According to the Global Plan to Stop TB, 2006-2015, “Encouraging and consistent scientific results from the laboratory and from early field trials indicate that the introduction of new, effective TB vaccines will be an essential component of any strategy to eliminate tuberculosis (TB) by 2050. New TB vaccines to prevent childhood and adult forms of tuberculosis, to reduce tuberculosis in persons co-infected with HIV, and to shorten drug treatment regimens will fundamentally alter our approach to TB control.”

A number of the new generation of TB vaccines may work best using a heterologous prime-boost strategy to complement the immune response induced by the current BCG. This “prime-boost” strategy could include administration of BCG or a new recombinant live replacement vaccine as the “prime”, followed by a “booster” inoculation with a different vaccine to infants and young children before they are exposed to TB (pre-exposure), as a separate booster to young adults, either before they are exposed or who may have already been exposed to TB (post-infection) or as an adjunct to chemotherapy (immunotherapy).

TB vaccines under development could work in several ways:

- Prevent infection
- Prevent primary disease
- Prevent latent infection
- Prevent reactivation of latent infection
- Shorten the course and improve the response to chemotherapy
In the following table, tuberculosis vaccine candidates are presented in three categories:

**Candidates Tested in Clinical Trials (Section I):** TB vaccine candidates that are in clinical studies in 2010. Certain candidates that have been in clinical studies but are not currently in clinical trials are listed as ‘completed.’

**Candidates in Preclinical Studies & GMP-2010 (Section II):** TB vaccine candidates that as of 2010 are not yet in clinical trials, but have been manufactured under good manufacturing practice (GMP) for clinical use and have undergone some preclinical testing that meets regulatory standards.

**Next Generation Candidates-2010 (Section III):** TB vaccine candidates that are in the research and development stage with some preclinical testing performed to show that they may confer protection.

Vaccine candidates are further divided into specific Vaccine Types: Recombinant Live; Viral Vectored; Recombinant Protein or Other and a brief description is provided. The Table lists vaccines intended to be used as a Prime (.FILL) or Booster (.FILL) vaccine, as a Post-infection vaccine (.FILL) or in immunotherapy (.FILL).

The information contained here was provided and updated by the vaccine developers unless otherwise indicated. In cases where an update regarding a previously listed vaccine candidate was not received in 2010, the 2009 listing was retained.
# TUBERCULOSIS VACCINE CANDIDATES – 2010

Stop TB Partnership Working Group on New TB Vaccines

## SECTION I: Candidates Tested in Clinical Trials

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Products</th>
<th>Product description</th>
<th>Sponsor</th>
<th>Indication</th>
<th>Status as of 2010</th>
<th>Citations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recombinant Live</strong></td>
<td>VPM 1002</td>
<td><em>rBCG Prague strain expressing listeriolysin and carries a urease deletion mutation</em></td>
<td>Max Planck, Vakzine Projekt Management GmbH, TBVI</td>
<td>![Prime] ![Boost]</td>
<td>Phase Ib</td>
<td>[1-4]</td>
</tr>
<tr>
<td></td>
<td>rBCG30</td>
<td><em>rBCG Tice strain expressing 30 kDa Mtb antigen 85B; phase I completed in U.S.</em></td>
<td>UCLA, NIH, NIAID, Aeras</td>
<td>![Prime]</td>
<td>Phase I [completed]</td>
<td>[5-9]</td>
</tr>
<tr>
<td></td>
<td>AERAS-422</td>
<td>Recombinant BCG expressing mutated <em>PfoA</em> and overexpressing antigens <em>85A</em>, <em>85B</em>, and Rv3407</td>
<td>Aeras</td>
<td>![Prime]</td>
<td>Phase I</td>
<td>[10-12]</td>
</tr>
<tr>
<td></td>
<td>AERAS-402/ Crucell Ad35</td>
<td>Replication-deficient adenovirus 35 vector expressing Mtb antigens <em>85A</em>, <em>85B</em>, <em>TB10.4</em></td>
<td>Crucell, Aeras</td>
<td>![Prime]</td>
<td>Phase IIb</td>
<td>[10-11, 18-20]</td>
</tr>
<tr>
<td></td>
<td>AdAg85A</td>
<td>Replication-deficient adenovirus 5 vector expressing Mtb antigen 85A</td>
<td>McMaster University</td>
<td>![Prime] ![Boost]</td>
<td>Phase I</td>
<td>[21-25]</td>
</tr>
<tr>
<td><strong>Recombinant Protein</strong></td>
<td>M72 + AS01</td>
<td>Recombinant protein composed of a fusion of <em>Mtb</em> antigens Rv1196 and Rv0125 &amp; adjuvant AS01</td>
<td>GSK, Aeras</td>
<td>![Prime] ![Post-infection]</td>
<td>Phase II</td>
<td>[26-29]</td>
</tr>
<tr>
<td></td>
<td>Hybrid-I+IC31</td>
<td>Adjuvanted recombinant protein composed of Mtb antigens <em>85B</em> and ESAT-6</td>
<td>Statens Serum Institute (SSI), TBVI, EDCTP, Intercell</td>
<td>![Prime] ![Post-infection]</td>
<td>Phase I</td>
<td>[30-34]</td>
</tr>
<tr>
<td><strong>Whole Cell, Inactivated or Disrupted</strong></td>
<td><em>M. vaccae</em></td>
<td>Inactivated whole cell non-TB mycobacterium; phase III in BCG-primed HIV+ population completed; reformulation pending</td>
<td>NIH, Immodulon</td>
<td>![Prime] ![Post-infection] ![Immunotherapy]</td>
<td>Phase III [completed]</td>
<td>[38-42]</td>
</tr>
<tr>
<td></td>
<td><em>Mw [M. indicus pranii (MIP)]</em></td>
<td>Whole cell saprophytic non-TB mycobacterium</td>
<td>Department of Biotechnology (Ministry of Science &amp; Technology, Government of India), M/s. Cadila Pharmaceuticals Ltd.</td>
<td>![Immunotherapy]</td>
<td>Phase III</td>
<td>[43-45]</td>
</tr>
</tbody>
</table>

