



Tuberculosis Vaccines

hope for the future



WORLD HEALTH
ORGANIZATION

Stop TB Partnership

TB Vaccines

The tuberculosis (TB) pandemic is growing and evolving, threatening public health worldwide. Drug-resistant forms of TB, including multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, and increasing rates of TB/HIV co-infection are making the pandemic even more deadly. The need for better tools - vaccines, drugs and diagnostics - to prevent and control TB has never been greater.

- Two billion people worldwide are infected with TB¹
- The majority of TB cases remain undetected
- Nearly 9 million new cases of TB are diagnosed each year
- TB kills nearly 1.7 million people a year-98% of them in developing countries
- One third of people living with HIV also suffer from TB², and TB is the leading cause of death for people with HIV/AIDS³
- TB primarily affects people at their most economically productive age, creating an additional \$16 billion in lost productivity⁴

The world has taken notice. There is a global target to eliminate TB as a public health threat by 2050⁵, and increased commitment and resources have been devoted to more aggressive TB control. However, without a new vaccine, elimination of this deadly disease will not be possible.

› Why a new vaccine?

The existing vaccine Bacille Calmette-Guérin (BCG) was developed more than 85 years ago and is routinely given to infants in much of the world. While it provides some protection against severe forms of TB in children, it does not protect well against pulmonary TB, which is the most infectious form of TB and accounts for most of the worldwide TB disease burden. Despite being widely used, BCG has had no apparent impact on reversing the growing global TB pandemic.

A new vaccine that is both effective and safe for children, adolescents and adults-including people infected with HIV-will decrease TB incidence overall and help prevent further spread of the disease. A recent WHO study indicates that new vaccines would make TB elimination by 2050 “far more likely”.⁶

Leading global health institutions agree on an urgent need for a comprehensive response, including new, more effective vaccines, to curb this deadly pandemic. In 2006, the World Health Organization (WHO) launched the “Stop TB Strategy,” a key component of which is enabling and promoting research of new vaccines, drugs and diagnostics.

¹ World Health Organization, Fact Sheet No. 104, Tuberculosis, March 2006.

² Stop TB Partnership/UNAIDS, Fight AIDS, Fight TB, Fight Now: TB/HIV Information Pack, July 2004

³ World Health Organization, Fact Sheet No. 104, Tuberculosis, March 2006.

⁴ BIO Ventures for Global Health, Tuberculosis Vaccines: The Case for Investment, October 2006.

⁵ Elimination is defined as less than one case per million people

⁶ Need Chris Dye citation.

The Stop TB Partnership, a network of international organizations, countries, public and private sector donors, governmental and non-governmental organizations and individuals, has recently developed the Global Plan to Stop TB 2005-2016. TB vaccine development is an integral element of this plan.

“The introduction of new, effective TB vaccines will be an essential component of any strategy to eliminate TB by 2050... New TB vaccines to prevent childhood and adult forms of TB, to reduce TB in people coinfecting with HIV, and to shorten drug treatment regimens will fundamentally alter our approach to TB control.” Global Plan to Stop TB 2006-2015

› Advances in TB vaccine development

A wealth of scientific insights and developments in the fields of microbiology, immunology, genetics, and biotechnology has transformed TB research in recent years, putting a new TB vaccine within reach. The decoding of the M. Tuberculosis (M.tb) genome has provided new vaccine targets, while additional research has developed new techniques to augment the effects of vaccines and closely monitor responsiveness. Researchers are examining delivery platforms that would be cost-effective and meet the needs of limited-resource settings. And new vaccine candidates have entered human clinical trials for the first time in decades.

Experts now say it is realistic to believe we can have an effective TB vaccine in the coming decade. And an effective TB vaccine could prevent over 40 million deaths due to TB over the next 50 years.

› Types of vaccines

Due to the complex nature of M.tb and its interactions with human hosts, scientists are examining multiple approaches for new TB vaccines.

- Pre-exposure TB vaccines: Intended for use in newborns or young infants to replace or amplify BCG early in life and before exposure to TB, these vaccines are intended to prevent TB in people who have not been infected with M.tb.
- Post-exposure TB vaccines: Given post-infancy, typically to school children, adolescents or adults, who have either been vaccinated or latently infected with the TB bacteria or both, these vaccines reduce progression to active disease.
- Therapeutic vaccines: These vaccines are given to individuals with active TB in conjunction with TB drug therapy with the aim of shortening the duration of the drug therapy.



› New clinical trial field sites

Much of the current optimism in the TB vaccine field reflects recent progress made in moving promising candidates from the laboratory and preclinical studies into human clinical trials.

For vaccine trials to be effective, investigators must go into the field and conduct trials with entire communities most at risk for TB as there is no way to know who will develop a disease in the future. Testing vaccines in these communities is also important to ensure the safety and efficacy of vaccine candidates in the populations that most need them. This requires creating vaccine trial sites within countries with high burdens of TB. Preparation of a field site capable of conducting large scale clinical trials involves substantial investment in physical infrastructure, local research capacity and human resource capacity - investments that will remain in the community even after trials are completed. Trials are often conducted by local research institutions and include programs to develop community interaction, regulatory compliance, diagnostic procedures and vaccine administration.

The Working Group has committed its members to a goal of supporting the development of clinical trial field sites in order to meet aggressive targets for distribution of new vaccines. By 2015, TB experts hope the world will have an improved vaccine ready for global distribution.

