SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

REPEVAX, suspension for injection, in pre-filled syringe

Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) 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
Poliovirus (Inactivated)**	
Type 1	40 D antigen units
Type 2	8 D antigen units
Type 3	32 D antigen units
Adsorbed on aluminium phosphate	1.5 mg (0.33 mg aluminium)

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

REPEVAX may contain traces of formaldehyde, glutaraldehyde, streptomycin, neomycin, polymyxin B and bovine serum albumin, 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

REPEVAX appears as a uniform, cloudy, white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

REPEVAX is indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis in persons from 3 years of age as a booster following primary immunization.

The use of REPEVAX should be determined on the basis of 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.

REPEVAX is a vaccine containing low-dose diphtheria toxoid plus tetanus toxoid in combination with pertussis and polio antigens for booster vaccinations.

In adolescents and adults with an unknown or incomplete diphtheria or tetanus vaccination status against diphtheria or tetanus, one dose of REPEVAX® can be administered as part of a vaccination series to protect against pertussis and poliomyelitis 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.

REPEVAX can be used for repeat vaccination to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 year intervals (see section 5.1). Repeat vaccination should be performed according to official recommendations.

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

Paediatric Population

REPEVAX should not be used in children under 3 years of age.

Children from the age of 3 years onwards and adolescents should receive the same dosage as adults.

Method of administration

A single injection of one dose (0.5 mL) of REPEVAX should be administered intramuscularly. The preferred site is into the deltoid muscle.

REPEVAX should 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

- REPEVAX should not be administered to persons with known hypersensitivity
  - to diphtheria, tetanus, pertussis or poliomyelitis vaccines
  - to any other component of the vaccine (see Section 6.1)
  - to any residual substances carried over from manufacture (formaldehyde, glutaraldehyde, streptomycin, neomycin, polymyxin B and bovine serum albumin), which may be present in undetectable trace amounts.

- REPEVAX 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 REPEVAX should be postponed in persons suffering from an acute severe febrile illness. The presence of a minor infection (e.g., mild upper respiratory infection) is not a contraindication.

4.4 Special warnings and precautions for use

REPEVAX should not be used for primary immunization.

Regarding the interval between a booster dose of REPEVAX and preceding booster doses of diphtheria and/or tetanus containing vaccines, the official recommendations should generally be followed. Clinical data in adults have demonstrated that there was no clinically relevant difference in rates of adverse reactions associated with administration of REPEVAX 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 REPEVAX 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 or brachial neuritis has occurred following receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

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

The rates and severity of adverse events in recipients of tetanus toxoid antigen are influenced by the number of prior doses and level of pre-existing antitoxins.

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 and following

official recommendations the administration of REPEVAX by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

Syncope (fainting) can occur in association with administration of injectable vaccines, including REPEVAX. Procedures should be in place to prevent falling injury and manage syncopal reactions.

Other considerations

As with any vaccine, a protective immune response may not be elicited in all vaccinees (see section 5.1).

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.

4.5 Interaction with other medicinal products and other forms of interaction

REPEVAX may be administered concomitantly with a dose of inactivated influenza vaccine, based on the results of a clinical trial conducted in persons 60 years of age and older.

REPEVAX may be administered concomitantly with a dose of hepatitis B vaccine.

REPEVAX may be administered concurrently with a dose of recombinant Human Papillomavirus vaccine with no significant interference with antibody response to any of the components of either vaccine. However, a trend of lower anti-HPV GMTs was observed in the concomitant group. The clinical significance of this observation is not known. This is based on the results from a clinical trial in which REPEVAX was administered concomitantly with the first dose of Gardasil (see section 4.8).

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy

The effect of REPEVAX on embryo-foetal development has not been assessed. No teratogenic effect of vaccines containing diphtheria or tetanus toxoids, or inactivated poliovirus has been observed following use in pregnant women.

Available data on exposures during pregnancy do not indicate any adverse foetal or maternal outcomes attributable to REPEVAX. The administration of REPEVAX to a pregnant woman should be on the basis of official recommendations or on an individual assessment of the benefits versus the risks.

