PRODUCT MONOGRAPH

ADACEL®-POLIO

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine

Suspension for injection

(For active immunization against Tetanus, Diphtheria, Pertussis and Poliomyelitis)

ATC Code: J07CA02

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Toronto, Ontario, Canada

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration

Intramuscular injection

Dosage Form / Strength

Suspension for injection

Each 0.5 mL dose is formulated to contain:

Active Ingredients

Tetanus toxoid, reduced diphtheria toxoid, acellular pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA), pertactin (PRN), fimbriae types 2 and 3 (FIM)], and inactivated poliomyelitis vaccine [type 1 (Mahoney), type 2 (MEF-1) and type 3 (Saukett)].

Clinically Relevant Non-medicinal Ingredients

Excipients: Aluminum phosphate (adjuvant), 2-phenoxyethanol, polysorbate 80.

Manufacturing process residuals: Bovine serum albumin, formaldehyde, glutaraldehyde, streptomycin, neomycin and polymyxin B are present in trace amounts.

For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING section.

DESCRIPTION

ADACEL®-POLIO [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine] is a sterile, uniform, cloudy, white suspension of tetanus and diphtheria toxoids and acellular pertussis vaccine adsorbed separately on aluminum phosphate, combined with inactivated poliomyelitis vaccine (vero cell origin) types 1, 2 and 3, and suspended in water for injection. The acellular pertussis vaccine is composed of five purified pertussis antigens (PT, FHA, PRN and FIM).

INDICATIONS AND CLINICAL USE

ADACEL®-POLIO is indicated for:

Active booster immunization for the prevention of tetanus, diphtheria, pertussis (whooping cough) and poliomyelitis in persons 4 years of age and above.

Vaccination during pregnancy for passive immunization against pertussis disease in young infants. (See DOSAGE AND ADMINISTRATION, Pregnant Women, and Immunogenicity in Pregnancy.)

In children 4 to 6 years of age, ADACEL®-POLIO may be considered as an alternative for the fifth dose of diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine (DTaP-IPV).

Persons who have had tetanus, diphtheria or pertussis should still be immunized since these clinical infections do not always confer immunity. (1) Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against tetanus, diphtheria and pertussis according to standard schedules. (1)

ADACEL®-POLIO is not to be used for the treatment of disease caused by *Bordetella pertussis, Corynebacterium diphtheriae, Clostridium tetani* or poliomyelitis infections.

Pediatrics

ADACEL®-POLIO has been used in clinical studies in children as young as 3 years of age. (2)

Geriatrics

ADACEL®-POLIO has been used in clinical studies in persons up to 91 years of age. (3).

Tetanus Prophylaxis in Wound Management

The need for active immunization with a tetanus toxoid-containing preparation (such as Td Adsorbed vaccine, ADACEL® or ADACEL®-POLIO) with or without passive immunization with Tetanus Immune Globulin, depends on both the condition of the wound and the patient's vaccination history. (1) (See DOSAGE AND ADMINISTRATION.)

CONTRAINDICATIONS

Hypersensitivity

Known systemic hypersensitivity reaction to any component of ADACEL®-POLIO or a life-threatening reaction after previous administration of the vaccine or a vaccine containing one or more of the same components are contraindications to vaccination. (See SUMMARY PRODUCT INFORMATION.) Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such persons may be referred to an allergist for evaluation if further immunizations are considered. (1)

Acute Neurological Disorders

Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of a previous dose of a pertussis-containing vaccine that is not attributable to another identifiable cause is a contraindication to administration of any pertussis-containing vaccine, (4) including ADACEL®-POLIO.

WARNINGS AND PRECAUTIONS

General

Before administration of ADACEL®-POLIO, health-care providers should inform the recipient or parent or guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the patient to be immunized, review the patient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the patient/guardian before immunization.

It is extremely important that the recipient, parent or guardian be questioned concerning any signs or symptoms of an adverse reaction after a previous dose of vaccine. (See CONTRAINDICATIONS and ADVERSE REACTIONS.)

The rates and severity of adverse events in recipients of tetanus toxoid are influenced by the number of prior doses and level of pre-existing antitoxins. (1)

Syncope (fainting) has been reported following vaccination with ADACEL®-POLIO. Procedures should be in place to prevent falling injury and manage syncopal reactions.

As with any vaccine, ADACEL®-POLIO may not protect 100% of vaccinated persons.

Administration Route Related Precautions: Do not administer ADACEL®-POLIO by intravascular injection: ensure that the needle does not penetrate a blood vessel.

Intradermal or subcutaneous routes of administration are not to be utilized.

ADACEL®-POLIO should not be administered into the buttocks.

Febrile and Acute Disease: Vaccination should be postponed in cases of an acute or febrile disease. (4) However, a disease with low-grade fever should not usually be a reason to postpone vaccination.

Hematologic

Because any intramuscular injection can cause an injection site hematoma in persons with any bleeding disorders, such as haemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with ADACEL®-POLIO should not be administered to such persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

Immune

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Hypersensitivity reactions may occur following the use of ADACEL®-POLIO even in persons with no prior history of hypersensitivity to the product components.

As with all other products, epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. (1) Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management. (1) For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website.

Immunocompromised persons (whether from disease or treatment) may not achieve the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. (1) Nevertheless, vaccination of persons with chronic immunodeficiency, such as HIV infection, is recommended even if the immune response might be limited. (4)

Neurologic

ADACEL®-POLIO should not be administered to individuals with progressive neurological disorder, uncontrolled epilepsy, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized. (5) (6)

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give ADACEL®-POLIO or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks. (4) (7)

Special Populations

Pregnant Women

ADACEL®-POLIO and ADACEL® vaccination during pregnancy for passive immunization against pertussis in early infancy has been evaluated in published studies. Safety data from 4 randomized controlled trials (outcomes for 310 pregnancies) (8) (9) (10) (11) and 6 observational studies (outcomes for 125,356 pregnancies) (12) (13) (14) (15) (16) (17) of women who received ADACEL®-POLIO or ADACEL® during pregnancy (the majority in the 3rd trimester) have shown no vaccine-related adverse effect on pregnancy or on the health of the fetus/newborn child. These studies support the administration of ADACEL®-POLIO during pregnancy. (See CLINICAL TRIALS: Immunogenicity in Pregnancy).

Nursing Women

The effect of administration of ADACEL®-POLIO during lactation has not been assessed. As ADACEL®-POLIO is inactivated, any risk to the mother or the infant is improbable. However, the effect on breast-fed infants of the administration of ADACEL®-POLIO to their mothers has not been studied. The risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.

The safety of ADACEL®-POLIO has been evaluated in a total of 1,636 participants who received a single dose of ADACEL®-POLIO in 7 clinical trials (644 children 3 to 7 years of age, 992 adolescents and adults 11 to 60 years of age). (2) (18) (19) (20) (21) (22) (23) (24) (25) Pain was the most common injection site reaction in all age groups. Most injection site reactions occurred within 3 days following vaccination. The most frequent systemic reaction was headache in adolescents and adults and tiredness in children. These reactions were usually transient and of mild to moderate intensity.

Table 1 presents the frequencies of the solicited injection site and systemic adverse events reported in 3 UK clinical trials in which children previously primed with 3 doses of PEDIACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine and Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate)] or a whole-cell pertussis combination vaccine, received a pre-school booster dose of ADACEL®-POLIO at 3 to 5 years of age. In addition, adverse events of irritability (7.3%), injection site bruising (3.3%), injection site pruritus (2.7%) and dermatitis (1.3%) were reported within 7 days of vaccination in two of these studies. (2) (18) (19)

In clinical trials in children ADACEL®-POLIO showed a comparable safety profile to that of ADACEL® [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed]. Therefore, the safety of ADACEL®-POLIO, in particular for use as a 4 to 6 years-old booster dose is further supported by a study conducted with ADACEL® in 298 children. (26) (27)

The frequency of the solicited injection site and systemic adverse events reported in a Canadian clinical trial in adolescents and adults are also presented in Table 1.

Table 1: Frequency (%) of Solicited Reactions Observed in Clinical Trials in Children, Adolescents and Adults, Following a Single Booster Dose of ADACEL®-POLIO (2) (18) (20) (23) (24)

Solicited Reactions	Children 3 to 5 Years of Age* (N = 307)	Adolescents 12 to 18 Years of Age† (N = 350)	Adults 19 to 60 Years of Age† (N = 366)
Injection Site Reactions			
Pain	46.5 – 71.3	88.3	86.3
Swelling	20.4 – 34.0	21.2	16.7
Redness	35.7 – 48.7	17.5	23.0
Systemic Reactions			
Fever‡	7.0 – 12.7	14.2	2.7
Headache	N.S.	41.3	37.7
Nausea	N.S.	17.5	14.5
Diarrhea	7.6 – 10.0	5.4	15.8
Vomiting	2.5 – 6.7	3.2	2.5
Body Ache	N.S.	26.1	24.0
Sore or Swollen Joints	1.3	11.2	11.2
Tiredness	35.7 – 52.7	37.2	29.8
Chills	N.S.	17.5	11.2
Rash	7.0 – 8.7	N.S.	N.S.

