SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM

RotaTeq® Solution

(rotavirus vaccine, live, oral, pentavalent, MSD)

COMPOSITION

Each 2 ml dose contains the following human-bovine rotavirus reassortants: G1, G2, G3, G4 and P1A[8]. The minimum dose levels of the reassortants are as follows:

G1 $2,2 \times 10^6$ infectious units

G2 $2,8 \times 10^6$ infectious units

G3 $2,2 \times 10^6$ infectious units

G4 $2,0 \times 10^6$ infectious units

P1A[8] $2,3 \times 10^6$ infectious units

The reassortants are propagated in Vero cells using standard tissue culture techniques in the absence of antifungal agents.

The reassortants are suspended in a buffered stabiliser solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80 and also Low Protein Kidney Medium-3 (LPKM-3) and rotavirus diluent. There are no preservatives or thimerosal present.

Contains sugar (sucrose).

PHARMACOLOGICAL CLASSIFICATION

A.30.1 Biologicals - Antigens

PHARMACOLOGICAL ACTION

RotaTeq is a live, oral pentavalent vaccine for use in the protection from rotavirus gastroenteritis. Protection is observed to last for at least 2 years. The vaccine contains 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express one of the outer capsid VP7 proteins (serotype G1, G2, G3 or G4) from the human rotavirus parent strain and the VP4 attachment protein (serotype P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein, P1A[8], from the human rotavirus parent strain and the outer capsid VP7 protein (serotype G6) from the bovine rotavirus parent strain (see **Table 1**).

Table 1

Name of Reassortant	**Human Rotavirus Parent Strains and Outer Surface Protein Compositions**	**Bovine Rotavirus Parent Strain and Outer Surface Protein Composition**	**Reassortant Outer Surface Protein Composition (Human Rotavirus Component in Bold)**
G1	WI79 - G1, P1A[8]	WC3 - G6, P7[5]	**G1**, P7[5]
G2	SC2 - G2, P2A[6]		**G2**, P7[5]
G3	WI78 - G3, P1A[8]		**G3**, P7[5]
G4	BrB - G4, P2A[6]		**G4**, P7[5]
P1A[8]	WI79 - G1, P1A[8]		G6, **P1A[8]**

Summary of Clinical Studies

Efficacy

The efficacy of RotaTeq was evaluated in 2 studies among infants who received vaccine (n=3 484) or placebo (n=3 499). The third dose was administered to infants as old as 32 weeks of age. Efficacy evaluations included efficacy against any severity (mild, moderate and severe) of rotavirus gastroenteritis and efficacy against severe rotavirus gastroenteritis. The effect on healthcare contacts for rotavirus gastroenteritis, including hospitalisations and emergency department visits (n=68 038), routine visits to a physician (n=5 673) and work loss (n=68 038), was also evaluated in the Rotavirus Safety and Efficacy Trial (REST). Concomitant administration of other licensed childhood vaccines except for oral poliovirus vaccine (OPV) was permitted in all phase III studies.

Efficacy against any severity of gastroenteritis caused by naturally occurring rotavirus of the composite of the G serotypes (G1-G4) included in the vaccine was 73,8 %, and efficacy against severe rotavirus gastroenteritis was 98,2 % through the first rotavirus season after completion of vaccination. RotaTeq also provided protection against non-vaccine G serotypes. Based on limited data, the efficacy against any severity of gastroenteritis caused by the non-vaccine G serotype (G9) was 74,1 %. The efficacy of RotaTeq through two rotavirus seasons after completion of vaccination against any severity of rotavirus gastroenteritis was 71,3 %.

