

To: Ambassador Deborah L. Birx, U.S. Global AIDS Coordinator & U.S. Special Representative for Global Health Diplomacy

CC: Dr. Lisa Nelson, Chief Medical Officer (Acting), The Office of the U. S. Global AIDS Coordinator and Health Diplomacy
Dr. Carlos Del Rio, Chair, PEPFAR Scientific Advisory Board

8 February 2017

Open Letter re: Urgent need to roll out LAM test for TB in some people with HIV

Dear Ambassador Birx,

As organizations concerned with ending the epidemics of HIV and tuberculosis (TB), we congratulate you on your excellent leadership of the President's Emergency Plan for AIDS Relief (PEPFAR). Acknowledging the continuing emergency that HIV, and TB—the leading killer of people with HIV¹—present worldwide, we welcome the PEPFAR Scientific Advisory Board and its TB/HIV Expert Working Group's prioritization of expediting diagnosis of TB in people with HIV. As such, we write to ask for PEPFAR's support for the immediate introduction of the LAM test—a simple, useful diagnostic to detect TB in extremely vulnerable people with HIV—in all PEPFAR-funded countries and programs.

As you know, until recently, TB has been particularly difficult to diagnose in people with HIV with low CD4 T cell counts and advanced disease, who are at extremely high risk of developing TB and of dying from TB. Fortunately, a simple, inexpensive, relatively new test called the lipoarabinomannan (LAM) test has demonstrated impact—including increased survival due to earlier initiation of anti-TB treatment—in this population. The test, marketed as the Determine TB LAM Ag test by Alere, is a rapid, urine-based, point-of-care test. As such, it is simpler to use and more sensitive in people with HIV than many other sputum-based diagnostic methods for TB, as sputum is difficult to produce, and extrapulmonary or paucibacillary TB disease are more common in people with HIV. Since 2015, the World Health Organization (WHO) has recommended the use of this test as a preliminary test to rule in TB in people with HIV with CD4 counts below 100/mm³ or who are seriously ill.² The test is especially useful in hospital or clinical settings.

A recent randomized controlled trial in four PEPFAR countries demonstrated the benefit of LAM testing in guiding TB treatment initiation and reducing mortality in people with advanced HIV.³ Researchers randomized over two thousand hospitalized people with HIV to receive either LAM plus routine diagnostic tests for TB (smear-microscopy, GeneXpert MTB/RIF, and culture) or routine diagnostic tests alone. The simple addition of LAM testing reduced all-cause 8-week mortality by four percentage points, with a relative risk reduction of 17%. Using LAM tests ensured more patients were started on TB treatment, and that treatment initiation occurred earlier. Earlier treatment is important not only for individual health, but also for reducing infectiousness, as TB rapidly becomes non-infectious once appropriate therapy is started.⁴

While LAM testing has limited sensitivity, it is the first TB diagnostic test ever to demonstrate a clear mortality benefit in a randomized study among HIV+ persons with advanced immunosuppression. It is also the first truly point-of-care test to be recommended by the WHO. It has no infrastructural or biosafety requirements. And, at a cost of just USD \$2.66 per test, it is extremely affordable. Yet despite being on the market and WHO-recommended for over one year, no country has scaled up to routinely procurement and use of LAM. We are concerned that people with advanced HIV are missing opportunities for simpler, faster diagnosis of TB and therefore survival. We are also troubled to learn that Alere may discontinue production of this important test if it does not start seeing sales volumes in the near future.

As such, we urge PEPFAR to support the provision of immediate access to the life-saving, simple, affordable (and likely cost-saving) intervention of LAM testing in the countries it supports. We have already recommended that the Office of the Global AIDS Coordinator include LAM testing in the PEPFAR 2017 COP/ROP Guidance. We furthermore request that PEPFAR i) directly procures LAM tests, ii) works with PEPFAR-funded countries and programs to incorporate LAM testing into their screening and testing algorithms, iii) encourages PEPFAR-funded countries to facilitate registration of LAM tests as soon as possible, and iv) supports PEPFAR-funded countries to conduct their own procurement of LAM tests.

We kindly request your response, which can be directed to Erica Lessem at erica.lessem@treatmentactiongroup.org, by February 27, 2017.

Respectfully submitted,
AIDS and Rights Alliance for Southern Africa (ARASA)
AIDS-Free World
Collectif des Organisations de Lutte contre la Tuberculose et les Maladies Respiratoires de Côte d'Ivoire (COLTMR-CI)
The Global Network of People Living with HIV (GNP+)
Health Global Access Project (Health GAP)
International Community Of Women Living with HIV Eastern Africa (ICWEA)
International Treatment Preparedness Coalition (ITPC)
International Treatment Preparedness Coalition – Eastern Africa (ITPC-EA)
RESULTS
Treatment Action Campaign (TAC)
Treatment Action Group (TAG)

¹ UNAIDS. Global HIV Statistics. Geneva: UNAIDS; 2016 November. Available from:

http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

² World Health Organization. The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis in people living with HIV. Geneva: World Health Organization; 2015. Available from: <http://www.who.int/tb/publications/use-of-lf-lam-tb-hiv/en/> ³ Peter

JG, Zijenah LS, Chanda D, et al. Effect on mortality of point-of-care, urine-based lipoarabinomannan testing to guide tuberculosis treatment initiation in HIV-positive hospital inpatients: a pragmatic, parallel-group, multicountry, open-label, randomised controlled trial. Lancet: 2016 Mar 9. [http://dx.doi.org/10.1016/S0140-6736\(15\)01092-2](http://dx.doi.org/10.1016/S0140-6736(15)01092-2).

⁴ Dharmadhikari AS, Mphahlele M, Venter K, et al. Rapid impact of effective treatment on transmission of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis. 2014Sep;18(9):1019-25. doi: 10.5588/ijtld.13.0834.