* Adverse reactions reported within 7 days of vaccination. Range of frequencies across 3 UK studies.

† Adverse reactions reported within 14 days of vaccination.

‡ Fever was defined as temperature ≥37.5°C in children, ≥38.0°C in adolescents and adults. Fever was solicited up to 7 days post-vaccination in children, up to 72 hours in adolescents and adults.

N.S.: Not solicited.

Post-market Adverse Drug Reactions

The following additional adverse events have been spontaneously reported during the post-marketing use of ADACEL®-POLIO. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Blood and Lymphatic Disorders

Lymphadenopathy

Immune System Disorders

Anaphylactic reactions, such as urticaria, face edema and dyspnea

Nervous System Disorders

Convulsions, vasovagal syncope, Guillain-Barré syndrome, facial palsy, myelitis, brachial neuritis, transient paresthesia/hypoesthesia of vaccinated limb, dizziness

Musculoskeletal and Connective Tissue Disorders

Pain in vaccinated limb

Gastro intestinal disorders

Abdominal pain

General Disorders and Administration Site Conditions

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 ADACEL®-POLIO. 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.

Malaise, pallor, injection site induration

DRUG INTERACTIONS

Vaccine-Drug Interactions

Immunosuppressive treatments may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS.)

Concomitant Vaccine Administration

ADACEL®-POLIO may be administered concurrently with a dose of hepatitis B vaccine. (25) Supportive data from a study conducted with ADACEL® suggests that ADACEL®-POLIO may be used concomitantly with trivalent influenza vaccine. (28) ADACEL®-POLIO has been safely administered concomitantly with measles-mumps-rubella vaccine in non-controlled clinical studies in children 3 to 5 years of age. (19) Data are not available on concomitant use of ADACEL®-POLIO and varicella vaccine.

Administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately. (1) Vaccines administered concomitantly should be given using separate syringes at separate sites. (1) Simultaneous administration is suggested, particularly when there is concern that a person may not return for subsequent vaccination.

ADACEL®-POLIO should not be mixed in the same syringe with other parenterals.

DOSAGE AND ADMINISTRATION

Recommended Dose

ADACEL®-POLIO should be administered as a single injection of 1 dose (0.5 mL) by the intramuscular route. The preferred site is the deltoid muscle.

Fractional doses (doses <0.5 mL) should not be given. The effect of fractional doses on safety and efficacy has not been determined.

If ADACEL®-POLIO is administered to a pregnant woman, it should ideally be done during the third trimester of pregnancy or according to recommendations from the National Advisory Committee on Immunization (NACI) (29).

Health-care professionals should also refer to the National Advisory Committee on Immunization (NACI) recommendations for tetanus prophylaxis in routine wound management shown in Table 2.

Table 2: NACI Recommended Use of Immunizing Agents in Wound Management (1)

	Clean, minor wounds		All other wounds	
History of Tetanus Immunization	**Td***	**TIG† (Human)**	**Td***	**TIG† (Human)**
Uncertain or <3 doses of an immunization series‡	Yes	No	Yes	Yes
≥3 doses received in an immunization series‡	No§	No	No**	No††

* Adult-type tetanus and diphtheria toxoid.

† Tetanus immune globulin, given at a separate site from the Td.

‡ Primary immunization is at least 3 doses at age appropriate intervals.

§ Yes, if >10 years since last booster.

** Yes, if >5 years since last booster.

†† Yes, if persons are known to have a significant humoral immune deficiency state (e.g., HIV, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Persons who have completed primary immunization against tetanus and who sustain wounds that are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (e.g., wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years. (1)

For adults who have not previously received a dose of acellular pertussis vaccine, a single tetanus-diphtheria (Td) booster dose should be replaced by a combined tetanus-diphtheria-acellular pertussis vaccine (Tdap). (1)

Administration

Inspect for extraneous particulate matter and/or discolouration before use. (See DESCRIPTION.) If these conditions exist, the product should be discarded.

Shake the vial or syringe well until a uniform, cloudy, suspension results. When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual patient to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines.

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. Administer the total volume of 0.5 mL **intramuscularly** (IM). The preferred site of injection is the deltoid muscle.

Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

Overdosage

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Tetanus and Diphtheria: Protection against disease attributable to *C. tetani* is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assay, is considered the minimum protective level. (4) (30) One month after a single booster dose of ADACEL®-POLIO, seroprotective tetanus antitoxin levels were achieved in 100% of adults and adolescents, and 100% of children 3.5 to 4.1 years of age.

Protection against disease attributable to *C. diphtheriae* is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective for diphtheria. (31) 83.8% of adults, 97.1% of adolescents and at least 97.6% of children 3.5 to 4.1 years of age achieved a seroprotective antitoxin level of 0.1 IU/mL against diphtheria. (20) (23) (24)

Pertussis: Pertussis (whooping cough) is a respiratory disease caused by *B. pertussis*. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined. The mechanism

of protection from *B. pertussis* disease is not well understood. However, in a clinical trial in Sweden (Sweden I Efficacy Trial) using TRIPACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed], the same pertussis components as present in ADACEL®-POLIO (i.e., PT, FHA, PRN and FIM) have been shown to prevent pertussis in infants with a protective efficacy of 85.2% using the World Health Organization (WHO) case definition (≥21 consecutive days of paroxysmal cough with culture or serologic confirmation or epidemiological link to a confirmed case). In the same study, the protective efficacy against mild disease was 77.9%. (32)

Minimum serum antibody levels to specific pertussis vaccine components that confer protection against the development of clinical pertussis have not been established. Nevertheless, a number of studies have demonstrated a correlation between the presence of serum antibody responses to pertussis vaccine components and protection against clinical disease. The acellular pertussis formulations of ADACEL®-POLIO and ADACEL® compared to TRIPACEL® differ only in the amount of PT (2.5 µg in ADACEL®-POLIO and ADACEL® versus 10 µg in TRIPACEL®) and the amount of diphtheria toxoid (2 Lf in ADACEL®-POLIO and ADACEL® versus 15 Lf in TRIPACEL®). Furthermore, the IPV antigens present in ADACEL®- POLIO are not included in the formulation of TRIPACEL®.

The efficacy of ADACEL®-POLIO is based on a comparison of pertussis antibody levels achieved in ADACEL®-POLIO recipients with those measured with TRIPACEL® in the Sweden I Efficacy Trial. (33) In particular, ADACEL®-POLIO was demonstrated, both in children and in adolescents and adults, to elicit antibody levels against pertussis antigens, which were consistently higher than those found to be protective in the Sweden I Efficacy Trial. (20) (23) (24) In addition, in a clinical study with ADACEL® among Canadian 4 to 6 year-olds, it was demonstrated that, in the context of the Canadian immunization schedule, the pertussis antigens formulation of ADACEL®-POLIO also elicited serum antibody levels that were consistently higher than those measured in the Sweden I Efficacy Trial. (26) (27)

Poliomyelitis: Inactivated poliomyelitis vaccine induces the production of detectable levels of neutralizing antibodies against each type of poliovirus. The detection of type-specific neutralizing antibodies has been correlated with protection. (34) In all clinical trials, 99.0% to 100% of vaccinees in all age groups achieved seroprotective levels (≥1:8 dilution) of anti-poliovirus antibodies for all three types. (2) (18) (19) (20) (23) (24)

STORAGE AND STABILITY

Store at 2° to 8°C (35° to 46°F). **Do not freeze**. Discard product if exposed to freezing (≤ 0°C). ADACEL®-POLIO has been shown to remain stable at temperatures above 8°C and up to 25°C, for a maximum of 3 days (72 hours). These data are not recommendations for shipping or storage, but may guide decision for use in case of temporary temperature excursions.

Do not use after expiration date.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

ADACEL®-POLIO is supplied as a sterile, uniform, cloudy, white suspension in a vial or prefilled syringe.

Composition

Each dose (0.5 mL) is formulated to contain:

Active Ingredients

Tetanus Toxoid	5 Lf
Diphtheria Toxoid	2 Lf
Acellular Pertussis:	
Pertussis Toxoid (PT)	2.5 µg
Filamentous Haemagglutinin (FHA)	5 µg
Pertactin (PRN)	3 µg
Fimbriae Types 2 and 3 (FIM)	5 µg
Inactivated Poliomyelitis Vaccine:	
Type 1 (Mahoney)	40 D-antigen units*
Type 2 (MEF-1)	8 D-antigen units*
Type 3 (Saukett)	32 D-antigen units*

* or the equivalent antigen quantity, determined by suitable immunochemical method

Other Ingredients

Excipients:

Aluminum Phosphate (adjuvant)	1.5 mg
2-phenoxyethanol	0.6% v/v
Polysorbate 80	<5 µg
Water for Injection	q.s. 0.5 mL

Manufacturing Process Residuals:

Bovine serum albumin, formaldehyde, glutaraldehyde, streptomycin, neomycin and polymyxin B are present in trace amounts.

