Call for applications to assess efficacy of *Mycobacterium tuberculosis* vaccine candidates in a mouse model

Call identifier: TBVAC-Horizon Call 2 (of 4)

Call open: 07 May 2024

Application deadline: 16 August 2024

With this application you will formally apply to include a vaccine candidate for inclusion in a mouse aerosol challenge experiment to be performed at the Medicines and Healthcare products Regulatory Agency (MHRA) within the TBVAC-HORIZON project as part of a gating and prioritisation process to identify new candidates to add to and diversify the preclinical vaccine pipeline (www.tbavcpathway.com). Details on the experimental setup and the parameters that are routinely assessed are described in **Annex I**.

The objective of this round is to perform head to head comparison with the BCG Danish 1331 reference standard of the-ability of new candidate TB vaccines to reduce bacterial load (CFU) in a standard mouse model of vaccination and pulmonary challenge with *Mycobacterium tuberculosis* (*M.tb*) H37Rv strain.
NOTE: this call is for preclinical vaccine candidates (BSL1 or BSL2 containment level). Prime-boost regimens involving BCG or another live vaccine candidate as the prime, would also be considered. The criteria and selection process for evaluation of submissions are described in **Annex II.**

In this current second round, up to 6 candidate vaccine slots are available in this mouse model, depending on the number of additional controls required plus one reference control group (BCG Danish 1331) as well as one unvaccinated control group. When submitting, please be aware that, if your candidate vaccine is selected, you will consent to provide the following:

- All necessary documentation needed for submission to the Biosafety committee of MHRA:
    - the use of genetically modified viral vectors or live vaccine strains (if applicable)
    - approval at the originating institute for what biocontainment conditions are required for use of live organisms – vaccine candidate and parent organism (for live vaccine candidate only)

  these documents must be approved by the MHRA Biosafety committee (and if necessary the UK HSE) prior to shipment and setting up the experiment.
- Detailed information on the composition of the vaccine, such as: antigen or bacteria, adjuvant, excipients and impurities if known. And for use of the vaccine candidate in the mouse model: dosing concentrations, administration route and schedule are required.

We anticipate an experiment will be able to begin for this call from 1 November 2024.
The selected vaccine candidates must be ready to dispatch to MHRA by this date.

How to Apply:
Using the **application form** (**Annex III**), provide a 4-page scientific background with relevant literature to address the criteria (Annex II) on the vaccine/adjuvant/delivery route and delivery system.

Send the completed application form to info@tbvi.eu 16 August 2024 at the latest.

Outcome
All applicants will receive an email on the selection outcome of their submitted candidate by 20 September 2024.
The successful applicants will be contacted with further information.

Future calls within the TBVAC Horizon Programme
A third and fourth call are foreseen in February 2025 and early 2026. At that time, in addition to the currently available mouse aerosol challenge model (Prevention of disease), the following models will be available:

Model	**Current call (2nd)**	**3rd call (2025)**	**4th call (2026)**
Mouse aerosol challenge model (Prevention of disease)	x	x	x
Low dose aerosol challenge guinea pig model (Prevention of disease)		x	x
TB meningitis mouse model (Prevention of dissemination)			x
Ultra-low dose proportional guinea pig model (Prevention of infection)			x

Candidates selected in this call may also apply for inclusion in subsequent rounds of the gating strategy calls– dependent on their performance in each model.

Annex I

Standard mouse *Mycobacterium tuberculosis* (*M.tb*) aerosol infection model

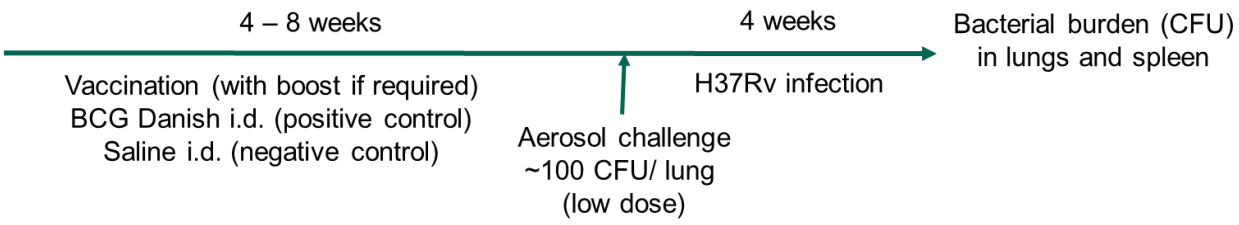
This mouse model is used for head to head evaluation of selected vaccine candidates, within and/or outside of the TBVAC-Horizon consortium. The experiment will be performed at the MHRA BSL2 (for vaccination prior *M.tb* infection) and 3 (post *M.tb* infection) laboratories in a designated facility for *in vivo* work. The following routes of vaccination can be used to assess protective potency of selected vaccine candidates when compared to intradermal (i.d) BCG vaccination: intradermal, subcutaneous, intranasal or aerosol.

