Meeting Report

“Maintaining European scientific excellence and global leadership in EU-funded collaborative TB Vaccine research and innovation”

Impact of 3 EU-funded TB vaccine Research and Innovation projects on the global TB vaccine pipeline
8 October 2019, Brussels
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Summary
Tuberculosis (TB) remains one of the biggest global public health burdens, with ten million new TB cases each year and 1.6 million TB-related deaths. Important progress is being made in diagnosis and treatment of TB. However, there is an urgent need for efficacious vaccines that protect against all different forms of TB disease, in all target groups and for all indications, to enable us to fight the global TB epidemic. Furthermore, the WHO indicates that Drug-Resistant TB is a persistent problem expected to be responsible for 25% of all deaths from resistant pathogens in the near future which indicates the importance of new tools including vaccines.

The EC framework programme Horizon2020 has invested over 120M€ in TB research and a good share of this went to TB vaccine research. Thanks to this investment substantial progress has been made in the innovation and development of vaccines against TB. This is shown by the promising results of the three H2020-funded TB vaccine Research and Innovation projects on the global TB vaccine pipeline - TBVAC2020, EMI-TB and STriTuVaD. During the workshop “Maintaining European scientific excellence and global leadership in EU funded collaborative TB Vaccine research and innovation” (8 October 2019, Brussels), scientists, policy makers and funders discussed the challenges, opportunities and recommendations on how to build on these achievements.

Recent policy and publications confirm that the EU is strongly committed to continue to support TB vaccine R&D. Continued support under the Horizon Europe programme will be essential for maintaining a strong European TB vaccine R&D community, to keep the momentum and foster the essential contribution of this unique collaboration in the global TB vaccine development space.

"New TB vaccines are vital to stop TB! Continued funding is needed to keep the momentum, to build on and learn from recent promising results in preclinical and clinical TB vaccine development." (Quote Helen McShane – Chair TBVI advisory committee and prof. Vaccinology at Oxford University)

The main achievements of these collaborative H2020-funded research projects on TB Vaccines presented during the workshop are:

- The impact of European investment in TB R&D is evidenced by the fact that over 50% of the TB vaccine candidates in the global preclinical and clinical pipeline originate from TBVAC2020, and its predecessors projects under FP 5, 6 and 7.

- By using head-to-head testing in ‘standardised’ centralised preclinical models and by applying a globally accepted stage gating and portfolio assessment, the TBVAC2020 and EMI TB project have identified 13 new promising candidates, 7 of which showed improved efficacy over the existing BCG vaccine.

- By evaluating a range of different and innovative approaches in vaccine discovery, TBVAC2020 and EMI-TB have identified 25 new vaccine approaches and platform technologies that are applied to the development of novel TB vaccine candidates, and to development of vaccines in a range of other infectious diseases.

- A unique global platform for TB biomarker research and development has emerged. This resulted in a rich pipeline of biomarkers.

1 https://ec.europa.eu/info/research-and-innovation/research-area/health/tuberculosis_en
2 the commission communication and Council recommendation in 2019 and the presented ten actions towards vaccination of all
A number of TB vaccine candidates discovered and developed with the support of TBVAC2020, and its FP6 and FP7 predecessors have progressed to clinical stages and secured support from EDCTP for further (clinical) development.

The goal-driven approach of EMI-TB focusing on mucosal immunity has accelerated early-stage vaccine development. This resulted in 3 new mucosal TB vaccine candidates.

To shorten the duration of therapy and reduce the costs of clinical trials, a new Horizon2020 project supported by the STriTuVaD project is advancing computer modelling and simulation to accelerate the development of TB vaccines.

