CEPI

Coalition for Epidemic Preparedness Innovations

Joint Coordination Group Meeting

November 18, 2016

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☒ Non-confidential

Summary of proceedings

High level summary

Purpose

Inform about the first JCG meeting, which intended to; clarify and discuss roles and responsibilities of the JCG, update stakeholders on CEPIs work and progress, get feedback on how CEPI should proceed and what considerations to take when working in the end-to- end spectrum.

Key considerations

- More clarity on the regulatory pathway is sought, as fast approval during outbreak is crucial. CEPI should support and facilitate a regulatory harmonization, but not take on a normative or direct coordinating role. Others should fulfil the latter.
- Funding and shared risks/rewards: Need guarantee for industry that no loss will incur by engaging. Some point at the necessity for allowing a small profit margin, in particular to ensure sustainability for smaller biotech companies, even if it might impede accessibility. Others disagree. Value-based pricing is discussed.
- To securing a diverse preclinical pipeline, CEPI should focus on what others are not. Focus on platform technologies and lead head-to head comparisons. Benchmarking is important in several aspects, and standardization and reference labs should therefore be considered.
- CEPI will play an important role in aligning investments and actors for clinical development and trials. Pull mechanisms, the use of prices and milestone payments should also be considered.
- In preparedness phase, CEPI could create clinical trial centers of excellence and a network of investigator sites to build capacity and preparedness in LMIC. Consider doing efficacy trials outside of outbreaks.
- Strong national level and community engagement necessary in countries when outbreaks occur. Ethical standards to be upheld.
- Secure stockpiles for emergency use and containment of outbreak: aligning interest with procurement agencies will be important. Transparency is necessary for more accurate forecasting of stockpile needs. Consider mechanisms for reserved manufacturing capabilities.

Strong appetite for setting up working groups. No objections to reconstituting the JCG into a smaller and more technical group, possibly also extending with additional meetings.

Document Administration

Version number	Approval process	Date
1.0	Prepared by: CEPI Secretariat	06.12.16
	Approved by: CEPI CEO	08.12.16

CEPI

Coalition for Epidemic Preparedness Innovations

CEPI Interim Joint Coordination Group (JCG) Meeting
November 18, 2016
WHO, Geneva

SUMMARY FROM JCG PROCEEDINGS (CEPI/JCG1)

The following participated at the JCG meeting:

- Ole Kristian Aars, CEPI Secretariat
- Kjetil Aasland, Norwegian Mission
- Bruce Altvogt, Pfizer
- Paul Anthony MacAry, Singapore
- Ashley Arabasadi , No More Epidemics
- Sina Bavari , USAMRIID
- Stephan Becker, DZIF
- Ahmed Bellah, WHO
- Seth Berkley, GAVI
- Catharina Boehme, FIND
- Daniel Brasseur, EMA
- Marco Cavaleri, EMA
- Mukesh Chawla, World Bank
- Jongkyun Choi, Permanent Mission of the Republic of Korea
- Gerard Cunningham , GHIF
- Serge Desnoyers, CIHR
- Peter Dull, Bill & Melinda Gates Foundation
- Laura Efros , PaxVax
- Mark Feinberg, IAVI
- Amy Finan, Sabin Vaccine Institute
- Gabrielle Fitzgerald, GPS Strategy
- Davinder Gill, Hilleman Laboratories
- Tore Godal, Ministry of Foreign Affairs, Norway
- Swati Gupta , Merck
- Shanelle Hall, UNICEF
- Margaret Hamburg, Chair, CEPI JCG
- Richard Hatchett, BARDA
- Adrian Hill, Jenner Institute
- Marit Holleman, Intravacc
- Akira Homma , Bio-Manguinhos
- Phil Hosbach , Sanofi Pasteur
- Jennifer Hurley, Institut Pasteur
- Johanne Iversen, CEPI Secretariat
- Suresh Jadhav, Serum Institute of India
- Karianne Johansen, CEPI Secretariat
- David C Kaslow, PATH
- Ken Kelley, Presidential Executive Fellow
- Marie-Paule Kieny, WHO
- Wayne Koff, Human Vaccines Project
- Daisuke Koga, Ministry of Health, Labour and Welfare, Japan
- Frederik Kristensen, CEPI Secretariat
- Nancy Lee, Wellcome Trust
- Odile Leroy, European Vaccine Initiative (EVI)
- Yves Levy, INSERM
- Thor-Erik Lindgren, Norwegian Mission
- Julia Lynch, International Vaccine Institute
- Sebastian Majewski, Bill & Melinda Gates Foundation
- Rohit Malpani, MSF
- Line Matthiessen, European Commission
- Alex Mclaughlin, DoH/UK Vaccines Network
- Makhoana Morena , Biovac Institute
- Aurellia Nguyen, GAVI
- Gunnstein Norheim, CEPI Secretariat
- Solomon Nwaka, ANDI
- Mark Page, National Institute for Biological Standards and Control (NIBSC)
- Sonia Pagliusi, DCVMN
- Gustavo Palacios, USAMRIID
- Vikram Paradkar, Biological E
- Panduranga Rao, Bharat Biotech/Ella Foundation
- Glenn Rockman, GHIF
- John-Arne Røttingen, CEPI Secretariat
- Samia Saad, Bill & Melinda Gates Foundation
- Desai Samir , Zydus Cadila
- Moncef Slaoui, GSK
- Jelle Thole, Intravacc
- Odette Tomescu-Hatto, INSERM
- Johan Van Hoof , Janssen Vaccines & Prevention B.V
- Rajeev Venkayya, Takeda Pharmaceuticals
- James Wassil, Pfizer
- Michael Watson, Valera
- David Wood, WHO
- Naoko Yamamoto, Ministry of Health, Labour and Welfare, Japan
- Marc Zheng Jie Marc Ho, Singapore

