NEW ZEALAND DATA SHEET

1. PRODUCT NAME

ADACEL® POLIO 0.5 mL suspension for injection

Pertussis Vaccine - Acellular and Diphtheria and Tetanus Toxoids (Adsorbed) Combined with Inactivated Poliovirus Type 1, 2 and 3 (Vero cell)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Adacel Polio is a sterile, uniform cloudy, white suspension for injection in prefilled syringes .

Each 0.5 mL dose of Adacel Polio contains:

Diphtheria toxoid	≥2 IU[2] (2 Lf)
Tetanus toxoid	≥20 IU[2] (5 Lf[1])
Pertussis toxoid	2.5 micrograms
Pertussis filamentous haemagglutinin	5 micrograms
Pertactin	3 micrograms
Pertussis fimbriae 2 + 3	5 micrograms
Poliovirus inactivated type 1, Vero (Mahoney)[3]	29 D antigen Units[4]
Poliovirus inactivated type 2, Vero (MEF1)[3]	7 D antigen Units[4]
Poliovirus inactivated type 3, Vero (Saukett)[3]	26 D antigen Units[4]
Adsorbed on aluminium phosphate	1.5 mg (0.33mg aluminium)

[1]The formulated content of 5LfU per 0.5 mL of tetanus toxoid is the same as in the related product Tripacel®.
[2] As lower confidence limit (p equals 0.95) of activity measured according to the assay described in the European Pharmacopoeia.
[3] Cultivated on vero cells
[4] These antigen quantities are strictly the same as those previously expressed as 40-8-32 D-antigen units, for virus type 1, 2 and 3 respectively, when measured by another suitable immunochemical method.

This vaccine may contain traces of formaldehyde, glutaral, streptomycin sulfate, neomycin, polymyxin B sulfate and bovine serum albumin, and Medium 199 Hanks without phenol red (including phenylalanine), which are used during the manufacturing process.

For the full list of excipients, see Section 6.1 List of excipients.

The vaccine is prepared from: purified formaldehyde detoxified and adsorbed diphtheria and tetanus toxins; purified and glutaral-detoxified and adsorbed pertussis toxin (pertussis toxoid or PT); purified formaldehyde treated and adsorbed filamentous haemagglutinin (FHA); adsorbed purified pertactin (PRN) and co-purified and adsorbed fimbriae types 2 and 3 (FIM); and poliomyelitis viruses type 1, 2 and 3 cultivated on Vero cells, purified and then inactivated by formaldehyde.

Adacel Polio is a diphtheria-tetanus-acellular pertussis combination vaccine (dTpa) combined with inactivated poliovirus vaccine with a reduced content of pertussis toxoid, filamentous haemagglutinin and diphtheria toxoid compared to paediatric diphtheria-tetanus-acellular pertussis (DTPa) formulations.

Adacel Polio should not be used as part of a primary course of immunisation for diphtheria, tetanus, pertussis or poliomyelitis.

The manufacture of this product includes exposure to bovine materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

3. PHARMACEUTICAL FORM

Adacel Polio is supplied in a prefilled syringe for single dose (0.5 mL) use.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adacel Polio is indicated for active immunisation against diphtheria, tetanus, pertussis and poliomyelitis in adults, adolescents and children aged 4 years and older as a booster following primary immunisation.

Children 4-6 years of age should have already received four doses of DTPa and IPV or OPV.

Adacel Polio is not intended for primary immunisation.

Adacel Polio may be administered during pregnancy for prevention of pertussis in young infants via transplacental antibody transfer from the pregnant woman to the fetus.

The use of Adacel Polio should be determined on the basis of official recommendations. For further information, refer to the current Immunisation Handbook.

4.2 Dose and method of administration

Adacel Polio should be administered as a single injection of one dose (0.5 mL) by the intramuscular route. The same dosage applies to all age groups. Adacel Polio may be administered from the age of four years onwards.

Adacel Polio can be used for repeat vaccination, after a previous dose of Adacel Polio or Adacel, to boost immunity to diphtheria, tetanus and pertussis at 5- to 10-year intervals. Repeat vaccination should be performed taking into account national recommendations.

