



A first for TB drug development

For the first time, pharmaceutical companies, civil society and regulatory officials are joining forces to address the urgent need to develop new combination drug regimens for TB. Through a new partnership called the Critical Path to TB Drug Regimens (CPTDR), and with guidance from the U.S. FDA, partners will work together to test promising TB drug candidates in combination and identify new regulatory pathways to speed the approval of these novel TB therapies.

New TB drug regimens are long overdue

While often perceived as a “disease of the past,” TB remains one of the world’s deadliest infectious diseases – second only to HIV/AIDS. Each year, TB kills more than 1.8 million people, and there are 9.4 million new cases, primarily in developing countries. TB’s complex and deadly interaction with HIV/AIDS has even further exacerbated the global TB epidemic.

The current first-line TB drug regimen of four drugs is more than 40 years old, takes six to nine months to complete and has significant side effects. All too often, these drawbacks cause patients to default on their treatment and, consequently, resistance to TB drugs is spreading in every corner of the world. Last year alone, there were more than half a million cases of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB reported globally. With the rapid and lethal spread of drug-resistant TB, speeding the development of new, simpler and more effective drug regimens is no longer just an option, but a major public health imperative.

Nine new drug candidates: An unprecedented opportunity for collaboration

In recent years, a number of factors aligned to create a historic opportunity to develop new combination TB drug regimens. The pipeline of new TB drugs is stronger than ever before, with nine promising compounds from at least six antibiotic classes in clinical trials or late pre-clinical development and others in discovery and early pre-clinical stages. This is thanks to government and philanthropic investments in TB R&D and increased industry focus on TB over the past decade. Through their participation in the CPTDR initiative, industry, academia and civil society are maximizing this critical moment so that innovation and patient need drive every aspect of TB drug development.

Clear and efficient pathways are needed to speed registration of and access to new combinations

Given the TB bacterium’s ability to rapidly develop resistance to a single antibiotic, treatment will always require a combination of multiple effective drugs. Currently, individual drug candidates are developed and registered separately by being substituted (or added) one at a time to existing combination therapies. Because each trial could take at least six years, the approval of a new four-drug regimen, through successive trials, could take 24 years or longer to obtain under this framework. The world cannot wait a quarter century for the development of appropriate tools to stop this devastating disease

To optimize the efficiency of regimen development, CPTDR will alter the development paradigm such that the regimen, and not an individual drug, is considered the unit of development. Advances in regulatory science will help clearly evaluate experimental TB drugs both on their own and within the context of a regimen.

CPTDR revolutionizes the existing paradigm of regimen development

Under CPTDR, drug companies and other product developers will work together to test promising combinations of individual TB drug candidates as early as possible and identify the best new combinations. At the same time, CPTDR partners will work with regulators to develop new pathways to evaluate and register these safe, effective combination TB therapies in record time. By testing promising drug combinations in parallel, the CPTDR initiative has the potential to reduce the timeline for developing novel TB drug regimens to as little as six years—cutting time to approval by up to 75 percent.

CPTR has the support of the U.S. FDA

Current regulatory guidelines allow for the development and approval of combination regimens, provided that the contribution of each individual drug in the regimen can be identified. The CPTR partners will now work with FDA scientists to identify the tools and methods appropriate to establish the value of each new TB drug as part of a regimen, which will significantly accelerate the registration of new TB combinations that meet the FDA's regulatory requirements.

FDA Commissioner Margaret Hamburg's support for CPTR mirrors recent investments by the FDA and other regulatory agencies in regulatory science to speed the development and delivery of effective new medical technologies – including combination therapies – to those who need them most. This strongly demonstrates the Agency's commitment to innovation in the service of public health.

CPTR is an innovative, multi-sectoral initiative

Introduction of new TB drug regimens cannot be accomplished by a single company or organization working alone. The CPTR initiative brings together leading organizations from the public and private sectors and academia to join forces in ways never thought possible to speed the development of effective combination therapies. CPTR partners recognize the need to tackle this major public health crisis through new, creative forms of cooperation.

The core partners and founders of the initiative are the **Global Alliance for TB Drug Development** (TB Alliance), the **Critical Path Institute** and the **Bill & Melinda Gates Foundation**. They will work with other CPTR partners to determine the optimal combinations of compounds to be tested together; orchestrate clinical and preclinical combination testing programs; strengthen the regulatory science and framework under which trials are conducted; and bolster the global capacity to carry out the trials to take place under the CPTR umbrella. The CPTR initiative will be coordinated by the Critical Path Institute, a non-profit organization that serves as a “neutral broker” for regulatory science collaborations between the FDA, scientists and industry.

By signing on to the initiative's “Statement of Principles,” pharmaceutical companies **Johnson & Johnson**, **Pfizer**, **GlaxoSmithKline**, **sanofi-aventis**, **AstraZeneca** and **Anacor** have already committed to participate in CPTR and make their compounds available for combination testing.

Additional signatories committed to the CPTR mission include representatives from the advocacy community, such as **Treatment Action Group** (TAG), and other clinical research funders, such as the **European & Developing Countries Clinical Trials Partnership** (EDCTP).

The initiative welcomes participation from any company or research organization with a promising TB drug candidate in development, as well as other groups providing the technical expertise or resources to help develop new TB regimens.

Setting the stage for future innovation

If the initiative succeeds, it could become the “gold standard” for rapid, safe and efficient development and testing of new TB drug combinations. The CPTR model could also be a trailblazer for similar initiatives in other disease areas for which combination treatment is a necessity, such as cancer and hepatitis.

