Two IPVs in Japan
- Salk vs. Sabin

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History of OPV and reported polio cases in Japan

Introduction of OPV by mass campaign (1961～)

Mass vaccination campaign of OPV for all the children with excellent achievement

Routine immunization of OPV (1964～)

(Reported Polio cases)

(Reported Polio cases)

(year)
Between 1960’s and 1990’s, Sabin live vaccine largely replaced Salk killed vaccine everywhere in the world.

However, because the live virus in the vaccine occasionally became strong enough to cause actual disease, Salk killed-type vaccine has replaced the live type in the United States, and also other countries.
### Milestone of the introduction of IPV in Japan

<table>
<thead>
<tr>
<th>Year</th>
<th>IPV</th>
<th>OPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958</td>
<td>Pilot production of Salk cIPV</td>
<td>Japan Live Poliovaccine Research Commission established</td>
</tr>
<tr>
<td>1960</td>
<td>Large-scale production of cIPV</td>
<td>Importation of tOPV from USSR and Canada for mass immunization campaign</td>
</tr>
<tr>
<td>1961</td>
<td>Introduction of cIPV for routine immunization</td>
<td>Mass immunization campaigns with imported mOPV and bOPV</td>
</tr>
<tr>
<td>1962~1963</td>
<td></td>
<td>Introduction of domestic tOPV for routine immunization</td>
</tr>
<tr>
<td>1964</td>
<td></td>
<td></td>
</tr>
<tr>
<td>late 1970s</td>
<td>sIPV development initiated by JPRI</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>Clinical studies of sIPV launched by JPRI</td>
<td></td>
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<tr>
<td>2001</td>
<td>Applied sIPV for manufacturing by JPRI</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>DTaP-sIPV development started by domestic manufactures</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Withdrew sIPV application due to GCP problems</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Call for urgent development of IPV by MHLW</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>Clinical studies of cIPV launched by Sanofi Pasteur</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Standalone cIPV introduced for routine immunization</td>
<td>Withdrawed from routine immunization</td>
</tr>
<tr>
<td>2014</td>
<td>DTaP-cIPV approved for manufacturing</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>DTaP-cIPV product will be introduced for routine immunization</td>
<td></td>
</tr>
</tbody>
</table>
How many doses of polio vaccine totally?
- from OPV to IPV transitional period -

• OPV 2 dose in the past
  ⇒ already completed

• Starting with IPV
  ⇒ 4 doses of IPV

• OPV 1 dose in the past
  ⇒ additional 3 doses of IPV
  (4 doses of polio vaccine, totally)

* when final dose vaccination?
  ⇒ 6 months interval after 3rd
Two types of method for transition from OPV to IPV

- **Total change**
- **Cohort change**

**Sequential schedule**
- Birth
- OPV
- IPV

**The day of transition**
- UK
- Australia
- Malaysia
- Russia
- USA

- Japan

- (~1996)
- (1997-99)
- (2000~)
Interchangeability in different polio vaccines

Group A
- OPV
- DTaP-sIPV
- DTaP-sIPV

Group B
- OPV
- cIPV
- cIPV

Group C
- DTaP-sIPV
- DTaP-sIPV
- cIPV

Group D
- cIPV
- cIPV
- DTaP-sIPV

Created based upon data from the Research Group of Analytical Epidemiologic Study on the Effectiveness and Safety of Vaccines (Principal Investigator: Dr.Yoshio Hirota), organized by the Ministry of Health, Labor and Welfare, Japan.
Routine OPV immunization coverage (Nationwide survey, JFY2004 - 2012)


Immunization rates for different poliovirus vaccines in 2013

MHWL. Routine polio immunization rates, 2013

Seroprevalence in different survey years, 1988～2014

## IPV products in Japan

<table>
<thead>
<tr>
<th>Product (Brand name)</th>
<th>Antigen</th>
<th>IPV antigen content/dose (D antigen unit; DU)</th>
<th>Manufacture</th>
<th>Status</th>
</tr>
</thead>
</table>
| IMOVAX POLIO subcutaneous | cIPV | Type 1: 40 cDU  
Type 2: 8 cDU  
Type 3: 32 cDU | Sanofi K.K | Application submitted (Feb 23, 2012)  
Approved for manufacturing (Apr 27, 2012)  
Introduced for routine immunization (Sept 1, 2012) |
| Quattrovac Subcutaneous Injection Syringe | DTaP-siPV | Type 1: 1.5 sDU  
Type 2: 50 sDU  
Type 3: 50 sDU | Kaketsuken | Application submitted (Jan 27, 2012)  
Approved for manufacturing (July 27, 2012)  
Introduced for routine immunization (Nov 1, 2012) |
| Tetrabik Subcutaneous Injection Syringe | DTaP-siPV | Type 1: 1.5 sDU  
Type 2: 50 sDU  
Type 3: 50 sDU | Biken | Application submitted (Dec 27, 2011)  
Approved for manufacturing (July 27, 2012)  
Introduced for routine immunization (Nov 1, 2012) |
| Squarekids Subcutaneous Injection Syringe | DTaP-clIPV | Type 1: 40 cDU  
Type 2: 8 cDU  
Type 3: 32 cDU | Kitasato | Application submitted (Feb 20, 2013)  
Approved for manufacturing (July 4, 2014)  
Introduce for routine immunization (Dec 9, 2015) |
| DTaP-siPV | | | Takeda | Withdraw |

Immunogenicity of booster doses of the inactivated polio vaccine (cIPV) among Japanese adult travelers

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Background

✓ A booster dose(s) of polio vaccine is recommended for adult travelers to polio-endemic or high-risk areas.

✓ According to the recommendation by WHO, one dose is given for adults who have previously received three or more doses of OPV or IPV.

✓ However, Japanese immunization program has been two doses of OPV, before the IPV introduction in Japan for routine immunization in 2012.

✓ Therefore, it is necessary to determine how many booster doses of IPV are required for Japanese adult travelers who have previously received OPV.

Methods

【Study Period】June 2011 ～ May 2013

【Subjects】Japanese healthy adults (≧20 years)

【Protocol】

Imovax Polio (Sanofi Pasteur) was administered at Day 0 and 28.

【Serological Methods】

・Serum neutralizing (NT) antibody titers were evaluated before the first booster dose and 28 days after each dose.

・Serum NT titers were measured against Sabin 1, Sabin 2, Sabin 3, Mahoney, MEF-1, Saukett, and type 2 vaccine-derived poliovirus (VDPV) isolated in Vietnam and Nigeria (SV3128, SV3130, 11196, 11198).
### Sabin strains

<table>
<thead>
<tr>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Day 0)</td>
<td>(Day 28)</td>
<td>(Day 56)</td>
</tr>
</tbody>
</table>
| - Blood sampling  
- clIPV 1st | - Blood sampling  
- clIPV 2nd | - Blood sampling |

### Wild poliovirus reference strains (clIPV antigens)

<table>
<thead>
<tr>
<th>Type2 Vaccine-derived poliovirus (VDPV) (Vietnam)</th>
<th>Type2 Vaccine-derived poliovirus (VDPV) (Nigeria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahoney, MEF-1, Saukett</td>
<td>SV3128, SV3130, 11196, 11198</td>
</tr>
</tbody>
</table>

We greatly appreciate Prof. Yoshio Hirota, Dr. Hiroyuki Shimizu, Dr. Shinji Fukushima, and all members for contributing to these studies and providing helpful advice.