If Adacel Polio is administered to a pregnant woman, it should be done according to official national recommendations for pertussis vaccination of a pregnant woman. For further information, refer to the current Immunisation Handbook.

Methods of administration

Inject 0.5 mL intramuscularly. The preferred site is into the deltoid muscle. The vaccine should not be injected into the gluteal area.

The vaccine's normal appearance is a cloudy, white suspension, which may sediment during storage. Shake the prefilled syringe~~,~~ well to distribute uniformly the suspension before administering the vaccine.

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

The intravascular or subcutaneous routes should not be used.

Separate syringes, separate injection sites and preferably separate limbs must be used in case of concomitant administration.

Product is for single use in one patient on one occasion only. Discard any residue.

4.3 Contraindications

Hypersensitivity

Adacel Polio should not be administered to individuals with a history of severe allergic reaction after previous administration of the vaccine or a vaccine containing the same components or constituents

Adacel Polio should not be administered to individuals with a history of severe allergic reaction to any component of the vaccine or residues carried over from manufacture (see components listed in Section 2 - Qualitative and quantitative composition and Section 6.1 – List of excipients) or residues carried over from manufacture (such as formaldehyde, glutaraldehyde, streptomycin, neomycin and polymyxin B).

Acute Neurological Disorders

Adacel Polio should not be administered to individuals who experienced an encephalopathy of unknown origin within 7 days of previous immunisation with a pertussis-containing vaccine, or to individuals who have experienced other neurological complications following previous immunisation with any of the antigens in Adacel Polio.

Febrile or Acute Disease

Generally vaccination must be postponed in cases of moderate or severe febrile and/or acute disease. Low-grade fever does not constitute a contraindication.

4.4 Special warnings and precautions for use

General

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.

Hypersensitivity

Anaphylaxis has been reported after receipt of some preparations containing diphtheria toxoid, tetanus toxoid, and/or pertussis antigens.

This product contains as residues trace amounts of formaldehyde, glutaral, streptomycin sulfate, neomycin, polymyxin B sulfate and bovine serum albumin, as well as medium 199 Hanks, a mixture of amino acids (including phenylalanine), salts, vitamins and other compounds (including glucose). This product contains, ethanol, phenoxyethanol and polysorbate 80 as excipients. Therefore, a hypersensitivity reaction may occur.

Neurological Adverse Events

If Guillain-Barré Syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid, including Adacel Polio should be based on careful consideration of the potential benefits and possible risks, such as whether or not the primary immunisation schedule has been completed.

Adacel Polio should not be administered to individuals with progressive or unstable neurological disorder, uncontrolled epilepsy, or progressive encephalopathy until a treatment regimen has been established, the condition has stabilised and the benefit clearly outweighs the risk.

Serious and Severe Adverse Events Related Precautions

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of the vaccine. As a precautionary measure, adrenaline (epinephrine) injection (1:1000) must be immediately available in case of unexpected anaphylactic or serious allergic reactions.

The vaccine must be given intramuscularly, as subcutaneous administration increased the chances of a local reaction. A persistent nodule at the site of injection may occur with all adsorbed vaccines, particularly if administered into the superficial layers of the subcutaneous tissue.

Administration Route Related Precautions

Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

As with all injectable vaccines, the vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these individuals.

Syncope

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

Altered Immune Status

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

Protection

As with any vaccine, immunisation with Adacel Polio may not protect 100% of susceptible individuals.

Paediatric population

Adacel Polio should not be used for primary immunisation.

Adacel Polio is indicated for use in children aged four years and over.

Use in the elderly

Adacel Polio has been used in clinical studies in elderly persons aged 59 to 91 years of age.

4.5 Interactions with other medicines and other forms of interaction

A clinical study has shown that Adacel Polio can be safely administered concomitantly with hepatitis B vaccine, using a separate limb for the site of injection. Adacel Polio has safely been given concomitantly with measles-mumps-rubella vaccine (MMR™ II). Interaction studies have not been carried out with other vaccines, biological products or therapeutic medications. However, in accordance with commonly accepted immunisation guidelines, since Adacel Polio is an inactivated product, there is no theoretical reason why it should not be administered concomitantly with other vaccines or immunoglobulins at separate sites.

