Measles-containing Vaccines
(Measles, MR, MMR)
Measles-containing vaccines include combination vaccines for measles and rubella (MR) and for measles, mumps and rubella (MMR) and monovalent measles vaccines.

Measles is a highly infectious viral disease. Vaccination against measles has been recommended as part of the Expanded Programme on Immunization (EPI) since the programme’s inception in 1974. Before that, 90% of individuals were infected with measles before the age of ten years. There were 122,000 measles deaths in 2012, most of which were among children aged under five years. Surveillance data show that there were 177,510 total reported measles cases globally for 2013, and 45,566 for the first five months of 2014.

The WHO recommends measles vaccination for all susceptible infants, young children and adults (in the absence of contraindications) as part of national immunisation programmes globally. The first dose of measles vaccine, if administered at 11–12 months of age, provides a seroconversion rate of 99%. Of children who fail to respond to the first dose, 97% (median value) develop immunity after the second dose. Mumps infection affects primarily the salivary glands and is most common among children aged between five and nine years. The disease is generally self-limiting but serious complications can occur; these include meningitis, encephalitis, deafness and orchitis.

Mumps incidence has declined dramatically since the 1960s, when vaccines against it were first introduced. Currently, global mumps incidence is 100–1,000 cases per 100,000 population, with epidemic peaks every two to five years.

The WHO recommends routine mumps vaccination in countries where reduction of mumps is a public health priority, provided the country has a well-established childhood vaccination programme and the capacity to maintain coverage for routine measles and rubella vaccination at >80%. All mumps vaccine strains (except the Rubini strain) confer short-term protective efficacy rates above 90% with administration of one dose.

Rubella is an acute, contagious and generally mild viral disease, usually affecting susceptible children and young adults. Rubella infections occurring before conception or in early pregnancy are of greatest concern because rubella can be teratogenic, potentially leading to miscarriage, fetal death, or congenital malformations as part of congenital rubella syndrome (CRS). CRS can cause ophthalmic, auditory, cardiac and brain anomalies and worldwide an estimated 110,000 children are born every year with CRS. Large scale rubella vaccinations over the past decade have substantially reduced rubella and CRS in many countries but more needs to be done to reach the measles and rubella elimination targets set out in the Global Measles and Rubella Strategic Plan.
The WHO recommends that all countries yet to introduce combined rubella vaccines (as part of MMR) should immediately consider adding them to national immunisation programmes. WHO also recommends reviewing national-level epidemiological factors, CRS burden and specific population profiles when determining the immunisation strategy for targeting rubella. To keep CRS in check and work towards rubella control and elimination, vaccination coverage needs to be sustained at or above 80% in an attempt to avoid shifting of rubella infection from childhood to fertile age groups. All licensed rubella vaccines (including those that are a component of MMR) induce seroconversion at a rate of 95% or higher after a single dose, with vaccine efficacy of 90–100%.\(^\text{190}\)

Nine months is the preferred age for the first dose for countries with ongoing measles transmission and high risk of measles mortality. In countries with low rates of measles infection among infants, 12 months is the preferred age for the first dose to achieve a seroconversion rate of >90%.

Giving the second dose at 15–18 months ensures early protection of the individual and slows accumulation of susceptible young children, thereby reducing the risk of an outbreak.\(^\text{124,185}\)

The choice of age for rubella vaccination depends entirely on when the first dose of measles vaccine is given. Vaccination in pregnant women should be avoided because of the theoretical risk of congenital rubella.\(^\text{124,190}\)