RotaTeq reduced the rate of hospitalisations, emergency department visits, non-urgent care visits and parent/legal guardian work loss days. Hospitalisations and emergency department visits were evaluated among 68 038 infants and non-urgent care visits were evaluated among 5 673 infants for a maximum of 2 years after vaccination. The rate reductions were as follows:

- 94,5 % for hospitalisations and emergency department visits
  - 95,8 % for hospitalisations
  - 93,7 % for emergency department visits
- 86,0 % for non-urgent care visits
- 86,6 % for parent/legal guardian work loss days

Efficacy of RotaTeq against rotavirus gastroenteritis through the first full rotavirus season after completion of vaccination and reduction in hospitalisations/emergency department visits for rotavirus gastroenteritis for up to 2 years post-vaccinations by G-serotype are shown in **Table 2**.

Table 2

Efficacy of RotaTeq against rotavirus (RV) gastroenteritis

Reduction in incidence of RV gastroenteritis through one full season post-vaccination in REST and Study 007 (RotaTeq n=3 484*) (% [95 % CI])						
Serotype						
Severe disease (G1-G4)	Any severity (G1-G4)	G1	G2	G3	G4	G9
98,2 % [89,6, 100]†	73,8 % [67,2, 79,3]†	75,0 % [68,2, 80,5]†	63,4 % [2,7, 88,2]†	55,6 % [< 0, 92,6]	48,1 % [< 0, 91,6]	74,1 % [< 0, 99,5]
Reduction in hospitalisations/emergency department visits for RV gastroenteritis for						

up to 2 years post-vaccination in REST (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]†

*n=Number Vaccinated

†Statistically Significant

Efficacy and Safety in Pre-term Infants

RotaTeq or placebo was administered to 2 070 pre-term infants (25 to 36 weeks gestational age), including 1 007 recipients of RotaTeq, according to their chronological age in a placebo-controlled study. Among a subset of 308 pre-term infants who were followed for all adverse experiences, the safety profile was generally similar among those infants receiving RotaTeq as compared with those receiving placebo. The incidence of fever, vomiting, diarrhoea or irritability was generally similar among vaccine and placebo recipients.

In a subset of 204 vaccinated infants (99 in the vaccine group), protective efficacy, as measured by a reduction in the incidence of rotavirus gastroenteritis of any severity caused by vaccine serotypes (G1-G4) that occurred at least 14 days after the third dose of vaccine through the first full rotavirus season after vaccination, was 70,3 % [95 % CI < 0, 94,7]. In 2 070 vaccinated infants (1 007 in the vaccine group), protective efficacy, as measured by a reduction in the rate of hospitalisations and emergency department visits for rotavirus gastroenteritis caused by G1-G4 from 14 days for up to 2 years after the third dose, was 100 % [95 % CI 74, 100]. Likewise, the protective efficacy, as measured by a reduction in the rate of hospitalisations and emergency department visits for rotavirus gastroenteritis caused

by any serotype from 14 days for up to 2 years after the third dose, was 100 % [95 % CI 82, 100].

Studies with Other Vaccines

The immunogenicity of RotaTeq and diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, inactivated poliovirus vaccine (IPV), *Haemophilus influenzae* type b conjugate vaccine (HIB), hepatitis B vaccine and pneumococcal conjugate vaccine was evaluated among 1 358 infants. The immune responses to the specified vaccines were unaffected by RotaTeq. In addition, the studies demonstrated the efficacy of RotaTeq (89,5 %) when administered with these vaccines.

Concomitant administration of RotaTeq and oral poliovirus vaccine (OPV) did not affect the immune response to the polio antigens in a controlled study of 735 vaccinated infants. Although concomitant administration of OPV reduced some immune responses to RotaTeq, the seroconversion rates (≥ 3-fold rise from baseline) for serum IgA were > 93 %. There is evidence that a high level of efficacy against severe rotavirus gastroenteritis is maintained. The immune responses to RotaTeq are unaffected when OPV is administered two weeks after RotaTeq.

The safety profile, including the incidences of fever, vomiting, diarrhoea and irritability, was generally similar among subjects receiving the specified concomitant vaccines with RotaTeq and subjects receiving the specified concomitant vaccines with placebo.

