ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

RotaTeq **oral** solution

Rotavirus vaccine (live)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (2 ml) contains:

rotavirus type* G1	not less than 2.2×10^6 IU[1, 2]
rotavirus type* G2	not less than 2.8×10^6 IU[1, 2]
rotavirus type* G3	not less than 2.2×10^6 IU[1, 2]
rotavirus type* G4	not less than 2.0×10^6 IU[1, 2]
rotavirus type* P1A[8]	not less than 2.3×10^6 IU[1, 2]

* human-bovine rotavirus reassortants (live), produced in Vero cells.

[1] Infectious Units
[2] As lower confidence limit (p = 0.95)

Excipients with known effect
This vaccine contains 1080 milligrams sucrose and 37.6 milligrams sodium (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solution
Pale yellow clear liquid that may have a pink tint

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RotaTeq is indicated for the active immunisation of infants from the age of 6 weeks to 32 weeks for prevention of gastroenteritis due to rotavirus infection (see sections 4.2, 4.4 and 5.1).

RotaTeq is to be used on the basis of official recommendations.

4.2 Posology and method of administration

Posology

From birth to 6 weeks
RotaTeq is not indicated in this subset of paediatric population.

The safety and efficacy of RotaTeq in individuals from birth to 6 weeks of age have not been established.

From 6 weeks to 32 weeks
The vaccination course consists of three doses.
The first dose may be administered from the age of 6 weeks and no later than the age of 12 weeks.

RotaTeq may be given to infants who were born prematurely provided that the period of gestation was at least 25 weeks. These infants should receive the first dose of RotaTeq at least six weeks after birth (see sections 4.4 and 5.1).

There should be intervals of at least 4 weeks between doses.

It is preferable that the vaccination course of three doses should be completed by the age of 20-22 weeks. If necessary, the third (last) dose may be given up to the age of 32 weeks (see section 5.1).

As no data exist regarding the interchangeability of RotaTeq with another rotavirus vaccine, it is recommended that infants who receive RotaTeq for the first immunisation against rotavirus should receive this same vaccine for the subsequent doses.

If it is observed or strongly suspected that an incomplete dose has been swallowed (e.g., infant spits or regurgitates the vaccine), a single replacement dose may be given at the same vaccination visit, however, this has not been studied in clinical trials. If the problem recurs, additional replacement doses should not be given.

No further doses are recommended after completion of the 3-dose vaccination course (see sections 4.4 and 5.1 regarding available information on persistence of protection).

From 33 weeks to 18 years
RotaTeq is not indicated in this subset of paediatric population.

Method of administration
RotaTeq is for **oral** administration only.

RotaTeq SHOULD UNDER NO CIRCUMSTANCES BE INJECTED.

RotaTeq may be given without regard to food, liquid, or breast milk.

See section 6.6 for administration instructions.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypersensitivity after previous administration of rotavirus vaccines.

Previous history of intussusception.

Subjects with congenital malformation of the gastrointestinal tract that could predispose to intussusception.

Infants who have known or suspected immunodeficiency (see sections 4.4 and 4.8).

Administration of RotaTeq should be postponed in infants suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication for immunisation.

The administration of RotaTeq should be postponed in subjects suffering from acute diarrhoea or vomiting.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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

No safety or efficacy data are available from clinical trials regarding administration of RotaTeq to immunocompromised infants, those exposed in utero to an immunosuppressive treatment, infants infected with HIV or infants who have received a blood transfusion or immunoglobulins within 42 days of dosing. Asymptomatic HIV infection is not expected to affect the safety or efficacy of RotaTeq. However, in the absence of sufficient data, administration of RotaTeq to asymptomatic HIV-infected infants is not recommended. Administration of RotaTeq to infants who have been exposed in utero to an immunosuppressive treatment should be based on careful consideration of potential benefits and risks.

