ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection
Measles, mumps, and rubella vaccine (live)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 ml) contains:

Measles virus[1] Enders' Edmonston strain (live, attenuated) ……..….not less than $1x10^3$ $CCID_{50}$*
Mumps virus[1] Jeryl Lynn™ [Level B] strain (live, attenuated)……...…not less than $12.5x10^3$ $CCID_{50}$*
Rubella virus[2] Wistar RA 27/3 strain (live, attenuated) ……..….not less than $1x10^3$ $CCID_{50}$*

*50% cell culture infectious dose

[1] produced in chick embryo cells.
[2] produced in WI-38 human diploid lung fibroblasts.

The vaccine may contain traces of recombinant human albumin (rHA).
This vaccine contains a trace amount of neomycin. See section 4.3.

Excipients with known effect:
The vaccine contains 14.5 mg of sorbitol. See section 4.4.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.
Before reconstitution, the powder is a light yellow compact crystalline cake and the solvent is a clear colourless fluid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

M-M-RVAXPRO is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals from 12 months of age (see section 4.2).

M-M-RVAXPRO can be administered to infants from 9 months of age under special circumstances (see sections 4.2, 4.4 and 5.1).

For use in measles outbreaks, or for post-exposure vaccination, or, for use in previously unvaccinated individuals older than 9 months who are in contact with susceptible pregnant women, and persons likely to be susceptible to mumps and rubella, see section 5.1.

M-M-RVAXPRO is to be used on the basis of official recommendations.

4.2 Posology and method of administration

Posology

Individuals 12 months of age or older:

Individuals 12 months or older should receive one dose at an elected date. A second dose may be administered at least 4 weeks after the first dose in accordance with official recommendation. The second dose is intended for individuals who did not respond to the first dose for any reason.

Infants between 9 and 12 months of age:
Immunogenicity and safety data show that M-M-RVAXPRO can be administered to infants between 9 and 12 months of age, in accordance with official recommendations or when an early protection is considered necessary (e.g., day-care, outbreak situations, or travel to a region with high prevalence of measles). Such infants should be revaccinated at 12 to 15 months. An additional dose with a measles-containing vaccine should be considered according to official recommendations (see sections 4.4 and 5.1).

Infants below 9 months of age:
No data on the efficacy and safety of M-M-RVAXPRO for use in children below 9 months of age are currently available.

Method of administration

The vaccine is to be injected intramuscularly (IM) or subcutaneously (SC).

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.

For precautions to be taken before handling or administering the medicinal product, and for instructions on reconstitution of the medicinal product before administration, see section 6.6.

DO NOT INJECT INTRAVASCULARLY.

4.3 Contraindications

History of hypersensitivity to any measles, mumps, or rubella vaccine, or to any of the excipients, including neomycin (see sections 2, 4.4, and 6.1).

Pregnancy. Furthermore, pregnancy should be avoided for 1 month following vaccination (see section 4.6).

Vaccination should be postponed during any illness with fever >38.5°C.

Active untreated tuberculosis. Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine. No studies have been reported to date on the effect of measles virus vaccines on children with untreated tuberculosis.

Blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the haematopoietic and lymphatic systems.

Current immunosuppressive therapy (including high doses of corticosteroids). M-M-RVAXPRO is not contraindicated in individuals who are receiving topical or low-dose parenteral corticosteroids (*e.g.* for asthma prophylaxis or replacement therapy).

Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia and AIDS or symptomatic HIV infection or an age-specific CD4+ T-lymphocyte percentage in children below 12 months: CD4+ <25% %; children between 12-35 months: CD4+ < 20%; children between 36-59 months: CD4+ < 15% (see section 4.4).

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.

Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

Adults and adolescents with a history of allergies may potentially be at increased risk of anaphylaxis or anaphylactoid reactions. Close monitoring is recommended following vaccination for the early signs of such reactions.

Since live measles vaccine and live mumps vaccine are produced in chick embryo cell culture, persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (*e.g.*, hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions. The potential risk-to-benefit ratio should be carefully evaluated before considering vaccination in such cases.

Due caution should be employed in administration of M-M-RVAXPRO to persons with individual or family history of convulsions, or a history of cerebral injury. The physician should be alert to the temperature elevation that may occur following vaccination (see section 4.8).

Infants from 9 to 12 months of age vaccinated with a measles-containing vaccine during measles outbreaks or for other reasons may fail to respond to the vaccine due to the presence of circulating antibodies of maternal origin and/or immaturity of the immune system (see sections 4.2 and 5.1).

This vaccine contains 14.5 mg of sorbitol as an excipient. Patients with rare hereditary problems of fructose intolerance should not take this vaccine.

Thrombocytopenia
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-RVAXPRO (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 section 4.8).

Other
Vaccination may be considered in patients with selected immune deficiencies where the benefits outweigh the risks (asymptomatic HIV patients, IgG subclass deficiencies, congenital neutropenia, chronic granulomatous disease, and complement deficiency diseases).

Immunocompromised patients who have no contraindication for this vaccination (see section 4.3) may not respond as well as immunocompetent patients; therefore, some of these patients may acquire measles, mumps, or rubella in case of contact, despite appropriate vaccine administration. These patients should be monitored carefully for signs of measles, parotitis, and rubella.

Vaccination with M-M-RVAXPRO may not result in protection in all vaccinees.

Transmission

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7 to 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 without any evidence of clinical disease (see section 4.6).

There are no reports of transmission of the more attenuated Enders' Edmonston strain of measles virus or the Jeryl Lynn™ strain of mumps virus from vaccinees to susceptible contacts.

Interference with laboratory tests: see section 4.5.

4.5 Interaction with other medicinal products and other forms of interaction

Immune globulin
Immune globulin (IG) is not to be given concomitantly with M-M-RVAXPRO.

Administration of immune globulins concomitantly with M-M-RVAXPRO may interfere with the expected immune response. Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

Administration of measles, mumps, or rubella antibody-containing blood products, including immune globulin preparations, should be avoided within 1 month after a dose of M-M-RVAXPRO unless considered to be essential.

Laboratory tests
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 4 to 6 weeks after vaccination with M-M-RVAXPRO.

Use with other vaccines
Currently no specific studies have been conducted on the concomitant use of M-M-RVAXPRO and other vaccines. However, since M-M-RVAXPRO has been shown to have safety and immunogenicity profiles similar to the previous formulation of the combined measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., experience with this vaccine can be considered.

Published clinical data support concomitant administration of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. with other childhood vaccinations, including DTaP (or DTwP), IPV (or OPV), HIB (*Haemophilus influenzae* type b), HIB-HBV (*Haemophilus influenzae* type b with Hepatitis B vaccine), and VAR (varicella). M-M-RVAXPRO should be given concomitantly at separate injection sites, or one month before or after administration of other live virus vaccines.

Based on clinical studies with the quadrivalent measles, mumps, rubella and varicella vaccine and with the previous formulation of the combined measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., M-M-RVAXPRO can be given simultaneously (but at separate injection sites) with Prevenar and/or hepatitis A vaccine. In these clinical studies, it was demonstrated that the immune responses were unaffected and that the overall safety profiles of the administered vaccines were similar.

4.6 Fertility, pregnancy and lactation

Pregnancy
Pregnant women should not be vaccinated with M-M-RVAXPRO.

Studies have not been conducted with M-M-RVAXPRO in pregnant women. It is not known whether M-M-RVAXPRO can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity.

However, foetal damage has not been documented when measles or mumps vaccines have been given to pregnant women. Although a theoretical risk cannot be excluded, no cases of congenital rubella syndrome have been reported in more than 3500 susceptible women who were unknowingly in early stages of pregnancy when vaccinated with a rubella-containing vaccine. Therefore, inadvertent vaccination of unknowingly pregnant women with measles-, mumps-, or rubella-containing vaccines should not be a reason for termination of pregnancy.

Pregnancy should be avoided for 1 month following vaccination. Women who intend to become pregnant should be advised to delay.

Breast-feeding
Studies have shown that breast-feeding postpartum women vaccinated with live attenuated rubella vaccines may secrete the virus in breast milk and transmit it to breast-fed infants. In the infants with serological evidence of rubella infection, none had symptomatic disease. It is not known whether measles or mumps vaccine virus is secreted in human milk; therefore, caution should be exercised when M-M-RVAXPRO is administered to a breast-feeding woman.

Fertility
M-M-RVAXPRO has not been evaluated in fertility studies.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
M-M-RVAXPRO is expected to have no or negligible influence on ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile
In clinical trials, M-M-RVAXPRO was administered to 1965 children (see section 5.1), and the general safety profile was comparable to the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc.

In a clinical trial, 752 children received M-M-RVAXPRO, 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%).

All adverse reactions were evaluated in 1940 children. Among these children, the vaccine-related adverse reactions, summarised in section b, were observed in individuals following vaccination with M-M-RVAXPRO (excluding isolated reports with frequency <0.2%).