Although impressive progress has been made, there are still many challenges to overcome to achieve the successful development and licensure of effective tuberculosis vaccines. To meet these challenges and to ensure the promising results and impact can be continued, the following opportunities and recommendations were concluded during the discussion sessions:

- Collaborative research and innovation efforts (consortia) have proven to be best able to provide the necessary interactive and integrative framework to generate new knowledge in TB Vaccine development.
- A long-term vision with appropriate and sustainable funding instruments is needed for TB vaccine research and development to accelerate promising vaccine candidates and to ensure continuous innovation and diversity in the TB vaccine pipeline.
- The complexity and disease-specific elements of bringing new, effective and affordable TB vaccines to market require a TB vaccine-specific focus in the relevant R&D agenda’s and funding programmes.
- Funding must be used to build on and strengthen existing networks and excellence.
- Public-private collaboration and collaboration between consortia should be endorsed.
- The TB vaccine research and innovation community must continue to create and be open to new collaboration in different areas: multi-disciplinarily, with global involvement, including endemic countries, exchanging knowledge between consortia and searching for synergy from both horizontal and other diseases.
- An initiative like the Global TB Vaccine Partnership could be the instrument to stimulate alignment of funding and connect project coordinators.
1. Key achievements TBV2020, EMI-TB and STriTuVaD

1.1 TBVAC2020

Aim: The overall aim of TBVAC2020 was to innovate and diversify the TB vaccine (and biomarker) pipeline, while at the same time applying portfolio management using entry, gating and priority setting criteria to select the most promising TB vaccine candidates as early as possible and accelerate their development.

Achievements:

- TBVAC2020 consortium consists of more than 40 partners and builds upon the TBVI TB vaccine R&D consortium that has been developed over the past 15 years.
- 50% of the current clinical TB vaccine pipeline resulted from the TBVAC2020 consortium or its predecessors.
- TBVAC2020 delivered on what was promised: prioritisation & selection, diversification, harmonisation, data sharing and global collaboration.

Discovery and innovation:

Throughout the four-year TBVAC2020 project, various novel concepts and vaccine strategies have been employed that, combined with most promising existing candidates, have led to a more diverse preclinical pipeline.

Preclinical and rational selection of TB vaccine candidates:

The preclinical evaluation infrastructure and procedure set up by the TBVAC2020 consortium has produced unique elements that have shown to work:

- **Selection criteria and stage-gating, including the use of the TB vaccine Stage Gate criteria ([www.tbvacpathway.org](http://www.tbvacpathway.org)), allow robust decision-making**
  
  By applying this approach, promising candidates progressed through the pipeline, or enabled iterative improvement of vaccine candidates.

- **Head-to-head testing in ‘standardised’ models allows prioritisation**
  
  Results and data of these tests were shared within the consortium, and transparency in sharing prioritisation decisions was applied.

Within TBVAC2020 these two elements were key. Thanks to the rational selection (Stage Gates) and the head-to-head evaluation in centralised preclinical models, promising candidates moved forward in the TB vaccine development pipeline (figure 1). This approach resulted in 13 new promising candidates of which 7 showed improved efficacy over the existing BCG vaccine. And thanks to funding of research to new vaccine candidates in H2020 and previous framework programmes, several vaccine candidates have transited from preclinical to clinical development stages, with some receiving funding from EDCTP.
Figure 1. Movement of TB vaccine candidates during TBVAC2020

Biomarkers for TB vaccine development:

The biomarker group under TBVAC2020/TBVI has been able to build a unique and open network of researchers working in biomarkers. A globally unique platform for TB biomarker research and development has emerged by combining the leading TB biomarker research groups in EU with leading African TB biomarker and clinical research sites (Figure 2). This has resulted in a rich pipeline of biomarkers, including potential correlates of protection that may enable the identification of protective antigens and effective vaccines at a much earlier stage in development.

This unique network resulted in:

- 25 potential biomarkers of risk, reduced risk, and of protection
- 15 potential biomarkers of disease
- 10 potential biomarkers of infection
- Human cohorts and potentially available sample repositories
- A database for TB biomarkers
Knowledge sharing:

The true sense of collaboration established through the sequential TB vaccine consortia has resulted from the length of funding that enabled the consortium led by TBVI to mature and develop. The TBVAC2020 consortium facilitates collaboration and early data sharing between partners, and facilitates independent research test facilities where potential vaccine candidates can be evaluated. Through this model, the consortium was able to provide an in-vivo testing capability offering objective assessment (head-to-head where possible) of the safety and potency of vaccines. Through its extensive network, TBVAC2020 contributed to (open) knowledge sharing and knowledge exchange. More than 124 publications were published in 28 scientific journals, and more than 175 presentations were given at scientific meetings and conferences. Furthermore, approximately 140 participants from 70 organisations attended the annual meetings that contributed to creating opportunities to exchange knowledge, including members from research institutes, universities, industry, SMEs, funding and technical agencies and partner organisations.

