Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Triaxis, suspension for injection in a pre-filled syringeDiphtheria, Tetanus, Pertussis (acellular component) Vaccine (adsorbed, reduced antigen(s) content)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Diphtheria Toxoid Not less than 2 IU* (2 Lf)
Tetanus Toxoid Not less than 20 IU* (5 Lf)
Pertussis Antigens
Pertussis Toxoid 2.5 micrograms
Filamentous Haemagglutinin 5 micrograms
Pertactin 3 micrograms
Fimbriae Types 2 and 3 5 micrograms
Adsorbed on aluminium phosphate 1.5 mg (0.33 mg Al^{3+})

* As lower confidence limit (p = 0.95) of activity measured according to the assay described in the European Pharmacopoeia.

This vaccine may contain traces of formaldehyde and glutaraldehyde which are used during the manufacturing process (see sections 4.3 and 4.4).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.
Triaxis appears as a cloudy white suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

TRIAXIS (Tdap) is indicated for:
Active immunization against tetanus, diphtheria and pertussis in persons from 4 years of age as a booster following primary immunization.

Passive protection against pertussis in early infancy following maternal immunization during pregnancy (see sections 4.2, 4.6, and 5.1).

TRIAXIS should be used in accordance with official recommendations.

4.2 Posology and method of administration

Posology
A single injection of one (0.5 mL) dose is recommended in all indicated age groups.

In adolescents and adults with an unknown or incomplete diphtheria or tetanus vaccination status against diphtheria or tetanus, one dose of TRIAXIS can be administered as part of a vaccination series to protect against pertussis and in most cases also against tetanus and diphtheria. One additional dose of a diphtheria- and tetanus- (dT) containing vaccine can be administered one month later followed by a 3rd dose of a diphtheria or dT containing vaccine 6 months after the first dose to optimize protection against disease (see section 5.1). The number and schedule of doses should be determined according to local recommendations.

TRIAXIS can be used for repeat vaccination to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 year intervals (see section 5.1).

TRIAXISscan be used in the management of tetanus prone injuries with or without concomitant administration of Tetanus Immunoglobulin according to official recommendations.

TRIAXIS may be administered to pregnant women during the second or third trimester to provide passive protection of infants against pertussis (see sections 4.1, 4.6 and 5.1).

Method of administration
A single injection of one dose (0.5 mL) of TRIAXIS should be administered intramuscularly. The preferred site is into the deltoid muscle.
TRIAXISshould not be administered into the gluteal area; intradermal or subcutaneous routes should not be used (in exceptional cases the subcutaneous route may be considered, see section 4.4).

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

4.3 Contraindications

TRIAXIS should not be administered to person with known hypersensitivity

- to diphtheria, tetanus or pertussis vaccines
- to any other component of the vaccine (see section 6.1)
- to any residual substances carried over from manufacture (formaldehyde and glutaraldehyde), which may be present in undetectable trace amounts.

TRIAXIS should not be administered to persons who experienced an encephalopathy of unknown origin within 7 days of previous immunization with a pertussis-containing vaccine.

As with other vaccines, administration of TRIAXIS should be postponed in persons suffering from an acute severe febrile illness. The presence of a minor infection is not a contraindication.

4.4 Special warnings and precautions for use

TRIAXIS should not be used for primary immunization.

Regarding the interval between a booster dose of TRIAXIS and preceding booster doses of diphtheria and/or tetanus containing vaccines, the official recommendations should generally be followed. Clinical data have demonstrated that there was no clinically relevant difference in rates of adverse reactions associated with administration of a tetanus-, diphtheria- and pertussis-containing booster vaccine as early as 4 weeks, compared to at least 5 years, after a preceding dose of tetanus and diphtheria-containing vaccine.

Prior to immunization
Vaccination should be preceded by a review of the person's medical history (in particular previous vaccinations and possible adverse events). In persons who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, administration of TRIAXIS vaccine must be carefully considered.

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of the vaccine.

If Guillain-Barré syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid, including TRIAXIS should be based on careful consideration of the potential benefits and possible risks.

TRIAXIS should not be administered to persons with progressive neurological disorder, uncontrolled epilepsy or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized.