In one study, 7 367 infants received a hexavalent (DTaP, IPV, HIB and hepatitis B) vaccine concomitantly with RotaTeq. The frequency of overall serious adverse experiences (SAEs), regardless of causal relationship, was 2,9 % in recipients of RotaTeq and 3,2 % in placebo

recipients. More detailed safety information was evaluated among a subset of 638 infants receiving RotaTeq with a hexavalent vaccine. The safety profile, including the incidences of fever, vomiting, diarrhoea and irritability, was generally similar among subjects receiving a hexavalent vaccine with RotaTeq and subjects receiving a hexavalent vaccine with placebo.

Immunogenicity

The immunologic mechanism by which RotaTeq protects against rotavirus gastroenteritis is unknown. A relationship between antibody responses to RotaTeq and protection against rotavirus gastroenteritis has not been established. However, RotaTeq induces antibodies that neutralise human serotypes G1, G2, G3, G4 and P1A[8]. In phase III studies, 92,9 % to 100 % of recipients of RotaTeq achieved a significant rise in serum anti-rotavirus IgA after a three-dose regimen.

INDICATIONS

RotaTeq is an oral pentavalent vaccine indicated for the prevention of rotavirus gastroenteritis in infants and children caused by the serotypes G1, G2, G3, G4 and G-serotypes that contain P1A[8] (e.g. G9). RotaTeq may be administered as early as 6 weeks of age.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine

Individuals who develop symptoms suggestive of hypersensitivity after receiving a dose of RotaTeq should not receive further doses of RotaTeq.

Individuals with Severe Combined Immunodeficiency Disease (SCID).

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

WARNINGS AND SPECIAL PRECAUTIONS

Adequate treatment provisions, including epinephrine injection (1:1 000), should be available for immediate use should an anaphylactic reaction occur.

No safety or efficacy data are available from clinical trials regarding the administration of RotaTeq to:

1. Immunocompromised patients such as
    - individuals with malignancies or who are otherwise immunocompromised
    - individuals receiving immunosuppressive therapy
2. Individuals infected with HIV or
3. Individuals who have received a blood transfusion or blood products, including immunoglobulins, within 42 days.

There are insufficient data from the clinical trials to support administration of RotaTeq to infants with indeterminate HIV status who are born to mothers with HIV/AIDS.

No faecal shedding of vaccine strains was seen in a small subset of infants with serious medical conditions (e.g. cystic fibrosis, failure to thrive, cancer, congenital heart disease and neutropenia) that were diagnosed after enrollment in the study. Healthcare providers may want to consider these data when assessing the benefits and potential risks of administering RotaTeq to infants with serious medical conditions while keeping in mind nearly all children are infected with naturally occurring rotavirus by age 5 years.

In clinical trials, RotaTeq was not administered to infants known to have immunodeficient household members. In these 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. Transmission of vaccine virus strains to non-vaccinated contacts has been observed post-marketing. Therefore, RotaTeq should be administered with caution to individuals with immunodeficient close contacts such as: Individuals with malignancies or who are otherwise immunocompromised; or individuals receiving immunosuppressive therapy. However, because nearly all children are infected with naturally occurring rotavirus by the age of 5 years, vaccination of infants may decrease the risk of exposure of immunodeficient household contacts to naturally occurring rotavirus. The healthcare provider should assess the potential risks and benefits of administering RotaTeq to infants known to have immunodeficient close contacts.

Infants with active gastrointestinal illness, chronic diarrhoea or growth retardation or a history of congenital abdominal disorders or intussusception were not to be included in the clinical studies. 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.

In worldwide post-marketing surveillance, cases of intussusception have been reported in temporal association with RotaTeq. (See **"SIDE EFFECTS, Post-Marketing Reports"**.)

Any acute infection or febrile illness may be reason for delaying use of RotaTeq except when, in the opinion of the physician, withholding the vaccine entails a greater risk. Low-grade fever itself and mild upper respiratory infection are not contraindications to vaccination with RotaTeq.