Separate injection sites and separate syringes must be used in case of concomitant administration.

Immunosuppressive treatment may interfere with the development of the expected immune response to Adacel Polio, refer to Section 4.4 Special warnings and precautions for use.

Effects on laboratory tests

Interference of Adacel Polio with laboratory and/or diagnostic tests has not been studied.

4.6 Fertility, pregnancy and lactation

Use in pregnancy (Category A)

Human Data

Multiple studies involving numerous pregnant women and their offspring have generated considerable safety, immunogenicity and effectiveness data on the use of Adacel Polio and Adacel, which contains the same tetanus, diphtheria and acellular pertussis components as Adacel Polio, primarily during the second and third trimesters of pregnancy.

Safety data are available from 4 randomised controlled trials (310 pregnancy outcomes), 6 observational studies (84,371 pregnancy outcomes) and from passive surveillance:

- Adacel Polio and Adacel led to no more than the expected (generally mild or moderate, and usually self-limited) adverse events for pregnant women who receive it. Safety outcomes for pregnant women were very similar to those seen when these vaccines were given to non-pregnant women of childbearing age.
- Adacel Polio and Adacel have not been shown to cause fetal harm when administered to the fetus or newborn.

Immunogenicity data from 13 studies and effective data from 3 studies have shown:

- Pertussis antibody responses following vaccination with Adacel are robust in most pregnant women, are amplified when measured in newborn cord blood, persist for 2 to 4 months in the infant, but appear to blunt (reduce) the infant's antibody responses to her or his own pertussis vaccinations later in infancy. There is no evidence to suggest that this blunting is clinically relevant in protection against pertussis.
- Adacel Polio and Adacel are > 90% effective when given to women during pregnancy in preventing pertussis disease and hospitalisation in their infants younger than 3 months of age as detailed in the following table.

Table 1 - Vaccine effectiveness (VE) against pertussis disease in young infants born to mothers vaccinated during pregnancy with Adacel Polio or Adacel 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	3 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
* over 80%-of the vaccine used in this study population was Adacel				

The decision to administer Adacel Polio to a pregnant woman should be made according to the official national recommendations for pertussis vaccination of a pregnant woman.

Breastfeeding

It is not known whether the active substances included in Adacel Polio are excreted in human milk, but antibodies to Adacel (which contains the same tetanus, diphtheria and acellular pertussis component as Adacel Polio) have been found to be transferred to the suckling offspring of rabbits.

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

Fertility

Adacel Polio has not been evaluated for impairment of fertility.

4.7 Effects on ability to drive or use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The reactions are listed within body systems and categorised by frequency according to the following definitions:

Very common	(≥ 1/10)
Common	(<1/10 and ≥1/100)
Uncommon	(<1/100 and ≥1/1,000)

Clinical Trial Experience

Adolescents and Adults (992 subjects)

In clinical studies in which Adacel Polio was administered to adolescents and adults, the most frequently reported adverse reactions occurring over all age groups during the first 24 hours after vaccination included the following:

Very common:	Injection site pain, erythema and swelling, tiredness, headache, bodyache, chills, nausea, fever, arthralgia or joint swelling
Common:	Diarrhoea, vomiting

There was a trend for higher rates of local and systemic reactions in adolescents than in adults. In both age groups, injection site pain was the most common adverse reaction.

Late-onset local adverse reactions (i.e. a local adverse reaction which had an onset or increase in severity 3 to 14 days post-immunisation), such as injection site pain, erythema and swelling, occurred in less than 1.2%.

Table 2 summarises adverse events (%) in Adacel Polio (dTpa-IPV) recipients 0 - 24 hours post vaccination:

Table 2 Adverse Events (%) in Adacel Polio (dTpa-IPV) recipients 0 - 24 hours post vaccination