Cases of gastroenteritis associated with vaccine virus have been reported post marketing in infants with severe combined immunodeficiency (SCID, see section 4.3).

In trials, RotaTeq was shed in the stools of 8.9 % of vaccine recipients almost exclusively in the week after dose 1 and in only one vaccine recipient (0.3 %) after dose 3. Peak excretion occurred within 7 days of dosing. Transmission of vaccine virus strains to non-vaccinated contacts has been observed post-marketing. RotaTeq should be administered with caution to individuals with close contacts who are immunodeficient (e.g., individuals with malignancies or who are otherwise immunocompromised or individuals receiving immunosuppressive therapy). Also, those caring for recent vaccinees should observe careful hygiene especially when handling excreta.

In a clinical study, RotaTeq was administered to approximately 1,000 infants who were born at a gestational age of 25 to 36 weeks. The first dose was administered from 6 weeks after birth. The safety and efficacy of RotaTeq were comparable between this subset of infants and infants born at term. However, 19 of the approximately 1,000 infants were born at a gestational age of 25 to 28 weeks, 55 were born at a gestational age of 29 to 31 weeks and the remainder was born at a gestational age of between 32 and 36 weeks. See sections 4.2 and 5.1.

Intussusception

As a precaution, healthcare professionals should follow-up on any symptoms indicative of intussusception (severe abdominal pain, persistent vomiting, bloody stools, abdominal bloating and/or high fever) since data from observational studies indicate an increased risk of intussusception, mostly within 7 days after rotavirus vaccination (see section 4.8). Parents/guardians should be advised to promptly report such symptoms to their healthcare provider.

For subjects with a predisposition for intussusception, see section 4.3.

Safety or efficacy data are not available for infants with active gastrointestinal illnesses (including chronic diarrhoea) or growth retardation. Administration of RotaTeq may be considered with caution in such infants when, in the opinion of the physician, withholding the vaccine entails a greater risk.

The level of protection provided by RotaTeq is based on the completion of all 3 doses. As with any vaccine, vaccination with RotaTeq may not result in complete protection in all recipients. RotaTeq does not protect against gastroenteritis due to other pathogens than rotavirus.

Clinical trials of efficacy against rotavirus gastroenteritis were performed in Europe, the United States, Latin America, and Asia. During these trials, the most common circulating rotavirus genotype was G1P[8], while rotavirus genotypes G2P[4], G3P[8], G4P[8], and G9P[8] were identified less often. The extent of protection that RotaTeq might provide against other rotavirus types and in other populations is unknown.

No clinical data are available on the use of RotaTeq for post-exposure prophylaxis.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunisation series to very premature infants (born ≤28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

RotaTeq SHOULD UNDER NO CIRCUMSTANCES BE INJECTED.

Sucrose
RotaTeq contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this vaccine. See section 2.

Sodium
This vaccine contains 37.6 mg sodium per dose, equivalent to 1.88% of the WHO recommended maximum daily intake of 2 g sodium for an adult. See section 2.

4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of RotaTeq with vaccines containing one or more of the following antigens at approximately 2, 4 and 6 months of age demonstrated that the immune responses and the safety profiles of the administered vaccines were unaffected:

- Diphtheria-tetanus-acellular pertussis vaccine (DTaP)
- *Haemophilus influenzae* type b vaccine (Hib)
- Inactivated poliomyelitis vaccine (IPV)
- Hepatitis B vaccine (HBV)
- Pneumococcal conjugate vaccine (PCV)

Co-administration of RotaTeq with DTaP-IPV-HBV-Hib vaccine (Infanrix hexa) at approximately 2, 3, and 4 months of age demonstrated that the immune responses and the safety profiles of the co-administered vaccines were unaffected compared to separate administrations.

Co-administration of RotaTeq with a group C meningococcal conjugate vaccine (MenCC, the vaccine studied was a tetanus toxoid conjugate) at 3 and 5 months of age (and mostly at the same time as DTaP-IPV-Hib vaccine), followed by a third dose of RotaTeq at approximately 6 months of age, demonstrated that the immune responses to RotaTeq and MenCC were unaffected. Co-administration resulted in an acceptable safety profile.