The following matters were on the agenda:

1. Opening of 1st CEPI JCG Meeting

Points discussed under this item:

- Welcome to members
- Objectives for the meeting

2. Duties of the JCG

- The functions of the JCG is to facilitate alignment between stakeholders and serve as an advisory body to the CEPI board and the CEPI secretariat on issues that fall under the end-to-end scope of vaccine development. CEPI has no intention of formally coordinating actors, but aims to facilitate appropriate interaction.
- The JCG has no executive or decision-making authority over CEPI's operations, and the recommendations the JCG gives will be made by consensus. Mechanisms will be put in place for the Scientific Advisory Committee (SAC) to seek input from the JCG and vice versa. More clarity has to be given on how the different governing bodies interact with each other.
- The current JCG is established for the interim phase, and changes will apply moving towards the permanent phase. Meetings are planned for once a year, but there may be other means of communication (phone, circulation of documents etc). Membership on the JCG was originally intended to be conditional on signing a Memorandum of Understanding. Moving forward, there is an intent of having a smaller, but representative JCG, and in addition establish a broader Partners Forum for all partners committing to supporting CEPI's mission.
- Optionally, the JCG can appoint task forces/working groups to explore more in-depth particular specific topics/challenges that fall within CEPI's scope.

3. Updates

3.1 Presentation of the business plan

John-Arne Røttingen presented key features of the CEPI business plan, including the vision, mission and scope of CEPI's end-to-end approach.

- The broad pictures is that CEPI will convene actors from the broader spectrum of vaccine development (from discovery to delivery), but focus its investments to identified gaps, in particular for moving vaccine candidates from the pre-clinical phase through phase II clinical trials. All CEPI activities will be guided by the strategic objectives; i) equitable access, ii) response speed, iii) market predictability and iv) equity.
- CEPI partners have identified a need for improved regulatory alignment and clear and predictable regulatory procedures, and will support and collaborate on efforts from WHO and other regulators to achieve this. Stockpiles and the associated capacity in an outbreak situation is also important.
- There is an intent of establishing a Partners' Forum that builds on a general assembly model where a larger group of CEPI partners can be engaged and endorse CEPI's mission. The Forum will be open to all partners signing an MoU, and for additional stakeholders who will endorse a high-level statement of support. The Partners Forum might be virtual, but will

likely also have annual meetings that are linked to meetings of the institutional bodies of CEPI.

- The JCG will thus be reconstituted and transition into a smaller group composed by both permanent members and members participating on a rotational basis following from the constituencies they represent. Participation on the JCG will therefore be on an invitational basis and not linked to an MoU, although organisations and CEPI are able to enter into separate agreements.

Comments and elaboration

- CEPI has demonstrated its ability for rapid evolution and is moving in the right direction, but specific issues need more discussion in smaller bodies. It will be important to facilitate sharing of information and workload among CEPI partners in order to make progress in the space of vaccine development.
- Acknowledging the substantial effort that has gone into the WHO blueprint, CEPI will use this as a point of departure for the Call for Proposals, but will consider widening it to cover more pathogens over time.
- Regulators are important and independent actors, and their work cannot be coordinated by CEPI. Since no single regulator can do all the work single handed, CEPI might however have an important role in supporting and facilitating regulatory scientific discussions and harmonisation in regulatory networks which in turn can lead to faster progress. The JCG might be the appropriate body to support this task, in addition to the important work that is being done in the already appointed working group on regulatory issues.
- CEPI must be mindful of value-based pricing with respect to its operations, and how this feeds into the CEPI policies on shared risks/rewards. This will be important for companies to engage, and especially so for the smaller ones. This also links to regulatory uncertainty and the possibility of making a profit.

3.2 Progress update on the WHO R&D Blueprint

Marie-Paule Kieny presented the progress update on the WHO R&D blueprint for action on preventing epidemics.

- The current approaches for improving preparedness were explained and a timeline was presented. It will be especially important to support discussions on regulatory science.
- The WHO collaboration with CEPI is grounded in an MoU, and includes principles of transparency of operations and that the vaccines funded by CEPI are affordable and accessible.

