Options for UNICEF’s engagement in outbreak vaccine R&D & supply: Zika Virus and beyond
Outline

I. Background
II. Zika epidemiology and vaccine R&D
III. Objectives, challenges and possible models for UNICEF engagement
Background
UNICEF’s interest in outbreak vaccine R&D grows out of three sources:

1. Increasing importance of emergency preparedness and response in UNICEF’s overall strategy, as codified in the Health Emergency Preparedness Initiative (HEPI)

2. The HEPI R&D component led by Supply Division

UNICEF’s engagement in Zika R&D to date

- Joint WHO/UNICEF Zika vaccine and diagnostic TPPs
- Industry consultation on Zika diagnostics and vaccines, May 2016
- Initial demand modeling
- Presentation at last year’s vaccine industry consultation (VIC)
- Zika diagnostics APC tender
Changes in context since last VIC

- Dramatic waning of LAC outbreak
- Increased uncertainty about future outbreaks
- BARDA decision on inactivated Zika vaccine candidate
- CEPI launch, pathogen prioritization, initial approach
- Inclusion of Zika in Gavi Vaccine Investment Strategy selection process
Framework for UNICEF R&D engagement (health products)

- Epidemiology
  - Mortality & morbidity
  - UNICEF priorities
  - Available control tools

- Scientific basis
  - Market prospects
  - Status of current pipeline
  - Desired product & market characteristics

- Objectives of intervention
  - UNICEF’s tools & resources
  - Industry decision-making

Need & impact

- Is the disease a major public health threat? Is it a UNICEF priority?
- Would the product have a large impact on disease burden or risk in UNICEF countries?
- Are alternative control or prevention interventions available?

R&D prospects & obstacles

- Is development of the product scientifically feasible?
- Is it likely to come to market without additional intervention?
- Is it likely to have appropriate characteristics and be available at affordable prices in UNICEF countries?
- What are the main obstacles to availability of an appropriate product?

UNICEF opportunities

- What are the market interventions available to UNICEF?
- At what scale could UNICEF hope to implement them?
- Does UNICEF have a comparative advantage in intervening?
- Are these interventions likely to overcome obstacles to availability of an appropriate product?
Zika epidemiology and vaccine development
Zika overview

Flavivirus transmitted by Aedes mosquitoes (as YF, JE, DEN, WN). Until recently, not considered a significant public health threat.

Zika outbreak in LAC

More than 200,000 confirmed cases so far; 3,400 cases of congenital syndrome.
Where might Zika go next? Vectors present in much of tropics.

But some evidence of previous exposure/possible immunity in much of SSA, Asia

Zika virus seroprevalence in countries with evidence of Zika virus infection in humans prior to 1 April 2007

Biggest question: Are there large regions vulnerable to an outbreak on the scale of the LAC outbreak?

Epidemiological scenarios

1. Prolonged lull
   LAC outbreak ends, no new large outbreaks for at least 10 years.

2. Endemic transmission with significant morbidity
   No large outbreaks, but endemic transmission in SSA, LAC, or elsewhere is shown to constitute a public health problem.

3. Regular localized outbreaks
   Sporadic outbreaks at the level of cities or subnational regions, similar to dengue pattern

4. New large outbreaks
   Outbreaks on national or regional scale in Africa or Asia

Initiatives addressing vaccines for outbreak diseases, including Zika, must somehow accommodate this uncertainty.
Zika vaccine development
WHO/UNICEF TPP for emergency use