Event	Children*	Adolescents†		Adults ‡	
	Sweden 5.5 Yr	TD9707	TD9809	TD9707	
	dTpa-IPV (N = 240)	dTpa-IPV (N = 350)	dTpa-IPV§ (N =144)	dTpa-IPV (N = 366)	dT (N = 126)
Local Reactions	%	%	%	%	%
Redness (Any)	-	13.5	25.0	19.7	19.8
Redness (≥2 cm)	7.5	-	-	-	-
Redness (≥5 cm)	3.3	-	-	-	-
Swelling (Any)	-	16.4	21.5	14.2	7.2
Swelling (≥2 cm)	11.7	-	-	-	-
Swelling (≥5 cm)	3.3	-	-	-	-
Pain	60.8	87.9	95.8	84.4	82.5
Systemic Reactions	%	%	%	%	%
Fever**	9.7	10.8	2.1	1.4	0.0
Headache	-	26.4	35.4	15.0	13.5
Chills	-	13.8	17.4	3.8	3.2
Body ache	-	19.8	41.0	13.4	11.9
Tiredness	11.7	29.9	40.3	15.6	16.7
Sore/Swollen Joints	-	9.2	18.1	4.1	4.8
Nausea	-	10.6	13.9	6.8	5.6
Vomiting	0.4	1.2	1.4	0.3	0.8
Diarrhoea	0.4	1.2	2.1	3.6	2.4

* ≥5 to < 6 years in Swedish children; these children were primed with DTPa at 3, 5 and 12 months of age.

† ≥12 to < 19 years of age in TD9707, and ≥11 to <14 years of age in TD9809

‡ ≥19 to 60 years of age

§ The rates for dTpa-IPV administered alone or concomitantly with Hepatitis B vaccine were comparable.

** includes fever ≥38.0 °C

Safety following repeat vaccination with Adacel

The safety and tolerability of repeat vaccination with Adacel was evaluated in two open-label, non-randomised clinical studies. Adacel Polio is identical to Adacel except for the addition of inactivated poliovirus antigen produced in Vero cells. In study Td518, adolescent and adult subjects received Adacel approximately 5 years after a previous dose of Adacel. In study Td526, adult subjects received Adacel 10 years after a previous dose of Adacel Polio or Adacel.

The frequency of solicited injection-site and systemic reactions reported following repeat administration of Adacel at 5 and 10 years are presented in Table 3

Table 3 - Frequency (%) of Solicited Reactions Observed in Adolescents and Adults Following Repeat Administration of Adacel at 5 and 10 years

Solicited Reactions	Repeat 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	28.6	23.1
Swelling	25.6	20.5
Systemic Reactions		
Myalgia	61.0	60.1
Headache	53.2	40.6
Malaise	38.2	29.4
Fever	6.5	4.2

N: Number of vaccinated subjects with a safety follow-up
* Adverse reactions observed within 0 to 14 days after vaccination
† Adverse reactions observed within 0 to 7 days after vaccination

Children 3 to 5 years old (150 subjects)

In two clinical studies (U01-Td5I-303 and U01-Td5I-402) 150 children primed at 2, 3 and 4 months of age with a DTPw vaccine (with no additional dose in the second year of life) received Adacel Polio at 3 to 5 years of age. The most frequently reported adverse reactions occurring during the first 7 days included the following:

Very common: Injection site pain, erythema and swelling; fatigue, fever ≥37.5˚C, irritability

Common: Injection site bruising and dermatitis; diarrhoea, vomiting and rash

Children 5 to 6 years old (240 subjects)

In a clinical study, children were primed at 3, 5 and 12 months of age with a DTPa vaccine with no additional dose in the second year of life. These children received Adacel Polio at 5 to 6 years of age. The most frequently reported adverse reactions occurring during the first 24 hours included the following:

Very common: Injection site pain and swelling; fatigue

Common: Injection site erythema and pruritus; fever ≥38˚C

Uncommon: Diarrhoea, vomiting

The rates of general symptoms after the first day but within 10 days after vaccination were low; only fever (≥38˚C) and fatigue were reported in >10% of subjects. Transient severe swelling of the upper arm was reported in <1% of subjects.

Children 4 to 6 years old (298 subjects)

In a clinical study, children primed with DTPa at 2, 4 and 6 months and a booster at 18 months of age received ADACEL® (dTpa) at 4 to 6 years of age. The most frequently reported adverse reaction that occurred during the first 3 days was pain at 38.3%. Erythema and swelling were also commonly reported.

Post-Marketing Experience

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. These events have been very rarely reported.