The immunogenicity of the vaccine could be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone the vaccination until the end of such disease or treatment if practical. Nevertheless, vaccination of

HIV infected persons or persons with chronic immunodeficiency, such as AIDS, is recommended even if the antibody response might be limited.

Administration precautions
Do not administer by intravascular or intradermal injection.

Intramuscular injections should be given with care in patients on anticoagulant therapy or suffering from coagulation disorders because of the risk of haemorrhage. In these situations, administration of TRIAXIS by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

Syncope (fainting) can occur following, or even before, administration of injectable vaccines, including TRIAXIS. Procedures should be in place to prevent falling injury and manage syncopal reactions.

The tip caps of the prefilled syringes contain a natural rubber latex derivative, which may cause allergic reactions in latex sensitive individuals.

Other considerations
As with any vaccine, vaccination with TRIAXIS may not protect 100% of susceptible individuals.
A persistent nodule at the site of injection may occur with all adsorbed vaccines, particularly if administered into the superficial layers of the subcutaneous tissue.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Based on the results of concomitant use clinical studies, TRIAXIS can be administered concomitantly with any of the following vaccines: inactivated Influenza vaccine, Hepatitis B vaccine, Inactivated or Oral Poliomyelitis vaccine and recombinant Human Papillomavirus vaccine (See section 4.8) according to local recommendations.

Separate limbs must be used for the site of injection of concomitant parenteral vaccines. Interaction studies have not been carried out with other vaccines, biological products, or therapeutic medications. However, in accordance with commonly accepted immunization guidelines, since TRIAXIS is an inactivated product it may be administered concomitantly with other vaccines or immunoglobulins at a separate injection site.

In the case of immunosuppressive therapy please refer to section 4.4.

4.6 Fertility, pregnancy and lactation

Pregnancy
TRIAXIS can be used during the second or third trimester of pregnancy in accordance with official recommendations (see section 4.2).
Safety data from 4 randomized controlled trials (310 pregnancy outcomes), 1 prospective observational study (546 pregnancy outcomes), 5 retrospective observational studies (124,810 pregnancy outcomes), and from passive surveillance of women who received TRIAXIS or REPEVAX (Tdap-IPV; containing the same amounts of tetanus, diphtheria and pertussis antigens as TRIAXIS) during the second or third trimester have shown no vaccine-related adverse effect on pregnancy or on the health of the fetus/newborn child.
As with other inactivated vaccines, it is not expected that vaccination with TRIAXIS during any trimester would harm the fetus. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development.

For information on immune responses to vaccination during pregnancy and its effectiveness at preventing pertussis in infants, see section 5.1.

Breast-feeding
It is not known whether the active substances included in TRIAXIS are excreted in human milk but antibodies to the vaccine antigens have been found to be transferred to the suckling offspring of rabbits. Two animal developmental studies conducted

in rabbits have not shown any harmful effects of maternal antibodies induced by the vaccine on offspring postnatal development.

However, the effect on breast-fed infants of the administration of TRIAXISto their mothers has not been studied. As TRIAXIS is inactivated, any risk to the infant is unlikely. The risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.

Fertility
TRIAXIS 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 or use machines have been performed. TRIAXIS has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
In clinical trials TRIAXIS was given to a total of 4,546 persons, including 298 children (4 to 6 years), 1,313 adolescents (11 to 17 years) and 2,935 adults (18 to 64 years). Most commonly reported reactions following vaccination included local reactions at the injection site (pain, redness and swelling) that occurred in 21% - 78% of the vaccinees, headache and tiredness that occurred in 16% - 44% of vaccinees. These signs and symptoms usually were mild in intensity and occurred within 48 hours following vaccination. They all resolved without sequelae.

Safety analysis was conducted in 1,042 healthy adolescent males and females aged 10 to 17 years during a clinical trial. They received quadrivalent human papillomavirus types 6/11/16/18 vaccine (Gardasil) concurrently with a dose of TRIAXIS and a dose of quadrivalent meningococcal conjugate vaccine serogroup A, C, Y and W135. The safety profiles were similar in both concomitant and non-concomitant groups. Higher frequencies of swelling at the Gardasil injection site, bruising and pain at TRIAXIS injection sites were observed in the concomitant administration group. The differences observed between concomitant and non-concomitant groups were less than 7% and in a majority of subjects the adverse events were reported as mild to moderate in intensity.

