ADACEL®

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed

Intramuscular injection
Suspension for injection

DESCRIPTION

ADACEL®, [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed], is a sterile, uniform, cloudy, white suspension of tetanus and diphtheria toxoids adsorbed separately on aluminum phosphate, combined with acellular pertussis vaccine and suspended in water for injection. The acellular pertussis vaccine is composed of 5 purified pertussis antigens (PT, FHA, PRN and FIM).

INDICATIONS AND CLINICAL USE

ADACEL® is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis (whooping cough) in persons 4 years of age and older.

ADACEL® may be considered as an alternative for the fifth dose of tetanus, diphtheria and acellular pertussis vaccine (DTaP) in children 4 through 6 years of age, concomitantly administered with Inactivated Poliomyelitis Vaccine (IPV) at separate sites to complete the vaccination series for this age, when indicated.

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

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

Pediatrics

ADACEL® is not indicated for immunization of children below the age of 4 years.

Tetanus Prophylaxis in Wound Management

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

CONTRAINDICATIONS

Hypersensitivity

Known systemic hypersensitivity reaction to any component of ADACEL® 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 DOSAGE FORMS, COMPOSITION AND PACKAGING.)

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.

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 not attributable to another identifiable cause is a contraindication to vaccination with any pertussis-containing vaccine, including ADACEL®.

WARNINGS AND PRECAUTIONS

General

Before administration of ADACEL®, health-care providers should inform the recipient or the parent or guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient'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 recipient/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.

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

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

Administration Route Related Precautions: Do not administer ADACEL® 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® should not be administered into the buttocks.

Febrile and Acute Disease: Vaccination should be postponed in cases of an acute or febrile disease. 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 hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with ADACEL® 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® 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. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management.

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. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited.

Neurologic

ADACEL® should not be administered to individuals with progressive or unstable neurological disorders, uncontrolled epilepsy or progressive encephalopathy until a treatment regimen has been established, the condition has stabilized and the benefit clearly outweighs the risk.

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

A few cases of demyelinating diseases of the central nervous system, peripheral mononeuropathies and cranial mononeuropathies have been reported following vaccines containing tetanus and/or diphtheria toxoids, although the IOM concluded that the evidence is inadequate to accept or reject a causal relation between these conditions and vaccination.

Pregnant Women

Safety

Adacel can be used during the second or third trimester of pregnancy in accordance with official recommendations (see section DOSAGE AND ADMINISTRATION)

Safety data from 4 randomized controlled trials (310 pregnancy outcomes), 1 prospective observational study (546 pregnancy outcomes), 5 retrospective observational studies (124,810 pregnancy outcomes), and from passive surveillance of women who received ADACEL® or ADACEL®-POLIO (Tdap-IPV; containing the Tdap component of ADACEL®) during the 2nd or 3rd 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 ADACEL® during any trimester would harm the fetus.

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

For information on immune responses to vaccination during pregnancy and its effectiveness at preventing pertussis in infants, see section **ACTION AND CLINICAL PHARMACOLOGY**

Nursing Women

The effect of administration of ADACEL® during lactation has not been assessed. As ADACEL® is inactivated, any risk to the mother or the infant is improbable. However, the effect on breast-fed infants of the administration of ADACEL® 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 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 the 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® was evaluated in a total of 5,818 participants who received a single dose of ADACEL® in 6 clinical trials (298 children ≥ 4 years of age, 1,508 adolescents, 2,842 adults < 65 years of age and 1,170 adults ≥ 65 years of age).

Pain at the injection site was the most common solicited injection site reaction. Most injection site reactions occurred within 3 days following vaccination and their mean duration was less than 3 days. The most frequent systemic reaction was tiredness in children and headache in adolescents and adults (18 – 64 years). Myalgia was the most frequently reported systemic reaction among older adults ≥ 65 years of age. Fever was reported in less than 10% of vacinees. These reactions were usually transient and of mild to moderate intensity. In addition, in adolescents and adults the incidence of injection site and systemic reactions following ADACEL® was comparable to those observed with a Td vaccine booster. In children the observed frequencies of injection site and fever following ADACEL® were significantly lower than those observed with QUADRACEL® (DTaP-IPV) when administered as a booster at 4 to 6 years of age. Except for fever, the observed rates for the systemic reactions were comparable between the two vaccines. The frequency of the solicited injection site and systemic reactions reported in two clinical trials are shown in Table 1.

Two serious adverse events were reported during Study Td506 which were considered related to the vaccination: a case of severe migraine with unilateral facial paralysis, and a diagnosis of nerve compression in the neck and left arm. Both of these conditions resolved spontaneously or with treatment.

