

TO: Portia Nkambule, Acting Chief Executive Officer and Director, Clinical Evaluation & Trials  
Helen Rees, Chair, Board  
Setlola Molepo, Assistant director  
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CC: Malebona Precious Matsoso, Director-General  
Yogan Pillay Deputy Director-General for Health  
Aaron Motsoaledi, Minister of Health  
Lindiwe Mvusi, Director, TB Control and Management Cluster  
Norbert Ndjeka, Director, Drug-Resistant TB, TB & HIV  
**National Department of Health**  
**Private Bag X828**  
**Pretoria, South Africa, 0001**

23 August 2018

**Open letter re: Urgent need to register essential medicines for the treatment and prevention of tuberculosis (TB) in South Africa**

Dear Dr. Nkambule and colleagues,

We welcome the establishment of South African Health Products Regulatory Authority (SAHPRA) as an advance to ensure transparent, efficient, and effective regulation of health products and research in South Africa. However, we are concerned that access to essential medicines and initiation of vital research remain delayed due to regulatory processes. In particular, we request your attention to ensure availability of and timely research into new prevention and treatment options, for tuberculosis (TB), which despite being preventable and curable, remains the leading cause of death in South Africa. Namely, we request your attention to 1) marketing approval of, and expedition of further research into, delamanid, an important medicine for treating drug-resistant strains of TB; 2) approval of rifapentine, which allows for dramatic shortening of preventive therapy for TB; and 3) approval of child-friendly formulations of TB medicines, which facilitate dosing and ease the burden of TB treatment on children and those administering treatment alike.

**1) Approving delamanid and expediting further research**

South African civil society and the global TB response community heralded South Africa's leadership in being the first country to scale up use of bedaquiline, one of only two new drugs developed for treating drug-resistant TB. Yet South Africa is lagging on utilizing the other drug, delamanid. Delamanid has been approved by the European Medicines Agency since 2014 and is recommended by the World Health Organization (WHO) for use in people with rifampicin-resistant TB as young as six years. It has been tested in randomized clinical trials—more than can be said for most other drugs currently used in South Africa and globally to treat drug-

resistant TB—and has been found to be safe, well-tolerated, and have no clinically significant interactions with antiretrovirals. Delamanid is an essential drug (indeed, it is on the WHO Model Lists of Essential Medicines for both adults and children) for treating drug-resistant TB, especially in those for whom a robust regimen cannot otherwise be constructed.

Approving delamanid will enable South Africans affected by TB to benefit from South Africa's bold and wise decision to move towards injectable-free regimens. Given its safety and tolerability relative to other TB drugs with even less evidence of efficacy, delamanid also has an essential role to play as a component of a robust regimen for adults with drug-resistant TB, and warrants approval. We need all the tools at our disposal to fight the TB epidemic, to ensure all persons with TB are given the best chance at a full cure.

We also encourage SAHPRA to rapidly review and approve research proposals that test novel drug candidates and/or regimens for TB. From early-stage monotherapy and early bactericidal activity studies of new investigational agents through late-stage trials to optimize regimens and shorten treatment, well-designed clinical trials in TB are urgently needed.

## **2) Approving rifapentine**

TB is not only curable but preventable. With its large burden of people at high risk for developing active TB—including people with HIV, close contacts of people with TB, clinicians, and miners—South Africa would benefit greatly from more prevention options. Rifapentine is an important product for preventing TB, as it reduces the length of TB preventive therapy from nine months of daily therapy to just 12 once-weekly doses (and new research indicates rifapentine can further shorten TB preventive therapy to just one month of daily dosing).

We appreciate the fast track review was granted to rifapentine, and are aware that SAHPRA has sent questions to the applicant Sanofi. We hope that, pending Sanofi's submission of its answers, the review can proceed with all due acceleration to allow for approval within this calendar year, thus facilitating use of the product starting in 2019. After being approved for active TB for decades, rifapentine received U.S. Food and Drug Administration approval for an indication for treatment of latent TB infection in 2014. Rifapentine is also approved for preventive therapy by regulatory authorities of the Philippines, Hong Kong, and Taiwan. We hope South Africa can soon follow suit.

