

## 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.

Passive protection against pertussis in early infancy following maternal immunization during pregnancy (see sections 4.2, 4.4, 4.6 and 5.1).

REPEVAX 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 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).

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

REPEVAX may be administered to pregnant women during the second or third trimester to provide passive protection of infants against pertussis (see sections 4.1, 4.4, 4.6 and 5.1).

#### 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.

#### **4.8 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 occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid, including REPEVAX 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 following, or even before, 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 vaccines (see section 5.1).

Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born to women vaccinated with REPEVAX during pregnancy. The clinical relevance of this observation is unknown.

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.

### **4.9 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

No teratogenic effect of vaccines containing diphtheria or tetanus toxoids, or inactivated poliovirus has been observed following use in pregnant women.

Safety data from 4 randomized controlled trials (310 pregnancy outcomes), 2 prospective observational studies (2670 pregnancy outcomes), 4 retrospective observational studies (81,701 pregnancy outcomes), and from passive surveillance of women who received REPEVAX or ADACEL (Tdap component of REPEVAX; containing the same amounts of diphtheria, tetanus and pertussis antigens) during the 2<sup>nd</sup> or 3<sup>rd</sup> 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 REPEVAX during any trimester would harm the fetus. The benefits versus the risks of administering REPEVAX during pregnancy should be evaluated.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development.

Limited clinical data have shown there is interference with the immune response to other antigens (i.e. diphtheria, tetanus, polio, pneumococcal, meningococcal) in infants born to women vaccinated with REPEVAX during pregnancy. However, in most of the cases, the antibody concentrations remain above the thresholds established as protective. The clinical relevance of this observation is unknown.

### 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.

#### 4.10 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	( $\geq 1/10$ )
Common	( $\geq 1/100$ to $< 1/10$ )
Uncommon	( $\geq 1/1,000$ to $\square 1/100$ )
Rare	( $\square 1/10,000$ to $\square 1/1,000$ )
Very rare	( $\square 1/10,000$ ), 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  $\geq 37.5^{\circ}\text{C}$  in Children groups and measured as temperature  $\geq 38^{\circ}\text{C}$  in Adolescents and Adults group

‡ See section c)

§ was observed at a frequency of very common in adolescents and adults, in studies with ADACEL (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 4<sup>th</sup> and 5<sup>th</sup> 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 ( $\geq 37.5^{\circ}\text{C}$ ) 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 Medicines and Healthcare products Regulatory Agency (MHRA), Yellow Card Scheme at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

### **4.11 4.9 Overdose**

Not-applicable.

## **5 PHARMACOLOGICAL PROPERTIES**

### **4.12 5.1 Pharmacodynamic properties**

Pharmaco-therapeutic 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)
<b>Diphtheria</b>	□0.1 IU/mL	92.8%	99.4%	100%
<b>Tetanus</b>	□0.1 IU/mL§	100%	99.5%	100%
<b>Pertussis</b>				
<b>Pertussis Toxoid</b>	□5 EU/mL**	99.7%	91.2%	99.3%
<b>Filamentous</b>	□5 EU/mL**	99.9%	99.1%	99.3%
<b>Haemagglutinin</b>	□5 EU/mL**	99.6%	100%	100%
<b>Pertactin</b>	□5 EU/mL**	99.8%	99.5%	100%
<b>Fimbriae Types 2 and 3</b>				
<b>Polio 1</b>	□1:8 Dilution	99.9%	100%	100%
<b>Polio 2</b>	□1:8 Dilution	100%	100%	100%
<b>Polio 3</b>	□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<sup>1</sup>)**

		Children (4-6 years) <sup>2</sup>	Adolescents (11-17 years) <sup>2</sup>			Adults (18-64 years) <sup>2</sup>		
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)	Sero-positivity <sup>3</sup>							
PT		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

<sup>1</sup>Eligible subjects for whom immunogenicity data was available for at least one antigen at the specified time-point.

<sup>2</sup>Age at which subjects received a dose of COVAXiS

<sup>3</sup>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

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  $\geq 98.5\%$  of study participants achieved seroprotective antibody levels ( $\geq 0.1$  IU/ml) for diphtheria and tetanus, and  $\geq 84\%$  achieved booster responses to the pertussis antigens. (A pertussis booster response was defined as a post-vaccination antibody concentration  $\geq 4$  times the LLOQ if the pre-vaccination level was  $< \text{LLOQ}$ ;  $\geq 4$  times the pre-vaccination level if that was  $\geq \text{LLOQ}$  but  $< 4$  times LLOQ; or  $\geq 2$  times the pre-vaccination level if that was  $\geq 4$  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  $\geq 40$  years of age that had not received any diphtheria- and tetanus-containing vaccine in the past 20 years:

- $\geq 95.8\%$  of adults were seropositive ( $\geq 5$  IU/mL) for antibodies to all vaccine-containing pertussis antigens,
- 82.4% and 92.7% were seroprotected against diphtheria at a threshold  $\geq 0.1$  and  $\geq 0.01$  IU/mL, respectively,
- 98.5% and 99.7% were seroprotected against tetanus at a threshold  $\geq 0.1$  and  $\geq 0.01$  IU/mL, respectively,
- and  $\geq 98.8\%$  were seroprotected against polio (types 1, 2 and 3) at a threshold  $\geq 1:8$  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% ( $\geq 0.1$  and  $\geq 0.01$  IU/mL, respectively), against tetanus 100% ( $\geq 0.1$  IU/mL), and against polio (types 1, 2 and 3) 100% ( $\geq 1:8$  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

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

#### **4.13 5.2 Pharmacokinetic properties**

Evaluation of pharmacokinetic properties is not required for vaccines.

#### **4.14 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**

#### **4.15 6.1 List of excipients**

Phenoxyethanol  
Polysorbate 80  
Water for injections

#### **4.16 6.2 Incompatibilities**

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

#### **4.17 6.3 Shelf life**

3 years.

#### **4.18 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.

#### **4.19 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.

#### **4.20 6.6 Special precautions for disposal**

##### 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**

Sanofi Pasteur Europe  
14 Espace Henry Vallée  
69007 Lyon  
FRANCE

Distributed in the UK by:

Sanofi  
One Onslow Street  
Guildford  
Surrey  
GU1 4YS

## **8     MARKETING AUTHORISATION NUMBER(S)**

PL 46602/0005

## **9     DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

15/12/2006

## **10    DATE OF REVISION OF THE TEXT**

20/02/2019