duncan Blair (Abbott): The clinical data in terms of the reduction in morbidity and mortality from using the TB LAM test speaks for itself. The question is whether to use nothing or use something that has been shown to have impact.

- Kathleen England (Fujifilm): From a scientific perspective, we also want to innovate. Our priority is to make better antibodies and other capture technologies that could make the test simpler. For example, using nanocages or magnetic affinity beads that pull LAM out and concentrate it on existing assays to improve the lower limit of detection and amplification of the signal. However, as with all technology there is a cost. The question is what cost will we pay for new technology, and this depends on how good the test is and the population the test will serve. If the test is only indicated for a small population, the costs will likely be higher.

- Samuel Schumacher (FIND): In term of the question of accessibility vs performance of test, I agree that some tests with relatively low sensitivity still have major impact if they can reach patients that we could simply not test with conventional diagnostics. A test should not be discounted based on low sensitivity alone. LAM tests clearly have particular value in patients who can’t give a sputum sample and may also enable more decentralized testing.

- Lara Vojnov (WHO): One thing we’ve definitely learnt in the HIV space is that competition can be a wonderful thing in terms of supporting the costing pieces.

Q: Are there going to be future guidelines for the TB LAM test in terms of HIV and advanced HIV, and when to offer prophylaxis? If so, what are the timelines for that? Current guidelines are reasonably complex for people in decentralized settings.

- Lara Vojnov (WHO): We developed the advanced HIV guidelines a few years ago, before we revised the TB LAM guideline. This year we are embracing guideline revision and working on a consolidated guideline looking at a number of key clinical and operational issues. This will happen over two phases. We hope to take these recommendations and refine them within the advanced disease package of care and see how we can combine that with our service delivery work within HIV programmes. As those working in TB will see TB LAM as being TB-specific, we’re looking at it as one consolidated package including cryptococcal screening and various prophylaxis guidelines. We don’t need any additional evidence for this piece, as it won’t go through a guideline process; it’s about revising the current advanced package language. Ideally, this will happen this year.
Q. We heard about how TB LAM can add value, but uptake has been low and there are a number of challenges. What challenges have NTP had in rolling out TB LAM?

- Charles Sandy (AIDS/TB Programmes, Zimbabwe): Despite evidence that TB LAM is a good test, there has been a delay in rolling out the programme, and issues with funding. Most national programmes depend on external funding as government budget allocations are usually insufficient to cover all the needs. We need to think about how to improve access, particularly for those living in rural areas.

Q. Marketing to healthcare workers is something Carol mentioned - we shouldn’t expect people in the field to get all the knowledge from one session. What is the experience in India?

- Nishant Kumar (Ministry of Health & Family Welfare, India): Most of the issues have been covered in the first panel, which discussed the science quite comprehensively. A key issue was that the initial recommendations weren’t clear. In addition, we have had to work to reduce the high number of missing (undiagnosed) cases of TB in India. I think we have managed to close that gap somewhat in India. Urine is definitely one of the best sample for patients for a diagnostic test. Another issue is the regulatory framework, as in India, TB and HIV are two different programmes. Accuracy is also important. Funding is not barrier in India, as TB and HIV have always been a priority and the budget has been increased.
Q. What’s the perspective of the Global Fund in terms of TB LAM access?

- Eliud Wandwalo (Global Fund): Our model depends on country ownership. We support diagnostics approved by WHO and once diagnostics are WHO approved, countries can use Global Fund funding to procure the product. After we put TB LAM in our recommendations and funding paper, we expected countries to come with requests, but there wasn’t a lot of demand. We think the earlier recommendations from WHO were a bit restrictive and may have limited applications from countries. Funding could be a barrier but did not appear to be a big issue for us, as countries can reprogramme what they have in the grant for TB funding if required. In the last cycle, we had a number of countries that could not use their full allocation for TB funding. Another issue could be the lack of clarity between the two programmes (TB and HIV) that procure the test. We have asked countries with both programmes to have single concept, but we still come up against these kinds of issues. We have a 20% higher allocation for TB in the upcoming cycle and we have been very clear that TB LAM can be used. We expect countries will be able to ask for this test and hope that use will increase with the broader, more flexible 2019 WHO guideline.

Q. You brought up the issue of procurement. I know GDF is significantly involved in the procurement of TB products. What has your experience been in last 5 years?

- Bibiana Angarita Zambrano (Stop TB Partnership): We believe in the product and we expected a boom in requests once available. However, nothing happened, and 6 months later we thought we have to do something. That’s why we started sharing information with country supply offices, ministries of health and regional technical advisors. After that, things got a bit better, but didn’t reach the levels of uptake we wanted. We then conducted a survey to understand what was happening. The findings were that clients mostly lacked funds for the TB LAM test. After pushing and sharing information on the benefits of TB LAM, we saw some increased uptake. However, we still need more communication, and greater clarity on which donor (TB or HIV) is procuring the test. We’ve also been asked to develop GDF technical information notes on TB LAM (which contain key supply information to make a procurement request) in different languages to be more client oriented; we are consequently planning to develop versions in French and Spanish. Another barrier is lack of in-country product registration and we have plans meet with the supplier to discuss more about what we are missing in terms of communication/dissemination to countries to improve the procurement of TB LAM in 2020.

Q: What could be done?

