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

CC: J. Sean Cavanaugh, Senior Tuberculosis Advisor, Office of the U.S. Global AIDS Coordinator
Dr. Carlos Del Rio, Chair, PEPFAR Scientific Advisory Board

5 April 2018

Open letter re: ensuring scaled up, expanded TB-LAM testing in all 2018 Country Operating Plans

Dear Ambassador Birx,

As organizations, researchers, and clinicians concerned with ending the epidemics of HIV and tuberculosis (TB), we thank you for your continued commitment to ensuring President's Emergency Plan for AIDS Relief (PEPFAR) support for evidence-based programming to address HIV and TB/HIV. TB remains the leading cause of death in people with HIV, and we remain concerned about underutilization of the TB-LAM test, a simple, inexpensive diagnostic proven to reduce TB deaths in people with HIV. In light of recent findings about TB-LAM's life-saving potential with expanded use in people with HIV, and in anticipation of the final Country Operating Plan (COP) 18 approval meetings (April 10-13 and April 17-20, 2018), **we ask you to ensure that 2018 COPs for all high TB/HIV burden countries include TB-LAM testing, including procurement, nationwide scale up, and expanded use of the test.**

We applaud PEPFAR's explicit support of optimal strategies and tools, including TB-LAM testing, to address TB/HIV in the comprehensive 2018 COP guidance. Yet the onus is currently still on countries to opt into using this test. Additionally, new data have emerged since the 2018 COP guidance supporting an expanded use of LAM.

The multi-country, randomized STAMP trial showed that using TB-LAM testing in addition to GeneXpert MTB/RIF in all HIV+, hospital-admitted adults resulted in a survival benefit in the most at-risk sub-populations in a pre-specified analysis, and resulted in an increase in TB diagnosis and treatment initiation in the general study population.[1] These data expand the previous evidence to indicate the value of using TB-LAM testing as a TB screening test in all hospital patients with HIV. Further, a separate prospective observational cohort study of both ambulatory and hospitalized HIV-positive adults in Kenya indicate the utility of expanding TB-LAM testing to people with CD4<200mm^3 to increase diagnostic yield.[2] We enclose with this letter the recently presented data from the STAMP trial demonstrating its clinical benefit and cost-

[1] Gupta-Wright A, Corbett EL, van Oosterhout JJ, et al. Rapid urine-based screening for TB to reduce AIDS-related mortality in hospitalized patients in Africa (STAMP) trial. CROI 2018. Abstract 38LB.

[2] Huerga H, et al. Incremental Yield of Including Determine-TB LAM Assay in Diagnostic Algorithms for Hospitalized and Ambulatory HIV-Positive Patients in Kenya. PLoSOne. 2017 Jan 26;12(1):e0170976. doi: 10.1371/journal.pone.0170976.

effectiveness as a screening test for all HIV-positive individuals admitted to hospital, as well as the Kenya observational cohort study.

These new data not only reiterate the need for TB-LAM uptake, but also favor expanding the use of TB-LAM testing in both inpatient and outpatient settings. The World Health Organization's 2015 recommendation, issued well before these data were available, recommends the TB-LAM test for use as in people with CD4<100 cells/mm^3 or who are seriously ill. Evidence now strongly suggests the dramatic benefits of using the TB-LAM test in high TB/HIV burden settings for all people with HIV admitted to hospital regardless of CD4 count or symptoms (plus GeneXpert MTB/RIF Ultra), and for all people with HIV with CD4<200 cells/mm^3 presenting to ambulatory care.

Despite the great potential of TB-LAM to enable earlier detection of TB and life-saving earlier treatment start in those at most risk of dying from TB, and its low cost and simple technology, it is still infrequently used. Only South Africa and Uganda have begun nationwide use of TB-LAM. PEPFAR could play a catalytic role in ensuring uptake of this important test—including its expanded use. But our analysis of the 11 current 2018 COPs available to us from PEPFAR-funded high TB/HIV burden countries (of which there are 24) indicates that only one includes use of TB-LAM. Three additional COPs included feedback related to the use of TB-LAM. None includes expanded use of TB-LAM in line with recent data (see Appendix for details).

To ensure the rights to health, life, and the benefits of scientific progress of people with HIV, we urge PEPFAR to take all steps possible to increase access to TB-LAM testing and prevent further needless TB deaths in people with HIV. **As such, we ask that you:**

1. **Require that high TB/HIV burden countries[3] include TB-LAM testing procurement and nationwide scale up in their 2018 COP (or Regional Operating Plan) as a condition of receiving PEPFAR funding, and**
2. **Encourage countries to include in such plans the expanded use of TB-LAM:**
    a. **as a hospital-based screening test (along with GeneXpert MTB/RIF Ultra) for all people with HIV, regardless of CD4 count or symptoms,**
    b. **in outpatient settings, to all people with HIV with CD4 counts <200 cells/mm^3.**

We thank you again for your excellent leadership, and look forward to your carrying forward the above in your meetings next week. Please do not hesitate to let us know if you have any questions. We request your response, which can be directed to Erica Lessem at erica.lessem@treatmentactiongroup.org, by April 10, 2018.

