

WHO Research and Development Blueprint

Evaluation of ideas for potential platforms to support development and production of health technologies for priority infectious diseases with epidemic potential

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Abbreviations & acronyms

ADEPT	Accelerated Defense against Emerging Pathogen Threats
ADP	Advanced Development Partnership
BNITM	Bernhard-Nocht-Institut für Tropenmedizin
BPO	biopreparedness organisation
BV	Bavarian Nordic A/S
CCHF	Crimean-Congo haemorrhagic fever
CE-IVD	in vitro diagnostics (CE-mark is a requirement for selling medical products and equipment in the EU)
CEPI	Coalition for Epidemic Preparedness Innovation
ChAd3	chimpanzee-based adenovirus vaccine type 3
DPP	Diagnostic Preparedness Platform
DZIF	German Centre for Infection Research
EID	epidemic-prone infectious disease
EUA	emergency use authorization
EUAL	Emergency Use Assessment and Listing Procedure
EVD	Ebola virus disease
FDA	U.S. Food and Drug Administration
GMP	good manufacturing practice
GSK	GlaxoSmithKline
INMI	Istituto Nazionale per le Malattie Infettive “Lazzaro Spallanzani”
IP	intellectual property
LICs	low-income countries
LMICs	low-middle income countries
MCMs	medical countermeasures
M&E	monitoring and evaluation
MoU	memorandum of understanding
MSF	Médecins Sans Frontières
MVA	modified vaccinia ankara
MVA-PP	modified vaccinia ankara Platform Partnership
NRAs	national regulatory authorities
PCR	polymerase chain reaction
PHE	Public Health England
POC	point-of-care
PQ	pre-qualification
RDT	rapid diagnostic test
R&D	research and development
RT-	real-time
USAMRIID	US Army Medical Research Institute of Infectious Diseases
VHF	viral haemorrhagic fever
VLP	virus like particle
WHO	World Health Organization

Executive Summary

On 21 July 2016, a 2nd Technical Workshop on R&D platform technologies was convened at the World Health Organization (WHO) headquarters in Geneva with the goal of presenting the 6 most meritorious proposals emerging from the **WHO public consultation¹ on platform technologies**, for consideration by interested WHO Member States and relevant R&D funders.

Launched by WHO in October 2015, this public consultation is one activity within the **WHO Research and Development (R&D) Blueprint²**, a global effort pioneered by WHO to increase R&D preparedness for future epidemics.

The focus of this 2nd technical workshop was on having concise technical presentations of the six final proposals while fostering an enabling environment for bilateral and/or multilateral discussions around potential future collaborations and/or support, between proponents and interested WHO members states and other organizations which fund R&D.

After a brief overview of the WHO R&D Blueprint, information was provided on the **Coalition for Epidemic Preparedness Innovation (CEPI)**; and following a summary of the public consultation process since its launch, the six finalists (3 vaccines, 1 diagnostics, 1 immunotherapy, 1 covering all product streams) presented their ideas in **open sessions**.

The groups presented to the Advisory Group, the WHO Secretariat, interested **member states³** (representatives of the Permanent Missions of Colombia, Germany, India, Korea, Norway, The Netherlands and The United Kingdom of Great Britain and Northern Ireland were present at the meeting), **potential funders** (CEPI and Wellcome Trust) and **other observers** (Médecins Sans Frontières - MSF). Each presentation was followed by a brief summary of the feedback given by the Advisory Group during their review process, and by an open discussion with participants.

The topics covered during the workshop included:

- Long term affordability, global access and intellectual property of proposed platform technologies
- Data transparency, social responsibility and the feasibility of the “no profit/ no loss” principle for the selected platforms and meaningful participation by entities in LMICs
- Linkages with other platforms technologies and availability to collaborate using technologies owned by another party
- Projected costs
- Engagement of the regulators and the role of WHO in the area of national regulatory authorities support
- Alignment of CEPI with the WHO Blueprint

The principle of “no profit/ no loss” and social responsibility and the subsequent approach of offering products at no cost to populations in need was agreed to be guiding the philosophy of the majority of the presenting groups, with the exception of those entities which, due to their structure and turnover, pointed to the fact that they needed to balance this principle with the requirement to be a sustainable and profitable business. As a follow-up to the process, WHO proactively engaged potential funders in order to advance funding for the most promising ideas.

¹ http://www.who.int/medicines/ebola-treatment/public_consult_platform-tech/en/

² <http://www.who.int/csr/research-and-development/en/>

³ 16 Permanent Missions to the UN in Geneva were invited to the workshop: Argentina, Brazil, China, Colombia, France, Germany, India, Japan, Kingdom of Saudi Arabia, Norway, Republic of Korea, Russian Federation, South Africa, Switzerland, Thailand, The Netherlands.

Introduction: public consultation on platform technologies

Background

Current, market-driven models of medical R&D do not cater for the development of medical technologies for diseases that are sporadic or unpredictable, especially when they occur in countries with low investment in health infrastructure and delivery. The challenge becomes even greater when faced with a wholly new disease such as SARS, MERS and Nipah virus infection, which are just three examples of diseases that have emerged at the human-animal interface in the last two decades. The international community needs to invest to improve our ability to respond to new threats and to prepare itself with a novel R&D paradigm to address future epidemics.

The World Health Organization (WHO) invited ideas through a public consultation process on how to improve research and development readiness against priority infectious disease threats through establishment of a set of technology development and production platforms.

Proposals were requested for flexible development and production platform technologies to manufacture candidate products for evaluation in Phase 1 clinical trials before any confirmed epidemic threat, as well as for Phase 2 and 3 clinical evaluations during a potential epidemic. The scope of health products which was considered included vaccines, therapeutics (drugs and blood products), and diagnostics against priority pathogens, defined by WHO.

WHO stipulated that candidate products developed through this mechanism and that were found to have a favourable benefit-risk profile should be available in sufficient quantity to enable potential use in disease control efforts. Therefore the proposals were requested to go beyond preparing materials for Phase 1 clinical studies only, and to include strategies to assure readiness for production at an appropriate scale to contribute to epidemic control.

Candidate products developed through this process should be affordable for use in populations in which they are tested and/or needed. The priority pathogens may affect any country but options to address affordability in low and middle income countries (LMICs) needed to be included in each proposal.

The manufacturing process must be capable of meeting WHO norms and standards, where they exist, and WHO-requirements for emergency listing of a product or, where appropriate, prequalification. Proposals that would result in a strategic geographic distribution of platform production sites, in countries with oversight by a WHO-recognized National Regulatory Authority, were especially welcomed.

Proposals received were evaluated in a first round by a panel of experts convened by the WHO. Successful Round 1 applicants were invited to develop in Round 2 an operational and costed plan, with agreed milestones. WHO reserved the right to suggest the grouping of complementary proposals into a larger collaborative project. Round 2 plans were likewise evaluated by a panel of experts, and the best proposals were presented to potential funders and interested Member States for their consideration during the 21 July meeting.

The public consultation on platform ideas did not result in funds being awarded. Rather, it enabled a selection of appropriate proposals to be presented to potential funders for decision-making. Proposers were therefore expected to include a justified budget needed to operationalize the plans contained in the proposal. The proposals needed also to explain what internal resources would be used and what external funding would be required to implement the platform concepts being proposed.

A key goal of the process was to encourage the development of options that include meaningful participation by entities in LMICs. The strength of the collaborations included in the application was one of the evaluation parameters. The scope of the collaborations was not pre-specified by WHO, but creative ideas were welcomed.

Session 1: CONTEXT

A research and development Blueprint for action to prevent epidemics

Dr Marie-Paule Kieny, Assistant Director-General, Health Systems and Innovation, WHO HQ, Geneva Switzerland. [presentation available electronically]

At the request of its **194 Member States in May 2015**, WHO has convened a broad global coalition of experts to develop a blueprint and a platform for accelerated R&D for infectious diseases for which few medical countermeasures currently exist⁴. WHO experts teams, an international Scientific Advisory Group and partners engaged through global forums have been collaborating to formulate this novel R&D model.

The **R&D Blueprint** is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crisis. With WHO as convener, the broad global coalition of experts who have contributed to the Blueprint come from several medical, scientific and regulatory backgrounds. WHO Member States welcomed the development of the Blueprint at the **World Health Assembly in May 2016**.

The vision the Blueprint is a world in which our R&D response to PHEIC⁵ caused by emerging pathogens is faster and more effective than ever before and in which the global community is able to ensure a continuous effort aiming not only to accelerate the results of research but also to adapt to the scientific, logistical and social challenges that are specific to epidemics.