Blood and lymphatic disorders:

Lymphadenopathy

Immune system disorders:

Anaphylactic reactions, such as urticaria, face oedema and dyspnoea.

Nervous system disorders:

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

Musculoskeletal and connective tissue disorders:

Pain in vaccinated limb

Gastrointestinal disorders:

Abdominal pain

General disorders and administration site conditions:

Malaise, Pallor, injection site induration

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 of the number of prior doses of dTpa/DTPa vaccine, with a greater risk following the 4th and 5th doses.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://pophealth.my.site.com/camreportnz/s/.

4.9 Overdose

For general advice on overdose management, contact the National Poisons Centre, 0800 POISON or 0800 764 766.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccine against diphtheria, tetanus, pertussis and poliomyelitis

ATC code: J07CA02.

Clinical efficacy and safety

Immune responses of adults, adolescents and children 3 to 6 years of age one month after vaccination with Adacel Polio are shown in Table 4 below.

Table 4: Immune Responses 4 Weeks After Vaccination

Antigen	Criteria	Adults and adolescents* (N = 986)	Children 5-6 years old† (N = 240)	Children 3-5 years old‡ (N = 148)
Seroprotection Rates				
Diphtheria (1)	≥0.1 IU/ mL	92.8%	99.4%§	100%
Tetanus (2)	≥0.1 IU/ mL**	100%	99.5%	100%
Polio 1	≥1:8 Dilution	99.9%	100%	100%
Polio 2	≥1:8 Dilution	100%	100%	100%
Polio 3	≥1:8 Dilution	100%	100%	100%
Seroconversion Rates				
Pertussis (3)				
PT	≥5 EU/mL††	99.7%	91.2%	99.3%
FHA	≥5 EU/mL††	99.9%	99.1%	99.3%
PRN	≥5 EU/mL††	99.6%	100%	100%
FIM	≥5 EU/mL††	99.8%	99.5%	100%
Pertussis				
PT	4-fold rise	84.0%	92.9%	92.6%
FHA	4-fold rise	78.4%	80.2%	91.2%
PRN	4-fold rise	95.1%	96.7%	96.0%
FIM	4-fold rise	88.9%	93.3%	86.5%

* From the age of 11 years onwards

† Primed with DTPa (Diphtheria toxoid (paediatric dose), tetanus toxoid and acellular pertussis vaccine) at 3 and 5 months with a booster at 12 months of age

‡ Primed with DTPw (Diphtheria toxoid (paediatric dose), tetanus toxoid and whole cell pertussis vaccine) at 2,3 and 4 months of age

§ Tested by Vero Cell Neutralization Assay (n=162)

** Measured by ELISA

†† EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis

The safety and immunogenicity profile of Adacel Polio in adults and adolescents was shown to be comparable to that observed with a single booster dose of an adult formulation diphtheria-tetanus (Td), aP or Td Polio adsorbed vaccines containing the same amount of tetanus and diphtheria toxoids, pertussis antigens and inactivated poliovirus types 1, 2 and 3 administered separately.

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

Serological correlates for protection against pertussis have not been established. On comparison with data from the two separate pertussis efficacy trials conducted in Sweden between 1992 and 1996, where primary immunisation with Sanofi Pasteur Limited's acellular pertussis infant DTPa formulations conferred a protective efficacy of 85% against pertussis disease, it was considered that Adacel Polio had elicited protective immune responses.

Immune responses of children 4 to 6 years of age, primed with 4 doses of DTPa, one month after vaccination with ADACEL are shown in Table 5 below.

Table 5**: Immune Responses 4 Weeks After Vaccination With ADACEL (dTpa)**

Antigen	Criteria	Children 4-6 years old* (N =265)
Seroprotection Rates		
Diphtheria (1)	≥0.1 IU/ mL	100%
Tetanus (2)	≥0.1 IU/ mL†	100%
Seroconversion Rates		
Pertussis (3)		
PT	≥5 EU/mL‡	99.6%
FHA	≥5 EU/mL‡	99.6%
PRN	≥5 EU/mL‡	100.0%
FIM	≥5 EU/mL‡	100.0%
Pertussis		
PT	4-fold rise	91.9%
FHA	4-fold rise	88.1%
PRN	4-fold rise	94.3%
FIM	4-fold rise	94.6%

* Primed with DTPa at 2, 4 and 6 months and with a booster at 18 months of age
† Measured by ELISA
‡ EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis

Antibody persistence

Seroprotection rates 3 years post-vaccination with Adacel Polio in adults and adolescents are shown in Table 6 below.

