Report of the high-level consultation on accelerating the development of the M72/AS01$_E$ tuberculosis vaccine candidate

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Geneva, Switzerland

Meeting Report

World Health Organization

ACKNOWLEDGEMENTS

We acknowledge with gratitude the participants of this consultation and administrative personnel who made this meeting possible and productive. We wish to thank particularly Dr. Jeremy Farrar for chairing the consultation. All the meeting participants contributed their time to the review of the final document; this support is also gratefully acknowledged.

Background

Tuberculosis (TB) is the deadliest infectious disease in human history and remains the leading cause of death from a single infectious agent globally. The World Health Organization (WHO) estimates that TB caused illness in 10 million people and claimed 1.6 million lives in 2017 alone[1]. The global TB community has made commendable efforts in the past decade to successfully attain the Millennium Development Goal and other international targets of halting and reversing TB incidence and mortality, respectively. However, despite the achievements to date, the global TB incidence is slowly declining at a rate of 1-2% per year only.

Recognizing these challenges, in May 2014 the World Health Assembly approved the new End TB Strategy with a set of ambitious targets, later incorporated within the Sustainable Development Goals for 2030. Targets include the reduction of TB deaths by 90% and of TB incidence by 80% between 2015 and 2030, and by 2020, the elimination of catastrophic costs due to TB in affected households. To achieve these targets, the three-pillar End TB Strategy comprises (i) integrated patient-centered care and prevention; (ii) bold policies and systems, with emphasis on social protection of vulnerable populations; and (iii) intensified research and innovation. The research and innovation pillar of the End TB Strategy highlights the need for new TB vaccines that are safe, affordable and more effective than Bacillus Calmette-Guérin (BCG), in providing protection against pulmonary TB in adolescents and adults. To assist with this, WHO has expressed preferred product characteristics for new TB vaccines, to stimulate and guide the scientific community, vaccine developers and regulatory bodies in development of impactful vaccine candidates[2]. Preference was expressed for a vaccine targeting adolescents and adults in different geographical settings, regardless of previous mycobacterial exposure, providing over 50% protection against pulmonary TB, the most clinically significant endpoint responsible for transmission.

Recently, an investigational TB vaccine candidate (M72/AS01$_E$) was found to be significantly protective against TB disease in a Phase IIb trial conducted in Kenya, South Africa and Zambia, in individuals with evidence of latent tuberculosis infection. The point estimate of vaccine efficacy was 54% (90% CI, 14-75; P = 0.04), over approximately two years of follow-up[3].

This result, unprecedented in decades of TB vaccine research in terms of clinical significance and strength of evidence, constitute a major scientific breakthrough. Key questions on this candidate emerge, such as whether the vaccine may provide protection against TB among uninfected people, or in other geographical areas beyond where it has been tested. Further investigations are warranted to support a more precise evaluation of impact and assess generalizability. A comprehensive value proposition analysis would help guide investment decisions.

In this context, the objective of this consultation is to discuss key strategies and actions needed to advance the research and development pathway of the M72 vaccine candidate. Specifically, key questions discussed during the meeting included:

- What are potential future vaccine use cases and associated data packages supportive of policy decision?
- What are the key clinical development options and associated priority studies to progress this vaccine candidate?
- What types of collaborative initiatives are needed to catalyze the development of this vaccine candidate?
- What actions should be taken in the future by WHO to facilitate this process?

Expected outcome: The expected outcome of this meeting was to define a way forward on the ideal pathway for the development of this vaccine, with a sense of collaboration and urgency.

[1] Global tuberculosis report. Geneva: WHO; 2017 (http://www.who.int/tb/publications/global_report/en/, accessed 6 Oct 2018).
[2] Schrager LK et al. WHO preferred product characteristics for new vaccines against tuberculosis. Lancet Infect Dis 2018;18(8):828-829.
[3] Van Der Meeren O et al. Phase 2b Controlled Trial of M72/AS01E Vaccine to Prevent Tuberculosis. N Engl J Med 2018;379(17):1621-1634.

Introduction

After a welcome by Dr. Soumya Swaminathan (Chief Scientist, WHO), Dr. Jeremy Farrar, Chair of the Consultation and Director of the Wellcome Trust, opened the meeting at 9:15 AM April 5, 2019. The Chair presented the programme of the 1-day meeting and introduced participants.