Packaging

ADACEL®-POLIO is supplied in 0.5 mL single dose vials or prefilled syringes.

The vials and syringes are made of USP Type 1 glass. The container closure system for all presentations of ADACEL®-POLIO is free of latex (natural rubber).

ADACEL®-POLIO may be available in packages of:

1 single dose vial

5 single dose vials

10 single dose vials

1 single dose syringe without attached needle and with or without 2 separate needles (1 x 25G x 16 mm, and 1 x 23G x 25 mm)

10 single dose syringes without attached needles and with or without 2 separate needles (5 x 25G x 16 mm, and 5 x 23G x 25 mm)

20 single dose syringes without attached needles

Vaccine Information Service: 1-888-621-1146.

Full product monograph available on request or visit us at www.sanofi.ca

Product information as of June 2020.

Manufactured and distributed by:

Sanofi Pasteur Limited
Toronto, Ontario, Canada

Fabricated by:
Sanofi Pasteur SA
Lyon, France

R6-0620 Canada

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine (Tdap-IPV)

Product Characteristics

ADACEL®-POLIO is a sterile, uniform, cloudy, white suspension of tetanus and diphtheria toxoids and acellular pertussis vaccine adsorbed separately on aluminum phosphate and combined with inactivated poliomyelitis vaccine (vero cell origin) types 1, 2 and 3, and suspended in water for injection. Acellular pertussis vaccine is composed of five purified pertussis antigens (PT, FHA, PRN and FIM).

C. diphtheriae is grown in modified Mueller's growth medium. (46) After purification by ammonium sulphate fractionation, diphtheria toxin is detoxified with formaldehyde and diafiltered. *C. tetani* is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (47) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulphate fractionation and diafiltration. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate.

The 5 acellular pertussis vaccine components are obtained from *B. pertussis* cultures grown in Stainer-Scholte medium (48) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. Pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) are isolated separately from the supernatant culture medium. Fimbriae types 2 and 3 (FIM) are extracted from the bacterial cells. These antigens are purified by sequential filtration, salt-precipitation, ultrafiltration and chromatography. PT is detoxified with glutaraldehyde and FHA is treated with formaldehyde and the residual aldehydes are removed by diafiltration. The individual antigens are adsorbed onto aluminum phosphate.

The adsorbed diphtheria, tetanus and acellular pertussis components are combined with aluminum phosphate (as adjuvant), 2-phenoxyethanol and water for injection, to formulate the Tdap concentrate.

Inactivated poliomyelitis vaccine (IPV) is a highly purified, inactivated poliovirus vaccine including three types of poliovirus: Type 1 (Mahoney), Type 2 (MEF-1) and Type 3 (Saukett). Each of the three strains of poliovirus is individually grown in vero cells, which are cultivated on microcarriers. The single virus harvest is concentrated and purified, then inactivated with formaldehyde to produce the type 1, 2 or 3 monovalent. Monovalents of each type are then combined in appropriate quantities to produce a trivalent concentrate.

The Tdap concentrate is combined with IPV, aluminum phosphate (as adjuvant), 2-phenoxyethanol and water for injection containing polysorbate 80.

When tested in guinea pigs, the tetanus component induces at least 20 IU and the diphtheria component induces at least 2 IU per single dose. The potency of the acellular pertussis vaccine components is verified by the antibody response of immunized mice to PT, FHA, PRN and FIM

as measured by enzyme-linked immunosorbent assay. The content in IPV components is verified by ELISA determination of D antigen content for each of the 3 types of IPV.

CLINICAL TRIALS

Four clinical trials, conducted in Canada and the United Kingdom, provide the clinical basis for the licensure of ADACEL®-POLIO in Canada. (See Table 3) In addition, clinical trial Td508, conducted with ADACEL® in Canadian children 4 to 6 years of age, further supports the safety and immunogenicity of ADACEL®-POLIO in the context of the Canadian immunization schedule.

Study demographics and trial design

Table 3: Summary of Demographics and Study Design of the Trials with ADACEL®-POLIO

Study	Study Design	Dosage and Route of Administration	ADACEL®-POLIO Recipients (N = ITT*)	Mean Age (Range)	Gender
U01-A5I-302 Part III (20)	Randomized, open-label trial.	0.5 mL I.M.	Children (N = 157)	3.7 years (3.5-4.1)	Males (N = 85) Females (N = 72)
U01-Td5I-303 (18) (19)	Randomized, controlled, open-label, comparative trial with ADACEL® used as control.	0.5 mL I.M.	Children (N = 100)	4.0 years (3.5-5.0)	Males (N = 47) Females (N = 53)
U02-Td5I-402 (2) (19)	Single-arm, open-label trial.	0.5 mL I.M.	Children (N = 50)	3.2 years (3.0-3.4)	Males (N = 27) Females (N = 23)
TD9707 (23) (24)	Randomized, controlled, single-blind, multicentre comparative trial with Td-IPV and ADACEL® used as controls in adolescents and adults, respectively.	0.5 mL I.M.	Adolescents (N = 350)	14.0 years (12.0-18.97)	Males (N = 177) Females (N = 173)
			Adults (N = 366)	38.2 years (19.4-65.2)	Males (N = 111) Females (N = 255)

* "Intent-to-Treat" (ITT) population includes all randomized participants who received ADACEL®-POLIO and were included in safety analyses.

Table 4: Summary of Demographics and Study Design of Supportive Trial with ADACEL®

Study	Study Design	Dosage and Route of Administration	Study Population (N = ITT)*	Mean Age (Range)	Gender
Td508 **(26) (27)**	Randomized, controlled, modified double-blind, multicentre comparative trial with DTaP-IPV used as control.	0.5 mL I.M.	Children (N = 298)	4.6 years (4.0 - 6.6)	Males (N = 144) Females (N = 154)

* "Intent-to-Treat" (ITT) population includes all randomized participants who received ADACEL® and were included in safety analyses.

Safety of ADACEL®-POLIO in Children 3 Years of Age and Above

Data from three studies conducted in the United Kingdom in children 3.0 to 5.0 years of age, further supported by a study of ADACEL® conducted in Canada in children 4.0 to 6.0 years of age, constitute the pivotal database supporting the safety of ADACEL®-POLIO as a pre-school booster of diphtheria, tetanus, acellular pertussis and poliomyelitis vaccine.

In study U01-A5I-302 conducted in the United Kingdom according to the British immunization schedule, 158 children 3.5 to 4.1 years of age, previously primed with PEDIACEL®[a] (N = 81) or DTwP vaccine used to reconstitute Hib vaccine administered concomitantly with OPV (N = 77), as well as meningococcal C conjugate (MenC) vaccine, at 2, 3, and 4 months of age, received the locally recommended pre-school booster dose of ADACEL®-POLIO concomitantly with measles, mumps, rubella (MMR) vaccine. (20) In this study, solicited adverse events following administration of ADACEL®-POLIO were monitored daily for 7 days post-vaccination using diaries. Unsolicited and serious adverse events were monitored up to 42 days post-vaccination. Table 5 presents the frequencies and severity of solicited injection site and systemic adverse reactions reported in study U01-A5I-302 within 7 days of the administration of ADACEL®-POLIO. This study demonstrated that, when administered to children primed with PEDIACEL®, ADACEL®-POLIO was safe and well tolerated, based on both frequency and severity of adverse reactions, in comparison to the safety profile observed with both ADACEL®-POLIO and ADACEL® in other studies in similar age groups, as reported below.

[a] Sanofi Pasteur Limited – PEDIACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine and Haemophilus b Conjugate Vaccine (Tetanus Protein Conjugate).