Table 6**: Seroprotection Rates 3 Years Post-Vaccination with Adacel Polio in Adults and Adolescents**

Antigen	Criteria	Adults and adolescents* (N = 251)
Seroprotection Rates		
Diphtheria (1)	≥0.01 IU/mL	95.6%
Tetanus (2)	≥0.01 IU/mL†	100%
Polio 1	≥1:8 Dilution	100%
Polio 2	≥1:8 Dilution	100%
Polio 3	≥1:8 Dilution	100%
Seroconversion Rates		
Pertussis (3)		
PT	≥5 EU/mL‡	96.8%
FHA	≥5 EU/mL‡	100.0%
PRN	≥5 EU/mL‡	100.0%
FIM	≥5 EU/mL‡	98.0%

* From the age of 11 years onwards
† Measured by ELISA
‡ EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis

Immunogenicity following repeat vaccination

In an open-label, non-randomised clinical trial (Td526), 743 adults were divided into two groups for the evaluation of immunogenicity and safety following repeat vaccination with Adacel. Group 1 comprised 324 persons who previously received Adacel or Adacel Polio vaccine approximately 10 years earlier as part of study TD9707 or Td9805. Group 2 consisted of age- balanced subjects who had not received any tetanus, diphtheria or pertussis-containing vaccine in the past 10 years

One month after vaccination, seroprotective tetanus antitoxin levels ≥ 0.1 IU/mL were achieved by 100% and 99.7% of Adacel vaccinees in Groups 1 and 2 respectively. Seroprotective diphtheria antitoxin levels ≥ 0.1 IU/mL were attained by 98.5% and 96.1% in Groups 1 and 2, respectively. (See Table 7)

Table 7 - Tetanus and Diphtheria Antitoxin Seroprotection Rates in Adults in Study Td526

IU/mL			% (95% CI)	
			Group 1: dTpa Repeat Dose (N=324)	Group 2: dTpa Naïve (N= 379-381)
Anti-Tetanus	**Pre-vaccination**	**≥ 0.1**	97.5 (95.2, 98.9)	93.1 (90.1, 95.5)
		≥ 1.0	44.8 (39.3, 50.3)	49.1 (43.9, 54.2)
	Post-vaccination	**≥ 0.1**	100 (98.9, 100)	99.7 (98.5, 100)
		≥ 1.0	100 (98.9, 100)	97.6 (95.6, 98.9)
Anti-Diphtheria	**Pre-vaccination**	**≥ 0.1**	73.5 (68.3, 78.2)	65.9 (60.9, 70.6)
		≥ 1.0	24.7 (20.1, 29.8)	21.8 (17.7, 26.3)
	Post-vaccination	**≥ 0.1**	98.5 (96.4, 99.5)	96.1 (93.6, 97.8)
		≥ 1.0	87.3 (83.2, 90.8)	83.5 (79.3, 87.1)

N: total number of subjects with available data

Group 1 received a previous dose of Adacel or Adacel Polio approximately 10 years earlier as part of Sanofi Pasteur trial Td9707 or Td9805.

Group 2 had not received any tetanus, diphtheria or pertussis-containing vaccine in the past 10 years.

GMCs and booster response rates for the pertussis antigens PT, FHA, PRN and FIM pre and post repeat vaccination with Adacel in adults are presented in Table 8. Post-vaccination anti- pertussis antibody GMCs were substantially higher compared to baseline. Non-inferiority for Group 1 (dTpa Repeat Dose) compared to Group 2 (dTpa Naïve) was achieved for antibodies to PT, FHA and PRN, but not FIM. Although non-inferiority was not achieved for FIM, the lower limit of the 95% CI of the GMC ratio (0.66) was only marginally lower than non-inferiority criterion (the lower bound of the 2-sided 95% CI > 0.67). Anti-pertussis booster response rates were high (> 84%) in both Group 1 and Group 2.