In comparison to the first dose, a second dose of M-M-RVAXPRO is not associated with an increase in the incidence and severity of clinical symptoms including those suggestive of hypersensitivity reaction.

Additionally, other adverse reactions reported with post-marketing use of M-M-RVAXPRO and/or in clinical studies and post-marketing use of previous formulations of monovalent and of the combined measles, mumps, and rubella vaccines manufactured by Merck & Co., Inc. without regard to causality or frequency are available and are summarised in section b (frequency *not known*). These data were reported based on more than 400 million doses distributed worldwide.

The most common adverse reactions reported with the use of M-M-RVAXPRO were: fever (38.5°C or higher); injection site reactions including pain, swelling and erythema.

b. Tabulated list of adverse reactions

Adverse reactions are ranked under headings of frequency using the following convention: [Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to ≤1/100); not known (cannot be estimated from the available data)]

Adverse reactions	Frequency
Infections and infestations	
Nasopharyngitis, Upper respiratory tract infection or Viral infection	Uncommon
Aseptic meningitis†, Atypical measles, Epididymitis, Orchitis, Otitis media, Parotitis, Rhinitis, Subacute Sclerosing Panencephalitis†	Not known
Blood and the lymphatic system disorders	
Regional lymphadenopathy, Thrombocytopenia	Not known
Immune system disorders	
Anaphylactoid reaction, Anaphylaxis and related phenomenon such as Angioneurotic oedema, Facial oedema, and Peripheral oedema	Not known
Psychiatric disorders	
Irritability	Not known
Nervous system disorders	
Afebrile convulsions or seizures, Ataxia, Dizziness, Encephalitis† , Encephalopathy† , Febrile convulsion (in children), Guillain-Barre syndrome, Headache, Measles inclusion body encephalitis (MIBE) (see section 4.3), Ocular palsies, Optic neuritis, Paraesthesia, Polyneuritis, Polyneuropathy, Retrobulbar neuritis, Syncope	Not known
Eye disorders	
Conjunctivitis, Retinitis	Not known
Ear and labyrinth disorders	
Nerve deafness	Not known
Respiratory, thoracic, and mediastinal disorders	
Rhinorrhoea	Uncommon
Bronchial spasm, Cough, Pneumonia, Pneumonitis (see section 4.3), Sore throat	Not known
Gastrointestinal disorders	
Diarrhoea or Vomiting	Uncommon
Nausea	Not known
Skin and subcutaneous tissue disorders	
Rash morbilliform or other Rash	Common
Urticaria	Uncommon
Panniculitis, Purpura, Skin induration, Stevens-Johnson syndrome, Pruritus	Not known
Musculoskeletal, connective tissue and bone disorders	
Arthritis† and/or Arthralgia† (usually transient and rarely chronic), Myalgia	Not known
General disorders and administration site conditions	
Fever (38.5°C or higher), Injection site erythema, Injection site pain, and Injection site swelling	Very common
Injection site bruising	Common
Injection site rash	Uncommon
Burning and/or Stinging of short duration at the injection site, Fever (38.5°C or higher), Malaise, Papillitis, Peripheral oedema, Swelling, Tenderness, Vesicles at the injection site, Wheal and Flare at the	Not known

injection site	
Vascular disorders	
Vasculitis	Not known

† see section c

c. Description of selected adverse reactions

Aseptic meningitis

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

Encephalitis and Encephalopathy

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 section 4.3); disseminated mumps and rubella vaccine virus infection has also been reported.

Subacute sclerosing panencephalitis

There is no evidence that measles vaccine can cause SSPE. There have been reports of SSPE in children who did not have a history of infection with wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. The results of a retrospective case-controlled study conducted by the US Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent risk of SSPE.

Arthralgia and/or arthritis

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of infection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. Following vaccination in children, reactions in joints are generally uncommon (0-3%) and of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (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 adult women. Even in older women (35-45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

Chronic arthritis

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V

4.9 Overdose

Administration of a higher than recommended dose of M-M-RVAXPRO was reported rarely and the adverse reaction profile was comparable to that observed with the recommended dose of M-M-RVAXPRO.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral vaccine, ATC code J07BD52

Evaluation of immunogenicity and clinical efficacy
A comparative study in 1279 subjects who received M-M-RVAXPRO or the previous formulation (manufactured with human serum albumin) of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. demonstrated similar immunogenicity and safety between the 2 products.

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralising antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons.

Evaluation of immunogenicity in children from 9 to 12 months of age at the time of first dose
A clinical study was conducted with the quadrivalent measles, mumps, rubella and varicella vaccine manufactured by Merck & Co., Inc., administered with a 2-dose schedule, the doses being given 3 months apart in 1,620 healthy subjects from 9 to 12 months of age at the time of first dose. The safety profile post-dose 1 and 2 was generally comparable for all age cohorts.

In the Full Analysis Set (vaccinated subjects regardless of their antibody titre at baseline), high seroprotection rates of >99% were elicited to mumps and rubella post-dose 2, regardless of the age of the vaccinee at the first dose. After 2 doses, the seroprotection rates against measles were 98.1% when the first dose was given at 11 months compared to 98.9% when the first dose was given at 12 months (non-inferiority study objective met). After two doses, the seroprotection rates against measles were 94.6% when the first dose was given at 9 months compared to 98.9% when the first dose was given at 12 months (non-inferiority study objective not met).

The seroprotection rates to measles, mumps, and rubella for the Full Analysis Set are given in Table 1.

Table 1: Seroprotection Rates to Measles, Mumps, and Rubella 6 Weeks Post-Dose 1 and 6 Weeks Post-Dose 2 of the quadrivalent measles, mumps, rubella and varicella vaccine manufactured by Merck & Co., Inc. – Full Analysis Set

Valence (seroprotection level)	**Time point**	**Dose 1 at 9 months / Dose 2 at 12 months N = 527**	**Dose–1 at 11 months / Dose 2 at 14 months N = 480**	**Dose 1 at 12 months / Dose 2 at 15 months N = 466**
		Seroprotection rates [95% CI]	**Seroprotection rates [95% CI]**	**Seroprotection rates [95% CI]**
Measles (titre ≥255 mIU/mL)	**Post-Dose 1**	72.3% [68.2; 76.1]	87.6% [84.2; 90.4]	90.6% [87.6; 93.1]
	Post-Dose 2	94.6% [92.3; 96.4]	98.1% [96.4; 99.1]	98.9% [97.5; 99.6]
Mumps (titre ≥10 ELISA Ab units/mL)	**Post-Dose 1**	96.4% [94.4; 97.8]	98.7% [97.3; 99.5]	98.5% [96.9; 99.4]
	Post-Dose 2	99.2% [98.0; 99.8]	99.6% [98.5; 99.9]	99.3% [98.1; 99.9]
Rubella (titre ≥10 IU/mL)	**Post-Dose 1**	97.3% [95.5; 98.5]	98.7% [97.3; 99.5]	97.8% [96.0; 98.9]
	Post-Dose 2	99.4% [98.3; 99.9]	99.4% [98.1; 99.9]	99.6% [98.4; 99.9]

The post-dose 2 geometric mean titres (GMTs) against mumps and rubella were comparable across all age categories, while the GMTs against measles were lower in subjects who received the first dose at 9 months of age as compared to subjects who received the first dose at 11 or 12 months of age.

A comparative study in 752 subjects who received M-M-RVAXPRO either by intramuscular route or subcutaneous route demonstrated a similar immunogenicity profile between both administration routes.

The efficacy of the components of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. was established in a series of double-blind controlled field trials, which demonstrated a high degree of protective efficacy afforded by the individual vaccine components. These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.

Post-exposure vaccination
Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours after exposure. If, however, the vaccine is given a few days before exposure, substantial protection may be afforded. There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.

Effectiveness
More than 400 million doses of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. have been distributed worldwide (1978 to 2003). Widespread use of a 2-dose vaccination schedule in the United States and countries such as Finland and Sweden has led to a >99% reduction in the incidence of each of the 3 targeted diseases.

Non-pregnant adolescent and adult females
Vaccination 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 sections 4.4 and 4.6). 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.

Previously unvaccinated individuals older than 9 months who are in contact with susceptible pregnant women should receive live attenuated rubella-containing vaccine (such as M-M-RVAXPRO or a monovalent rubella vaccine) to reduce the risk of exposure of the pregnant woman.

Individuals likely to be susceptible to mumps and rubella
M-M-RVAXPRO is preferred for vaccination of persons likely to be susceptible to mumps and rubella. Individuals who require vaccination against measles can receive M-M-RVAXPRO regardless of their immune status to mumps or rubella if a monovalent measles vaccine is not readily available.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder
Sorbitol
Sodium phosphate
Potassium phosphate

Sucrose
Hydrolysed gelatin
Medium 199 with Hanks' salts
Minimum Essential Medium, Eagle (MEM)
Monosodium L-glutamate
Neomycin
Phenol red
Sodium bicarbonate
Hydrochloric acid (to adjust pH)
Sodium hydroxide (to adjust pH)

Solvent
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, the vaccine must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

After reconstitution, the vaccine should be used immediately; however, in-use stability has been demonstrated for 8 hours when refrigerated at 2°C-8°C.