Table 5: Frequency (%) of Solicited Adverse Reactions Observed in Clinical Trial U01-A5I-302 in Children 3.5 to 4.1 Years of Age, 0 to 7 Days Following a Single Dose of ADACEL®-POLIO (20)

Solicited Reactions		Children 3.5 to 4.1 years of age (N = 157)
Injection Site Reactions		
Pain	**Any**	46.5
	Severe*	1.3
Swelling	**Any**	20.4
	Severe (≥35 mm)	5.7
Redness	**Any**	35.7
	Severe (≥35 mm)	12.7
Systemic Reactions		
Fever	**Any (≥37.5°C)**	7.0
	Severe (≥39.0°C)	1.9
Diarrhea	**Any**	7.6
Vomiting	**Any**	2.5
	Severe†	0.6
Rash	**Any**	7.0
Swollen Joints	**Any**	1.3
	Severe*	0.0
Tiredness	**Any**	35.7
	Severe*	1.3

* Severe: incapacitating, unable to perform usual activities, may have or did require medical care or absenteeism
† Severe: more than 5 times

In UK study U01-Td5I-303, among participants 3.5 to 5.0 years of age previously primed with 3 doses of diphtheria, tetanus and whole-cell pertussis pediatric vaccine (DTwP) and MenC vaccine at 2, 3, and 4 months of age, 100 participants received a single dose of ADACEL®-POLIO concomitantly with MMR vaccine and were compared to 100 participants who received a single dose of ADACEL® concomitantly with OPV and MMR vaccine. In study U02-Td5I-402, 50 participants 3.0 to 3.5 years of age previously primed with 3 doses each of DTwP and MenC vaccines at 2, 3, and 4 months of age received a single dose of ADACEL®-POLIO concomitantly with MMR vaccine. (2) (18) (19) In both studies, solicited adverse events were monitored daily for 7 days post-vaccination using diaries; unsolicited and serious adverse events were monitored up to 42 days post-vaccination. Table 6 presents the frequencies, and severity, of solicited adverse events reported 7 days after a single dose of ADACEL®-POLIO in children 3.0 to 5.0 years of age in these two studies separately, in comparison with those reported in U01-Td5I-303 after immunization with ADACEL® + OPV. In these two studies, the safety profile of ADACEL®-POLIO, both in frequency and severity of adverse reactions, was shown to be very similar to that of ADACEL® when given in children 3.0 to 5.0 years of age as a pre-school booster.

Table 6: Frequency (%) of Adverse Reactions Observed in Children 3.0 to 5.0 Years of Age, 0 to 7 Days Following a Single Dose of ADACEL®-POLIO or ADACEL® + OPV (2) (18) (19)

Adverse Reactions		U02-Td5I-402 3.0 to 3.5 Years of Age	U01-Td5I-303 3.5 to 5.0 Years of Age	
		ADACEL®-POLIO (N = 50)	ADACEL®-POLIO (N = 100)	ADACEL® + OPV (N = 100)
Injection Site Reactions				
Pain	**Any**	70.0	72.0	71.0
	Severe*	0.0	1.0	1.0
Swelling	**Any**	28.0	37.0	40.0
	Severe (≥35 mm)	8.0	17.0	13.0
Erythema	**Any**	52.0	47.0	61.0
	Severe (≥35 mm)	28.0	27.0	34.0
Bruising	**Any**	4.0	3.0	6.0
	Severe*	0.0	0.0	0.0
Pruritus	**Any**	0.0	4.0	3.0
	Severe*	0.0	0.0	0.0
Systemic Reactions				
Fever	**Any (≥37.5°C)**	8.0	15.0	13.0
	Severe (≥39.0°C)	0.0	2.0	2.0
Diarrhea	**Any**	10.0	10.0	12.0
Vomiting	**Any**	4.0	8.0	5.0
	Severe†	0.0	0.0	0.0
Rash	**Any**	6.0	10.0	21.0
Sore or Swollen Joints	**Any**	2.0	1.0	3.0
	Severe*	0.0	0.0	0.0
Tiredness	**Any**	60.0	49.0	49.0
	Severe*	2.0	1.0	1.0
Dermatitis	**Any**	2.0	1.0	0.0
	Severe*	0.0	0.0	0.0
Irritability	**Any**	14.0	4.0	7.0
	Severe*	0.0	0.0	0.0

* Severe: incapacitating, unable to perform usual activities, may have or did require medical care or absenteeism

† Severe: more than 5 times

Clinical trial Td508 was conducted in children 4 to 6 years of age, who had previously been immunized with PENTACEL®[a], the Canadian standard of care for infant immunization at the time (1997-2007). 590 children were randomized and received a single dose of either QUADRACEL®[b] (N = 292), or ADACEL® concomitantly with IPV (N = 298). (26) (27) Solicited local and systemic reactions were monitored for 14 days post-vaccination using a diary card. Participants were monitored for 28 - 42 days for unsolicited adverse events, visits to an emergency room, unexpected visits to an office physician, hospitalization and serious adverse events. Table 7 presents the frequency and severity of solicited adverse events reported within 14 days following administration of ADACEL® + IPV or QUADRACEL® in study Td508. There were no reports of whole-limb swelling in either vaccine group. The rates of solicited local reactions and fever were significantly lower in ADACEL® recipients compared to those who received QUADRACEL®. The rates of erythema, swelling, pain and fever following the administration of ADACEL® were shown to be non-inferior to those observed after QUADRACEL®. Except for fever, the observed rates for the systemic adverse events were comparable between the two vaccines. ADACEL®-POLIO contains the same Tdap formulation (in antigens and concentrations) as ADACEL®. Comparative studies of the two products in the UK have demonstrated that they have similar safety profiles. Therefore, the demonstrated improved safety profile of ADACEL® compared to QUADRACEL® in study Td508 supports the safety of ADACEL®-POLIO as a 4 - 6 year-old pre-school booster, within the Canadian immunization schedule.

[a] Sanofi Pasteur Limited – PENTACEL® [Haemophilus b Conjugate Vaccine (Tetanus Protein Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine].

[b] Sanofi Pasteur Limited - QUADRACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine].

Table 7: Frequency (%) of Solicited Adverse Events Reported in Clinical Trial Td508 in Children 4 to 6 Years of Age, 0 to 14 Days Following a Single Dose of ADACEL® + IPV or QUADRACEL® (32) (33)

Solicited Reactions	Severity	ADACEL® (N = 298)	QUADRACEL® (N = 290)
Injection Site Reactions			
Pain	**Any**	39.6	67.2
	Severe*	0.3	1.0
Swelling	**Any**	24.2	33.8
	≥35 mm	10.1	17.2
Erythema	**Any**	34.6	51.7
	≥35 mm	11.7	29.0
Systemic Reactions			
Headache	**Any**	16.4	16.9
	Severe*	0.0	0.7
Body Ache or Muscle Weakness	**Any**	6.4	8.3
	Severe*	0.0	0.7
Tiredness	**Any**	31.5	36.6
	Severe*	0.3	3.1
Chills	**Any**	7.1	10.0
	Severe*	0.0	0.3
Nausea	**Any**	9.4	10.0
	Severe*	0.0	0.3
Sore or Swollen Joints	**Any**	4.0	4.5
	Severe*	0.0	0.0
Diarrhea	**Any**	14.4	9.7
	Severe*	0.7	0.7
Lymph Node Swelling	**Any**	5.4	8.3
	Severe*	0.0	0.0
Fever	**≥38.0°C**	8.7	16.9
	≥39.5°C	1.7	1.4
Vomiting	**Any**	8.1	10.0
	Severe*	1.3	0.0
Rash	**Any**	8.4	14.1
Anorexia	**Any**	21.5	22.1
	Severe*	0.7	2.1

* Incapacitating, prevented the performance of usual activities, may have/or did necessitate medical care or absenteeism

Safety of ADACEL®-POLIO in Adolescents and Adults

In clinical trial TD9707, a total of 1214 Canadian individuals were randomized to ten treatment groups. Among adolescents 12 to 18 years of age, 351 received a single dose of ADACEL®-POLIO, and 117 received a single dose of Td-IPV vaccine, followed by a dose of acellular pertussis vaccine one month later. Among adults 19 to 60 years of age, 372 received a single dose of ADACEL®-POLIO, and 126 received a single dose of ADACEL®, followed by a dose of IPV one month later. (23) (24) The safety profile was assessed by monitoring solicited, unsolicited and serious adverse events at 24 and 72 hours, and at 14 - 15 days post-vaccination. The frequency and severity of solicited adverse events reported after a single dose of ADACEL®-POLIO compared to Td-IPV vaccine in adolescents and to ADACEL® in adults are presented in Table 8 and Table 9, respectively. Except for an increased frequency in mild fever, the frequency and severity of solicited adverse reactions reported within 14 days of administration of a booster dose of ADACEL®-POLIO were comparable to those reported after Td-IPV vaccine. Similarly, the frequency and severity of solicited adverse events reported by adults within 14 days after administration of ADACEL®-POLIO were comparable or lower than after ADACEL®. These results support the safety of ADACEL®-POLIO administered as a booster in adolescents and adults, when an additional poliomyelitis vaccination is recommended.