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)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known cannot be estimated from the available data

Table 1 presents adverse reactions observed in clinical trials and also includes additional adverse events which have been spontaneously reported during the post-marketing use of TRIAXIS worldwide. Because post-marketing adverse events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Therefore, the frequency category "Not known" is assigned to these adverse events.

Table 1: Adverse events from trials and worldwide post-marketing experience

System Organ Class	**Frequency**	**Children (4 to 6 Years)**	**Adolescents (11 to 17 Years)**	**Adults (18 to 64 Years)**
Immune system disorders	Not known	Hypersensitivity (Anaphylactic) reaction (Angioedema, Oedema, Rash, Hypotension)*		
Metabolism and nutrition disorders	Very common	Anorexia		

		(decreased appetite)		
Nervous system disorders	Very common	Headache		
	Not known	Paraesthesia*, Hypoaesthesia*, Guillain-Barré Syndrome*, Brachial Neuritis*, Facial Palsy*, Convulsions*, Syncope*, Myelitis*		
Cardiac disorders	Not known	Myocarditis*		
Gastrointestinal disorders	Very common	Diarrhoea	Diarrhoea, Nausea	Diarrhoea
	Common	Nausea, Vomiting	Vomiting	Nausea, Vomiting
Skin and subcutaneous system disorders	Common	Rash		
	Not known	Pruritus*, Urticaria*		
Musculoskeletal and connective tissue disorders	Very common		Generalized aching or Muscular weakness, Arthralgia or Joint swelling	Generalized aching or Muscular weakness
	Common	Generalized aching or Muscular weakness, Arthralgia or Joint swelling		Arthralgia or Joint swelling
	Not known	Myositis*		
General disorders and administrative site conditions	Very common	Fatigue/Asthenia	Fatigue/Asthenia, Malaise, Chills	Fatigue/Asthenia, Malaise
		Injection site pain, Injection site erythema, Injection site swelling		
	Common	Pyrexia, Chills, Axillary adenopathy	Pyrexia, Axillary adenopathy	Pyrexia, Chills, Axillary adenopathy
	Not known	Injection site bruising*, Injection site sterile abscess*, Injection site nodule*		

* Post-marketing Adverse Events

Description of selected adverse reactions

General Disorders and Administration Site Conditions:

Large injection site reactions (>50 mm), including extensive limb swelling from the injection site beyond one or both joints occur after administration of TRIAXIS in adolescents and adults. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 - 5 days.

Paediatric population
The safety profile of TRIAXIS as presented in Table 1 includes data from a clinical trial in 298 children 4 to 6 years of age who had previously received a total of 4 doses, including primary immunization, with DTaP-IPV combined with Hib, at approximately 2, 4, 6 and 18 months of age. In this clinical study, the most common adverse events reported within 14 days post-vaccination were pain at the injection site (in 39.6 % of subjects) and tiredness (in 31.5 % of subjects).

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.

Ireland
Healthcare professionals are asked to report any suspected adverse reactions via the Health Products Regulatory Authority (HPRA) Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pertussis, purified antigen, combination with toxoids.
ATC code: J07AJ52

Clinical trials
The immune responses observed one month after vaccination with TRIAXIS in 265 children, 527 adolescents and 743 adults are shown in the table below.

Table 2: Immune response of children, adolescents and adults one month after vaccination with TRIAXIS

Antibody	**Criteria**	**Children (4 - 6 years)[1] (N=265) %**	**Adolescents (11 - 17 years)[2] (N=527) %**	**Adults (18 - 64 years)[2] (N=743) %**
Diphtheria (SN, IU/mL)	≥0.1	100	99.8	94.1
Tetanus (ELISA, IU/mL or EU/mL)	≥0.1	100	100	100
Pertussis (ELISA, EU/mL)				
PT	Booster Response[3]	91.9	92.0	84.4
FHA		88.1	85.6	82.7
PRN		94.6	94.5	93.8
FIM		94.3	94.9	85.9

DTaP: diphtheria toxoid [paediatric dose], tetanus and acellular pertussis; ELISA: Enzyme Linked Immunoassay; EU: ELISA units; IU: international units; N: number of participants with available data; SN: seroneutralisation.
[1] Study Td508was conducted in Canada with children 4-6 years of age.
[2] Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age.
[3] For children in Study Td508 who were previously primed with DTaP at 2, 4, 6 and 18 months of age, a booster response is defined as a 4-fold increase in concentration of anti-pertussis antibodies. For adolescents and adults in Study Td506, a booster response is defined as a 2-fold increase in concentration of anti-pertussis antibodies in participants with high pre-vaccination concentration and a 4-fold increase in participants with low pre-vaccination concentration.

