WHO DRAFT Target Product Profile:
A vaccine to protect against congenital Zika virus syndrome in neonates, for use during an emergency

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Proposed regulatory strategy for expedient availability of a ZIKV vaccine

- WHO’s aim is to enable availability of a safe, effective vaccine to priority populations, as soon as possible
- Initial development efforts should focus on generating data to support emergency use authorization or accelerated approval, considering the risk:benefit ratio in that particular context
- Development efforts and generation of data that will support conventional licensure, also need to be considered
- This TPP focuses on defining the characteristics of a ZIKV vaccine for emergency use

Timeline of ZIKV vaccine development

World Health Organization
WHO’s Product Development for Vaccines Advisory Committee (PDVAC) oversees activities related to global vaccine R&D including TPPs

- WHO Zika TPP will allow funders, manufacturers and other stakeholders to take into account WHO preferences in their development decision-making

- A PDVAC working group of subject matter experts was established in April 2016 to develop a TPP for a Zika vaccine for use during an emergency

- The draft was posted for public consultation from the 4th - 23rd May 2016

- SAGE members had the opportunity to comment

- Extensive comments from 15 organizations/individuals were received and considered

The TPP focuses on vaccines characteristics for priority populations, during an emergency.

- The TPP prioritizes prophylactic vaccination as a strategy to prevent or reduce congenital Zika virus syndrome in neonates.
- Immunization of women of child-bearing age is considered to be of highest priority.
- Although not the explicit target population, some women may receive the vaccination who are not aware they are pregnant.
- Whilst men contribute to disease transmission and are a target population, they may not be prioritized in the context of constrained resources or vaccine supply.
- Once a vaccine is available, recommendation for use is made by SAGE.
**Indication:** prevention of Zika virus-associated clinical illness

- Clinical illness refers to a virologically-confirmed case of symptomatic ZIKV illness, as defined by WHO/PAHO

- Prevention of clinical illness, and not ZIKV infection has been retained, considering:
  - Practicality of detecting ZIKV infection in the high proportion of asymptomatic carriers, and the short period of viraemia
  - Sterilizing immunity has not been achieved for other effective flavivirus vaccines

- Does not include prevention of congenital abnormalities and GBS as an indication, but will be assessed as AESIs in clinical studies and post-licensure

**World Health Organization**
Platform technologies: safety and speed of development (as well as efficacy!) are of primary consideration

• WHO does not intend to discourage the development of replication competent approaches, or novel platforms for ZIKV vaccine development
  – However, in the context of an emergency situation, non-replicating platforms, that have no documented safety concerns and for which related vaccines have been licensed, are likely to be faster to authorization/approval

• Safety and reactogenicity must be at least comparable to other WHO-recommended routine vaccines

• Absence of data may not preclude the exceptional use during pregnancy or in lactating women during an outbreak
  – Therefore platforms that may be contra-indicated will not be prioritised.
Measures of efficacy: Demonstration of prevention of virologically confirmed ZIKV illness

- VE target of 80% accepted. Need to consider minimal VE criterion.
- If feasible, the vaccine should demonstrate efficacy against a well-defined clinical endpoint (virol. confirmed ZIKV illness) in a placebo controlled study.
- However, immunological end-points may be considered if:
  - demonstration of clinical efficacy is unfeasible
  - an acceptable analytically validated immunologic correlate or surrogate of protection is identified (requires availability of preclinical disease models)
  - In this context, vaccine effectiveness studies will be needed.
- Reduction in congenital abnormalities and the effect on GBS will be considered exploratory outcomes, assessed post-licensure.
- A vaccine with impact against transmission is highly desirable although is not a prerequisite in the emergency use scenario.
Dose regimen and duration of protection: ...complexities of cross reactivity with other flaviruses

- Single dose, administered i.m. or s.c. preferred, but up to 2 doses (1mo apart) is acceptable
- Co-administration with other vaccines is not required for emergency use
- Protection for at least 1 year required in an emergency scenario, but multi-year protection is preferred
- If booster doses are required, must be no more frequent than annually or at time of new outbreak
  - It may be necessary to infer duration of protection, and therefore appropriate timing of a booster dose, from immune response kinetics.
  - Recommend measurement of neutralising antibody titres to ZIKV and other flaviviruses, pre- and post-vaccination, over extended follow up, to evaluate the need and timing for booster doses in primed individuals.
Product presentation, storage and stability

• A liquid formulation in mono-dose or multi-dose (5-10) presentations with a maximal dosage volume of 0.5mL for i.m. or s.c. administration is preferred.
• Shelf life of at least 24 months at -20 °C, or preferentially above, and demonstration of at least 6 months stability at 2-8°C is desired.
• Lyophilised doses of 1mL for i.m. and s.c. administration is acceptable, with a shelf life of at least 6 months at -20 °C, and stability for at least 6 hours at 2-8°C.
Feasibility of manufacture and supply

- Process and yield scalable to produce at least 100 million doses per year.
- Capacity and flexibility available to manufacture vaccine as expeditiously as possible following scale-up.
- Dosage, regimen and cost of delivery amenable to high volume and affordable supply
Next steps...

• To consider the TPP in the context of the regulatory considerations at this meeting
• To potentially revise, and then finalise the ZIKV vaccine TPP for emergency use and make this publically available by the end of June 2016
• To develop an accompanying position paper on regulatory considerations for the emergency use TPP
• To revise the TPP and proposed regulatory considerations as appropriate, with the emergence of new data.