Prime, Boost, Post-infection, Immunotherapy

Tuberculosis Vaccine Pipeline - 2010

[3]
## SECTION II: Candidates in Preclinical Studies & GMP - 2010

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Products</th>
<th>Product description</th>
<th>Sponsor</th>
<th>Indication</th>
<th>Citations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant Live</td>
<td>Mtb [ΔlysA ΔpanCD ΔsecA2]</td>
<td>Non-replicating, Mtb strain auxotrophic for lysine and pantothenate; attenuated for secA2 gene</td>
<td>Albert Einstein College of Medicine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MTBVAC [ΔphoP, Δfad D26]</td>
<td>Live vaccine based on attenuation of Mtb by stable inactivation by deletion of phoP and fad D26 genes</td>
<td>University of Zaragoza, Institute Pasteur, BIOFABRI, TBVI</td>
<td></td>
<td>[53-57]</td>
</tr>
<tr>
<td>Recombinant Protein</td>
<td>HBHA</td>
<td>Naturally methylated 21-kDa purified protein from M.bovis BCG</td>
<td>INSERM, TBVI</td>
<td></td>
<td>[58-62]</td>
</tr>
<tr>
<td>Hybrid 56 + IC31</td>
<td>Adjuvanted recombinant protein composed of Mtb antigens 85B, ESAT-6 and Rv2660</td>
<td>SSI, Aeras, Intercell</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>HGB5 A/B</td>
<td>Chimeric DNA vaccines—Ag85A/Ag85B</td>
<td>Shanghai H&amp;G Biotech</td>
<td></td>
<td>[63-67]</td>
</tr>
</tbody>
</table>