The West Africa Ebola epidemic saw the mobilization of numerous actors globally to find medical technologies to address the disease and save lives. Some of those efforts brought results, such as the VSV-EBOV vaccine, which so far has shown to be highly effective, while on the other hand large gaps were apparent in the way the global scientific and R&D community organises itself during an epidemic. The Blueprint coalition has considered those lessons gained and has developed a plan that leverages the successes and addresses the gaps so that next time the world can be prepared.

Four principles have guided the elaboration of the Blueprint plan:

1	2	3	4
An inclusive process with a clear mandate and defined milestones	Building on the efforts of others in the community	A collaborative effort with the Member States in the affected countries at its core	Driven by scientific knowledge

The Blueprint is both a convening mechanism and an instrument to articulate technical guidance for R&D preparedness, especially in the area of coordination (e.g. avoiding unnecessary duplication, addressing priorities), which can be implemented effectively through appropriate incentives and other measures.

In parallel to the Emergency Response Reform, WHO aims to develop innovative ways of promoting R&D preparedness for priority pathogens with a focus on LMICs. The R&D Blueprint seeks to create an enabling environment through which the R&D community, through increased funding, data sharing and partnerships, can drive change in the public health landscape to provide an elevated level of global impact.

⁴ For further details please visit <http://www.who.int/csr/research-and-development/blueprint/en/>

⁵ Public Health Emergency of International Concern (PHEIC)

Figure one shows the **three approaches** that are currently being used to improve preparedness under the R&D Blueprint. These 3 approaches are aligned with the lessons learned during the 2014–2016 Ebola epidemic and the recommendations of the various reviews on the Ebola epidemic conducted to date.

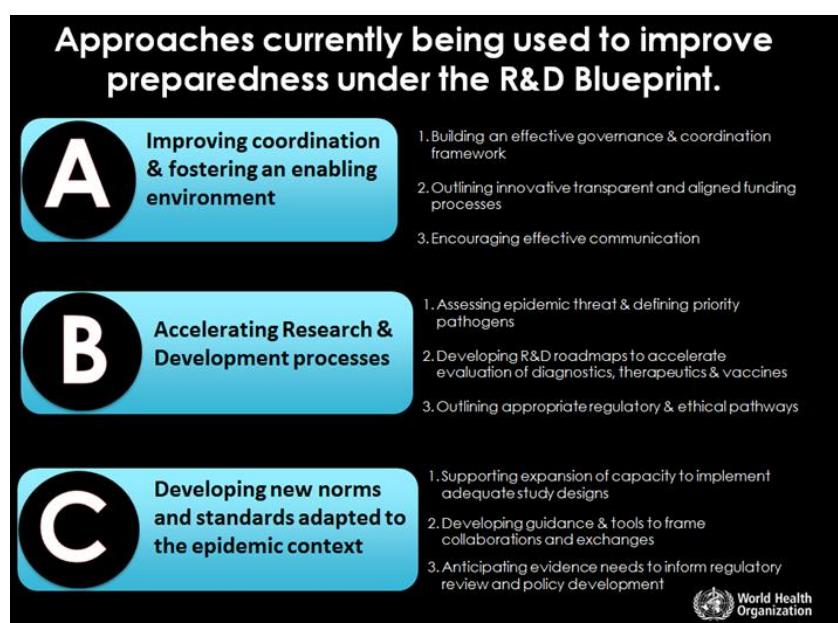


Figure 1 Approaches currently being used to improve preparedness under the R&D Blueprint

The first Blueprint **Deliverables**⁶ were described in the areas of:

- Prioritization of key pathogens
- Building an effective governance and coordination framework
- Increasing investment into R&D
- Data sharing
- Development of R&D Roadmaps for priority pathogens
- Monitoring and evaluation
- Platform Technologies

A number of new initiatives have been put in place or are under discussion by international stakeholders to increase R&D preparedness for severe and emerging infectious disease threats. These could complement the efforts of the Blueprint in ensuring coordination and alignment of efforts. One example of such initiatives is the **Coalition for Epidemic Preparedness Innovation (CEPI)**.

⁶ For further information on the Blueprint deliverables please consult the “AN R&D BLUEPRINT FOR ACTION TO PREVENT EPIDEMICS, Action Plan May 2016” available at http://www.who.int/csr/research-and-development/WHO-R_D-Final10.pdf?ua=1

The Coalition for Epidemic Preparedness Innovations (CEPI): an overview

Dr John-Arne Røttingen, Interim CEO, CEPI and Executive Director Infection Control and Environmental Health Norwegian Institute of Public Health, Oslo, Norway. [presentation available electronically]

The Coalition for Epidemic Preparedness Innovations (CEPI) is an initiative established following the Annual Meeting of the World Economic Forum in Davos in January 2016, where stakeholders from governments, foundations, industry and civil society discussed the urgent need for new and sustainable partnership models for product development (vaccines, diagnostics therapeutics) to contain outbreaks of emerging and epidemic-prone infectious disease (EID).

The Davos meeting reached a consensus that new mechanisms are required to finance and otherwise support vaccine development in cases of market failure, and that a partnership linking different sectors would be the best approach to delivering this. Recent outbreaks revealed gaps that such partnership should fill.

A process to create such a partnership is now underway (CEPI preparatory Phase: January-June 2016; CEPI start-up phase June 2016- December 2017), with an adopted interim entity, CEO and secretariat; a finalized strategic plan; established cross task teams to consider issues such as prioritisation, clinical development, manufacturing capacity and regulation, potential models for partnership, and potential innovative financing arrangements; and nominated candidates for interim Board of Directors and Scientific Advisory Committee. CEPI will operate according to the principles of no loss, shared benefits and equitable access with the following objectives: preparedness; response speed; “market” security; and equity.

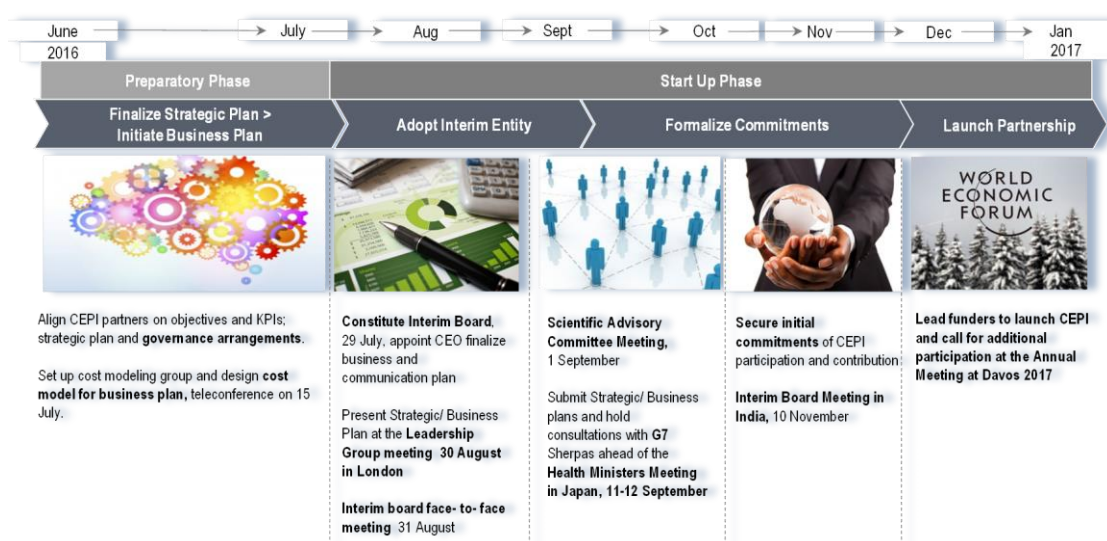


Figure 2 CEPI preparatory and start up phases

CEPI envisions a comprehensive policy ecosystem where epidemic outbreaks of infectious diseases will be managed at an early stage to prevent them from becoming public health emergencies that result in loss of life, undermine social and economic development and emerge into humanitarian crises.

An end-to-end approach to vaccine development to application, the CEPI initiative is separate from but intends to be complementary to the WHO-led process to develop the R&D Blueprint, and both CEPI stakeholders and WHO are taking steps to ensure the two are properly aligned (an memorandum of understanding (MoU) is currently in development between CEPI and WHO). CEPI will rely on WHO as the global normative lead agency in health and collaborate with it to respond to vaccine R&D needs for emerging infectious diseases, ensuring that the developed vaccines will be available to all in need, in order to achieve the highest possible public health impact; to focus on diseases on which the market fails to provide adequate incentives; and to strategically leverage the existing diverse set of national and

international mechanisms that support vaccine R&D, avoid duplication, and maximize synergies essential gaps in product development due to market failure.

The initial focus will be to move new vaccines through development from preclinical to proof of principle in humans and the development of platforms that can be used for rapid vaccine development against unknown pathogens. If successful the model could be extended to cover drugs, diagnostics or other products.