Breastfeeding

The effect of administration of REPEVAX during lactation has not been assessed. Nevertheless, as REPEVAX contains toxoids or inactivated antigens, no risk to the breastfed infant should be expected. The

benefits versus the risk of administering REPEVAX to breastfeeding women should be evaluated by the health-care providers.

Fertility

REPEVAX 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. REPEVAX 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 REPEVAX was given to a total of 1,384 persons including 390 children 3 through 6 years of age and 994 adolescent and adults. Most commonly reported reactions following vaccination included local reactions at the injection site (pain, redness and swelling). These signs and symptoms usually were mild in intensity and occurred within 48 hours following vaccination (Adverse Events have been observed within 24 hours and 7 days following vaccination in children 3 through 6 years). They all resolved without sequelae.

There was a trend for higher rates of local and systemic reactions in adolescents than in adults. In both age groups, injection site pain was the most common adverse reaction.
Late-onset local adverse reactions (i.e. a local adverse reaction which had an onset or increase in severity 3 to 14 days post-immunization), such as injection site pain, erythema and swelling occurred in less than 1.2%. Most of the reported adverse reactions occurred within 24 hours after the vaccination.

In a clinical trial of 843 healthy adolescent males and females 11-17 years of age, administration of the first dose of Gardasil concomitantly with REPEVAX showed that there was more injection-site swelling and headache reported following concomitant administration. The differences observed were < 10% and in the 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), including individual cases
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 REPEVAX worldwide. Adverse events in children were collected from clinical trials conducted in 3 to 5 years of age and 5 to 6 years of age. The highest frequency from either study is presented. 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 clinical trials and worldwide post marketing experience

System Organ Class	Frequency	Children 3 through 6 years	Adolescents and Adults
Blood and lymphatic system disorders	Not known	Lymphadenopathy*	
Immune system disorders	Not known	Anaphylactic reactions, such as urticaria, face oedema and dyspnea*	
Nervous system disorders	Very common		Headache
	Common	Headache	
	Not known	Convulsions, Vasovagal Syncope, Guillain Barré syndrome, Facial Palsy, Myelitis, Brachial Neuritis, Transient paresthesia/hypoesthesia of vaccinated limb, Dizziness*	
Gastrointestinal disorders	Very common	Diarrhoea	Nausea
	Common	Vomiting, Nausea	Diarrhoea, Vomiting
	Not known	Abdominal pain	
Skin and subcutaneous system disorders	Common	Rash	
Musculoskeletal and connective tissue disorders	Very common		Arthralgia/joint swelling, Myalgia
	Common	Arthralgia/joint swelling	
	Not known	Pain in vaccinated limb*	
General disorders and administration site conditions	Very common	Fatigue/Asthenia, Fever†	Fatigue/Asthenia, Chills
		Injection site pain, Injection site swelling, Injection site erythema	
	Common	Irritability, Injection site dermatitis, Injection site bruising, Injection site pruritus	Fever†
	Not known	Malaise§, Pallor*, Extensive limb swelling‡, Injection site induration*	

* Post marketing adverse events

† Fever was measured as temperature ≥37.5°C in Children groups and measured as temperature ≥38°C in Adolescents and Adults group

‡ See section c)

§ was observed at a frequency of very common in adolescents and adults, in studies with COVAXiS (Tdap component of REPEVAX; containing the same amounts of diphtheria, tetanus and pertussis antigens)

Description of selected adverse reactions

Extensive limb swelling which may extend from the injection site beyond one or both joints and is frequently associated with erythema, and sometimes with blisters has been reported following administration of REPEVAX. The majority of these reactions appeared within 48 hours of vaccination and spontaneously resolved over an average of 4 days without sequelae.

The risk appears to be dependent on the number of prior doses of d/DTaP vaccine, with a greater risk following the 4th and 5th doses.

Paediatric population

The safety profile of REPEVAX in 390 children 3 to 6 years of age as presented in Table 1 is derived from two clinical studies:

- In a clinical study, 240 children were primed at 3, 5 and 12 months of age with a DTaP vaccine with no additional dose in the second year of life. These children received REPEVAX at 5 to 6 years of age.
- One hundred and fifty children primed at 2, 3, and 4 months of age with a DTwP vaccine (with no additional dose in the second year of life) received REPEVAX at 3 to 5 years of age.