As with any vaccine, vaccination with RotaTeq may not result in complete protection in all recipients.

The clinical studies were not designed to assess the level of protection provided by only 1 or 2 doses of RotaTeq. *Post hoc* analyses of data from a large clinical study suggest that RotaTeq provides protection against hospitalisations and emergency department visits for rotavirus gastroenteritis during administration of the 3-dose vaccination series starting from 14 days post-dose 1.

No clinical data are available for RotaTeq when administered after exposure to rotavirus.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this vaccine.

INTERACTIONS

Concomitant administration of oral poliovirus vaccine (OPV) may reduce some immune responses to rotavirus vaccine; however, there is evidence that a high level of efficacy against severe rotavirus gastroenteritis is maintained (see **"PHARMACOLOGICAL ACTION, Studies with Other Vaccines"** and **"DOSAGE AND DIRECTIONS FOR USE, Use with Other Vaccines"**).

PREGNANCY AND LACTATION

RotaTeq is a paediatric vaccine and is not indicated for use in adults. There have been no adequate, well-controlled studies in women or animals. Information on the safety of the vaccine when used during lactation is not available.

DOSAGE AND DIRECTIONS FOR USE

FOR ORAL USE ONLY. NOT FOR INJECTION.

Paediatric Use

RotaTeq has been shown to be generally well tolerated and highly efficacious in preventing rotavirus gastroenteritis when administered to infants 6 weeks through 32 weeks of age.

Safety and efficacy have not been established in infants < 6 weeks of age.

Posology

The vaccination series consists of 3 ready-to-use liquid doses of RotaTeq administered orally to infants.

The first dose of RotaTeq should be administered at 6 to 12 weeks of age; the subsequent doses should be administered at a minimum interval of 4 weeks between each dose.

There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination with RotaTeq.

RotaTeq may be given to pre-term infants according to their chronological age.

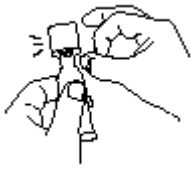
If for any reason an incomplete dose is administered (e.g. infant spits or regurgitates the vaccine), a replacement dose is not recommended, since such dosing was not studied in the clinical trials. The infant should continue to receive any remaining doses in the recommended series.

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

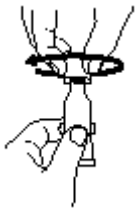
Each dose is supplied in a container consisting of a squeezable plastic, latex-free dosing tube with a twist-off cap, allowing for direct oral administration. The dosing tube is contained in a pouch.

To administer the vaccine:

Tear open the pouch and remove the dosing tube.

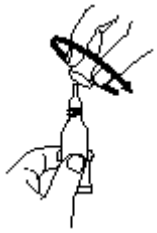


Clear the fluid from the dispensing tip by holding tube vertically and tapping cap.



Open the dosing tube in 2 easy motions:

Puncture the dispensing tip by screwing cap clockwise until it becomes tight.



Remove cap by turning it counter-clockwise.

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.

Use with Other Vaccines

RotaTeq can be administered with diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, whole cell pertussis vaccine, inactivated or oral poliovirus vaccine (IPV or OPV), *Haemophilus influenzae* type b conjugate vaccine, hepatitis B vaccine, pneumococcal conjugate vaccine, meningococcal group C conjugate vaccine and hexavalent vaccines.

Concomitant administration of RotaTeq and oral poliovirus vaccine (OPV) does not affect the immune response to the polio antigens. Although concomitant administration of OPV may reduce some immune responses to rotavirus vaccine, there is evidence that a high level of efficacy against severe rotavirus gastroenteritis is maintained. The immune responses to RotaTeq are unaffected when OPV is administered two weeks after RotaTeq.

Instructions to Healthcare Provider

The healthcare provider should determine the current health status and previous vaccination history of the vaccine recipient.