6.4 Special precautions for storage

Store and transport refrigerated (2°C – 8°C).
Do not freeze.
Keep the vial of powder in the outer carton in order to protect from light.

For storage conditions after the reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Powder in a vial (glass) with a stopper (butyl rubber) and solvent in a vial (glass) with stopper (chlorobutyl rubber) in a pack size of 1 and 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

To reconstitute, use the solvent supplied. The solvent is a clear colourless liquid. Before mixing with the solvent, the powder is a light yellow compact crystalline cake. When completely reconstituted, the vaccine is a clear yellow liquid.

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

Reconstitution instructions
Withdraw the entire volume of solvent into a syringe to be used for reconstitution and injection. Inject the entire content of the syringe into the vial containing the powder. Gently agitate to mix thoroughly. The reconstituted vaccine must not be used if any particulate matter is noted or if the appearance of the solvent or powder or of the reconstituted vaccine differs from that described above.

Withdraw the entire content of the reconstituted vaccine vial into the same syringe and inject the entire volume.

If two needles are provided: use one needle to reconstitute the vaccine and the other for its administration to the person to be vaccinated.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/001
EU/1/06/337/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 May 2006
Date of latest renewal: 11 May 2011

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps, and rubella vaccine (live)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 ml) contains:

Measles virus[1] Enders' Edmonston strain (live, attenuated) …….not less than $1x10^3$ $CCID_{50}$*
Mumps virus[1] Jeryl Lynn™ [Level B] strain (live, attenuated)……not less than $12.5x10^3$ $CCID_{50}$*
Rubella virus[2] Wistar RA 27/3 strain (live, attenuated) …….not less than $1x10^3$ $CCID_{50}$*

*50% cell culture infectious dose

[1] produced in chick embryo cells.
[2] produced in WI-38 human diploid lung fibroblasts.

The vaccine may contain traces of recombinant human albumin (rHA).
This vaccine contains a trace amount of neomycin. See section 4.3.

Excipients with known effect:
The vaccine contains 14.5 mg of sorbitol. See section 4.4.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection in pre-filled syringe.
Before reconstitution, the powder is a light yellow compact crystalline cake and the solvent is a clear colourless fluid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

M-M-RVAXPRO is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals from 12 months of age (see section 4.2).

M-M-RVAXPRO can be administered to infants from 9 months of age under special circumstances (see sections 4.2, 4.4 and 5.1).

For use in measles outbreaks, or for post-exposure vaccination, or, for use in previously unvaccinated individuals older than 9 months who are in contact with susceptible pregnant women and persons likely to be susceptible to mumps and rubella, see section 5.1.

M-M-RVAXPRO is to be used on the basis of official recommendations.

4.2 Posology and method of administration

Posology

Individuals 12 months of age or older:

Individuals 12 months or older should receive one dose at an elected date. A second dose may be administered at least 4 weeks after the first dose in accordance with official recommendation. The second dose is intended for individuals who did not respond to the first dose for any reason.

Infants between 9 and 12 months of age:
Immunogenicity and safety data show that M-M-RVAXPRO can be administered to infants between 9 and 12 months of age, in accordance with official recommendations or when an early protection is considered necessary (e.g., day-care, outbreak situations, or travel to a region with high prevalence of measles). Such infants should be revaccinated at 12 to 15 months. An additional dose with a measles-containing vaccine should be considered according to official recommendations (see sections 4.4 and 5.1).

Infants below 9 months of age:
No data on the efficacy and safety of M-M-RVAXPRO for use in children below 9 months of age are currently available.

Method of administration

The vaccine is to be injected intramuscularly (IM) or subcutaneously (SC).

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.

For precautions to be taken before handling or administering the medicinal product, and for instructions on reconstitution of the medicinal product before administration, see section 6.6.

DO NOT INJECT INTRAVASCULARLY.

4.3 Contraindications

History of hypersensitivity to any measles, mumps, or rubella vaccine, or to any of the excipients, including neomycin (see sections 2, 4.4, and 6.1).

Pregnancy. Furthermore, pregnancy should be avoided for 1 month following vaccination (see section 4.6).

Vaccination should be postponed during any illness with fever >38.5°C.

Active untreated tuberculosis. Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine. No studies have been reported to date on the effect of measles virus vaccines on children with untreated tuberculosis.

Blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the haematopoietic and lymphatic systems.

Current immunosuppressive therapy (including high doses of corticosteroids). M-M-RVAXPRO is not contraindicated in individuals who are receiving topical or low-dose parenteral corticosteroids (*e.g.* for asthma prophylaxis or replacement therapy).

Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia and AIDS or symptomatic HIV infection or an age-specific CD4+ T-lymphocyte percentage in children below 12 months: CD4+ <25% ; children between 12-35 months: CD4+ < 20%; children between 36-59 months: CD4+ < 15% (see section 4.4).

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.

Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

Adults and adolescents with a history of allergies may potentially be at increased risk of anaphylaxis or anaphylactoid reactions. Close monitoring is recommended following vaccination for the early signs of such reactions.

Since live measles vaccine and live mumps vaccine are produced in chick embryo cell culture, persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (*e.g.*, hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions. The potential risk-to-benefit ratio should be carefully evaluated before considering vaccination in such cases.

Due caution should be employed in administration of M-M-RVAXPRO to persons with individual or family history of convulsions, or a history of cerebral injury. The physician should be alert to the temperature elevation that may occur following vaccination (see section 4.8).

Infants from 9 to 12 months of age vaccinated with a measles-containing vaccine during measles outbreaks or for other reasons may fail to respond to the vaccine due to the presence of circulating antibodies of maternal origin and/or immaturity of the immune system (see sections 4.2 and 5.1).

This vaccine contains 14.5 mg of sorbitol as an excipient. Patients with rare hereditary problems of fructose intolerance should not take this vaccine.

Thrombocytopenia
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-RVAXPRO (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 section 4.8).

Other
Vaccination may be considered in patients with selected immune deficiencies where the benefits outweigh the risks (asymptomatic HIV patients, IgG subclass deficiencies, congenital neutropenia, chronic granulomatous disease, and complement deficiency diseases).

Immunocompromised patients who have no contraindication for this vaccination (see section 4.3) may not respond as well as immunocompetent patients; therefore, some of these patients may acquire measles, mumps, or rubella in case of contact, despite appropriate vaccine administration. These patients should be monitored carefully for signs of measles, parotitis, and rubella.

Vaccination with M-M-RVAXPRO may not result in protection in all vaccinees.

Transmission

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7 to 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 without any evidence of clinical disease (see section 4.6).

There are no reports of transmission of the more attenuated Enders' Edmonston strain of measles virus or the Jeryl Lynn™ strain of mumps virus from vaccinees to susceptible contacts.

Interference with laboratory tests: see section 4.5.

4.5 Interaction with other medicinal products and other forms of interaction

Immune glogulin
Immune globulin (IG) is not to be given concomitantly with M-M-RVAXPRO.

Administration of immune globulins concomitantly with M-M-RVAXPRO may interfere with the expected immune response. Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

Administration of measles, mumps, or rubella antibody-containing blood products, including immune globulin preparations, should be avoided within 1 month after a dose of M-M-RVAXPRO unless considered to be essential.

Laboratory tests
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 4 to 6 weeks after vaccination with M-M-RVAXPRO.

Use with other vaccines
Currently no specific studies have been conducted on the concomitant use of M-M-RVAXPRO and other vaccines. However, since M-M-RVAXPRO has been shown to have safety and immunogenicity profiles similar to the previous formulation of the combined measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., experience with this vaccine can be considered.

Published clinical data support concomitant administration of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. with other childhood vaccinations, including DTaP (or DTwP), IPV (or OPV), HIB (*Haemophilus influenzae* type b), HIB-HBV (*Haemophilus influenzae* type b with Hepatitis B vaccine), and VAR (varicella). M-M-RVAXPRO should be given concomitantly at separate injection sites, or one month before or after administration of other live virus vaccines.

Based on clinical studies with the quadrivalent measles, mumps, rubella and varicella vaccine and with the previous formulation of the combined measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., M-M-RVAXPRO can be given simultaneously (but at separate injection sites) with Prevenar and/or hepatitis A vaccine. In these clinical studies, it was demonstrated that the immune responses were unaffected and that the overall safety profiles of the administered vaccines were similar.

4.6 Fertility, pregnancy and lactation

Pregnancy
Pregnant women should not be vaccinated with M-M-RVAXPRO.

Studies have not been conducted with M-M-RVAXPRO in pregnant women. It is not known whether M-M-RVAXPRO can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity.

