TO: Dr. Edward Cox
CC: Dr. Janet Woodcock
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

24 May 2012

Open Letter Re: Crucial Regulatory Harmonization on Endpoints and Pharmacokinetic Studies for Tuberculosis Drug Development

Dear Dr. Cox,

As a group of concerned advocates for people infected and affected by tuberculosis (TB) worldwide, we urge the US Food and Drug Administration (FDA) to adopt two important measures to expedite research and development for desperately needed novel combinations of new drugs for TB.

First, we appeal to you to accept two-month sputum culture conversion (SCC) as a valid clinical endpoint. This shortened time frame will facilitate accelerated approval for new TB drugs and regimens, thereby benefitting TB patients and affected communities in urgent need of access to improved treatment options.

The European Medicines Agency (EMA) revised their regulations to reflect the two month criteria for measurement of SCC in 2010.[1] The time has come for a similar revision of this duration from FDA, both to assure harmonization between regulatory authorities, and to shorten the unacceptably long regulatory pathway for approval of novel TB drugs candidates.

Secondly, we are concerned that the two new investigational TB drugs which are farthest along in development, bedaquiline and delamanid -- both of which are being studied in people with multi-drug resistant TB, extensively drug resistant TB (XDR-TB) and pre-XDR-TB, and both of which are entering phase III studies and have or are likely to be submitted to regulatory authorities this year -- have not been studied together in the pharmacokinetic (PK) studies that will tell us how they interact and whether they are safe to use together.

However, when they are approved, it is inevitable that they will be used together in the field, because people with XDR-TB desperately need effective new oral drugs to shorten their time to culture conversion, and hopefully, cure.

Therefore, we call upon the FDA to require that the respective drug sponsors, Janssen and Otsuka, conduct the necessary PK studies to demonstrate whether the drugs are safe to use together. This requirement should be a condition for accelerated approval.

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[1] European Medicines Agency. Addendum to the Note for Guidance on the Evaluation of Medicinal Prodcuts Indicated for Treatment of Bacterial Infections to Specifcally Address the Clinical Development of New Agents to Treat Disease due to Mycobacterium Tuberculosis. London, UK. 20 January 2010. www.ema.europa.eu/pdfs/human/ewp/1437708enfin.pdf

We are similarly making this request to the European Medicines Agency (EMA). We are also in discussions with the drug sponsors to encourage the expeditious commencement of the necessary PK studies to ensure that sufficient data are available to inform guidance for the appropriate use of the two drugs in combination, once they are both approved.

We are readily available to dialogue further and look forward to a favorable response. Please respond to Erica Lessem at erica.lessem@treatmentactiongroup.org at your earliest convenience.

Yours truly,

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Nathan Geffen, South Africa
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for the Global Tuberculosis Community Advisory Board (TB CAB)