

The Working Group on New TB Vaccines - Workplan 2008-2009

Development of new vaccines against tuberculosis is gaining substantial momentum. The aim of the Working Group on New TB Vaccines is to foster and support collaborative efforts to develop new safe, effective and affordable TB vaccines that will help reduce the burden of this disease in the world. During 2006-2007, work continued to focus on (a) keeping the vaccine research and discovery pipeline filled (b) supporting the progression of candidate TB vaccines to Phase I/II human clinical trials and (c) preparations for future Phase III efficacy trials. Progress has been excellent and by the end of 2007 or early 2008 at the latest, 7 TB vaccine candidates will have entered clinical evaluation in humans. Particular challenges for the next two-year period, i.e. 2008-2009, include:

- Ensuring the smooth transition of "second generation" TB vaccine candidates and/or delivery systems, e.g. "latency vaccines", from the research/discovery stage into the vaccine development pipeline.
- Bringing the remaining "first generation" TB vaccine candidates into clinical testing.
- Initiating Phase IIb/Test-of-Concept trials of the most advanced vaccine candidates.
- Completing the preparation of a first set of Phase III trial sites in TB-high burden countries in at least two epidemiological subregions, i.e. sub-Saharan Africa and Asia.
- Developing plans for manufacturing and roll-out, in order to achieve maximal coverage once a new vaccine is licensed.
- Providing templates for national strategic planning and community preparedness towards the evaluation and introduction of new TB vaccines.
- Assuring continued interaction with existing and new donors to close the existing downstream funding gap.

The following are proposed activities for 2008 and 2009 with their roughly estimated cost, which the Working Group will carry out in close collaboration with the relevant key stakeholders:

Objective: Maintain and improve BCG vaccination programmes

Functioning high-coverage BCG vaccination programmes will be an important prerequisite to ensure fast implementation of new BCG-based TB vaccination paradigms once a new vaccine becomes available. While the Working Group has few possibilities to influence national vaccination programmes, it will be important to ensure that the BCG used is of good and defined quality and that state-of-the-art Quality Control methodologies for BCG are in place. The Working Group, together with WHO and BCG manufacturers has initiated an effort to update methodologies to BCG identity and potency. It is planned to continue this work and to organize one coordinating workshop per year.

Product: one annual coordinating workshop including meeting preparation and implementation, report and follow-up communications and activities (estimated cost: US\$ 80,000).

Objective: "Keep the pipeline filled" - Discovery & translational research

A number of "first generation" TB vaccine candidates are currently in early clinical evaluation. However, it is currently unknown if any of these vaccines will be superior to BCG in providing improved and/or extended protection against pulmonary TB in particular. It is therefore important to ensure that new innovative vaccine antigens are tested, new adjuvants and delivery routes and devices are evaluated for their use in TB and new talent is attracted to work on TB vaccines. To this end, the Working Group has established an "Innovative Approaches" Task Force, which will meet at least once a year to scan beyond the horizon of the traditional TB vaccine development community.

Product: one annual workshop of the Innovative Approaches Task Force including meeting preparation and implementation, report and follow-up communications and activities (estimated cost US\$ 80,000).

Objective: Build capacity at vaccine trial sites

Vaccine trials and in particular large and complex and often multi-centered Phase III efficacy trials require enormous scientific, technical, logistical and infrastructural capacities that are not a priori available in developing country trial sites. The Vaccine WG wants to facilitate the exchange among developing country researchers across trial sites and trial sponsors by establishing a "TB Vaccine trialists network".

Product: One annual forum of the TB vaccine clinical trialists network including meeting preparation and implementation, report and follow-up communications and activities, in conjunction with the UNION conference, if feasible (estimated cost: US\$ 100,000).

Product: Strengthening of regulatory and ethical capacity in TB endemic countries where clinical trials are being performed: prepare and present TB vaccine specific modules for existing networks and fora, e.g. African Vaccine Regulators Forum - AVAREF (estimated cost: US\$ 70,000)

Objective: Perform clinical trials

2008-2009 will largely be a period of Phase I and Phase II clinical trials. However, this will also be a period where laboratory assays for efficacy trials should be developed and validated and diagnostic paradigms as well as clinical endpoints need to be defined. This is all the more urgent since towards the end of the 2008-2009 biennium one or two phase IIb or "Test-of-Concept" clinical trials will likely be initiated. These are small trials that provide preliminary indications of vaccine efficacy and which will use the same or similar assays and endpoints as the subsequent Phase III efficacy trials. The Vaccine WG

has established two Task Forces that aim at accelerating these processes: one on development and validation of laboratory assays and one on diagnosis and endpoints.

Product: one annual meeting of the laboratory assays TF including meeting preparation and implementation, report and follow-up communications and activities (estimated cost: US\$80,000).

Product: a collaborative research study on the development of a functional assay (estimated cost: US\$ 100,000).

Product: one annual meeting of the TF on diagnostic paradigms and clinical endpoints including meeting preparation and implementation, report and follow-up communications and activities (estimated cost: US\$80,000).

Product: Development of a "white book" on clinical evaluation of TB vaccines (estimated cost: US\$ 70,000).

Objective: Provide an enabling infrastructure

The Vaccine WG has established two Task Force to facilitate and accelerate vaccine development, access and introduction:

- A TF on economics and product profiles, which will be providing guidance on questions of cost effectiveness considerations, market size, vaccine pricing, vaccine indications and formulations for different target populations, etc.
- A TF on advocacy, communication and social mobilization, which works in tight collaboration with the WG of the same name. This task force will raise awareness globally of the need for new TB vaccines and the status of TB vaccine development, and endeavor to ensure that endemic country governments and affected communities are informed and involved in TB vaccine development and clinical trials. In order to reach out to communities, it is of paramount importance to undertake advocacy and social mobilization work in close collaboration with community-based organizations. The fact that vaccines follow pathways that are different and independent from all other areas of TB control, in development , but even more so in procurement and implementation, made it seem inevitable to establish a group that provides vaccines-specific inputs to the ACSM WG and the recently formed Task Force on Retooling.

In addition, working group operations such as full WG meetings, core group meetings and chair travel fall under this objective and a "core budget" is requested for these activities.

Product: one annual workshop of the TF on economics and product profiles including meeting preparation and implementation, report and follow-up communications and activities (estimated cost: US\$ 80,000).

Product: Preparation of studies/reports by consultants on specific areas being addressed by the TF on economics and product profiles (estimated cost: US\$150,000).

Product: one annual workshop of the ACSM TF, if possible in conjunction with ACSM WG meetings, including meeting preparation and implementation, report and follow-up communications and activities (estimated cost: US\$80,000).

Product: production of advocacy material and development of community outreach activities (estimated cost: US\$ 100,000).

Product: Retooling TF: Vaccine WG contribution (estimated cost: US\$ 40,000).

Core funding: one annual full WG meeting, one annual core group meeting between full WG meetings plus travel of the Chair to visit donors, trials sites, etc (estimated budget: US\$ 180,000).

Requested budget 2008-2009 - GRAND TOTAL: US\$ 1,290,000