



Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade

A comprehensive strategy to introduce the safest and most effective TB vaccines that reduce tuberculosis worldwide, through partnerships, innovative strategies and creative mechanisms





“No one organization or country can do this alone. The TB Vaccine Blueprint, created through international collaboration, outlines “five keys to progress” that can guide our work and speed the global TB vaccine development effort.”

Peggy Johnston – Bill & Melinda Gates Foundation

The way forward for TB vaccine development

Safe and effective tuberculosis (TB) vaccines are urgently needed. Despite recent progress, TB continues to take the lives of almost one and a half million people per year and devastates the lives of millions more. Over the past decade, researchers have made significant progress in TB vaccine development, and more than a dozen TB vaccine candidates are now being evaluated in clinical trials. However, developing new TB vaccines is a costly, complex and time-consuming undertaking, requiring a coordinated global effort.

A unified global strategy is needed. A consensus approach to TB vaccine development can identify research priorities, maximise limited available resources and provide guidance to scientists, regulators, advocates, donors, investors and decision makers.

Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade, developed in consultation with stakeholders from the whole TB vaccine research community, provides such a strategy, and sets out a renewed, intensified and well integrated international effort to develop more effective TB vaccines as quickly and cost-effectively as possible. The *Blueprint* outlines the major scientific challenges and priorities, and describes the critical activities and crucial questions that need to be addressed to develop life-saving TB vaccines.

The *Blueprint* is a follow-up of the 1998 *Blueprint for Tuberculosis Vaccine Development* and represents consensus in the TB vaccine development field, clearly articulating the most efficient path forward for the next decade. Building on the tremendous progress that has been made over the past decade, the new *Blueprint* will not only look at advancing new and existing vaccine candidates but also lay the groundwork for licensure and distribution of new TB vaccines.

A Deadly Epidemic

With nearly 9 million new cases and almost 1.5 million deaths per year, tuberculosis (TB) is the second deadliest infectious disease in the world.

TB is an airborne infectious disease caused by *Mycobacterium tuberculosis*. It is estimated that around two billion people, a third of the world's population, are infected with the bacterium and may develop the disease in their lifetimes. The disease causes great human suffering, a huge financial burden and significant, worldwide economic damage.

Immunisation is one of the most cost-effective health interventions, yet the only currently available vaccine against tuberculosis, Bacille Calmette-Guérin (BCG), provides very limited protection against pulmonary TB, the most prevalent and contagious form of the disease. Mathematical modelling shows that without new, more effective vaccines, TB cannot be eliminated.

“Only a highly efficacious TB vaccine will ensure elimination of TB worldwide. The challenge is not only to invest more in research to understand better what to target in designing a vaccine, but also the time that this will take. The more quickly we invest, the sooner we will succeed.”

Dr Mario Raviglione - WHO Stop TB Department





“The new Blueprint provides a roadmap for close collaboration among all stakeholders and for scientists to address practical and relevant fundamental and translational questions, and for funders to maximize resources in the current economic climate.”

*Christine Sizemore and Anthony S. Fauci
US National Institutes of Health
Tuberculosis, March 2012*

Five Keys to Progress

Delivering more effective, safe TB vaccines will require creative thinking, innovative approaches and new and enhanced forms of partnership. *Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade* outlines five key areas where collaboration is crucial to accelerate development of successful TB vaccines over the next decade.

Creativity in Research and Discovery

Scientific advances over the past decade have produced a rich TB vaccine pipeline, with candidates in various phases of discovery and development. Yet there is still much that we do not understand about the interaction between the bacterium and the human immune system. Creativity is needed to:

- Identify mechanisms of protective immunity for TB that increase our understanding of the disease, the bacterium and the body's response.
- Introduce new vaccine mechanisms that broaden our vaccine development approach beyond protein-based antigens.
- Facilitate translational research, comparative preclinical studies and animal models so that we can advance promising scientific ideas into the clinic quickly and effectively—and with as much knowledge as possible.