The healthcare provider should question the parent or guardian about reactions to a previous dose of RotaTeq or other rotavirus vaccine.

Information for Parents/Guardians

The healthcare provider should provide the vaccine information required to be given with each vaccination to the parent or guardian.

The healthcare provider should inform the parent or guardian of the benefits and risks associated with vaccination, as well as the importance of completing the immunisation series. For risks associated with vaccination, see **"WARNINGS AND SPECIAL PRECAUTIONS"**.

Parents or guardians should be instructed to report any adverse reactions to their healthcare provider.

SIDE EFFECTS

71 725 infants were evaluated in 3 placebo-controlled clinical trials including 36 165 infants who received RotaTeq and 35 560 infants who received placebo. Parents/guardians were contacted on days 7, 14 and 42 after each dose regarding intussusception and any other serious adverse events.

The vaccine is generally well tolerated.

In the large-scale (34 837 vaccine recipients and 34 788 placebo recipients), placebo-controlled Rotavirus Efficacy and Safety Trial (REST), RotaTeq did not increase the risk of intussusception relative to placebo (see **Table 3**). Active surveillance was employed to identify potential cases of intussusception at days 7, 14 and 42 after each dose and every 6 weeks thereafter for 1 year after dose one. There were no confirmed cases of intussusception during the 42-day period after dose one, and there was no clustering of cases among vaccine recipients at any time period after any dose. Following the 1-year

safety follow-up period, 4 cases of intussusception were reported in children who had received placebo during the study.

Table 3

Confirmed Cases of Intussusception in Recipients of RotaTeq as Compared with Placebo Recipients during REST

	RotaTeq (n=34 837)	Placebo (n=34 788)
Confirmed intussusception cases within 42 days after each dose	6	5
Relative Risk (95 % CI)†	1,6 (0,4; 6,4)	--
Confirmed intussusception cases within 365 days after dose one	13	15
Relative Risk (95 % CI)	0,9 (0,4; 1,9)	--

†Relative Risk and 95 % Confidence Interval based upon group sequential design stopping criteria employed in REST

Kawasaki's disease was reported in the phase III clinical trials in < 0,1 % (5/36 150) of vaccine recipients and < 0,1 % (1/35 536) of placebo recipients within 42 days of any dose (not statistically significant).

In 11 711 infants (6 138 recipients of RotaTeq) from the 3 studies, a Vaccination Report Card was used by parents/guardians to record the child's temperature and any episodes of diarrhoea and vomiting on a daily basis during the first week following each vaccination. **Table 4** summarises the frequencies of these adverse events, regardless of cause.

Table 4

Adverse Experiences of Special Clinical Interest within the First Week after the First Dose

Adverse Event	First Dose	
	RotaTeq	Placebo
Elevated Temperature (≥ 100,5 °F [38,1 °C] rectal equivalent)	17,1 %	16,2 %
Vomiting	6,7 %	5,4 %
Diarrhoea	10,4 %	9,1 %

Parents/guardians of the 11 711 infants were also asked to report the presence of other events on the Vaccination Report Card for 42 days after each dose. The following vaccine-related adverse experiences were observed among recipients of RotaTeq at a frequency at least 0,3 % greater than that observed among placebo recipients.

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)

Infections and infestations

Uncommon: Nasopharyngitis (0,6 % vaccine recipients, 0,3 % placebo recipients)

Gastrointestinal disorders

Very Common: Diarrhoea (17,6 % vaccine recipients, 15,1 % placebo recipients), vomiting (10,1 % vaccine recipients, 8,2 % placebo recipients)

General disorders and administration site conditions

Very Common: Pyrexia (20,9 % vaccine recipients, 18,7 % placebo recipients).

Other Adverse Events

Otitis media and bronchospasm occurred in more vaccine than placebo recipients (14,5 % versus 13,0 % and 1,1 % versus 0,7 %, respectively) overall; however, among cases that were considered to be vaccine-related in the opinion of the study investigator, the incidence was the same for vaccine and placebo recipients for otitis media (0,3 %) and bronchospasm (< 0,1 %).

