HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use QUADRACEL® safely and effectively. See full prescribing information for QUADRACEL.

QUADRACEL (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine) injectable suspension, for intramuscular use

Initial U.S. Approval: 2015

----------INDICATIONS AND USAGE----------

Quadracel is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis. A single dose of Quadracel is approved as a fifth dose in the diphtheria, tetanus, pertussis (DTaP) vaccination series, and as a fourth or fifth dose in the inactivated poliovirus (IPV) vaccination series in children 4 through 6 years of age whose previous DTaP vaccine doses have been with Pentacel, DAPTACEL and/or VAXELIS. (1)

----------DOSAGE AND ADMINISTRATION----------

For intramuscular use. (2)

Administer Quadracel as a single 0.5 mL dose. (2)

----------DOSAGE FORMS AND STRENGTHS----------

- Injectable suspension. A single dose is 0.5 mL. (3)

----------CONTRAINDICATIONS----------

- Severe allergic reaction (e.g., anaphylaxis) to any ingredient of Quadracel, or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine or inactivated poliovirus vaccine. (4.1)
- Encephalopathy within 7 days of a previous pertussis-containing vaccine with no other identifiable cause. (4.2)
- Progressive neurologic disorder until a treatment regimen has been established and the condition has stabilized. (4.3)

----------WARNINGS AND PRECAUTIONS----------

- Carefully consider benefits and risks before administering Quadracel to persons with a history of:
  - fever ≥40.5°C (≥105°F), hypotonic-hyporesponsive episode (HHE) or persistent, inconsolable crying lasting ≥3 hours within 48 hours after a previous pertussis-containing vaccine. (5.2)
  - seizures within 3 days after a previous pertussis-containing vaccine. (5.2)
- If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including Quadracel, should be based on careful consideration of the potential benefits and possible risks. (5.3)

----------ADVERSE REACTIONS----------

In a clinical study, the most common solicited injection site reactions were pain (>75%), increase in arm circumference (>65%), erythema (>55%), and swelling (>40%). Common solicited systemic reactions were myalgia (>50%), malaise (>35%), and headache (>15%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Vaccines US Inc., at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or http://vaers.hhs.gov

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Quadracel® is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis. A single dose of Quadracel is approved for use as a fifth dose in the diphtheria, tetanus, pertussis (DTaP) vaccination series, and as a fourth or fifth dose in the inactivated poliovirus (IPV) vaccination series in children 4 through 6 years of age whose previous DTaP vaccine doses have been with Pentacel® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus and Haemophilus b conjugate (Tetanus Toxoid Conjugate) Vaccine], DAPTACEL® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) and/or VAXELIS (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine).

2 DOSAGE AND ADMINISTRATION

For intramuscular use.

Just before use, shake the vial or prefilled syringe well, until a uniform, white, cloudy suspension results.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the product should not be administered.

Administer a 0.5 mL dose of Quadracel intramuscularly. Discard unused portion in vial.

Quadracel should not be combined through reconstitution or mixed with any other vaccine.

When Quadracel is given at the same time as another injectable vaccine(s), the vaccines should be administered with different syringes and at different injection sites.

3 DOSAGE FORMS AND STRENGTHS

For injectable suspension. A single dose is 0.5 mL.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Severe allergic reaction (e.g., anaphylaxis) to any ingredient of Quadracel *[see Description (11)]* or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, or inactivated poliovirus vaccine, is a contraindication to administration of Quadracel.

4.2 Encephalopathy

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, including Quadracel.

4.3 Progressive Neurologic Disorder

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy is a contraindication to administration of any pertussis-containing vaccine including Quadracel. Pertussis vaccine should not be administered to individuals with such conditions until a treatment regimen has been established and the condition has stabilized.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Quadracel.

5.2 Adverse Reactions Following Prior Pertussis Vaccination

If any of the following events have occurred within the specified period after administration of a pertussis vaccine, the decision to administer Quadracel should be based on careful consideration of benefits and risks.

- Temperature of ≥40.5°C (≥105°F) within 48 hours, not attributable to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode [HHE]) within 48 hours.
- Persistent, inconsolable crying lasting ≥3 hours within 48 hours.
- Seizures with or without fever within 3 days.

