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EDITORIALS

Developing a vaccine against Zika

We've made a good start but substantial challenges remain

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The race to develop a vaccine against Zika began in February 2016, when the unusual clustering of cases of microcephaly and other neurological disorders associated with Zika virus infection led to the declaration of a public health emergency of international concern. When the World Health Organization held its first consultation in March, 14 active vaccine projects had already been announced.[1] Today, WHO's pipeline tracker counts about 30 active projects, pursued by developers from endemic and non-endemic countries, private and public sector.[2]

Such a jump start in vaccine development is rare, and several candidates have already progressed to clinical development. This pace is facilitated by our collective experience in developing vaccines against flaviviruses, the availability of novel vaccine technologies that greatly facilitate manufacturing of vaccines appropriate for trials in humans, and generous funding from some governments to support both basic research and product development.

However, there is no guarantee that the pace we have seen in early development will continue for the clinical evaluation of vaccine candidates, nor that the technical feasibility of developing a vaccine will ultimately result in products capable of effectively protecting the public. To overcome such difficulties WHO established the Research and Development Blueprint for Action to Prevent Epidemics.[3] This framework sets out to guide the preclinical and clinical development of vaccines, diagnostics, and therapeutics for various priority diseases, including Zika.[3] The blueprint builds on lessons learnt from the Ebola epidemic, where substantial delays occurred as stakeholders sought consensus on the best path forwards and tried to establish the necessary agreements. It aims to minimise delays and uncertainty. Providing guidance on development of Zika vaccine candidates is the first test of this blueprint.

At the March 2016 consultation, WHO proposed that priority should be given to developing vaccines to protect women from developing Zika disease during pregnancy, which could prevent microcephaly and related pathologies in newborn infants. In the following months WHO, Unicef, and other partners developed a target product profile (TPP) for Zika vaccines for use in an emergency context.[4] The TPP describes the minimal and preferred characteristics of a product destined for a specific public health purpose. Although it is not a regulatory document, it describes performance characteristics that are both technologically achievable and able to fulfil a public health function. The aim of the TPP is not to narrow the scope of scientific work but to direct the scientific, regulatory, and public health communities to priority characteristics.

Developing the TPP for Zika vaccine was challenging, mostly because we have a limited understanding of the epidemiology of the infection and the relative importance of different routes of transmission. Safety is paramount because the priority target group is women of childbearing age and some women may already be pregnant when vaccinated. Pregnancy has repercussions for most suitable vaccine technologies. The TPP may be revised as our understanding of the epidemiology, disease, and disease modulating factors evolves.

Regulatory implications exist for all new vaccines, especially if they build on technologies that are not used in existing "routine" vaccines, and it's still too early to identify a definitive regulatory strategy for any new Zika vaccine. A continuous dialogue is needed between developers, regulators, and public health professionals to identify how best to achieve rapid, robust, safe, and evidence based licensing.

The design of trials testing new Zika vaccines, including choice of outcomes, is another key consideration. WHO has established a process to develop generic annotated trial protocols for priority diseases,[5] including Zika.

Although the WHO blueprint provides a framework for identifying what a Zika vaccine should aim to achieve, and establishing mechanisms and partnerships to test candidate vaccines, WHO is not directly involved in the development of vaccine candidates. This is being done by various public and private entities, most notably in the US, Brazil, and India. The

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recently set up Coalition for Epidemic Preparedness Innovations (www.cepi.net), a new alliance to finance and coordinate the development of new vaccines to prevent epidemics, might also be well placed to participate.

Should a future Zika vaccine be used only during outbreaks to protect women of childbearing age and their babies, or should it be incorporated in routine vaccination programmes? We won't know the answer until we have more detailed information on the evolving epidemiology of the virus, the risk and scale of neurological outcomes, and the level of herd immunity induced by a first wave of infection. Development of a Zika vaccine started well, but all players need to keep up the momentum if a vaccine is to become a reality within the next three to five years.

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3 WHO. A research and development blueprint for action to prevent epidemics. 2016. http://www.who.int/csr/research-and-development/en/
4 WHO, Unicef. Zika virus vaccine target product profile for emergency use. 2016. http://www.who.int/immunization/research/meetings_workshops/WHO_Zika_vaccine_TPP.pdf?ua=1
5 WHO. Designing a vaccine efficacy trial during public health emergencies: progress in developing adequate study designs. 2016. http://www.who.int/csr/research-and-development/consultations/chamonix-meeting/en/