## SECTION III: Next Generation Candidates – 2010

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Products</th>
<th>Product description</th>
<th>Sponsor</th>
<th>Indication</th>
<th>Citations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant Live</td>
<td>HG856-BCG</td>
<td>rBCG overexpressing chimeric ESAT-6/Ag85A DNA fusion protein</td>
<td>Shanghai Public Health Clinical Center</td>
<td></td>
<td>[63-65, 69-70]</td>
</tr>
<tr>
<td>IKEPLUS M. smegmatis with ESX-3 deletion/ complementation</td>
<td>Live M. smegmatis with deletion of ESX-3 encoding locus and complementation with Mtb locus</td>
<td>Albert Einstein College of Medicine, Aeras</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>paBCG</td>
<td>BCG with reduced activity of anti-apoptotic microbial enzymes including SodA, GlnA1, thioredoxin, and thioredoxin reductase</td>
<td>Vanderbilt University</td>
<td></td>
<td>[71]</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Candidate information communicated by the Wuhan Institute of Biological Products. 
\(^b\) Candidate information communicated by TBVI.
<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Description</th>
<th>Institution</th>
<th>Prime</th>
<th>Boost</th>
<th>Post-infection</th>
<th>Immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proapoptotic rBCG</td>
<td>Recombinant BCG expressing mutated PfoA and including mutations shown at AECOM to induce macrophage apoptosis</td>
<td>Aeras, Albert Einstein College of Medicine</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rBCG38</td>
<td>rBCG  Tice strain overexpress the 38 kDa protein</td>
<td>Universidad Nacional Autónoma de México</td>
<td>P</td>
<td>B</td>
<td></td>
<td>[77-80]</td>
</tr>
<tr>
<td>rBCG overexpressing L,D-Transpeptidase</td>
<td>Recombinant M. bovis BCG overexpressing an Mtb L,D-Transpeptidase</td>
<td>Johns Hopkins University</td>
<td>P</td>
<td></td>
<td></td>
<td>[82]</td>
</tr>
<tr>
<td>Replication deficient rBCG</td>
<td>Recombinant BCG expressing PfoA and classical, latency, and resuscitation antigens in live, non-replicating background</td>
<td>Aeras</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rM.microti30, rM.microti38</td>
<td>rM.microti strain overexpress the 30 or 38kDa protein</td>
<td>Universidad Nacional Autónoma de México</td>
<td>P</td>
<td></td>
<td></td>
<td>[78, 83]</td>
</tr>
<tr>
<td>ID93 in GLA-SE adjuvant</td>
<td>Subunit fusion protein composed of 4 Mtb antigens</td>
<td>Infectious Disease Research Institute</td>
<td>B</td>
<td>P</td>
<td>T</td>
<td>[85-86]</td>
</tr>
<tr>
<td>Latency fusion proteins</td>
<td>Recombinant fusion proteins composed of antigens 85A-85B-Rv3407, Rv3407-Rv1733c-Rv2626c, Rv0867c-Rv-1884-Rv2389c</td>
<td>Aeras</td>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r30</td>
<td>30kDa Mtb Ag85B protein purified from rM. Smegmatis</td>
<td>UCLA, NIH, NIAID</td>
<td>B</td>
<td>P</td>
<td>T</td>
<td>[87-91]</td>
</tr>
<tr>
<td>Recombinant LCMV</td>
<td>Recombinant lymphocytic choriomeningitis virus expressing Ag85A, Ag85B, or Ag85B-ESAT6</td>
<td>University of Geneva</td>
<td>P</td>
<td>B</td>
<td>P</td>
<td>T</td>
</tr>
<tr>
<td>pND vector</td>
<td>pND 14 vector with tpa factor expressing esat6, cfp10, hspx, Ag85A, Ag85B, or Ag85c</td>
<td>HEC-Pakistan</td>
<td>P</td>
<td>P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tuberculosis Vaccine Pipeline - 2010**
<table>
<thead>
<tr>
<th>Candidate Information</th>
<th>Vaccine Description</th>
<th>Manufacturing Company</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liporale-BCG</td>
<td>Live attenuated BCG Danish Strain in a novel lipid adjuvant and delivery system for an oral vaccine</td>
<td>Immune Solutions Ltd.</td>
<td>[107-111]</td>
</tr>
<tr>
<td>NasL3/AM8SB conjugate</td>
<td>Nasal vaccine with man-capped Arabinomannan oligosaccharide conjugated to Ag85B in Eurocine L3™ adjuvant</td>
<td>Karolinska Institute</td>
<td>[112-116]</td>
</tr>
<tr>
<td>NasL3/HtkBCG (BCG adjuvant)</td>
<td>Intra-nasal heat-killed whole BCG Copenhagen strain in Eurocine L3™ adjuvant</td>
<td>Karolinska Institute</td>
<td>[117-119]</td>
</tr>
<tr>
<td>PS- conjugate</td>
<td>Subunit Mtb polysaccharide protein conjugate</td>
<td>Albert Einstein College of Medicine</td>
<td></td>
</tr>
<tr>
<td>TBVax</td>
<td>T cell epitope-based DNA-prime peptide boost vaccine</td>
<td>EpiVax, Inc.</td>
<td>[123-125]</td>
</tr>
</tbody>
</table>

* Candidate information acquired from published literature.
The aim of the Stop TB Working Group on New Vaccines is to bring together the wide range of international groups with an interest in TB vaccine development, acting as a "broker" to promote synergy and to accelerate identification and introduction of the most effective vaccination strategy. This is achieved by representation of national and international public health organisms, major funding organizations, TB endemic countries, commercial and non-profit institutions involved in TB vaccine development, as well as experts in regulatory issues associated with vaccine development.
References