AUSTRALIAN PRODUCT INFORMATION
M-M-R® II (Measles, Mumps and Rubella Virus Vaccine Live)

1 NAME OF THE MEDICINE

Measles, Mumps and Rubella Virus Vaccine Live

2 QUALITATIVE AND QUANTITATIVE COMPOSITION and 3 PHARMACEUTICAL FORM

M-M-R II is a sterile lyophilised preparation containing a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell cultures; the Jeryl Lynn (B level) strain of mumps virus propagated in chick embryo cell cultures; and the Wistar RA 27/3 strain of live attenuated rubella virus propagated in human diploid cell (WI-38) culture. The three viruses are mixed before being lyophilised.

The reconstituted vaccine is for subcutaneous (SC) or intramuscular (IM) administration. When reconstituted as directed, the dose for injection is approximately 0.5 mL and contains not less than the equivalent of 1000 $TCID_{50}$ (50% tissue culture infectious doses) of Measles Virus; 12,500 $TCID_{50}$ of Mumps Virus; and 1000 $TCID_{50}$ of Rubella Virus.

Powder for injection

Before reconstitution, the lyophilised vaccine is a light yellow compact crystalline plug.
M-M-R II, when reconstituted, is clear yellow.

Excipients with known effect: The vaccine contains 14.5 mg of sorbitol.

For the full list of excipients, see section 6.1 List of excipients.

This product may also contain residual recombinant human albumin, foetal bovine serum and other buffer and media ingredients.

The product contains no preservative.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

M-M-R II is indicated for simultaneous immunisation against measles, mumps and rubella.

Refer to the NHMRC Australian Immunisation Handbook (AIH) for vaccination recommendations and schedule.

There is some evidence to suggest that infants immunised against measles at less than 12 months of age, or who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later

revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunisation.

Infants who are less than 12 months of age may fail to respond to one or more components of the vaccine due to presence in the circulation of residual antibodies of maternal origin, the younger the infant, the lower the likelihood of seroconversion. In geographically isolated or other relatively inaccessible populations for whom immunisation programmes are logistically difficult, and in population groups in which wild-type measles infections may occur in a significant proportion of infants before 15 months of age, it may be desirable to give the vaccine to infants at an earlier age. Infants vaccinated under these conditions at less than 12 months of age should be revaccinated after reaching 12 to 15 months of age.

Previously unvaccinated children older than 12 months who are in contact with susceptible pregnant women should receive live attenuated rubella vaccine to reduce the risk of exposure of the pregnant woman.

Non-Pregnant Adolescent and Adult Females

Immunisation of susceptible non-pregnant adolescent and adult females of childbearing age with live attenuated rubella virus vaccine is indicated if certain precautions are observed (See 4.4 Special Warnings and Precautions for Use and 4.6 Fertility, Pregnancy and Lactation). Vaccinating susceptible postpubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infection of the foetus and consequent congenital rubella injury. Congenital malformations do occur in up to seven percent of all live births, and their chance appearance after vaccination should be borne in mind.

Women of childbearing age should be advised not to become pregnant for one month after vaccination against rubella (which is included in M-M-R II) and should be informed of the reasons for this precaution (See 4.6 Fertility, Pregnancy and Lactation, Use in Pregnancy).

The Australian Immunisation Handbook recommends that effort should be made to identify and immunise non-pregnant seronegative women of child-bearing age.

Women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing. Please refer to AIH for recommendations for further information regarding serological testing for immunity to rubella.

Postpubertal females should be informed of the frequent occurrence of generally self-limited arthralgia and/or arthritis beginning 2 to 4 weeks after vaccination against rubella (see 4.8 Adverse Effects (Undesirable Effects)).

Post-Partum Women

It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period using an appropriate rubella-containing vaccine. (See 4.6 Fertility, Pregnancy and Lactation, *Use in Lactation*).

Revaccination

Children vaccinated when younger than 12 months of age should be revaccinated at 12 to 15 months of age. Persons who were vaccinated originally when 12 months of age or older should be revaccinated with a MMR-containing vaccine, as per the recommended vaccination schedule. Revaccination is intended to seroconvert those who did not respond to the first dose. However, data on long term persistence of antibodies are limited and continued surveillance will

be required to allow firm recommendations to be made on revaccination. However, persons should be revaccinated if there is evidence to suggest that initial immunisation was ineffective.

4.2 DOSE AND METHOD OF ADMINISTRATION

FOR SUBCUTANEOUS OR INTRAMUSCULAR ADMINISTRATION - **Do Not Inject Intravascularly**

The preferred injection sites are the anterolateral area of the thigh in younger children and the deltoid area in older children, adolescents, and adults.
The vaccine should be administered subcutaneously in patients with thrombocytopenia or any coagulation disorder.