- Karen Heichman (Bill & Melinda Gates Foundation): I can’t speak much about uptake for TB LAM from Global Fund perspective. However, we’re thinking about a next-generation TB LAM test, rooted in science and performance. Usage remains quite complicated as the guidelines are strict, but can be interpreted as containing ambiguous and confusing directives. We need to improve the performance of the test in all patients, not just people living with HIV, then recommendations for usage will be clearer. Ideally, we’d like to get to a place where all HIV-positive patients in high-risk settings will be tested for TB.

- Eliud Wandwalo (Global Fund): I think country-level guidelines are important, and we need countries to be quick to adapt guidelines at the country level. There is also work to be done in terms of training healthcare workers. The area of diagnostics is still the weakest link in TB. Diagnostics is not very well integrated, and we get a lot of questions for our Technical Review
Panel. Countries still need a lot of technical assistance to understand which diagnostic test can be used where.

- Charles Sandy (AIDS/TB Programmes, Zimbabwe): For me, we need to be clear about the population for the test. For example, when we started using TB LAM, our assumption was that we don’t give the test to those with advanced HIV, mainly because of the test and treat all campaign. But over the years, we’ve realised that a number of people with advanced HIV are still coming, so we will need guidance on where to target the test for better effectiveness. The other issue that could be supported by the Global Fund is the price of the test. The funding envelope for TB programmes will improve marginally in the new funding window (although for us, funding has been reduced). If the test remains at current costs (~$10 USD), this could be a limitation when it comes to privatization. We’re looking to use the test at a primary care level, as it’s easy to use. In that case, we need to consider the unit cost to improve coverage and we might need to advocate for lower costs to drive market improvement. Another issue is training, which is very critical. It would also be valuable to hold sessions on the test at future standalone meetings or symposia, but unfortunately there aren’t many of these meetings in our region. There’s an opportunity there to highlight benefits to programme managers.

- Nishant Kumar (Ministry of Health & Family Welfare, India): Yes, I agree it’s not WHO mandate to generate evidence but pace of new evidence generation and recommendations is slow.

- Alexei Korobitsyn (WHO): Yes, we receive a lot of criticism about the guidelines. However, our role is to systematically assess evidence and provide guidance based on this evidence. The 2019 guideline is better than the 2015 guideline, but the 2015 guideline is still good. I understand it would be easier to say that the test could be used in all people, but there are conditions and groups that are more appropriate. It’s very clear in the guidelines that the test can save lives.

Q: Abbott are developing a next-generation test to face challenges. What plans do Fujifilm have to address barriers?

- Ryo Kobayashi (Fujifilm): I think there are a lot of challenges to face. In terms of pricing, we’re working on solutions right now. We’re also manufacturing small pilot production, then we will move up to mid-scale production once we receive a clearer idea of market demand, and this will lower the pricing. In terms of specific goals, we are working with FIND and other global stakeholders to understand how to reach those in need.

- Duncan Blair (Abbott): These discussions are needed in other forums, e.g. with those in finance, to make sure resources get allocated, otherwise FujiLAM will face the same issues as the AlereLAM.
In his closing remarks, Sergio asked the group to keep in mind Carol’s story and the difficulties and delays patients like Carol face in getting a TB diagnosis. Sergio stressed that demand for the TB LAM test can be driven by patients and communities, who are currently underserved by existing diagnostics. He pointed out the missed opportunities for clinicians in leaving people with single-digit CD4 counts untested, when a test for TB in those living with advanced HIV disease is already available. Stakeholders were urged to ensure regulatory and associated access issues are cleared quickly in the near future. Sergio also called for new ways to address funding needs, improve communication with countries on new innovative approaches to diagnose TB and effective ways to provide sustainable technical support. Finally, Sergio asked the group to consider whether future TB diagnostics could be simple enough for patients like Carol to use, noting that technological developments are not only about improving sensitivity, but also about making tools easier to use.
ABBREVIATIONS

- AlereLAM, Alere Determine™ TB LAM Ag
- CEO, Chief Executive Officer
- CITAM+, Community Initiative For TB, HIV/AIDS & Malaria
- FIND, Foundation for Innovative New Diagnostics
- FujiLAM, Fujifilm SILVAMP TB LAM
- GHIT, Global Health Innovative Technology Fund
- HIV, Human immunodeficiency virus
- POC, Point of care
- TB, Tuberculosis
- TPP, Target product profile
- WHO, World Health Organization
### APPENDIX: PARTICIPANT LIST AND MEETING AGENDA

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<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Adam</td>
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###
TB LAM
Paving the way for next-generation point-of-care testing

6 FEBRUARY 2020
15:00–17:00
FOLLOWED BY TEA
6 FLOOR,
SALLE B1.06
CAMPUS BIOTECH
GENEA, SWITZERLAND

WELCOME AND INTRODUCTION
WELCOME REMARKS
OPENING REMARKS
WHY POC TOOLS MATTER
THE PROMISE OF TB LAM TESTS
POLICY UPDATE

PANEL DISCUSSION
TB LAM tests: from development to policy uptake and implementation – where do we stand today?

PANEL DISCUSSION
Bringing POC LAM-based diagnostics to scale – can this bridge deadly TB testing gaps?

SUMMARY & CLOSE

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Chiaki Noguchi, Ministry of Health, Labour and Welfare, Japan
Carol Nawina Nyirenda, CITAM+
Morten Ruhwald, FIND
Alexei Korobitsyn, WHO

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Duncan Blair, Abbott
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Karen Heichman, Bill & Melinda Gates Foundation
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Sergio Carmona, FIND