Session 1: Progress in the M72 vaccine development and its potential role in ending TB

1.1 The role of vaccines in ending the TB epidemic and priority use case scenarios

Dr Philippe Glaziou, Global TB Programme, WHO

Dr. Glaziou presented WHO's End TB Strategy, which articulates the need for research and innovation to end the epidemic as a public health threat by 2030. The rationale of why research and innovation was adopted as a pillar in the End TB Strategy was presented using modelling data that shows the need for new tools, including new vaccines by 2025, to significantly decrease TB incidence to achieve the target of <10/100,000 new TB cases by 2035. Dr. Glaziou also presented potential use scenarios of pre and post exposure, as well as therapeutic vaccine candidates together with their potential impact on the global TB epidemic. ***Slide access***

1.2 WHO's Preferred Product Characteristics (PPCs) for new TB vaccines

Dr Johan Vekemans, Initiative for Vaccine Research, WHO

Dr. Vekemans presented WHO's PPCs for new TB vaccines[4], which was developed to assist TB vaccine developers in identifying important vaccine features aligned with patient and programmatic needs at country level. The proposed PPCs, which describe prioritized characteristics, specify the clinical indication of the PPCs, the goals to be met, the measure of efficacy, the main safety aspects, the target population that will receive the vaccine, and the intended end-users. ***Slide access***

1.3 TB vaccines in context: history & pipeline analysis

Dr Barry Bloom, Harvard School of Public Health

Dr. Bloom presented the history of TB vaccine research, including the nuances on the discrepancies of protective efficacy of BCG in different geographic settings. Considering the presence of inherent non-TB mycobacteria in different parts of the world that potentially impacts vaccine efficacy, Dr. Bloom emphasized that the TB field needs to test a diverse portfolio of TB vaccines, to identify candidates with maximum efficacy. Dr. Bloom also presented future questions that would allow fully exploiting the potential of the M72 vaccine. ***Slide access***

1.4 The M72/AS01E TB vaccine candidate:

- vaccine profile, early clinical data

Dr Olivier Van Der Meeren, GSK

Dr. Van Der Meeren presented the product profile of the M72/AS01$_E$ vaccine, and early clinical data assessing immunogenitcy, safety and reactogenicity, in different groups, as well as the target indication of the vaccine candidate. While waiting for the year 3 data of the M72 Phase IIb trial, Dr. Van Der Meeren recommended future studies to assess adjuvant dosage, and longer interval dosing schedule, to lay a sustainable pathway to Phase III development. ***Slide access***

- safety and efficacy results of a phase IIb trial

Dr Ann Ginsberg, IAVI

Dr. Ginsberg presented the results of the M72 vaccine candidate Phase IIb trial primary analysis , the results of which have been published. Dr. Ginsberg also announced that ancillary biobank studies are being planned from samples collected from the study, with funding from BMGF, US-NIH and potentially other funders, and in collaboration with Gates MRI and other key stakeholders, to support discovery of vaccine-induced correlates of TB disease risk and protection. **Participants** asked if vaccine efficacy varies by study site (country), to which, Dr. Ginsberg explained that most of the cases were located in South Africa, and such analysis may not be conclusive (detailed information will be available later in the year as part of the final analysis). Because entering Phase III is a very important decision, as it carries both financial and opportunity cost/risk, some participants suggested smaller Phase II studies to answer Phase III preparatory questions, such as likelihood of achieving a clinically relevant response with an adjuvant dose lower than what was used in the published Phase IIb study or an alternate dosing regimen. ***Slide access***

[4] Schrager LK et al. WHO preferred product characteristics for new vaccines against tuberculosis. Lancet Infect Dis 2018;18(8):828-829.

Session 2: Advancing clinical and product development pathways of M72/AS01$_E$

2.1 Possible next steps in clinical development

Dr Mark Feinberg, IAVI

Dr. Feinberg presented options for taking forward the M72 vaccine candidate with an end-to-end perspective, linking product development, manufacturing, regulatory and policy pathways, as well as financing. He emphasized the need for novel partnerships and collaborations across key public and private sector stakeholders and funders to ensure efficient development and delivery of an effective, accessible product. Dr. Feinberg iterated the need for a global health value proposition for this vaccine as soon as possible, to support decision making by stakeholders during the different stages of product development. ***Slide access***