Comments and elaboration

- In previous outbreaks, industry has invested millions without any return. As such, they should not incur any losses by engaging, but at the same time cannot expect any larger profits. Others pointed to the need for a small profit, and especially so for smaller companies who might not have separate income streams to support full dedication to a specific project. If prices are set too low, companies might not engage, thereby impeding the number one task of bringing products to those in need.
- The differentiation between GAVI and non-GAVI eligible countries must be taken into account, and ensure that those countries who are close to being GAVI eligible are guaranteed access through affordable pricing.

- In ensuring that products are developed, CEPI should also consider extending its financial framework by including more pull mechanisms, including by instruments as advanced market commitment.

3.3 Finishing the job on Ebola – what role for CEPI?

Mark Feinberg presented where we are today on development of Ebola vaccines and provided future outlooks for gaps that need to be addressed

- The international community, including regulators, were unprepared for Ebola, but the accelerated development of products that occurred showed that that the community can pull together in times of crisis. Regional regulatory support platforms, like AVAREF, were extremely useful for Ebola and provided regulatory support to the affected countries.
- The remaining scientific gaps are: i) Correlate and mechanism of protection in humans and if the correlate will be different for the different vaccines ii) Duration of immunity in humans iii) clarity on what data are needed for efficacy testing for vaccines with no current efficacy data iv) development of vaccines with suitable cold-chain requirement.
- In terms of licensure, no vaccine candidate is licenced, accepted and available for use. A pathway to licensure for some candidates are very uncertain, in particular for those with no efficacy data in humans.
- The EUAL mechanism established under a public health emergency (PHEIC) will assist UN procurement agencies and member states on the applicability to use a medical product during a PHEIC. The question remain if there is a regulatory or policy framework in place to enable vaccine introduction and stockpiling in advance of licensure, after PHEIC termination.
- In terms of readiness for the next outbreak, the WHO-led Global Ebola Vaccine Implementation Team (GEVIT) aims to cover vaccine implementation policies. However, credible demand forecasts are needed, stockpile policies and financial support for procurement should be secured and sustainable manufacturing strategies should be defined.
- Overall, this is work in progress and it will be important to not create redundancy on collaborative efforts – and weigh against other priorities and definition of CEPI scope.

Comments and elaboration

- SAGE has reviewed initial data and made provisional recommendations for use of Ebola vaccines and vaccination in outbreak response. Long-term immunity data is currently not available. It will be important to have the candidate vaccines assessed by the regulators. Ebola target product profiles (TPPs) for emergency and prophylactic response are published on the WHO website, as well as a TTP for multivalent filovirus.
- Regarding the EUAL process, as of today validity will only be in the case of a public health emergency of international concern. Stockpiles should be ready in order to achieve effectiveness, but might be difficult for cases where there is no efficacy data available.
- Assay verification tools have been developed but technical specifications of the work on Ebola should be discussed with CEPI.
- More clarity on the regulatory pathways was sought, whilst others stated that the uncertainty was tied to regulatory *science* and not necessarily *pathways*. As such, CEPI might take a facilitating role in providing clarity on the regulatory scientific issues and gaps in order to secure efficient deployment of vaccines in future outbreaks.

- A number of Ebola vaccine projects are ongoing, including INSERM/NIH project with MNCs with a co-funded trial using a prime-boost strategy. CIHR is conducting work on a phase 2 trial. The industry also assured that Ebola projects are not being seized.

3.4 Plans for Call for Proposals

John-Arne Røttingen gave a short introduction of the plans for Call for Proposals (CFP). With the WHO Blueprint list as starting point, the SAC – facilitated by Secretariat analyses - is currently determining a short list of 3-5 priority pathogens against which R&D projects will be funded. This process will be finalized by mid-December through a decision made by the Board. The CFP will be a two-stage process where applicants are invited to give a short expression of interest during the first stage, of whom a selected number will be invited to submit a complete proposal in the second stage.

3.5 Update from Regulatory Working group

Daniel Brasseur presented the work of the Regulatory working group. It's mission is to cooperate with WHO and other regulators to help product developers better understand the regulatory and ethics processes around i) The data requirements and regulatory vehicles for product development in the absence of an outbreak, ii) The regulatory issues around stockpiling and iii) Clarifying regulatory and ethical issues surrounding the use of stockpiled investigational products during outbreaks.

Future steps include

- Promoting early and continuing engagement and discussion of vaccine development and evaluation plans, including for pre-clinical, clinical studies and manufacturing and quality issues with all implicated partners.
- Contributing to the development and implementation of the WHO R&D Blueprint regulatory science agenda including by being supportive of global coordination mechanisms established by WHO and facilitating communications of regulatory guidance.
- Implementing guidance and standardized templates for issues such as data and sample sharing and liability issues, to optimize the product development process.