The safety and immunogenicity of TRIAXIS in adults and adolescents was shown to be comparable to that observed with a single dose of an adult formulation diphtheria-tetanus (Td) adsorbed vaccine containing the same amount of tetanus and diphtheria toxoids.

Serological correlates for protection against pertussis have not been established. On comparison with data from the Sweden I pertussis efficacy trials conducted between 1992 and 1996, where primary immunization with Sanofi Pasteur _acellular pertussis infant DTaP formulation confirmed a protective efficacy of 85% against pertussis disease, it is considered that TRIAXIS had elicited protective immune responses. The pertussis antibody levels for all antigens following a booster dose of TRIAXIS in adolescents and adults exceeded those observed in a household contact study nested within the efficacy trial.

Table 3: Ratio of pertussis antibody GMC observed one month after a dose of TRIAXIS in adolescents and adults compared with those observed in infants one month following vaccination at 2, 4 and 6 months of age in the Sweden I efficacy trial with DTaP (PPI Population[1])

	Adolescents (11-17 years)[2]	**Adults (18-64 years)[2]**
	TRIAXIS/DTaP[3] GMC Ratio (95% CIs)[4]	**TRIAXIS/DTaP[3] GMC Ratio (95% CIs)[4]**
Participants	**N=524-526**	**N=741**
Anti-PT	3.6 (2.8, 4.5)	2.1 (1.6, 2.7)
Anti-FHA	5.4 (4.5, 6.5)	4.8 (3.9, 5.9)
Anti-PRN	3.2 (2.5, 4.1)	3.2 (2.3, 4.4)
Anti-FIM	5.3 (3.9, 7.1)	2.5 (1.8, 3.5)

DTaP: diphtheria toxoid [paediatric dose], tetanus and acellular pertussis; GMC: Geometric Mean Concentration; N: number of participants with available data; PPI: per protocol immunogenicity

[1] Eligible participants for whom immunogenicity data were available.

[2] Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age. Antibody GMCs, measured in ELISA units were calculated separately for infants, adolescents and adults.

[3] N = 80, number of infants who received DTaP at 2, 4 and 6 months of age with available data post-dose 3 (sera from the Sweden I Efficacy Trial tested contemporaneously with samples from study Td506).

[4] GMCs following TRIAXIS were non-inferior to GMCs following DTaP (lower limit of 95% CI on the ratio of GMCs for TRIAXISdivided by DTaP >0.67).

Antibody persistence

Serology follow-up studies were conducted at 3, 5 and 10 years, in individuals previously immunized with a single booster dose of TRIAXIS. Persistence of seroprotection to diphtheria and tetanus, and seropositivity to pertussis is summarised in Table 4.

Table 4: Persistence of Seroprotection/Seropositivity Rates (%) in Children, Adolescents and Adults at 3-, 5- and 10-years following a dose of TRIAXIS (PPI Population[1])

		Children (4-6 years)[2]	**Adolescents** (11-17 years)[3]			**Adults** (18-64 years)[3]		
Time since TRIAXIS dose		**5 years**	**3 years**	**5 years**	**10 years**	**3 years**	**5 years**	**10 years**
Participants		N=128-150	N=300	N=204-206	N=28-39	N=292	N=237-238	N=120-136
Antibody		% Seroprotection/Seropositivity						
Diphtheria (SN, IU/mL)	≥ 0.1	86.0	97.0	95.1	94.9	81.2	81.1	84.6
	≥ 0.01	100	100	100	100	95.2	93.7	99.3
Tetanus (ELISA, IU/mL)	≥ 0.1	97.3	100	100	100	99.0	97.1	100
Pertussis (ELISA, EU/mL)	Sero-positivity[4]							
PT		63.3	97.3	85.4	82.1	94.2	89.1	85.8
FHA		97.3	100	99.5	100	99.3	100	100
PRN		95.3	99.7	98.5	100	98.6	97.1	99.3
FIM		98.7	98.3	99.5	100	93.5	99.6	98.5