Mumps vaccination is recommended as part of the combined measles, mumps and rubella vaccine.\(^\text{124,188}\)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age at 1st dose</th>
<th>Doses in primary series (interval between doses)</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>9 or 12 months (not &lt;6 months)(^\text{1})</td>
<td>2 doses (minimum 4 weeks)</td>
<td>No booster</td>
</tr>
<tr>
<td>Mumps</td>
<td>12–18 months with measles-containing vaccine</td>
<td>2 doses (2nd dose at least 1 month before school entry)</td>
<td>No booster</td>
</tr>
<tr>
<td>Rubella</td>
<td>9 or 12 months with measles-containing vaccine</td>
<td>1 dose</td>
<td>No booster</td>
</tr>
<tr>
<td>Product</td>
<td>Manufacturer</td>
<td>WHO PQ date</td>
<td>Form and presentation*</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
<td>-------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Measles vaccine</td>
<td>Bio Farma</td>
<td>Apr 1997 (10-dose) Sep 2006 (20-dose)</td>
<td>Lyophilised, 10- or 20-dose vials + water diluent</td>
</tr>
<tr>
<td>Measles vaccine</td>
<td>GPO-Merieux</td>
<td>Sep 2010</td>
<td>Lyophilised, 10-dose vial + water (5 ml) diluent</td>
</tr>
<tr>
<td>Rouvax Measles vaccine</td>
<td>Sanofi Pasteur</td>
<td>May 2002</td>
<td>Lyophilised, 10-dose vial + water for injection (5 ml) diluent</td>
</tr>
<tr>
<td>Measles vaccine (live, attenuated)</td>
<td>Serum Institute of India</td>
<td>Feb 1993</td>
<td>Lyophilised, 1-, 2-, 5- and 10-dose vials + ampoule water diluent</td>
</tr>
<tr>
<td>Measles and rubella vaccine (live, attenuated)</td>
<td>Serum Institute of India</td>
<td>Jul 2000</td>
<td>Lyophilised, 1-, 2-, 5- and 10-dose vials + ampoule water diluent</td>
</tr>
<tr>
<td>Priorix Measles, mumps and rubella vaccine</td>
<td>GSK</td>
<td>Mar 2001 (1-dose) Dec 2011 (2-dose)</td>
<td>Lyophilised, 1- and 2-dose vials + ampoule water for injection diluent</td>
</tr>
<tr>
<td>M-M-R II Measles, mumps and rubella vaccine</td>
<td>Merck Sharp &amp; Dohme</td>
<td>Jan 2009</td>
<td>Lyophilised, 1-dose vial</td>
</tr>
<tr>
<td>M-M-R II Measles, mumps and rubella vaccine</td>
<td>Sanofi Pasteur</td>
<td>Apr 2002</td>
<td>Lyophilised, 1-dose vial + 1-dose ampoule (diluent); and 10-dose vial + 5 ml vial diluent</td>
</tr>
<tr>
<td>Measles, mumps and rubella vaccine (live, attenuated)</td>
<td>Serum Institute of India</td>
<td>Aug 2003</td>
<td>Lyophilised, 1-, 2-, 5- and 10-dose vials (+ ampoule diluent)</td>
</tr>
</tbody>
</table>

*All reconstituted multidose vials must be discarded no more than six hours after opening (WHO multi-dose open-vial policy).172*
PIPELINE PRODUCTS

A live, attenuated MMR vaccine from GSK is in Phase III of development.194

Bio-Manguinhos, in association with the Bill & Melinda Gates Foundation, is developing an MR vaccine.195,196

CHALLENGES

Outbreaks of both mumps and measles have surged in developed countries in recent years. This is largely because public misconceptions about vaccine safety are causing parents to choose not to vaccinate their children,193 in spite of conclusive independent evidence disproving the alleged causal link between MMR and autism, among other safety concerns, claimed by anti-vaccine advocates.197,198

The Global Measles and Rubella Strategic Plan lists several challenges to the elimination of these diseases. These include establishing and guaranteeing sustained and predictable financing for immunisation efforts; improving data and reporting of vaccination coverage; and addressing concerns on the capacities of health systems. The plan also calls for working with governments to reach areas of high population density, areas with highly mobile populations and countries facing complex humanitarian emergency situations, where measles case fatality rates can be as high as 25%.193

Alternative vaccine delivery methods, such as by the nasal route, are in development after research indicating they can provide a viable pathway for delivery, with improved vaccine seroconversion rates.199

The measles monovalent vaccine supply is fragile because a single manufacturer (Serum Institute of India) produces 80% of the supply and is also the sole manufacturer of the only WHO prequalified MR vaccine.200
Prices and affordability

PRICE EVOLUTION: UNICEF AND PAHO
(See Annex A for more information on prices used in this section)

MEASLES VACCINE

The price of the measles vaccine is relatively low, but has followed an upward trend in the past decade [Graph 11]. This likely reflects reduced demand for the monovalent product, as countries progressively switch to combination vaccines such as MR and MMR (for instance, PAHO ceased orders for measles vaccines in 2006), and a decreasing number of manufacturers.

The number of different products procured by UNICEF has declined from seven in 2002 to only three, two of which are produced by emerging manufacturers. Mono-dose measles vaccines were purchased by UNICEF for the last time in 2003; since then the much less expensive multi-dose vial presentation has been preferred.

MR VACCINE

Recent recommendations by WHO (2011) to include rubella in routine immunisation have increased demand for MR and MMR vaccines.