Comments and elaboration

- CEPI's role depends on whether it will focus on preparedness or be an emergency responder. The associated regulatory pathways are quite different, and one should therefore look more into the corresponding approaches. One way forward might be to have a "ready-to-use" procedure in order to prepare for the unpredictable.
- In making the regulatory requirements, one must ensure that these are communicated to companies early in order to speed up transition into phase 3. Accordingly, CEPI's scope should not stop at phase 2, but help ensure that vaccines make it through the whole regulatory pathway.
- CEPI will seek to have validated technology platforms ahead, but might use existing platforms initially. Mock-up dossiers are available for influenza and this is a platform for approval in EU, which could be an option to be explored in other areas as well, where the concept is to approve at early stages of the development, based on immunogenicity or an animal model for the vaccine to only be used in case of an emergency. However, when dealing with a completely unknown pathogen it might be a very different process.

4. Discussion on end to end spectrum – Six questions

1. How can we secure a sufficient and diverse preclinical pipeline for EID vaccines?

Representatives from NIH, the Jenner Institute and the Department of Health shared the following views in the panel discussion:

- To secure a sustainable funding base, CEPI should use co-funding arrangements with established actors to complement its efforts. CEPI can also consider looking into the use of prizes (for candidates ready for phase I) as an additional incentive for companies to engage. Early phase I trials would be more informative with comparative immunogenicity data across platforms.
- Cognizant that Ebola did not make the priority list before the outbreak, one must be weary of other potential threats outside of the identified diseases. In order for basic research funders and others to engage, priorities must in turn be clearly communicated. Moreover, animal models have to be assessed and comparative immunogenicity assays and facilities (i.e. reference labs) should be prioritized.
- An important part of CEPI is galvanizing funding and securing a diverse financial base to hedge against changing political priorities. When CEPI prioritizes its activities, it should focus on what others are not doing, and ensure that the products funded are also possible to scale up. The latter should be done in close collaboration with the SAC.

Comments and elaboration

- Assay samples should be sent to a central reference lab. The appropriate entity that has control of the field sites and funding, possibly CEPI, WHO or even journals, should help determine what are the appropriate reference labs. Without a reference lab, it's hard compare and verify results.
- Important for CEPI to have a portfolio management approach to follow up specific targets. It should also pay attention to the natural history of disease. This will also help inform what are the best animal models, and what are the best immunization platforms. CEPI can use this as a guideline to direct its funding.
- At the moment, no one is willing to do head-to-head comparison between different products/platforms, and CEPI should pay specific attention to this. Moreover, CEPI should work with regulators to clearly define what type of studies they are interested in, that being GLP or non-GLP format.

2. How can we secure the development of adaptable vaccine technologies and keep track of new promising technologies?

Representatives from the Human Vaccines Project, the Bill & Melinda Gates Foundation and PATH shared the following views in the panel discussion:

- Single shot with lifelong protection should be the ultimate goal for CEPI. Historically, animal models have been imperfect, but should be used to a larger extent and be considered for CEPI. There are a range of tools that should be applied, including biological (assays), computational (amount of data will need informatics tools) and engineering (using nanotechnology). The above should be done in a coherent manner, including by the use of networks and standardization of sample acquisition and clinical trial design.

- CEPI must be leveraged for engaging on innovative platforms, which in turn can be used to pivot quickly in the right direction. RNA vaccines should be investigated more closely. In the end-to-end discussion, products should be ready for phase 3 – this means that CMC facilities can be leveraged quickly.
- As with other areas of work, CEPI needs to use benchmarks for new products. Having a relevant challenge/infection model to evaluate unproven technology is therefore very helpful, and the right incentives need to be in place for this to happen. On novel platforms, the wisest way is not to use the unproven technology to the hardest problem. There also has to be in place mechanisms to track the corresponding progress.

Comments and elaboration

- In order for challenge models to be effective, clinical data has to be collected at the time of emergencies and mechanisms need to be in place for sharing this. WHO is the natural coordinator in this space, but more can be done.
- On the proposal on new technologies being tried first in existing vaccines and then in new targets, one should consider doing this in parallel to reflect the sense of urgency that CEPI is operating under.

3. How can we facilitate alignment and predictability of pathways for clinical development and regulatory approval?

Representatives from the WHO and EMA shared the following views in the panel discussion:

- To foster regulatory science and facilitate rapid regulatory decision-making, there should be standardisation of the animal- and human challenge models particularly when efficacy data is unavailable. Although CEPI can play a role, the regulatory discussion should be handled by the regulators and should be fostered to take place more on a global scale and with a global scope, e.g. global scientific advice. Early approval is an important area, and there needs to be increased awareness and information sharing at an early stage – particularly with regulators that do not have such frameworks. Lastly, data on vulnerable populations is desired.
- Idea of AVAREF is to help in assisting countries to expedite regulatory and ethics review, promote convergence and build technical capacity. During the Ebola outbreak, AVAREF brought together regulators for a joint review. This helped expedite the timeline for regulatory and ethical approval of clinical trials by responding to questions from manufacturers on a timely basis and providing to-do lists for facilitating swift

Comments and elaboration

- AVAREFs approach is a single regional approval, although there might be country-specific needs that need to be tackled bilaterally. However, the aim of AVEREF is regulatory convergence between partner countries.
- Many countries accept WHO prequalification as a standard which is based on a review of a licenced vaccine from a national regulatory agency. WHO has also established an Emergency Use Assessment and Listing (EUAL) process. This is for situations where there is insufficient data for prequalification. A possible role for CEPI could be providing funding for standards and assays, and thereby advance regulatory harmonization. The same goes for funding of the development of animal models.