WHO Public Consultation on Platform Technologies: context and objective of the workshop

Dr David Wood, Coordinator, Technologies Standards and Norms, Essential Medicines and Health Products, Health Systems and Innovation, WHO HQ, Geneva, Switzerland. [presentation available electronically]

An efficient and effective research response during an infectious disease epidemic requires preparedness – work done between epidemics to fill knowledge gaps, identify potentially useful candidate medical products and other interventions, and to ensure the timely availability of such when the next epidemic occurs.

The epidemic of Ebola Virus Disease (EVD) in West Africa showed that the world is unable to develop effective interventions in a timely manner for control of severe emerging infectious diseases using current R&D approaches to vaccine, drug and diagnostics development.

Launched in October 2015, as one of the activities within the WHO R&D Blueprint, this public consultation, open to non-profit organizations, for-profit companies, international organizations, government agencies and academic institutions, solicited ideas for platform technology solutions that are sufficiently flexible to develop and manufacture candidate products for clinical trials in a timely manner (months rather than years) against a variety of infectious disease threats. The scope of health products considered included vaccines, therapeutics (drugs and blood products), diagnostics and enabling technologies. The platforms had to be targeted against three or more of the priority pathogens defined through the R&D Blueprint process.

Candidate products developed through this process should be affordable for use in populations in which they are tested and/or needed. The priority pathogens may affect any country but options to address affordability in low and middle income countries (LMICs) needed to be included in each proposal. The submissions needed also to explain how intellectual property (IP) issues will be managed to ensure fair and equitable access, especially for LMICs, to any product(s) developed through the proposed platform(s). Additionally, candidate products developed through this mechanism and that are found to have a favourable benefit-risk profile should be available in sufficient quantity to enable potential use in disease control efforts. Therefore submissions needed to include strategies to assure readiness for production at an appropriate scale to contribute to epidemic control.

By the closing date in February 2016 **35 responses** were received. After an initial screening by the WHO Secretariat to determine if the submissions were within the scope, **33 ideas were selected** addressing: vaccines (8); monoclonal antibodies (2); polyclonal immunoglobulin (3); antiviral (1); diagnostics (8); two or more product streams (4); and enabling technologies (7). Submissions that were out of scope were removed from further consideration and the applicant(s) informed.

Reviews of the 33 submissions that were within scope (Annex 1) were conducted by an **ad hoc Advisory Group** (AG, Annex 2), convened specifically by WHO.

The reviews were informed by a **3-day technical workshop, in Geneva, April 4-6 2016**, at which the ideas were presented. Based on this review and on ad hoc teleconferences of the Advisory Group, **13 proponents** were invited to submit more detailed proposals for a second round of review.

PLATFORM TECHNOLOGIES*	Accepted for round 2	Not accepted for round 2
2 or more product streams	1	4
Vaccines	4	4
Monoclonal antibodies		2
Polyclonal immunoglobulin	1	2
Antivirals		1
Diagnostics	5	3
Enabling technologies	2	4

Round 2 submission were also evaluated by the Advisory Group which met by teleconference for initial discussions and identified the **six most meritorious proposals** (3 vaccines, 1 diagnostics, 1 immunotherapy, 1 covering all product streams) to be presented to potential funders and interested Member States during the 2nd technical workshop.

The purpose of this workshop was twofold:

- to have concise technical presentations of the six final proposals for consideration by interested Member States and relevant R&D funders, and
- to create an enabling environment for bilateral and/or multilateral discussions around potential future collaborations, or support, as appropriate.

A timeline of the selection process, an explanation of the scoring systems used by WHO to make decisions on the projects that were submitted and the criteria that informed it, are summarized in Annexes 2 and 3.

Session 2: PRESENTATIONS

Improving R&D readiness for priority infectious disease threats through the development and utilisation of vaccine platform technologies

Lead Institution: GlaxoSmithKline, LLC

Dr Moncef Slaoui, Chairman of Vaccines, GlaxoSmithKline, Philadelphia, USA. [presentation available electronically]

Recent epidemics and threats provoked emergency actions and accelerated responses from many stakeholders, often in an uncoordinated way. This situation is both sub-optimal and unstable. An alternative strategic “ready to run” approach, based on proactive preparedness, would allow timely readiness when a threat materialises and facilitate management of the financial uncertainty associated with an ‘emergency response’.

GSK proposes to create a dedicated Biopreparedness Organisation (BPO) to improve R&D readiness for priority infectious disease threats that lack market incentives through the development and utilisation of vaccine platform technologies. The BPO will develop and manufacture vaccines to anticipate and improve preparedness for global health threats, including pandemics and epidemics. Such threats primarily impact developing countries, but also create financial and security challenges for developed nations. The BPO could make a practical and sustainable contribution to global health security by delivering a rapid, predictable, and high quality way to enable quick provision of needed global preparedness vaccines.

GSK has developed the concept of a dedicated, permanent BPO to continuously design and develop vaccines against previously identified and newly occurring pathogens that present a threat to global health without traditional market incentives. The BPO would operate alongside already established approaches and organisations focused on biopreparedness. However, it would differentiate itself in a number of ways. First, it would be permanent and proactive, ensuring a state of readiness to respond. Second, it would be fully embedded in an established, highly-experienced vaccine R&D organisation, to ensure that the BPO stays at the cutting-edge of production know-how and platform technology, and employs methodologies with a high likelihood of successful scale-up and acceptance by regulators. Third, it would offer a fully integrated, end-to-end approach, from vaccine design to a clinically evaluated vaccine and readiness for mass manufacturing.

By continuously and proactively developing needed vaccines and shifting to crisis response as required, the BPO would provide a fast, flexible, predictable, and high - quality approach to the challenges of global preparedness. For this purpose, GSK would make its proprietary technologies [adjuvant recombinant proteins; live-attenuated viral vectors; self-amplifying mRNA (SAM); chemical conjugation; and bio conjugation technology] available to the BPO. If so required, the BPO would also consider producing candidate vaccines based on technologies that GSK does not own (e.g. Recombinant Measles vector, MVA, VSV). It is the primary intent of the BPO to develop vaccines up to the point of clinical proof of concept with a 200,000 to 3 million - dose vaccine stockpile. Once a vaccine is developed to the point of clinical proof of concept and dose selection, decisions can be made, depending on the urgency of the threat, to either suspend the clinical development or, at the other extreme, to deploy vaccine and/or to progress to full approval by regulators with manufacturing from one or more permanent manufacturing sites outside the BPO. The BPO could transfer the technology to facilities around the world, including developing countries, to allow for expanded production.

GSK does not seek a return, nor would the company incur costs related to the BPO. GSK wants to work with a limited number of governments and other agencies to secure the funding required allowing the BPO to advance. Based on the assumption that the BPO will deliver two vaccine programmes on an ongoing basis, GSK estimates standing maintenance and operating costs at approximately \$55m per annum over the initial 7 years.

WHO R&D Blueprint: Janssen Vaccines – Jenner Institute complementary Vaccines Platform Technologies

Lead Institution(s): Janssen Vaccines & Prevention B.V. ("Janssen Vaccines" or "Janssen") and Jenner Institute, University of Oxford

Dr Olga Popova, Vice President Global Vaccine Policy & Partnership, and Dr Jerome Custer, SR. Scientific Director, Janssen Vaccines & Prevention B.V., Leiden, The Netherlands.

Professor Sarah Gilbert, Professor of Vaccinology and Head of Influenza Vaccine Development, The Jenner Institute, Oxford, UK. [presentation available electronically]

Janssen Vaccines (an affiliate of Johnson & Johnson) and the Jenner Institute of Oxford University achieved Phase I selection by the WHO R&D Blueprint to address future emergencies via priority disease vaccine development. WHO Scientific Advisory Group found these applications complementary and both organizations were approved to proceed into phase II of the public consultation for potential funding, subject to the single joint submission - through leveraging respective strengths and capabilities: Jenner Institute's established platforms of adenoviral vectors and Modified Vaccinia vectors, research laboratory capabilities, rapid transfer of candidate vaccines into GMP manufacturing and human studies – coupled with Janssen leveraging its own adenovirus, protein and inactivated vaccines know-how together with PER.C6® mammalian cell culture vaccine manufacturing platform technology for large scale high yield production.

Oxford University and Janssen already partnered on Ebola vaccine development over the last two years in both first-in-human phase I and phase II clinical trials, and share a strong commitment to addressing emerging epidemic diseases.

The Jenner Institute and Janssen Vaccines have a wide range of vaccine technologies to offer for rapid development of vaccines to be deployed in an emergency response setting. Key attributes for use in an emergency situation are rapid scale up of manufacturing capacity and formulations compatible with facilitated storage, stockpiling and vaccine use in remote areas. Vaccine technologies available to us include the human cell line PER.C6® for manufacturing of biologics like inactivated virus vaccines, recombinant proteins, attenuated viruses and adenoviral vectors. The Jenner Institute and Janssen Vaccines jointly have access to a panel of distinct adenoviral vectors for development of different vector based vaccines. In addition Modified Vaccinia viral vector technology and Virus Like Particle (VLP) antigen delivery systems are available.