However, foetal damage has not been documented when measles or mumps vaccines have been given to pregnant women. Although a theoretical risk cannot be excluded, no cases of congenital rubella syndrome have been reported in more than 3500 susceptible women who were unknowingly in early stages of pregnancy when vaccinated with a rubella-containing vaccine. Therefore, inadvertent vaccination of unknowingly pregnant women with measles-, mumps-, or rubella-containing vaccines should not be a reason for termination of pregnancy.

Pregnancy should be avoided for 1 month following vaccination. Women who intend to become pregnant should be advised to delay.

Breast-feeding
Studies have shown that breast-feeding postpartum women vaccinated with live attenuated rubella vaccines may secrete the virus in breast milk and transmit it to breast-fed infants. In the infants with serological evidence of rubella infection, none had symptomatic disease. It is not known whether measles or mumps vaccine virus is secreted in human milk; therefore, caution should be exercised when M-M-RVAXPRO is administered to a breast-feeding woman.

Fertility
M-M-RVAXPRO has not been evaluated in fertility studies.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
M-M-RVAXPRO is expected to have no or negligible influence on ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile
In clinical trials, M-M-RVAXPRO was administered to 1965 children (see section 5.1), and the general safety profile was comparable to the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc.

In a clinical trial, 752 children received M-M-RVAXPRO, 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%).

All adverse reactions were evaluated in 1940 children. Among these children, the vaccine-related adverse reactions, summarised in section b, were observed in individuals following vaccination with M-M-RVAXPRO (excluding isolated reports with frequency <0.2%).

In comparison to the first dose, a second dose of M-M-RVAXPRO is not associated with an increase in the incidence and severity of clinical symptoms including those suggestive of hypersensitivity reaction.

Additionally, other adverse reactions reported with post-marketing use of M-M-RVAXPRO and/or in clinical studies and post-marketing use of previous formulations of monovalent and of the combined measles, mumps, and rubella vaccines manufactured by Merck & Co., Inc. without regard to causality or frequency are available and are summarised in section b (frequency *not known*). These data were reported based on more than 400 million doses distributed worldwide.

The most common adverse reactions reported with the use of M-M-RVAXPRO were: fever (38.5°C or higher); injection site reactions including pain, swelling and erythema.

b. Tabulated list of adverse reactions

Adverse reactions are ranked under headings of frequency using the following convention: [Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to ≤1/100); not known (cannot be estimated from the available data)]

Adverse reactions	Frequency
Infections and infestations	
Nasopharyngitis, Upper respiratory tract infection or Viral infection	Uncommon
Aseptic meningitis†, Atypical measles, Epididymitis, Orchitis, Otitis media, Parotitis, Rhinitis, Subacute Sclerosing Panencephalitis†	Not known
Blood and the lymphatic system disorders	
Regional lymphadenopathy, Thrombocytopenia	Not known
Immune system disorders	
Anaphylactoid reaction, Anaphylaxis and related phenomenon such as Angioneurotic oedema, Facial oedema, and Peripheral oedema	Not known
Psychiatric disorders	
Irritability	Not known
Nervous system disorders	
Afebrile convulsions or seizures, Ataxia, Dizziness, Encephalitis† , Encephalopathy† , Febrile convulsion (in children), Guillain-Barre syndrome, Headache, Measles inclusion body encephalitis (MIBE) (see section 4.3), Ocular palsies, Optic neuritis, Paraesthesia, Polyneuritis, Polyneuropathy, Retrobulbar neuritis, Syncope	Not known
Eye disorders	
Conjunctivitis, Retinitis	Not known
Ear and labyrinth disorders	
Nerve deafness	Not known
Respiratory, thoracic, and mediastinal disorders	
Rhinorrhoea	Uncommon
Bronchial spasm, Cough, Pneumonia, Pneumonitis (see section 4.3), Sore throat	Not known
Gastrointestinal disorders	
Diarrhoea or Vomiting	Uncommon
Nausea	Not known
Skin and subcutaneous tissue disorders	
Rash morbilliform or other Rash	Common
Urticaria	Uncommon
Panniculitis, Purpura, Skin induration, Stevens-Johnson syndrome, Pruritus	Not known
Musculoskeletal, connective tissue and bone disorders	
Arthritis† and/or Arthralgia† (usually transient and rarely chronic), Myalgia	Not known
General disorders and administration site conditions	
Fever (38.5°C or higher), Injection site erythema, Injection site pain, and Injection site swelling	Very common
Injection site bruising	Common
Injection site rash	Uncommon
Burning and/or Stinging of short duration at the injection site, Fever (38.5°C or higher), Malaise, Papillitis, Peripheral oedema, Swelling, Tenderness, Vesicles at the injection site, Wheal and Flare at the	Not known

injection site	
Vascular disorders	
Vasculitis	Not known

† see section c

c. Description of selected adverse reactions

Aseptic meningitis

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

Encephalitis and Encephalopathy

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 section 4.3); disseminated mumps and rubella vaccine virus infection has also been reported.

Subacute sclerosing panencephalitis

There is no evidence that measles vaccine can cause SSPE. There have been reports of SSPE in children who did not have a history of infection with wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. The results of a retrospective case-controlled study conducted by the US Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent risk of SSPE.

Arthralgia and/or arthritis

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of infection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. Following vaccination in children, reactions in joints are generally uncommon (0-3%) and of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (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 adult women. Even in older women (35-45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

Chronic arthritis

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V

4.9 Overdose

Administration of a higher than recommended dose of M-M-RVAXPRO was reported rarely and the adverse reaction profile was comparable to that observed with the recommended dose of M-M-RVAXPRO.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral vaccine, ATC code J07BD52

Evaluation of immunogenicity and clinical efficacy
A comparative study in 1279 subjects who received M-M-RVAXPRO or the previous formulation (manufactured with human serum albumin) of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. demonstrated similar immunogenicity and safety between the 2 products.

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralising antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons.

Evaluation of immunogenicity in children from 9 to 12 months of age at the time of first dose
A clinical study was conducted with the quadrivalent measles, mumps, rubella and varicella vaccine manufactured by Merck & Co., Inc., administered with a 2-dose schedule, the doses being given 3 months apart in 1,620 healthy subjects from 9 to 12 months of age at the time of first dose. The safety profile post-dose 1 and 2 was generally comparable for all age cohorts.

In the Full Analysis Set (vaccinated subjects regardless of their antibody titre at baseline), high seroprotection rates of >99% were elicited to mumps and rubella post-dose 2, regardless of the age of the vaccinee at the first dose. After 2 doses, the seroprotection rates against measles were 98.1% when the first dose was given at 11 months compared to 98.9% when the first dose was given at 12 months (non-inferiority study objective met). After two doses, the seroprotection rates against measles were 94.6% when the first dose was given at 9 months compared to 98.9% when the first dose was given at 12 months (non-inferiority study objective not met).

The seroprotection rates to measles, mumps, and rubella for the Full Analysis Set are given in Table 1.

Table 1: Seroprotection Rates to Measles, Mumps, and Rubella 6 Weeks Post-Dose 1 and 6 Weeks Post-Dose 2 of the quadrivalent measles, mumps, rubella and varicella vaccine manufactured by Merck & Co., Inc. – Full Analysis Set

Valence (seroprotection level)	**Time point**	**Dose 1 at 9 months / Dose 2 at 12 months N = 527**	**Dose–1 at 11 months / Dose 2 at 14 months N = 480**	**Dose 1 at 12 months / Dose 2 at 15 months N = 466**
		Seroprotection rates [95% CI]	**Seroprotection rates [95% CI]**	**Seroprotection rates [95% CI]**
Measles (titre ≥255 mIU/mL)	**Post-Dose 1**	72.3% [68.2; 76.1]	87.6% [84.2; 90.4]	90.6% [87.6; 93.1]
	Post-Dose 2	94.6% [92.3; 96.4]	98.1% [96.4; 99.1]	98.9% [97.5; 99.6]
Mumps (titre ≥10 ELISA Ab units/mL)	**Post-Dose 1**	96.4% [94.4; 97.8]	98.7% [97.3; 99.5]	98.5% [96.9; 99.4]
	Post-Dose 2	99.2% [98.0; 99.8]	99.6% [98.5; 99.9]	99.3% [98.1; 99.9]
Rubella (titre ≥10 IU/mL)	**Post-Dose 1**	97.3% [95.5; 98.5]	98.7% [97.3; 99.5]	97.8% [96.0; 98.9]
	Post-Dose 2	99.4% [98.3; 99.9]	99.4% [98.1; 99.9]	99.6% [98.4; 99.9]

The post-dose 2 geometric mean titres (GMTs) against mumps and rubella were comparable across all age categories, while the GMTs against measles were lower in subjects who received the first dose at 9 months of age as compared to subjects who received the first dose at 11 or 12 months of age.

