Strategies for Affordable IPV

Manufacturer's Meeting, Geneva, 30 October 2008

Research and Product Development Team, Polio Eradication Initiative, WHO, Geneva
Presentation Overview

• Background
• Strategies for "affordable" IPV
  – Reduce number of IPV dose in schedule
  – Reduce antigen: Fractional dose use
  – Enhance immunity of IPV: Adjuvant use
  – Optimize production processes
  – S-IPV for developing country production
• Develop of alternative seed strains as a longterm strategy for "safe" IPV production
• Conclusions
Prerequisites for OPV Cessation

1. Wild virus certification & containment.
2. Global surveillance & notification.
3. mOPV stockpile & response.
4. Affordable IPV & use in poliovirus-retaining countries.
5. Synchronization of OPV cessation.
IPV Schedule Assessment
# Seroconversion After 2 or 3 doses of IPV, Puerto Rico and Cuba

<table>
<thead>
<tr>
<th>Country</th>
<th>6-10-14 weeks</th>
<th>2-4 mos</th>
<th>2-4-6 mos</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puerto&amp; Rico</td>
<td>86% P1</td>
<td>97% P3</td>
<td>97% P1</td>
<td>100% P2</td>
</tr>
<tr>
<td></td>
<td>86% P2</td>
<td></td>
<td>100% P2</td>
<td>99% P3</td>
</tr>
<tr>
<td>Cuba*</td>
<td>94% P1</td>
<td>90% P1</td>
<td>0% P1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>83% P2</td>
<td>89% P2</td>
<td>0% P2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100% P3</td>
<td>90% P3</td>
<td>0% P3</td>
<td></td>
</tr>
</tbody>
</table>


Poliovirus Isolation after tOPV Challenge, by Study Group, Cuba, 2003

INACTIVATED POLIOVIRUS VACCINE IN CUBA

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Infants</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Any Type of Poliovirus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>% (95% CI)</td>
<td>No.</td>
<td>% (95% CI)</td>
<td>No.</td>
</tr>
<tr>
<td>A</td>
<td>52</td>
<td>10 (10–33)</td>
<td>45</td>
<td>87 (74–94)</td>
<td>5</td>
</tr>
<tr>
<td>B</td>
<td>54</td>
<td>9 (8–29)</td>
<td>48</td>
<td>89 (77–96)</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>72</td>
<td>13 (10–29)</td>
<td>67</td>
<td>93 (85–98)</td>
<td>10</td>
</tr>
</tbody>
</table>

* All stool samples taken from study participants just before the challenge dose were negative for poliovirus. Exact confidence intervals (CIs) are based on the binomial distribution.

† Group A received a combination of diphtheria–pertussis–tetanus vaccine, *Haemophilus influenzae* type b vaccine, and inactivated poliovirus vaccine (DPT-Hib-IPV) at 6, 10, and 14 weeks of age. Group B, the control group, received a combination of DPT vaccine and Hib vaccine at 6, 10, and 14 weeks. Group C received the DPT-Hib-IPV combination at 8 and 16 weeks.

‡ Mean values are given for excretors of poliovirus.
Studies on Routine IPV Schedules

• Cuba1 (sp combination vaccine):
  – 2-dose schedule 2 + 4 mos ~90% for each serotype
  – 3-dose schedule 6, 10, 14 wks ~ 83-100%
  – Modest decrease (1/2 log10) in excretion in IPV groups following tOPV challenge

• Puerto Rico2 (sp IPV):
  – 3 dose schedule 6, 10, 14 wks ~ 80-90%
  – 3 dose schedule 2, 4, 6 mos almost 97-100% for each serotype

Fractional IPV Dose
Seroconversion After 3 IPV Doses at 6, 10, and 14 Weeks, Country A, 2006-2007

<table>
<thead>
<tr>
<th>Type of Poliovirus</th>
<th>Seroconversion, %</th>
<th>ID n=188</th>
<th>IM n=179</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>53.2%</td>
<td>89.4%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td>85.1%</td>
<td>95.5%</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Type 3</td>
<td>69.2%</td>
<td>98.9%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
## Seroconversion After IPV at 2, 4 and 6 Months, by Study Arm, Country B

<table>
<thead>
<tr>
<th></th>
<th>ID n=187</th>
<th>IM n=186</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poliovirus type 1</td>
<td>98.4%</td>
<td>100%</td>
<td>0.25</td>
</tr>
<tr>
<td>seroconversion, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliovirus type 2</td>
<td>95.7%</td>
<td>100%</td>
<td>0.004</td>
</tr>
<tr>
<td>seroconversion, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliovirus type 3</td>
<td>97.9%</td>
<td>100%</td>
<td>0.06</td>
</tr>
<tr>
<td>seroconversion, %</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Studies on Fractional Dose IPV

• **Safety:**
  – Only minimal severity local adverse events associated with needle-free jet injector
  – No serious adverse events attributable to trial intervention

• **Immunogenicity:**
  – Fractional dose IPV given intradermally at 2, 4, 6 mos virtually comparable to full dose IPV intramuscular
  – Fractional dose IPV given intradermally at 6, 10, 14 weeks suboptimal because of maternal antibody effect

• **Parental survey:**
  – Overwhelming preference for intradermal route – "baby doesn't cry"
Adjuvant Use
Adjuvants for IPV

- Often combined with DTP → higher immunogenicity
- FDA, NIBSC, manufacturers, others, have evaluated different adjuvants
- Project to evaluate new adjuvants, including "oil and water emulsion" in wIPV (IVR & IDRI Seattle)
- Adjuvants also evaluated as part of the Sabin-IPV development project with NVI
1,25-Dihydroxyvitamin D3 Enhances Systemic and Mucosal Immune Responses to Inactivated Poliovirus Vaccine in Mice

Optimizing Production Processes
Optimizing Production Processes

- Current production process developed in the 1950s and revised in the late 1960s
- Sabin-IPV project offers the opportunity to review and all aspects of IPV production
- Assessing cell densities, "suspended" cell lines (VERO) in Sabin-IPV project
- Project to evaluate alternative inactivation methods ($\beta$-propriolactione)
Production of S-IPV by Developing Country Manufacturers
Developing Country Production

- Interest by a number of vaccine manufacturers in the developing world to produce S-IPV
- Large countries appear to be especially interested in producing S-IPV, incl. China, India and others
- To produce S-IPV safely, prospective manufacturer need to make **substantial capital and human resource investments** to meet not only the GMP but also the containment requirements for S-IPV
- Production in developing countries could lead to **substantial reductions in cost** of S-IPV production
Alternate Seed Strains for IPV Production

• Ultimate objective is be able to produce IPV safely under lower or no bio-containment requirements
• Prospective strains would potentially not replicate in humans (only in tissue culture)
• 4 research groups working on these strains
• This is a longterm project with a time horizon of ~10 years
Conclusions

• A number of strategies are being pursued to make S-IPV affordable for developing country use

• Some strategies may be more promising and will be followed-up, others may be discontinued if results not supportive

• To make IPV affordable, GPEI need only few successful strategies
Thank You for Your Attention!