Refer to the Australian NHMRC Immunisation Handbook for vaccination recommendations and schedule. This handbook is available online at http://www.immunise.health.gov.au

Do not give immune globulin (Ig) concurrently with M-M-R II. (See 4.5 Interactions with Other Medicines and Other Forms of Interactions).

The dosage of vaccine is the same for all persons. Inject the total volume of the single dose vial (approximately 0.5 mL) intramuscularly or subcutaneously, preferably into the outer aspect of the upper arm.

CAUTION: A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine.

To reconstitute, use only the diluent supplied, since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

Single Dose Vial

Product is for single use in one patient only. Discard any residue.

The product may be reconstituted using diluent supplied in a vial or pre-filled syringe. If using diluent from a vial, first withdraw the entire volume of diluent into the syringe to be used for reconstitution.

Inject all the diluent in the syringe into the vial of lyophilised vaccine, and agitate to mix thoroughly. Withdraw the entire contents into a syringe and inject the total volume of reconstituted vaccine intramuscularly or subcutaneously.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of infectious agents from one person to another.

Each dose contains not less than the equivalent of 1000 $TCID_{50}$ of Measles Virus, 12,500 $TCID_{50}$ of Mumps Virus and 1000 $TCID_{50}$ of Rubella Virus. Each dose contains approximately 25 µg neomycin, an antibiotic.

4.3 CONTRAINDICATIONS

- Hypersensitivity to any component of the vaccine, including gelatin.

- Do not give M-M-R II to pregnant females. If vaccination of post pubertal females is undertaken for protection against rubella, pregnancy should be avoided for one month following vaccination. (See 4.6 Fertility, Pregnancy and Lactation, *Use in Pregnancy*)

- Anaphylactic or anaphylactoid reaction to neomycin (each dose of reconstituted vaccine contains approximately 25 µg of neomycin). A history of contact dermatitis to neomycin is not a contraindication; however, the possibility of a flare-up of skin lesions should be borne in mind.

- History of anaphylactic or anaphylactoid reaction to eggs (see 4.4 Special Warnings and Precautions for Use, *Hypersensitivity to Eggs*)

- Any febrile respiratory illness or other active febrile infection

- Active untreated tuberculosis

- Patients receiving immunosuppressive therapy. This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, eg for Addison's disease

- Individuals with blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems

- Primary and acquired immunodeficiency states, including patients who are immunosuppressed in association with AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinaemic and dysgammaglobulinaemic states.

Measles inclusion body encephalitis (MIBE), pneumonitis and death as a direct consequence of disseminated measles vaccine virus infection have been reported in severely immunocompromised individuals inadvertently vaccinated with measles-containing vaccine.

- Individuals with a family history of congenital or hereditary immunodeficiency, until the immune competence of the potential vaccine recipient is demonstrated.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Adequate treatment provisions including adrenaline (epinephrine), should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

Patients should be observed for a sufficient period (at least 20 minutes) for the occurrence of early onset reactions seen with measles vaccine (see 4.8 Adverse Effects (Undesirable Effects)).

Due caution should be employed in administration of M-M-R II to persons with individual or family histories of convulsions, cerebral injury or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur following vaccination (see 4.8 Adverse Effects (Undesirable Effects)).

Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7-28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk. However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see 4.6 Fertility, Pregnancy and Lactation, *Use in Lactation*).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either any time before, simultaneously with, or at least 4 to 6 weeks after M-M-R II.

As for any vaccine, vaccination with M-M-R II may not result in seroconversion in 100% of susceptible persons given the vaccine.

Hypersensitivity to Eggs
Live measles vaccine and live mumps vaccine are produced in chick embryo cell culture. Persons with a history of anaphylactic or anaphylactoid or other immediate reactions (eg hives, swelling of the mouth and throat, difficulty in breathing, hypotension or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions after receiving vaccines containing traces of chick embryo antigen and should not be vaccinated with M-M-R II.

The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases. Such individuals may be vaccinated with extreme caution, having adequate treatment on hand should a reaction occur.

Thrombocytopenia and Coagulation disorders
This vaccine should be given subcutaneously to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination. In addition, individuals who experienced thrombocytopenia with the first dose of M-M-R II (or its component vaccines) may develop thrombocytopenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see 4.8 Adverse Effects (Undesirable Effects)).

Use in the elderly
No data available.

Paediatric use
Safety and effectiveness of measles vaccine in infants below the age of 6 months have not been established. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established.