Table 8: Frequency (%) of Solicited Adverse Reactions Observed in Clinical Trial TD9707 in Adolescents, 0 to 14 Days Following a Single Dose of ADACEL®-POLIO or Td-IPV Vaccine (23)

Solicited Reactions		ADACEL®-POLIO (N = 350)	Td-IPV Vaccine (N = 116)
Injection Site Reactions			
Pain	**Any**	88.3	93.1
	Severe *	1.7	0.9
Swelling	**Any**	21.2	21.6
	Severe (≥35 mm)	11.2	7.8
Redness	**Any**	17.5	17.2
	Severe (≥35 mm)	2.6	2.6
Systemic Reactions			
Fever †	**Any (≥38.0°C)**	14.2	4.3
	Severe (≥40.5°C)	0.3	0.0
Headache	**Any**	41.3	37.1
	Severe *	1.4	0.9
Nausea	**Any**	17.5	13.8
	Severe *	0.3	0.9
Diarrhea	**Any**	5.4	7.8
	Severe *	0.0	0.0
Vomiting	**Any**	3.2	2.6
	Severe *	0.0	0.0
Body Ache	**Any**	26.1	20.7
	Severe *	0.3	0.9
Sore or Swollen Joints	**Any**	11.2	12.1
	Severe *	0.0	0.0
Tiredness	**Any**	37.2	28.4
	Severe *	0.6	0.0
Chills	**Any**	17.5	16.4
	Severe *	0.9	0.0

* Severe: incapacitating, unable to perform usual activities. Required medical care or absenteeism from school or work.

† Fever was solicited up to 72 hours post-vaccination.

Table 9: Frequency (%) of Solicited Adverse Reactions Observed in Clinical Trial TD9707 in Adults, 0 to 14 Days Following a Single Dose of ADACEL®-POLIO or ADACEL® (23)

Solicited Reactions		ADACEL®-POLIO (N = 366)	ADACEL® (N = 116)
Injection Site Reactions			
Pain	**Any**	86.3	87.9
	Severe *	0.5	0.8
Swelling	**Any**	16.7	10.5
	Severe (≥35 mm)	8.2	4.0
Redness	**Any**	23.0	26.6
	Severe (≥35 mm)	4.1	7.3
Systemic Reactions			
Fever †	**Any (≥38.0°C)**	2.7	4.8
	Severe (≥40.5°C)	0.0	0.0
Headache	**Any**	37.7	41.1
	Severe *	3.3	6.5
Nausea	**Any**	14.5	12.1
	Severe *	0.8	1.6
Diarrhea	**Any**	15.8	13.7
	Severe *	0.8	0.0
Vomiting	**Any**	2.5	1.6
	Severe *	0.5	0.0
Body Ache	**Any**	24.0	29.8
	Severe *	0.8	2.4
Sore or Swollen Joints	**Any**	11.2	15.3
	Severe *	0.3	0.8
Tiredness	**Any**	29.8	29.0
	Severe *	1.9	4.0
Chills	**Any**	11.2	14.5
	Severe *	0.3	1.6

* Severe: incapacitating, unable to perform usual activities. Required medical care or absenteeism from school or work.

† Fever was solicited up to 72 hours post-vaccination.

Immunogenicity of ADACEL®-POLIO in Children

The Canadian immunization schedule recommends an infant series during the first 2 years of life using PEDIACEL®, the current standard of care in Canada. This infant series should be followed by a booster dose of tetanus, diphtheria, acellular pertussis and poliomyelitis vaccine be given to children at school entry (4 to 6 years of age) to ensure a continued protection against these diseases through childhood until they receive a further booster as teenagers.

As previously described (see Safety of ADACEL®-POLIO in Children 3 Years of Age and Above), in study U01-A5I-302, 158 children 3.5 to 4.1 years of age received a booster dose of ADACEL®-POLIO concomitantly with MMR vaccine. (20) Serum antibody levels were measured on sera collected 28 days post-vaccination with ADACEL®-POLIO. Table 10 presents the pooled immunogenicity results for children 3.5 to 4.1 years of age immunized with ADACEL®-POLIO, independent of the vaccine used for the primary series. For all antigens, the increase in antibody levels demonstrated a strong response to the booster dose of ADACEL®-POLIO. Although these children had not received a booster dose of diphtheria, tetanus, pertussis and poliomyelitis-containing vaccine in their second year of life, as would be recommended for Canadian children, almost all participants achieved seroprotective antibody levels for diphtheria, tetanus and poliomyelitis. The Geometric Mean Titres (GMT) observed for pertussis were also consistently higher than those found to be protective in the Sweden I Efficacy Trial (i.e., 49.8 EU/mL for anti-PT antibodies, 33.3 EU/mL for anti-FHA antibodies, 352.4 EU/mL for anti-FIM antibodies and 116.7 EU/mL for anti-PRN antibodies). (32)

Table 10: Antibody Responses Observed Prior To and One Month Following a Dose of ADACEL®-POLIO in Clinical Trial U01-A5I-302 in Children 3.5 to 4.1 Years of Age (20)

Antigen		Criteria	Pre Booster Dose (N = 126-131)	Post Booster Dose (N = 127-132)
Diphtheria		**≥0.1 IU/mL**	23.8%	97.6%
Tetanus		**≥0.1 IU/mL**	84.0%	100.0%
Pertussis	**PT**	**GMT (EU/mL)**	5.0	128.1
	FHA	**GMT (EU/mL)**	7.5	110.5
	PRN	**GMT (EU/mL)**	4.6	142.3
	FIM	**GMT (EU/mL)**	13.8	789.5
IPV	**Type 1**	**≥1:8 dilution**	91.5%	100.0%
	Type 2	**≥1:8 dilution**	91.5%	100.0%
	Type 3	**≥1:8 dilution**	93.8%	99.2%

The demonstrated immunogenicity of ADACEL® in Canadian clinical trial Td508 (see Safety of ADACEL®-POLIO in Children 3 Years of Age and Above) further supports the use of Sanofi Pasteur Limited's Tdap formulations, including ADACEL®-POLIO, for the NACI-recommended booster dose at 4 to 6 years of age. (26) (27) The diphtheria and tetanus post-vaccination seroprotection rates following vaccination with ADACEL® were shown to be non-inferior to those obtained with QUADRACEL®. 100% of vaccinees achieved diphtheria and tetanus antitoxin levels ≥0.1 IU/mL (see Table 11). Post-vaccination GMTs for diphtheria were lower in the ADACEL® group compared to the QUADRACEL® group, consistent with the lower diphtheria content in ADACEL®. GMTs for the pertussis antigens PT, FHA, PRN and FIM, at 1-month post-vaccination are presented in Table 11. The GMTs and four-fold response rates were generally comparable between both vaccine groups, although anti-PT and anti-FHA were slightly higher in QUADRACEL® vaccinees, consistent with higher PT and FHA content of QUADRACEL®, while anti-PRN and anti-FIM were slightly higher in those who received ADACEL®. Pertussis antibody GMTs following ADACEL® were also consistently higher than those found to be protective in the Sweden I Efficacy Trial (i.e., 49.8 EU/mL for anti-PT antibodies, 33.3 EU/mL for anti-FHA antibodies, 352.4 EU/mL for anti-FIM antibodies and 116.7 EU/mL for anti-PRN antibodies). (32)

Table 11: Antibody Responses Observed One Month Following a Dose of ADACEL® or QUADRACEL® in Clinical Trial Td508 in Children 4 to 6 Years of Age (26) (27)

Antigen		Criteria	ADACEL® (N = 259-265)	QUADRACEL® (N = 248-254)
Tetanus		**≥0.1 IU/mL**	100%	100%
Diphtheria		**≥0.1 IU/mL**	100%	100%
Pertussis	**PT**	**GMT (EU/mL)**	297.1	331.1
	FHA	**GMT (EU/mL)**	198.0	258.1
	PRN	**GMT (EU/mL)**	303.8	243.1
	FIM	**GMT (EU/mL)**	1177.2	737.6

Antibody Persistence in Children

In clinical trial U01-Td5I-303 conducted in the United Kingdom, among participants 3.5 to 5 years of age previously primed with 3 doses of DTwP vaccine at 2, 3, and 4 months of age, 100 participants received a single dose of ADACEL®-POLIO concomitantly with MMR vaccine. (18) (19). A long-term serology follow-up study was later conducted on these children. The immunogenicity results 1 month, 1 year and 3 years following immunization with ADACEL®-POLIO are provided in Table 12. Paired serum samples were obtained from 40 children at 1 year post-vaccination and from 47 children at 3 years post-vaccination. The robust responses against diphtheria, tetanus and polio (types 1, 2, and 3) achieved by the children one month post-vaccination was sustained after 1 and 3 years, with 97.9 to 100.0% of children demonstrating seroprotective levels of the respective antibodies (diphtheria: ≥0.01 IU/mL; tetanus: ≥0.01 IU/mL; polio: ≥1:8). The GMTs of antibodies against pertussis antigens in ADACEL®-POLIO 1 and 3 years post-vaccination remained higher than pre-vaccination levels, suggesting continued protection against pertussis disease. (36)