1.2 EMI-TB

The Eliciting Mucosal Immunity in TuBerculosis (EMI-TB) consortium comprised 14 academic, SME and public health institutions across Europe and Africa and was coordinated by St. Georges’ University in London, UK. EMI-TB focused on investigating the airways as an administration site for novel, rationally designed, mucosal TB vaccine candidates. Operating at the pre-clinical level, EMI-TB has been able to screen a large number of candidate vaccines. Building on this work, EMI-TB partners have now developed novel approaches for the aerosolisation of the most promising vaccines and successfully delivered them for further testing in the pivotal non-human primate (NHP) model, advancing the pipeline of pre-clinical vaccine candidates for mucosal application.

In parallel, volunteers and patients were recruited at two TB clinics in Spain and in Mozambique with the goal of identifying human transcriptomic, proteomic and immunological parameters associated with the lack of disease acquisition in close TB case contacts. The biomarker discovery work emphasised the analysis of samples from the airways, and is the first to directly compare biomarkers in saliva and sputum.
In summary, EMI-TB has delivered the following achievements:

- EMI-TB tested 36 formulations and selected 3 novel vaccine candidates: Spore-FP1, Nano-FP1 and Lipo-AE (mouse and guinea pig studies)
- All 3 candidates were designed as mucosal boost to systemic BCG
- All 3 candidates were safe in NHP when used mucosally or systemically
- Spore-FP1 is the first protein-based aerosolised TB vaccine candidate
- NHP Immunogenicity evidence for Spore-FP1:
  - Antigen-specific cellular responses observed in PBMC
  - Antibody responses observed in serum and mucosa
  - Induced antibodies conferred significant protection when transferred to naïve mice
- Spore-FP1 did not improve significantly on BCG protection in non-human primates
- Further refinement of Spore-FP1 aerosolised delivery in NHP is needed

The EMI-TB project was built around specific goals. The main goal was to select a mucosal vaccine candidate through a rigorous and controlled screening procedure and advance it through pre-clinical development. EMI-TB has shown that such a goal-driven approach can rapidly accelerate early-stage vaccine development. Moreover, by effective communication and co-operation between research consortia, we were able to effectively share resources to deliver the best possible research outcomes. To achieve this, partners work closely with other organisations supporting the development of TB vaccines, including TBVI/TBVAC2020, StriTuVad, Euripred and CTVD.

**Key messages:**

- EMI-TB as a new consortium has made substantial progress in the mucosal vaccination field
- We have generated new knowledge and made technological advances
- We have set up new collaborations and initiatives and created opportunities
- We have had an excellent cooperation with TBVI and TBVAC2020
- We have learned and we will continue to make improvements with our aerosolised vaccine formulations
- It is an imperative that the current momentum is maintained to ensure that progress continues to be achieved

### 1.3 STriTuVaD

The STriTuVaD (In Silico Trial for Tuberculosis Vaccine Development) consortium is the youngest consortium of the three projects highlighted. It consists of eight partners and is coordinated by Etna Biotech in Italy. The goal of STriTuVaD is to demonstrate how advanced computer modelling and simulation can be used to reduce the costs of the clinical trials required to test the efficacy of new therapies for tuberculosis.

One promising possibility to shorten the duration of the therapy is new host-reaction therapies (HRT) offered in combination with the antibiotic therapy. The endpoints in the clinical trials for HRTs are time to inactivation and incidence of recurrence. With inactivation it is possible, in some cases, to have statistically powered evidence for efficacy in a Phase II clinical trial. However, recurrence almost always requires a Phase III clinical trial with thousands of patients involved and very high costs.