ELISA: Enzyme Linked Immunoassay; EU: ELISA units; IU: international units; N: number of participants with

available data; PPI: per protocol immunogenicity; SN: seroneutralisation;[1] Eligible participants for whom immunogenicity data were available for at least one antibody at the specified
time-point.
[2] Study Td508 was conducted in Canada with children 4-6 years of age.
[3] Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age.
[4] Percentage of participants with antibodies ≥ 5 EU/mL for PT, ≥ 3 EU/mL for FHA and PRN, and ≥ 17 EU/mL for FIM for the 3 year follow-up; ≥ 4 EU/mL for PT, PRN and FIM, and ≥ 3 EU/mL for FHA for the 5-year and 10-year follow-up.

Immunogenicity in persons not previously vaccinated or with an unknown vaccination status
After administration of one dose of REPEVAX (Tdap-IPV; containing the same amounts of tetanus, diphtheria and pertussis antigens as TRIAXIS) to 330 adults ≥40 years of age that had not received any diphtheria- and tetanus-containing vaccine in the past 20 years:

- ≥95.8% of adults were seropositive (≥ 5 EU/mL) for antibodies to all vaccine-containing pertussis antigens,
- 82.4% and 92.7% were seroprotected against diphtheria at a threshold ≥0.1 and ≥0.01 IU/mL, respectively,
- 98.5% and 99.7% were seroprotected against tetanus at a threshold ≥0.1 and ≥0.01 IU/mL, respectively,
- and ≥98.8% were seroprotected against polio (types 1, 2 and 3) at a threshold ≥1:8 dilution.

After administration of two additional doses of diphtheria- tetanus- and polio-containing vaccine to 316 subjects, one and six months after the first dose, the seroprotection rates against diphtheria were 94.6% and 100% (≥0.1 and ≥ 0.01 IU/mL, respectively), against tetanus 100% (≥0.1 IU/mL), and against polio (types 1, 2 and 3) 100% (≥1:8 dilution).

Immunogenicity following repeat vaccination
The immunogenicity of TRIAXIS following repeat vaccination 10 years after a previous dose of TRIAXIS or REPEVAX, has been evaluated. One month post-vaccination ≥ 98.5% of study participants achieved seroprotective antibody levels (≥ 0.1 IU/ml) for diphtheria and tetanus, and ≥ 84% achieved booster responses to the pertussis antigens. (A pertussis booster response was defined as a post-vaccination antibody concentration ≥ 4 times the LLOQ if the pre-vaccination level was < LLOQ; ≥ 4 times the pre-vaccination level if that was ≥ LLOQ but < 4 times LLOQ; or ≥ 2 times the pre-vaccination level if that was ≥ 4 times the LLOQ).

Based on the serology follow-up and repeat vaccination data, TRIAXIS can be used instead of a dT vaccine to boost immunity to pertussis in addition to diphtheria and tetanus.

Immunogenicity in pregnant women
Pertussis antibody responses in pregnant women are generally similar to those in non-pregnant women. Vaccination during the second or third trimester of pregnancy is optimal for antibody transfer to the developing fetus.