Concomitant administration of RotaTeq and oral poliomyelitis vaccine (OPV) did not affect the immune response to the poliovirus antigens. Although concomitant administration of OPV slightly reduced the immune response to rotavirus vaccine, there is currently no evidence that clinical protection against severe rotavirus gastroenteritis would be affected. The immune response to RotaTeq was unaffected when OPV was administered two weeks after RotaTeq.

Therefore, RotaTeq can be given concomitantly with monovalent or combination infant vaccines containing one or more of the following antigens: DTaP, Hib, IPV or OPV, HBV, PCV and MenCC.

4.6 Fertility, pregnancy and lactation

RotaTeq is intended for use in infants only. Thus human data on use during pregnancy or lactation are not available and animal fertility or reproduction studies have not been performed.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

a. Summary of the safety profile

In a subset of infants from 3 placebo-controlled clinical trials (n=6,130 recipients of RotaTeq and 5,560 placebo recipients), RotaTeq was evaluated for all adverse events within 42 days of vaccination with or without concomitant use of other paediatric vaccines. Overall, 47 % of infants given RotaTeq experienced an adverse reaction compared with 45.8 % of infants given placebo. The most commonly reported adverse reactions that occurred more frequently with vaccine than with placebo were pyrexia (20.9 %), diarrhoea (17.6 %) and vomiting (10.1 %).

Serious adverse reactions were assessed in all participants (36,150 recipients of RotaTeq and 35,536 placebo recipients) of 3 clinical trials for up to 42 days after each dose. The overall frequency of these serious adverse reactions was 0.1 % among recipients of RotaTeq and 0.2 % among placebo recipients.

b. Tabulated summary of adverse reactions

Adverse reactions more common in the vaccine group in clinical trials are listed below per system organ class and frequency. Based on pooled data from 3 clinical trials in which 6,130 infants received RotaTeq and 5,560 received placebo, the adverse reactions listed occurred with excess incidences in RotaTeq recipients compared to placebo recipients of between 0.2 % and 2.5 %.

Frequencies are reported as:
Very common (≥1/10); Common (≥1/100, <1/10); Uncommon (≥1/1,000, <1/100); Rare (≥1/10,000, <1/1,000), Very rare (< 1/10,000), Not known (cannot be estimated from the available data)

Adverse reactions following administration of RotaTeq in clinical trials and adverse events reported post-marketing (in italics)		
System Organ Class	Frequency	Adverse Reaction/Event
Infections and infestations	Common	Upper respiratory tract infection
	Uncommon	Nasopharyngitis, otitis media
Immune system disorders	Not known	*Anaphylactic reaction*‡
Respiratory, thoracic and mediastinal disorders	Rare	Bronchospasm
Gastrointestinal disorders	Very common	Diarrhoea, vomiting
	Uncommon	*Haematochezia*†, Abdominal pain upper
	Very Rare	*Intussusception* α *
Skin and subcutaneous tissue disorders	Uncommon	Rash
	Rare	*Urticaria*†
	Not known	*Angioedema*‡
General disorders and administration site conditions	Very common	Pyrexia
	Not known	*Irritability*‡

† This adverse reaction was identified through post-marketing surveillance. The frequency category was estimated based on relevant clinical trials.

α The frequency category was estimated based on observational study data.

* See section 4.4.
‡ Post-marketing adverse events (frequency cannot be estimated from the available data).

c. Description of selected adverse reactions
Kawasaki disease was reported in 5 of 36,150 vaccine recipients (<0.1 %) and 1 of 35,536 placebo recipients (<0.1 %) with a relative risk (RR) of 4.9 [95 % CI, 0.6 – 239.1] (not statistically significant). No increased risk of Kawasaki disease was observed among infants receiving RotaTeq in a large post-marketing observational safety surveillance study (see section 5.1).