2.2 Future perspective of developing the M72/AS01E vaccine candidate: challenges and opportunities

Dr Olivier Van Der Meeren, GSK

Dr. Van Der Meeren presented the industry perspective of what it takes to advance the clinical development of M72 towards public health impact in the context of financial, scientific and practical preparations needed before entering Phase III, (including dose–schedule, adjuvant dosage, and, boostability testing). Currently, limited but ready to use vaccine GMP lots are available (around 9000 doses, with a stability plan up to 2020, potentially extendable). Before advancing to Phase III, production would typically need process upgrade. This being considered, it would be unlikely that Phase III could start before 2022. Considering the likelihood that post licensure implementation research would likely be needed, global vaccine delivery may not be implemented until 2030. It was confirmed that adjuvant production according to current technology requires the natural extract of QS21 for AS01 and synthetic development is not available. Examples of potential Phase II/ III scenarios were presented against timeline. In terms of development cost, greater than USD 800 million was estimated to bring the product to market. Further financial perspective from industry was presented by Dr. Breuer (Session 4.2). ***Slide access***

Discussion

Participants reflected that

- Estimated financial cost of M72 vaccine development presented in sessions 2.1 and 2.2, are conservative and this needs to be revisited together with communication strategy that provides clarity on risks during the various stages of product development.
- In future studies, inclusion of people living with HIV (PLHIV) and other groups at high risk of developing TB disease, should be considered.
- Globally representative data needs to be generated through future studies to support optimal policy decision making, by including trial sites in different continents and epidemiological settings.
- Adaptive clinical trial designs need to be considered to allow for efficient, responsive and expedited research, without compromising quality.
- Scientific questions and data supportive of policy decision need to be clearly articulated before initiating Phase II/III studies.

2.3 Panel session: Regulatory pathways to facilitate expedited and equitable access

Dr. Marco Cavaleri, EMA

Dr. Cavaleri commented that from a regulatory assessment perspective, there is expectation that pivotal clinical trials are designed with a primary endpoint that is clinically meaningful and/or relevant from a public health perspective (e.g. prevention of disease), together with due consideration to factors such as environmental Mycobacteria exposure that can influence efficacy in different geographic settings and context of use in view of current standard of care for persons infected with Mtb. Dr. Cavaleri also iterated the EMA's readiness to discuss vaccines, in the context of European authorization, as well as under Article 58 rule (in collaboration with WHO), if the vaccine will be used outside of the EU. A priority scheme is available that allows more contact with developers, to allow for continuous discussions.

Dr Jeffrey Roberts, FDA

From a broader point of view of whether to do a very large Phase III or to go smaller, there are two opportunities to consider: (i) there is opportunity to use *biomarkers*, if identified, to support regulatory decision making (e.g. using surrogate markers, instead of clinical endpoint), which can expedite the clinical pathway, and (ii) using *"real world evidence"* approach to support vaccine effectiveness analysis. For example, a vaccine can be approved for a narrow indication (background of LTBI), and following real world evidence analysis, it can be approved for broader indication.

Dr Emer Cooke, WHO

Dr. Cooke presented WHO's prequalification process, preparation for which needs to concretely take place at least 2 years before licensure but the thinking into the 'how' needs to take place now. ***Slide access***

Mr Esteban Burrone, MPP

Mr. Burrone started his presentation by emphasizing that preparation needs to take place in parallel and not sequentially to address access issues; in particular, to ensure that immediately after approval, there is(are) manufacturers ready to supply product at an affordable cost to low-income countries. Understanding the regulatory pathways in low- and middle-income countries is key to avoid delays in access. Furthermore, considering the prevalence of coinfection with HIV, vaccine/ drug interaction needs to be assessed as early as possible. If there is a role for licensing and tech transfer in this vaccine development, preparations are needed to ensure economies of scale (avoid market fragmentation) by engaging high TB burden countries, and supporting competitive supply, to incentivize innovation in manufacturing process which is ultimately needed to drive prices to affordable but sustainable levels. Finally, market forecasting should be considered to support the vaccine development pathway.

Session 3: Perspectives of high TB burden countries in advancing the development of M72

Panel session

Dr Tereza Kasaeva, GTB/WHO introduced the panellists and opened the session by emphasizing that high TB-burden countries have an important role to increase health research activity for TB. This is particularly so for the BRICS countries (i.e., Brazil, Russia, India, China, and South Africa), which account for more than 40% of the global TB disease burden in terms of both TB incidence and TB deaths, and about 50% of the burden of DR-TB. Increased financial investment coupled with greater use of institutions by the BRICS countries can help transform the TB vaccine field by bringing in new resources and innovation.

