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CEPI

Answers by CEPI to questions posed by MPs

German Parliament's Subcommittee on Global Health on 23 January 2023

*Question by MP Tina Rudolph: *So-called platform technologies are of enormous importance for preparing for the pandemics of the future. Now there is the WHO mRNA technology transfer hub specifically for mRNA platform technology. There is also the WHO C-TAP (Covid- Technologies Access Pool) structure. How important do you consider such technology transfer platforms for distributing new platform technologies (other than mRNA technology) in the world, in order to be prepared in the best possible way for pandemics of the future, or to be able to react quickly to a pandemic and to contain it?*

Developing new vaccines *from scratch* in response to a future outbreak from an unknown pathogen with sufficient speed, scale and access will not be possible without the necessary preparatory research. Developing vaccine platform technologies that can be used in advance to maximize our scientific, technical, clinical effectiveness and safety, as well as manufacturing experience (including scale-up technology transfer to globally diverse facilities) are going to be critical. Hence, when a future epidemic or pandemic occurs, the new pathogen can be applied to the platform in a "plug-and-play" approach in order to test viability on that platform (or at least as much as possible; the ease of doing this will vary considerably by platform). This not only allows for a more rapid response, but also more rapid large-scale manufacturing at globally diverse sites to facilitate equitable access. mRNA-based platforms are one the most useful vaccine platform technologies for this purpose because of their suitability for rapid adaptation to novel pathogens.

The WHO mRNA Hub and C-TAP can be useful tools to progress toward improving global capabilities and experience with mRNA platforms (and, with caveats, similar approaches could plausibly be used for other platforms as well). A critical component of diversifying global capabilities, which it isn't clear these initiatives by themselves can address, is building technical 'know-how' and skills using these technologies (and this even more so for other platforms). I think preparedness will be best served if we support multiple complementary initiatives, bringing in the many globally diverse public, private and commercial organizations that are currently working on and/or have extensive experience with mRNA and other technologies. The vaccine manufacturing network that CEPI is assembling is one such complementary effort also seeking to support geographically diverse capabilities; another is the Regional Vaccine Manufacturing Collaborative that we are sponsoring in partnership with the U.S. National Academy of Medicine and the World Economic Forum.

*Question by MP Kordula Schulz-Asche: *What role does the diversification of production sites across continents play (for CEPI)? How can it help to improve access and mitigate against shortages? This refers to vaccines as well to other medical products.*

Based on our experience and observations during the pandemic, CEPI believes that geo-diversification of vaccine production will be critical to ensure the rapid equitable access to vaccines in underserved regions. CEPI, for example, is supporting broad global efforts to expand access to rapid-response vaccine development and production technologies by establishing a network of manufacturers, suppliers and Contract Development and Manufacturing Organizations (CDMOs) to ensure that emergency disease outbreaks can be prepared for and responded to with agility and in a timely manner. Increasing the geographical diversity of vaccine manufacturing capacity, so that all regions can take control of their health security, is important for achieving equitable access to vaccines for future pandemics.

Coordinating such networks and efforts will be critical if they are to deliver on their promise. A potential template for such coordination is being developed in Germany under the VAXMAN project, to which CEPI has provided advice and support. Since 2021, the German Vaccine Task Force and now the ZEPAI Center for Pandemic Vaccines and Therapeutics (at the Paul Ehrlich Institute) have been working to create a network of vaccine developers, manufacturers, CDMOs and suppliers. This VAXMAN project network may also supply emergency outbreak response vaccines both within and externally to the EU.

CEPI is also co-leading the Regional Vaccine Manufacturing Collaborative (RVMC), together with the US National Academy of Medicine under the convening power of the World Economic Forum. This initiative was launched at the 2022 World Economic Forum's Annual Meeting in Davos, in order to identify common needs, best practices, and facilitate the establishment of regional manufacturing efforts. RVMC has developed a global framework to help guide regional partners seeking to establish regionalized vaccine manufacturing and is now beginning to work with specific sovereign partners that are well positioned to lead such efforts.

**Question by MP Dr. Karamba Diaby: Refers to the importance of vaccine equity and local manufacturing capacity and the related infrastructure and the lessons learned from COVID-19 in this context. What is expected from parliamentarians/policy makers over the coming years? What are the main lessons learned with regards to international cooperation in the COVID-19 context? Main take aways for the cooperation with WHO and CEPI?*

The experience of COVID-19 saw both international collaboration to tackle a global challenge and self-serving behavior by high-income countries that resulted in significant disparities of access to COVID-19 vaccines that persist to this day. The rapidly established COVAX Facility supported the fastest and broadest vaccine roll-out in history but failed to eliminate these disparities.