Correlates of Immunity and Biomarkers for TB Vaccines

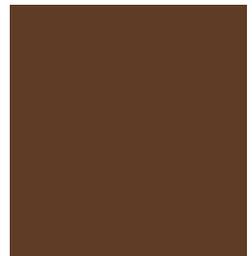
Next to the identification of safe and effective candidates, no issue is more critical to successful development of new TB vaccines than the discovery of biomarkers: indicators that predict natural protection or susceptibility to disease and that may predict vaccine efficacy and reduce time, cost and number of participants needed for large-scale clinical trials. To find these markers, we should:

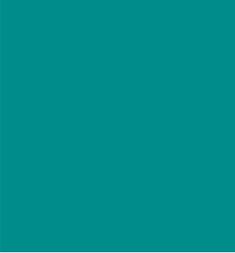
- Explore novel approaches to identify correlates of immunity using new technologies and partnerships across scientific fields.
- Introduce novel assays in efficacy trials to help establish correlates of immunity.
- Identify signatures of vaccine efficacy to guide the selection of the most promising vaccine candidates much earlier in the process.

Clinical Trials – Harmonisation and Cooperation

Clinical testing of new TB vaccines is expensive and complicated on both a scientific and a logistical level and presents major hurdles as candidates advance toward Phase III trials for potential licensure. To overcome these challenges, we can:

- Determine TB prevalence and incidence, select trial sites and choose target populations for TB vaccines that result in the greatest reduction in disease.
- Design clinical trials to determine efficacy using better defined clinical endpoints—until we find clear indicators of protection.
- Address regulatory, ethical and sustainability issues by engaging authorities early in the development process and deploying creative strategies to obtain timely review by regulatory bodies and speed access.





Rational Selection of TB Vaccine Candidates

The need to advance the most promising new TB vaccines and the limitations of both financial and clinical resources demand a structured and transparent 'rational selection' process. To accomplish this, the vaccine community should:

- Establish global criteria for assessing vaccine candidates in clinical studies so we can select and assess the best candidates to move forward.
- Obtain consensus on criteria to move new candidates through stages of development that consider safety, immunogenicity and efficacy issues, as well as production, regulatory and business challenges.

Building Support through Advocacy, Communications and Resource Mobilisation

It is critically important to inform and engage the media, government officials, NGOs, affected communities and other key stakeholders at the local, national and global levels. This will help generate support and political will, to increase investment, to ensure transparency and generate a supportive environment for clinical trials, and to lay the groundwork for acceptance and adoption of new TB vaccines once licensed. Together we can:

- Expand financing to provide sufficient resources through new funders, including emerging economies with high TB burdens, as well as new, innovative partnerships and financing models.
- Raise awareness and build support for the role of new TB vaccines through greater collaboration between advocates and researchers.
- Broaden the base of TB vaccine advocates to include scientists, politicians, funders, advocates and community representatives—all critical to development and introduction of new TB vaccines.

Moving forward

The *Blueprint* lays out an ambitious agenda to move the field towards its goal of developing new, more effective TB vaccines. Its success will rely on commitment, collaboration, partnerships and leadership. Links to organisations that develop similar products for other diseases, and close cooperation with organisations that develop new TB drugs and diagnostics will serve to advance the key issues outlined in the *Blueprint*. People in communities and countries affected by TB will play a crucial role in supporting the development and introduction of new vaccines. Together we can overcome challenges and build on lessons learned. The global problem of TB—and the global need for TB vaccines—demands global solutions.

Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade was produced under the auspices of the Stop TB Partnership Working Group on New Vaccines and published in the journal *Tuberculosis* (Brennan, MJ and Thole, J, Vol. 92, Supplement 1, ppS1-S35, March 2012). The complete *Blueprint*, including relevant opinion editorials, is available at www.stoptb.org/wg/new_vaccines.



"The TB community welcomes the Blueprint as it provides a sound framework to jointly face challenges in research, development and deployment of effective TB vaccines. The fact that it addresses issues along the entire value chain from innovation and discovery through clinical trials to community mobilisation is very commendable."

*Charles Mgone
European and Developing Countries Clinical Trials Partnership (EDCTP)*