Dr Julio Croda, Brazil presented the perspective of Brazil on potential use cases for M72 in the context of high TB incidence amongst prisoners, PLHIV and close contacts of TB patients. Dr. Croda also outlined Brazil's strong record of Universal Health Coverage that ensures access to vaccines to all who need them. Several examples were presented showing Brazil's capacity in vaccine development, regulatory oversight, and manufacturing for the Americas market, some including in partnership with GSK. Brazil's government expressed willingness to discuss co-funding a Phase 3 programme for M72 and associated technology transfer for manufacturing. ***Slide access***

Professor Irina Vasilyeva, Russian Federation commented on the declining incidence and mortality from TB in the Russian Federation, attributed to strong efforts by the government to scale-up and efficiently implement existing interventions, including BCG immunization. However, drug-resistant TB and HIV coinfection continue to present challenges to controlling the TB epidemic. Ongoing research is mainly focused on the development of diagnostics and therapeutics, but Russia acknowledges the importance of vaccines in the fight against TB. ***Slide access***

Professor Balram Bhargava, India reiterated that M72 development project can be a glue for BRICS to exert joint research efforts. After discussing the epidemiological profile of TB in India, Dr. Bhargava proposed India's readiness to contribute to smaller studies to validate and expand Phase II results. TB vaccines are a priority for India, and currently, Indian Medical Research Council is funding the clinical development of several vaccine candidates, including VPM1002 and MIP. ***Slide access***

Dr Zhao Yanlin, China shared China's TB epidemiological context as a high TB burden (including drug-resistant forms) but low TB/HIV incidence country. Dr Zhao presented currently ongoing TB vaccine research in China, including clinical trial capacity, and ongoing collaborative works with Pharma in vaccine development including with GSK and Merck. Regulatory nuances for vaccine approval were also presented. Specifically, a Phase II level study must be implemented in-country to register a new vaccine in China.

Dr Glenda Gray, South Africa shared South Africa's challenge in battling TB, fuelled by the HIV epidemic, particularly in people between 16-22 years of age. As such, M72 vaccine discussion in South African context should ideally be inclusive of PLHIV. Financial commitment from government will require understanding Pharma's commitment, global problem with adjuvant access, tech transfer, and better understanding of cost, and the investment model required for vaccine development. South Africa has strong clinical trial capacity and efficient regulatory pathway, and is in a strong position to conduct clinical development studies. However, multi-site study across the BRICS may require strategies to support regulatory harmonization.

Session 4: Financial and technological considerations in advancing the M72 vaccine development

4.1 Financing late stage development and vaccine introduction: effective models and best practices

Dr Seth Berkley, GAVI

Dr. Berkley presented examples of financial/non-financial incentives for late stage vaccine development that would allow end products to be used equitably in both low-and high-income countries. Examples on pull financial mechanisms, such as vaccine bonds based on long-term binding agreements from donor governments[5], and advance market commitment were presented. Dr Berkley also presented the decision pathway to vaccine introduction to advocate for early preparation needed to overcome potential complexities and challenges. As part of the discussion, **Dr Tore Godal**, former GAVI CEO suggested that a public health value proposition for new TB vaccines be developed (e.g., how much life will be saved, the cost of inaction, etc) to help mobilize resources. ***Slide access***

4.2 Financing the further development of M72/AS01E vaccine candidate

Dr Thomas Breuer, GSK

Dr. Breuer presented GSK's position on advancing further development of the M72 vaccine. Previously, GSK has followed a co-funding model (joint internal and external) to fund the malaria RTS,S vaccine candidate, with GSK maintaining proprietary control of the vaccine. For the M72 vaccine, a proposal was put forward for partner(s) to take a license from GSK to further develop, license, manufacture, be liable for, and supply the vaccine for the 'developing world' (GSK will maintain proprietary control for the 'non-developing world'). For the adjuvant component, GSK proposes to maintain proprietary control with willingness to produce and supply AS01, with full support from external fundingAS01 is part of GSK's SHINGRIX, RTS,S and other new candidate vaccines. Currently, there is sufficient AS01 supply for internal clinical research work, for pilot phase of the malaria vaccine, and up to 15 million doses for malaria (post pilot phase) until 2042. Additional capacity needs to be created within GSK to meet further demands of the AS01 adjuvant , financed externally. Indicative figures of costs for clinical development, manufacturing investment and procurement were provided. With such a development plan, the cost of the M72 vaccine is estimated to be between 3.50-5 USD per dose. *Slide access*

