Plenary Session 2: Landscape
Vaccine Thermostability

Next-Generation Vaccine Delivery Technology Meeting
Geneva, Switzerland

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**Thermostability & immunization goals**

**Increase coverage...**
- by stocking vaccines at facilities that do not have cold chain equipment

**Improve efficacy and safety...**
- by decreasing probability of administering vaccines that are not potent or harmful

**Reduce System Cost...**
- by decreasing waste due to heat & freeze exposure
- by decreasing cold chain footprint
- by reducing cold chain complexity

**Improving thermostability is critical to achieve immunization goals**
We have identified and investigated a range of technology options that may offer improved heat stability, including:

<table>
<thead>
<tr>
<th>Technologies</th>
<th>Details</th>
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<tbody>
<tr>
<td>Heat stabilization</td>
<td>Addition of excipients to increase stability of existing vaccines on market</td>
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<tr>
<td>Re-labeling</td>
<td>No change in formulation; can require clinical trials to create label that reflects Vx thermostability</td>
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<tr>
<td>Freeze</td>
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<tr>
<td>Bulk freeze</td>
<td>Freezing liquid solutions to form more stable dried powders via a lyophilization process (which includes freezing &amp; sublimation)</td>
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<tr>
<td>Spray freeze</td>
<td>Atomizing liquid solutions and drying droplets via heat to create a more stable powder</td>
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<tr>
<td>Spray</td>
<td></td>
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<tr>
<td>Bubble</td>
<td>Converting solution into micro particles that can be dried through warm carrier gas</td>
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<tr>
<td>Foam</td>
<td>Forming a dry foam through desiccation under a vacuum and evaporation of solvent</td>
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<tr>
<td>Microspheres</td>
<td>Various types of antigen encapsulation or coating mechanisms to minimize degradation and / or provide thermostability</td>
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<tr>
<td>Nanoparticles</td>
<td></td>
</tr>
<tr>
<td>Microcrystals</td>
<td></td>
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<tr>
<td>Silk proteins</td>
<td></td>
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<tr>
<td>Sugar glassification</td>
<td></td>
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</table>
However these technologies are not applicable to all vaccines.

<table>
<thead>
<tr>
<th>RI HEAT STABILITY</th>
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<tbody>
<tr>
<td>Heat stability at 40C (unless noted below)</td>
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</tbody>
</table>

**Rota**

- **Short-term**
  - <5 yrs
  - 14 days
  - Freeze-dry: ~2 months @ 40-45°C
  - Spray dry: 14 days

- **Long-term**
  - >6 months @ 40-45°C

**IPV**

- **Short-term**
  - No technologies showing promise of >2 month heat stability

- **Long-term**
  - 14 days
  - Lyophilized IPV: ~6 months @ 37°C

**Pneumo**

- Stability would require maintaining stability of all 10/13 serotypes
- May require clinical bridging

**Penta**

- Requires stabilization of all five components, with HiB most challenging
- D, T, and wP assays would need complete revamp

Additional work needed to understand:
- Technical feasibility
- Incentives to encourage mfgs.

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1 Based on Rotarix (GSK); VVM for Rotatet currently unavailable (as of May 24, 2013, WHO)
2 Based on Hilleman Labs spray dry of Rotatet: No loss of potency at 40-45C
3 Based on Hilleman Labs lyo formulation; Potential for additional thermostability with testing
4 Refers to liquid formulation (SSI VVM = 7 days, GSK VVM = 14 days)
5 Six months without loss for type 2 and 3; 10-20% loss for type 1, at 37C; Stand-alone only

**As there are multiple manufacturers of each vaccine, stability improvements would need to be made across the board to ensure good market dynamics**

SOURCE: WHO, PATH, expert interviews
CampaigNS/special strategy vaccines can benefit more easily from thermostability, but more work is needed to unlock this value.

35-45% savings projected in Chad due to leverage of a CTC

Modeled savings for MenA campaign by region

<table>
<thead>
<tr>
<th>Region</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chari</td>
<td>0.28</td>
<td>0.13</td>
</tr>
<tr>
<td>Baguirmi</td>
<td>0.16</td>
<td>0.28</td>
</tr>
<tr>
<td>Mayo</td>
<td>0.26</td>
<td>0.15</td>
</tr>
<tr>
<td>Kebbi Est</td>
<td>0.20</td>
<td>0.16</td>
</tr>
<tr>
<td>N’Djamena</td>
<td>0.20</td>
<td>0.13</td>
</tr>
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</table>

Current Collaborations
- Yellow fever –
- Birth dose HepB
- Cholera –
- HPV –

Proposed Collaborations
- Additional studies to validate existing stability for measles, MR, TT vaccines
- Defining benefits from increasing thermostability of other maternal vaccines (HepB, TT, flu)

Industry collaborations for CTC migration already underway, with opportunity for more

A range of other issues also need to be addressed
- Improving market incentives to make CTC development an attractive business decision,
- Continuing pilots to demonstrate benefits of CTC migration to drive behavior change
- Need for development of a dual peak/threshold VVM
- Addressing regulatory issues to match product label with actual stability

SOURCE: “Economic benefits of leveraging the true stability of vaccines: The case of Meningitis A in Chad”
Way Forward: Our investments need to be targeted and evidence based

3 priority issues emerge to enable success long-term:

- **Building increased thermostability into the development path for all priority vaccines in development**, to reduce wastage and provide flexibility in use cases.
- **Take advantage of existing thermostability**
- **Making seed investments in proven technologies for specific vaccines** (e.g., rota and IPV) – managed risk;
- **Stay focused on broader immunization coverage and cost effective ways to achieve outcomes** – other delivery technologies; cold chain technology and assess their ability to achieve stability for the full portfolio.