“...TB remains a leading cause of death in adults in South Africa, one of the top-10 high-burden TB countries of the world. The situation is worsening as a consequence of the exploding HIV epidemic. We need a new, more effective vaccine to prevent TB to address this pandemic; and clinical trial sites in high burden countries will play a crucial role in the development of new vaccines.” Dr. Gregory Hussey, Director, South African Tuberculosis Vaccine Initiative (SATVI), Cape Town, South Africa

Dr. Lydia Mungherera, TASO, Uganda (focus on need for new TB vaccines from a community perspective)

› Challenges to vaccine development

Scientific challenges: The greatest scientific challenge in meeting the 2015 target is related to the uncertainty about identifying vaccine candidates that provide consistent protection against TB and the lack of experience with new TB vaccines in human populations. As a result, the scientific community is pursuing a dual strategy of maintaining support for relevant activities in vaccine discovery research while maximizing the number of candidates introduced into clinical trials. This approach increases the chances for developing an effective vaccine.

Operational challenges: Definitive diagnosis in infants and children, main targets for new vaccines and therefore indispensable in clinical testing, is demanding and may be possible in no more than 50% of suspect cases. [NOTE: Is anything specific being done to address this, that could be noted here?]

Financial challenges: Despite impressive commitments by philanthropic organizations and the public sector, the Global Plan to Stop TB 2006-2015 estimates at least a \$1.5 billion funding gap to achieve the objectives of the TB vaccine development plan in time. Funds are being prioritized to support the maintenance of the vaccine delivery pipeline, performance of clinical trials, and the creating of an enabling infrastructure. Without increased investment, promising vaccine candidates will not advance through large-scale efficacy trials and new, second generation candidates will not be brought into the pipeline.

› Global partnerships

The development of a new TB vaccine is a complex and challenging goal that requires collaborative efforts and global partnerships that combine financial resources, scientific discoveries, and technological expertise. Such partnerships have developed in recent years, and are a key reason that progress in TB vaccine development has come so far. These partnerships rely on active participation across sectors - public, private and academic - to contribute the elements needed for successful vaccine development.

“The only way we can develop a truly effective response to the global TB pandemic is by forging global private-public partnerships,” said Dr. Jerald C. Sadoff, Chief Executive Officer of the Aeras Global TB Vaccine Foundation, a Product Development Partnership focused exclusively on the development of new TB vaccines. “Through these partnerships we can harness the best resources of government, industry, academics and philanthropies, to develop a comprehensive approach that will speed development of better TB tools, ensure access for those who need them most, and minimize cost.”

*] Michel Gréco, Chair,
Working Group on New
TB Vaccines (focus on
overall need for new TB
vaccines)*

› Stop TB Partnership: Working Group on New TB Vaccines

To facilitate the enormous task of developing a new TB vaccine, the Stop TB Partnership has established a Working Group on New TB Vaccines, which is one of the seven working groups within the Partnership. The other Working Groups include New TB Drugs, New TB Diagnostics, DOTS Expansion, MDR-TB, TB/HIV, and Advocacy, Communications and Social Mobilization (ACSM).



The Working Group on New TB Vaccines seeks involvement of a cross-section of parties interested in accelerating the development and availability of a new TB vaccine. Partners include the private sector, academia, philanthropic organizations, research institutions and non-governmental organizations. The Working Group secretariat is provided by

the WHO Initiative for Vaccine Research, which is also the entity in charge of executing many of the Working Group's strategic recommendations.

One of the Working Group's main roles is as a broker and facilitator, helping to coordinate and publicize the activities of the various actors in TB vaccine research and development, including international and national public health organizations, regulatory agencies, academic scientists, pharmaceutical manufacturers, funding organizations, and other research groups.

› Key goals

In order to speed up the development of a new TB vaccine, the Working Group has identified a portfolio of key facilitating actions with the following objectives:

1 › Facilitate preclinical evaluation of candidate vaccines

- Develop and promote consensus guidelines, normative references, standardized protocols, experimental models and standardized reagents.
- Build capacity at animal testing centres for integration into the WHO preclinical vaccine-testing network.
- Facilitate the rapid exchange of information among laboratory and clinical scientists and key Working Group partners.

2 › Provide normative support

- Support harmonization of regulatory guidelines for TB vaccine production.
- Build up regulatory capacity of countries where vaccines will be tested.
- Strengthen Institutional Review Board capacity to evaluate TB vaccine protocols.

3 › Prepare for clinical trials

- Facilitate research to determine the incidence of TB in countries targeted for possible clinical studies.
- Help to develop and design appropriate clinical trials and identify possible field trial sites.
- Focus coordinated research and funding to address key scientific vaccine challenges such as correlates of immune protection against TB.

4 › Prepare to introduce vaccines to the market

- Facilitate economic and marketing analyses of the potential and emerging market for TB vaccines.
- Develop adolescent and adult immunization strategies and vaccine campaigns.
- Reach out to other partners in developing countries to assure a global investment in the goal of producing a new TB vaccine.

5 › Advocacy, communication, networking

- Facilitate community and public discussions about concerns that may arise with regard to clinical trials of candidate vaccines and future vaccine campaigns.
- Help communities with TB vaccine preparedness activities.
- Promote the global public health need and potential impact of pre-exposure, post-exposure and therapeutic TB vaccines.

**Stop TB is a partnership hosted
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