A comparative study in 752 subjects who received M-M-RVAXPRO either by intramuscular route or subcutaneous route demonstrated a similar immunogenicity profile between both administration routes.

The efficacy of the components of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. was established in a series of double-blind controlled field trials, which demonstrated a high degree of protective efficacy afforded by the individual vaccine components. These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.

Post-exposure vaccination
Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours after exposure. If, however, the vaccine is given a few days before exposure, substantial protection may be afforded. There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.

Effectiveness
More than 400 million doses of the previous formulation of the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc. have been distributed worldwide (1978 to 2003). Widespread use of a 2-dose vaccination schedule in the United States and countries such as Finland and Sweden has led to a >99% reduction in the incidence of each of the 3 targeted diseases.

Non-pregnant adolescent and adult females
Vaccination 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 sections 4.4 and 4.6). 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.

Previously unvaccinated individuals older than 9 months who are in contact with susceptible pregnant women should receive live attenuated rubella-containing vaccine (such as M-M-RVAXPRO or a monovalent rubella vaccine) to reduce the risk of exposure of the pregnant woman.

Individuals likely to be susceptible to mumps and rubella
M-M-RVAXPRO is preferred for vaccination of persons likely to be susceptible to mumps and rubella. Individuals who require vaccination against measles can receive M-M-RVAXPRO regardless of their immune status to mumps or rubella if a monovalent measles vaccine is not readily available.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder
Sorbitol
Sodium phosphate
Potassium phosphate

Sucrose
Hydrolysed gelatin
Medium 199 with Hanks' salts
Minimum Essential Medium, Eagle (MEM)
Monosodium L-glutamate
Neomycin
Phenol red
Sodium bicarbonate
Hydrochloric acid (to adjust pH)
Sodium hydroxide (to adjust pH)

Solvent
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, the vaccine must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

After reconstitution, the vaccine should be used immediately; however, in-use stability has been demonstrated for 8 hours when refrigerated at 2°C-8°C.

6.4 Special precautions for storage

Store and transport refrigerated (2°C – 8°C).
Do not freeze.
Keep the vial of powder in the outer carton in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Powder in a vial (glass) with a stopper (butyl rubber) and solvent in a pre-filled syringe (glass) with attached needle with plunger stopper (chlorobutyl rubber) and needle-shield (natural rubber) in a pack size of 1 and 10.

Powder in a vial (glass) with a stopper (butyl rubber) and solvent in a pre-filled syringe (glass) with plunger stopper (chlorobutyl rubber) and tip cap (styrene-butadiene rubber), without needle, in pack size 1, 10, and 20.

Powder in a vial (glass) with a stopper (butyl rubber) and solvent in a pre-filled syringe (glass) with plunger stopper (chlorobutyl rubber) and tip cap (styrene-butadiene rubber), with one or two unattached needles, in pack size 1, 10 and 20.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

To reconstitute, use the solvent supplied. The solvent is a clear colourless liquid. Before mixing with the solvent, the powder is a light yellow compact crystalline cake. When completely reconstituted, the vaccine is a clear yellow liquid.

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

Reconstitution instructions
Inject the entire content of the syringe into the vial containing the powder. Gently agitate to mix thoroughly.
The reconstituted vaccine must not be used if any particulate matter is noted or if the appearance of the solvent or powder or of the reconstituted vaccine differs from that described above.

Withdraw the entire content of the reconstituted vaccine vial into the same syringe and inject the entire volume.

If two needles are provided: use one needle to reconstitute the vaccine and the other for its administration to the person to be vaccinated.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/003
EU/1/06/337/004
EU/1/06/337/005
EU/1/06/337/006
EU/1/06/337/007
EU/1/06/337/008
EU/1/06/337/009
EU/1/06/337/010
EU/1/06/337/011
EU/1/06/337/012
EU/1/06/337/013

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 May 2006
Date of latest renewal: 11 May 2011

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTION REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Merck Sharp & Dohme Corp.
Sumneytown Pike
PO Box 4
West Point
Pennsylvania 19486
USA

Name and address of the manufacturer responsible for batch release

Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2.of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified , especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

M-M-RVAXPRO - Powder in vial and solvent in vial- Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection
Measles, mumps, and rubella vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Measles virus Enders' Edmonston strain (live attenuated)	not less than 1 $x10^3$ CCID50*
Mumps virus Jeryl Lynn™ [Level B] strain (live attenuated)	not less than 12,5 $x10^3$ CCID50*
Rubella virus Wistar RA 27/3 strain (live attenuated)	not less than 1 $x10^3$ CCID50*

* 50% cell culture infectious dose

3. LIST OF EXCIPIENTS

Sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatine, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid , sodium hydroxide and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection
1 single dose vial (powder) + 1 vial (solvent).
10 single dose vials (powder) + 10 vials (solvent).

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular or subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C-8°C)
Do not freeze
Keep the vial of powder in the outer carton in order to protect from light
After reconstitution, use immediately or within 8 hours if stored in a refrigerator

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/001 – pack of 1
EU/1/06/337/002 – pack of 10

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS IN USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL OF POWDER

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

M-M-RVAXPRO powder for suspension for injection

2. METHOD OF ADMINISTRATION

IM or SC use

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

Sanofi Pasteur MSD SNC

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL OF SOLVENT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for M-M-RVAXPRO

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

Sanofi Pasteur MSD SNC

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

M-M-RVAXPRO - Powder in vial and solvent in prefilled syringe with attached needle - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps, and rubella vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Measles virus Enders' Edmonston strain (live attenuated)	not less than $1x10^3$ CCID50*
Mumps virus Jeryl Lynn™ [Level B] strain (live attenuated)	not less than $12,5\ x10^3$ CCID50*
Rubella virus Wistar RA 27/3 strain (live attenuated)	not less than $1\ x10^3$ CCID50*

*50% cell culture infectious dose

3. LIST OF EXCIPIENTS

Sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatin medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid , sodium hydroxide and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection in pre-filled syringe
1 single dose vial (powder) + 1 prefilled syringe (solvent) with needle.
10 single dose vials (powder) + 10 prefilled syringes (solvent) with needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular or subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C-8°C)
Do not freeze
Keep the vial of powder in the outer carton in order to protect from light
After reconstitution, use immediately or within 8 hours if stored in a refrigerator

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/003 – pack of 1
EU/1/06/337/004 – pack of 10

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

M-M-RVAXPRO - Powder in vial and solvent in prefilled syringe without needle - Pack of 1, 10, 20

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps, and rubella vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Measles virus Enders' Edmonston strain (live attenuated)	not less than 1 $x10^3$ CCID50*
Mumps virus Jeryl Lynn™ [Level B] strain (live attenuated)	not less than 12,5 $x10^3$ CCID50*
Rubella virus Wistar RA 27/3 strain (live attenuated)	not less than 1 $x10^3$ CCID50*

*50% cell culture infectious dose

3. LIST OF EXCIPIENTS

Sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatine, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid , sodium hydroxide and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection in pre-filled syringe
1 single dose vial (powder) + 1 prefilled syringe (solvent) without needle.
10 single dose vials (powder) + 10 prefilled syringes (solvent) without needle.
20 single dose vials (powder) + 20 prefilled syringes (solvent) without needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular or subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C-8°C)
Do not freeze
Keep the vial of powder in the outer carton in order to protect from light
After reconstitution, use immediately or within 8 hours if stored in a refrigerator

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/005 – pack of 1
EU/1/06/337/006 – pack of 10
EU/1/06/337/007 – pack of 20

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

M-M-RVAXPRO - Powder in vial and solvent in pre-filled syringe with one unattached needle – Pack of 1, 10, 20

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps, and rubella vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Measles virus Enders' Edmonston strain (live attenuated)	not less than 1 $x10^3$ CCID50*
Mumps virus Jeryl Lynn™ [Level B] strain (live attenuated)	not less than 12,5 $x10^3$ CCID50*
Rubella virus Wistar RA 27/3 strain (live attenuated)	not less than 1 $x10^3$ CCID50*

*50% cell culture infectious dose

3. LIST OF EXCIPIENTS

Sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatine, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid , sodium hydroxide and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection in pre-filled syringe
1 single dose vial (powder) + 1 prefilled syringe (solvent) + 1 needle.
10 single dose vials (powder) + 10 prefilled syringes (solvent) + 10 needles.
20 single dose vials (powder) + 20 prefilled syringes (solvent) + 20 needles.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular or subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C-8°C)
Do not freeze
Keep the vial of powder in the outer carton in order to protect from light
After reconstitution, use immediately or within 8 hours if stored in a refrigerator

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/008 – pack of 1
EU/1/06/337/009 – pack of 10
EU/1/06/337/010 – pack of 20

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

M-M-RVAXPRO - Powder in vial and solvent in pre-filled syringe with two unattached needles - Pack of 1, 10, 20