5.3 Guillain-Barré Syndrome

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

5.4 Limitations of Vaccine Effectiveness

Vaccination with Quadracel may not protect all individuals.

5.5 Altered Immunocompetence

If Quadracel is administered to immunocompromised persons, including persons receiving immunosuppressive therapy, the expected immune response may not be obtained.

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to Quadracel.

5.6 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines including Quadracel. Procedures should be in place to avoid injury from fainting.

6 ADVERSE REACTIONS

In a clinical study, the most common solicited injection site reactions were pain (>75%), increase in arm circumference (>65%), erythema (>55%), and swelling (>40%). Common solicited systemic reactions were myalgia (>50%), malaise (>35%), and headache (>15%).

6.1 Clinical Trials Experience

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 poliovirus component (poliovirus types 1, 2, and 3) of this formulation of Quadracel is grown in Vero cells *[see Description (11)].* The clinical study data in this section were accrued with a Quadracel formulation in which poliovirus component was grown in MRC-5 cells.

In a randomized, controlled, multicenter study conducted in the US and Puerto Rico (Study M5I02; ClinicalTrials.gov Identifier: NCT01346293), 3,372 children, 4 to 6 years of age, who had received 4 doses of DAPTACEL and/or Pentacel vaccine(s) received Quadracel, or DAPTACEL + IPOL (Poliovirus Vaccine Inactivated) vaccines administered concomitantly but at separate sites. Subjects also received Measles, Mumps, and Rubella Virus Vaccine Live (MMR) (Merck & Co., Inc.) and Varicella Virus Vaccine Live (Varicella vaccine) (Merck & Co., Inc.) administered concomitantly at separate sites. Safety was evaluated in 2,733 subjects who received Quadracel and 621 subjects who received DAPTACEL + IPOL vaccines.

Among these subjects, 51.5% were male, 48.5% were female, 75.7% were Caucasian, 8.6% were Black, 7.9% were Hispanic, 0.9% were Asian, and 7.8% were of other racial/ethnic groups. The mean age for both groups was 4.4 years and the ratio of male to female subjects and ethnicity were balanced between both groups.

Solicited injection site reactions and systemic reactions were collected daily for 7 days following vaccination, via diary cards. Participants were monitored for unsolicited adverse events for 28 days and serious adverse events (SAEs) for 6 months after vaccination.

Solicited Adverse Reactions

The incidence and severity of solicited injection site and systemic adverse reactions that occurred within 7 days after vaccination in each study group are shown in Table 1.

Table 1: Percentage of Children 4 through 6 years of Age with Solicited Adverse Reactions by Intensity Within 7 Days of Vaccination with Quadracel or Concomitant but Separate DAPTACEL and IPOL vaccines Co-Administered with MMR and Varicella Vaccines*

	Quadracel (N[†]= 2,500-2,689)	**DAPTACEL + IPOL (N[†] = 598-603)**
Injection Site Reactions	**Quadracel site**	**DAPTACEL or IPOL site**
Pain[‡], Any	77.4	76.5
Pain[‡], Grade 1	56.4	54.9
Pain[‡], Grade 2	19.0	18.6
Pain[‡], Grade 3	2.0	3.0
Change in limb circumference[§], Any	68.1	65.1
Change in limb circumference[§], Grade 1	59.8	58.6
Change in limb circumference[§], Grade 2	8.2	6.5
Change in limb circumference[§], Grade 3	0.2	0.0
Erythema, Any	59.1	53.4
Erythema, >0 to <25 mm	31.6	31.8
Erythema, ≥25 to <50 mm	9.5	9.6
Erythema, ≥50 mm	18.0	11.9
Swelling, Any	40.2	36.4
Swelling, >0 to <25 mm	23.5	23.1
Swelling, ≥25 to <50 mm	8.1	6.1
Swelling, ≥50 mm	8.6	7.1
Extensive limb swelling[¶], Any	1.5	1.3
Systemic Reactions		
Myalgia[#], Any	53.8	52.6
Myalgia[#], Grade 1	36.0	33.5
Myalgia[#], Grade 2	15.8	16.3
Myalgia[#], Grade 3	1.9	2.8
Malaise[#], Any	35.0	33.2
Malaise[#], Grade 1	21.7	18.7
Malaise[#], Grade 2	10.6	11.1
Malaise[#], Grade 3	2.6	3.3
Headache[#], Any	15.6	16.6
Headache[#], Grade 1	11.9	11.9
Headache[#], Grade 2	3.1	4.0
Headache[#], Grade 3	0.6	0.7
Fever, Any	6.0	6.9
Fever ≥38.0°C to ≤38.4°C	2.6	3.0