4. How should we align investments for clinical development in preparedness phase?

Representatives from BARDA, GSK and CIHR shared the following views in the panel discussion:

- CEPI must be mindful of the requirements under the animal rule if it chooses to go forward on this path. When preparing for studies conducted in an outbreak setting, one must be weary of ethical and strategic considerations that relate to collection of data and social mobilization. CEPI can furthermore play an important role in aligning investments. Depending on the existing investments being done by either private sector, US-based entities or non US based funders, CEPI must consider a relevant mix of cost-sharing and gap-filling to achieve the overall goal of access.
- In order to align investments, it is proposed to create a clinical trial centre of excellence where all CEPI funded vaccines can be assessed on safety and immunogenicity. This will serve as a benchmarking exercise. Moreover, a network of investigator sites can uphold standards and give capabilities in LMICs.
- Important to invest in excellence, and the decision maker should be aware of urgency for investing in preparedness. Glopid-R is doing important work in supporting this, as is a number of Canadian initiatives and networks that speeds the process through cross-sectorial collaboration. CEPI should consider leveraging such existing efforts, including CIRN (Canadian Immunization Research Network)

Comments and elaboration

Please see annex for comments received after the meeting.

5. How can we quickly conduct clinical phase 3 trials in emergencies?

Representatives from the European Commission, MSF, EMA and the WHO shared the following views in the panel discussion:

- Clinical trial sights in an outbreak is important, and there are ongoing initiatives that are looking at training the appropriate staff. There is a need to mobilize funding for phase 3 trials quickly in the event of an outbreak. CEPI and other funders should interact closely to ensure the dissemination of knowledge around what is in the pipeline.
- As things often do not pan out as anticipated, CEPI should not plan too much in order to maintain its flexibility. This will allow a quick response, although ethical standards must be upheld. Joint review processes need to be improved, including the EUAL. To make CEPI more accountable and balanced, there needs to be a stronger presence of affected countries in its governing bodies.
- Fast approval is important, and as such, there is a need to have in place a network of authorities to allow for flexible submission processes.
- Although the WHO has significant knowledge in the field, it will not conduct clinical trials. The Ebola affected countries did not have scientific review committees, and there is accordingly a need for normative guidance and other gap-filling efforts. Good community engagement should be a priority in addition to discussing appropriate clinical trial designs for demonstrating efficacy.

Comments and elaboration

- CEPI should consider doing efficacy trials outside of outbreaks when possible, and include such feasibility as one criterion in the Call for Proposals. Others highlighted the many

instances when this is not possible, also underscoring that it might be opposing to CEPI's need to operate in a flexible manner.
- CEPI should consider building capacity for clinical research for routine and in-emergencies assessment. Phase 2 trials might also seek to target health workers.

6. How can we secure stockpiles for emergency use and containment of outbreaks?

Representatives from the UNICEF, Gavi and No More Epidemics shared the following views in the panel discussion:

- UNICEF's has an extensive health portfolio and its work has a focus on partnering with other organisations. Experiences with Ebola and other diseases has shown the need for surge capacity in the event of an outbreak. The amount of resources that go into maintaining this (i.e. stockpiles) is considerable, and one must not neglect the importance of governance of deployments.
- CEPI and Gavi has shared interests and complementary roles for emerging infectious diseases, and should make efforts to align investment strategies. This is especially important in the short-term, as Gavi is currently reviewing its vaccine investment strategy. Stockpiles are a part of a broader disease strategy, and there has to be a transparent way of allocating doses. This means that forecasting has to be made and information shared across actors in the space, including recipients of the product. In addition to the stockpiling aspect, one should also considering other mechanisms like reserved manufacturing capabilities.
- Without appropriate health systems, vaccines are useless. Although there might be solid health infrastructure at the national level, this is often not the case for the community level. Especially important for the latter is creating a level of trust and awareness that allows effective interventions. Funding of piloting for vaccines at the country level should be considered by CEPI as a part of its broader strategy.

Comments and elaboration

Please see annex for comments received after the meeting.

Peggy Hamburg closed the meeting and invited for written inputs on the questions for discussions and on the issue of potentially establishing working groups.

6. ANNEX

This is a summary of feedback in the questback to meeting participants.

