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RESEARCH PAPER

Vaccines for epidemic infections and the role of CEPI

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ABSTRACT
The author reviews the foundation of the Coalition for Epidemic Preparedness and Innovations and the choices it has made for funding of vaccine development against epidemic diseases. He comments on those decisions as well as proposing how CEPI could remain relevant for the long term.

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Whither CEPI? short term and long term development

Viruses and bacteria, like other organisms, are always trying to extend their host range by mutation and selection, as well as by adaptation to new hosts. Humans have witnessed this phenomenon ever since we have lived in organized settlements. Thus, recent outbreaks of Ebola and Zika viruses, as well as historical outbreaks of plague, West Nile virus, and SARS are not unexpected, and future outbreaks of pathogens now known and unknown are certain to occur.

The human responses to outbreaks of infectious agents include flight, quarantine, antibiotics, antivirals, control of vectors, and more recently vaccination. However, the development of vaccines is a long, complicated and expensive process, such that epidemics may be over by the time vaccines are available. The 2015–16 outbreak of Ebola virus in West Africa with its high death toll illustrates this point: vaccines became available only at the end of the epidemic, when the incidence was declining.

The need for a new way of doing things became obvious to many observers, including the author of this article.[1] By the end of 2015, several groups proposed the creation of a fund for development of vaccines against emerging pathogens, both those now known, and in anticipation of new ones. The need for a fund was underlined by the paradigmatic case of Zika, in that the virus was discovered in 1947 but despite its spread from Africa to Asia and Polynesia did not cause concern until its importation into Brazil, probably in 2013, where its clinical effects became notorious.[2,3]

A large part of the problem with regard to epidemic response relates to the vaccine industry and the process of vaccine licensure. Vaccine manufacturers must choose their targets carefully because the cost of development for a single vaccine ranges between half a billion and a billion dollars,[4] to which must be added the construction costs for a manufacturing facility. Much of this cost relates to the phase III trial that is normally necessary to demonstrate safety and efficacy in comparison to a placebo, and which allows licensure. Licensing authorities in the United States and Europe place a high bar of safety and efficacy for licensure. This is not a criticism, because the public demands that a product used in healthy people to avoid possible infection be free of serious side effects and also highly effective.

Aside from the cost of development, manufacturers face uncertainty as to whether once developed, a vaccine will be recommended and used. An example of this problem is meningococcal Group B vaccines, which seemed high on the priority list for development once vaccines against the other meningococcal serogroups were put into routine use, but when once developed, the enthusiasm of recommending bodies for the use of a Group B vaccine had waned.[5] The partial remedy for this type of situation may be Advanced Marketing Commitments, meaning that once licensed, a government would commit itself to recommend and purchase a particular vaccine. Of course, epidemiology might change in the interval between a commitment and licensure, as it did for Group B meningococcus,[6] in which case there is no mechanism for the manufacturer to be recompensed for the costs of development.

Recent history has seen the emergence and expansion of many new threats to public health, from AIDS to Zika. In some cases the agent had an animal reservoir from which it passed to humans via an arthropod vector, or there was a mutation that adapted the animal virus to humans. The former was the case for Zika and the latter was the case for HIV/AIDS and SARS.[7-9]

The remarkable although unsurprising fact is that once an agent is identified as a threat to humans, scientists always rush to attempt prophylaxis, whether through antibodies, drugs, or vaccines. However, moving from animal studies to human clinical trials is inhibited by both safety concerns and insufficient

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funds. Thus, possible preventive measures are rapidly developed but may not be licensed for lack of commercial interest or other sources of funding. There are many infections that have been known for years, but for which vaccine development is stalled for perceived lack of a market.

The WHO and other organizations have made lists of pathogens for which vaccine development is a priority, but there has been no mechanism for acting on those priorities. A central problem has been that the likely recipients of a vaccine against those pathogens will be in Asia and Africa, whereas the markets that enable an acceptable return on investment, as well as the competent regulatory authorities are largely in North America and Europe.

Market failure

A significant part of the difficulty in responding to epidemics of emerging diseases with vaccines is the vaccine industry itself. The high cost of vaccine development alluded to above means that marketing departments of vaccine companies are loath to recommend allocation of resources to a project unlikely to result in financial recompense, and markets of less than hundreds of millions of dollars annually are unattractive.