	Quadracel (N†= 2,500-2,689)	DAPTACEL + IPOL (N† = 598-603)
Fever, ≥38.5°C to ≤38.9°C	2.1	1.8
Fever, ≥39.0°C	1.3	2.0

***** ClinicalTrials.gov Identifier: NCT01346293.
† N = The number of subjects with available data.
‡ Grade 1: Easily tolerated, Grade 2: Sufficiently discomforting to interfere with normal behavior or activities, Grade 3: Incapacitating, unable to perform usual activities.
§ Grade 1: >0 to <25 mm increase over pre-vaccination measurement, Grade 2: ≥25 to ≤50 mm increase over pre-vaccination measurement, Grade 3: >50 mm increase over pre-vaccination measurement.
¶ Swelling of the injected limb including the adjacent joint (i.e., elbow and/or shoulder) as compared to baseline.
# Grade 1: No interference with activity, Grade 2: Some interference with activity, Grade 3: Significant; prevents daily activity.

Serious Adverse Events

In Study M5I02, within 28 days following vaccination with Quadracel, or DAPTACEL + IPOL vaccines, and concomitant MMR and varicella vaccines, 0.1% of subjects (3/2,733) in the Quadracel group experienced a serious adverse event. During the same time period, 0.2% subjects (1/621) in the DAPTACEL + IPOL group experienced a SAE. Within the 6-month follow-up period after vaccination, SAEs were reported in 0.8% of subjects (21/2,733) who received Quadracel and 0.5% of subjects (3/621) who received DAPTACEL + IPOL vaccines, none of which were assessed as related to vaccination.

6.2 Postmarketing Experience

The following adverse events have been spontaneously reported, during the postmarketing use of Quadracel outside the US, in infants and children from 2 months through 6 years of age. Because these events are reported voluntarily from a population of uncertain size, it is not possible to estimate their frequency reliably or establish a causal relationship to vaccine exposure. This list includes adverse reactions based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Quadracel.

- *Immune system disorders*
  Anaphylactic reaction, hypersensitivity and allergic reactions (such as rash, urticaria, dyspnea)
- *Psychiatric disorders*
  Screaming
- *Nervous system disorders*
  Somnolence, convulsion, febrile convulsion, HHE, hypotonia
- *Cardiac disorders*
  Cyanosis
- *Vascular disorders*
  Pallor
- *General disorders and administration site conditions*
  Listlessness
  Injection site reactions (including inflammation, mass, sterile abscess, and edema)

Large injection site reactions (>50 mm), including limb swelling which may extend from the injection site beyond one or both joints

- *Infections and Infestations*
  Injection site cellulitis, injection site abscess

8 USE IN SPECIFIC POPULATIONS

8.4 Pediatric Use

The safety and effectiveness of Quadracel has not been established in children less than 4 years of age or children 7 through 16 years of age and is not approved for use in these age groups.

11 DESCRIPTION

Quadracel (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine) is a sterile injectable suspension for intramuscular use.

Each 0.5 mL dose is formulated to contain 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, acellular pertussis antigens [20 mcg detoxified pertussis toxin (PT), 20 mcg filamentous hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM)], and inactivated polioviruses [29 D-antigen units (DU) Type 1 (Mahoney), 7 DU Type 2 (MEF-1), 26 DU Type 3 (Saukett)].

Corynebacterium diphtheriae is grown in modified Mueller's growth medium. (1) After purification by ammonium sulfate fractionation, the diphtheria toxin is detoxified with formaldehyde and diafiltered.

Clostridium tetani is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (2) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and diafiltration. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate.