The vaccine platforms proposed have been progressed and tested in early clinical trials and have shown to be fit for purpose and feasible in terms of manufacturing, scalability and deployment.

While it is too early to define specific governance details, potential Blueprint programs / projects can be covered by collaborative agreements outlining each partner's individual contributions. The structure, governance and management of the potential R&D Blueprint collaboration between Janssen and Jenner Institute and beyond, as well as the geographic distribution of the particular programs, would be driven by the program selected and disease prevalence.

The two applicants would be prepared to identify and leverage, as relevant, the respective internal organizational support functions and experience in their many different types of arrangements to implement appropriate structures for beneficial collaborations. The stringent deadline for phase II application does not allow for establishment of meaningful collaborative framework, so the proposal is therefore made "bona fide", to be further developed.

The estimated average running cost would amount to \$48m per annum (with estimated joint base – fixed- costs of \$18.5m/year), with a total of \$240m for a 5 year period.

MVA Platform Partnership

Lead Institution: Bavarian Nordic A/S

Participating Institutions: German Centre for Infection Research (DZIF); Public Health England (PHE)

Dr David Noll, Director, Governmental Affairs at Bavarian Nordic A/S, Washington, US; Prof. Dr. Gerd Sutter and Prof. Dr. Stephan Becker, German Centre for Infection Research (DZIF), Germany.

[presentation available electronically]

The German Centre for Infection Research (DZIF), Public Health England (PHE) and Bavarian Nordic (BN) proposed the formation of a public-private partnership with the mission of rapidly advancing the development of MVA-vectored vaccines against key WHO priority pathogens.

The MVA Platform Partnership (MVA-PP) would advance a portfolio of MVA-based vaccines including both on-going and new preclinical and clinical programs. In general, the MVA-PP would combine the disease expertise, preclinical vaccine development infrastructure and animal testing capabilities of DZIF and PHE, with the advanced development and manufacturing capabilities of BN.

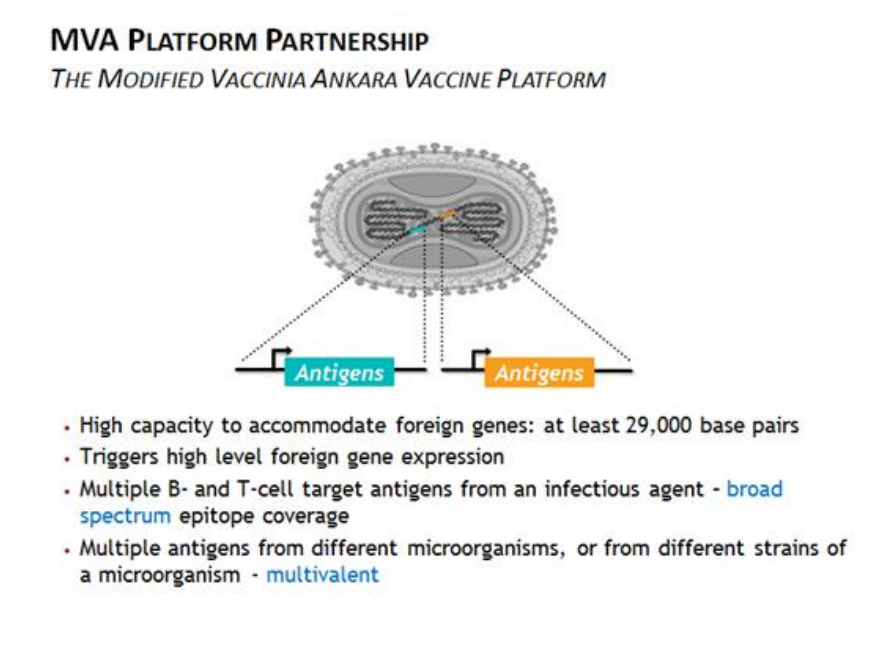
Clinical evaluation of vaccine candidates developed under the MVA-PP would leverage DZIF infrastructure and their existing relationships with partner sites in Africa.

The MVA-PP would utilize the MVA-BN vaccine platform as a “plug-and-play” technology to rapidly and reliably produce vaccines for known and unknown infectious diseases.

The MVA-PP would design, generate and initiate clinical evaluation of multiple MVA-BN-based vaccine candidates for six WHO priority pathogens. Development activities include vaccine design, generation and manufacturing (research grade, clinical trial material and a mixed stockpile of BDS and FDP), assay development to support clinical studies, preclinical studies in appropriate animal models and all necessary testing and regulatory submissions to initiate and perform a Phase 1 clinical trial.

The MVA-PP estimates that approximately €13m would be required to transition a single candidate MVA-BN-based vaccine from concept to stockpiling. By leveraging existing funding, the MVA-PP anticipates that €60m would be required to operationalize the plans contained in the proposal and produce stockpiled vaccines for five of the WHO Priority Pathogens over a 7 year period.

Figure 3 MVA Platform Partnership



Diagnostic Preparedness Platform

Lead institution(s): Altona Diagnostics GmbH / Alere Inc.

Dr Hans Khun, Finance & Administration, and Dr. Stephan Ölschläger, Scientist, Research and Development, Altona Diagnostics GmbH, Hamburg, Germany; Dr John Glenn, Director, Global Health Diagnostics R&D Alere, Inc., San Diego CA, US. [presentation available electronically]

The partners of the Diagnostic Preparedness Platform (DPP) would develop and manufacture diagnostic assay panels each comprised of pathogens with similar clinical presentation, and collectively covering each of the WHO priority pathogens.

Technology platforms that could be exploited to detect the pathogens of interest are 1) nucleic acids tests in a central laboratory format; 2) high-throughput testing by use of the automated workflow solution based on real-time (RT-) PCR assays; 3) nucleic acid detection at the Point-of-Care (POC) in cartridges; and 4) a lateral-flow rapid diagnostic immunoassay format (RDT).

The initially proposed panels would be a viral hemorrhagic fever panel including Ebola- and Marburg virus, Lassa virus, Rift Valley fever virus, and CCHF virus; a respiratory panel including MERS-CoV and SARS-CoV; and an encephalitis panel including Nipah virus, Japanese encephalitis virus, Enterovirus, rabies virus, and measles virus. Given the epidemiology and co-endemic distribution of these priority pathogens, more comprehensive panels could be considered such as a combined VHF panel with Zika virus, Chikungunya virus, and dengue virus, as well as malaria parasites.

The DPP is based on an existing collaboration between Alere and Altona along with scientific and clinical partners (BNITM, Germany; PHE, UK; INMI, Italy; and FIND, Switzerland). This collaboration has already demonstrated the feasibility of transferring real-time (RT-) PCR assay for filoviruses into cartridges. This POC system for filoviruses is currently under clinical validation and will be submitted for FDA EUA, WHO EUL and CE-IVD and would form the basis for a transfer into cartridges. Many of Altona's assays already have CE-IVD, FDA EUA, and WHO EUL. Additionally, where it's applicable such as for remote screening and triage, Alere could also leverage its capabilities in lateral flow testing.

The project goals are for assays and panels to be developed and validated by determining analytical performance characteristics and, where relevant, submitted for regulatory approvals in advance of potential disease outbreaks. This will allow much faster deployment and a more efficient response to directly support timely research, clinical diagnosis, and public health interventions in the event of an outbreak. To this end, the project partners have proven track records in the fast ramp-up of production capacity in order to supply increasing demand with a short turnaround time. If successful, Altona Diagnostics and Alere would execute an agreement to formalize their relationship, and delivery on the agreed project goals will ultimately be their responsibility. However, a network of external collaborators would also play vital roles in developing user specifications, product profiles, prototype testing, verification and validation testing, and generating field data.

Since the WHO priority pathogens potentially impact LMIC, the partners would utilize existing networks and seek to expand networking opportunities with leading scientific and public health institutions in these countries for joint validation work and deployment strategies for the project's diagnostic systems. Based on their experience with similar projects, they anticipate development and validation costs of approximately \$2-2.5m per assay panel per molecular POC or centralized test, and similarly approximately \$1.5m per product panel on the lateral-flow RDT platform. An additional \$0.5-1m would be required for clinical evaluation and field testing per panel or RDT. Depending on the complexity of the respective assay panels, and the amount of development work already done, the partnership aims for the availability of products within a 12-18 month time frame per panel or RDT.