In both studies the rates of most systemic adverse events within 7 to 10 days following vaccination were less than 10%. Only fever (≥37.5°C) and fatigue were reported in more than 10 % of subjects 3 to 6 years of age. In addition, irritability was reported in more than 10% of subjects 3 to 5 years of age. (See Table 1).

Transient severe swelling of the injected upper arm was reported in <1% of children aged 5 to 6 years.

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

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Vaccine against diphtheria, tetanus, pertussis and poliomyelitis
ATC Code: J07CA02

Clinical trials

The immune responses of adults, adolescents and children 3 to 6 years of age one-month after vaccination with REPEVAX are shown in the table below. The use of REPEVAX in children aged 3 to 5 years is based upon studies in which REPEVAX was given as the fourth dose (first booster) of diphtheria, tetanus, pertussis and poliomyelitis vaccines.

Table 2: Immune responses 4 weeks after vaccination

Antigen	Criteria	Adults and Adolescents* (n = 994)	Children 5-6 years old† (n = 240)	Children 3-5 years old‡ (n = 148)
Diphtheria	≥0.1 IU/mL	92.8%	99.4%	100%
Tetanus	≥0.1 IU/mL§	100%	99.5%	100%
Pertussis				
Pertussis Toxoid	≥5 EU/mL**	99.7%	91.2%	99.3%
Filamentous Haemagglutinin	≥5 EU/mL**	99.9%	99.1%	99.3%
Pertactin	≥5 EU/mL**	99.6%	100%	100%
Fimbriae Types 2 and 3	≥5 EU/mL**	99.8%	99.5%	100%
Polio 1	≥1:8 Dilution	99.9%	100%	100%
Polio 2	≥1:8 Dilution	100%	100%	100%
Polio 3	≥1:8 Dilution	100%	100%	100%

* From the age of 10 years onwards
† Primed with DTaP at 3 and 5 months with a booster at 12 months of age
‡ Primed with DTwP at 2, 3 and 4 months of age
§ Measured by ELISA
** EU = ELISA units: Antibody levels of >5 EU/mL were postulated as possible surrogate markers for protection against pertussis by Storsaeter J. et al, Vaccine 1998;16:1907-16.

The safety and immunogenicity of REPEVAX in adults and adolescents was shown to be comparable to that observed with a single booster dose of Td adsorbed or Td Polio adsorbed vaccines containing a similar amount of tetanus and diphtheria toxoids and inactivated poliovirus types 1, 2 and 3.

The lower response to diphtheria toxoid in adults probably reflected the inclusion of some participants with an uncertain or incomplete immunization history.

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 Limited's acellular pertussis infant DTaP formulation confirmed a protective efficacy of 85% against pertussis disease, it is considered that REPEVAX had elicited protective immune responses.

In a subsequent study, robust immune responses were observed following a single dose of REPEVAX in UK children 3.5 to 4.0 years of age previously primed with either an acellular pertussis combination vaccine (DTaP-IPV-Hib) or whole cell pertussis combination vaccine (DTwP//Hib) and OPV.

Antibody persistence

Pivotal studies conducted with COVAXiS (Tdap component of REPEVAX; containing the same amounts of diphtheria, tetanus and pertussis antigens) provide serology follow-up data at 3, 5 and 10 years, in individuals previously immunized with a single booster dose of COVAXiS. Persistence of seroprotection to diphtheria and tetanus, and seropositivity to pertussis is summarised in Table 3.