Table 12: Antibody Persistence Observed 1 and 3 Years After a Dose of ADACEL®-POLIO in Clinical Trial U01-Td5I-303 in Children 3.5 to 5.0 Years of Age at the Time of Vaccination (36)

Antigen		Criteria	1 Month Post-Vaccination (N = 99)	1 Year Post-Vaccination (N = 39-40)	3 Years Post-Vaccination (N = 46-47)
Diphtheria		**≥0.01 IU/mL**	100.0%	100.0%	100.0%
Tetanus		**≥0.01 IU/mL**	100.0%	100.0%	100.0%
Pertussis	**PT**	**GMT (EU/mL)**	161.4	20.7	6.1
	FHA	**GMT (EU/mL)**	128.6	22.8	18.4
	PRN	**GMT (EU/mL)**	240.4	31.1	18.6
	FIM	**GMT (EU/mL)**	835.9	77.6	62.6
IPV	**Type 1**	**≥1:8 dilution**	100.0%	100.0%	100.0%
	Type 2	**≥1:8 dilution**	100.0%	100.0%	100.0%
	Type 3	**≥1:8 dilution**	100.0%	100.0%	97.9%

Immunogenicity of ADACEL®-POLIO in Adolescents and Adults

Clinical trial TD9707 evaluated the immunogenicity of ADACEL®-POLIO in 351 adolescents 12 to18 years of age and in 372 adults 19 to 60 years of age. (23) (24) Immunogenicity analyses were conducted on sera collected 28 days post-vaccination with ADACEL®-POLIO. The immunogenicity of ADACEL®-POLIO in adolescents and adults is presented in Table 13. In both age groups the responses to diphtheria, tetanus and poliomyelitis was strong, with high percentages of participants achieving seroprotective antibody levels. The response to pertussis antigens was consistent between the two age groups. The adolescents and adult participants achieved GMTs against PT, FHA, PRN and FIM, which were consistently higher than those found to be protective in the Sweden I Efficacy Trial (i.e., 49.8 EU/mL for anti-PT antibodies, 33.3 EU/mL for anti-FHA antibodies, 352.4 EU/mL for anti-FIM antibodies and 116.7 EU/mL for anti-PRN antibodies). (32) (33). In study TD9707, the immune response in adolescent recipients of ADACEL®-POLIO was compared to that of adolescents having received Td-IPV vaccine, and the immune response in adult recipients of ADACEL®-POLIO was compared to that of adults having received Td vaccine or ADACEL® + IPV vaccine. In both age groups, ADACEL®-POLIO demonstrated a comparable immunogenicity profile to that of the control vaccines.

Table 13: Antibody Responses Observed One Month After a Dose of ADACEL®-POLIO in Adolescents and Adults in Clinical Trial TD9707 (23) (24)

Antigen		Criteria	Adolescents (N = 346-348)	Adults (N = 361-364)
Diphtheria		**≥0.01 IU/mL**	99.7%	96.2%
		≥0.1 IU/mL	97.1%	83.8%
Tetanus		**≥0.01 EU/mL**	100.0%	100.0%
		≥0.1 EU/mL	100.0%	100.0%
Pertussis	**PT**	**GMT(EU/mL)**	172.4	114.5
	FHA	**GMT(EU/mL)**	243.0	229.0
	PRN	**GMT(EU/mL)**	253.3	210.1
	FIM	**GMT(EU/mL)**	1199.1	633.3
IPV	**Type 1**	**≥1:8 dilution**	99.7%	100.0%
	Type 2	**≥1:8 dilution**	100.0%	100.0%
	Type 3	**≥1:8 dilution**	100.0%	100.0%

Antibody Persistence in Adolescents and Adults

A long-term serology follow-up study was conducted on adolescents (11 - 18 years of age at time of vaccination with ADACEL®-POLIO) and adults (19 - 60 years of age at time of vaccination with ADACEL®-POLIO), who had been immunized with a single booster dose of ADACEL®-POLIO in study TD9707. Serum samples were obtained from 118 adolescents and 136 adults at 3 years post-vaccination, and from 109 adolescents and 128 adults at 5 years post-vaccination. Both adolescent and adult recipients achieved robust immune responses that were sustained through to the 5-year time period for all antigens, the exception being diphtheria antibodies in the adult group in which a decline in antibodies was observed (See Table 14). For both adolescent and adult analyses of diphtheria and tetanus responses, seroprotection rates and GMT responses with ADACEL®-POLIO were similar to the responses in adolescents and adults who had received the then current standard-of-care vaccines for their age groups (Td-IPV and Td vaccines, respectively), used as comparators in study TD9707. GMTs for all pertussis antigens at 5-years remained at least 2-fold higher than pre-immunization levels, indicating a sustained long-term immune response for both adolescents and adults. For polio, the seroprotective levels (≥1:8) for each type (1, 2 and 3) were maintained for 98.2-100% of the adolescent groups and at 100% of the adult groups at the 5-year follow-up period. The long-term antibody profile observed in this study indicates that long-term protection against diphtheria, tetanus, and polio clinical disease is maintained for at least 5-years following administration of ADACEL®-POLIO in both adolescents

and adults. The pertussis responses for both adults and adolescents were indicative of long-term persistence and suggested on-going protection against pertussis. (35)

Table 14: Antibody Persistence Observed 3 and 5 Years After a Dose of ADACEL®-POLIO in a Clinical Trial in Adolescents and Adults (35)

Antigen		Criteria	3 Years Post-Vaccination		5 Years Post-Vaccination	
			Adolescents (N = 115-118)	Adults (N = 134-136)	Adolescents (N = 105-109)	Adults (N = 125-128)
Diphtheria		**≥0.01 IU/mL**	99.1%	91.9%	96.2%	79.2%
Tetanus		**≥0.01 EU/mL**	100.0%	100.0%	100.0%	100.0%
Pertussis	**PT**	**GMT (EU/mL)**	56.0	40.4	54.5	39.8
	FHA	**GMT (EU/mL)**	65.4	59.2	52.6	53.4
	PRN	**GMT (EU/mL)**	50.3	71.9	42.2	55.9
	FIM	**GMT (EU/mL)**	228.2	169.0	208.9	142.6
IPV	**Type 1**	**≥1:8 dilution**	100.0%	100.0%	100.0%	100.0%
	Type 2	**≥1:8 dilution**	100.0%	100.0%	100.0%	100.0%
	Type 3	**≥1:8 dilution**	100.0%	100.0%	98.2%	100.0%

ADDITIONAL RELEVANT INFORMATION

Tetanus is an acute and often-fatal disease caused by an extremely potent neurotoxin produced by *Clostridium tetani*. The organism is ubiquitous and its occurrence in nature cannot be controlled. Immunization is highly effective, provides long-lasting protection and is recommended for the whole population. Only 1 to 7 cases of tetanus were reported annually in Canada during the 1990s. (1)

Diphtheria is a serious communicable disease caused by toxigenic strains of *Corynebacterium diphtheriae*. The organism may be harboured in the nasopharynx, skin or other sites of asymptomatic carriers, making eradication of the disease difficult. Routine immunization against diphtheria in infancy and childhood has been widely practiced in Canada since 1930. Fewer than 2 cases are now reported annually in Canada. The case-fatality rate remains at 5 to10%, with the highest death rates in the very young and elderly. The disease occurs most frequently in unimmunized or partially immunized persons. (1)

Pertussis (whooping cough) results from an acute infection of the respiratory tract by *Bordetella pertussis*. The most serious complications and deaths occur in young infants, particularly those who have not yet had the opportunity to be immunized or are not yet fully immunized (e.g., 1 or 2 doses). (33) Despite widespread use in Canada of pertussis vaccines in childhood, there was resurgence in the incidence of pertussis disease in the 1990s. (49) (50) A pattern of steadily

increasing age of cases and higher incidence among adolescents and adults has been observed. (51) However, epidemiological reviews in Newfoundland and Labrador and in the Northwest Territories demonstrated a significant reduction in cases of pertussis after introduction of pertussis booster vaccination in provincial immunization programs, particularly among children and adolescents. (52) (53) Because of waning immunity, many vaccinated children become susceptible to pertussis in adolescence or adulthood. Pertussis is a frequent cause of cough illness with significant morbidity in adolescents and adults (54) (55) (56) (57), who are a source of transmission to infants. (58) (59)

To prevent pertussis in adolescents and adults and indirectly protect susceptible infants, the National Advisory Committee on Immunization (NACI) recommends that adolescents and adults receive a booster with an adolescent/adult acellular pertussis formulation combined with Td (Tdap). (51)

Poliomyelitis is caused by infection with one of the three antigenic types of poliovirus. Following introduction of poliovirus vaccine in Canada in 1955, the indigenous disease has been virtually eliminated. However, the persistence of wild virus cases in polio endemic regions of Africa and Asia (60) necessitates that the highest possible level of vaccine-induced immunity be maintained in the Canadian population.