The STriTuVaD project will extend the Universal Immune System Simulator to include all relevant determinants of such a clinical trial. The project will establish predictive accuracy against the individual patients recruited in the trial, use it to generate virtual patients and predict their response to the HRT
being tested, and then combine them with the observations made on physical patients using a new in silico-augmented clinical trial approach that uses a Bayesian adaptive design. This approach, if found effective, could drastically reduce the cost of innovation in this critical sector of public healthcare and make advanced therapies available at reasonable costs.

Milestone 31 July 2019:

- Computational modelling of two vaccination strategies tested on a virtual cohort of TB

Future perspective:

- Computational prediction of the effect of any intervention for pulmonary TB
- EMA qualification of the computational model

1.4 Conclusions and challenges

Thanks to collaborative research and development efforts in EU-funded TB consortia (TBVAC2020, EMI-TB and STRiTuVaD), substantial progress has been made in the development of vaccines against TB. The three collaborative projects have helped to strengthen and diversify the vaccine candidate pipeline.

The following unique elements of these TB vaccine consortia contributed to this impact made on the vaccine pipeline by:

- Independent head-to-head comparison
- Rational selection
- Support of independent Product and Clinical development experts
- Diversification (supporting and applying a diversity of vaccine approaches and technologies)
- Unique collaboration on Biomarkers
- Transit of resulting candidates to EDCTP
- Global integration by bringing key R&D partners together
- EC funding that leveraged national and international funds.

Recent studies have shown positive signals that give faith (hope?) in the further research and development of effective TB vaccines. Still many challenges remain to overcome and to achieve successful development and introduction of a TB vaccine to the market.

At the end of the morning session it was concluded that continued investment in TB vaccine R&I from discovery to clinical development is needed to overcome the challenges and bring new TB vaccines to the market. In the afternoon these challenges were discussed in three panel sessions which resulted in proposed recommendations for continued collaborative research on TB vaccine R&D.
2. Discussion panels

2.1 High-level R&I elements, areas and relevant technical support
infrastructures and processes of TB vaccine R&I consortia

*Driving research and innovation through lessons learned in the past years in TB vaccine R&D and
clinical development. Applying an evidence-based and transparent process in portfolio assessment.*

Chair: Gerald Voss

Panel members: Rajko Relic (St George’s University), Helen Mc Shane (Oxford University), Frank
Verreck (BPRC), Flora Musuamba Thsinanu (EMA)

**Scientific challenges and opportunities:**
The TB vaccine field has seen exciting new results in clinical studies over the past year³. While the
recent results need to be confirmed and the potential path to licensure be devised, these recent
findings offer possibilities to guide TB vaccine development through re-iterative research and
development cycles. It is therefore important to maintain a broad portfolio of early to mid-stage
vaccine candidates while progressing the promising candidates to the next stages of development.

While it is important to invest in and maintain a sustained and diverse pipeline of TB vaccine
candidates, addressing the most important gaps and challenges will accelerate the development of
novel TB vaccines. Better tools, including the identification and validation of immune correlates of
protection, improved preclinical animal models, controlled human infection models, and *in-vitro*
functional killing assays will provide valuable data for assessing vaccine candidates. The independent
head-to-head testing of candidates will assess the relative merits of different candidates and the use
of stage gating criteria as described in the TB vaccine development pathway (www.tbvacpathway.org)
will help to manage the global TB vaccine pipeline.

**Conclusions:**

**Innovation in TB vaccine R&D from discovery to clinical development**

Sustained innovation will contribute:

- New technologies and diversification of the vaccine pipeline on all levels (tools and
  approaches) and more of a **high risk-high gain** approach to move the field forward and ensure
  faster progress.

- To test new and existing candidates with new tools and technologies, including new delivery
  systems, vaccine tools, adjuvants, adopting from other pathogens.