Administration of other licensed vaccines was permitted in all studies. The safety of RotaTeq when administered concomitantly with pre-specified licensed vaccines including *Haemophilus influenzae* type b and hepatitis B vaccine, diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, inactivated poliovirus vaccine (IPV), pneumococcal conjugate vaccine and hexavalent vaccines was evaluated in all 3 phase III placebo-controlled studies. In subsequent controlled studies, the safety and immunogenicity of RotaTeq when administered concomitantly with oral poliovirus vaccine, meningococcal group C conjugate vaccine or hexavalent vaccine were evaluated. In all these studies, concomitant use with these vaccines was well tolerated; the frequency of adverse experiences observed was generally similar to that seen in the control group.

Post-Marketing Reports

The following adverse experiences have been spontaneously reported during post-approval use of RotaTeq. Because these experiences were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to vaccine exposure.

Gastrointestinal disorders: Gastroenteritis with vaccine viral shedding in infants with severe combined immunodeficiency (SCID), intussusception

Immune system disorders: Anaphylactic reaction

Skin and subcutaneous tissue disorders: Urticaria, angioedema.

Post-Marketing Observational Safety Surveillance Study

In a prospective post-marketing observational study conducted using a large medical claims database, the risks of intussusception or Kawasaki disease resulting in emergency department visits or hospitalisations during the 30 days following any dose of vaccine were analysed among 85 150 infants receiving one or more doses of RotaTeq. Medical charts were reviewed to confirm these diagnoses. In addition, general safety was monitored by electronic search of the automated records database for all emergency department visits and hospitalisations. The study included an independent, external Safety Monitoring Committee.

During the 0 to 30 day follow-up period after vaccination, there were no statistically significant differences in the rates of intussusception or Kawasaki disease compared with the expected background rates. In addition, there was no statistically significant increased risk of these adverse events during the 0 to 30 day follow-up period when comparing the 17 433 person-years of follow-up among infants receiving RotaTeq (n=85 150) with the 12 339 person-years of follow-up among a concurrent control group of infants who received DTaP, but not RotaTeq (n=62 617). There were 6 confirmed cases of intussusception among infants vaccinated with RotaTeq compared with 5 among the concurrent controls vaccinated with DTaP (relative risk = 0,8, 95 % CI: 0,22 to 3,52). There was one chart-confirmed case of Kawasaki disease identified among infants vaccinated with RotaTeq and one chart-confirmed case of Kawasaki disease among concurrent DTaP controls (relative risk = 0,7, 95 % CI: 0,01 to 55,56). In the general safety analyses, the Safety Monitoring Committee did not identify any specific safety concerns.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

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.

IDENTIFICATION

RotaTeq is a pale yellow clear liquid that may have a pink tint.

PRESENTATION

RotaTeq is available as a single, pre-filled 2 ml unit dose in a slightly opaque plastic dosing tube with a twist-off cap. The dosing tube is embossed with ROTAVIRUS VACCINE on both sides and is contained in a pouch. The container and delivery system are latex-free.
RotaTeq is available in packs of 1, 10 and 25.

STORAGE INSTRUCTIONS

Store and transport refrigerated at 2 °C to 8 °C. Protect from light.
DO NOT STORE FROZEN. While it is acceptable for the product to freeze during distribution from the manufacturer, the product should be discarded if it freezes during storage.
Keep out of reach of children.

The product must be used before the expiration date.

RotaTeq should be administered as soon as possible after being removed from refrigeration. When out of refrigeration at room temperature at or below 25 °C, administration may be delayed for up to 48 hours. After this time, the vaccine should be discarded in approved biological waste containers according to local regulations.

REGISTRATION NUMBER

A40/30.1/0730

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

MSD (Pty) Ltd

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