Investment in preparedness *before* outbreaks and pandemic threats emerge will be critical to moving fast, equitably and at scale when they occur in the future – and to being positioned to achieve the admittedly ambitious goal of having new vaccines ready for first approval within 100 days. Investments will be needed in developing prototype vaccines against priority viral families that can be adapted quickly to a specific threat and with which regulators already have familiarity so they can make decisions more quickly; clinical trial networks, including in regions most at risk for the emergence of new pathogens, that are ready to pivot to test new vaccines; regionally diversified manufacturing networks that can flex to produce different vaccine products at scale; and financing mechanisms that can very rapidly mobilise at-risk funds for R&D and manufacturing scale-up when needed; and agreement on how

international, regional and country partners will work together end-to-end from R&D to delivery to respond to an emergency.

Obviously, the world is faced with many competing priorities – from climate change to the impact of conflicts. But the links between climate change, conflict and emerging disease outbreaks need to be recognized. Political leadership will be needed to maintain investments in pandemic preparedness and response capabilities between emergencies and the principle of equitable access to new medical countermeasures both before and during crises.

The Pandemic Accord, being negotiated through the WHO, provides an opportunity for member states to establish an international framework for pandemic preparedness and response that makes equitable access to medical counter measures a key commitment.

Policy innovation, sustained political commitment and investment will be vital to the world's ability to rapidly develop and manufacture vaccines at-scale against future threats and to enable equitable access to them where they are needed. Parliamentarians can play key roles:

- Advocating for and monitoring government investment in and enabling policies for pandemic preparedness and response capacity – sustained investment before outbreak and pandemic threats emerge is essential to responding quickly when they occur and avoiding the health, economic, social and political impacts of a pandemic.
- Ensuring that important investment in national and regional R&D programmes and production capacity also supports and is complemented by investment in global networking, multi-sector collaboration and the multilateralism needed to accelerate innovation and to prepare for and respond to *global* biological and health threats.
- Be bold in defining what equitable access is and how it is achieved. Institute policies that require public investment in outbreak and pandemic R&D to include provisions to support access to successful products. Be steadfast in the application and enforcement of such provisions.
- Ensure that policy development supports the free cross-border movement of medical counter measures and technology that contributes to the preservation of health security. Responsive policies on trade measures, harmonisation of response and health threat containment are required.
- Governments need to take a broader perspective on response than just vaccines. A strategic package of responses to further COVID-19 outbreaks should comprise a role for Diagnostics Therapeutics and Vaccines and non-medical countermeasures. This would provide for a more dynamic human health response and management of the impact on healthcare systems.
- Engage all constituencies in the formulation of health policy. The perspectives of CSOs and community health workers, amongst others, can facilitate the development of more robust and relevant health emergency policies.

**Question by MP Dr. Georg Kippels: The 100-days mission is ambitious. In the Covid-19 context, we had the opportunity to build on the existing, and multi-year research on and experience with mRNA-technology. CEPI refers to a pivotal paradigm shift to make the offering of a vaccine against a new pathogen within 100 days possible. Which*

key decisions are needed to realize this paradigm shift? Which of them have been taken already and which are still pending?

At the heart of the new paradigm is a fundamental shift towards preparedness. This shift towards preparedness would need to be a global effort with appropriate attention in both higher- and lower-income settings.

Our research has identified a number of key scientific and technological prerequisites that could underpin this paradigm shift: 1) the ability to develop a pathogen-specific vaccine during an outbreak by adapting previously developed and well-characterised prototype vaccines against closely related viruses; 2) the availability and readiness of global clinical trial infrastructure, standards and tools; 3) the ability to develop and use more rapid measures of vaccine-induced immune response and protection thereby shortening the time to determine trial outcomes; 4) an ability to rapidly manufacture and validate the first batch of experimental vaccines that are suitable for human use; and 5) the ability for early characterisation of the outbreak and pathogen.

Success will likely require advancements in the organisation, governance, and financing of global preparedness systems, and multiple, interconnected scientifically guided collaborative efforts. CEPI has a US$3.5 billion 5-year plan that lays out how we think CEPI can contribute to this global effort to reducet the risk of pandemics and epidemics. This plan will urgently address the critical remaining COVID-19 vaccine R&D gaps, including the ever-evolving threat of COVID-19 variants; and enable preparation to address future threats in a way which benefits the entire world. This 5-year plan is not yet fully funded and CEPI will continue working with partners to close this gap in funding.

**Questions by MP Knut Gerschau: How have the lessons learned from the epidemics Ebola and the swine flu been relevant (to the management of COVID-19)? The 100-days mission study refers to the further advancement and optimization of vaccine manufacturing. What could this exactly look like?*

The principal lesson from the 2013-2016 Ebola epidemic in West Africa was that opportunities to develop definitive Ebola countermeasures (particularly vaccines) in advance – countermeasures that could have stopped the epidemic in its tracks – were neglected, at great cost to the affected countries and to the world. More than 11,000 people died and the health care systems of Guinea, Sierra Leone, and Liberia suffered devastating losses, at an estimated global cost of more than USD 50 billion.