Duration of Effect

Long-term follow-up of serum antibody levels in adolescents and adults who received a single dose of ADACEL®-POLIO shows that protective levels for tetanus antitoxin (≥0.01 IU/mL) and diphtheria antitoxin (≥0.01 IU/mL) persist in 100% and at least 79.2% of participants, respectively, after at least 5 years. Protective levels of anti-poliovirus antibodies (≥1:8) persist in 98.2% to 100.0% of both adolescents and adults after 5 years. While protective levels against pertussis have not yet been clearly defined, pertussis antibody levels remain several-fold higher than pre-immunization levels after 5 years. (35)

Long-term follow-up of serum antibody levels in children who received a single dose of ADACEL®-POLIO at 3.5 to 5 years of age shows that protective levels for tetanus antitoxin (≥0.01 IU/mL) and diphtheria antitoxin (≥0.01 IU/mL) persist in 100.0% of participants, 3 years after immunization. Protective levels of anti-poliovirus antibodies (≥1:8) persist in 97.9 to 100.0% of participants after 3 years. While protective levels against pertussis have not yet been clearly defined, after 3 years, pertussis antibody levels remain higher than pre-immunization levels. (36)

According to NACI, tetanus and diphtheria toxoid boosters are recommended every 10 years (1), however, the optimal interval for administering subsequent booster doses with ADACEL®-POLIO has not been determined. Nevertheless, a clinical study conducted with ADACEL® demonstrated that the incidence and severity of adverse events reported after administration of ADACEL® as early as 2 years after the last dose of tetanus and diphtheria vaccine were similar to those observed after administration at greater time intervals, up to 10 years. (37)

Immunogenicity in pregnancy

The assessment of pertussis antibody responses in pregnant women and newborn infants is based on 4 published randomized controlled studies with ADACEL® (8) (9) (10) (11) and one observational study with ADACEL®-POLIO (41).

Maternal antibody directed against pertussis antigens persists for at least 2 months after birth and may be associated with blunting of the infant immune response to active immunization against pertussis. The clinical relevance of the blunting of the immune response is unknown.

The effectiveness of vaccine in infants whose mothers were vaccinated with ADACEL® or ADACEL®-POLIO during pregnancy was evaluated in three published observational studies in UK and US (43) (44) (45). The vaccine was administered during the third trimester of pregnancy for passive protection against pertussis in infants below 3 months of age.

REFERENCES

1 National Advisory Committee on Immunization (NACI): Parts 1 - 4. In: Canadian immunization guide. Public Health Agency of Canada. https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html.

2 Data on file at Sanofi Pasteur Limited - Clinical trial U01-Td5I-402.

3 Kaml M, et al. Booster vaccination in the elderly: their success depends on the vaccine type applied earlier in life as well as on pre-vaccination antibody titers. Vaccine 2006;24:6808-11.

4 CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2006;55(RR-15):1-46.

5 CDC. Preventing tetanus, diphtheria and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and Recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. MMWR 2006;55(RR-17):1-33.

6 CDC. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on immunization (ACIP). MMWR 2006;55(RR-03):1-34.

7 Stratton K, Ford A, Rusch E, et al, editors. Adverse effects of vaccines; Evidence and causality. Washington D.C.: National Academies Press; p. 557-558.

8 Munoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. JAMA 2014;311:1760-1769.

9 Hoang HTT, Leuridan E, et al. Pertussis vaccination during pregnancy in Vietnam : Results of a randomized controlled trial Pertussis vaccination during pregnancy. Vaccine. 2016; 34:151-159.

10 Villarreal Perez JZ, Ramirez Aranda JM, et al. Randomized clinical trial of the safety and immunogenicity of the Tdap vaccine in pregnant Mexican women. Human Vaccines and Immunotherapeutics. 2017; 13:1:128-135.

11 Halperin SA, Langley JM, Ye L. et al. A randomized, controlled trial of the safety and immunogenicity of tetanus, diphtheria, and acellular pertussis vaccine (Tdap) immunization during pregnancy and subsequent infant immune response. Clinical Infectious Diseases, 2018;67:1063-1071.

12 Perry J, Towers CV, Weitz B, Wolfe L. Patient reaction to Tdap vaccination in pregnancy. Vaccine. 2017; 35:3064-3066.

13 Donegan K, King B, Bryan P. Safety of pertussis vaccination in pregnant women in UK: observational study. BMJ 2014;349:g4219.

14 Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Evaluation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. JAMA 2014;312:1897-1904.

15 Morgan JL, Baggari SR, McIntire DD, Sheffield JS Pregnancy outcomes after antepartum tetanus, diphtheria, and acellular pertussis vaccination. Obstetrics and Gynecology. 2015; 125:1433-1438.

16 Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Maternal Tdap vaccination: Coverage and acute safety outcomes in the vaccine safety datalink, 2007-2013. Vaccine 2016;34:968-973.

17 DeSilva M, Vazquez-Benitez G, Nordin JD et al. Maternal Tdap vaccination and risks of infant morbidity. Vaccine. 2017; 35:3655-3660.

18 Data on file at Sanofi Pasteur Limited - Clinical trial U01-Td5I-303.

19 Collins CL, et al. Immunogenicity and safety of a low-dose diphtheria, tetanus and acellular pertussis combination vaccine with either inactivated or oral polio vaccine as a pre-school booster in UK children. Vaccine 2004;22:4262-9.

20 Data on file at Sanofi Pasteur Limited - Clinical trial U01-A5I-302.

21 Data on file at Sanofi Pasteur Limited - Clinical Trial Sweden Booster Study.

22 Diez-Domingo J, et al. Immunogenicity and reactogenicity of a combined adsorbed tetanus toxoid, low dose diphtheria toxoid, five component acellular pertussis and inactivated polio vaccine in six-year-old children. Pediatr Infect Dis J 2005;24(3):219-24.

23 Data on file at Sanofi Pasteur Limited - Clinical trial TD9707.

24 Halperin SA, et al. Adult formulation of a five component acellular pertussis vaccine combined with diphtheria and tetanus toxoids and inactivated poliovirus vaccine is safe and immunogenic in adolescents and adults. Pediatr Infect Dis J 2000;19(4):276-83.

25 Data on file at Sanofi Pasteur Limited - Clinical trial TD9809.

26 Langley JM, et al. An adolescent-adult formulation tetanus and diphtheria toxoids adsorbed combined with acellular pertussis vaccine has comparable immunogenicity but less reactogenicity in children 4-6 years of age than a pediatric formulation acellular pertussis vaccine and diphtheria and tetanus toxoids adsorbed combined with inactivated poliomyelitis vaccine. Vaccine 2007;25(6):1121-5.

27 Data on file at Sanofi Pasteur Limited - Clinical trial Td508.

28 McNeil SA, et al. Comparison of the safety and immunogenicity of concomitant and sequential administration of an adult formulation tetanus and diphtheria toxoids adsorbed combined with acellular pertussis (Tdap) vaccine and trivalent inactivated influenza vaccine in adults. Vaccine 2007;25:3464-74.

29 National Advisory Committee on Immunization (NACI). Update on Immunization in Pregnancy with Tetanus Toxoid, Reduced Diphtheria Toxoid and Reduced Acellular Pertussis (Tdap) Vaccine [cited 2018 Mar 1]. Public Health Agency of Canada. https://www.canada.ca/en/public-health/services/publications/healthy-living/update-immunization-pregnancy-tdap-vaccine.html

30 Wassilak SGF, et al. Tetanus toxoid. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 5th ed. Philadelphia, PA: Elsevier Inc; 2008. p. 818.

31 Vitek CR, Wharton M. Diphtheria toxoid. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 5th ed. Philadelphia, PA: Elsevier Inc; 2008. p. 147.

32 Gustafsson L, et al. A controlled trial of a two-component acellular, a five-component acellular and a whole-cell pertussis vaccine. N. Engl J Med 1996;334(6):349-55

33 Halperin SA, et al. Epidemiological features of pertussis in hospitalized patients in Canada, 1991-1997: Report of the Immunization Monitoring Program - Active (IMPACT). Clin Infect Dis 1999;28:1238-43.

34 Plotkin SA. Immunologic correlates of protection induced by vaccination. Pediatr Infect Dis J 2001;20(1):63-75.

35 Data on file at Sanofi Pasteur Limited - Clinical trial TD9707 3 and 5 Year Serology Follow-up Report.

36 Data on file at Sanofi Pasteur Limited - Clinical trial U01-Td5I-303 3 Years Serology Follow-up Executive Summary

37 Halperin SA, et al. How soon after a prior tetanus-diphtheria vaccination can one give adult formulation tetanus-diphtheria-acellular pertussis vaccine? Pediatr Infect Dis J 2006;25(3):195-200.