The acellular pertussis vaccine antigens are produced from *Bordetella pertussis* cultures grown in Stainer-Scholte medium (3) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. PT, FHA and PRN are isolated separately from the supernatant culture medium. FIM are extracted and copurified from the bacterial cells. The pertussis antigens are purified by sequential filtration, salt-precipitation, ultrafiltration and chromatography. PT is detoxified with glutaraldehyde. FHA is treated with formaldehyde and the residual aldehydes are removed by ultrafiltration. The individual antigens are adsorbed separately onto aluminum phosphate.

The Type 1, Type 2, and Type 3 polioviruses are individually grown in Vero cells (a continuous line of monkey kidney cells). Prior to viral propagation, the cells are grown in Iscove's medium, supplemented with calf serum. For viral propagation, the culture medium is replaced by M199 medium without calf serum. The viral harvests are concentrated and purified, then inactivated with formaldehyde to produce monovalent suspensions of each serotype. Specified quantities of monovalent suspensions of each serotype are mixed to produce the trivalent poliovirus concentrate. The adsorbed diphtheria, tetanus and acellular pertussis antigens are combined with aluminum phosphate, 2-phenoxyethanol (not as a preservative) and water for injection, into an intermediate concentrate. The trivalent poliovirus concentrate is added and the vaccine is diluted to its final concentration.

Each 0.5 mL dose contains 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, <8.1 mcg polysorbate 80, 3.3 mg (0.6% v/v) 2-phenoxyethanol (not as a preservative), 2 mcg to 7 mcg residual formaldehyde, <50 ng residual glutaraldehyde, ≤10 ng residual bovine serum albumin, <0.0001 pg streptomycin sulphate, <0.01 pg of neomycin and <0.000001 pg polymyxin B sulphate.

Quadracel does not contain a preservative.

The potency of diphtheria and tetanus toxoids is measured by *in vitro* diphtheria and tetanus antigenicity enzyme-linked immunosorbent assay (ELISA) which detects immunologically relevant epitopes. The potency of the acellular pertussis antigen PT is evaluated by the antibody response of immunized mice to detoxified forms as measured by ELISA. The potency of the acellular pertussis antigen PRN, FHA and FIM is measured by *in vitro* PRN, FHA and FIM antigenicity ELISA. The potency of the inactivated poliovirus antigens is determined by using an *in vitro* D-Antigen ELISA for each serotype.

The vial stopper, syringe plunger stopper, and syringe tip cap are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease 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. (4) Levels of 1.0 IU/mL have been associated with long-term protection. (5)

Tetanus

Tetanus is an acute disease caused by an extremely potent neurotoxin produced by *C. tetani*. Protection against disease 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) (6). A tetanus antitoxoid level ≥0.1 IU/mL as measured by the ELISA used in clinical studies of Quadracel is considered protective.

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.

There is no well-established serological correlate of protection for pertussis. Because DAPTACEL contains the same pertussis antigens manufactured by the same process as those in Quadracel, the effectiveness of Quadracel against pertussis was based on a comparison of pertussis immune responses following Quadracel to those following DAPTACEL (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) [*see Clinical Studies (14)*]. The efficacy of the pertussis component of DAPTACEL was determined in clinical trials of DAPTACEL administered to infants (*see* DAPTACEL prescribing information). Quadracel

contains twice as much detoxified PT and four times as much FHA as DAPTACEL. Quadracel contains the same quantity of the same pertussis antigens manufactured by the same process as those in Pentacel and VAXELIS.

Poliomyelitis

Polioviruses, of which there are three serotypes (Types 1, 2, and 3), are enteroviruses. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliomyelitis. (7)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Quadracel has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility in animals.

14 CLINICAL STUDIES

The poliovirus component (poliovirus types 1, 2 and 3) of this formulation of Quadracel is grown in Vero cells *[see Description (11)]*. The clinical study data in this section were accrued with a Quadracel formulation in which the poliovirus component was grown in MRC-5 cells. The poliovirus component of the two formulations of Quadracel are analytically comparable.