- By developing better tools for vaccine selection, including controlled human infection models,
  correlates of protection/*in vitro* functional assays, and independent head-to-head animal
testing. Because capacity for large-scale human efficacy trials remains low, new tools that
facilitate vaccine selection, such as controlled human infection models and *in vitro*-functional
assays would help to accelerate TB vaccine development. Together with identification and

³ https://www.nejm.org/doi/full/10.1056/NEJMoa1803484 Phase 2b Controlled Trial of M72/AS01E Vaccine to
Vaccine or BCG Revaccination.
validation of correlates of protection and validated preclinical animal models, it would greatly facilitate tuberculosis vaccine development.

- By applying a coordinated "bottom-up approach". This approach stimulates and enables scientists to bring forward their innovative ideas, concept and technologies.

**Rational selection of TB vaccine candidates**

Given the limited resources, rational progression of promising innovations and standardised processes will contribute to mitigating development risks. Policymakers can promote and support an aligned and coordinated bottom-up approach to stimulate innovation and discovery by encouraging and enabling scientists to bring forward their innovative ideas, concepts and technologies. A rational prioritisation process like the TB vaccine development pathway with pre-defined criteria (www.tbvacpathway.org) will help to accelerate vaccine development and manage the global pipeline. This principle can be applied from discovery to late-stage clinical development.

**Translation of recent clinical trial data**

It is essential to translate the recent clinical study results through re-iterative research and development cycles. This will contribute to improve next generation TB vaccine approaches currently in discovery and the preclinical models available for the evaluation of TB vaccines.

**End-to-end approach and early dialogue with regulatory agencies**

The current TB vaccine landscape with two late-stage efficacy signals and several candidates in clinical development and further upstream requires an end-to-end perspective to rationalise and focus vaccine development. The definition of desired vaccine properties through the establishment of target product profiles that are aligned with WHO’s Preferred Product Characteristics is an essential prerequisite. A validation with regulatory agencies of these properties and corresponding development plans offers a valuable opportunity for guidance for vaccine developers and should occur re-iteratively.

**Recommendation:**

Despite a great and increasing body of knowledge there are still gaps. The complexity of host responses against the TB infection and in latency can now benefit from unbiased research approaches and big data platforms that have matured over the last decade. **Collaborative research and innovation efforts (consortia) are best able to provide the necessary interactive and integrative framework to generate new knowledge in this area.**

To address the challenges of TB vaccine R&D, synergies from both horizontal and other diseases should be strengthened. The complexity and disease-specific elements of bringing new, effective and affordable TB vaccines to market require a **TB vaccine-specific focus in the relevant R&D agenda’s and funding programmes.**
2.2 Composition/structure (incl. partners and stakeholders) of collaborative TB vaccine R&I consortia: which partners and structures are needed to deliver the key R&I content

Opportunities and ways to strengthening collaborative R&I consortia and build on EU excellence to advance the TB vaccine field

Chair: Hazel Dockrell

Panel members: Tonnie Rijkers (Netherlands Enterprise Agency RVO), Olga Rue (Archivel), Andrew Mcdonell (UK ERC), Georges Thiry (P&CDT TBVI)

In the discussion with the panel members and the audience, the overall conclusion was that the existing European TB vaccine network that has been built up during the last decades, has become mature and has delivered an important contribution to the diversification and expansion of the TB vaccine pipeline. It was also mentioned that the Global TB vaccine field was fractured five to ten years ago, but that collaboration and cooperation have been central and have resulted in initiatives like TBVI, BMGF-CTVD and the Global TB Vaccine Partnership.

There was consensus about the role of TBVI that has provided effective neutral leadership to several TB consortia (TBVAC, NEWTBVAC, TBVAC2020), by managing these complex consortia effectively and providing access to a network of experts and enabling research scientists to learn how to translate research findings into vaccines ready for clinical trials.

To continue the positive developments, it is important to maintain, improve, strengthen and adjust the consortium and seize new opportunities.