6.1 Feedback on panels

1. How can we secure a sufficient and diverse preclinical pipeline for EID vaccines?

Benchmarking and comparative studies

- Comparative immunogenicity can be best achieved through the production of standard reagents that permit calibration and harmonisation of assays to a physical standard. It will be important to provision for such standards in co-ordination with vaccine development programmes since the production of such high order materials (WHO endorsed) can take some time (>1 year) and this would need to be factored into development timelines so that these standards are ready for use in time for vaccine immunogenicity studies. Recognition of this activity should be included in CEPI's documentation/objectives, and investment plans.
- CEPI might consider contracting for a dedicated pre-clinical screening unit, perhaps with small animal and non-human primates model capabilities, with standard assays, to enable comparative analyses of the preclinical pipeline for EID vaccines. This unit might chair a small working group to develop an annual landscape analysis of the preclinical pipeline, and report back to CEPI. Additionally, at an annual scientific forum of CEPI, there could be a section on the preclinical pipeline with abstracts from those scientists/institutions working in this area
- CEPI could identify or setup regional R&D facilities, possibly BSL3 or 4 facilities, to rapidly cope with emerging infectious agents. Information sharing between labs would be essential to advance quickly to vaccine clinical development.

Financing and incentives

- Although both will probably needed, pull incentives and prizes should be favoured above push mechanisms for preclinical candidates.
- Ensure sufficient long-term financing to support and sustain the development of a robust pre-clinical pipeline and provide industry an opportunity to hedge the risks associated with early phases of vaccine development
- Create an incremental incentive mechanism that fully funds development in a stepwise way through to the end of phase 2 (establishing safety (in 3000 to 5000 subjects) and immunogenicity (in an appropriately sized subgroup) in the target population.)

Predictability and scope

- Even to get preclinical development kick-started we need to give researchers, developers and producers a clear line of sight to the end of the development, i.e. what use will be made of the vaccine/s when it/they have proven safety and immunogenicity. This assumes that efficacy cannot be demonstrated until an outbreak.
- CEPI should have in house/or insourced 'scouting' resources, who have the scientific/development experience to 'scout' for interesting vaccine candidates in the academic/biotech/industrial ecosystem, focusing on the target diseases prioritized by CEPI. The same goes for platform technologies.
- Look beyond obvious avenues. E.g. there are interesting things happening in places like Cuba and Russia.

- Although outside CEPI scope, one should consider encouraging ongoing basic research funding on the key RNA vaccine technologies and perhaps the DNA vaccine technologies
- Create a precise description of the products being sought (i.e. TPPs or PPCs) or the problems we want to solve

2. How can we secure the development of adaptable vaccine technologies and keep track of new promising technologies?

Scope and incentives

- We need to develop some basic profiles of the technologies we need and promote those as part of our calls or engagement with stakeholders. CEPI should develop and agree clear incentives and M&E mechanisms for the development, registration and deployment of these vaccines.
- CEPI could consider funding laboratory networks with the capabilities to conduct new assays/technology development, including but not limited to the Human Vaccines Project. HVP is currently developing a template for experimental medicine/Phase 1 clinical trials of vaccines, which can be shared with CEPI/JCG for input.
- CEPI can act as a bridge between innovators and influential public and private sector agencies through using tiered pricing models, forging strong public-private partnerships.
- There should be a horizon scanning and venture capital team within CEPI that is charged with tracking but more importantly being the go-to point for emerging technologies. They should also have seed money that can be used for milestone-based investment/co-investment in promising technologies. Finally, they should have a public list of technologies and their status

Validation and prioritization

- CEPI could identify four flexible technology platforms (different from each other), from in different regions and from different "owners" and provide support to validate such platforms as to usefulness to produce safe antigens that can be used as vaccines.
- With limited resources, CEPI must have a carefully crafted execution strategy in order to prioritize between vaccine development and platform technologies.

3. How can we facilitate alignment and predictability of pathways for clinical development and regulatory approval?

Pathways

- Ensure prior regulatory commitment on pathways and requirements. They will be specific for each pathogen but at least there needs to be a pre-agreed roadmap.
- Will be important to define more innovative regulatory pathways and keep a list of proven and preferred clinical trials designs. These efforts have to be made jointly by regulators and expert process innovators.
- Prepare in advance clear and relevant, detailed guidance documents that have been thoroughly vetted through normative processes at the global (e.g., WHO) and national levels

Networks and collaboration

- The establishment of sustainable clinical trial networks in developing countries would be important. CEPI can collaborate with established actors like ANDI and leverage this capacity

to identify suitable centres to support its work. On the regulatory approval pathways, WHO should play an important role

- CEPI could foster the creation of a discussion platform, to allow for early interaction between the teams tasked to develop the vaccine, and the 'global regulators'. Lesson could be drawn from the WHO meetings on the 'regulatory pathways' for Ebola vaccines, which were initiated in the period from September 2014 and onwards. A scientific advice mechanism between US/Europe/WHO/AVAREF might advance these efforts.
  If CEPI develops a close working relationship and trusted partnership with key regional regulatory bodies (EMA, US FDA) and with the WHO prequalification team, this will be a huge value-add for technologies that are supported by CEPI as it should improve predictability of acceptable development pathways and regulatory approval strategies at the country and public sector procurement levels.

