

To: Dr. G. N. Singh, Drugs Controller General, India  
Central Drugs Standard Control Organization  
Directorate General of Health Services  
Ministry of Health and Family Welfare  
Government of India  
FDA Bhavan, ITO, Kotla Road, New Delhi -110002

CC: Dr. Jagdish Prasad, Director General of Health Services, Ministry of Health & Family Welfare, Government of India  
Dr. Sunil Khaparde, Deputy Director General (TB), Central TB Division, Ministry of Health & Family Welfare Government of India  
Dr. V.S. Salhotra, Deputy Commissioner, National Health Mission, Ministry of Health & Family Welfare, Government of India  
Dr. Soumya Swaminathan, Director General, Indian Council of Medical Research  
David Budd, Chief Executive Officer, Epistem Holdings Plc  
Gino Miele, Director of Research and Development, Epistem Holdings Plc  
Gordon Powell, Global Commercial Director, Epistem Holdings Plc

30 June 2016

**Open Letter: Recommendation for Drug Controller General of India to withdraw GeneDrive test for tuberculosis from the Indian market**

Dear Dr. Singh,

In light of recent independent findings published by the *Journal of Clinical Microbiology* demonstrating the poor performance of Epistem's GeneDrive Tuberculosis Test<sup>1</sup>, and as advocates for communities affected by TB, we are writing to express concern regarding Epistem's recent announcement of its plans to commercially launch GeneDrive in India.<sup>2</sup> Further, we request immediate action to rescind the marketing approval granted to Epistem by the Drug Controller General of India (DCGI) in April 2015 and to implement more stringent requirements and higher standards for future diagnostic tests.

The World Health Organization (WHO) recommends that rapid sputum-based tests for tuberculosis achieve greater than 68 percent sensitivity in smear-negative, culture-positive samples and 99 percent sensitivity in smear-positive, culture-positive samples.<sup>3</sup> With 0 percent sensitivity in smear-negative samples and 45.4 percent sensitivity in smear-

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<sup>1</sup> Shenai, Shubhada, Derek T. Armstrong, et al. "Analytical and Clinical Evaluation of the Epistem Genedrive Assay for Detection of Mycobacterium Tuberculosis." *J. Clin. Microbiol. Journal of Clinical Microbiology* 54.4 (2016): 1051-057. Web.

<sup>2</sup> Epistem Holdings PLC. Epistem begins full commercial launch for GeneDrive Tuberculosis Tests in India [Press Release]. 18 April 2016. Available from : <http://www.publicnow.com/view/F29A9F8DA9E0AEA8714A469AE1DA1B25BBE01F0B?2016-04-18-11:00:36+01:00-xxx4802>.

<sup>3</sup> World Health Organization. High-priority target product profiles for new tuberculosis diagnostics: Report of a consensus meeting. Geneva: World Health Organization; 2014. Available from: [http://www.who.int/tb/publications/tpp\\_report/en/](http://www.who.int/tb/publications/tpp_report/en/).

positive samples<sup>4</sup>, GeneDrive fails to meet the performance standards set by the WHO for a smear microscopy replacement test. Further, GeneDrive yielded false positive results in 9.4 percent of negative control samples, and when tested with three different species of non-tuberculous mycobacteria (NTM), demonstrating the test's lack of reliability and problematic cross-reactivity with NTM.

Even if Epistem was able to optimize Genedrive's performance to achieve sensitivity and specificity more similar to smear microscopy, we are unconvinced that this test offers substantial benefits to justify its price and introduction into the market, which could very likely cause confusion and off-label use. Especially as the pricing for Genedrive is similar to a far more sensitive test, GeneXpert MTB/RIF (which also has advantages in terms of biosafety, of detecting rifampicin resistance, and of less concern of cross-reactivity with NTM) and other, lower priced tests with far better sensitivity and specificity are expected to enter the market in the next year, we believe it is unethical to introduce a more expensive test that is far below the WHO performance standards for a smear microscopy replacement test.

GeneDrive's clear inferiority to existing and forthcoming TB tests, its high price, and potential for rampant misuse, especially in the private sector, support our call for immediate revocation of Epistem's marketing authorization in India. If Epistem is allowed to go forward with its planned commercial launch in India, we have no doubts that GeneDrive will squander resources and do more harm than good for TB patients.

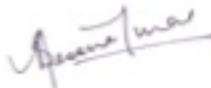
We look forward to prompt revocation of the marketing authorization granted to Epistem and withdrawal of Genedrive from the Indian market. We also strongly recommend that future marketing authorizations granted to diagnostic tests in India be contingent upon data from large multi-center evaluations demonstrating test performance in line with standards laid out by the World Health Organization.<sup>5</sup>

Before July 20th, please direct your response and any further correspondence to Wim Vandeveldde at [wim.vandeveldde@eatg.org](mailto:wim.vandeveldde@eatg.org).

Respectfully submitted,



Mr. Ketholelie Angami  
Director, Nagaland User's Network (NUN)



Mrs. Blessina Kumar, Chair Global Coalition of TB Activists (GCTA)

On behalf of the Global Tuberculosis Community Advisory Board (TB CAB)

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<sup>4</sup> Shenai, Shubhada, Derek T. Armstrong, et al. "Analytical and Clinical Evaluation of the Epistem Genedrive Assay for Detection of Mycobacterium Tuberculosis." *J. Clin. Microbiol. Journal of Clinical Microbiology* 54.4 (2016): 1051-057. Web.

<sup>5</sup> World Health Organization. High-priority target product profiles for new tuberculosis diagnostics: Report of a consensus meeting. Geneva: World Health Organization; 2014. Available from: [http://www.who.int/tb/publications/tpp\\_report/en/](http://www.who.int/tb/publications/tpp_report/en/).