Table 1: Frequency (%) of Solicited Reactions Observed Within 0 to 14 Days in Clinical Trials in Children, Adolescents and Adults, Following a Single Dose with ADACEL®

Solicited Reactions	Children 4 – 6 years (N = 298)	Adolescents 11 – 17 years (N = 1,184)	Adults 18 – 64 years (N = 1,752)	Adults ≥ 65 years (N = 1,153)
Injection Site Reactions				
Pain	39.6	77.8	65.7	43.0
Swelling	24.2	20.9	21.0	18.1
Erythema	34.6	20.8	24.7	24.3
Systemic Reactions				
Fever (≥38.0°C)	8.7	5.0	1.4	0.5
Headache	16.4	43.7	33.9	N.S.*
Nausea	9.4	13.3	9.2	N.S.*
Diarrhea	14.4	10.3	10.3	N.S.*
Vomiting	8.1	4.6	3.0	N.S.*
Anorexia	21.5	N.S*	N.S*	N.S.*
Rash	8.4	2.7	2.0	N.S.*
Body Ache or Muscle Weakness†/Myalgia ‡	6.4	30.4	21.9	28.4
Sore or Swollen Joints	4.0	11.3	9.1	N.S.*
Tiredness§/Malaise**	31.5	30.2	24.3	17.2
Chills	7.1	15.1	8.1	N.S.*
Axillary Lymph Node Swelling	5.4	6.6	6.5	N.S.*

* Not Solicited

† Body ache or muscle weakness was the solicited term in the trials in children, adolescents and adults 18 – 64 years of age.
‡ Myalgia was the solicited term in the trial in adults ≥ 65 years of age.
§ Tiredness was the solicited term in the trials in children, adolescents and adults 18 – 64 years of age.
** Malaise was the solicited term in the trial in adults ≥ 65 years of age.

Table 2: Frequency (%) of Solicited Reactions Observed in Adolescents and Adults Following Re-administration of ADACEL® at 5 and 10 years Respectively

Solicited Reactions	Re-administration of ADACEL®	
	After 5 years*	After 10 years†
	Adolescents and Adults 16- 69 years (N = 544)	Adults 20 – 72 years (N = 361)
Injection Site Reactions		
Pain	87.6	87.8
Erythema/ Redness	28.6	23.1
Swelling	25.6	20.5
Systemic Reactions		
Fever	6.5	4.2
Headache	53.2	40.6
Myalgia	61.0	60.1
Malaise	38.2	29.4

* Adverse reactions observed within 0 to 14 days after vaccination.

† Adverse reactions observed within 0 to 7 days after vaccination.

Data from Post-Marketing Experience

The following additional adverse events have been spontaneously reported during the post marketing use of ADACEL®. Because these 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. Decisions to include these events in labelling were based on one or more of the following factors: 1) severity of the event, 2) frequency of reporting, or 3) strength of causal connection to ADACEL®.

Immune System Disorders
Hypersensitivity (anaphylactic) reaction (angioedema, edema, rash, hypotension)

Nervous System Disorders
Paraesthesia, hypoesthesia, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis

Cardiac Disorders

Myocarditis

Skin and Subcutaneous Tissue Disorders
Pruritus, urticarial

Musculoskeletal and Connective Tissue Disorders
Myositis, muscle spasm

General Disorders and Administration Site Conditions
Large injection site reactions (> 50 mm) and extensive limb swelling from the injection site beyond one or both joints have been reported after administration of ADACEL® in adolescents and adults. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 - 5 days. The risk appears to be dependent on the number of prior doses of acellular pertussis containing vaccine.
Injection site bruising, injection site nodule, sterile abscess.

DRUG INTERACTIONS

Vaccine-Drug Interactions

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

Concomitant Vaccine Administration

In clinical studies, Adacel vaccine was administered concomitantly with one of the following vaccines: Hepatitis B vaccine or trivalent inactivated influenza vaccine.

The concomitant use of ACACEL® and trivalent inactivated influenza vaccine was evaluated in a clinical trial involving 696 adults 19 to 64 years of age. The safety and immunogenicity profiles in adults that received the vaccines concomitantly were comparable to those observed when the vaccines were given on separate occasions one month apart.

The concomitant use of ADACEL® and hepatitis B vaccine was evaluated in a clinical trial involving 269 adolescents 11 to 12 years of age. The safety and immunogenicity profiles in adolescents that received the vaccines concomitantly were comparable to those observed when the vaccines were given on separate occasions one month apart. No interference was observed in the immune responses to any of the vaccine antigens when ADACEL® and hepatitis B vaccines were given concurrently or separately.