Table 3: Persistence of Seroprotection/Seropositivity Rates ~~to Diphtheria and Tetanus~~ in Children, Adolescents and Adults at 3-, 5- and 10- years following a dose of COVAXiS (Tdap component of REPEVAX) (PPI Population~~*~~[1])

		Children (4-6 years)[2]	Adolescents (11-17 years)[2]			Adults (18-64 years)[2]		
Time point		**5 years**	**3 years**	**5 years**	**10 years**	**3 years**	**5 years**	**10 years**
Antibody		N=128-150	N=300	N=204-206	N=28-39	N=292	N=237-238	N=120-136
Diphtheria (SN, IU/mL)	≥ 0.1	86.0	97.0	95.1	94.9	81.2	81.1	84.6
	≥ 0.01	100.0	100.0	100.0	100.0	95.2	93.7	99.3
Tetanus (ELISA, IU/mL)	≥ 0.1	97.3	100.0	100.0	100.0	99.0	97.1	100.0
Pertussis (ELISA, IU/mL)								
PT	Sero-positivity[3]	63.3	97.3	85.4	82.1	94.2	89.1	85.8
FHA		97.3	100.0	99.5	100.0	99.3	100.0	100.0
PRN		95.3	99.7	98.5	100.0	98.6	97.1	99.3
FIM		98.7	98.3	99.5	100.0	93.5	99.6	98.5

N = number of subjects with available data; SN: seroneutralisation; ELISA: Enzyme Linked Immunoassay

~~*~~[1]Eligible subjects for whom immunogenicity data was available for at least one antigen at the specified time-point.

[2]Age at which subjects received a dose of COVAXiS

[3]Percentage of subjects with antibodies ≥ 4 EU/mL for PT, FHA and PRN, and ≥ 17 EU/mL for FIM for the 3 year follow-up; ≥ 4 EU/mL for PT, FIM and PRN, and ≥ 3 EU/mL for FHA for the 5-year and 10-year follow-up

~~Seropositivity to pertussis antigens – defined as an antibody concentration ≥ the lower limit of quantitation (LLOQ) – was maintained 5 years later in 63% to 99% of children, and 10 years later in 82% to 100% of adolescents / adults. (The LLOQ was ≥ 4 EU/mL for antibodies to PT, PRN and FIM, and ≥ 3 EU/mL for antibody to FHA.)~~

In serology follow-up studies conducted with REPEVAX, seroprotective antibody levels (≥1:8 dilution) for each poliovirus (type1, 2 and 3) were maintained in 95% to 100% of the children, adolescents and adults at the 5-year follow-up time point, and in 100% of the adolescents at the 10-year follow-up time point.

Immunogenicity following repeat vaccination

The immunogenicity of COVAXiS (Tdap component of REPEVAX) following repeat vaccination 10 years after a previous dose of COVAXiS 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, REPEVAX can be used instead of a dT vaccine or dT-IPV vaccine to boost immunity to pertussis in addition diphtheria, tetanus and polio.

Immunogenicity in naïve subjects

After administration of one dose of REPEVAX 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 IU/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) (see Table 4).

Table 4: Serological immune status (seroprotection/seroresponse rates and GMC/GMT) before vaccination and after each dose of a 3 dose-vaccination schedule including REPEVAX® (Dose 1) followed by 2 doses of REVAXIS® 1 and 6 months later (Dose 2 and 3) in subjects vaccinated according to protocol (FAS)