Other
Children and young adults who are known to be infected with human immunodeficiency viruses and are not immunosuppressed may be vaccinated. However, the vaccinees who are infected

with HIV should be monitored closely for vaccine-preventable diseases because immunisation may be less effective than for uninfected persons (see 4.3 Contraindications).

Children under treatment for tuberculosis have not experienced exacerbation of the diseases when immunised with live measles virus vaccine; no studies have been reported to date of the effect of measles virus vaccines on untreated tuberculosis children.

Effects on laboratory tests
Please refer to 4.4 Special Warnings and Precautions for Use for further information.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Administration of immune globulins concurrently with M-M-R II may interfere with the expected immune response. Vaccination should be deferred for 3 months or longer following administration of immune globulin (human) and blood or plasma transfusions.

Use With Other Vaccines
M-M-R II should not be given less than one month before or after administration of other live viral vaccines.

Routine administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral poliovirus vaccine) concomitantly with measles, mumps and rubella vaccines is not recommended because there are insufficient data relating to the simultaneous administration of these antigens. However, in some circumstances, particularly when the patient may not return, some practitioners prefer to administer all these antigens on a single day. If done, separate sites and syringes should be used for DTP and M-M-R II.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available

Use in pregnancy (Category B2)
Currently available live virus vaccines have not caused teratogenic effects in humans. Caution needs to be exercised as live virus vaccines have been shown to cross the placenta and infect the foetus. Some live virus vaccines have caused birth defects in animals.

The vaccine should not be administered to pregnant females; furthermore pregnancy should be avoided for one month following vaccination (see 4.3 Contraindications).

Women of child bearing age should be tested for rubella antibodies prior to pregnancy. All seronegative women, provided they are not pregnant, should be offered rubella vaccine.

Wild-type rubella infection during pregnancy, especially in the first trimester, can lead to miscarriage, stillbirth, or Congenital Rubella Syndrome (CRS). In an 18-year survey involving over 1200 pregnant women who received rubella vaccine within 3 months before or after conception (of whom 683 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with CRS. Subsequent post-marketing surveillance identified CRS associated with a rubella vaccine strain following inadvertent vaccination of a pregnant female with a measles, mumps, and rubella vaccine.

Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion. Although mumps vaccine virus has been shown to infect the placenta and foetus, there

is no evidence that it causes congenital malformations in humans. Reports have indicated that contracting of wild-type measles during pregnancy enhances foetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects and prematurity have been observed subsequent to infection with wild-type measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse foetal effects. Based on this experience, rubella vaccination during pregnancy need not be the reason to recommend interruption of pregnancy. The final decision must be made by the patient and her physician.

Use in lactation
It is not known whether measles or mumps vaccine virus is secreted in human milk. Recent studies have shown that lactating postpartum women immunised with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants.

In the infants with serological evidence of rubella infection, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella. Caution should be exercised when M-M-R II is administered to a nursing woman (See 4.1 Therapeutic Indications, *Post-Partum Women*).

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The adverse reactions associated with the use of M-M-R II are those which have been reported following administration of the combination vaccines.

COMMON
Burning and/or stinging of short duration at the injection site.

OCCASIONAL
Body as a whole
Fever (38.3°C or higher)
Skin
Rash, or measles-like rash, usually minimal but may be generalised
Generally, fever, rash, or both appear between the 5th and the 12th day.

RARE
Body as a whole
Mild local reactions such as erythema, induration and tenderness; sore throat, malaise, atypical measles, irritability
Cardiovascular
Vasculitis
Digestive
Parotitis, nausea, vomiting, diarrhoea
Haematologic/Lymphatic
Regional lymphadenopathy, thrombocytopenia including immune thrombocytopenia (ITP), purpura
Hypersensitivity
Allergic reactions such as wheal and flare at injection site, anaphylaxis and anaphylactoid reactions, as well as related phenomena such as angioneurotic

oedema (including peripheral or facial oedema) and bronchial spasm, urticaria in individuals with or without an allergic history

Musculoskeletal

Arthralgia and/or arthritis (usually transient and rarely chronic [see below]), myalgia

Nervous/Psychiatric

Febrile convulsions in children, afebrile convulsions or seizures, headache, dizziness, paresthesia, polyneuritis, polyneuropathy, Guillain-Barre syndrome, ataxia, acute disseminated encephalomyelitis (ADEM), transverse myelitis, aseptic meningitis (see below), measles inclusion body encephalitis (MIBE) (See 4.3 Contraindications), encephalitis/encephalopathy (see below), syncope.