41 Ladhani SN, Andrews NJ, et al. Antibody responses after primary immunization in infants born to women receiving a Pertussis-containing vaccine during pregnancy. Single arm observational study with a historical comparator. Clinical Infectious Diseases 2015;61:11:1637-1644.

43 Amirthalingam G, Campbell H, Ribeiro S, et al. Sustained effectiveness of the maternal pertussis immunization program in England 3 years following introduction. Clin Infect Dis 2016;63(S4):S236-243.

44 Baxter R, Bartlett J, Fireman B, Lewis E, Klein NP. Effectiveness of vaccination during pregnancy to prevent infant pertussis. Pediatrics 2017; 139:5.

45 Dabrera G, Amirthalingam G, Andrews N, et al. A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012-2013. Clin Infect Dis 2015;60:333-337.

46 Stainer DW. Production of diphtheria toxin. In: Manclark CR, editor. Proceedings of an informal consultation on the World Health Organization requirements for diphtheria, tetanus, pertussis and combined vaccines. United States Public Health Service, Bethesda, MD: DHHS (FDA) no 91-1174. 1991. p. 7-11.

47 Mueller JH, Miller PA. Variable factors influencing the production of tetanus toxin. J Bacteriol 1954;67(3):271-7.

48 Stainer DW, Scholte MJ. A simple chemically defined medium for the production of phase I Bordetella pertussis. J Gen Microbiol 1971;63:211-20.

49 Ntezayabo B, et al. Pertussis resurgence in Canada largely caused by a cohort effect. Pediatr Infect Dis J 2003;22(1):22-7.

50 Skowronski DM, et al. The changing age and seasonal profile of pertussis in Canada. J Infect Dis 2002;185:1448-53.

51 National Advisory Committee on Immunization (NACI). Prevention of pertussis in adolescents and adults. CCDR 2003;29(ACS-5):1-9.

52 Disease Control and Epidemilogy, Newfoundland and Labrador Department of Health and Community Services. Pertussis in Newfoundland and Labrador: 1991-2004. CCDR 2005;31(22):235-7.

53 Kandola K, et al. A comparison of pertussis rates in the Northwest Territories: pre- and postacellular pertussis vaccine introduction in children and adolescents. Can J infect Dis Med Microbiol 2005;16(5):271-4

54 De Serres G, et al. Morbidity of pertussis in adolescents and adults. J Infect Dis 2000;182:174-9.

55 Senzilet LD, et al. Pertussis is a frequent cause of prolonged cough illness in adults and adolescents. Clin Infect Dis 2001;32:1691-97.

56 Wirsing von Konig CH, et al. Pertussis in adults: frequency of transmission after household exposure. Lancet 1995;346:1326-29.

57 Deville JG, et al. Frequency of unrecognized Bordetella pertussis infections in adults. Clin Infect Dis 1995;1:639-42.

58 CDC. Transmission of pertussis from adult to infant - Michigan, 1993. MMWR 1995;44(4):74-6.

59 Bisgard KM, et al. Infant pertussis: who was the source? Pediatr Infect Dis J 2004; 23(11):985-9.

60 World Health Organization. Polio News. 2002;16:2.

Vaccine Information Service: 1-888-621-1146.

Full product monograph available on request or visit us at www.sanofi.ca

Product information as of June 2020.

Manufactured and distributed by:

Sanofi Pasteur Limited
Toronto, Ontario, Canada

Fabricated by:

Sanofi Pasteur SA
Lyon, France

R6-0620 Canada

PART III: CONSUMER INFORMATION

ADACEL®-POLIO

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine

This leaflet is part III of a three-part "Product Monograph" published when ADACEL®-POLIO was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ADACEL®-POLIO. Contact your doctor, nurse or pharmacist if you have any questions about the drug.

ABOUT THIS VACCINE

What the medication is used for:

ADACEL®-POLIO is a vaccine that is used to boost the body's protection against tetanus, diphtheria, pertussis (whooping cough) and poliomyelitis. This vaccine may be given to children, adolescents and adults from the age of 4 and above.

The majority of people who are vaccinated with ADACEL®-POLIO will produce enough antibodies to protect them against these 4 diseases. However, as with all vaccines, 100% protection cannot be guaranteed.

ADACEL®-POLIO may be given to a pregnant woman to help protect her baby against whooping cough.

What it does:

ADACEL®-POLIO causes your body to produce its own natural protection against tetanus, diphtheria, pertussis and polio viruses. After you receive the vaccine, your body begins to make substances called antibodies. Antibodies help your body to fight disease. If a vaccinated person comes into contact with one of the germs that cause these diseases, the body is usually ready to destroy it.

When it should not be used:

Do not give ADACEL®-POLIO to:

- Persons who are known to have a severe allergy to any ingredient in the vaccine or its container, or who have had a severe allergic reaction after receiving a vaccine that contained similar ingredients.
- Persons who have had a serious nervous system disorder within 7 days after a previous pertussis vaccine.

What the medicinal ingredient is:

Each 0.5 mL dose of ADACEL®-POLIO contains: tetanus toxoid, diphtheria toxoid, pertussis toxoid, filamentous haemagglutinin, pertactin, fimbriae types 2 and 3, and killed, purified viruses from three strains of poliomyelitis viruses.

What the important non-medicinal ingredients are:

Aluminum phosphate, 2-phenoxyethanol, polysorbate 80. Formaldehyde, glutaraldehyde, calf serum protein, neomycin, polymyxin B and streptomycin are present in trace amounts.

What dosage forms it comes in:

ADACEL®-POLIO is a liquid vaccine that is injected into a muscle. A single dose is 0.5 mL.

WARNINGS AND PRECAUTIONS

If you or your child have or have had any of the following conditions, talk to your doctor, nurse or pharmacist BEFORE you or your child receive ADACEL®-POLIO:

- **A high fever or serious illness.** Delay the vaccination until the person is better.
- **An allergy to any component of the vaccine or the container.**
- **A serious nervous system adverse event (Guillain-Barré syndrome or brachial neuritis) following a previous tetanus vaccination.**
- **A progressive nervous system disorder** or uncontrolled epilepsy, vaccination may be considered only after a treatment has been established.
- **Pregnant women or nursing mothers.** It is important that you understand the risks and benefits of vaccination. Tell the person giving you the injection if you are pregnant or breast-feeding. The health care professional will recommend whether you should receive ADACEL®-POLIO.
- **A weakened immune system.** The vaccine may provide you with a lower level of protection than it does for people with healthy immune systems. If possible, try to postpone the vaccination until after you have completed the treatment that affects your immune system.
- **A bleeding disorders or taking blood-thinning medications.** Tell the person giving you the injection about your condition. The injection must be done carefully to prevent excessive bleeding.

- **Fainted with a previous injection.** Fainting can occur following vaccination. Appropriate measures should be taken to prevent falling injury.

INTERACTIONS WITH THIS VACCINE

Do not mix ADACEL®-POLIO with other vaccines or medicinal products in the same syringe.

ADACEL®-POLIO may be given at the same time, but at separate sites with:

- Inactivated Flu vaccine
- Hepatitis B vaccine.

PROPER USE OF THIS VACCINE

Usual dose:
For persons 4 years of age and above who have previously been immunized against tetanus, diphtheria, pertussis and poliomyelitis, the recommended single dose is 0.5 mL.

The vaccination should be given in the muscle, preferably in the deltoid (shoulder) region.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
Not applicable to this vaccine.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A vaccine, like any medicine, may cause serious problems, such as severe allergic reactions. The risk of ADACEL®-POLIO causing serious harm is extremely small. The small risks associated with ADACEL®-POLIO are much less than the risks associated with getting the diseases.

Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well after receiving ADACEL®-POLIO.

Serious side effects are extremely rare.

Some people who receive ADACEL®-POLIO may have mild side effects such as redness, swelling or pain at the site of the injection. They may also feel tired, or have a headache, generalized body ache and sore or swollen joints. These side effects usually go away within a few days.

This is not a complete list of side effects. For any unexpected effects while taking ADACEL®-POLIO, contact your doctor, nurse or pharmacist.

HOW TO STORE IT

Store the vaccine in a refrigerator at 2° to 8°C (35° to 46°F). **Do not freeze**. Throw the product away if it has been exposed to freezing.

Do not use vaccine after the expiration date.

Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For health care professionals:
If a patient experiences an adverse event following immunization, please complete the Adverse Events following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit in **your province/territory.**

For the General Public:
Should you experience a side effect following immunization, please report it to your doctor, nurse or pharmacist.
Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Sanofi Pasteur Limited cannot provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.sanofi.ca

You may also contact the vaccine producer, Sanofi Pasteur Limited, for more information. Telephone: 1-888-621-1146 (no charge)

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