1. NAME OF THE MEDICINAL PRODUCT

M-M-RVAXPRO powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps, and rubella vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution,1 dose (0.5 ml) contains:

Measles virus Enders' Edmonston strain (live attenuated)	not less than 1 $x10^3$ CCID50*
Mumps virus Jeryl Lynn™ [Level B] strain (live attenuated)	not less than 12,5 $x10^3$ CCID50*
Rubella virus Wistar RA 27/3 strain (live attenuated)	not less than 1 $x10^3$ CCID50*

*50% cell culture infectious dose

3. LIST OF EXCIPIENTS

Sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatine, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid , sodium hydroxide and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection in pre-filled syringe
1 single dose vial (powder) + 1 prefilled syringe (solvent) + 2 needles.
10 single dose vials (powder) + 10 pre-filled syringes (solvent) + 20 needles.
20 single dose vials (powder) + 20 pre-filled syringes (solvent) + 40 needles.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular or subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C-8°C)
Do not freeze
Keep the vial of powder in the outer carton in order to protect from light
After reconstitution, use immediately or within 8 hours if stored in a refrigerator

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur MSD SNC
162 avenue Jean Jaurès
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/337/011 – pack of 1
EU/1/06/337/012 – pack of 10
EU/1/06/337/013 – pack of 20

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL OF POWDER

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

M-M-RVAXPRO powder for suspension for injection in pre-filled syringe

2. METHOD OF ADMINISTRATION

IM or SC use

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

Sanofi Pasteur MSD SNC

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE OF SOLVENT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for M-M-RVAXPRO

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

Sanofi Pasteur MSD SNC

B. PACKAGE LEAFLET

Package leaflet: Information for the user

M-M-RVAXPRO
Powder and solvent for suspension for injection
Measles, mumps and rubella vaccine (live)

Read all of this leaflet carefully before you or your child is vaccinated because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- If you get any of the side effects, talk to your doctor of pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What M-M-RVAXPRO is and what it is used for

M-M-RVAXPRO is a vaccine containing measles, mumps, and rubella viruses that have been weakened. When a person is given the vaccine, the immune system (the body's natural defences) will make antibodies against the measles, mumps, and rubella viruses. The antibodies help protect against infections caused by these viruses.

M-M-RVAXPRO is given to help protect you or your child against measles, mumps, and rubella. The vaccine may be administered to persons 12 months of age or older.
M-M-RVAXPRO can be administered to infants from 9 to 12 months of age under special circumstances.

M-M-RVAXPRO can also be used in measles outbreaks, or for post-exposure vaccination, or for use in previously unvaccinated persons older than 9 months who are in contact with susceptible pregnant women, and persons likely to be susceptible to mumps and rubella.

Although M-M-RVAXPRO contains live viruses, they are too weak to cause measles, mumps, or rubella in healthy people.

2. What you need to know before you receive M-M-RVAXPRO

Do not use M-M-RVAXPRO:
- If you or your child are allergic to any of the components of this vaccine (including neomycin or any of the other ingredients listed in section 6)
- If you or your child are pregnant (in addition, pregnancy should be avoided for 1 month after vaccination, see Pregnancy)
- If you or your child have any illness with fever higher than 38.5°C; however, low-grade fever itself is not a reason to delay vaccination
- If you or your child have active untreated tuberculosis
- If you or your child have a blood disorder or any type of cancer that affects the immune system
- If you or your child are receiving treatment or taking medicines that may weaken the immune system (except low-dose corticosteroid therapy for asthma or replacement therapy)
- If you or your child have a weakened immune system because of a disease (including AIDS)

- If you or your child have a family history of congenital or hereditary immunodeficiency, unless the immune competence of you or your child is demonstrated.

Warnings and precautions
Talk to the doctor or pharmacist before you or your child receive M-M-RVAXPRO if you have experienced any of the following:
- If you or your child have an allergic reaction to eggs or anything that contained egg
- If you or your child have a history or family history of allergies or of convulsions (fits)
- If you or your child have a side effect after vaccination with measles, mumps, or rubella vaccine (in a single component vaccine or a combined vaccine, such as the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., or M-M-RVAXPRO) that involved easy bruising or bleeding for longer than usual
- If you or your child have infection with Human Immunodeficiency Virus (HIV) but do not show symptoms of HIV disease. You or your child should be monitored closely for measles, mumps, and rubella because vaccination may be less effective than for uninfected persons (see section **Do not use M-M-RVAXPRO**).

As with other vaccines, M-M-RVAXPRO may not completely protect all persons who are vaccinated. Also, if the person who is to be vaccinated has already been exposed to the measles, mumps, or rubella virus but is not yet ill, M-M-RVAXPRO may not be able to prevent the illness from appearing.

M-M-RVAXPRO can be given to persons who have been in recent (within 3 days) contact with a case of measles and may be incubating the disease. However, M-M-RVAXPRO may not always be able to prevent measles developing in these cases.

Other medicines and M-M-RVAXPRO:

Tell your doctor or pharmacist if you or your child are taking or have recently taken any other medicines (or other vaccines).

The doctor may delay vaccination for at least 3 months following blood or plasma transfusions, or immune globulin (known as IG). After vaccination with M-M-RVAXPRO, IG should not be given for 1 month, unless your doctor tells you otherwise.

If a tuberculin test is to be performed, it should be done either any time before, simultaneously with, or 4 to 6 weeks after vaccination with M-M-RVAXPRO.

M-M-RVAXPRO may be given with Prevenar and/or hepatitis A vaccine at the same visit at a separate injection site (e.g. the other arm or leg).

M-M-RVAXPRO may be given with some routine childhood vaccines that may be due to be given at the same time. For vaccines that cannot be given at the same time, M-M-RVAXPRO should be given 1 month before or after administration of those vaccines.

Pregnancy and breast-feeding
M-M-RVAXPRO should not be given to pregnant females. Females of child-bearing age should take the necessary precautions to avoid pregnancy for 1 month, or according to doctor's recommendation, after they have been given the vaccine.

Persons who are breast-feeding or intend to breast-feed should tell the doctor. The doctor will decide if M-M-RVAXPRO should be given.

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist for advice before taking this vaccine.

Driving and using machines

There is no information to suggest that M-M-RVAXPRO affects the ability to drive or operate machinery.

M-M-RVAXPRO contains sorbitol.

If you have been told by your doctor that you or your child have an intolerance to some sugars, inform your doctor before you or your child receive this vaccine.

3. How to use M-M-RVAXPRO

M-M-RVAXPRO should be injected into the muscle or under the skin either in the area of the outer thigh or of the upper arm. Usually for injections into the muscle the thigh area is preferred in young children whereas for older individuals the upper arm area is the preferred injection site. M-M-RVAXPRO is not to be injected directly into any blood vessel.

M-M-RVAXPRO is given as follows:
One dose is given at an elected date usually from 12 months of age. Under special circumstances, it can be given from 9 months of age. Further doses should be administered according to your doctor's recommendation. The interval between 2 doses should be at least 4 weeks.

Reconstitution instructions intended for medical and healthcare professionals are included at the end of the package leaflet.

4. Possible side effects

Like all vaccines and medicines, this vaccine can cause side effects, although not everybody gets them.

The following side effects were reported with the use of M-M-RVAXPRO:

Frequency	Side effect
Very common (may affect more than 1 in 10 vaccinees)	• Fever (38.5°C or higher). • Injection-site redness; injection-site pain; injection-site swelling.
Common (may affect 1 to 10 in 100 vaccinees)	• Rash (including measles-like rash). • Injection-site bruising.
Uncommon (may affect 1 to 10 in 1000 vaccinees)	• Nasal congestion and sore throat; upper respiratory tract infection or viral infection; runny nose. • Diarrhoea, vomiting. • Hives. • Injection-site rash.
Not known (Frequency cannot be estimated from the available data)*	• Aseptic meningitis (fever, feeling sick, vomiting, headache, stiff neck, and sensitivity to light); swollen testicles; infection of the middle ear; inflamed salivary glands; atypical measles (described in patients who received a killed measles virus vaccine, usually given before 1975). • Swollen lymph nodes. • Bruising or bleeding more easily than normal. • Severe allergic reaction that may include difficulty in breathing, facial swelling, localised swelling, and swelling of the limbs. • Irritability. • Seizures (fits) without fever; seizures (fits) with fever in children;

	walking unsteadily; dizziness; illnesses involving inflammation of the nervous system (brain and/or spinal cord). • An illness consisting of muscle weakness, abnormal sensations, tingling in the arms, legs, and upper body (Guillain-Barré syndrome). • Headache; fainting; nerve disorders which can cause weakness, tingling, or numbness; eye nerve disturbances. • Discharge and itching of the eyes with crusting of eyelids (conjunctivitis). • Inflammation of the retina (in the eye) with changes in sight. • Deafness. • Cough; lung infection with or without fever. • Feeling sick (nausea). • Itching; inflammation of the fatty tissue under the skin; red or purple, flat, pinhead spots under the skin; hardened, raised area of the skin; serious illness with ulcers or blistering of the skin, mouth, eyes, and/or genitals (Stevens-Johnson syndrome). • Joint pain and/or swelling (usually transient and rarely chronic); muscle pain. • Burning and/or stinging of short duration at the injection site; blisters and/or hives at the injection site. • Generally feeling unwell (malaise); swelling; soreness. • Inflammation of blood vessels.