4. How should we align investments for clinical development in preparedness phase?

Incentives and scope

- If CFPs (Call for Proposals) are written acceptably, the current proposal from CEPI will likely drive investment. For lower priority targets, offering prizes for milestones in lieu of full funded research might be better to incentivize biotechs and industry.
- CEPI should create a detailed line-of-sight of pull and push funding mechanisms with clear Go/No-go criteria at each stage gate and funding mechanism transition.
- Long term agreements/volume guarantees for manufacturing scale up
- As things tend to cost more than anticipated, CEPI should be prepared to spend 1.5x or even 2x more when moving into the development phase
- Prioritise targets, issue incentivising CFPs and set off parallel, competitive projects covering at least 3-5 targets. Preparedness without breadth will almost certainly miss the next epidemic and investment without competition will reduce speed and innovation.

Networks and clinical trials

- A network of appropriate trial sites should be established in regions where targeted diseases are likely to manifest themselves.
- CEPI has critical path issues that need to be addressed to achieve stockpiling of vaccines for EIDs, but has a tremendous opportunity to enhance the broader field of vaccinology by conducting clinical trials where innate and adaptive immune assays are included, microbiome and other day 0 factors are incorporated, tissue sampling where applicable etc. Clinical networks and laboratory networks should be made available to CEPI for these purposes, and trials designed to achieve both product development/critical path issues, and vaccine research issues.

5. How can we quickly conduct clinical phase 3 trials in emergencies?

Guidance and pre-approval

- Prepare in advance clear and relevant, detailed guidance documents that have been thoroughly vetted through normative processes at the global (e.g., WHO) and national levels
- Will be important to have pre-approved investigational stockpiles (for which there are substantial safety and immunogenicity data available) and phase III study protocols. To achieve this, there needs to be collaboration with agencies such as AVAREF, in addition to ethical committees etc.

- Accelerated approval or conditional approval pathways could expedite the vaccine availability in the market. Standardized clinical trial protocols with appropriate of pre-approvals for different types of pathogens can be pre-positioned to ensure rapid initiation of clinical trials during outbreaks

Networks and infrastructure

- We need to engage with countries as part of preparedness and start training and preparing a network of clinical trial centres in developing countries.
- If CEPI is considering Phase 3 trials, then infrastructure/capacity needs to be considered in regions of the developing world where such capacity is limited. Novel clinical trial designs should also be considered.
- Establish a clinical and regulatory coordination network that can give advice on regulatory pathways for vaccines to be used in epidemics.
- Should consider having a 'clinical operations emergency team' ready to support local studies in case such sites are not available in the affected region

Stockpiling and healthcare workers

- Have protocols, CRFs, databases and trial centres etc. and vaccines ready as a stockpile, ready to deploy as soon as an outbreak is suspected.
- Do phase 2 in healthcare workers in at-risk geographies and follow them up regularly so that you have their contact details. They are most likely to bear the brunt of any epidemic even before we know that it is an epidemic. By doing this we will get real time effectiveness data to inform use of the vaccine

6. How can we secure stockpiles for emergency use and containment of outbreaks?

Collaboration

- Engagement of experienced organizations like GAVI, UNICEF, etc would be important here. The use of emerging mobile technologies can enhance tracking and access to the vaccines in emergency.

Surge capacity

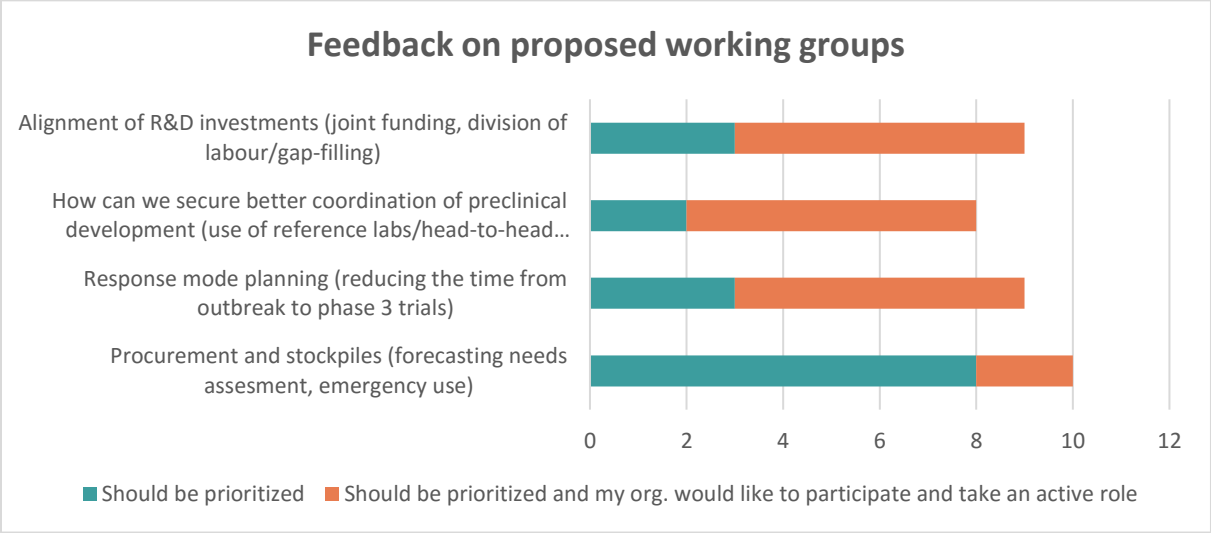
- To induce manufacturers to keep significant production capacity and stock on hand for emergency use, one should consider advance purchase commitments, volume guarantees and committed annual budgets for stockpile purchases. The success and cost of these efforts however, will be specific to the technical and economic realities of each vaccine product.
- Prioritise technologies with the ability to store large amounts of vaccine in small volumes for long periods of time and/or technologies that can produce and release vaccine in the shortest possible time period. Also prioritize technologies that don't have to have a dedicated warm-base facility for production (e.g. smallpox) but that can be produced by a platform able to produce either a range of epidemic vaccines or that will be in use producing routine vaccines.
- CEPI should contract for manufacturing of stockpiles, and warehousing of stockpiles

