

## New Vaccines Against Epidemic Infectious Diseases

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The vaccine-development response to the 2014 Ebola epidemic in West Africa, though a valiant effort, was too little, too late. Three vaccine candidates were tested successfully under challenging conditions.(1-3) Governments and foundations mobilized funds quickly. Companies and research-and-development institutions brought vaccine candidates into the field. Collaborations among the World Health Organization (WHO), funders, academia, civil society, and industry saw vaccines advancing through more than 15 accelerated clinical trials in a year. But the testing of Ebola vaccine candidates had previously stalled, though several candidates could have been ready for efficacy testing before the epidemic if the necessary investments had been made. In the absence of data on safety, immunogenicity, and dosing in humans, it was challenging to progress quickly with efficacy trials in West Africa. As a result, people who could have been protected instead became infected, and too many of them died. Moreover, there is no guarantee of similar risk-taking efforts in the future, especially given the poor market potential and the great clinical and regulatory uncertainties.

Vaccines can prevent outbreaks of emerging infectious disease from becoming humanitarian crises. The WHO recently deemed 11 pathogens as the most likely to cause severe outbreaks in the near future and will regularly update its list. There are feasible vaccine candidates for some of these diseases. When such candidates exist, timely vaccine development can avert global public health emergencies, contain loss of life, and limit social and economic damage. An efficient global system of vaccine research-and-development preparedness is needed. Since we generally have poor clinical vaccine-development pipelines for epidemic infectious diseases,(4) such diseases can emerge and spread faster than we can successfully develop vaccines. Platform technologies that

could reduce development times in an emergency are often not validated for human use in advance, which delays the start of clinical trials. Delays can also result from the time taken to reach agreement on appropriate clinical trial design, even when products are ready for testing. And regulatory pathways are not easily adaptable to epidemic contexts, especially in regions with weaker regulatory capacity and where outbreaks are more likely. Current vaccine-development efforts are fragmented, with no sustainable mechanism to support them across national borders and direct them toward global epidemic risks. Several countries have invested in research targeting prevention of the emergence and spread of pathogens likely to cause outbreaks that could affect them. But countries at the epicenter of outbreaks of emerging infectious diseases usually lack such research capacity. Vaccine developers end up spending their own resources to test products for epidemic conditions without any guarantee of risk sharing by governments seeking their help.

To address these problems, leaders from governments, foundations, industry, and civil society came together at the January 2016 World Economic Forum meeting in Davos, Switzerland, and agreed to explore new ways to drive vaccine innovation for high-priority public health threats. The meeting was inspired by a call for a new vaccine fund<sup>5</sup> and by proposals and expressions of interest from major vaccine manufacturers for new and dedicated partnership structures. It was supported by an emerging consensus from the 2015 Oslo consultation on Financing of R&D Preparedness and Response to Epidemic Emergencies and the process outlined in the WHO Research and Development Blueprint for creating a global financing facility for developing bio-medical countermeasures against emerging infections. Since the Davos meeting, more than 80 organizations and more

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than 200 individuals have collaborated to create the Coalition for Epidemic Preparedness Innovations (CEPI). Its mission is to stimulate, finance, and coordinate the development of vaccines against epidemic infectious diseases, especially in cases in which market incentives alone are insufficient.(5)

Between February and June 2016, CEPI convened three expert task teams to assess challenges and potential solutions for pathogen prioritization, clinical development, manufacturing capacity, and regulatory pathways; partnership models; and funding strategies. CEPI will initially focus on investments in essential gaps in product development, especially from late preclinical studies to proof of concept in humans (phase 2 trials); support for technical and institutional platforms that can be used for rapid vaccine development against known and unknown pathogens in the event of a new epidemic; partnership arrangements building on capabilities of advanced vaccine developers and manufacturers; and end-to-end coordination among stakeholders through plans to mobilize resources, manage and distribute stockpiles, and accelerate vaccine testing and approval during epidemics. Priority will also be given to contributions to finishing the job on Ebola vaccines. Building on the task teams' recommendations, CEPI has transitioned into a startup phase. An international nonprofit association has been founded by the governments of Norway and India, the Wellcome Trust, the Bill and Melinda Gates Foundation, and the World Economic Forum, and CEPI stakeholders are invited to become formal partners. An interim board and scientific advisory committee have been appointed. An interim secretariat is ensuring CEPI's launch, with functional nodes in Norway, the United Kingdom, and India.

CEPI plans to ensure the sustainability of its partnership approach by securing industry participation in collaborations in which the risks and benefits of vaccine development are shared and by supporting the development of regional capabilities for epidemic vaccine preparedness. To ensure achievement of public benefit, CEPI and its partners will need to agree to reasonable obligations for making investigational stockpiles and vaccines available in sufficient quantities in affected

territories and for setting prices as low as possible. Product costs should also be minimized through these risk-sharing arrangements.

A Joint Coordination Group was established in November 2016 to help align CEPI's efforts with those of other organizations in order to facilitate early development and to address clinical, regulatory, access, and manufacturing issues. CEPI will soon issue its first requests for proposals for funding, focusing on pathogens prioritized by its scientific advisory committee. We have already partnered with experienced vaccine manufacturers with global reach, members of the Developing Countries Vaccine Manufacturers Network, and vaccine biotechnology companies. We have accumulated expertise through our task teams and working groups and have benefited from the evidence generated through the WHO Research and Development Blueprint process. To succeed, we will have to continue to attract and retain a broad range of top experts and institutional champions.

Without cross-sector coordination or focus on timely vaccine-development capabilities, even the effort mounted against Ebola will be hard to replicate. We hope that CEPI's capabilities and partnerships will enable it to adequately address epidemic vaccine-development needs and help contain outbreaks quickly, providing a sort of global health insurance policy. We look forward to collaborating with all relevant actors to achieve these goals.

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