During the panel discussion the following challenges and opportunities were identified to maintain and strengthen the TB vaccine R&D collaborative efforts:

- Organise multidisciplinary involvement early on in projects, by for example including the regulatory authorities at an early stage of product development, and by involving researchers/scientists in the design of clinical trials early on.

- Integrate the translation of research into product development. The opportunity to learn from those who have product development expertise is valuable and consortia could do more to exploit this, for instance by working with companies and those with relevant expertise. Smaller companies can also benefit from this kind of advice and interactions.

- Involve non-European partners as it can leverage funding, giving value for money, but also provide access to clinical samples (in case of endemic countries) as well as new perspectives and expertise.

- Find ways to maintain expertise and not lose trained people in the gap between funding schemes such as between Horizon2020 and Horizon Europe calls that could fund work on TB vaccines.

- Educate the next generation of research scientists to lead TB vaccine R&D.

- Involve and communicate with the public, with other consortia, academia and involve industrial partners.

- Use experience from other consortia to adapt different products with different approaches.
Recommendations:

Build on and strengthen existing networks and infrastructures

The EU support over the last decade enabled the European TB vaccine R&D to establish a true sense of collaboration which contributed to a more diversified and filled pipeline. Collaborative efforts are essential for the highly scientific innovation needed for new vaccine production, through cross-fertilisation between different disciplines (multi-disciplinary).

Following the discussion, there are a number of (policy) measures to promote the formation and sustainability of these collaborative efforts and to build further on the EU excellence to advance the TB vaccine field:

- Stimulate **public-private collaborations** for product development and to improve access to the market.

- Encourage **knowledge sharing**, learning and communication. International collaborations increase knowledge transfer, causing significant improvements in chances of finding new vaccines, while at the same time EU excellence can used to build capacity in low- and middle-income countries. This diversity and international breadth of collaborations creates robust networks and infrastructures, fostering new vaccine development.
  
  o The three projects can learn a lot from each other and learn from other disease areas. Informal meetings and discussions are very important, and consortia should be encouraged to reach out to other consortia with similar issues and expertise.
  
  o It will be important to develop the next generation of scientists. Funders could help by recognising the need for a career path.
  
  o Create opportunities to learn from those who can translate research into product development by working with companies and those with relevant expertise.

- **Emphasize the importance of consortia with an independent and neutral coordinator** who leaves ownership in the hands of the developers. This increases confidence and stimulates knowledge exchange.

- Collaborative consortia should maintain, strengthen and **create new opportunities in different areas**:
  
  o Technical and scientific: by stimulating innovative research and development and including independent product and clinical development teams in consortia to translate discovery into a product and accelerate the process.
  
  o Geographical: to foster existing collaborations and be open to new partners
  
  o Cultural: to keep the ability to work in a multi-cultural and heterogeneous environment like with academia, biotech, large pharma, SMEs, NGOs, research institutes, and funders.
2.3 Funding instruments for collaborative R&I

A long-term vision with appropriate and sustainable funding instruments is needed for TB vaccine R&I to accelerate promising vaccine candidates and ensure continuous innovation and diversity in the TB vaccine pipeline.

Chair: Beatrice De Vos

Panel members: Hannu Laang (EC), Ole Olesen (EDCTP), Martin Broadstock (MRC), with written input from Katrin Eichelberg (NIH) and Willem Hanekom (BMGF).

Funding challenges and opportunities

The recent developments in TB have led to a new momentum that cannot be interrupted. To translate the new advances into real impact, global TB vaccine funding will need to increase. This will stimulate innovations, bring candidates to licensure and ultimately, delivery to the populations that need the vaccines most.