Antigen	Criteria	Pre-vaccination	Post-dose 1 REPEVAX®	Post-dose 2 REVAXIS®	Post-dose 3 REVAXIS®
		N=330	N=330	N=325	N=316
Diphtheria (SN, IU/mL)	GMC 95%CI	0.059 [0.046; 0.077]	0.813 [0.624; 1.059]	1.373 [1.100; 1.715]	1.489 [1.262; 1.757]
	≥0.1 95%CI	44.5% [39.1; 50.1]	82.4% [77.9; 86.4]	90.5% [86.7; 93.4]	94.6% [91.5; 96.8]
	≥0.01 95%CI	72.4% [67.3; 77.2]	92.7% [89.4; 95.3]	96.0% [93.3; 97.9]	100% [98.8; 100]
Tetanus (ELISA, IU/mL)	GMC 95%CI	0.48 [0.39;0.60]	6.82 [5.92;7.87]	7.60 [6.77;8.52]	5.46 [5.01;5.96]
	≥0.1 95%CI	81.2% [76.6; 85.3]	98.5% [96.5; 99.5]	100% [98.9; 100]	100% [98.8; 100]
	≥0.01 95%CI	92.4% [89.0; 95.0]	99.7% [98.3; 100]	100% [98.9; 100]	100% [98.8; 100]
Poliomyelitis (SN, 1/dil)					
Type 1	GMT 95%CI	162.6 [133.6; 198.0]	2869.0 [2432.9; 3383.4]	2320.2 [2010.9; 2677.0]	1601.9 [1425.4; 1800.3]
	≥8 95%CI	93.3% [90.1; 95.8]	99.4% [97.8; 99.9]	100% [98.9; 100]	100% [98.8; 100]
Type 2	GMT 95%CI	164.5 [137.6;196.8]	3829.7 [3258.5;4501.1]	3256.0 [2818.2;3761.7]	2107.2 [1855.7;2392.8]
	≥8 95%CI	95.5% [92.6; 97.4]	100% [98.9; 100]	100% [98.9; 100]	100% [98.8; 100]
Type 3	GMT 95%CI	69.0 [56.9; 83.6]	5011.4 [4177.4; 6012.0]	3615.6 [3100.5; 4216.4]	2125.8 [1875.5; 2409.6]
	≥8 95%CI	89.1% [85.2; 92.2]	98.8% [96.9; 99.7]	99.7% [98.3; 100]	100% [98.8; 100]
Pertussis (ELISA, EU/mL)					
PT	GMC 95%CI	7.7 [6.8; 8.7]	41.3 [36.7; 46.5]		
	≥5 95%CI	-	96.3% [93.6; 98.1]	-	-
FHA	GMC 95%CI	28.5 [25.5; 31.8]	186.7 [169.6; 205.6]		
	≥5 95%CI	-	100% [98.9; 100]	-	-
PRN	GMC 95%CI	7.7 [6.7; 8.9]	328.6 [273.0; 395.6]		
	≥5 95%CI	-	99.4% [97.8; 99.9]	-	-
FIM2&3	GMC 95%CI	6.1 [5.2; 7.1]	149.6 [123.6; 181.0]		
	≥5 95%CI	-	95.8% [93.0; 97.7]	-	-

GMC: Geometric mean of antibody concentrations; GMT: Geometric mean of antibody titres; CI: Confidence Interval; SN: seroneutralisation; ELISA: Enzyme Linked Immunoassay; dil: dilution

FAS: Full Analysis Set – includes all subjects who received the study vaccine dose and for whom the post-vaccination immunogenicity evaluation was available.

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 doses toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenoxyethanol
Polysorbate 80
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 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 container in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 mL of suspension in pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl or bromobutyl or chlorobutyl elastomer), without attached needle, with a tip-cap (chlorobromobutyl elastomer or synthetic isoprene-bromobutyl elastomer) - pack size of 1, 10 or 20.

0.5 mL of suspension in pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl or bromobutyl or chlorobutyl elastomer), without attached needle, with a tip-cap (chlorobromobutyl elastomer or synthetic isoprene-bromobutyl elastomer) and 1 or 2 separate needles - pack size of 1 or 10.

0.5 mL of suspension in pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl or bromobutyl or chlorobutyl elastomer) with attached needle and needle guard (translucent polypropylene rigid safeshield and polyisoprene) - pack size of 1, 10 or 20.

The stoppers, plunger stoppers and caps for all presentations of REPEVAX are latex-free.

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 discoloration 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 prefilled syringe well to uniformly distribute the suspension before administering the vaccine.

For needle free syringes, the needle should be pushed firmly on to the end of the prefilled 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

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

REPEVAX, suspension for injection in pre-filled syringe

[To be completed nationally]

1. NAME OF THE MEDICINAL PRODUCT

REPEVAX, suspension for injection in pre-filled syringe

Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) Vaccine (adsorbed, reduced antigen(s) content)

[To be completed nationally]

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 mL) contains:
≥ 2 IU (2 Lf) diphtheria toxoid, ≥ 20 IU (5 Lf) tetanus toxoid, 2.5 µg pertussis toxoid, 5 µg filamentous haemagglutinin, 3 µg pertactin, 5 µg fimbriae types 2 and 3, poliomyelitis viruses (inactivated, produced in Vero Cells): 40 D antigen units - type 1, 8 D antigen units - type 2, 32 D antigen units - type 3; adsorbed on 1.5 mg aluminium phosphate (0.33 mg Al).