6.2 Feedback on the functions of the JCG

- Several suggested that JCG meetings should be held more often than once a year. The possibility of having 2-day meetings was also raised.
- The JCG should serve as a forum for creating and maintaining line of sight from early preclinical research to full-scale implementation
- If the JCG mission is 'technical', it will be important to clarify its role vs the SAC, and the secretariat
- Several agreed to reconstituting the JCG into a smaller and more technical/strategic group, and that broader stakeholder engagement could be facilitated through a partners forum. On the composition of the JCG, it was suggested to keep a "strict" balance that allows industry to be well represented, as they are the only ones with the expertise and experience to deliver as when products are urgently needed. Such a group could have 33% industry/33% public health including CSOs (because they work for the public)/ 33% government-financing--regulatory. Another model would be to a small Executive Group consisting of the /Co-Chairs of working groups for questions 1-6, representatives from the SAC, Secretariat, and if appropriate Board of Directors.
- It would be helpful for the JCG to view the data emerging from CEPI sponsored clinical trials. Conflicts of interest need to be monitored carefully here, as it's likely that SAC/JCG member institutions will be the recipients of CEPI funding.

6.3 Feedback on working groups

The figure below shows responses from the questback that was shared with JCG meeting participants after the meeting.



The results show that there is a great interest in initiating new working groups. The three first working groups had the greatest interest from actors to take an active role, and the last working group had the most interest in total. Since the voter turnout was quite limited, the results are however not necessarily representative of the broader group. In addition the proposed working groups, respondents suggested the following to be considered:

- **Oversight of the Call for Proposals** - ensure equity, smooth process, adjust as necessary

- Include **fast-track registration** in one of the proposed working groups above, as well as BSL3-4 preparedness.
- **New Technologies in Clinical trials**- ensuring state of the art assays and technologies are incorporated in such trials, to achieve both critical path and vaccine research data for CEPI and the broader vaccine field.
- **Pricing models**
- **Development of standards for assay calibration**, as this activity needs to resourced effectively through co-ordination with the vaccine developers as soon as the pathogen target is identified.
- **Liability issues** – under mechanisms such as an EUAL and/or any other situation in which vaccines could be used prior to licensure, this remains a significant unaddressed issue/gap where progress will be important.
- **Stockpiling and new processes/bodies:** Working group that starts to discuss the current processes available for making decisions on stockpiling and new processes/bodies that might be needed to make decisions on stockpiles prior to licensure. A working group who could adequately describe the issue and ways that it could be addressed would be great. This will ensure that capacity is adequately planned for in advance and key opportunities for scale up are not missed. This will also force alignment up front on assumptions for anticipated target populations, indication, etc. until actual data are available.
- **Regional approval mechanisms**: The regulatory issues working group should also include regional approval mechanisms. For outbreak driven diseases, it will not be possible for companies to obtain licensure in "all" countries. Therefore expansion of AVAREF's current work and/or a better understanding of where these efforts stand is key.

Lastly, participants suggested to start working groups related to the following questions discussed in the different panels:

- **Panel 2**: How can we secure the development of adaptable vaccine technologies and keep track of new promising technologies? ***Specifically:***
    - Could be the task of a scientific working group, to report to the JCG annually or biannually, for information, though perhaps the most promising will then be decided by the board, based on SAC recommendations. Still, reporting to the JCG annually may keep the discussion open, and not "bother" the board if not relevant.
    - A small working group, from across academia, government, industry, and NGO would be useful to monitor technologies. It should include DARPA and other defense organizations that routinely fund new technology development in commercial firms.
- **Panel 3**: How can we facilitate alignment and predictability of pathways for clinical development and regulatory approval?
- **Panel 5:** How can we quickly conduct clinical phase 3 trials in emergencies?
- **Panel 6:** How can we secure stockpiles for emergency use and containment of outbreaks?

The most important take-out would be that there is an appetite for initiating working groups, and the secretariats recommendation is therefore that it will establish working groups based on the received feedback and following the guidance from the Board.