Accelerated Defense against Emerging Pathogen Threats (ADEPT)

Lead Institution: The Geneva Foundation

Participating Institutions: US Army Medical Research Institute of Infectious Diseases (USAMRIID)

Dr Gustavo Palacios, Director of the Center for Genomic Sciences (CGS), US Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, Maryland, US. [presentation available electronically]

The Geneva Foundation together with the US Army Medical Research Institute of Infectious Diseases (USAMRIID) proposed to create the Accelerated Defense against Emerging Pathogen Threats (ADEPT) platform, which is designed to provide a logical and effective plan for developing MCMs for both known and novel threats.

ADEPT is an “R&D toolbox” comprised of parallel programs that will converge to generate candidate MCMs ready for clinical trials within 12 months of implementation. The ADEPT platform would be fully integrated and completely open access, in order to maximize resources and expedite research while assuring that the data generated is available in real time to the entire research community.

The ADEPT platform would encompass numerous approaches and technologies that can be quickly adapted to generate candidate products in sufficient quantities to enable use in outbreak conditions. The modular framework of ADEPT could be immediately applied to known agents, including emerging diseases likely to cause major epidemics, such as those identified by WHO, for which some of the knowledge gaps are already filled. Importantly, ADEPT could be maintained in “standby” mode, where only table-top and wet-lab exercises are performed until WHO becomes concerned with an outbreak situation and activate the ADEPT platform. Such exercises would not only ensure the readiness of ADEPT for responding to known agents, but would also establish roadmaps that could be applied to the development of MCMs for future unknown pathogens.

The cost of ADEPT in “standby” mode is anticipated to be ~\$3m per annum; while the cost of the activation mode would depend on the type of outbreak involved: a worst case scenario of an outbreak including a completely uncharacterized novel agent is anticipated to be ~\$30m per annum.

Although ADEPT is focused on viral pathogens, it would be possible to adapt this model for other types of pathogens if needed. The key parallel R&D components within ADEPT are: identifying and characterizing the known or novel pathogen; developing a suitable animal model to assess MCMs; determining gene sequences for use in molecular vaccine technologies; providing an isolate of the pathogen for testing MCMs; developing and validating tailored molecular and serological diagnostic tools; activating a biopharmaceutical approach to identify small molecule therapeutic candidates; characterizing the immune B cell repertoire from survivors and resistant individuals for immune therapy or prophylaxis; and, obtaining clinical bio-samples to facilitate plasmapheresis and future human clinical trials.

Targeted Human Immunoglobulin to WHO Priority Pathogens Using Transchromosomal (Tc) Bovine

Lead institution: SAB Biotherapeutics Inc.

Participating Institutions: LFB (France), Novavax, Inc. (USA), United States Naval Medical Research Center, (USA); CSIRO Health and Biosecurity Australian Animal Health Laboratory, Australia.

Dr Eddie J. Sullivan, President, CEO and Co-Founder, SAB Biotherapeutics Inc., Sioux Falls, SD, US. [presentation available electronically]

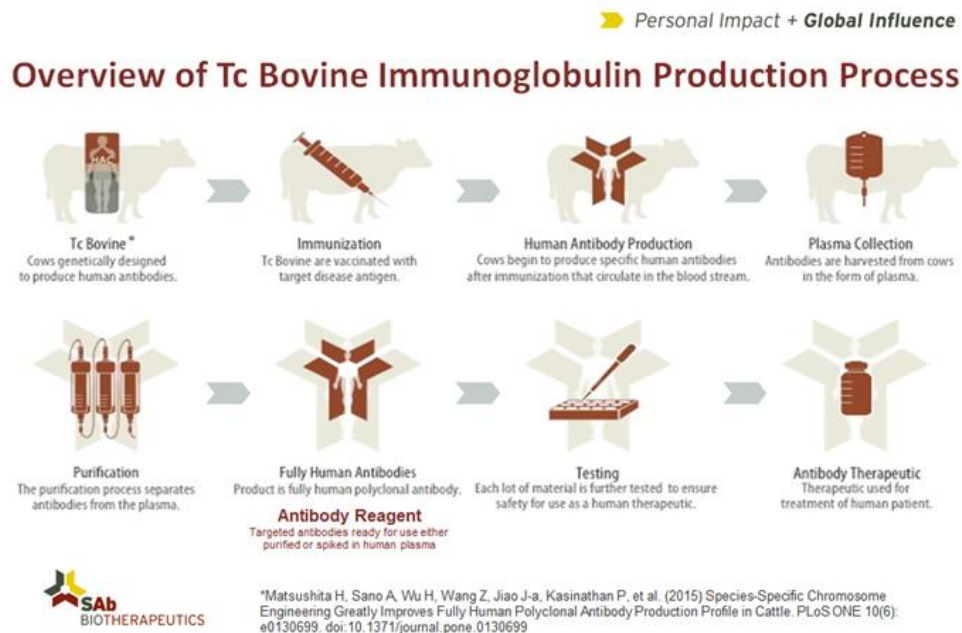
This proposal aimed to fill the need for effective therapeutics by utilizing the unique transchromosomal (Tc) bovine platform to rapidly produce potent, fully human immunoglobulins against a variety of disease targets, including viruses, bacteria, and toxins, in significant quantities (up to 600g/month/animal of highly purified immunoglobulin).

Targeted human polyclonal immunoglobulins produced in the Tc bovine platform would allow for rapid development for new products and provides an approach that is quickly scalable to be an effective global response.

Using the Tc Bovine system, SAB Biotherapeutics Inc. proposed to rapidly respond to WHO priority pathogens and to emerging infectious disease by increasing their response capability, maintaining a herd of Tc animals to be readily available for an outbreak, and to utilize the Tc bovine to quickly develop, test, and manufacture product.

Overall, the proposal would be completed at cost by the collaboration. The estimated average cost of the project would amount to \$~39m over a 2 year period.

Figure 4 Overview of Tc Bovine Immunoglobulin Production Process



Ad hoc Advisory Group's high level feedback on the 6 finalists

Improving R&D readiness for priority infectious disease threats through the development and utilisation of vaccine platform technologies

Lead Institution: GlaxoSmithKline, LLC

- Considered as the most promising platform among those presented;
- A robust proposal with five platforms to offer against all the priority pathogens, capable of integrating across several other streams and with a plan of active participation of LMICs;
- Vertically integrated, multiple technologies, high capability and capacity; open to collaboration and transparency;
- The safety and immunogenicity of many of the technologies in the platform have already been demonstrated in large trials; scale-up is already known; deliverables and timelines appear feasible and the reputation of the company suggests they can achieve them;
- *Challenges*: funding required for a relatively long initial time period (7 years);

WHO R&D Blueprint: Janssen Vaccines – Jenner Institute complementary Vaccines Platform Technologies

Lead Institution(s): Janssen Vaccines & Prevention B.V. ("Janssen Vaccines" or "Janssen") and Jenner Institute, University of Oxford

- A joint proposal covering a variety of established vaccine platforms of both partners with a track record of R&D, manufacturing, clinical evaluation, and licensing vaccines;
- Example that illustrates how two partners that came separately in the platform process then came together with the ability to merge their complementary strengths;
- *Challenges*: there is certainly clinical work envisioned in LMICs but it is still not very clear what kind of opportunity there will be for technology transfer;

MVA Platform Partnership

Lead Institution: Bavarian Nordic A/S

Participating Institutions: German Centre for Infection Research (DZIF); Public Health England (PHE)

- A well-known (though only one) vaccine platform and experienced manufacturer;
- *Challenges*: the proposal is based on the use of MVA only. While the partnership has extensive experience with this, a single technology platform is potentially less reliable than multiple technology platforms bringing in other viral vectors or recombinant protein; therefore it seems a less robust approach to vaccine development for the priority pathogens; clinical trial data suggest that boosting may be needed, and that MVA vector works best as the booster, not the priming agent;

Diagnostic Preparedness Platform

Lead institution(s): Altona Diagnostics GmbH / Alere Inc.

- The proposed portfolio covers a range of diagnostic platforms for different needs (generic PCR for standard lab, low-throughput cartridge PCR for less trained staff, and immuno-POC test for bedside testing);
- Both Altona and Alere have a track record in R&D for these three types of assays, manufacturing, and in getting these products on the market; both companies have collaborated together before, making this a proven partnership;
- Another plus for this proposal is the multilevel validation;
- *Challenges*: access to specimens; additionally, the proposal is based on existing technologies and IP and data acquired remain clearly with the companies; transfer of manufacturing to locations

other than the ones indicated is deemed neither practical nor desirable by the two companies and therefore there is limited LMICs involvement;

Accelerated Defense against Emerging Pathogen Threats (ADEPT)

Lead Institution: The Geneva Foundation

Participating Institutions: US Army Medical Research Institute of Infectious Diseases (USAMRIID)

- Sound platform for biopreparedness of priority pathogens and prior experience of proposers in Ebola outbreak; since it is a consortium of different platforms it has readability for easy test addition from other countries;
- Very comprehensive coverage of product streams and the supporting technologies (non-clinical and clinical testing capabilities). The proposal presents an established platform to develop animal models (experience with pre-clinical evaluation of products in non-human primates) and appropriate analytical reagents by which to test things;
- Designed to be reactive to need and completely open access (data sharing is the basic aim of the platform which is designed to integrate parallel R& D effort under one roof);
- *Challenges*: focussed on early discovery and proof of concept; the proposals doesn't cover late stage development and manufacturing and did not identify or mention its industrial partners; vaccine platforms (rVSV, DNA vaccines; RNA vaccines) are not the strongest portfolio;

Targeted Human Immunoglobulin to WHO Priority Pathogens Using Transchromosomal (Tc) Bovine

Lead institution: SAB Biotherapeutics Inc.