3. LIST OF EXCIPIENTS

Excipients: Phenoxyethanol, Polysorbate 80, Water for injections

[To be completed nationally]

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in prefilled syringe without attached needle – 0.5 ml – pack of 1.
Suspension for injection in prefilled syringe without attached needle – 0.5 ml – pack of 10.
Suspension for injection in prefilled syringe without attached needle – 0.5 ml – pack of 20.

Suspension for injection in prefilled syringe with one separate needle – 0.5 ml – pack of 1.
Suspension for injection in prefilled syringe with one separate needle – 0.5 ml – pack of 10.

Suspension for injection in prefilled syringe with two separate needles – 0.5 ml – pack of 1.
Suspension for injection in prefilled syringe with two separate needles – 0.5 ml – pack of 10.

Suspension for injection in prefilled syringe with attached needle – 0.5 ml – pack of 1.
Suspension for injection in prefilled syringe with attached needle – 0.5 ml – pack of 10.
Suspension for injection in prefilled syringe with attached needle – 0.5 ml – pack of 20.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Shake well before use.

Intramuscular use.

Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

[Not applicable]

[To be completed nationally]

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the syringe 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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

[Not applicable]

16. INFORMATION IN BRAILLE

[Not applicable]

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

REPEVAX, suspension for injection in pre-filled syringe

[To be completed nationally]

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

REPEVAX, suspension for injection in pre-filled syringe

Diph.-Tet.-ac. Pertussis-IPV

i.m.

[To be completed nationally]

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

[To be completed nationally]

6. OTHER

Sanofi Pasteur MSD

PACKAGE LEAFLET

Package leaflet: Information for the user

REPEVAX

Suspension for injection in pre-filled syringe

Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) Vaccine (adsorbed, reduced antigen(s) content)

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

What is in this leaflet:

1. What REPEVAX is and what it is used for

REPEVAX is a vaccine. Vaccines are used to protect against infectious diseases. They work by causing the body to produce its own protection against the bacteria and viruses that cause the targeted diseases.

This vaccine is used to boost protection against diphtheria, tetanus, pertussis (whooping cough) and poliomyelitis (polio) in children from the age of three years, adolescents and adults following a complete primary course of vaccination.

Limitations in the protection provided

REPEVAX will only prevent these diseases if they are caused by the bacteria or viruses targeted by the vaccine. You or your child could still get similar diseases if they are caused by other bacteria or viruses.

REPEVAX does not contain any live bacteria or viruses and it cannot cause any of the infectious diseases against which it protects.

Remember that no vaccine can provide complete, life long protection in all people who are vaccinated.

2. What you need to know before REPEVAX is given to you or your child

To make sure that REPEVAX is suitable for you or your child, it is important to tell your doctor or nurse if any of the points below apply to you or your child. If there is anything you do not understand, ask your doctor or nurse to explain.

Do not use REPEVAX if you or your child

- Has had an allergic reaction:
  - to diphtheria, tetanus, pertussis or poliomyelitis vaccines
  - to any of the other ingredients (listed in section 6)
  - to any residual component carried over from manufacture (formaldehyde, glutaraldehyde, streptomycin, neomycin, polymyxin B and bovine serum albumin) which may be present in trace amounts.
- has ever had
  - a severe reaction affecting the brain within one week after a previous dose of a whooping cough vaccine
- has an acute illness with or without fever. The vaccination should be delayed until you or your child has recovered. A minor illness without fever is not usually a reason to defer vaccination. Your doctor will determine if you or your child should receive REPEVAX.