Intussusception
Data from observational safety studies performed in several countries indicate that rotavirus vaccines carry an increased risk of intussusception, with up to 6 additional cases per 100,000 infants within 7 days of vaccination. There is limited evidence of a smaller increased risk following the second dose. The background incidence of intussusception in infants less than one year of age in these countries ranged from 25 to 101 per 100,000 infants per year. It remains unclear whether rotavirus vaccines affect the overall incidence of intussusception based on longer periods of follow up (see section 4.4).

d. Other special populations
Apnoea in very premature infants (born ≤28 weeks of gestation) (see section 4.4)

Gastroenteritis with vaccine viral shedding in infants with Severe Combined Immunodeficiency Disease (SCID) has been reported post-marketing.

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

There have been reports of administration of higher than recommended doses of RotaTeq.

In general, the adverse event profile reported with overdose was comparable to that observed with recommended doses of RotaTeq.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, Viral Vaccine ATC code: **J07BH02**.

Efficacy

In clinical trials, efficacy was demonstrated against gastroenteritis due to rotavirus of genotypes G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8].

The protective efficacy of RotaTeq was evaluated in two ways in the placebo-controlled Rotavirus Efficacy and Safety Trial (REST):

1. In 5,673 vaccinated infants (2,834 in the vaccine group) protective efficacy was measured as a reduction in the incidence of rotavirus (RV) gastroenteritis caused by vaccine G genotypes (G1-G4) that occurred at least 14 days after the third dose of vaccine through the first full rotavirus season after vaccination.

2. In 68,038 vaccinated infants (34,035 in the vaccine group) protective efficacy was measured as a reduction in the rate of hospitalisations and emergency department visits for RV gastroenteritis from 14 days after the third dose.

The results of these analyses are presented in the following tables.

Reduction in incidence of RV gastroenteritis through one full season post-vaccination (RotaTeq n=2,834) (% [95 % CI])						
		Efficacy against any severity by rotavirus genotype				
Severe* disease (G1-G4)	Any severity (G1-G4)	G1	G2	G3	G4	G9
98.0 % [88.3, 100.0]†	74.0 % [66.8, 79.9]†	74.9 % [67.3, 80.9]†	63.4 % [2.6, 88.2]†	82.7 % [<0, 99.6]	48.1 % [<0, 91.6]	65.4 % [<0, 99.3]

* Severe defined as a score >16/24 using a validated clinical scoring system based on the intensity and duration of symptoms (fever, vomiting, diarrhoea and behavioural changes)
† Statistically significant

Reduction in hospitalisations and emergency department visits for RV gastroenteritis for up to 2 years post-vaccination (RotaTeq n=34,035) (% [95 % CI])					
G1-G4	G1	G2	G3	G4	G9
94.5 % [91.2, 96.6]†	95.1 % [91.6, 97.1]†	87.6 % [<0, 98.5]	93.4 % [49.4, 99.1]†	89.1 % [52.0, 97.5]†	100 % [69.6, 100]†

† Statistically significant

The reduction in incidence of RV gastroenteritis caused by genotypes G1-G4 during the second rotavirus season after vaccination was 88.0 % [95 % CI 49.4, 98.7] for severe disease and 62.6 % [95 % CI 44.3, 75.4] for disease of any severity.

Efficacy against genotypes G2P[4], G3P[8], G4P[8] and G9P[8] rotavirus was based on fewer cases than for G1. The efficacy observed against G2P[4] most likely resulted from the G2 component of the vaccine.

In a combined post-hoc analysis of REST and another phase III study, the vaccine efficacy against G1-, G2-, G3- and G4-serotype RVG cases (any severity) was 61.5 % [95 % CI: 14.2; 84.2] among infants who were >26 to ≤32 weeks of age at dose 3.

