Development of a more affordable IPV

Objective of area-of-work

Affordable IPV
- achieve GPEI target of affordable IPV (~$0.5/immunizing dose)
- develop alternative intradermal delivery technologies for house-to-house campaigns

Safer-for-production IPV
- develop further attenuated IPV strains to enable "safer" production with reduced containment
- Ultimately, develop non-infectious production processes (i.e., packaging cells, VLPs) which may eliminate containment
**Current and anticipated prices**

IPV price per dose (US$)

- **Current lowest price**: 2.25 - 2.50
- **Volume purchase for GAVI**: 1.0 - 1.5
- **Gap**: 0.5
- **Post-endgame Target**: 0.5
# Affordable & safer-for-production IPV

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Approach</th>
<th>Description</th>
<th>Likely availability</th>
<th>Expected dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affordable IPV</td>
<td>Adjuvant</td>
<td>Adjuvant (e.g., aluminum) to reduce antigen</td>
<td>2016-17</td>
<td>2-3 fold</td>
</tr>
<tr>
<td>ID IPV</td>
<td>Intradermal administration for dose-sparing</td>
<td>2014</td>
<td>5 fold</td>
<td></td>
</tr>
<tr>
<td>Process optimization</td>
<td>Improve production yield with alternative media (e.g., ACF) or cell-line (e.g., Per C6)</td>
<td>2016-17</td>
<td>2-fold (with ACF) to 4-5 fold (with Per C6)</td>
<td></td>
</tr>
<tr>
<td>Safer-for-production IPV</td>
<td>Sabin IPV</td>
<td>Sabin strain</td>
<td>2012-18</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Alternate IPV strains</td>
<td>Further attenuated strains</td>
<td>2020~</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>VLPs</td>
<td>Virus-like particles</td>
<td>2020~</td>
<td>NA</td>
</tr>
</tbody>
</table>
Affordable IPV: Alum adjuvant

- Previous pre-clinical & clinical studies with Sabin- and Salk IPV suggest that alum adjuvant could achieve a 2-3-fold dose sparing effect.

- At least two IPV producers are working on optimization and development of aluminum adjuvant-IPV (with preliminary results in 2014).

- This may not be sufficient to achieve $0.5/dose price target, but could be important in some countries (e.g., self-suppliers).
SAGE concluded, "studies of a fractional intradermal IPV dose appeared very promising" and recommended to "fast track ID IPV immediately" (April 2012)

SAGE WG noted that ID is the only near-term option to achieve the price target ($0.5/dose) (June 2013)
Intradermal delivery options

- Current ID delivery [syringe&needle] represents significant operational issues:
  - Logistical and programmatic challenges (e.g., training)
  - Significant burden on healthcare providers and infants (e.g., time and pain)

- To make ID delivery feasible for campaign use, alternative delivery approaches will be needed:
  - Outbreak control and catch-up campaign use
  - Routine (e.g., low-cost option for some countries)
Highest priority: Label-change to allow ID delivery

- Two NRAs confirmed that a non-inferiority study in adults (w/ one dose boosting) would potentially be sufficient for a "boosting indication"
- WHO will sponsor such a trial in Q4 2013-Q1 2014
  - Protocols have been reviewed and approved by NRAs & manufacturers
  - Permission process for trial implementation
- A label change is feasible in 2014 (if trial data supportive)
### ID development: A step-wise approach

<table>
<thead>
<tr>
<th>Description</th>
<th>Adapter &amp; ID needle</th>
<th>Needle-free jet injector</th>
<th>Microneedle patch</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>&quot;Low hanging fruits&quot; (some already licensed)</td>
<td>ID Devices are ready for licensure after optimization</td>
<td>Enables house-to-house campaign use</td>
</tr>
<tr>
<td></td>
<td>Can be used in RI and the campaign</td>
<td>Provide more options for outbreak response</td>
<td>Requires extensive development and production scale-up</td>
</tr>
<tr>
<td></td>
<td>Price comparable to N&amp;S</td>
<td>Pre-filled cartridge may enable HtH campaign but it requires label change of IPV</td>
<td>Self-administration or volunteer use</td>
</tr>
<tr>
<td></td>
<td>Requires trained health workers</td>
<td>Requires restrained health workers</td>
<td>2016-17</td>
</tr>
<tr>
<td><strong>Timeline</strong></td>
<td>2014-15</td>
<td>2015-16</td>
<td>$0.5-1.0</td>
</tr>
<tr>
<td><strong>Price</strong></td>
<td>$0.1-0.2</td>
<td>$0.3-0.5</td>
<td><em>Excluding vaccine cost</em></td>
</tr>
</tbody>
</table>
**Intradermal IPV: licensed ID adapters**