Moreover, the vaccine industry is constricted. Today there are only 4 transnational major manufacturers that have the resources to focus on research and development of multiple vaccines: GlaxoSmithKline, Merck, Pfizer and Sanofi Pasteur. There are also smaller organizations that are growing in size, such as Astellas, Astra Zeneca, Johnson & Johnson, the Serum Institute of India, and Takeda. There is a growing vaccine industry in China, Brazil, and India, as well as many smaller national companies, but by and large they do not spend large amounts of money on research vaccines. In any case, when an outbreak occurs even the larger companies must decide to deviate resources from more remunerative projects such as drugs to pursue vaccine development against the new target. Aside from the financial issue, switching personnel from more profitable projects is disruptive.

The origin of CEPI

The organization now called the Coalition for Epidemic Preparedness and Innovations (CEPI) came into being because in the light of Ebola and Zika there were multiple proposals to establish an international fund to develop vaccines against emerging epidemic infections.[10] The lists of such infections vary, but Table 1 gives a consensus of the most important. The basic idea of CEPI is that when there is a perception that the commercial market is insufficient to justify private investment in vaccine development against an emerging pathogen, that manufacturers be reimbursed for the production of candidates that can be taken through phases 1 and 2 to provide initial evidence for safety and efficacy, followed by the production and maintenance of a stockpile for emergency use [Table 2]. Inherent in this concept is that applicants must have a means of producing the candidate under Good Manufacturing Practice. In situations where a phase III trial is feasible owing to continued incidence of infection it would be done, although identification of a correlate of protection might be sufficient for confidence that the particular vaccine could be deployed in the event of an outbreak. Licensure might be obtained eventually if efficacy is confirmed in a phase III trial or if that is not feasible, by showing protection in 2 relevant animal models.

Table 1. Pathogens for which vaccines are needed selected by various organizations.

Recommended by all as first priority
Ebolavirus
Recommended by most for immediate development
Lassa
Nipah
MERS
Recommended for later development
Crimean-Congo Hemorrhagic Fever
Rift Valley Fever
Zika
Recommended by some for later development
Chikungunya
Coxsackie A16
Enterovirus 68
Enterovirus 71
Hepatitis E Virus
Marburg
Paratyphoid A
SARS
SFTS
Yersinia pestis

Organizations: Foundation for Vaccine Research, CEPI Scientific Committee, Norwegian Institute of Public Health, UK Vaccine R&D Committee, WHO

To select pathogens against which immediate vaccine development will be supported by CEPI, various lists have been proposed [Table 3]. One list put together by the Foundation for Vaccine Research was long and it is clearly not possible to attack all listed, although it had the virtue of completeness; another list put together by a WHO group was more restricted, but had the disadvantages of excluding bacteria and including pathogens for which vaccine candidates do not yet exist. Their defects, common to all lists, is that they cannot include a pathogen yet unknown that could emerge tomorrow. Another defect is that they focus on infections that are or have been epidemic, excluding those that are endemic but not yet prevented by vaccination.

An important aspect of CEPI's mission is to create stockpiles for emergency use. This is not as easy as it sounds, since those stockpiles must be properly maintained over years with demonstration of stability, requiring periodic replenishment; rules must be established for the use of vaccine from the stockpile, perhaps without the vaccine having been licensed; and epidemics may require urgent expansion of production, for which arrangements must be made in advance. Regulatory issues for the use of CEPI-produced vaccines are still unsettled.

Table 2. Stages of development supported by CEPI.

Immunogenicity and safety in mice
Protection in relevant animal challenge model
GMP production, validation of methods – CEPI
Toxicity studies
Phase I
Phase IIa
Phase IIb – if possible
Stockpile
Conditional approval for emergencies – CEPI
Phase III
Licensure

Table 3. Prioritization of pathogens by different groups.