4.3 Achieving impact through responsible research and innovation: civil society perspective

Stacey Hannah, AVAC

Ms. Hannah presented Good Participatory Practice (GPP) Guidelines, which were developed to guide the research community towards partnerships between health researchers and sponsors on the one hand, and patients, communities and advocates on the other. Experiences from HIV prevention research were presented as a case study to showcase the opportunities meaningful community engagement can present in increasing the quality and acceptability of trial results. The position statement from the Global Tuberculosis Community Advisory Board and Treatment Action Group regarding the next steps of M72 vaccine development was also presented. ***Slide access***

4.4 Perspective from Stop TB Partnership

Dr Lucica Ditiu, Stop TB Partnership

Dr. Ditiu presented the importance of strengthening public private partnership, as well as civil society engagement to move new TB vaccine development forward, especially considering the significant gap in investment in TB research when benchmarked against diseases like HIV. The Stop TB Working Group on New TB Vaccines is one platform through which the Stop TB partnership will continue to contribute to this field, as well as by strengthening civil society engagement in creating demand for TB vaccines. Dr Ditiu reminded participants that the TB field is different from malaria, and further research on this vaccine needs to be done with renewed commitment, sense of urgency and collaboration (engaging new partners), recognizing that the investment ask is small when compared to the cost of inaction. Regarding the sense of urgency, **participants** asked if regulatory agencies are open to approve vaccines for use based on Phase IIb results (conditionally). EMA and FDA representatives commented that this is 'theoretically possible' but will depend on the evidence that Phase IIb studies are able to generate to allow decision-making. Currently available data is not sufficient to allow this discussion.

[5] https://www.iffim.org/about/

4.5 Perspectives of leading TB R&D funding institutions and partners

Bill & Melinda Gates Foundation, Gates MRI, BRICS countries, European Commission, EDCTP, GAVI, Global Fund, IAVI, PATH, US-NIH NIAID, TBVI, UNITAID, USAID, Wellcome Trust

After the presentations, a round table discussion was facilitated by the Chair to understand institutional perspectives regarding M72 vaccine development, among organizations engaged in funding / implementation/use of TB research and innovation.

BMGF recognizes the potential of this vaccine for ending the TB epidemic. The path forward will need to account for risk (financial and opportunity cost). Extensive pre-planning is needed as we risk failure if the science is not done well, for example, which populations to target, adjuvant dosing and dosage schedule, geography, etc. The scientific questions that guide a Phase II/Phase III programme need to be clearly and thoughtfully articulated and this should be the immediate next step. The Foundation is otherwise supportive of this research effort.

Gates MRI, subsidiary of BMGF ('nonprofit biotech'), was established to facilitate product development for priority diseases, including TB. Gates MRI has specific expertise in clinical trial design/simulation and biomarker/correlates studies that it can contribute with regard to M72 research. However, guiding principles are needed at this early stage to understand what questions need to be answered in Phase II/III research. This includes understanding country needs in terms of product profile, as well as data needs for policy recommendation so a Phase III programme can be designed that will not require a pilot implementation step, including through adaptive trial models (accounting for risk when using such approaches, so that speed does not compromise quality).

Brazil reiterated that government funding requires understanding future perspective of M72 vaccine development (i.e. the issue of tech transfer, access and sustainability). Brazil is otherwise open and willing to support further Phase II/III studies.

China mentioned the need to keep in mind regulatory nuances as early as possible, and the need to have direct agreement between government and Pharma if government funding is required for the further development of this vaccine.

European Commission acknowledged the importance of the M72 vaccine development but highlighted the need to invest in wider range of vaccine candidates to maximize the chance of success. In the context of funding, the EC is transitioning into a new commission and a 'post horizon 2020' strategy, hence political discussions will determine future funding opportunities. The current financing model operates on a 'call' basis, and is not suited for targeted funding sought by this meeting. Stakeholders may explore financial mechanisms under Infectious Diseases Finance Facility of the European Investment Bank.

EDCTP supported the European Commission's position on diversifying investment across various TB vaccine candidates. The majority of EDCTP's investment portfolio is focused on the TB field and the partnership is open to discuss on how to bring the whole TB vaccine field forward.