- Very promising and interesting idea considering all aspects, including technology, manufacturing, ability to move into clinical trials, and partners in the R&D process;
- *Challenges*: very significant investment for a product that has limited clinical data about safety and efficacy in humans (cost for production of \$2000/gram at 10,000 doses is very high); LMICs access is likely to be limited to final preparation as the primary biological production in bovines is not amenable to export; therefore affordability and suitability of manufacturing facility in LMICS currently is an issue;

CONCLUSION

Discussion

The aim of this public consultation was to enable a selection of appropriate proposals to be presented to interested R&D funders and Member States for their consideration and decision-making for potential support. During the discussion, it was highlighted how the **different rounds of review** and the **criteria used to score the proposals** helped narrow down the selection from a broad spectrum with very upstream ideas to projects that could offer a variety of near-term solutions.

Larger collaborative efforts among proponents were encouraged and suggested, based on WHO Secretariat's knowledge of potential partners for the proposed work. One successful example of alignment, coordination and merge of complementary strengths between two partners that entered separately into the platform process was the joint proposal submitted for round 2 by the Janssen Vaccines & Prevention B.V. and the Jenner Institute, University of Oxford. When asked whether they would be willing and interested in accepting and/or combining into their platform, when appropriate, technologies owned by another party, all proponents declared themselves open to the possibility.

Discussions also focused on **global access** and **management of intellectual property (IP)** rights. The description of these elements included in the applications were two of the evaluation parameters: both play an important role for the **viability of the platforms**, especially in an effort to ensure **fair and equitable access for LMICs**. Emphasis was made on the importance of ensuring appropriate IP protection (for some proposals this meant no access to the broad platform itself but IP made available to cover pathogen-specific vaccines), while making technology transfer **as available as possible** (e.g. "access should be driven by science and optimal outbreak control", even though it was noted that for specific technologies transfer to locations in LMICs could be neither practical or desirable). Even in those instances where proponents indicated that ownership of background IP would remain with the respective developing partners, discussion highlighted a strong intention from the groups to explore options to make products available free of charge, or at the least available and affordable in case of an emergency. Most proponents also stated that they are envisaging access provisions based on existing policies. A strong commitment was voiced to ensure **transparency of data** (some companies will make both raw and interpretative data available, some other have strong policies in place to ensure transparency): an example is the approach to publish data from studies and clinical trials.

Global access was also discussed in relation to **CEPI**. The *ad interim* CEO of CEPI stated that agreements would be negotiated between the coalition and vaccine developers to encourage affordability and availability in Low Income Countries (LICs), and contracts should include reasonable royalty payment provisos for products or patents. Currently the focus is on **technologies for pathogens where there is no commercial incentive**: however should a CEPI-sponsored vaccine develop economic value above and beyond a pre-agreed set point, vaccine developers could benefit from these rewards and pay back CEPI funding (for example seed funding to commence operations, to be augmented with longer term funding and shared-risks agreements). Additionally, rewards to vaccine developers would be proportional to levels of risk, R&D, infrastructural or other types of commitments. CEPI has very much engaged with the **private sector** (e.g. biotech companies, vaccine manufacturers from emerging countries). The partnership model explored for CEPI is a hybrid Advanced Development Partnership (ADP) that can accommodate both permanently dedicated and project-based capabilities, providing a mixture of warm base funding and project-based funding; and a clinical and regulatory coordination network.

The principle of **"no profit/ no loss"** and **social responsibility** and the subsequent approach of offering vaccines/ other health technologies at no cost were discussed and seemed to be guiding the philosophy of the majority of the presenting companies, with the exception of those entities which, due to their structure and turnover, stated that they needed to balance these approaches with the requirement to be a sustainable and profitable business.

Lastly, the discussion focused on **regulators**. Each regulators has its own jurisdiction that is not fully aligned with the ones from other countries. **CEPI** has engaged with regulators and has been analysing legal and regulatory gaps to vaccine development. The Coalition would like to see WHO as a convening force. The **role of WHO** in the area of **NRA support** is two-fold: one aspect relates to **regulatory system strengthening**. The second aspect relates to providing **guidance and technical assistance** in order to enable countries to implement global guidelines to meet their specific regulatory environment and needs⁷. WHO is engaging in different activities such as mapping regulatory pathways worldwide: many country do not have the necessary flexibility to respond to emergencies, and they have therefore requested the development of a framework.

Interim evaluation of the platform technologies process

The WHO Secretariat has worked with the R&D Blueprint Monitoring and Evaluation (M&E) team on an interim evaluation of the platform technologies consultation⁸.

Data and information were extracted from 14 survey questionnaires completed by proponents, supplemented by one phone interview. The purpose of the questionnaire was to try to capture some of the intangible outcomes of the platform technology process and document the benefits to groups taking part in this exercise.

The survey analysis highlighted that the consultation process generated a **new focus on preparedness** and renewed the **urgency to respond to public health emergencies**, while providing an opportunity to **increase awareness about the R&D Blueprint**. It also provided **stimulus and impetus for plans to operationalize proponents ideas** and improved their alignment with public health priorities, while providing an **opportunity for expert review of ideas**.

The consultation influenced the work of the proponents through refining and focusing their plans in order to prepare submissions, and responding to suggestions from the Advisory Group to create complimentary linkages. Furthermore **57% of respondents** created **new collaborations** or **partnerships**, typically with 3-4 other groups, to respond to the call.

Particularly the **April workshop** (the evaluation covered the period October 2015-April 2016) promoted an informal “market-place” atmosphere that was conducive to new networking opportunities, creating an enabling environment where participants had the opportunity to initiate discussions around awareness and potential collaborations. The meeting contributed to a better understanding of the public consultation and its facets: proponents realized other groups were not necessarily “competitors” but potential partners with valuable resources for referrals and best-practices that could suggest new partnerships and spark inspiration for new collaborative projects.

The survey analysis also highlighted some opportunities for improvement particularly in regard to dissemination of information about the call, process and outcomes, and clarity on how the process and outcomes link with, and will be used by, donors and interested Member States.

⁷ WHO does this through its prequalification (PQ) program which aims to ensure that key health products (i.e. diagnostics, medicines, vaccines and immunization-related equipment and devices for high burden diseases) meet global standards of quality, safety and efficacy, in order to optimize use of health resources and improve health outcomes. However the 2014/2015 Ebola outbreak has demonstrated the need for a special procedure for vaccines in the case of a public health emergency when the community may be more willing to tolerate less certainty about the efficacy and safety of products, given the morbidity and/or mortality of the disease and the shortfall of treatment and/or prevention options : the WHO emergency use assessment and listing procedure (EUAL) for candidate vaccines for use in the context of a public health emergency was thus designed.

⁸ “Public Consultation” refers to the entire process and may be used interchangeably with the Platform Technologies “call, process, & meeting”. The public consultation meeting refers to the first meeting which took place on 4-6 April 2016. The “Public Consultation” is inclusive of the public consultation April meeting.

Feedback from the Secretariat to groups that submitted ideas

The WHO Secretariat had the opportunity to interact with the groups following the successive rounds of reviews. Proponents indicated that they had appreciated receiving feedback, especially groups that did not progress to the final list, on the strengths and weaknesses of their ideas.

Groups also expressed a strong interest in creating synergies with groups that have complimentary ideas.

Some types of ideas e.g. enabling technologies, that are not necessarily product-specific, and relatively novel diagnostic platforms, in spite of their merit, did not meet the criteria of the call.

Next Steps

The WHO Secretariat intends to prepare **an article for submission** to a scientific peer reviewed journal.

With permission from the groups that participated in the platform technologies consultation, the Secretariat will also proactively share information on the ideas with interested funders.