However, the number of manufacturers of the MR vaccine has always been limited to two, and following Crucell’s exit from the market in 2012, Serum Institute of India was left as the sole manufacturer of a WHO prequalified MR vaccine.113

Increasing demand from UNICEF and a diminishing number of manufacturers have driven up prices of the MR vaccine [Graph 12, overleaf].

In 2013, Gavi announced its support of large-scale catch up campaigns with the MR vaccine, provided that countries self-finance the introduction of the vaccine into their routine immunisation programmes.201

MMR VACCINE

MMR vaccines are more expensive than MR or measles vaccines. For instance, the lowest price per dose offered to UNICEF for the MMR vaccine (10-dose presentation by Serum Institute of India at US$1.025) is almost twice that of the MR vaccine offered in the same presentation by the same manufacturer (at US$0.55) [Graph 13, overleaf].

There are large price differences between the products containing different strains of mumps. For instance, the PAHO price in 2014 for the single-dose MMR Jeryl Lynn strain vaccine (manufactured by GSK and Merck) was about 2.4 times more expensive than the single-dose MMR Urabe strain vaccine (manufactured by Sanofi Pasteur), and five times more expensive than the lowest-priced presentation of the MMR Zagreb strain vaccine (manufactured by Serum Institute of India).

Graph 11: Price evolution of measles vaccines for PAHO and UNICEF

Sources:
PAHO Revolving Fund, UNICEF Supply Division

Notes:
- Products omitted from graph because of data discontinuity. A 10-dose presentation was sold to UNICEF by Tanabe Seiyaku from 2002 to 2003; and Eisai Co from 2001 to 2003.
- Sanofi Pasteur product was sold under Aventis Pasteur Canada from 2001 to 2003.
- Novartis supplied measles vaccines to UNICEF in 2005 but has not agreed to the publication of prices.
Graph 12: Price evolution of Measles-Rubella (MR) vaccines for PAHO and UNICEF

![Graph 12: Price evolution of Measles-Rubella (MR) vaccines for PAHO and UNICEF](image)

Sources: PAHO Revolving Fund, UNICEF Supply Division

Note:
Products omitted from graph because of data discontinuity: PAHO purchased a two-dose presentation of the vaccine from 2003–2005.

Graph 13: Price evolution of Measles-Mumps-Rubella (MMR) vaccines for PAHO and UNICEF

![Graph 13: Price evolution of Measles-Mumps-Rubella (MMR) vaccines for PAHO and UNICEF](image)

Sources: PAHO Revolving Fund, UNICEF Supply Division

Notes:
- Products omitted from graph because of data discontinuity: UNICEF purchased a 10-dose MMR Jeryl Lynn strain from GSK in 2002, and a Sanofi Pasteur Urabe-strain MMR vaccine in 2010 and 2012. Serum Institute of India also offers a two-dose MMR vaccine since 2010, priced similarly to its 10-dose presentation.
- Novartis has supplied MMR to UNICEF but has not agreed to the publication of prices.
**PRICES IN COUNTRIES: FOCUS ON MMR**

- Vaccines made with the Jeryl Lynn mumps strain are more expensive; countries opting for a measles or MR vaccine instead of an MMR product will unfortunately lose a disease-control opportunity to vaccinate against mumps.197

- In countries where only measles is included in the Expanded Programme on Immunization (EPI), MMR is available only through the private sector, often at very high prices. In South Africa, for instance, the price of the measles vaccine from the government is US$0.59, while a dose of MMR through the private sector will cost US$13.51 [Graph 14].

- The price of the MMR vaccine in the retail market in the US (MMRII, by Merck, at US$56.14) is extremely high compared to that in other countries; it is double the price paid in Belgium, the next high-income country included in our analysis (for Priorix, by GSK, at US$29.27), and triple the price paid in France.

Graph 14: Prices for MMR vaccines in several countries, by manufacturer and price type, 2013/2014*

![Graph showing prices for MMR vaccines](image)

**Sources:** PAHO Revolving Fund, UNICEF Supply Division, MSF Supply; country price analysis.

*Annex A, Section C

**Notes:**
- Prices for UNICEF, MSF, PAHO, Thailand and the Philippines are for multidose vials; those for the other countries are for single-dose vials.
- MSF price is Incoterm Carriage Paid To (named destination) (see Annex C).
- When a country or organisation purchases several presentations of a same vaccine, only the lowest price is presented in the graph.