Warnings and precautions

Tell your doctor or nurse before vaccination if you or your child has:

- received a booster dose of a vaccine for diphtheria and tetanus within the last 4 weeks. In this case you or your child should not receive REPEVAX and your doctor will decide on the basis of official recommendations when you or your child can receive a further injection.
- ever had a Guillain-Barré syndrome (temporary loss of movement and feeling in all or part of the body) or brachial neuritis (loss of movement, pain and numbness of the arm and the shoulder) following a previous dose of a tetanus containing vaccine. Your doctor will decide if you or your child should receive REPEVAX.
- a progressive illness affecting the brain/nerves or uncontrolled fits. Your doctor will first start treatment and vaccinate when the condition has stabilized.
- a poor or reduced immune system, due to:
  - medication (e.g. steroids, chemotherapy or radiotherapy)
  - HIV infection or AIDS
  - any other illness.

  The vaccine may not protect as well as it protects people whose immune system is healthy. If possible, vaccination should be postponed until the end of such disease or treatment.
- any problems with the blood that causes easy bruising, or bleeding for a long time after minor cuts (for instance due to a blood disorder such as haemophilia or thrombocytopenia or treatment with blood thinning medicines).

Fainting can occur following, or even before, any needle injection. Therefore tell the doctor or nurse if you or your child fainted in connection with a previous injection.

Other medicines or vaccines and REPEVAX

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

As REPEVAX does not contain any live bacteria or viruses it can generally be given at the same time as other vaccines or immunoglobulins, but at a different injection site. Studies have demonstrated that REPEVAX can be used at the same time as any of the following vaccines: an inactivated influenza vaccine, a hepatitis B vaccine, and a recombinant Human Papillomavirus vaccine respectively. Injections of more than one vaccine at the same time will be given in different limbs.

If you or your child is receiving medical treatment affecting your or your child's blood or immune system (such as blood thinning medicines, steroids, chemotherapy), please refer to the section "Warnings and precautions" above.

Pregnancy, breast-feeding and fertility

Tell your doctor or nurse if you or your child is pregnant or breast-feeding, think you or your child might be pregnant or planning to have a baby. Your doctor or nurse can advise you whether or not vaccination should be delayed.

Driving and using machines:

It has not been studied if the vaccine affects the ability to drive or use machines. The vaccine has no or negligible influence on the ability to drive and use machines.

3. How and when REPEVAX is given

When you or your child will be given the vaccine

Vaccination history

Your doctor will determine if REPEVAX is suitable for you or your child, depending on:
- what vaccines have been given to you or your child in the past
- how many doses of similar vaccines have been given to you or your child in the past
- when the last dose of a similar vaccine was given to you or your child

Your doctor will decide how long you have to wait between vaccinations.

Dosage and method of administration

Who will give you REPEVAX?

REPEVAX should be given by healthcare professionals who have been trained in the use of vaccines and at a clinic or surgery that is equipped to deal with any rare severe allergic reaction to the vaccine.

Dosage

All age groups for whom REPEVAX is indicated will receive one injection (half a millilitre).

In case you or your child experience an injury which requires preventative action for tetanus disease, your doctor may decide to give REPEVAX with or without tetanus immunoglobulin.

REPEVAX can be used for repeat vaccination. Your doctor will give you advice on repeat vaccination.

Use in children and adolescents

REPEVAX should not be used in children under 3 years of age.

Children from the age of 3 years onwards and adolescents should receive the same dosage as adults.

Method of administration

Your doctor or nurse will give you the vaccine into a muscle in the upper outer part of the arm (deltoid muscle).

Your doctor or nurse will **not** give you the vaccine into a blood vessel, into the buttocks or under the skin. In case of blood clotting disorders they may decide to inject under the skin, although this might result in more local side effects, including a small lump under the skin.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, REPEVAX can cause side effects, although not everybody gets them.

Serious allergic reactions

If any of these symptoms occur after leaving the place where you or your child received the injection, you must consult a doctor IMMEDIATELY.

- difficulty in breathing
- blueness of the tongue or lips
- a rash
- swelling of the face or throat
- low blood pressure causing dizziness or collapse

When these signs or symptoms occur they usually develop very quickly after the injection is given and while you or your child is still in the clinic or doctor's surgery. Serious allergic reactions are a very rare possibility (may affect up to 1 in 10,000 people) after receiving any vaccine.