There was an extension of REST conducted in Finland only. This Finnish Extension Study (FES) included a subset of 20,736 subjects that had been enrolled previously in REST. The infants were followed for up to 3 years post-vaccination in the FES.

In REST there were 403 healthcare encounters (20 in the vaccine group and 383 in the placebo group) associated with G1-G4 and G9 RV gastroenteritis in the per protocol population. The additional data from the FES increased the number by 136 encounters in total, including 9 in the vaccine group and 127 in the placebo group. Overall, 31 % and 25 % of the encounters in the respective groups occurred during the FES.

Based upon combined data from REST and the FES, the reduction up to 3 years post-vaccination in the rate of hospitalisations and emergency department visits for RV gastroenteritis was 94.4 % (95 % CI: 91.6, 96.2) for genotypes G1-G4**,** 95.5 % (95 % CI: 92.8, 97.2) for genotype G1, 81.9 % (95 % CI: 16.1, 98.0) for genotype G2, 89.0 % (95 % CI: 53.3, 98.7) for genotype G3, 83.4 % (95 % CI: 51.2, 95.8) for genotype G4, and 94.2 % (95 % CI: 62.2, 99.9) for genotype G9. During year 3, there were no health care contacts for RV gastroenteritis in the vaccine group (n=3,112) and one (non-typeable) in the placebo group (n=3,126).

A complete 3-dose vaccination series of RotaTeq should be administered (see section 4.2) to provide the level and duration of protection against rotavirus gastroenteritis that was observed in the clinical studies. However, post hoc analyses indicated that RotaTeq achieved some reduction in the numbers of cases of rotavirus gastroenteritis of sufficient severity to require hospitalisation or an emergency department visit before completion of all three doses (i.e. from approximately 14 days after administration of the first dose onwards).

Efficacy in premature infants
In REST, RotaTeq was administered to approximately 1,000 infants who were born at a gestational age of 25 to 36 weeks. The efficacy of RotaTeq was comparable between this subset of infants and infants born at term.

Post-marketing observational safety surveillance study
In a large prospective post-marketing observational study in the US, the risk of Kawasaki disease was analysed among 85,150 infants receiving one or more doses of RotaTeq (17,433 person-years of follow-up).

During the 0-30 day follow-up period after vaccination, there were no statistically significant difference in the rate of Kawasaki disease compared with the expected background rate. In addition, there was no statistically significant increased risk of this adverse event during the 0-30 day follow-up period compared with a concurrent control group of infants who received DTaP, but not RotaTeq (n=62,617, 12,339 person-years of follow-up). One chart-confirmed case was recorded among infants vaccinated with RotaTeq compared with one chart-confirmed case among concurrent DTaP controls (relative risk = 0.7, 95 % CI: 0.01-55.56). In the general safety analyses, no specific safety concerns were identified.

Effectiveness study data
Post marketing studies demonstrating effectiveness to prevent RV gastroenteritis (RVGE)

Study design (Region)	Study population	Endpoints	Effectiveness % [95%CI]	RV seasons
Claims database analysis (US)	33,140 vaccinated 26,167 unvaccinated Aged ≥7 months Received 3 doses	Hospitalization and Emergency Department (ED) visits due to RVGE	100% [87,100]	2007-2008
		Outpatients due to RVGE	96% [76,100]	
		Hospitalization and ED visits due to all cause gastroenteritis	59% [47,68]	
Cohort study (France)	1,895 vaccinated with 3 doses 2,102 unvaccinated Aged <2 years	Hospitalization due to RVGE	98% [83,100]	2007-2008 2008-2009
Case-control study (US)	402 cases 2,559 controls* Aged <8 years Received 3 doses	Hospitalization and ED visits due to RVGE	80% [74,84]	2011-2012 2012-2013
		Strain-specific		
		- G1P[8]	89% [55,97]	
		- G2P[4]	87% [65,95]	
		- G3P[8]	80% [64,89]	
		- G12P[8]	78% [71,84]	
		Age-specific		
		- 1st year of life	91% [78,96]	
		- 2nd year of life	82% [69,89]	
		- 3rd year of life	88% [78,93]	
		- 4th year of life	76% [51,88]	
		- 5th year of life	60% [16,81]	
		- 6th-7th year of life	69% [43,84]	

