MODEL INSERT
MEASLES, MUMPS AND RUBELLA (MMR) COMBINED VACCINE

DESCRIPTION
The vaccine is a freeze-dried powder containing three viruses - measles, mumps and rubella.

a) The measles vaccine component is a live, attenuated viral vaccine. Each dose of 0.5 ml contains not less than.....(specify) CCID50 (cell culture infective doses 50%) of viral vaccine strain.....(specify), prepared in … (specify substrate: diploid cell (MRC5), chick embryo fibroblast cells) and not more than .....µg of residual antibiotic………..(specify)

b) The mumps vaccine component is an attenuated live virus vaccine. Each dose contains not less than.....(specify) CCID50 (cell culture infective doses 50%) of viral vaccine strain. .....(specify), prepared in … (specify substrate: diploid cell (MRC5), chick embryo fibroblast cells or embryonated eggs)) and not more than .....µg of residual antibiotic…. (specify).

b) The rubella vaccine component is also a live, attenuated viral vaccine. Each dose of 0.5 ml contains not less than.....(specify) CCID50 (cell culture infective doses 50%) of viral vaccine strain.....(specify), prepared in … (specify substrate: diploid cells, MRC5 /WI-38) and not more than .....µg of residual antibiotic….. (specify).

<table>
<thead>
<tr>
<th>COMPOSITION</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Measles</td>
<td>XXX CCID50</td>
</tr>
<tr>
<td>Mumps</td>
<td>XXX CCID50</td>
</tr>
<tr>
<td>Rubella</td>
<td>XXX CCID50</td>
</tr>
<tr>
<td>Nature / amount of excipient</td>
<td>XX mg/ml</td>
</tr>
<tr>
<td>Nature / amount of stabilizer</td>
<td>XX mg/ml</td>
</tr>
<tr>
<td>Nature and amount of residual antibiotic</td>
<td>XX µg/ml</td>
</tr>
</tbody>
</table>

Diluent composition

ADMINISTRATION
Immunization consists of a single dose of 0.5 ml injected subcutaneously, preferably in the upper arm. The lyophilizate must be reconstituted by adding the entire content of the supplied container of diluent to the vaccine vial. The vaccine pellet should be completely dissolved in the diluent. Following reconstitution, the vaccine should be inspected visually for any foreign particulate matter prior to administration. If observed, the vaccine must be discarded.
A sterile needle and sterile syringe must be used for the reconstitution of the vaccine and for each injection. Because of sensitivity to ultraviolet light, the vaccine must be stored in the dark at +2°C and +8°C and used within six (6) hours. Any opened vials remaining at the end of an immunization session (within six [6] hours of reconstitution should be discarded. The vaccine vial monitor for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.

The diluent supplied is specially designed for use with this vaccine. Only this diluent may be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or for measles vaccine from other manufacturers. Using an incorrect diluent will result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen but must be cooled between +2°C and +8°C before used for reconstitution.

**IMMUNIZATION SCHEDULE**

In countries where the incidence and mortality from measles is high in the first year of life, the recommended age for immunization using MMR is at 9 months of age (270 days) or soon after. In countries where measles infection occurs later in life (due to sustained high vaccine coverage), the age of immunization can be moved to 12-15 months. A second opportunity is needed both to increase the chance that every child receives at least one dose of measles-containing vaccine and to increase the proportion of the population that is fully immunized. The second dose of measles-containing vaccine can be given through routine or supplemental activities.

MMR vaccine can be given safely and effectively simultaneously with DTP, Td, TT, BCG, polio (OPV and IPV), *Haemophilus influenzae* type b, hepatitis B, or yellow fever vaccines or vitamin A supplementation.

The combination MMR vaccine produces an immunological response to each antigen (e.g. measles, mumps, rubella) equivalent to that following administration of each of the single antigen products. The safety and immunogenicity of this combination vaccine appears to be similar to that of its individual constituents.

**SIDE EFFECTS**

The type and rate of severe adverse reactions with the combined MMR vaccine do not differ significantly from the measles, mumps and rubella vaccine reactions described separately.