Repeat vaccination with Adacel Polio at 10 year intervals induces robust immune responses to tetanus, diphtheria and pertussis in adolescents and adults.

Table 8 - Anti-pertussis GMCs and Booster Response Rates in Adults in Study Td526

Group		Pre-Vaccination		Post-Vaccination		Booster response rates*	
		N	GMCs (95% CI)	N	GMCs (95% CI)	N	% (95% CI)
Anti-PT (EU/mL)	dTpa Repeat Dose	291	15.1 (12.9; 17.6)	318	116† (105; 129)	285	87.7 (83.3; 91.3)
	dTpa Naïve	353	9.42 (8.20; 10.8)	357	89.2 (80.2; 99.3)	330	84.2 (79.9; 88.0)
Anti-FHA (EU/mL)	dTpa Repeat Dose	324	34.8 (31.2; 38.7)	324	214† (199; 231)	324	88.0 (83.9; 91.3)
	dTpa Naïve	380	20.0 (17.7; 22.5)	380	249 (229; 272)	379	93.9 (91.0; 96.1)
Anti-PRN (EU/mL)	dTpa Repeat Dose	324	28.2 (24.4; 32.7)	324	266† (243; 292)	324	90.4 (86.7; 93.4)
	dTpa Naïve	381	8.54 (7.41; 9.85)	381	216 (188; 247)	381	92.7 (89.6; 95.1)
Anti-FIM (EU/mL)	dTpa Repeat Dose	324	124 (111; 139)	324	779 (720; 843)	324	84.3 (79.8; 88.0)
	dTpa Naïve	374	37.8 (32.7; 43.7)	378	1015 (894; 1154)	371	93.0 (89.9; 95.4)

* Booster response is defined as subjects whose post-vaccination antibody concentrations are ≥ 4 x LLOQ, if the pre-vaccination concentration was < LLOQ; ≥ 4 x the pre-vaccination antibody concentration, if the pre-vaccination concentration was ≥ LLOQ but < 4 x LLOQ; ≥ 2 x the pre-vaccination antibody concentration, if the pre-vaccination concentration was ≥ 4 x LLOQ

LLOQ: PT=4 EU/mL; FHA=3 EU/mL; PRN=4 EU/mL; FIM=4 EU/mL.

N: Number of subjects with available data

† Non-inferiority for GMCs was achieved (the lower bound of the two sided 95% CI is greater than 0.67)

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been performed.

5.3 Preclinical safety data

Genotoxicity

Adacel Polio has not been evaluated for genotoxic potential.

Carcinogenicity

Adacel Polio has not been evaluated for carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium phosphate

ethanol

phenoxyethanol

polysorbate 80

water for injections

Manufacturing process residuals per dose include ≤5 µg formaldehyde, ≤0.02 mg glutaral, ≤0.2 µg streptomycin sulfate, ≤0.02 µg neomycin, ≤0.025 µg polymyxin B sulfate, Medium 199 Hanks (without phenol red) and bovine serum albumin.

6.2 Incompatibilities

The vaccine must not be mixed with other vaccines or medicinal products.

6.3 Shelf life

48 months at 2° to 8°C.

6.4 Special precautions for storage

Store at 2º to 8ºC. REFRIGERATE. DO NOT FREEZE. Do not use after expiry date.

In the absence of photostability studies, store the vaccine container in its original packaging.

6.5 Nature and contents of container

0.5 mL of suspension in pre-filled syringe – pack size of 1 syringe with or without separate needles

6.6 Special precautions for disposal

After use, any remaining vaccine and container must be disposed of safely according to locally agreed procedures.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Freecall: 0800 283 684
Email: medinfo.australia@sanofi.com

Manufacturer

SANOFI PASTEUR LIMITED
Toronto, Ontario, Canada

9. DATE OF FIRST APPROVAL

28 February 2008

10. DATE OF REVISION OF THE TEXT

26 March 2024

Summary Table of Changes

Section changed	Summary of new information
2, 3, 4.2 and 6.5	Removal of references to vials and 5 packs