*RV-negative acute gastroenteritis controls

Immunogenicity
The immunological mechanism by which RotaTeq protects against rotavirus gastroenteritis is not completely understood. No immunological correlate of protection has currently been identified for rotavirus vaccines. In phase III studies between 92.5 % and 100 % of recipients of RotaTeq achieved a significant rise in serum anti-rotavirus IgA after a three-dose regimen. The vaccine induces an immune response (i.e., appearance of serum neutralising antibody) to the five human-rotavirus proteins expressed on the reassortants (G1, G2, G3, G4 and P[8]).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

A single and repeated dose oral toxicity study in mice suggests no special hazard to humans. The dose administered to mice was approximately 2.79 x 10^8 infectious units per kg (about 14-fold the projected infant dose).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Sodium citrate

Sodium dihydrogen phosphate monohydrate
Sodium hydroxide
Polysorbate 80
Culture media (containing inorganic salts, amino acids and vitamins)
Purified water

6.2 Incompatibilities

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

6.3 Shelf life

2 years

RotaTeq should be administered promptly after removal from refrigeration.

6.4 Special precautions for storage

Store and transport refrigerated (2 °C to 8 °C).

Keep the dosing tube in the outer carton in order to protect from light.

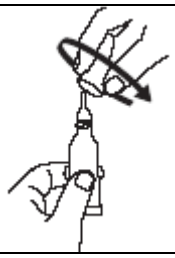
6.5 Nature and contents of container

2 ml solution in a pre-filled squeezable tube (LDPE), with a twist-off cap (HDPE) in a protective bag, pack size of 1 or 10 pre-filled squeezable tube(s).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine is to be administered orally without mixing with any other vaccines or solutions. Do not dilute.

To administer the vaccine:	
	Tear open the protective bag and remove the dosing tube.
	Clear the fluid from the dispensing tip by holding tube vertically and tapping the twist-off cap.
	Open the dosing tube in 2 easy motions: 1. Puncture the dispensing tip by screwing cap **clockwise** until it becomes tight.
	2. Remove cap by turning it **counterclockwise**.
	Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty. (A residual drop may remain in the tip of the tube.)
	Discard the empty tube and cap in approved biological waste containers according to local regulations.

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

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBERS

EU/1/06/348/001
EU/1/06/348/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 June 2006

Date of latest renewal: 18 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 RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITION OR RESTRICTION 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 LLC
770 Sumneytown Pike
West Point, Pennsylvania 19486
USA

Name and address of the manufacturer responsible for batch release

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

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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 (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates 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 marketing authorisation holder (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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RotaTeq – Pack size of 1 single-dose (2 ml) Tube
RotaTeq – Pack size of 10 single-dose (2 ml) Tubes

1. NAME OF THE MEDICINAL PRODUCT

RotaTeq oral solution
Rotavirus vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (2 ml) contains rotavirus type*:

G1	≥ 2.2 x 10^6 IU[1]
G2	≥ 2.8 x 10^6 IU[1]
G3	≥ 2.2 x 10^6 IU[1]
G4	≥ 2.0 x 10^6 IU[1]
P1A[8]	≥ 2.3 x 10^6 IU[1]

* human-bovine rotavirus reassortants (live), produced in Vero cell.

[1]Infectious Units

3. LIST OF EXCIPIENTS

Sucrose, sodium

4. PHARMACEUTICAL FORM AND CONTENTS

2 ml oral solution in a tube
pack size of 1 tube
pack size of 10 tubes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

FOR ORAL USE ONLY
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.
Keep the dosing tube in the outer carton in order to protect from light.