WHO	NIPH	FVR
• Crimean-congo hemorrhagic fever	• Ebolavirus	• Ebola hemorrhagic fever virus
• Filovirus diseases (i.e., EVD & Marburg)	• Hepatitis E virus	• Lassa hemorrhagic fever virus
• Highly pathogenic emerging coronaviruses relevant to humans (MERS Co-V & SARS)	• Enterovirus 71	• Marburg hemorrhagic fever virus
• Lassa Fever	• West Nile virus	• MERS coronavirus
• Nipah	• Chikungunya virus	• SARS cornoavirus
• Rift Valley Fever	• Marburg virus	• Crimean-Congo hemorrhagic fever virus
• R&D preparedness for a new disease	• Yersinia pestis	• Chikungunya virus
• Chikungunya	• Rift valley fever virus	• Nipah virus
• Severe fever with thrombocytompenia syndrome	• SARS-CoV	• Hepatitis E virus
• Zika	• MERS-CoV	• Zika virus
	• Lassa virus	• Entervirus 71
	• Nipah virus	• Enterovirus 68
	• Coxsackievirus A16	• Coxsackievirus 16
	• Crimean-Congo hemorrhagic fever virus	• Paratyphoid A (Salmonella enterica)
	• SFTS virus	• West Nile virus
	• Zika virus	• Rift Valley fever virus
	• Enterovirus 68	• Plague (Yersinia pestis)

All of this means that CEPI must be a real organization, with a leader, a staff, a sufficient budget, and a continuing mission that must not fade in the temporary absence of an epidemic. Memories are short, whereas funding must be regular and uninterrupted. It should be remembered that despite the disruption caused by the SARS outbreak it was insufficient to generate new mechanisms, leading to a lack of preparedness for the West African Ebola epidemic, to say nothing of MERS and Zika. Fortunately, multiple governments and philanthropic organizations have contributed at least 800 million dollars to launch CEPI, as announced on January 19, 2017.[10]

Platforms

With regard to possible outbreaks of agents yet unknown, it would be desirable to have platforms that can be readily used for rapid development of vaccines, even if those vaccines are temporary stopgaps while better prophylactics are developed. Two general classes of platforms suggest themselves at this juncture: nucleic acids and vectors [Table 4]. DNA plasmids are readily developed from viral sequences and although they are better at inducing cellular responses than antibody responses, recent improvements have made them attractive in emergencies.[11] RNA vaccines of different types are less advanced but commercial development is moving rapidly and ultimately they may offer advantages.[12]

Table 4. Platforms that might be made constantly available for unforeseen epidemics.

DNA Plasmids
mRNA (self-applifying)
VSV vector
Measles vector
Animal adenoviruses vectors
MVA vector

On the vector side there are multiple possibilities, although at this point 4 vectors are obvious candidates: vesicular stomatitis virus,[13] measles virus,[14] animal adenoviruses,[15] and vaccinia mutants.[16] Many of these approaches were used to develop candidate vaccines to prevent Ebola Zaire strain infections. Efficacy in humans could be demonstrated with the VSV vector before the West African epidemic subsided, and the other platforms have shown protection in non-human primates.

A question that CEPI will have to answer is how many of these platforms should be maintained in a state that would allow them to respond urgently to a new pathogen? Or to put it another way, will manufacturers using these platforms be willing to immediately move personnel and facilities to a project responding to an urgent health problem? Note that better surveillance may identify outbreaks when they are small, with less terror and disruption than that seen with Ebola. It may be necessary to contract with manufacturers to maintain the readiness of platforms and to divert resources toward synthesis of vaccines against new pathogens at the request of CEPI. The maintenance of these platforms should permit at least rapid development of stopgap vaccines, while not excluding vaccines developed by other technologies.

The short term: Filoviruses and chikungunya

Memories are short and needs for financial support are many. My view is that CEPI must have rapid successes early on, or funders will lose interest. The Scientific Advisory Committee of CEPI has given priority to fund efforts to develop vaccines against Filoviruses, MERS, Nipah and Lassa. No one can doubt the importance and relevance of these diseases to the concept of CEPI, but one can doubt the ease of vaccine development.

The success of the VSV vectored Ebola Zaire vaccine in human trials implies that vaccines can be made against the other related filoviruses, and there is general agreement that protection should be ensured against at least Ebola Sudan, Bundibugyo, and Marburg viruses.[17-19] However, unless fortuitous outbreaks occur we will be unable to demonstrate the efficacy of those other filovirus vaccines except by determination of correlates of protection in 2 relevant animal models or by analogy to human responses to Ebola Zaire vaccine. It is not yet clear how CEPI will choose among the many filovirus candidate vaccines.

In the case of MERS, it appears clear that the Spike glycoprotein of coronaviruses, and particularly its receptor binding domain, is the best target for a vaccine, although cellular immunity may be important.[20-26] Also, SARS and MERS teach us that animal coronaviruses may be infectious from human to human and that new coronaviruses are evolving. However, as MERS appears to be an infection of young dromedaries a fair question is should we develop and deploy a veterinary vaccine to prevent exposure and infection of humans.[27,28] A veterinary vaccine would be much easier and faster to develop.