**ID adapter (West Pharma)**
- Guides the angle and depth of penetration
- No extra dead space
- Usability study with adults is available

**MicronJet 600 (Nanopass)**
- Array of 3 microneedles, mounted on a regular syringe
- Multiple studies with flu; CDC clinical trial in Bangladesh

**Solvivia (BD)**
- Glass,prefillable microinjection system for ID vaccination
- Licensed in EU for flu vaccine by Sanofi (ID flu)

**ID needle and syringe (Star)**
- Glass microinjection system for ID vaccination
- GMP product will be available in November 2013
Jet Injectors: Selected devices in Cuba study

ID Pen (Bioject)

Tropis (Pharmajet)

Biojector2000 (Bioject)
Microneedle patch options
Microneedle patch: Target product profile

Pre-requisites
• Self-administration or volunteer use (no trained healthcare worker needed)
• Improved heat stability
• [Availability of pre-clinical data (e.g., vaccines, drugs)]

Preferable
• Simpler to use
  – No sharp wastage
  – No applicator
• Affordable cost (<$0.5)
• GMP material available in short-term (12-18 months)
• Investment requirements reduced (i.e., GMP-production facility available)
Microneedle patch: Development pathway

**Supply of IPV bulk**
- 2013: Bulk
- 2014: Supplier A (Test), Supplier B (Test), Supplier C (Test)
- 2015: Ph I/IIa
- 2016: Non-inferiority

**Production of GMP material**
- 2017: Scale-up/Establish a commercial line*

**Clinical study**
- Path agreed

**Registration**

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* Could be done either at IPV supplier site or patch producer
<table>
<thead>
<tr>
<th>Description</th>
<th>sIPV Development</th>
<th>Alternate Strains</th>
<th>Virus-Like Particles</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sIPV Development</strong></td>
<td>IPV produced from Sabin strains</td>
<td>IPV produced from genetically modified strains (&quot;safer than Sabin&quot; strains)</td>
<td>Stabilized poliovirus capsid</td>
</tr>
<tr>
<td><strong>Alternate Strains</strong></td>
<td>Safer-to-produce, lower containment requirements</td>
<td></td>
<td>No containment required</td>
</tr>
<tr>
<td><strong>Virus-Like Particles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Progress to date</strong></td>
<td>Japanese NRA licensed 2 products</td>
<td>PRC selected NIBSC strain for evaluation by Intravacc (May '12)</td>
<td>University of Leeds demonstrated technical feasibility</td>
</tr>
<tr>
<td><strong>First product available</strong></td>
<td>WHO/Intravacc completed phase I/IIa and technology transfer is ongoing</td>
<td>PRC developed evaluation criteria for the other strains</td>
<td>Currently evaluating multiple production system</td>
</tr>
<tr>
<td>2013-4 (China)</td>
<td></td>
<td>2020~</td>
<td>2020~</td>
</tr>
<tr>
<td>2017~ (Others)</td>
<td></td>
<td></td>
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Conclusions

- The development of affordable IPV is necessary to achieve the ultimate GPEI price target ($0.5/dose) & to allow volunteer use of IPV for campaign use.
- Substantial progress in developing affordable & "safer-for-production" IPV
  - Regulatory pathway for IPV label change to include ID for a "booster indication".
  - Adjuvant optimization studies are underway, and the results will become available in 2014-15.
  - Preliminary results from production process optimization may enable a production of full-dose IPV at ~$0.5/dose
  - Different options for safer IPV production are under evaluation.
Thank you for your attention!