We understand Sanofi in process of making required updates to its chemistry, manufacturing, and control (CMC) dossier, and in several countries approval was granted on the condition of approval of updates being entered at a later date. Similar arrangements should be possible for South Africa, if this is contributing to the delay in the product's approval.

## **3) Approving paediatric formulations of TB medicines**

Children are particularly vulnerable to TB. To facilitate TB treatment in children, there is an urgent need for SAHPRA to approve the paediatric fixed dose combinations and reformulated stand-alone dispersible tablets of first-line drugs and to allow the importation of dispersible tablets of second-line TB medicines so that acceptability can be confirmed and a long-term access plan can be developed. While these first- and second-line TB medicines have been approved and available for use in South Africa for decades, they are inappropriately dosed and

formulated for children, requiring higher pill burdens and crushing and splitting tablets to approximate correct dosages. Fixed-dose dispersible combinations and stand-alone dispersible tablets of these same medicines, developed by Macleods, facilitate administration and accurate dosing, reduce pill burden, and improve taste and acceptability for children, easing the difficulties of TB treatment for children and those who care for them. We look forward to these formulations, some of which have been available on the global market since 2015, being available to South African children.

Finally, we request SAHPRA to make its decision-making processes about health products, including but not limited to, TB, transparent and have a venue for input from affected communities such as those we represent.

We hope to see the registration of delamanid, rifapentine, and the paediatric formulations of first- and second-line TB medicines shortly, as well as the continuation of high quality TB research in South Africa. We appreciate your consideration of our letter, and look forward to your response, which can be directed to Lindsay McKenna, [lindsay.mckenna@treatmentactiongroup.org](mailto:lindsay.mckenna@treatmentactiongroup.org) and Ingrid Schoeman, [Ingrid.tbproof@gmail.com](mailto:Ingrid.tbproof@gmail.com) by 5 September 2018.

Respectfully submitted,  
On behalf of the undersigned organizations and individuals

### **Organizations**

Activists Coalition on TB - Asia Pacific (ACT! AP), Asia Pacific  
AIDS Foundation East West (AFEW International), The Netherlands  
Alliance for Public Health, Ukraine  
Desmond Tutu TB Centre, South Africa  
Drug Resistant Tuberculosis Treatment Action Team (DR-TB STAT), USA  
Eurasian Harm Reduction Association (EHRA), Lithuania  
European AIDS Treatment Group, Belgium  
Global Coalition of TB Activists (GCTA), Global TB Community Advisory Board (TB CAB),  
Global  
HAYAT, National Humanitarian Public Union, Azerbaijan  
Médecins Sans Frontières (MSF) South Africa, South Africa  
Norwegian Heart and Lung Patient Organisation (LHL International), Norway  
Romanian Angel Appeal Foundation, Romania  
Saglamliga Khidmat, Azerbaijan  
School of Public Health & Family Medicine, Faculty of Health Sciences, University of Cape  
Town, South Africa  
Sentinel Project on Pediatric Drug Resistant Tuberculosis, USA  
Southern African HIV Clinicians Society, South Africa  
Speranta terrei, Moldova  
Stop Stockouts Project, South Africa  
Support of people living with HIV Kuat, Kazakhstan  
TB Europe Coalition, Regional network of Eastern and Western Europe, Caucuses and Central  
Asia  
TB Proof, South Africa

Treatment Action Campaign (TAC), South Africa  
Treatment Action Group (TAG), USA  
WACI Health, South Africa

### **Individuals**

Andrea von Delft, TB Proof, South Africa  
Andreas Diacon, Founder, Director and CEO Task Applied Science, South Africa  
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Colleen Daniels, CD Global Consulting, South Africa  
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Ingrid Schoeman, Registered Dietitian, Pre-XDR TB Survivor, TB Proof, Pretoria, South Africa  
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James Seddon, Desmond Tutu TB Centre, Stellenbosch University, South Africa  
Jennifer Furin, Harvard Medical School, Department of Global Health & Social Medicine, Boston, MA, USA  
Jeroen van Gorkom, KNCV Tuberculosis Foundation, The Netherlands  
Judy Caldwell, TB Programme Manager, City of Cape Town, South Africa  
Lauren Jankelowitz, The Southern African HIV Clinicians Society, South Africa  
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