The 2009 pandemic ominously foreshadowed the challenges that the COVID pandemic presented, but because H1N1, the causative virus, was so mild, many of the lessons that should have been learned were not. The acute challenges of rapidly and equitably deploying novel vaccines to the world seen during the H1N1 pandemic prompted the early decision of CEPI and its partners WHO, Gavi, and UNICEF to establish the COVAX Facility. We remain deeply vulnerable to future influenza pandemics, with a manufacturing infrastructure for licensed vaccines that is inherently slow and not scalable, and we should anticipate dreadful shortfalls in vaccine if a much more lethal influenza pandemic caused by an agent such as H5N1 were to emerge. Improving our vaccine preparedness for flu by developing new vaccines on recently validated rapid response platforms such as mRNA should be an urgent priority.

CEPI itself is the manifestation of lessons learned from these epidemics. One of the principal reasons CEPI was created in 2017 was to prevent epidemics by developing safe and effective vaccines against

known infectious disease threats that could be deployed rapidly to contain outbreaks, before they become global health emergencies. CEPI was also created to shorten the time it takes to develop new vaccines to protect against viruses that emerge suddenly as public health threats – like COVID-19 – by capitalizing on innovations in adaptable vaccine technology and investing in facilities that could respond quickly to previously unknown pathogens. Meanwhile, global funding for Disease X countermeasures – including rapid response platform technologies – "rose tenfold between 2016 and 2020" according to the World Economic Forum. These prescient investments in preparedness meant, for example, that CEPI was able to rapidly pivot its portfolio of MERS coronavirus vaccine developers to work on developing a SARS-COV-2 vaccine in the first few weeks of the COVID-19 pandemic. Oxford and AstraZeneca, with CEPI support, similarly pivoted the ChadOx1 platform to develop a SARS-COV-2 vaccine that went on to be the most widely available and administered vaccine in the world by the end of 2021.

With respect to the 100-day mission, this is not something that a single country or organization can achieve alone. Success will require advances in the organization, governance, and financing of global-preparedness systems and the development of multiple interconnected, scientifically guided collaborative efforts. With respects to vaccine manufacturing such efforts must undergo a paradigm shift to focus on:

- Preparedness pre-100 days - requiring development of rapid response platforms, vaccine libraries, critical reagents, infrastructure, and partnerships across the manufacturing sectors.
- Reaction within the 100 days - requiring a shift following a disease outbreak trigger to rapidly advance prototype vaccines through clinical testing allowing early emergency use authorization, scale-up, manufacture, and supply.
- Roll-out post-100 days - requiring continued manufacture, release, continuing clinical efficacy evaluations and real world effectiveness monitoring, and intervention evaluation.

**Additional question by MP Tina Rudolph, posed to CEPI by email: Dr. Hatchett, you yourself made the statement at the height of the Covid-19 pandemic, as did your colleague Dr. In-Kyu Yoon a few months ago in a workshop at the World Health Summit. Namely, you said that it is important that governments should attach conditions to the allocation of public R&D funding - so-called access conditions - in order to actually be able to ensure, in case of doubt, that in the event of a next global crisis, sufficient vaccines are produced and made available to everyone everywhere in the world. Can you elaborate on why that's important, please?*

Elected officials have a clear primary duty to serve and protect their own populations. Securing access to products to protect their own populations is essential to protect those populations. No one would argue otherwise, and national governments play a vital role in securing access for their own populations by making investments in, for example, research and development, procurement and advance purchase agreements. Both before and during a crisis such investments are necessary to offset the risks that companies must take to develop new vaccines rapidly. That governments will take these risks provides a tremendous amount of leverage.

CEPI's proposal is that if elected officials making such investments use this leverage only to secure doses for their own country, and effectively turn over full control over products they have helped pay to develop to the private sector once local needs are met, they are underutilizing the leverage they have.

At CEPI, using the limited funds (less than USD 1.5 billion) we were able to raise at the beginning of the pandemic, we were able to secure dose or output commitments from supported partners of approximately 2 billion doses for COVAX (although not all of these commitments were realized).

By contrast, Operation Warp Speed in the United States invested approximately 10 times more than CEPI did but secured doses only for the U.S. population, because U.S. decision makers focused only on their own national needs. We would argue that they could have secured access to many hundreds of millions or even billions more doses for global allocation if they had included access provisions in their funding and purchase agreements such as a requirement to allow export, to provide a portion of manufacturing output to the global south, to agree to tech transfer technology to regional partners and otherwise support access to global populations in need. Procurement of which could have been handled by others (e.g., COVAX).

In the future, measures for equitable access in investment can be mandated through national legislation or serve as guidance for public funding of medical countermeasures as well as through individual funding agreements.

The G7 Pandemic Preparedness Partnership, the Global Preparedness and Monitoring Board and The Independent Panel for Pandemic Preparedness and Response, support individual action by governments and regional institutions through terms for funding research and development as well as procurement and advance purchase agreements terms. Moreover, equitable access measures have already been included in some agreements with private sector partners.

As innovations in research, development and manufacturing can only deliver real-world impact if they are made equitably accessible, it is important that governments attach broader, more globally focused access conditions to their investments, recognizing of course that the investing country should be the first beneficiary of any successful development programs.