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

Please read the package leaflet for disposal of medicines no longer required

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/06/348/001 pack of 1 tube
EU/1/06/348/002 pack of 10 tubes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Text for the protective bag

1. NAME OF THE MEDICINAL PRODUCT

RotaTeq oral solution
Rotavirus vaccine (live)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

MSD

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

1 dose

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Tube label

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

RotaTeq
Oral solution
Oral use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (2 ml)

6. OTHER

MSD

B. PACKAGE LEAFLET

Package Leaflet: Information for the user
RotaTeq oral solution
Rotavirus vaccine (live)

Read all of this leaflet carefully before 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 pharmacist.
- If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What RotaTeq is and what it is used for

RotaTeq is an oral vaccine that helps protect infants and young children against gastroenteritis (diarrhoea and vomiting) caused by rotavirus infection and may be given to infants from the age of 6 weeks to 32 weeks (see section 3). The vaccine contains five types of live rotavirus strains. When an infant is given the vaccine, the immune system (the body's natural defences) will make antibodies against the most commonly occurring types of rotavirus. These antibodies help protect against gastroenteritis caused by these types of rotavirus.

2. What you need to know before your child receives RotaTeq

Do not use RotaTeq if

- your child is allergic to any of the components of this vaccine (see section 6 Contents of the pack and other information).
- your child developed an allergic reaction after receiving a dose of RotaTeq or other rotavirus vaccine.
- your child has previously had intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment).
- your child was born with a malformation of the gastrointestinal system that might predispose for intussusception.
- your child has any disease which reduces his/her resistance to infection.
- your child has a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first.
- your child has diarrhoea or is vomiting. It might be necessary to postpone the vaccination until recovery.

Warnings and precautions

Talk to your doctor or pharmacist before using RotaTeq if your child:
- has received a blood transfusion or immunoglobulins within the last 6 weeks.
- has a close contact such as a household member who has a weakened immune system, e.g., a person with cancer or who is taking medicines that may weaken the immune system.
- has any disorder of the gastrointestinal system.
- has not been gaining weight and growing as expected.
- or the mother has taken any medicine during pregnancy that weakens the immune system.

After your child has received RotaTeq, contact a doctor/health care professional right away if your child experiences severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever (see also section 4 “Possible side effects”).

As always, please take care to wash your hands thoroughly after changing soiled nappies.

As with other vaccines, RotaTeq may not completely protect all children who are vaccinated even after all three doses have been given.

If your child has already been infected with rotavirus but is not yet ill when vaccinated, RotaTeq may not be able to prevent the illness.

RotaTeq does not protect against diarrhoea and vomiting due to causes other than rotavirus.

Other medicines and RotaTeq

RotaTeq may be given at the same time as your child receives other normally recommended vaccinations, such as diphtheria, tetanus, pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated or oral poliomyelitis, hepatitis B, pneumococcal conjugate and meningococcus group C conjugate vaccines.

Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines (or other vaccines).

RotaTeq with food and drink

There are no restrictions on taking food or liquid, including breast milk, either before or after vaccination with RotaTeq.

RotaTeq contains sucrose

If you have been told that your child has an intolerance to some sugars, inform your doctor/health care professional before the vaccine is administered.

RotaTeq contains sodium

This vaccine contains 37.6 mg sodium (main component of cooking/table salt) in each dose. This is equivalent to 1.88% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use RotaTeq

RotaTeq IS FOR ORAL USE ONLY.

A doctor or nurse will administer the recommended doses of RotaTeq to your child. The vaccine will be given by gently squeezing the tube and delivering the vaccine into your child's mouth.
The vaccine can be given without regard to food, liquid, or breast milk.
In case your child spits out or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit.

Under no circumstance should this vaccine be administered by injection.