Annexes

Annex 1 – Advisory Group and WHO Secretariat

Advisory Group⁹

Biographies of all Advisory Group members were published, for public comment, on the WHO website two weeks in advance of the meeting. No comments were received. All Advisory Group members also completed WHO Declaration of Interest forms prior to the meeting. These were assessed by the Secretariat and no declared interests were considered to be in conflict with participation in the meeting. Specific Advisory Group members recused themselves from decision making on specific projects.

The Advisory Group advised the WHO Secretariat on the strengths and weaknesses of each presented ideas, specifically addressing the likelihood of meaningful participation by entities in LMICs; the strengths of the proposed organizational and management structures and the budget needed to operationalize the plans contained in the proposal(s); and the management of intellectual property (IP) rights.

The following members were of the Advisory Group:

Professor Miles Carroll
National Infections Service
Public Health England, UK

Doctor Karen Midthun (Chair)
Biological Drug Development,
USA

Professor Stephan Günther*
Bernhard-Nocht-Institute of Tropical
Medicine, Germany

Professor Rosanna Peeling (Co-Chair)*
International Diagnostics Centre, London School of
Hygiene and Tropical Medicine, UK

Doctor Isao Hamaguchi*
Department of Safety Research on Blood and
Biological Products, Japan

Professor Helen Rees*
Wits Reproductive Health and HIV Institute,
South Africa

Professor Ahmad Hersi*
Cardiac Sciences Department, Faculty of
Medicine King Saud University, KSA

Professor Larisa Rudenko*
Department of Virology, Institute of Experimental
Medicine RAMS, Russia

Professor Surinder Singh
National Institute of Biologicals, Ministry of
Health and Family Affairs, India

Professor Junzhi Wang*
Institute of Biological Product Control, National
Institutes for Food and Drug Control, China

Doctor John Horton
Tropical Project, UK

Doctor Graeme Bilbe
Drugs for Neglected Diseases Initiative, Switzerland

** Unable to attend the July 21 meeting*

⁹ For further details, please visit http://www.who.int/medicines/ebola-treatment/platform_techs_bios/en/

Written comments from Advisory Group members unable to attend the meeting were also taken into account in the decision making process.

The following member of the WHO R&D Blueprint Strategic Advisory Group (SAG) also provided comments and advice:

Dr Chris Wilson

Global Health Discovery and Translational Science Programme
The Bill and Melinda Gates foundation, USA

WHO Secretariat

The WHO secretariat for this initiative was assumed by the WHO Essential Medicines and Health Products (EMP) Department of the Health Systems and Innovation (HIS) Cluster. Dr David Wood, Coordinator, Technologies, Standards and Norms in this Department, was in charge of leading the process.

Other WHO experts participating in the discussions

Dr Martin Friede – *vaccines*

Coordinator Initiative for Vaccine Research
Immunization Vaccines and Biologicals
Family, Women's and Children's Health
WHO HQ, Geneva Switzerland

Dr Marie-Paule Kieny – *all product categories*

Assistant Director-General
Health Systems and Innovation
WHO HQ, Geneva Switzerland

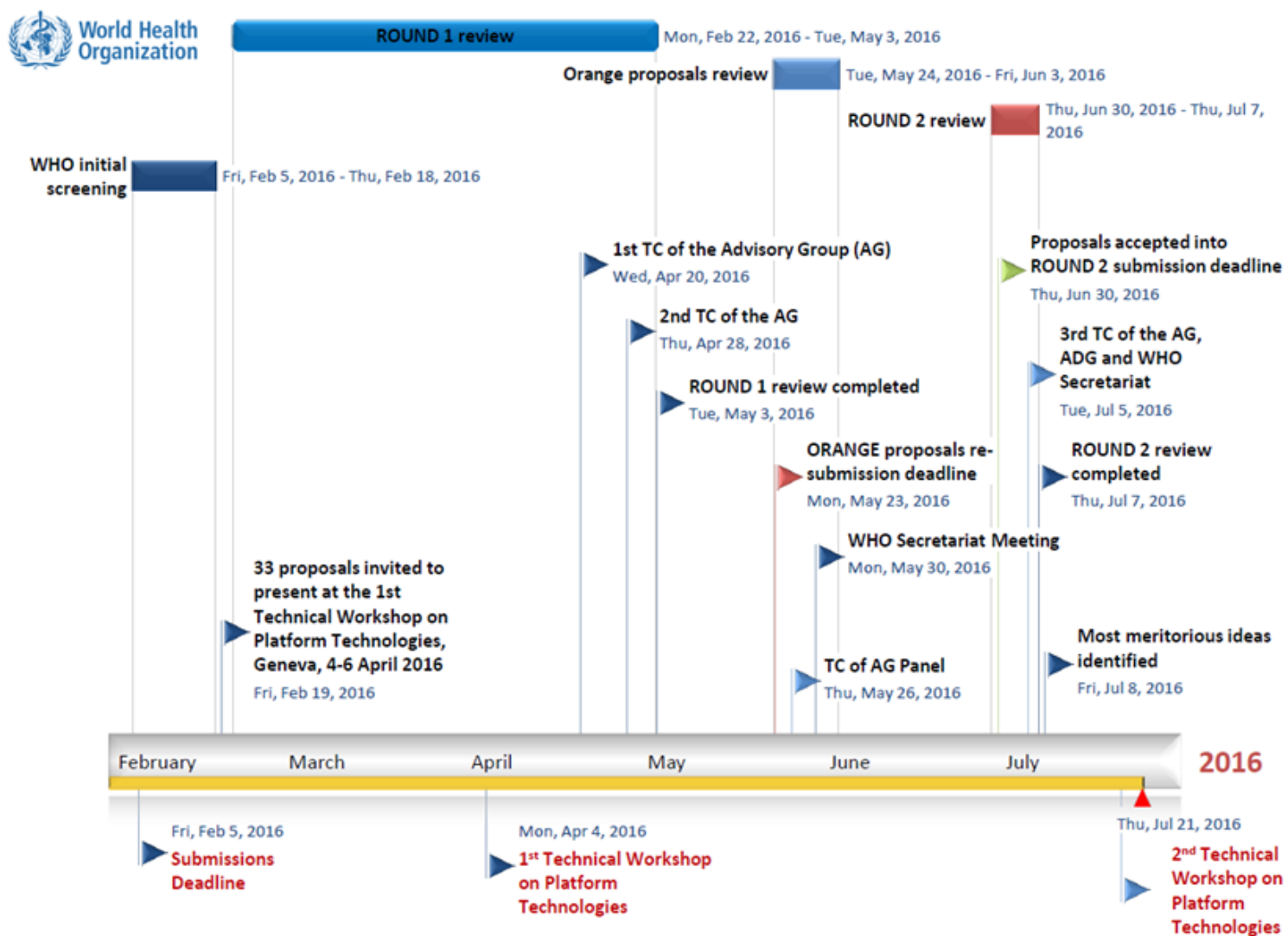
Dr Francis Moussy – *diagnostics*

Scientist, Public Health, Innovation and Intellectual Property
Essential Medicines and Health Products
Health Systems and Innovation
WHO HQ, Geneva Switzerland

Dr David Wood – *all product categories*

Coordinator, Technologies Standards and Norms
Essential Medicines and Health Products
Health Systems and Innovation
WHO HQ, Geneva Switzerland

Annex 2 – Platform Technologies Public Consultation Timeline



Annex 3 – Public Consultation scoring system and criteria

As a pre-screening tool in preparation of the 1st technical workshop in April, the WHO Secretariat drafted and circulated among the Advisory Group members, a revision **template** consisting of 13 questions covering the criteria set forth in the published request.

Following the April meeting and in consultation with the Advisory Group, a more detailed matrix was drafted for ROUND 1 of review. The matrix included a general colour coded rating (green, orange and red) on the overall quality of the proposals and the following questions (Y/N and rating from 3 to 1).

