WHO/UNICEF Zika Vaccine TPP and vaccine landscape

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What is a WHO vaccine TPP?

- Developed with input from **external independent experts** and a **broad consultative process**.

- Provides **technical guidance as to WHO’s criteria** in response to **emergency** or **epidemic** scenarios.

- Developed when there is a **commitment to accelerated vaccine development** and **rapid direction** is needed.

- Allows funders, manufacturers, and other stakeholders to take into account **WHO preferences** in development decision-making.

- Intended to **reduce the timeline** between vaccine licensure and introduction into countries that have the greatest need.

Public Health Objective

The public health objective in the emergency/outbreak context is the prevention of congenital ZIKV syndrome through the protection of pregnant women throughout the duration of their pregnancy.

Vaccination of women of reproductive age, and/or vaccination of women during pregnancy
# Format for WHO Zika vaccine TPP

<table>
<thead>
<tr>
<th></th>
<th>Preferred</th>
<th>Minimally acceptable/Critical</th>
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<tbody>
<tr>
<td>Indication</td>
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<td>Target Population</td>
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<td>Contraindications</td>
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<td>Platforms</td>
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<td>Safety/reactogenicity</td>
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<tr>
<td>Measures of efficacy</td>
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<td>Dose regimen</td>
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<td>Durability of protection</td>
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<td>Route of administration</td>
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<td>Stability and storage</td>
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<td>Co-administration</td>
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<tr>
<td>Presentation</td>
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</table>

None of the characteristics in the tables dominates over any other. Therefore should a vaccine’s profile be sufficiently superior to the minimal characteristics under one or more categories, this may outweigh deficiencies in meeting another specific minimal characteristic.
Key Points: Target population

Minimal/Preferred: Females of reproductive age*, and males of the same ages

– If supply limited, vaccination would be prioritized to women of reproductive age, which may include pregnant women, as this group is considered at high risk

*including adolescent and pre-adolescent girls 9 years of age or older
Key Points: Contraindication

Minimal/Preferred: No contraindication for use during pregnancy or in lactating women

– Theoretical risk may not preclude the exceptional use during pregnancy or in lactating women during an outbreak

– Immunization advisory groups may recommend vaccination of pregnant women with due consideration of risks and benefits

– Women who are unknowingly pregnant may be vaccinated, as screening with pregnancy tests is considered infeasible during an emergency campaign
**Key Points: Vaccine Platform**

**Preferred:** Non-replicating platforms, platforms with licensed human vaccines, inactivated / virus-like particle / subunit vaccines are preferred from the safety perspective given the potential exposure of pregnant women; **alum** adjuvants.

- Likely to be faster to authorization/approval

**Minimal:** Single-cycle replicating vector platform, replication-competent vaccine platform, **novel technologies**, non-alum adjuvants

- with acceptable safety data, including from pregnancy (e.g. inadvertent use)
Key Points: **Measures of efficacy (1)**

**Preferred:** Demonstration of prevention of virologically confirmed ZIKV illness in 80% of the population or higher.

- Based on assumption that prevention of illness also reduces the risk of infection of the fetus

- Evidence of prevention of infection also desirable

- Assumed that effectiveness against the longer term sequelae of GBS and congenital ZIKV syndrome will only be possible to assess post-authorization
Key Points: Measures of efficacy (2)

**Minimal:** Immunological surrogate in >70% of vaccination population.

- If surrogate established through animal models or cohort studies, likely ZIKV-specific neutralising antibody titre
- May play important role if demonstration of clinical efficacy is infeasible
- Vaccine effectiveness would then need to be demonstrated as a follow-up commitment
- Pending study approval by regulatory authorities, data from a controlled human infection model may complement immunogenicity data
### WHO Vaccine Pipeline Tracker

- Trial registries
- Literature reviews
- Outreach to developers
- Public meeting reports

<table>
<thead>
<tr>
<th>Coordinating Center</th>
<th>Status</th>
<th>Platform</th>
<th>Technology</th>
<th>Trial Phase</th>
<th>Start Date</th>
<th>End Date</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>In Proc</td>
<td>WWV</td>
<td>mRNA</td>
<td>Phase 2</td>
<td>Nov-16</td>
<td>Sep-17</td>
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<tr>
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<td>WWV</td>
<td>mRNA</td>
<td>Phase 2</td>
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<td>Nov-16</td>
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</table>

Note: The table above summarizes the status of vaccine trials as of the specified dates.
WHO Vaccine Pipeline Tracker

45 candidates in “development”

Distribution of Candidates in WHO Tracker

Subunit N=18
- Protein
- DNA
- RNA

Whole Virus N=27
- Inactivated
- Non-replicating
- Replicating

Slide adapted courtesy of D. Kaslow

http://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/
https://docs.google.com/spreadsheets/d/19otvlNcayJURCMg76xWO4KvuyedYbMZDcXqbyJGdcZM/pubhtml#
Clinical ZIKV Vaccine Development Pipeline – June 2016
Clinical ZIKV Vaccine Development Pipeline – June 2017

Phase I
- GLS-5700
  GeneOne / Inovio
- ZIKV PIV
  WRAIR / BIDMC / NIAID / Sanofi Pasteur
- mRNA-1325
  Valera Moderna
- MV-Zika
  Themis Bioscience
- AGS-v
  SEEK / NIH
- BBV121
  Bharat Biotech

Phase II
- VRC ZIKV DNA
  VRC / NIAID

Phase IIb

Phase III

Registration

Nucleic Acid
- Inactivated
- Peptide
- Live attenuated (recombinant)
# Overview of Clinical Candidates

<table>
<thead>
<tr>
<th>Platform</th>
<th>GLS-5700</th>
<th>VRC DNA</th>
<th>PIV</th>
<th>mRNA-1325</th>
<th>MV-Zika</th>
<th>AGS-v</th>
<th>BBV121</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA</td>
<td>DNA</td>
<td>Inactivated</td>
<td>mRNA</td>
<td>Viral Vector</td>
<td>Synthetic Peptide</td>
<td>Inactivated</td>
<td></td>
</tr>
</tbody>
</table>

### Published Preclinical Data

1. Immunogenic in NHP, protection post-challenge against death, reduced viral load in mice
2. Immunogenic and protection post-challenge against virema in NHP
3. Immunogenic and protection post-challenge against virema in NHP
4. None found

### Most Advanced Phase

<table>
<thead>
<tr>
<th>Study Locations</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 1</th>
<th>Phase 1/2</th>
<th>Phase 1</th>
<th>Phase 1</th>
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<td>US, Puerto Rico</td>
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<td>Austria</td>
<td>US</td>
<td>India</td>
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### Primary Completion Dates

Biggest challenge: uncertainty

• **Clinical outcomes**
  – How do viremia, clinical illness, and severe outcomes correlate?
  – What is the full spectrum of clinical illness? Are there other priority risk groups?

• **Zika epidemiology**
  – How can clinical benefit be established?
  – What is the burden of / risk of Zika in Africa? In Asia?
  – Is there endemic transmission or sporadic outbreaks?

• **What will be the future need for a Zika vaccine?**
  – What will be the global demand of a Zika vaccine?
Thank you!

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