Critical Path to TB Drug Regimens

Accelerating New TB Regimens:
Effective coordination across the US Government

After decades of neglect, TB research and development is experiencing a renaissance, thanks in part to strategic investments by and visionary leadership from the US Government. Ten years of concerted effort has brought about the largest pipeline of TB drugs in history, with 10 experimental drugs in clinical trials, making it feasible to develop novel combination regimens. Several US agencies have worked together, and with non-profit drug developers and the pharmaceutical industry, each contributing expertise, to speed new drugs and regimens from the bench to the bedside.

US Government involvement in TB regimen development is an example of effective coordination across agencies and collaborative partnership with the public, private, and non-profit sectors. Working in concert, these efforts have already yielded tangible results and promise to deliver impactful changes in the treatment of TB patients around the world in the near to mid-term.

- *Centers for Disease Control and Prevention (CDC)* –CDC's TB Trials Consortium (TBTC) has been a key partner in research on TB for 15 years. CDC's early research on moxifloxacin, an existing drug used for the treatment of respiratory and skin infections, provided data on the use of the drug for TB in humans, contributing to the knowledge base that enabled the TB Alliance and Bayer to embark on a Phase III trial for registration. Today, moxifloxacin is also being tested with other TB drugs to form a novel regimen. CDC has also played a key role in advancing rifapentine by sponsoring the PREVENT TB trial, which demonstrated the efficacy of a 3-month regimen for treatment of latent TB infection.

- *National Institutes of Health (NIH) -* NIH plays a fundamental role in generating scientific discoveries and enabling their translation into products for public health. The NIH's National Institute of Allergy and Infectious Diseases (NIAID) has been involved in the development of many candidate TB drugs, vaccines, and diagnostics, several of which are currently in clinical development. For example, NIAID provided critical preclinical and clinical contract support for several drug candidates, including PA-824, a novel TB drug developed by the not-for-profit drug developer TB Alliance, which may serve as an important component of several new regimens being tested. Furthermore, in 2009, NIAID announced that it would make its AIDS clinical trials infrastructure available for TB trials, providing much needed clinical capacity. In 2011, four AIDS Clinical Trials Group (ACTG) sites came on line to participate in a global Phase III trial sponsored by the TB Alliance, collaborating with pharmaceutical partner, Bayer AG.

- *US Agency for International Development (USAID) -* USAID's field presence in many developing countries makes it uniquely well-placed to advise on product appropriateness for low-resource settings and liaise with country decision makers for rapid uptake of innovations. USAID plays a particularly crucial role in funding late-stage field trials to evaluate the efficacy of new TB regimens in the populations in which they will ultimately be used. Since 2004, USAID has supported clinical evaluation of several new TB regimens that are poised for delivery to the field within the next five years. These new regimens will dramatically improve health systems' response to TB.

- *US Food and Drug Administration (FDA)* - In 2010, FDA drafted progressive new guidance for evaluating TB drugs in combination, enabling product developers to test and register new regimens in a quarter of the time. Furthermore, investments through FDA's Critical Path Initiative are supporting the coordination framework and regulatory science that underpins the combination testing approach to improve the evaluation and registration of new TB regimes and preclinical development of optimized regimens. This includes support for qualifying new pre-clinical models for TB drug development, discovering biomarkers for TB disease and evaluation of treatment efficacy, and developing tools to improve TB diagnosis.

cptrinitiative.org