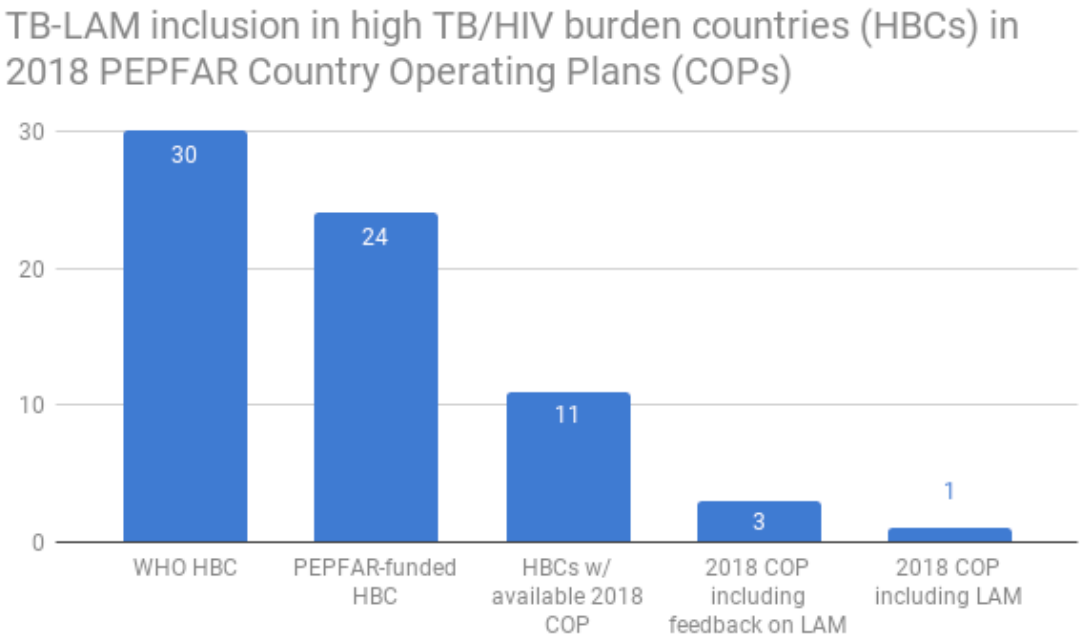
[3] World Health Organization-listed high TB/HIV burden countries (countries with 2018 bilateral PEPFAR support in **bold**; with regional PEPFAR support in ***italics and bold***) **Angola**, **Botswana**, Brazil, **Burma**, **Cameroon**, Central African Republic, Chad, ***China***, Congo, **Democratic Republic of the Congo**, **Ethiopia**, **Ghana**, Guinea-Bissau, **India, Indonesia**, **Kenya**, **Lesotho**, Liberia, **Malawi**, **Mozambique**, **Namibia**, **Nigeria**, **Papua New Guinea**, **South Africa**, **Swaziland**, ***Thailand***, **Uganda**, **Tanzania**, **Zambia**, **Zimbabwe**

Respectfully submitted,

Organizational endorsements
AIDS and Rights Alliance for Southern Africa, Regional (Southern and East Africa)
AIDS-Free World, Global
Global TB Community Advisory Board (TB CAB), Global
Health GAP (Global Access Project), Global
International Community of women living with HIV, Regional (Eastern Africa Uganda, Kenya, Tanzania, Rwanada and Burundi)
International Treatment Preparedness Coalition (ITPC), Global
RESULTS, USA
TB Centre, London School of Hygiene & Tropical Medicine, UK and Global
The Global Network of People Living with HIV (GNP+), Global
Treatment Action Campaign, South Africa
Treatment Action Group (TAG), USA and Global

Individual endorsements
Institution noted for affiliation purposes and does not reflect institutional endorsement
Yvan Jean Patrick Agbassi, Global TB CAB, Senegal
Professor Liz Corbett, London School of Hygiene & Tropical Medicine, and Malawi Liverpool Wellcome Research Programme
Paul Drain, University of Washington
Ankur Gupta-Wright, London School of Hygiene & Tropical Medicine
Blessina Kumar, Global Coalition of TB Activists
Adrienne E. Shapiro, MD, PhD, University of Washington

Appendix: Analysis of Inclusion of TB-LAM in Available 2018 COPs for High TB/HIV Burden Countries



World Health Organization-designated high TB/HIV burden countries[4] (N=30): Angola, Botswana, Brazil, Burma, Cameroon, Central African Republic, Chad, China, Congo, Democratic Republic of the Congo, Ethiopia, Ghana, Guinea-Bissau, India, Indonesia, Kenya, Lesotho, Liberia, Malawi, Mozambique, Namibia, Nigeria, Papua New Guinea, South Africa, Swaziland, Thailand, Uganda, Tanzania, Zambia, Zimbabwe

PEPFAR-supported high TB/HIV burden countries[5] (N=24): Angola, Botswana, Burma, Cameroon, China, Democratic Republic of the Congo, Ethiopia, Ghana, India, Indonesia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Papua New Guinea, South Africa, Swaziland, Thailand, Uganda, Tanzania, Zambia, Zimbabwe

PEPFAR-supported high TB/HIV burden countries for which COPs were obtained (N=11): Botswana, Democratic Republic of the Congo, Kenya, Malawi, Mozambique, Nigeria, Swaziland, South Africa, Tanzania, Uganda, Zimbabwe

PEPFAR-supported high TB/HIV burden countries that include TB-LAM in COP (N=1): Democratic Republic of Congo

PEPFAR-supported high TB/HIV burden countries that have feedback on use of TB-LAM in COP (N=3): Kenya, Mozambique, South Africa

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[4] World Health Organization. Use of high burden country lists for TB by WHO in the post-2015 era. Geneva: World Health Organization; 2015. Available from: http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020.pdf

[5] PEPFAR support is defined here as either bilateral or regional support