Respiratory System

Pneumonia, pneumonitis (see 4.3 Contraindications), cough, rhinitis

Skin

Erythema multiforme, Stevens-Johnson syndrome, Henoch-Schőnlein purpura, Acute Haemorragic Oedema of Infancy, vesiculation at injection site, swelling, pruritus

Special senses

Forms of optic neuritis, including retrobulbar neuritis, papillitis, and retinitis; ocular palsies, otitis media, nerve deafness, conjunctivitis

Urogenital

Epididymitis, orchitis

Other

Death from various, and in some cases unknown, causes has been reported rarely following vaccination with measles, mumps and rubella vaccines; however, a causal relationship has not been established in healthy individuals (see 4.3 Contraindications). No deaths or permanent sequelae were reported in a published post-marketing surveillance study in Finland involving 1.5 million children and adults who were vaccinated with M-M-R II during 1982 to 1993.

UNKNOWN FREQUENCY

Skin

Skin granuloma associated with vaccine derived rubella virus

Children who received M-M-R II intramuscularly

In a clinical trial of 752 children aged 12-19 months who received M-M-R II, either intramuscularly or subcutaneously. The general safety profile of either administration routes were comparable, although injection-site reactions were less frequent in the IM group (15.8%) compared with the SC group (25.8%).

Arthralgia and/or arthritis

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of injection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children.

Chronic arthritis has been associated with wild-type rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%; women: 12-20%), and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or, on rare occasions, for

years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35-45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

Subacute Sclerosing Panencephalitis (SSPE)
There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognised measles in the first year of life or possibly from the measles vaccination. Based on estimated measles vaccine distribution in the U.S.A., the Centers for Disease Control and Prevention have estimated that the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with wild-type measles, 6-22 cases of SSPE per million cases of measles in the U.S.A. The results of a retrospective case-controlled study conducted by the Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine appears to be to protect against SSPE by preventing measles with its inherent high risk of SSPE.

Aseptic meningitis
Cases of aseptic meningitis have been reported following measles, mumps, and rubella vaccination. Although a causal relationship between the Urabe strain of mumps vaccine and aseptic meningitis has been shown, there is no evidence to link Jeryl Lynn mumps vaccine to aseptic meningitis.

Encephalitis/encephalopathy
Encephalitis/encephalopathy have been reported approximately once for every 3 million doses of the measles, mumps, and rubella vaccine manufactured by Merck Sharp & Dohme LLC, Rahway, NJ 07065 USA. Since 1978, post-marketing surveillance indicates that serious adverse events such as encephalitis and encephalopathy continue to be rarely reported. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with wild type measles (one per one thousand reported cases).

In severely immunocompromised individuals inadvertently vaccinated with measles-containing vaccine, measles inclusion body encephalitis, pneumonitis, and fatal outcome as a direct consequence of disseminated measles vaccine virus infection have been reported (see 4.3 Contraindications); disseminated mumps and rubella vaccine virus infection have also been reported.

The Centers for Disease Control and Prevention has pointed out that a certain number of cases of encephalitis may be expected to occur in a large childhood population in a defined period of time even when no vaccines are administered. However, CNS adverse reactions, such as encephalitis and encephalopathy occurring within 30 days after vaccination, have been associated with measles vaccine approximately once every million doses. The risk of such serious neurological disorders following live measles virus vaccine administration is believed to be far less than that for encephalitis and encephalopathy with wild-type measles (one per two thousand reported cases).

Panniculitis
Panniculitis has been reported rarely following administration of measles vaccine.

In a clinical trial, 752 children received M-M-R II, either intramuscularly (n=374) or subcutaneously (n=378). The general safety profiles of the intramuscular and subcutaneous administration routes were comparable; however, fewer subjects experienced injection site

adverse reactions in the intramuscular group.

Forms of optic neuritis, including retrobulbar neuritis, papillitis and retinitis, may infrequently follow viral infections, and have been reported to occur 1 to 3 weeks following inoculation with some live virus vaccines; otitis media and conjunctivitis.

Infrequently, reactions comprising choking or cough, vomiting, respiratory difficulty and cyanosis have been reported within 30 minutes of vaccination. These reactions generally pass off without any treatment. However, appropriate equipment, medicines and personnel to manage the acute reaction should be readily available (see 4.4 Special Warnings and Precautions for Use).

Clinical experience with live attenuated measles, mumps, and rubella virus vaccines given individually indicates that encephalitis and other nervous system reactions have occurred very rarely. These might occur also with M-M-R II.