Vaccines administered simultaneously should be given using separate syringes at separate injection sites and preferably in separate limbs. ADACEL® should not be mixed in the same syringe with other parenterals.

DOSAGE AND ADMINISTRATION

Recommended Dose

The immunization schedule with ADACEL® should follow local recommendations.

ADACEL® may be administered to pregnant women during the second or third trimester to provide passive immunization of infants against pertussis (see sections INDICATIONS AND CLINICAL USE, WARNINGS AND PRECAUTIONS and Special Populations-Pregnant Women).

ADACEL® (0.5 mL) should be administered as a booster dose by the intramuscular route.
Re-dosing with ADACEL® can be used to boost immunity to diphtheria, tetanus and pertussis at 5- to 10-year intervals.

The preferred site is into the deltoid muscle.

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

The use of ADACEL® in management of tetanus-prone wounds should follow local recommendations. Canada's National Advisory Committee on Immunization (NACI) and US Advisory Committee on Immunization Practices (ACIP) have issued guidelines for tetanus prophylaxis in routine wound management as shown in Table 3.

Table 3: NACI Recommended Use of Immunizing Agents in Wound Management

History of Tetanus Immunization	Clean, Minor Wounds		All Other Wounds	
	Td*	TIG† (Human)	Td*	TIG† (Human)
Uncertain or < 3 doses of an immunization series‡	Yes	No	Yes	Yes
≥ 3 doses received in an immunization	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.

Administration

Inspect for extraneous particulate matter and/or discolouration before use. (See DESCRIPTION) If these conditions exist, the product should not be administered.

Shake the vial well until a uniform, cloudy, suspension results. Cleanse the vial stopper with a suitable germicide prior to withdrawing the dose. Do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient, to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines. (See WARNINGS AND PRECAUTIONS.)

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.

ACTION AND CLINICAL PHARMACOLOGY

Tetanus and Diphtheria: Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *C. tetani*. The toxin causes neuromuscular dysfunction, with rigidity and spasms of skeletal muscles. 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. A tetanus antitoxin level of at least 0.1 IU/mL as measured by the ELISA used in clinical studies of ADACEL® is considered as protective for tetanus. Levels of 1.0 IU/mL have been associated with long-term protection.

Strains of *C. diphtheriae* that produce diphtheria toxin can cause severe or fatal illness characterized by membranous inflammation of the upper respiratory tract and toxin-induced damage to the myocardium and nervous system. 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. Levels of 1.0 IU/mL have been associated with long-term protection.

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), the same pertussis components as in ADACEL® (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%. A household contact study that was nested in this efficacy trial demonstrated that there were statistically significant correlations between clinical protection and the presence of antibodies against PT, PRN and FIM in pre-exposure sera.

Minimum serum antibody levels to specific pertussis vaccine components that confer protection against the development of clinical pertussis have not been identified. 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. In ADACEL® clinical trials, in children, adolescents and adults < 65 years of age, post-vaccination Geometric Mean Concentrations (GMCs) for all pertussis antibodies were consistently above those of TRIPACEL® in the Sweden I Efficacy Trial.

In a clinical study, individuals 65 years of age and older received a single dose of Adacel vaccine. Based on pre-specified criteria, persons 65 years of age and older who received a dose of Adacel vaccine had lower geometric mean concentrations of antibodies to PT, PRN and FIM when compared to infants who had received a primary series of TRIPACEL®, Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP). Nevertheless, their post-immunization anti-pertussis antibody levels were 4.4 – 15.1-fold higher than pre-immunization levels.

Duration of Effect

Long-term follow-up of serum antibody levels in adolescents and adults who received a single dose of ADACEL® show that protective levels for tetanus antitoxin (≥ 0.01 EU/mL) and diphtheria antitoxin (≥ 0.01 IU/mL) persist in 99.2% and 92.6% of participants, respectively, 10 years post-vaccination. While protective levels against pertussis have not yet been clearly defined, pertussis antibody levels remain 2 to 9 fold higher than pre-immunization levels after 5 years. However at 10 years post-vaccination pertussis antibody levels were observed to decline towards pre-vaccination levels.

Tetanus and diphtheria toxoid boosters are recommended every 10 years. The serology follow-up and redosing data for ADACEL® suggests that it can be used instead of tetanus and diphtheria toxoid vaccine for boosting at 10-year intervals in adults.