However, the amount of funding is not the only challenge. There are fundamental structural challenges to be addressed in the way vaccine development policy and funding programmes are formulated and aligned:

- Although vaccine development can take decades, funding programmes are often available for a relatively short period and cause interruptions or even discontinuation in the development efforts, especially during a so-called ‘funding gap’. Also, a certain level of flexibility is needed to re-allocate funding to support the most promising product during the funding programmes.
- Another challenge is the transit from EC H2020 projects or other more early vaccine discovery projects to the next steps of development and introduction of a vaccine to the market. Research and development are only the first phases of the long way to get a vaccine to the market. Further (clinical and product) development and the related regulatory path are also important phases and are now often not included in H2020 R&D-projects.
- Often there is no funding for efficient communication between different consortia and with funders.
- EC encourages collaboration between public and private entities, but this does not arise easily on its own, and needs support through national and international policy formulation.
- The market does not naturally create strong bridges to the low- and medium-income countries that are the primary targets of TB vaccine development. This is an area where trans-national policy can foster the effective ties needed between countries.

There are a few main funders in the TB vaccine R&D field like EC, EDCTP, NIH, MRC and BMGF with their own focus and perspective, and with a clear commitment to TB with the following scope:

- The EU is strongly committed to continue TB research and considers vaccines as important in the fight against TB. It becomes more important to find the right constellation of future consortia. Growth of consortia is an important consideration. Consortia should become more and more interdisciplinary in which TB R&D should be integrated with areas like Artificial Intelligence, ‘One Health’, Ethics, Social Sciences etc. This requires broad expertise and communication between consortia and funders.
- BMGF remains committed to TB vaccine discovery and development. BMGF’s prioritisation is based on science: modelling has shown that a new, effective vaccine would be an impactful intervention in the TB epidemic.
- NIH has large funding programmes including TB, and with a focus on biomedical research.
- MRC has a long term commitment to TB and has its focus on discovery up to Phase I and diagnostics.
- EDTCP has a well-defined focus on clinical trials, also in TB, and stimulates collaboration between different continents.

Recommendations
As a result of the collaborative research and development efforts, substantial progress has been made over the last few years in the innovation and development of vaccines against tuberculosis. However, it was also agreed during this panel discussion that many challenges remain before we achieve the successful licensure and introduction of a TB vaccine to the market. The following recommendation were discussed that could contribute to sustained funding:

- **Align funding tools for collaborative R&I to ensure sustainability**
  A long-term vision with appropriate and sustainable funding instruments is needed for TB vaccine research and development to accelerate promising vaccine candidates and ensure continuous innovation and diversity in the TB vaccine pipeline. Sustained funding for collaborative research to reach that goal is essential. A critical look at how to overcome funding gaps is essential. EDCTP is an important funder for promising vaccines resulting from EC collaborative projects and could help the transition between discovery and early development into clinical development.

- **TB is a global problem that needs global solutions**
  TB is a global problem that needs global solutions. There is a variety of funders in the TB vaccine field like EC, EDCTP, NIH, MRC, BMGF and national governments with their own focus and perspective. The Global TB Vaccine Partnership is a collaboration of vaccine researchers and developers, EC, the World Health Organization (WHO), national governments and major funders in the TB vaccine field that aims at making novel TB vaccines a reality. The GTBVP could be an excellent platform that allows facilitation of partnerships among the different global funding organisations and timely exchange of funding priorities for TB vaccine research. The GTBVP could be the instrument that stimulates the alignment of funding and should also bring project coordinators together.

  To be able to continue and implement the chosen path to accelerate the development of the most promising vaccine candidates and to overcome the scientific challenges, it will be important not to only rely on a few key funders as EC and NIH, but also to further expand and include funding from national governments.

  EC is still strongly committed to the research and development of TB vaccines and emphasizes the importance for more variety in funders, such as national governments. TB is a global problem, and the responsibility to support research activities should be shared. The EU has built partnerships between its Member States and the global TB research field, and work has been done to integrate European efforts with the global TB research agenda.

- **A clear steering from funders to encourage interactions and low-hanging fruits is necessary**
  Consortia will be challenged more and more to become interdisciplinary. TB R&D should be integrated with other disciplines and knowledge should be exchanged with other consortia. This requires communication between consortia and between consortia and funders. Funders should encourage these interactions by including these activities in funding programmes. Also, funders could encourage innovation by including specific possibilities for high-risks activities and or low-hanging fruits into funding programmes.
Word of thanks

We would like to thank all the participants for their valuable contributions to this meeting.