The first dose (2 ml) of RotaTeq may be given from the age of 6 weeks and should be given before 12 weeks of age (about 3 months). RotaTeq may be given to infants who were born early provided that the pregnancy had lasted at least 25 weeks. These infants should receive the first dose of vaccine between 6 and 12 weeks after birth.

Your child will receive 3 doses of RotaTeq given at least four weeks apart. It is important that your child receives all 3 doses of the vaccine for protection against rotavirus. It is preferred that all three doses should be given by the age of 20-22 weeks and at latest all three doses should be given by the age of 32 weeks.

When RotaTeq is given to your child for the first dose, it is recommended that your child also receives RotaTeq (and not another rotavirus vaccine) to complete the vaccination course.

If you forget an appointment for RotaTeq

It is important that you follow the instructions of your doctor/health care professional regarding your child's return visits for the follow-up doses. If you forget or are not able to go back to your doctor/health care professional at the scheduled time, ask him or her for advice.

4. Possible side effects

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

Contact a doctor/health care professional right away if your child experiences one of the following symptoms:

- Allergic reactions (frequency cannot be estimated from the available data), which may be severe (anaphylaxis), and may include: allergic swelling that may affect the face, lips, tongue or throat.

- Bronchospasm (rare, may affect up to 1 in 1000 infants). This may present as wheezing, coughing or difficulty breathing.

- Severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever. These could be symptoms of a very rare (may affect up to 1 in 10,000 infants), but serious, side effect called intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment).

The following other side effects reported with the use of RotaTeq were:

- Very common (may affect more than 1 in 10 infants): fever, diarrhoea, vomiting

- Common (may affect up to 1 in 10 infants): infections of the upper respiratory system

- Uncommon (may affect up to 1 in 100 infants): stomach pains (see also above for signs of a very rare side effect of intussusception), runny nose and sore throat, ear infection, rash, blood in stool

- Rare (may affect up to 1 in 1000 infants): hives

- Not known (frequency cannot be estimated from the available data): irritability

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

Ask your doctor/health care professional if you want more information about side effects for RotaTeq.

Reporting of side effects
If your child gets 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 RotaTeq

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Store and transport refrigerated (2 °C to 8 °C). Keep the dosing tube in the outer carton in order to protect from light.

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

6. Contents of the pack and other information

What RotaTeq contains

The active substances in RotaTeq are 5 human-bovine reassortant rotavirus strains:

G1 2.2×10^6 Infectious Units
G2 2.8×10^6 Infectious Units
G3 2.2×10^6 Infectious Units
G4 2.0×10^6 Infectious Units
P1A[8] 2.3×10^6 Infectious Units

The other ingredients in RotaTeq are: sucrose, sodium citrate, sodium dihydrogen phosphate monohydrate, sodium hydroxide, polysorbate 80, culture media (containing inorganic salts, amino acids and vitamins), and purified water.

What RotaTeq looks like and contents of the pack

Oral solution

This vaccine is contained in a single-dose tube and is a pale yellow clear liquid that may have a pink tint.

RotaTeq is available in pack size of 1, 10 dosing tubes. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Merck Sharp & Dohme B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands.

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

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This leaflet was last revised in:

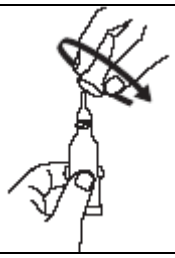
Other sources of information

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

The following information is intended for health care professionals only:

Instructions

To administer the vaccine:

	Tear open the protective bag and remove the dosing tube.
	Clear the fluid from the dispensing tip by holding tube vertically and tapping the twist-off cap.
	Open the dosing tube in 2 easy motions: 1. Puncture the dispensing tip by screwing cap **clockwise** until it becomes tight.
	2. Remove cap by turning it **counterclockwise**.
	Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty. (A residual drop may remain in the tip of the tube.)
	Discard the empty tube and cap in approved biological waste containers according to local regulations.

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

See also section 3. How to use RotaTeq.