Inactivated Poliovirus Vaccines (IPV)
WHO recommendations & general information

Poliomyelitis (polio) is an acute viral infection consisting of three distinct serotypes (1, 2 and 3). Before the introduction of the Expanded Programme on Immunization (EPI) in 1974, the disease was the leading cause of disability among children.

WHO member states resolved at the 1988 World Health Assembly to eradicate polio by the year 2000. At the time global polio incidence was estimated to be around 350,000 cases per year. Sustained immunisation activities reduced polio incidence by >99% between 1988 and 2012, and there were 223 and 403 reported cases of polio in 2012 and 2013 respectively. In 2013, India, and with it the entire WHO South-East Asia region, was declared polio free. The only remaining polio-endemic countries are Afghanistan, Nigeria and Pakistan. For the year 2014, as of 30 April, there had been 68 reported polio cases worldwide, with Pakistan accounting for 54 of them.

The WHO recommends that all children worldwide should be fully vaccinated against polio and that countries using only the oral polio vaccine (OPV) should include at least one dose of inactivated polio vaccine (IPV). IPV was first used in the 1950s. Current formulations of IPV are highly immunogenic, with 94–100% seroconversion rates for all three polio serotypes. The addition of the functionally trivalent IPV has been recommended to mitigate against potential re-emergence of polio serotype 2, following the withdrawal of type 2-strains from OPV (making it bivalent). IPV is less effective than OPV in inducing mucosal immunity among previously unvaccinated children, but administering both formulations in immunisation campaigns has resulted in uniformly high antibody titres against all three poliovirus types.

Recent research shows that fractional doses of IPV can be administered intradermally with specialised adapters to auto-disposable syringes or jet injectors. Use of fractional doses allows a lower dose to be given without reduction in immunogenicity and can provide overall cost savings. Research also underlines the potential for combining fractional IPV doses with hexavalent vaccine formulations.

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**Recommended schedules**

<table>
<thead>
<tr>
<th>Schedules</th>
<th>Age at 1st dose</th>
<th>Doses in primary series (interval between doses)</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 doses OPV + 1 dose IPV (OPV plus IPV)*</td>
<td>OPV: birth dose</td>
<td>OPV: 1st dose at 6 weeks (4 weeks between doses 1, 2 and 3) IPV: dose at 14 weeks</td>
<td>No booster</td>
</tr>
<tr>
<td>1 – 2 doses IPV+ ≥2 OPV (Sequential IPV OPV)**</td>
<td>IPV: 14 weeks</td>
<td>IPV: 2nd dose at 3–4 months OPV: 2nd dose 4–8 weeks after 1st dose</td>
<td>No booster</td>
</tr>
<tr>
<td></td>
<td>IPV: 2 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPV: after last IPV dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 doses IPV (IPV only)†</td>
<td>2 months</td>
<td>4 weeks between 1st and 2nd doses, and between 2nd and 3rd doses</td>
<td>If primary series is begun at &lt;2 months, booster recommended at ≥6 months (becomes a 4-dose schedule).</td>
</tr>
</tbody>
</table>

*WHO no longer recommends OPV-only schedules. The OPV plus IPV schedule is applicable to polio-endemic countries and those with high risk of importation.

**Applicable to countries with 90–95% immunisation coverage, low importation risk and where vaccine-acquired polio is a significant concern.

†Applicable to countries with sustained high immunisation coverage and lowest risk of wild poliovirus importation and transmission.
### Products & manufacturers

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>WHO PQ date</th>
<th>Form and presentation</th>
<th>Lowest known price (UNICEF, US$)</th>
<th>Vaccine vial monitor (VVM) type and cold chain volume (per dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated polio vaccine (IPV)</strong></td>
<td>Bithoven Biologicals BV*</td>
<td>Dec 2010</td>
<td>Liquid; 1-dose vial</td>
<td>2.80</td>
<td>VVM 7</td>
</tr>
<tr>
<td><strong>Inactivated polio vaccine (IPV)</strong></td>
<td>Serum Institute of India/Bithoven Biologicals</td>
<td>N/A</td>
<td>Liquid; 5-dose vial**</td>
<td>2.00†</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Poliorix</strong> Inactivated polio vaccine</td>
<td>GSK</td>
<td>Aug 2012</td>
<td>Liquid; 1-dose and 2-dose vials ‡</td>
<td>N/A</td>
<td>VVM 7 (1-dose vial) VVM 14 (2-dose vial)</td>
</tr>
<tr>
<td><strong>Imovax Polio</strong> Inactivated polio vaccine</td>
<td>Sanofi Pasteur</td>
<td>Dec 2005</td>
<td>Liquid; 10-dose vial †</td>
<td>1.04‡</td>
<td>No VVM</td>
</tr>
<tr>
<td><strong>IPV Vaccine SSI</strong> Inactivated polio vaccine</td>
<td>Statens Serum Institut</td>
<td>Dec 2010</td>
<td>Liquid; 1-dose vial</td>
<td>N/A</td>
<td>VVM 7</td>
</tr>
</tbody>
</table>