Groups of five female C57BL/6 mice (commercially available; about 8 weeks old with 15-20 g body weight) will be given saline or vaccinated with either BCG (lyophilised Danish 1331 reference standard to be provided by the modeller; at about 3×10^4 CFU/mouse via i.d. route) or candidate vaccines (to be provided by the applicants). The route of administration and detailed immunisation schedule of selected candidates will be discussed and agreed with the successful applicants. As the experiment will be designed for head to head comparison of different vaccine candidates, some degree of compromising in immunisation schedule may be required.

A low dose (~100 CFU/ lung) aerosol challenge of *M.tb* (H37Rv, challenge stock to be provided by the modeller) is used to assess protective potency of vaccine candidates by measuring the bacterial burden in lungs and spleen of vaccinated mice at 4 weeks post *M.tb* infection. Each round of experiment will be performed testing up to 3 candidates.

Limited biological samples (e.g. frozen/formaldehyde-fixed tissues and/or splenocytes) from this animal model may be provided if requested by the successful applicants. Detail of requirement and preparation will be discussed and agreed prior the start of the experiment.

A typical experiment is as shown below.



Annex II

Evaluation criteria & process

Selection procedure involves the assessment of the following criteria, against data specific to the vaccine candidate being considered for the call:

A. Go /no go criteria:

In *in vivo* mammalian model show:

- Existing safety data in immunocompetent model.
    - Of note: for live vaccine candidates existing safety data on residual virulence in immunocompromised SCID mice is desirable.
- Existing immunogenicity data.
- Existing protection data (demonstrating equivalent to, or better than BCG or other comparator).

B. Priority setting criteria

The proposed vaccine candidates that meet the go/no go criteria will be assessed against the criteria listed below and will be ranked in order of priority by the Portfolio Advisory Committee (PAC) of TBVAC-Horizon whose members are independent of laboratories that may apply for slots in the experiments. The final priority ranking will be approved by the TBVAC-Horizon Steering Committee (SC).
The criteria which need to be met or will influence decisions for the Standard Mouse Efficacy Model are described below:

Priority setting criteria are concerning the following 4 topics:

1. **Innovation / diversification**: the project is offering potential advantages over existing technologies and/or ensuring portfolio diversity
2. **Feasibility:** the project could lead to a new vaccine provided it meets quality, safety and efficacy criteria. i.e. it must be scalable for clinical use.
3. **Relevance:** the project is compatible with unmet medical needs
4. **Business environment** of the project can ensure successful access to market

Selection procedure:

- Go / no go criteria have to be passed
- Ranking by PAC, with hierarchy in the selection along 2 layers: First “Layer 1” criteria (specified in the table below) are used for ranking. If those criteria do not lead to clear ranking, “Layer 2” criteria will be used.

These priority setting criteria are further specified below:

1. Innovation / diversification			
a	**Scientific concept:** the choice of the vaccine composition is scientifically documented and relevant to the expected impact of the vaccine candidate.	**Layer 1**	
b	**Mechanism of action and vaccine delivery system** (including route of administration): the mechanism of action is defined and the delivery system proposed is expected to be efficient (e.g. adjuvant) and scalable.	**Layer 1**	
c	**Technology:** the technology used to process the vaccine / antigen(s) is explained and it is substantiated why the vaccine is (expected to be) effective and innovative.	**Layer 1**	
2. Feasibility			
a	**Laboratory**: the lab facilities are adapted to early development and formulation of the candidate.	**Layer 1**	
b	**Industrial**: GMP facilities are available/identified and adapted to large scale production, including adjuvant formulation where applicable.		**Layer 2**
c	**Preclinical and clinical development** are feasible and can be conducted by a development team properly established (commitment, competency capability, management, staff, skills…).	**Layer 1**	
d	**Regulatory pathway** is defined/identified and no major hurdles identified (acceptable safety profile based on available data).		**Layer 2**
3. Relevance			
a	**The concept vaccine aligns with the overall strategy** of the TBVAC-HORIZON project, including diversity of the portfolio.		**Layer 2**
b	**The public health need** is recognized (target population is defined) and the public health impact is measurable.		**Layer 2**
4. Business environment			
a	**Intellectual property**: IPRs are robust or do not represent an issue, FTO is not an issue.		**Layer 2**
b	**Budget:** resources are available (at least to take the project to next stage gate).		**Layer 2**
c	**Partnership** necessary to conduct the project (to next stage gate) is identified.		**Layer 2**
d	**Market access** is supported by a (robust) business plan.		**Layer 2**

The above criteria are derived from the Stage gate A criteria of the vaccine development pathway. This can be used as further guidance.