Outline

- Polio Epidemiology, VDPVs and current vaccines
- Why new products
- Pipeline
- Some thoughts on mRNA vaccines for Polio
Types of Polioviruses

Wild (WPV)
- Type 1 (still circulating in Pakistan and Afghanistan, with risks of exportations worldwide)
- Type 2 (certified as eradicated)
- Type 3 (certified as eradicated)

Vaccine derived polioviruses (VDPV) (from OPV)
- VDPVs are mutated Sabin (OPV vaccine) polioviruses
- Most become circulating VDPVs (cVDPVs)
- Epidemiology, neurovirulence and control measures for VDPVs is similar to wild polioviruses
- VDPV may emerge in immunodeficient persons (iVDPVs)
**Polio Vaccines**

**Inactivated Polio Vaccine (Salk)**
Killed virus administered by injection
1955
Problem: manufactured with live virus; low impact on mucosal immunity

**Oral Polio Vaccine (Sabin)**
Live weakened virus
1961
Problem: VDPVs – novel OPVs under development and use
Why new products?

Current products (IPV and OPV): Strengths
- Regulatory: licensed and PQd
- Availability: currently adequate supply through UN supply and WHO stockpile
- Acceptance: long history with well accepted safety and effectiveness

Current products: Weaknesses
- IPV: no mucosal immunity, live virus needed for manufacturing (containment)
- OPV: VDPVs, live virus needed for manufacturing (containment)

Treatment for chronic poliovirus excretors under development (antivirals, monoclonal antibodies)
Issues to be addressed with new products

cVDPVs:
- Increase genetic stability of OPVs to Reduce / avoid cVDPVs
- Use vaccines without live virus (CAVEAT: mucosal immunity)

Containment:
- Produce vaccines without using live virus

Chronic Excretors:
- Produce treatments that reduce / eliminate shedding
## Pipeline

<table>
<thead>
<tr>
<th>Products</th>
<th>Issue to be addressed</th>
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<tbody>
<tr>
<td><strong>Vaccines</strong></td>
<td></td>
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<tr>
<td>nOPV2 (used under EUL)</td>
<td>cVPDPVs, containment, could replace OPV2</td>
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<tr>
<td>nOPV1&amp;3</td>
<td>cVPDPVs, containment, could replace OPV1&amp;3</td>
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<tr>
<td><strong>Virus-Like Particles (VLPs)</strong></td>
<td>Long process however best non-infectious option at present to replace IPVs</td>
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<tr>
<td>sIPV (licensed)</td>
<td>containment</td>
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<tr>
<td>S19</td>
<td>Containment, could replace IPVs</td>
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<td><strong>Monoclonal Antibodies</strong></td>
<td>Chronic excretors</td>
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<tr>
<td><strong>Antivirals</strong></td>
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<tr>
<td>Pocapavir</td>
<td>Chronic excretors</td>
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<tr>
<td>V7404</td>
<td>Chronic excretors</td>
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Currently no mRNA vaccine in pipeline. Brainstorming phase
Some thoughts on mRNA for Polio

Positive:
- Manufacturing capacity available
- Manufacturers seek to extend portfolio
- Potentially short development timescales

Challenges:
- Poliovirus RNA contains 7433 nucleotides
- Whole capsid needed as antigenic entity, in situ assembly
- Reactogenicity
- Duration of protection