Nipah is a paramyxovirus, and therefore the target antigens are the F and G proteins. Multiple candidate vaccines exist, but all are in the preclinical stage. The most advanced is a vaccine

against the related Hendra virus that is cross-protective against Nipah and VSV vectors for Nipah have shown promise in animals.[29-32] Passive protection with antibodies has also been successful in experimental studies. Although a vaccine is probably feasible, problems may arise as they have with vaccine development against another paramyxovirus, respiratory syncytial virus.

Lassa virus is an arenavirus, and a vaccine already exists for another arenavirus, Argentine Hemorrhagic Fever.[33] However, there appear to be multiple distinct strains of Lassa.[34] Moreover, passively administered antibody doesn't work[35] and protection against arenaviruses is mediated through cellular immunity.[36,37] The vaccine world has little experience with vaccines that depend on T cell responses to protect, the exceptions being vaccines against tuberculosis and zoster. That fact creates the need for extensive safety studies to show that unwanted cellular immune responses are not also evoked.

Thus, the first targets chosen by CEPI are certainly ones for which vaccines are needed, but except for the filoviruses, for which efficacy has been demonstrated, one may doubt that success will be achieved with lightning speed. In contrast, the mosquito-borne Chikungunya virus suggests itself as an easier target, with multiple candidates in far advanced development. Chikungunya has spread from Africa to around the world, including to the Western Hemisphere in 2013, and in the process picked up a mutation that allows it to infect *Aedes albopictus* as well as *Aedes aegypti*.[38] It is far from benign, causing residual arthralgia in about half of those infected and a chronic rheumatoid arthritis-like syndrome in 5%.[39,40] Among the factors that make vaccine development relatively easy is the fact that Chikungunya is an αvirus with a genome that synthesizes envelope proteins against which antibodies are typically effective.[41] Although there are multiple lineages of the virus, depending on geography, there is only one serotype. Moreover, years ago formalin-inactivated and attenuated Chikungunya vaccines were developed and shown to induce neutralizing antibodies in humans. Those antibodies were protective in multiple models, including primates.

In contrast to some other pathogens, the cupboard of Chikungunya candidate vaccines is full. A list of already developed candidates, probably incomplete, is given in Table 5. At least 4 vaccines have been tested in humans, and at least 17 others have shown promise in animals.[41-48] The most advanced are a virus-like particle vaccine using the envelope proteins;[49,50] 2 live, attenuated vaccines (one of which is a recombinant with another αvirus); and a measles-vectored Chikungunya envelope.[51] Neutralizing antibodies at a level of 1/10 have been shown to be the correlate of protection.[52] The VLP vaccine and the measles-vectored vaccine have both been tested in phase 2 trials. If a review of those results by CEPI were satisfactory, manufacture of stockpiles could be immediately financed, and given a supply of vaccine, trials could be done in countries where Chikungunya is endemic. Thus, CEPI could quickly show its abilities and value for the world.

Note that with Chikungunya or any other disease, if a candidate not supported by CEPI appears to have a faster track to licensure, funding could be terminated. In all cases, CEPI will have to carefully assess the field to avoid inhibiting competing candidates.

Another relatively easy target is West Nile Virus.[53] This infection started in Africa, spread to North Africa, Europe and eventually the United States, where it migrated from New York City to virtually the entire country through mosquito-borne infection of birds, from which vector mosquitoes could transmit the virus to humans.[54] Although the incidence of West Nile Virus has decreased recently, presumably because the reservoir has diminished due to death of many infected birds and post-infection immunity in others, there were still over 2,000 cases in the US in 2015. Moreover, chronic sequelae of the infection in humans have recently been identified involving premature deaths of previously West Nile infected individuals.[55] This shows that survival is not always unaccompanied by consequences.[56] Moreover, it appears that transmission can occur between mosquitoes during multiple bites, lessening the possibility of viral extinction.[57]

Military strategy teaches us to attack weak points of an enemy, not the strongly defended ones. Mortality is easy to measure, and I do not suggest that death due to MERS, Nipah, or Lassa isn't a major disability (!), but strategically it may be desirable for CEPI to attack an easier target first rather than a highly fatal disease if the candidate vaccines are uncertain to work. A practical step would be to replace MERS with Chikungunya and to use a veterinary vaccine approach to control MERS.