Immunogenicity against pertussis in infants (<3 months of age) born to women vaccinated during pregnancy
Data from 2 published randomized controlled trials demonstrate higher pertussis antibody concentrations at birth and at 2 months of age, (i.e., prior to the start of their primary vaccinations) in infants of women vaccinated with TRIAXIS during pregnancy compared with infants of women not vaccinated against pertussis during pregnancy.
In the first study, 33 pregnant women received TRIAXIS and 15 received saline placebo at 30 to 32 weeks gestation. The geometric mean concentrations (GMC) in EU/mL for the anti-pertussis antibodies to the PT, FHA, PRN, and FIM antigens in infants of vaccinated women were, respectively, 68.8, 234.2, 226.8, and 1867.0 at birth, and 20.6, 99.1, 75.7, and 510.4 at 2 months of age. In the control-group infants, the corresponding GMCs were 14.0, 25.1, 14.4, and 48.5 at birth, and 5.3, 6.6, 5.2, and 12.0 at 2 months. The GMC ratios (TRIAXIS/control group) were 4.9, 9.3, 15.8, and 38.5 at birth, and 3.9, 15.0, 14.6, and 42.5 at 2 months.
In the second study, 134 pregnant women received TRIAXIS and 138 received a tetanus and diphtheria control vaccine at a mean gestational age of 34.5 weeks. The GMCs (EU/mL) for the anti-pertussis antibodies to the PT, FHA, PRN, and FIM antigens in infants of vaccinated women were, respectively, 54.2, 184.2, 294.1, and 939.6 at birth, and 14.1, 51.0, 76.8, and 220.0 at 2 months of age. In the control-group infants, the corresponding GMCs were 9.5, 21.4, 11.2, and 31.5 at birth, and 3.6, 6.1, 4.4, and 9.0 at 2 months. The GMC ratios (TRIAXIS/control group) were 5.7, 8.6, 26.3, and 29.8 at birth, and 3.9, 8.4, 17.5, and 24.4 at 2 months.
These higher antibody concentrations should provide passive immunity against pertussis for the infant during the first 2 to 3 months of life, as has been shown by observational effectiveness studies.

Immunogenicity in infants and toddlers born to women vaccinated during pregnancy

For infants of women vaccinated with TRIAXIS or REPEVAX during pregnancy, the immunogenicity of routine infant vaccination was assessed in several published studies. Data on the infant response to pertussis and non-pertussis antigens were evaluated during the first year of life.
Maternal antibodies derived after TRIAXIS or REPEVAX vaccination in pregnancy may be associated with blunting of the infant immune response to active immunization against pertussis. Based on current epidemiological studies, this blunting may not have clinical relevance.
Data from several studies did not show any clinically relevant blunting from vaccination in pregnancy with TRIAXIS or REPEVAXand the infants' or toddlers' responses to diphtheria, tetanus, *Haemophilusinfluenzae* type b, inactivated poliovirus, or pneumococcal antigens.
Effectiveness against pertussis in infants born to women vaccinated during pregnancy
The vaccine effectiveness in the first 2-3 months of life for infants born to women vaccinated against pertussis during the third trimester of pregnancy has been evaluated in 3 observational studies. The overall effectiveness is > 90%.

Table 5: Vaccine effectiveness (VE) against pertussis disease in young infants born to mothers vaccinated during pregnancy with TRIAXIS or REPEVAX in 3 retrospective studies.

Location	Vaccine	VE (95% CI)	VE estimation method	Infant follow-up period
UK	REPEVAX	93% (81, 97)	unmatched case-control	2 months
US	TRIAXIS*	91.4% (19.5, 99.1)	cohort regression model	2 months
UK	REPEVAX	93% (89, 95)	screening (case-coverage)	3 months
* Approximately 99% of women were vaccinated with TRIAXIS				

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity in pregnancy, embryonal/foetal development, parturition and postnatal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenoxyethanol
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store in a refrigerator at 2°C to 8°C.
Do not freeze. Discard the vaccine if it has been frozen.
Keep the syringe in the outer carton in order to protect from light.
Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period, Triaxis should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.5 Nature and contents of container

0.5 mL of suspension in pre-filled syringe (glass) with a plunger stopper (bromobutyl elastomer), without needle, with a tip-cap (rubber compound) - pack size of 1 or 10.

0.5 mL of suspension in pre-filled syringe (glass) with a plunger stopper (bromobutyl elastomer), with a tip-cap (rubber compound) and 1 or 2 separate needles - pack size of 1 or 10.
The tip caps of the prefilled syringes contain a natural rubber latex derivative.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use

Parenteral products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. In the event of either being observed, discard the medicinal product.

The normal appearance of the vaccine is a uniform, cloudy, white suspension which may sediment during storage. Shake the pre-filled syringe well to uniformly distribute the suspension before administering the vaccine.

The needle should be pushed firmly on to the end of the pre-filled syringe and rotated through 90 degrees.

Disposal

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

Needles should not be recapped.

7 MARKETING AUTHORISATION HOLDER

Sanofi Pasteur
14 Espace Henry Vallee
Lyon
69007
France

8 MARKETING AUTHORISATION NUMBER

PA2131/010/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3rd June 2016
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May 2023