<table>
<thead>
<tr>
<th>Vaccine characteristic</th>
<th>TPP</th>
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<tbody>
<tr>
<td>Target population</td>
<td>Women of reproductive age</td>
</tr>
<tr>
<td>Contraindication</td>
<td>No contraindication for use during pregnancy</td>
</tr>
<tr>
<td>Measure of efficacy</td>
<td>Demonstration of prevention of ZIKV illness</td>
</tr>
<tr>
<td>Duration of protection</td>
<td>More than 1 year</td>
</tr>
<tr>
<td>Vaccine platform</td>
<td>Non-replicating preferred</td>
</tr>
<tr>
<td>Dose regimen</td>
<td>Single dose preferred</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Injectable, IM or SC</td>
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<tr>
<td>Stability and storage</td>
<td>At least 12 months at -20 and 6 months at 2-8</td>
</tr>
<tr>
<td>Presentation</td>
<td>Liquid, single or multi-dose</td>
</tr>
</tbody>
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Considerations not included in TPP
- Price/manufacturing cost
- Length of production cycle/speed of scale up
Zika vaccine R&D: status and obstacles

Current status
• Six candidates in safety trials; many others at earlier stages
• Many platforms, promising preclinical data
• Substantial push funding, from US government and others

Possible obstacles
• Demonstration of safety in pregnant women
• Risk of interaction with other flaviviruses (dengue)
• Withdrawal of donor support
• Lack of incidence for efficacy trials
• Uncertain or inadequate market
  o Market could be large, in the event of an outbreak, but highly uncertain.

UNICEF can help with other obstacles, but a UNICEF incentive would primarily address market challenges.
Options for UNICEF engagement
Potential objectives of UNICEF intervention

1. Prepare for rapid late-stage development and scale-up when an outbreak occurs

2. Incentivize adaptation for countries served by UNICEF of a vaccine mainly developed for other (HIC) markets

3. Ensure adequate supply of vaccine to UNICEF in the event of an outbreak

4. Promote long-term competition
Challenges

1. Epidemiological uncertainty
   - Will a vaccine be needed? When, where, and in what quantity?
   - Will efficacy trials be possible?

2. Incentive size: Can UNICEF create an incentive large enough to influence vaccine developers?
   - If there’s a new outbreak, UNICEF’s intervention may not be necessary
   - If concern recedes, intervention might have to be very large

3. Defining institutional roles
   - UNICEF’s appropriate role relative to others (WHO, CEPI, Gates, USG, Gavi)? Engagement should be based on comparative advantages.

Approach must incorporate epi uncertainty. Engagement will require partnership.
Instruments that UNICEF could deploy to influence R&D

• Demand signaling (unfunded): TPPs, expressions of interest

• Demand forecasting, help with pilot introduction, stimulating uptake in other ways

• Advance purchase or market commitments

• Upstream incentives: procurement of R&D services?

UNICEF SD’s comparative advantage is in pull incentives linked to procurement
Potential for complementarity with push funders (e.g. CEPI, Gates, BARDA, NIH)
Specific options under consideration

Two forms of purchase commitment, which could be combined to create a tiered mechanism.

Notes:
- Options could apply to other outbreak vaccines
- Implementation would almost certainly be in partnership.
A. Advance purchase commitment for a vaccine stockpile

Objectives:
• Secure specified number of doses for stockpile
• Send signal about product characteristics

Approach:
• Advance commitment to purchase vaccine for a stockpile, using funds set aside in advance for this purpose
• Commitment would be hard: Would depend only on regulatory approval/prequalification and attainment of technical specifications, not on demand.

Approximate size of commitment: $US 10-20 million
B. Larger conditional commitment

Objectives:
• Influence product characteristics
• Encourage establishment of supply capacity for UNICEF market

Approach:
• Advance commitment to purchase vaccine in an outbreak
• Commitment would be conditional: triggered by outbreak

Approximate size of commitment: $US 50-500 million, drawing on conditional commitments from donors (binding commitments to make funding available in the event of an outbreak, with predefined criteria)
Next steps

- Further design work on APC structures
- Consultations with industry
- Discussions with partners on roles and comparative advantage
Questions
EXTRA SLIDES
Potential Zika vaccine demand (excludes Americas)

Demand could be very large. But extremely uncertain: depends on epidemiology and use.

Commercial interest will depend critically on US, travelers’ market, UMIC countries.