* Acquired by Serum Institute of India in July 2012.
** 5-dose vial presentation from Serum Institute of India/Bithoven was put forward for the UNICEF bid tender although not WHO prequalified. It is anticipated to be prequalified and available for procurement by the end of 2014.† Price listed is the Gavi price, converted from euros to US dollars.‡ Currently UNICEF procures Imovax Polio from Sanofi Pasteur for non-Gavi countries at three different price tiers that are based on adjusted Gross National Income per capita (see ‘Prices and affordability’ section, opposite).‡ This arrangement does not cover all middle-income countries, prices for which are country- and supplier specific.§ All multidose opened vials must be discarded not more than six hours after opening (WHO multidose open-vial policy).†

### PIPELINE PRODUCTS

- **DTP-HepB-IPV-Hib (PR5):** paediatric hexavalent vaccine in Phase III of development from Sanofi Pasteur. 173
- **DTP-HepB-IPV-Hib (V419):** paediatric hexavalent vaccine in Phase III from Merck. 134
- **DPT-IPV (TAK-3615):** tetravalent vaccine in Phase II from Takeda and Japan Polio Research Institute. 174
- **Sabin IPV (sIPV) products from Panacea, Takeda and Intravacc (Netherlands Vaccine Institute) in varying phases of development.** 173,176

### CHALLENGES

- **On 5 May 2014, WHO declared the international spread of polio to date in 2014 to be a Public Health Emergency of International Concern and an “extraordinary event” posing a “public health risk to other states for which a coordinated international response is essential”**, 161,177,178 WHO identified Pakistan, Cameroon and Syria as states posing the greatest risk of wild poliovirus exportation, and a further seven countries (including Afghanistan and Nigeria) as infected with wild poliovirus but not currently exporting. WHO recommendations include vaccination of all country residents, visitors and travellers and maintenance of the recommended measures for a period of 12 months with no evidence of transmission. 161,177,178
- **There are significant supply bottlenecks relating to IPV. With five-dose and new versions of the 10-dose vials only made available from mid- to late 2014, current availability of one- and two-dose vials will be heavily constrained.** 169
- **To expedite supply of IPV, UNICEF recommends that countries provide timely information on preferred vial size, acceptable alternatives, and national licensing requirements and their anticipated timetable for introduction.** 167,169,179
THE GLOBAL POLIO ERADICATION INITIATIVE

The Global Polio Eradication Initiative (GPEI) was created in 1988, following a resolution passed at the World Health Assembly. GPEI is a public–private partnership with the goal to eradicate polio worldwide. Thus far more than US$8.2 billion has been spent on polio eradication. Efforts intensified after 2008 and since 2012 WHO has declared ending polio a “programmatic emergency for global public health”, as a result of which the Polio Eradication and Endgame Strategic Plan 2013–2018 was developed. The plan includes the phasing-out of OPV and progressive introduction of IPV into routine immunisation schedules as a key element of eradication and post-eradication activities, reducing the risk of re-emerging type-2 polio while also accelerating wild poliovirus eradication.

PRICE EVOLUTION: UNICEF AND PAHO

(See Annex A for more information on prices used in this section)

- Before 2010, there was only one WHO prequalified IPV product (Sanofi Pasteur’s Imovax Polio). In 2010, Statens Serum Institute, GSK and Bilthoven obtained WHO prequalification status for their IPV vaccines. In July 2012, Serum Institute of India purchased Bilthoven Biologicals, and in 2013, the newly created Intravacc (the Dutch Institute for Translational Vaccinology) and Bilthoven Biologicals started their collaboration to improve the IPV production process, with the aim of a more affordable vaccine.

- PAHO has benefited from the entry of these new manufacturers into the market. In 2013, the price of IPV was reduced as a result of Bilthoven’s participation in the Revolving Fund. PAHO purchased IPV at US$4.14 from GSK in 2013, but purchased the Bilthoven vaccine the same year at US$2.90 and then at US$2.80 in 2014, a 30% price drop [Graph 9, overleaf].

- In February 2014, price announcements were made following UNICEF’s IPV tender. Sanofi Pasteur and Serum Institute of India/Bilthoven Biologicals responded to the tender and offered their IPV vaccines at a reduced price. Sanofi Pasteur offered different prices based on groups of countries, while Serum Institute of India offered one price for all countries.