Global Fund and GAVI are supportive of TB vaccine development with high public health impact, including the current candidate under discussion, and look forward to engaging at later stages of product development, in keeping with their institutional mandates.

UNITAID's mandate is focused on investing on late stage innovations to overcome access barriers and pave the way for scalability. It notes with interest the potential of the M72 vaccine's impact on the TB epidemic and will continue following up on its development with a view to engage during advanced stages of product development.

US-NIH NIAID supports ongoing discussions on further research on M72 and is open to potential collaborations as research goes forward (Phase II and III), assuming the efficacy results hold in the final analysis of the phase IIb trial and the development path through delivery can be mapped. US-NIH uses specific grant/contract mechanisms for funding, to which collaborative initiatives will need be aligned. Additionally, NIAID supports well-established clinical trial infrastructure with experience in HIV clinical research, which has expanded to TB research.It may be possible to engage these networks to help move M72 clinical development forward. It is important to consider as early as possible how M72 can be developed for PLHIV, for example in Phase II efficacy trials, to move the agenda forward in an inclusive manner. This can also be facilitated through NIH's clinical trial infrastructure but will require advanced planning for site selection according to target disease epidemiology and capacity. US-NIH is also in discussion with IAVI and Gates Foundation to move the TB vaccine immune correlates work related to M72 forward.

USAID will have a role in supporting implementation and

scale-up of products post licensure. At this early stage, small funding is usually available to support clinical trial site preparation and capacity building, epidemiological studies, and procurement of small equipments to assist with trial preparation.

PATH encouraged participants to support a consortium model (that may evolve overtime) to drive M72 development, with clarity and transparency on the roles and responsibilities of each partner. Sustainable and long-term commitment is key to distribute risk and facilitate decision making. WHO should support discussion around regulatory and financing pathways, as well as scientific discussions on next steps, in a manner that can eliminate the need for pilot implementation programme from the vaccine development and introduction pathway.

IAVI reiterated that a public-private partnership (consortium model with multiple partners) is key to take this product forward. Alignment among public, philanthropic and private sectors is key to facilitate a clear end-to-end process, responsive to county demand and needs, and such alignment can only be achieved in a consortium model where there is a transparent flow of information.

TBVI supported IAVI's remarks and added that examples of such collaborative partnerships exist in European TB vaccine development partnerships, which can serve as examples/models. TBVI can also support ongoing and future biomarker/correlate studies.

Wellcome Trust is committed to work in partnership with others to support this going forward: the M72 agenda fits well with Wellcome's current priority on vaccine and drug-resistant infection research. Wellcome also has clinical trial sites in different parts of the world and can also support additional sites where the target disease epidemiology is present, in partnership with other institutions. In addition, further discussion of this topic should take place with heads of international research organizations, including high TB burden countries, in 2020 to keep the momentum going.

Conclusions and way forward

At the conclusion of the meeting, the Chair presented a brief summary of the day. All participants agreed that the meeting was productive and agreed to continue engaging in further discussions. As a next step, it was suggested that WHO would establish and convene a working group (s) as soon as possible, to support the development of the M72 vaccine, in a manner that boosts the overall TB vaccine agenda. Priorities for such working group(s)* include to

- define priority evidence that needs to be collected for regulatory and policy decision making, with a view to inform future clinical development plans and study designs;
- provide guidance on robust, efficient and well-structured clinical trial designs that facilitate regulatory, clinical and health policy decision making;
- foster functional collaborative platforms that can help implement the required next steps of product development, with an end-to-end perspective. This will require input and contribution from scientists, civil society, research institutions, countries, regulators, funders and other relevant stakeholders in the private, public and philanthropic sectors, also taking account of relevant activities and strategic value added by exisiting working groups on new TB vaccines;
- promote the development of innovative financing models; and,
- develop an overall public health value assessment of new TB vaccines, to support decision making by various stakeholders in the R&D cycle.

**The WHO Secretariat will work with/support partners and institutions that have effective systems already in place to make progress on these action points.*

Dr. Kasaeva (WHO/Director/ Global TB Programme), Dr. Kate O'Brien (WHO/Director/ Department of Immunization, Vaccines and Biologicals), and Dr. Soumya Swaminatan (WHO/Chief Scientist) thanked the participants and emphasized WHO's commitment and support to the TB vaccine field. The Chair closed the meeting at 5:15 PM.