The long term — Emerging pathogens

All of the lists of pathogens for which vaccine development is needed have relied on current epidemiology. Let us suppose that CEPI is successful in developing and stockpiling vaccines for the known epidemic agents. Is there a role for continued existence of CEPI?

I submit that science is progressing to the point where prediction of epidemic potential is possible. To make this claim I rely on the work of several groups of theoretical biologists, who

Table 5. Chikungunya candidate vaccines.

Phase 2	VLPs
	Measles vector
Phase 1	Formalin inactivated
Preclinical	Envelope proteins
	Chimeric alphavirus
	Live, attenuated
	VSV (live) vector
	Chimp adeno vector
	MVA vector
	DNA plasmids (several)

Nota bene: Neut titers $\geq$ 1/10 are a good correlate of protection

Table 6. Viruses isolated from bats (selected).

Rabies	Duvenhage
SARS	Sindbis
Hendra	Nipah
Ebola	VEE
Marburg	Rift Valley Fever
Tacaribe reovirus	Kyasanur flavivirus

Table 7. The five stages through which pathogens of animals evolve to cause diseases confined to humans. Virtually all animal-derived human pathogens arose from pathogens of other warm-blooded vertebrates, primarily mammals plus in two cases (influenza A and ultimately *falciparum* malaria) birds. Primates constitute only 0.5% of all vertebrate species but have contributed about 20% of our major human diseases. (Adapted from Ref. 62.)

Stage	Characteristic	Example	Transmission to Humans	Reproductive Number
1	Only in animals	Foot and Mouth Disease	Present only in animals	Ro = 0
2	Primary infection	Rabies	Only from animals	Ro = >0
3	Limited outbreak	MERS	From animals	Ro = <1
4	Long outbreak	Ebola	Bats (?), then human-to-human	Ro = 1
5	Exclusively humans	Measles	Only human-to-human	Ro = >1

have studied multiple pathogens that have reservoirs in bats or are transmitted by mosquitoes. The inherent mutability of genomes of RNA viruses which may allow those viruses to adapt to humans is important to keep in mind in this regard. Ebola is a good example of this. The divergence of the West African virus from the Central African virus occurred about 2004, presumably in the primate population. The closest virus sequence to that found in the West African epidemic from a human case was that from the 2007 epidemic in the Democratic Republic of the Congo, 7 y before the human epidemic in Guinea started in 2014.[58] Rapid accumulation of genetic variation was seen in the Ebola virus genomes. I don't think we know if the West-African virus is better adapted to humans than the Congo virus, but that is possible.

However, we know that increases in Ro, the reproductive number, often accompanies genetic changes, resulting in an increase in outbreak size. Arinamipathy and McLean have compared the outbreak size for an agent with an Ro of 0.1 and an agent with an Ro of 0.9.[59] Even though the latter is less than 1, many more outbreaks will occur with that increase in infectivity.

Cross-species transmission is exemplified by the origin of HIV. Many primates carry simian immunodeficiency lentiviruses related to HIV. Crossover to humans has apparently happened 4 times, leading to several different clades of HIV 1 and also to HIV2. HIV-1 Clade M has been the best-adapted to humans.[60]

Innumerable agents have been isolated from bats, as shown in Table 6. Carriage by bats is suspected to be at the origin of many epidemic viruses, including notably rabies and Nipah, and their biology, which includes hibernation and torpor leading to extended incubation times, permits survival of infectious agents. Coronaviruses and filoviruses may also be derived from bats, SARS being an example.[61]

Other mammals can be carriers of both RNA and DNA viruses. These agents may become adapted to humans through occasional infections. Table 7 shows 5 stages of adaptation to humans proposed by Wolfe et al.[62] These levels of adaptation are influenced by the factors listed in Table 8, which include whether they are already adapted to primates, whether they already have a broad host range, whether they mutate readily, the absence of host barriers, the transmission route, and of course the virulence of the agent in the host species.[63] These are traits that make certain viruses more likely to cause disease in humans. Another factor that increases the likelihood of epidemic spread are the height and duration of virus replication in human hosts.