*These side effects were reported with the use of M-M-RVAXPRO or with the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., or with its monovalent (single) components, during post-marketing use and/or during clinical studies.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store M-M-RVAXPRO

Keep out of the sight and reach of children.
Do not use this vaccine after the expiry date which is stated on the outer carton after EXP. The expiry date refers to the last day of that month.
Store and transport refrigerated (2°C- 8°C).
Keep the vial of powder in the outer carton in order to protect from light.
Do not freeze the vaccine.

Once the vaccine has been mixed with the solvent supplied, it should be either used immediately or stored in the refrigerator and used within 8 hours.

Do not throw away any vaccines via wastewater or household waste. Ask your pharmacist how to throw away vaccines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What M-M-RVAXPRO contains

The active substances are:

After reconstitution, one dose (0.5 ml) contains:

Measles virus[1] Enders' Edmonston strain (live, attenuated) ……..…….not less than $1x10^3$ $CCID_{50}$*
Mumps virus[1] Jeryl Lynn™ [Level B] strain (live, attenuated)……not less than $12.5x10^3$ $CCID_{50}$*
Rubella virus[2] Wistar RA 27/3 strain (live, attenuated) ……..….not less than $1x10^3$ $CCID_{50}$*

* 50% cell culture infectious dose

[1] produced in chick embryo cells.
[2] produced in WI-38 human diploid lung fibroblasts.

The other ingredients are:

Powder:
sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatin, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid (to adjust pH), and sodium hydroxide (to adjust pH)

Solvent:
water for injections

What M-M-RVAXPRO looks like and contents of the pack

The vaccine is a powder for suspension for injection contained in a single-dose vial, which should be mixed with solvent provided.

The solvent is a clear and colourless liquid. The powder is a light yellow compact crystalline cake.

M-M-RVAXPRO is available in packs of 1 and 10. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Sanofi Pasteur MSD SNC, 162 avenue Jean Jaurès, 69007 Lyon, France

Manufacturer Responsible for Batch Release: Merck Sharp and Dohme, B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien
Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

България
Мерк Шарп и Доум България ЕООД
Тел.: +359 2 819 3737

Česká republika
Merck Sharp & Dohme s.r.o. Tel.: +420.233.010.111

Danmark
Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Lietuva
UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Luxembourg/Luxemburg
Sanofi Pasteur MSD, Tél: +32.2.726.95.84

Magyarország
MSD Pharma Hungary Kft., Tel.: + 36.1.888.5300

Malta
Merck Sharp & Dohme Cyprus Limited., Tel: 8007 4433 (+356 99917558)

Deutschland
Sanofi Pasteur MSD GmbH, Tel: +49 30 499198-0
Eesti
Merck Sharp & Dohme OÜ, Tel: +372.6144 200
Ελλάδα
ΒΙΑΝΕΞ Α.Ε., Τηλ: +30.210.8009111

España
Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00
France
Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00
Hrvatska
Merck Sharp & Dohme d.o.o., Tel: +385 1 66 11 333
Ireland
Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland
Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia
Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11
Κύπρος
Merck Sharp & Dohme Cyprus Limited
Τηλ: +80000 673 (+357 22866700)
Latvija
SIA "Merck Sharp & Dohme Latvija"
Tel: +371 67364 224

Nederland
Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Norge
Sanofi Pasteur MSD, Tlf: +47.67.50.50.20
Österreich
Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91 14
Polska
MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00
Portugal
Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50
România
Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00
Slovenija
Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201
Slovenská republika
Merck Sharp & Dohme, s. r. o., Tel: +421.2.58282010
Suomi/Finland
Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30
Sverige
Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom
Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last revised in:

Other source of information

Detailed information on this vaccine is available on the European Medicines Agency website: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

Reconstitution instructions
The solvent is a clear colourless liquid. Before mixing with the solvent, the powder is a light yellow compact crystalline cake. When completely reconstituted, the vaccine is a clear yellow liquid.

Do not use the reconstituted vaccine if you notice any particulate matter or if the appearance of the solvent or powder or of the reconstituted vaccine differs from that described above.

Withdraw the entire volume of solvent into a syringe. Inject the entire content of the syringe into the vial containing the powder. Gently agitate to dissolve completely. Withdraw the entire content of the reconstituted vaccine vial into the same syringe and inject the entire volume.

If two needles are provided: use one needle to reconstitute the vaccine and the other for its administration to the person to be vaccinated.

It is recommended that the vaccine be administered immediately after reconstitution or stored in the refrigerator and used within 8 hours to minimize loss of potency. Discard if reconstituted vaccine is not used within 8 hours.

Do not freeze the reconstituted vaccine.

Any unused product or waste material should be disposed of in accordance with local requirements.

See also section 3 **How to use M-M-RVAXPRO**.

Package leaflet: information for the user

M-M-RVAXPRO
Powder and solvent for suspension for injection in pre-filled syringe
Measles, mumps and rubella vaccine (live)

Read all of this leaflet carefully before you or your child is vaccinated because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- If you get any of the side effects, talk to your doctor of pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What M-M-RVAXPRO is and what it is used for

M-M-RVAXPRO is a vaccine containing measles, mumps, and rubella viruses that have been weakened. When a person is given the vaccine, the immune system (the body's natural defences) will make antibodies against the measles, mumps, and rubella viruses. The antibodies help protect against infections caused by these viruses.

M-M-RVAXPRO is given to help protect you or your child against measles, mumps, and rubella. The vaccine may be administered to persons 12 months of age or older.
M-M-RVAXPRO can be administered to infants from 9 to 12 months of age under special circumstances.

M-M-RVAXPRO can also be used in measles outbreaks, or for post-exposure vaccination, or for use in previously unvaccinated persons older than 9 months who are in contact with susceptible pregnant women, and persons likely to be susceptible to mumps and rubella.

Although M-M-RVAXPRO contains live viruses, they are too weak to cause measles, mumps, or rubella in healthy people.

2. What you need to know before you receive M-M-RVAXPRO

Do not use M-M-RVAXPRO:
- If you or your child are allergic to any of the components of this vaccine (including neomycin or any of the other ingredients listed in section 6)
- If you or your child are pregnant (in addition, pregnancy should be avoided for 1 month after vaccination, see Pregnancy)
- If you or your child have any illness with fever higher than 38.5°C; however, low-grade fever itself is not a reason to delay vaccination
- If you or your child have active untreated tuberculosis
- If you or your child have a blood disorder or any type of cancer that affects the immune system
- If you or your child are receiving treatment or taking medicines that may weaken the immune system (except low-dose corticosteroid therapy for asthma or replacement therapy)
- If you or your child have a weakened immune system because of a disease (including AIDS)

- If you or your child have a family history of congenital or hereditary immunodeficiency, unless the immune competence of your or your child is demonstrated.

Warnings and precaution
Talk to the doctor or pharmacist before you or your child receive M-M-RVAXPRO if you have experienced any of the following:
- If you or your child have an allergic reaction to eggs or anything that contained egg
- If you or your child have a history or family history of allergies or of convulsions (fits)
- If you or your child have a side effect after vaccination with measles, mumps, or rubella vaccine (in a single component vaccine or a combined vaccine, such as the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., or M-M-RVAXPRO) that involved easy bruising or bleeding for longer than usual
- If you or your child have infection with Human Immunodeficiency Virus (HIV) but do not show symptoms of HIV disease. You or your child should be monitored closely for measles, mumps, and rubella because vaccination may be less effective than for uninfected persons (see section **Do not use M-M-RVAXPRO**).

As with other vaccines, M-M-RVAXPRO may not completely protect all persons who are vaccinated. Also, if the person who is to be vaccinated has already been exposed to the measles, mumps, or rubella virus but is not yet ill, M-M-RVAXPRO may not be able to prevent the illness from appearing.

M-M-RVAXPRO can be given to persons who have been in recent (within 3 days) contact with a case of measles and may be incubating the disease. However, M-M-RVAXPRO may not always be able to prevent measles developing in these cases.

Other medicines and M-M-RVAXPRO:
Tell your doctor or pharmacist if you or your child are taking or have recently taken any other medicines (or other vaccines).

The doctor may delay vaccination for at least 3 months following blood or plasma transfusions, or immune globulin (known as IG). After vaccination with M-M-RVAXPRO, IG should not be given for 1 month, unless your doctor tells you otherwise.

If a tuberculin test is to be performed, it should be done either any time before, simultaneously with, or 4 to 6 weeks after vaccination with M-M-RVAXPRO.