Criteria used to score the proposals invited to ROUND 1 of reviews:

A. The proposed activity is intended for and reasonably likely to be useful for 3 or more priority pathogens/diseases

Yes – moves forward for further review - please see below points B, B(Bis), C and D;

No – not responsive

B. Goal is to develop vaccines, drugs/biologics or diagnostics

Rating 1 – vertically integrated entity with established capability and capacity to discover candidate products, to advance them into and through phase 1-3 clinical trials, to register them via SRAs and to produce final high quality products at scale in a time frame relevant for outbreak response

Rating 2 – potentially able to discover, develop and manufacture high quality products and to meet some but not all of the other criteria required for rating 1; would require collaboration within a consortium of one or more additional partners with needed capabilities and/or capacities to provide SRA approvable quality products in a time frame relevant for outbreak response

Rating 3 – insufficient evidence at this time for the potential to develop and produce high quality products in a time frame relevant for outbreak response

B(bis). Goal is to provide one or more tools or technologies (e.g., standards, surveillance/detection, manufacturing capacity, clinical trial capability, capacity and coordination) to enable more timely and efficient response to an outbreak

Rating 1 – fully integrated capability and capacity to meet an essential need that can be broadly applied in a timely manner at meaningful scale

Rating 2 – potentially able to provide full capability and capacity in partnership with another applicant as part of a consortium

Rating 3 – insufficient evidence that the tool or technology would be useful or if useful that fully integrated capability and capacity could be achieved with or without partnership

C. LMIC participation

Rating 1 – LMIC participation in relevant geographies is integral to the program and is likely to result in sustainable capacity development

Rating 2 – LMIC participation in relevant geographies is described but is in the current description not integral and may not results in sustainable capacity development

Rating 3 – inadequate consideration of LMIC participation

The proposal: (Y/N)

a. Explains how IP issues will be managed to ensure fair and equitable access, especially for LMICs, to any product(s) developed through the proposed platform(s)

b. The manufacturing process presented in the proposal meets WHO norms and standards, where they exist, and WHO-requirements for emergency listing of a product or, where appropriate, prequalification

c. Utilizes technologies that are known to regulatory authorities

d. Includes a justified budget needed to operationalize the plans

e. Explains what internal resources will be used and what external funding will be required to implement the platform concepts being proposed

The Secretariat summarized the results of the scoring and the AG met via teleconferences for discussion and final agreement. The proposals classified as orange were invited to ROUND 2 provided they satisfactorily addressed the additional request for clarification put forward by the AG.

When preparing their submissions for ROUND 2, proponents were strongly encouraged to provide further details on the following elements:

- The likelihood of meaningful participation by entities in LMICs (the strength of the collaborations included in the application will be one of the evaluation parameters);
- The strengths of the proposed organizational and management structures and the budget needed to operationalize the plans contained in the proposal(s); and
- The management of intellectual property (IP) rights: the proposals should explain how IP issues will be managed to ensure fair and equitable access, especially for LMICs, to any product(s) developed through the proposed platform;

Criteria used to score the proposals invited to ROUND 2 of reviews:

The scoring matrix for ROUND 2 of review was further modified, after discussion with the WHO Panel and ratification by the AG, to take into account the specificities of the each product category.

For “vaccines” and “two or more product streams, polyclonal immunoglobulin, enabling technologies”:

A. Does the platform apply only to one or two targets?	0 = one or to two targets
	1 = all targets
	2 = all targets as well as routine

B. Does the platform have demonstrated safety and immunogenicity in human population?	0 = NO
	1 = small trials
	2 = big trials
C. Do the partners have capacity to scale up production rapidly in event of need?	0 = NO
	1 = small/slow capacity
	2 = big/fast capacity
D. Deliverables and timeline 1. Are the deliverables clearly defined? 2. Is the timeline realistic?	0 = not present or not favourable
	1 = meets certain aspects of the criteria
	2 = fully meets the criteria
E. Costs 1. Based on your expert opinion, is the detailed budget reasonable? 2. Will there be internal resources allocated for this project?	Comments
F. <u>ACCESS</u>: does the consortium/group have an access policy which is going to be supportive of equitable access in LMICs? <i>Management of the intellectual property (IP)</i>	
D. <u>DATA SHARING</u>: Does the proposal include plans for data-sharing and bio-banking?	

Where for YES/NO questions the value was as follows: 0 = NO, 2= YES; and the weight of criteria was A to D= 10 and E to G were qualitative criteria.

For “**diagnostics**”:

A. <u>Proposed technical approach</u> 1. Please rate the technical details of the technology platform according to appropriateness and feasibility to the priority pathogens 2. Please rate the platform in terms of its suitability for use in LMICs 3. Does the proposal describe an appropriate data-connectivity?	0 = not present or not favourable
	1 = meets certain aspects of the criteria
	2 = fully meets the criteria
B. <u>Quality, Production and Distribution</u> 1. Please rate the proposal based on ability to scale up production during an outbreak 2. Does the proposal have a distribution network in LMICs?	0 = not present or not favourable
	1 = meets certain aspects of the criteria
	2 = fully meets the criteria

3. Has the technology platform received any previous approval from a stringent NRA (e.g. for other pathogens) or WHO PQ?	
C. <u>Proposed collaborative approach</u>	0 = not present or not favourable
1. Is there a clear and detailed description of the structure and management of the collaboration with other partners?	1 = meets certain aspects of the criteria
2. Based on your experience, would the proposed participation of partners from LMIC be meaningful? (i.e. would there be reasonable resources available to enable meaningful participation of LMIC collaborator)	2 = fully meets the criteria
3. Please rate the proposal in terms of its intended platform production site in LMICs	
D. Deliverables and timeline	0 = not present or not favourable
3. Are the deliverables clearly defined?	1 = meets certain aspects of the criteria
4. Is the timeline realistic?	2 = fully meets the criteria
E. <u>Costs</u>	Comments
3. Based on your expert opinion, is the detailed budget reasonable?	
4. Will there be internal resources allocated for this project?	
F. <u>Management of intellectual property (IP) rights and terms of access</u>	Comments
1. 'Openness': Does the platform allow easy test additions from other companies?	
2. Please rate the proposal of IP management in terms of its effect to ensure fair and equitable access. A table describing the common ways of how IP is managed is provided and scored according to its effect on access. [Refer to Annex 1.]	
3. Would the terms of access described in the proposal ensure the affordability of the product in affected countries in LMIC?	

G. <u>Data sharing</u>	Comments
<ol style="list-style-type: none"> 1. If the collaboration includes obtaining samples for product development, does the proposal include a plan to participate in future/relevant bio bank for sample sharing? 2. Will final validation data be made publicly available? 3. Will any data generated from the proposal be published in an open access journal? 	

Where for YES/NO questions the value was as follows: 0 = NO, 2= YES; and the weight of criteria was A=4, B=2, C=1, D=2 and E to G were qualitative criteria.

The Secretariat summarized and analysed the results of the scoring and distributed the analysis to the WHO Panel and AG members for clearance and agreement. The matrix served as a tool to identify the six most meritorious proposals that were presented at the workshop, among the 13 invited to round 2.

Annex 4 – Agenda

Time	Topic	Presenter*/**
<u>Context</u>		
09:00	Welcome address	Marie-Paule Kieny
09:15	The WHO R&D Blueprint: updates	Marie-Paule Kieny
09:45	Connections with new initiatives: WHO and CEPI	John-Arne Røttingen
10:15	Context and objectives of the workshop, review of the agenda	David Wood
10:30	<i>Coffee/Tea</i>	
<u>Presentation of selected Platforms (moderated by Advisory group members)</u>		
11:00	Improving R&D Readiness for Priority Infectious Disease Threats through the Development and Utilisation of Vaccine Platform Technologies	Moncef Slaoui, Chris Strutt (GlaxoSmithKline, UK)
11:45	WHO R&D Blueprint: Janssen Vaccines – Jenner Institute complementary Vaccines Platform Technologies	Olga Popova (Janssen, The Netherlands) and Sarah Gilbert (Jenner Institute, University of Oxford, UK)
12:30	<i>Lunch break</i>	
13:45	MVA Platform Partnership	David Noll, Gerd Sutter, Stephan Becker, Miles Carroll (Bavarian Nordic, the German Centre for Infection Research (DZIF), and Public Health England (PHE) are independent participants of the consortium)
14:30	Diagnostics Preparedness Platform DPP	Hans Kuhn, Stephan Ölschläger, (Altona Diagnostics, Germany) Glenn Johns, Oliver Lemuth (Alere, Switzerland)
15:15	<i>Coffee</i>	
15:30	Accelerated Defence against Emerging Pathogen Threats (ADEPT)	Sina Bavari, Louise Pitt, Gustavo Palacios, Connie Schmaljohn (USAMRIID, USA)
16:15	Targeted Human Immunoglobulin to WHO Priority Pathogens Using Transchromosomal (Tc) Bovine	Eddie Sullivan (SAB Biotherapeutics, USA), James Cumming (Novavax), John Lowenthal (CSIRO Australia), Sami Chtourou (LFB, France)
17:00	General Discussion	Karen Midthun, chair of the Advisory group
18:00	<i>End of meeting</i>	

** presenters may be subject to change ** additional team members (up to a max of 6 people) may join the session*

Annex 5 – List of Participants to the 21 July 2016, workshop

Advisory Group Experts

Graeme Bilbe

R&D Director
Drugs for Neglected Diseases initiative
Geneva, Switzerland

Miles Carroll

Head of Research, Deputy Director
National Infections Service
Public Health England
Salisbury, United Kingdom

Stephan Günther*

Professor
Bernhard-Nocht-Institute for Tropical Medicine
Hamburg, Germany

Isao Hamaguchi*

Director
Department of Safety Research on Blood and
Biological Products
National Institute of Infectious Diseases
Tokyo, Japan

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