Certainly, our ability to predict which viruses will adapt to humans is far from perfect, and rapid or so-called punctual adaptation may defy prediction, but on the other hand gradual adaptation is predictable by the increasing size of outbreaks, a phenomenon which was observed with Ebola-Zaire.[64]

A list of viruses known or suspected of being transmissible has been proposed by Mark Woolhouse and collaborators at the University of Edinburgh and is shown in Table 9.[65] Obviously, this list exceeds the lists of targets that have been proposed by various organizations. Note that the ability of a virus to spread may depend on a change in route of transmission. An example of this is HIV, which apparently spread from a chimpanzee in the Cameroun through exposure to SIV in blood infecting a wound in a human, whereas between humans it spreads mainly by the sexual route,[8] which has allowed the virus to become epidemic.

What we need, then, is heightened surveillance for small outbreaks of agents that do not currently attract much attention. Such surveillance could be undertaken by WHO based on electronic reporting from around the world. If such surveillance could be organized, then CEPI could establish a DNA plasmid library of those agents, which would enable rapid development of at least DNA vaccines and rapid translation to other types of vaccine platforms. As a result there would be less chance of being surprised by a large outbreak of an unknown agent, and a faster development of candidate vaccines against such an agent.

In addition to viral diseases, there are several uncontrolled bacterial and parasitic diseases, which have been largely ignored by CEPI. The former include various species of salmonella, including paratyphoid organisms,[66] whereas the latter include schistosomiasis and leishmaniasis.[67,68] Perhaps an even better example in relation to the need for a vaccine is the recent discovery that the cryptosporidia protozoa are a common cause of infantile diarrhea, second only to rotavirus.[69]

Table 8. Virus traits potentially relevant for capacity to emerge and cause disease in human populations (modified from Ref. 65).

Trait	Definition
Reservoir host relatedness	Viruses derived from primate species
Height and duration of virus replication	Increases exposure
Virus host range	Viruses with a broad host range are of greater concern
Evolvability	Higher substitution rates make it easier to adapt to human hosts
Transmission route	Certain transmisssion routes are more infectious
Virulence	Determines whether a virus causes mild or severe disease in humans
Host-virus coevolution	Lack of a shared evolutionary history is associated with higher virulence

Table 9. Viruses (n = 37) that are known or suspected of being transmissible (directly or indirectly) between humans but to date have been restricted to short transmission chains or self-limiting outbreaks (modified from Ref. 65).

Genome, virus family	Virus name
Single stranded RNA (ambisense)	
Arenaviruses	Guanarito, Junin, Lassa, Lujo, Machupo, Sabia, Dandemong*, lymphocytic choriomeningitis*Single stranded RNA (ambisense)
Bunyaviruses	Andes, Bwamba, Crimean-Congo Hemorrhagic fever, Oropouche, Rift Valley, severe fever with thrombocytopenia syndrome
Single-stranded RNA (positive sense)	
Flaviviruses	Japanese encephalitis,* Usutu,* West Nile*
Coronaviruses	Middle East respiratory syndrome
Togaviruses	Bamah Forest, o'nyong-nyong, Ross River, Semliki Forest, Venezuelan equine encephalitis
Single-stranded RNA (negative sense)	
Filoviruses	Bundibugyo Ebola, Lake Victoria Marburg, Sudan Ebola
Paramyxoviruses	Nipah
Rhabdoviruses	Bas-Congo, rabies*
Double-stranded RNA	
Reoviruses	Nelson Bay, Colorado tick fever*
Double-stranded DNA	
Adenoviruses	Titi monkey
Herpesviruses	Macacine herpesvirus 1
Polyomaviruses	Simian virus 40
Poxviruses	Monkeypox, Orf, vaccinia

*human transmission of these viruses is known only by iatrogenic or vertical routes

I would argue that if the mission of CEPI is to create vaccines for diseases that do not interest industry because those vaccines are not likely to be profitable, then that mission should be extended into the long-term future to include infections that are prevalent or that if rare, have the potential for increased infectiousness to humans. The lists that CEPI, WHO and other organizations began with were limited to diseases already known to be threats to human health. If we use more of the tools of modern biology those lists could be expanded to include other agents and therefore to justify the extension of CEPI over the long-term future to act as a worldwide safeguard against an unanticipated epidemic of an agent not yet well known. This is a worthy long-term goal for this fledgling organization.

Conclusion

Isaac Newton famously said "if I have seen further it is because I stand on the shoulders of giants." CEPI stands on the shoulders of numerous scientists, on the shoulders of vaccine manufacturers and on the shoulders of WHO. However, neither vaccine developers, nor manufacturers nor WHO can accomplish what CEPI can do if it learns from the past, sets the right targets for the present and looks far into the future.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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