- *Side effects following measles vaccination* are generally mild and transient. Slight pain and tenderness at the site of injection may occur within 24 hours of vaccination, sometimes followed by mild fever and local lymphadenopathy. About 7 - 12 days after vaccination up to 5% of measles vaccine recipients may experience fever > 39.4 °C for 1 - 2 days. A transient rash may occur in approximately 2% of vaccinees, usually starting 7-10 days following vaccination and lasting 2 days. Side effects, with the exception of anaphylactic reactions, are less likely to occur after receipt of a second dose of measles-containing vaccine. Encephalitis has been reported following measles vaccination at a frequency of approximately one (1) case per one (1) million doses administered although a causal link is not proven.

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- *The mumps component* may result in parotitis in up to 3% of recipients, and the onset is usually 5-24 days following vaccination. Orchitis occurs rarely. Aseptic meningitis, with onset 15-35 days following vaccination, has been reported at widely varying frequencies. The delayed onset of aseptic meningitis may limit the ability to detect these cases by passive surveillance. Vaccine-associated aseptic meningitis resolves spontaneously in less than one week without sequelae. The risk of developing aseptic meningitis may vary with the mumps vaccine strain. However, the available data are not strong enough to form the basis of a recommendation not to use the specific strain. It was noted that higher rates of aseptic meningitides have been described for the Urabe, the Leningrad-Zagreb and the Leningrad-3 strain vaccines compared with the Jeryl-Lynn strain vaccine. The possible basis for this difference and/or the other characteristics of the product that might explain these differences are not known. Some of the variability observed in the risk of aseptic meningitides following use of the various mumps vaccine strains may reflect pre-immunity, in particular in older age groups, as well as the variable levels of sensitivity of surveillance and of diagnostic practices in different settings.

- *The rubella component* may commonly result in transient arthralgias (25%) and arthritis (10%) among adolescent and adult females that begin 1-3 weeks after vaccination and last from 1 day to 2 weeks. However, arthralgias and arthritis are very rare in children and in men receiving MMR vaccine (0% -3%). These transient reactions seem to occur in non-immunes only, for whom the vaccine is important. Low grade fever and rash, lymphadenopathy, myalgia and paraesthesiae are commonly reported. Thrombocytopenia is rare and has been reported in less than 1 case per 30 000 doses administered. Anaphylactic reactions are also rare.

**CONTRAINDICATIONS**

A previous allergic reaction to measles, MR or MMR vaccine is a contraindication. Persons with a history of an anaphylactic reaction to any components of the vaccine should not be vaccinated.

Apart from this, there are few contraindications to the administration of MMR vaccine. It is particularly important to immunize children with malnutrition. Low-grade fever, mild respiratory infections or diarrhoea, and other minor illnesses should not be considered as contraindications.

MMR vaccine should not be administered during pregnancy because of the theoretical but never demonstrated teratogenic risk. Inadvertent receipt of MMR vaccine during pregnancy is not an indication for an abortion. If pregnancy is planned, then an interval of one month should be observed after MMR vaccination.

**Immune deficiency**

Children with known or suspected HIV infection are at increased risk of severe measles. Such children should be offered measles vaccine as early as possible. The standard WHO recommendation for children at high risk of contracting measles is to immunize with measles vaccine at 6 months of age with a second dose at 9 months. This recommendation should be applied to children with known or suspected HIV infection. The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukaemia, lymphoma or generalized malignancy.

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STORAGE
Freeze-dried MMR vaccine should be kept in the refrigerator between +2°C and +8°C until used. The vials of vaccine and the diluent should be transported together, but the diluent must not be frozen. Because of sensitivity to ultraviolet light the vaccine must be stored in the dark.

Freeze-dried measles vaccine should also be kept frozen at -20°C

PRESENTATION
The vaccine comes in vials of .... dose (s).

Fig. The Vaccine Vial Monitor

The vaccine vial monitor...

- Inner square lighter than outer circle.
  - If the expiry date has not been passed, USE the vaccine.

- At a later time, inner square still lighter than outer circle.
  - If the expiry date has not been passed, USE the vaccine.

- Discard point: Inner square matches colour of outer circle.
  - DO NOT use the vaccine.

- Beyond the discard point: Inner square darker than outer ring.
  - DO NOT use the vaccine.

The Vaccine Vial Monitors (VVMs) are on the cap of .... (specify vaccine) supplied through .......... (specify supplier or manufacturer). The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

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The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.