- However, the price announcement raised some concerns as it was the first time that a manufacturer responded to a UNICEF tender with a clear tiered-pricing offer. Sanofi’s price offer classified countries in four tiers: three groups of countries that pay three distinct prices, and the Gavi-supported group comprising the lowest tier. According to the UNICEF website, tiers were determined on the basis of “GNI per capita, and by considering each country’s overall level of development by adjusting the GNI per capita to account for inequities in wealth distribution within each country”.

- Sanofi’s announcement to sell IPV to UNICEF at a lower price was supported by the Bill & Melinda Gates Foundation and is heralded as critical in light of the Global Polio Endgame Strategy. But despite efforts to reduce prices, the lowest price for IPV remains more than seven times as expensive as the lowest price for OPV: in 2014, the lowest price to UNICEF for OPV is US$0.12 per dose (Bio Farma, 20-dose presentation), while IPV is priced at US$1 (Sanofi Pasteur, Gavi countries only, 10-dose presentation).
**Graph 9: Price evolution of Inactivated Poliovirus (IPV) vaccines for PAHO, UNICEF and Gavi**

**Sources:**
PAHO Revolving Fund, UNICEF Supply Division

* Forecasted data. Prices remain the same between 2015 and 2018.

** Special terms apply except for a single-dose liquid presentation. MSF requested details from UNICEF on these special terms but the information was not provided.

*** Sanofi Pasteur and the Gates Foundation have designed a price mechanism with additional financial contributions to attain the Gavi IPV price. MSF requested details on these subsidies but the information was not provided.

**Notes and methodology:**
- For PAHO, a weighted average price is used for 2006–2012, an average of the two available actual prices (from GSK and Bilthoven Biologicals) is used for 2013 and the actual price from Bilthoven Biologicals (sole supplier) is used in 2014.
- The rise in price for PAHO from 2006 to 2013 occurred because, prior to 2013, only one country had introduced IPV in its routine immunisation programme.
- Tiers for Sanofi Pasteur’s vaccine are:**
  - Tier 1 countries: Cape Verde, Egypt, Morocco, Palestine, Philippines, Samoa, Swaziland, Vanuatu (GNI/capita: <US$4,000).
  - Tier 2 countries: Albania, Algeria, Fiji, Iran, Macedonia, Maldives, Namibia, Serbia, Thailand, Tonga, Tunisia, Turkmenistan (GNI/capita: US$4,000–6,000).
  - Tier 3 countries: Botswana, Gabon, Lebanon, Mauritius, Seychelles, Tuvalu (GNI/capita: >US$6,000).
PRICES IN COUNTRIES

There are few data points from countries on IPV as several countries have introduced IPV through pentavalent or hexavalent combination vaccines that contain IPV. Therefore, prices of standalone IPV listed here might be higher in countries that have also introduced one of these combination vaccines (e.g. South Africa).

The graph below [Graph 10] demonstrates that despite Sanofi Pasteur’s tiered prices being aligned with country GNI per capita for countries who procure through UNICEF, the end result continues to be high and unaffordable prices for many countries. Comparing the PAHO price to the UNICEF price, the PAHO price appears pegged to the UNICEF price gradation despite UNICEF and PAHO procuring two different products. Regarding prices of IPV in countries that do not procure through UNICEF, the relationship between the price of the vaccine and the country’s wealth is much less obvious, even when keeping in mind that there are different price categories represented in the graph.

Prices of combination vaccines such as hexavalent DTaP-HepB-Hib-IPV vaccine or the DTaP-Hib-IPV vaccine have been explored in the pentavalent vaccines product card [see page 65].

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Graph 10: Prices for Inactivated Poliovirus (IPV) vaccines by GNI/capita in several countries, 2013/2014

Sources: PAHO Revolving Fund, UNICEF Supply Division, country price analysis (see Annex A for more information).
*Annex A, Section C
** Special terms apply except for a single-dose liquid presentation. MSF requested details from UNICEF on these special terms but was not given information.
*** Sanofi Pasteur and the Gates Foundation have designed a price mechanism with additional financial contributions to attain the Gavi IPV price. MSF requested details on these subsidies but was not given information.

Notes and methodology:
- All prices are for Sanofi Pasteur products (Ipol in the US, Imovax Polio in other countries), across presentations, except the PAHO price, which is for Bhlhoven Biologicals vaccine.
- For the Sanofi Pasteur vaccine purchased through UNICEF, GNI per capita thresholds are: Tier 1: up to US$4,000; Tier 2: US$4,000 – 6,000; Tier 3: over US$6,000.184
- PAHO GNI per capita estimated at US$7,500.184