Other side effects

The following side effects were observed during clinical studies carried out in specific age groups.

In children 3 to 6 years of age

Very common (may affect more than 1 in 10 people):

- pain
- swelling and redness in the area where the vaccine was injected

- tiredness
- fever (a temperature at or above 37.5°C)
- diarrhoea.

Common (may affect up to 1 in 10 people):
- bruising
- itching and skin inflammation in the area where the vaccine was injected
- headache
- nausea
- vomiting
- rashes
- aching or swollen joints
- irritability.

In adolescents (11 years of age and older) and adults

Teenagers are a little more likely than adults to have side effects. Most side effects occur within the first 3 days after vaccination.

Very common (may affect more than 1 in 10 people):
- pain
- swelling and redness in the area where the vaccine was injected
- headache
- nausea
- aching or swollen joints
- aching muscles
- weakness
- chills.

Common (may affect up to 1 in 10 people):
- vomiting
- diarrhoea
- fever (a temperature at or above 38.0°C).

The following additional adverse events have been reported in the various recommended age groups during the commercial use of REPEVAX. The frequency of these adverse events cannot be precisely calculated, as it would be based on voluntary reporting in relation to the estimated number of vaccinated persons.

Lymph node disorder, allergic/serious allergic reactions, fits (convulsions), fainting, paralysis of part or all the body (Guillain-Barré syndrome), facial paralysis, inflammation of the spinal cord, inflammation of the nerves in the arm (brachial neuritis), temporary loss or alteration of sensation in vaccinated limb, dizziness, pain in vaccinated limb, extensive limb swelling (frequently associated with redness, and sometimes with blisters), feeling ill, pale skin, a hard lump (induration) in the area where vaccine was injected, abdominal pain.

Reporting side effects

If you or your child get any side effects, talk to your doctor, pharmacist or nurse. 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 REPEVAX

Keep out of the sight and reach of children.

REPEVAX must not be used after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (at 2°C to 8°C). Do not freeze. Discard the vaccine if it has been frozen.

Keep the container 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 protect the environment.

6. Contents of the pack and other information

What REPEVAX contains

The active substances in each dose (0.5 mL) of vaccine are:

Diphtheria Toxoid	not less than 2 International Units (2 Lf)
Tetanus Toxoid	not less than 20 International Units (5 Lf)
Pertussis Antigens:	
Pertussis Toxoid	2.5 micrograms
Filamentous Haemagglutinin	5 micrograms
Pertactin	3 micrograms
Fimbriae Types 2 and 3	5 micrograms
Inactivated Poliomyelitis Virus (produced in Vero cells):	
Type 1	40 D antigen units
Type 2	8 D antigen units
Type 3	32 D antigen units
Adsorbed on aluminium phosphate	1.5 mg (0.33 mg aluminium)

The other ingredients are: phenoxyethanol, polysorbate 80, water for injections

What REPEVAX looks like and contents of the pack

REPEVAX is presented as a suspension for injection in pre-filled syringes (0.5 mL):

- without attached needle – pack size of 1, 10 or 20
- with 1 or 2 separate needles – pack size of 1 or 10
- with attached needle – pack size of 1, 10 or 20

Not all pack sizes may be marketed.

The normal appearance of the vaccine is a uniform cloudy white suspension, which may sediment during storage. After shaking well it is a uniformly white liquid.

Marketing Authorisation Holder and Manufacturer

[TO BE COMPLETED LOCALLY]

The manufacturer responsible for batch release is:
Sanofi Pasteur
2, avenue pont Pasteur
69007 Lyon
France

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Norway, Portugal, United Kingdom:	REPEVAX
Belgium, Luxembourg, Netherlands:	TRIAXIS POLIO

This leaflet was last revised in {month YYYY}.

The following information is intended for healthcare professionals only:

Instructions for use

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

Parenteral products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. If these conditions exist, the product should not be administered.

For needle-free syringes, the needle should be pushed firmly onto the end of the pre-filled syringe and rotated through 90 degrees.

Needles should not be recapped.