Immunogenicity

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

Immunogenicity against pertussis in infants (<3 months of age) born to women vaccinated during pregnancy
Data from 2 published randomized controlled trials demonstrate higher pertussis antibody concentrations at birth and at 2 months of age, (ie, prior to the start of their primary vaccinations) in infants of women vaccinated with ADACEL® during pregnancy compared with infants of women not vaccinated against pertussis during pregnancy.

In the first study, 33 pregnant women received ADACEL® and 15 received saline placebo at 30 to 32 weeks gestation. The geometric mean concentrations (GMC) in EU/mL for the anti-pertussis antibodies to the PT, FHA, PRN, and FIM antigens in infants of vaccinated women were, respectively, 68.8, 234.2, 226.8, and 1867.0 at birth, and 20.6, 99.1, 75.7, and 510.4 at 2 months of age. In the control-group infants, the corresponding GMCs were 14.0, 25.1, 14.4, and 48.5 at birth, and 5.3, 6.6, 5.2, and 12.0 at 2 months. The GMC ratios (ADACEL® /control group) were 4.9, 9.3, 15.8, and 38.5 at birth, and 3.9, 15.0, 14.6, and 42.5 at 2 months.

In the second study, 134 pregnant women received Tdap and 138 received a tetanus and diphtheria control vaccine at a mean gestational age of 34.5 weeks. The GMCs (EU/mL) for the anti-pertussis antibodies to the PT, FHA, PRN, and FIM antigens in infants of vaccinated women were, respectively, 54.2, 184.2, 294.1, and 939.6 at birth, and 14.1, 51.0, 76.8, and 220.0 at 2 months of age. In the control-group infants, the corresponding GMCs were 9.5, 21.4, 11.2, and 31.5 at birth, and 3.6, 6.1, 4.4, and 9.0 at 2 months. The GMC ratios (ADACEL® /control group) were 5.7, 8.6, 26.3, and 29.8 at birth, and 3.9, 8.4, 17.5, and 24.4 at 2 months.

These higher antibody concentrations should provide passive immunity against pertussis for the infant during the first 2 to 3 months of life, as has been shown by observational effectiveness studies.

Immunogenicity in infants and toddlers born to women vaccinated during pregnancy
For infants of women vaccinated with ADACEL® or ADACEL®-POLIO during pregnancy, the immunogenicity of routine infant vaccination was assessed in several published studies. Data on the infant response to pertussis and non-pertussis antigens were evaluated during the first year of life.

Maternal antibodies derived after ADACEL® and ADACEL®-POLIO vaccination in pregnancy may be associated with blunting of the infant immune response to active immunization against pertussis. Based on current epidemiological studies, this blunting may not have clinical relevance.

Data from several studies did not show any clinically relevant blunting from vaccination in pregnancy with ADACEL® and ADACEL®-POLIO and the infants' or toddlers' responses to diphtheria, tetanus, *Haemophilus influenzae* type b, inactivated poliovirus, or pneumococcal antigens.

Effectiveness
Effectiveness against pertussis in infants born to women vaccinated during pregnancy
The vaccine effectiveness in the first 2-3 months of life for infants born to women vaccinated against pertussis during the third trimester of pregnancy has been evaluated in 3 observational studies. The overall effectiveness is > 90%.

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

Location	Vaccine	VE (95% CI)	VE estimation method	Infant follow-up period
UK	ADACEL®-POLIO	93% (81, 97)	Unmatched case-control	2 months
US	ADACEL®*	91.4% (19.5, 99.1)	cohort regression model	2 months
UK	ADACEL®-POLIO	93% (89, 95)	Screening (case-coverage)	3 months

* Approximately 99% of women were vaccinated with ADACEL®

STORAGE AND STABILITY

Store at 2° to 8°C. **Do not freeze**. Discard product if exposed to freezing. Do not use after expiration date.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

ADACEL® is supplied as a sterile uniform, cloudy, white suspension in a vial.

Composition

Each single dose (0.5 mL) contains:

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

Other Ingredients

Excipients

Aluminum Phosphate (adjuvant)	1.5 mg
2-phenoxyethanol	0.6% v/v

Manufacturing Process Residuals
Formaldehyde and glutaraldehyde are present in trace amounts.

Packaging

ADACEL® is supplied in 0.5 mL single dose glass vials.

The vials are made of Type 1 glass. The container closure system of ADACEL® is free of latex (natural rubber).

ADACEL® is available in a package of:
1 single dose vial
5 single dose vials
10 single dose vials

Manufactured by:
Sanofi Pasteur Limited
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