There have been isolated reports of ocular palsies and Guillain-Barre syndrome occurring after immunisation with vaccines containing live attenuated measles virus. The ocular palsies have occurred approximately 3-24 days following vaccination. No definite causal relationship has been established between either of these events and vaccination. Isolated reports of polyneuropathy including Guillain - Barre syndrome have also been reported after immunisation with rubella containing vaccines. Measles inclusion body encephalitis (MIBE) has occurred (see 4.3 Contraindications).

Reporting suspected adverse effects
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Overdose has been reported rarely and was not associated with any serious adverse events.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
See Section 5.1 Pharmacodynamics Properties, Clinical trials

Clinical trials
Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that subcutaneously administered M-M-R II is immunogenic in a high proportion of cases and generally well tolerated. In these studies, a single subcutaneous injection of the vaccine induced measles haemagglutination inhibition (HI) antibodies in 95 percent, mumps neutralising antibodies in 96 percent and rubella HI antibodies in 99 percent of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose.

The RA 27/3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralising antibody levels than other strains of rubella vaccine and has

been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies. The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses. The increased levels and broader profile of antibodies produced by RA 27/3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild-type virus.

Vaccine induced antibody levels following administration of M-M-R II have been shown to persist for at least two years without substantial decline. However, continued surveillance will be required to establish the long-term persistence of antibodies following vaccination with M-M-R II.

A comparative study in 752 subjects aged 12 to 19 months who received M-M-R II either by intramuscular route or subcutaneous route demonstrated a similar immunogenicity profile between both administration routes.

5.2 PHARMACOKINETIC PROPERTIES

Absorption
Not applicable

Distribution
Not applicable

Metabolism
Not applicable

Excretion
Not applicable

5.3 PRECLINICALSAFETY DATA

Genotoxicity
No data available

Carcinogenicity
No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

sorbitol
monobasic sodium phosphate
dibasic potassium phosphate
dibasic sodium phosphate
monobasic potassium phosphate
hydrolysed porcine gelatin*
phenolsulfonphthalein
sodium bicarbonate
sucrose
neomycin
monosodium glutamate monohydrate
*contains sulfites

Diluent

Water for injections

6.2 INCOMPATIBILITIES

Not applicable. Please refer to 4.5 Interactions with Other Medicines and Other Forms of Interactions for further information.

6.3 SHELF LIFE

The expiry date can be found on the packaging. In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG).

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Before reconstitution, store the vial of lyophilised vaccine at 2-8°C or colder. The diluent (prefilled syringe or vial) should be stored in the refrigerator with the lyophilised vaccine or separately at room temperature. **Do not freeze the diluent.**

To reduce microbiological hazard, it is recommended the vaccine be used as soon as possible after reconstitution. If storage of reconstituted vaccine is necessary, store in a dark place at 2°C-8°C and discard if not used within 8 hours.

The vaccine must be maintained at a temperature of 2-8°C during shipment, to ensure that there is no loss of potency. Freezing during shipment will not affect potency of the vaccine.

Protect the vaccine from light at all times, since such exposure may inactivate the viruses.

6.5 NATURE AND CONTENTS OF CONTAINER

M-M-R II is supplied as:
(1) a combination pack of a single-dose vial of lyophilised vaccine and a diluent-containing syringe.

(2) a box of ten combination packs of single-dose vials of lyophilised vaccine with diluent-containing syringes.

(3) a single-dose vial of lyophilised vaccine and a vial of diluent.

(4) a box of five combination packs of single-dose vials of lyophilized vaccine with diluent-containing vials.

(5) a box of ten combination packs of single-dose vials of lyophilised vaccine with diluent-containing vials.

(6) a single-dose vial of lyophilised vaccine, with diluent supplied separately.

(7) a box of ten single-dose vial of lyophilized vaccine, with diluent supplied separately.

Combination pack containing lyophilised vaccine and diluent together should be stored at 2-8°C.

Not all presentations and pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure
Not applicable

CAS number
Not applicable

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine S4

8 SPONSOR

Merck Sharp & Dohme (Australia) Pty Limited
Level 1, Building A, 26 Talavera Road
Macquarie Park NSW 2113
www.msd-australia.com.au

9 DATE OF FIRST APPROVAL

14 February 2006

10 DATE OF REVISION

27 January 2026

Summary table of changes

Section changed	Summary of new information
2, 3, 4.2	Included the use of sterile diluent prefilled syringes for reconstitution and changes for consistency within the M-M-R, VARIVAX, and ProQuad product family
6.1	Updated to reflect presence of sulfite and to include information on the diluent
6.4	Update to the diluent storage text to specify prefilled syringe or vials.
Multiple	Minor editorial revisions were made throughout the document

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