M-M-RVAXPRO may be given with Prevenar and/or hepatitis A vaccine at the same visit at a separate injection site (e.g. the other arm or leg).

M-M-RVAXPRO may be given with some routine childhood vaccines that may be due to be given at the same time. For vaccines that cannot be given at the same time, M-M-RVAXPRO should be given 1 month before or after administration of those vaccines.

Pregnancy and breast-feeding
M-M-RVAXPRO should not be given to pregnant females. Females of child-bearing age should take the necessary precautions to avoid pregnancy for 1 month, or according to doctor's recommendation, after they have been given the vaccine.

Persons who are breast-feeding or intend to breast-feed should tell the doctor. The doctor will decide if M-M-RVAXPRO should be given.

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, a sk your doctor or pharmacist for advice before taking this vaccine.

Driving and using machines
There is no information to suggest that M-M-RVAXPRO affects the ability to drive or operate machinery.

M-M-RVAXPRO contains sorbitol.

If you have been told by your doctor that you or your child have an intolerance to some sugars, inform your doctor before you or your child receive this vaccine.

3. How to use M-M-RVAXPRO

M-M-RVAXPRO should be injected into the muscle or under the skin either in the area of the outer thigh or of the upper arm. Usually for injections into the muscle the thigh area is preferred in young children whereas for older individuals the upper arm area is the preferred injection site. M-M-RVAXPRO is not to be injected directly into any blood vessel.

M-M-RVAXPRO is given as follows:
One dose is given at an elected date usually from 12 months of age. Under special circumstances, it can be given from 9 months of age. Further doses should be administered according to your doctor's recommendation. The interval between 2 doses should be at least 4 weeks.

Reconstitution instructions intended for medical and healthcare professionals are included at the end of the package leaflet.

4. Possible side effects

Like all vaccines and medicines, this vaccine can cause side effects, although not everybody gets them.

The following side effects were reported with the use of M-M-RVAXPRO:

Frequency	Side effect
Very common (may affect more than 1 in 10 vaccinees)	• Fever (38.5°C or higher). • Injection-site redness; injection-site pain; injection-site swelling.
Common (may affect 1 to 10 in 100 vaccinees)	• Rash (including measles-like rash). • Injection-site bruising.
Uncommon (may affect 1 to 10 in 1000 vaccinees)	• Nasal congestion and sore throat; upper respiratory tract infection or viral infection; runny nose. • Diarrhoea, vomiting. • Hives. • Injection-site rash.
Not known (Frequency cannot be estimated from the available data)*	• Aseptic meningitis (fever, feeling sick, vomiting, headache, stiff neck, and sensitivity to light); swollen testicles; infection of the middle ear; inflamed salivary glands; atypical measles (described in patients who received a killed measles virus vaccine, usually given before 1975). • Swollen lymph nodes. • Bruising or bleeding more easily than normal. • Severe allergic reaction that may include difficulty in breathing, facial swelling, localised swelling, and swelling of the limbs. • Irritability. • Seizures (fits) without fever; seizures (fits) with fever in children; walking unsteadily; dizziness; illnesses involving inflammation of the nervous system (brain and/or spinal cord).

	• An illness consisting of muscle weakness, abnormal sensations, tingling in the arms, legs, and upper body (Guillain-Barré syndrome). • Headache; fainting; nerve disorders which can cause weakness, tingling, or numbness; eye nerve disturbances. • Discharge and itching of the eyes with crusting of eyelids (conjunctivitis). • Inflammation of the retina (in the eye) with changes in sight. • Deafness. • Cough; lung infection with or without fever. • Feeling sick (nausea). • Itching; inflammation of the fatty tissue under the skin; red or purple, flat, pinhead spots under the skin; hardened, raised area of the skin; serious illness with ulcers or blistering of the skin, mouth, eyes, and/or genitals (Stevens-Johnson syndrome). • Joint pain and/or swelling (usually transient and rarely chronic); muscle pain. • Burning and/or stinging of short duration at the injection site; blisters and/or hives at the injection site. • Generally feeling unwell (malaise); swelling; soreness. • Inflammation of blood vessels.

*These side effects were reported with the use of M-M-RVAXPRO or with the measles, mumps, and rubella vaccine manufactured by Merck & Co., Inc., or with its monovalent (single) components, during post-marketing use and/or during clinical studies.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store M-M-RVAXPRO

Keep out of the sight and reach of children.
Do not use this vaccine after the expiry date which is stated on the outer carton after EXP. The expiry dates refers to the last day of that month.
Store and transport refrigerated (2°C- 8°C).
Keep the vial of powder in the outer carton in order to protect from light.
Do not freeze the vaccine.

Once the vaccine has been mixed with the solvent supplied, it should be either used immediately or stored in the refrigerator and used within 8 hours.

Do not throw away any vaccines via wastewater or household waste. Ask your pharmacist how to throw away vaccines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What M-M-RVAXPRO contains

The active substances are:

After reconstitution, one dose (0.5 ml) contains:

Measles virus[1] Enders' Edmonston strain (live, attenuated) ……..….not less than $1x10^3$ $CCID_{50}$*
Mumps virus[1] Jeryl Lynn™ [Level B] strain (live, attenuated)……not less than $12.5x10^3$ $CCID_{50}$*
Rubella virus[2] Wistar RA 27/3 strain (live, attenuated) ……..….not less than $1x10^3$ $CCID_{50}$*

* 50% cell culture infectious dose

[1] produced in chick embryo cells.
[2] produced in WI-38 human diploid lung fibroblasts.

The other ingredients are:

Powder:
sorbitol, sodium phosphate, potassium phosphate, sucrose, hydrolysed gelatin, medium 199 with Hanks' salts, MEM, monosodium L-glutamate, neomycin, phenol red, sodium bicarbonate, hydrochloric acid (to adjust pH), and sodium hydroxide (to adjust pH)

Solvent:
water for injections

What M-M-RVAXPRO looks like and contents of the pack

The vaccine is a powder for suspension for injection contained in a single-dose vial, which should be mixed with solvent provided.

The solvent is a clear and colourless liquid. The powder is a light yellow compact crystalline cake.

M-M-RVAXPRO is available in packs of 1, 10 and 20, with or without needles. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Sanofi Pasteur MSD SNC, 162 avenue Jean Jaurès, 69007 Lyon, France

Manufacturer Responsible for Batch Release: Merck Sharp and Dohme, B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien
Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

България
Мерк Шарп и Доум България ЕООД
Тел.: +359 2 819 3737

Česká republika
Merck Sharp & Dohme s.r.o. Tel.: +420.233.010.111

Danmark
Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Deutschland

Lietuva
UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Luxembourg/Luxemburg
Sanofi Pasteur MSD, Tél: +32.2.726.95.84

Magyarország
MSD Pharma Hungary Kft., Tel.: + 36.1.888.5300

Malta
Merck Sharp & Dohme Cyprus Limited., Tel: 8007 4433 (+356 99917558)

Nederland

Sanofi Pasteur MSD GmbH, Tel: +49 30 499198-0

Eesti
Merck Sharp & Dohme OÜ, Tel: +372.6144 200

Ελλάδα
BIANEΞ A.E., Τηλ: +30.210.8009111

España
Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

France
Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Hrvatska
Merck Sharp & Dohme d.o.o., Tel: +385 1 66 11 333

Ireland
Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland
Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia
Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος
Merck Sharp & Dohme Cyprus Limited
Τηλ: +80000 673 (+357 22866700)

Latvija
SIA "Merck Sharp & Dohme Latvija"
Tel: +371 67364 224

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Norge
Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Österreich
Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91 14

Polska
MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

Portugal
Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

România
Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija
Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika
Merck Sharp & Dohme, s. r. o., Tel: +421.2.58282010

Suomi/Finland
Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige
Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom
Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last revised in:

Other sources of information

Detailed information on this vaccine is available on the European Agency website: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

Reconstitution instructions

The solvent is a clear colourless liquid. Before mixing with the solvent, the powder is a light yellow compact crystalline cake. When completely reconstituted, the vaccine is a clear yellow liquid.

Do not use the reconstituted vaccine if you notice any particulate matter or if the appearance of the solvent or powder or of the reconstituted vaccine differs from that described above.

Inject the entire content of the pre-filled syringe into the vial containing the powder. Gently agitate to dissolve completely. Withdraw the entire content of the reconstituted vaccine vial into the same syringe and inject the entire volume.

If two needles are provided: use one needle to reconstitute the vaccine and the other for its administration to the person to be vaccinated.

It is recommended that the vaccine be administered immediately after reconstitution or stored in the refrigerator and used within 8 hours to minimize loss of potency. Discard if reconstituted vaccine is not used within 8 hours.

Do not freeze the reconstituted vaccine.

Any unused product or waste material should be disposed of in accordance with local requirements.

See also section 3 **How to use M-M-RVAXPRO**.