14.1 Immunogenicity

In Study M5I02, children 4 through 6 years of age received Quadracel or DAPTACEL + IPOL as the fifth dose in the diphtheria, tetanus, and pertussis vaccination series and the fourth or fifth dose in the inactivated poliovirus vaccination series. Subjects also received their second dose of MMR and Varicella vaccines, concomitantly. The immunogenicity subset comprised 263 subjects in the Quadracel group and 253 subjects in the DAPTACEL + IPOL vaccines group *[see Adverse Reactions (6.1)]*.

Antibody levels to diphtheria, tetanus, pertussis (PT, FHA, PRN and FIM) and poliovirus antigens were measured in sera obtained immediately prior to vaccination and 28 days after vaccination. The co-primary endpoints were booster response rates and antibody geometric mean concentrations/titers (GMCs/GMTs) to diphtheria, tetanus, pertussis and poliovirus antigens elicited after vaccination. Booster response rates and antibody GMCs/GMTs following Quadracel vaccination were compared to those after DAPTACEL + IPOL vaccination.

Quadracel was noninferior to DAPTACEL + IPOL vaccines administered concomitantly at separate sites, as demonstrated by comparison of the postvaccination antibody booster response rates and GMCs/GMTs to diphtheria and tetanus (Table 2), to all pertussis antigens (Table 3) and to poliovirus 1, 2 and 3 (Table 4).

Table 2: Booster Response Rates, Pre- and Postvaccination Seroprotection Rates and Postvaccination Antibody Levels to Diphtheria and Tetanus Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines*

	Quadracel (N†=253-262)	DAPTACEL + IPOL (N†=248-253)
Anti-Diphtheria		
% Booster Response‡	97.3§	99.2
Pre-vaccination % ≥0.1 IU/mL¶	90.7	83.1
Postvaccination % ≥0.1 IU/mL¶	100.0	99.6
Postvaccination % ≥1.0 IU/mL¶	99.6	99.6
Postvaccination GMC (IU/mL)	18.6#	15.5
Anti-Tetanus		
% Booster Response‡	84.2§	84.3
Pre-vaccination % ≥0.1 IU/mL¶	91.7	89.1
Postvaccination % ≥0.1 IU/mL¶	100.0	99.2
Postvaccination % ≥1.0 IU/mL¶	98.9	96.8
Postvaccination GMC (IU/mL)	6.4#	5.5

***** ClinicalTrials.gov Identifier: NCT01346293.

† N = The number of subjects with available data.

‡ Booster response: In subjects with pre-vaccination antibody concentrations <0.1 IU/mL, a postvaccination level ≥0.4 IU/mL; in subjects with pre-vaccination antibody concentrations ≥0.1 IU/mL but <2.0 IU/mL, a 4-fold rise in postvaccination level; in subjects with pre-vaccination antibody level ≥2.0 IU/mL, a 2-fold rise in postvaccination level.

§ Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination booster response rates for diphtheria and tetanus (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were >-10%).

¶ Seroprotection: anti-diphtheria and anti-tetanus antibody concentrations ≥ 0.1 IU/mL and ≥ 1.0 IU/mL.

Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination GMCs for diphtheria and tetanus (lower limits of the 2-sided 95% CIs of the ratio [Quadracel / DAPTACEL + IPOL] were >2/3).

Table 3: Booster Response Rates and Postvaccination Antibody Levels to Pertussis Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines*

	Quadracel (N†=250-255)	DAPTACEL + IPOL (N†=247-249)
Anti-PT		
% Booster Response‡	95.2§	89.9
Postvaccination GMC (EU/mL)	120.7¶	61.3
Anti-FHA		
% Booster Response‡	94.9§	87.5
Postvaccination GMC (EU/mL)	123.5¶	79.0
Anti-PRN		
% Booster Response‡	96.9§	93.1
Postvaccination GMC (EU/mL)	282.6¶	187.5
Anti-FIM		
% Booster Response‡	97.2§	92.4
Postvaccination GMC (EU/mL)	505.8¶	378.9

* ClinicalTrials.gov Identifier: NCT01346293.

† N = The number of subjects with available data.

‡ Booster response: In subjects with pre-vaccination antibody concentrations <LLOQ, a postvaccination level ≥4xLLOQ; in subjects with pre-vaccination antibody concentrations ≥LLOQ but <4xLLOQ, a 4-fold rise in postvaccination level; in subjects with pre-vaccination antibody level ≥4xLLOQ, a 2-fold rise in postvaccination level.

§ Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination booster response rates for all pertussis antigens (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were > -10%).

¶ Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination GMCs for all pertussis antigens (lower limits of the 2-sided 95% CIs of the ratio [DTaP-IPV / DAPTACEL + IPOL] were >2/3).

Table 4: Booster Response Rates, Pre- and Postvaccination Seroprotection Rates and Postvaccination Antibody Levels to Poliovirus Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines*

	Quadracel (N†=247-258)	DAPTACEL + IPOL (N†=248-253)
Anti-Poliovirus 1		
% Booster Response‡	85.9§	82.3
Pre-vaccination % ≥1:8 dilution	98.4	98.8
Postvaccination % ≥1:8 dilution	100.0	99.6
Postvaccination GMT	3,477¶	2,731
Anti-Poliovirus 2		
% Booster Response‡	78.3§	79.0
Pre-vaccination % ≥1:8 dilution	99.6	99.6
Postvaccination % ≥1:8 dilution	100.0	100.0
Postvaccination GMT	3,491¶	3,894
Anti-Poliovirus 3		
% Booster Response‡	85.0§	84.7
Pre-vaccination % ≥1:8 dilution	96.8	93.1
Postvaccination % ≥1:8 dilution	100.0	100.0
Postvaccination GMT	4,591¶	3,419

* ClinicalTrials.gov Identifier: NCT01346293.

† N = The number of subjects with available data.

‡ Booster response: In subjects with pre-vaccination antibody concentrations <1:8 dilution, postvaccination levels ≥1:8 dil; in subjects with pre-vaccination antibody concentrations ≥1:8 dilution, a 4-fold rise in postvaccination antibody levels.

§ Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination booster response rates for polio types 1, 2 and 3 (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were > -10%).

¶ Quadracel was noninferior to DAPTACEL + IPOL based on the postvaccination GMTs for polio types 1, 2 and 3 (lower limits of the 2-sided 95% CIs of the ratio [Quadracel / DAPTACEL + IPOL] were >2/3).

15 REFERENCES

1 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 91-1174. 1991:7-11.

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

3 Stainer DW, Scholte MJ. A simple chemically defined medium for the production of phase I Bordetella pertussis. J Gen Microbiol 1970;63:211-20.

4 Department of Health and Human Services, Food and Drug Administration. Biological products; bacterial vaccines and toxoids; implementation of efficacy review; proposed rule. Federal Register 1985;50(240):51002-117.

5 Vitek CR, Tiwari TSP, Wharton M. Diphtheria toxoid. In: Plotkin SA, Orenstein WA, and Offit PA, editors. Vaccines. 7th ed. Philadelphia, PA: WB Saunders; 2018;7:261-75.

6 Roper M, Wassilak SGF, Tiwari TSP, Orenstein WA. Tetanus toxoid. In: Plotkin SA, Orenstein WA, and Offit PA, editors. Vaccines. 7th ed. Philadelphia, PA: WB Saunders; 2018;18:1052-79.

7 Sutter RW, et al. Defining surrogate serologic tests with respect to predicting protective vaccine efficacy: Poliovirus vaccination. In: Williams JC, et al. eds. Combined vaccines and simultaneous administration. Current issues and perspectives. New York, NY: The New York Academy of Sciences. 1995:289-99.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- Single-dose vial (NDC No. 49281-564-58) is supplied as package of 10 vials (NDC No. 49281-564-10).
- Single-dose, prefilled syringe, without needle, (NDC No. 49281-564-88). Supplied as package of 10 prefilled syringes (NDC No. 49281-564-15).

16.2 Storage and Handling

Store refrigerated at 2° to 8°C (35° to 46°F).

Do not freeze. Do not use product which has been frozen. Do not use after expiration date shown on the label.

17 PATIENT COUNSELING INFORMATION

Inform the parent or guardian of the following:

- The potential benefits and risks of immunization with Quadracel.
- The common adverse reactions that have occurred following administration of Quadracel or other vaccines containing similar components.
- Other adverse reactions can occur. Call a healthcare provider with any adverse reactions of concern.

Provide the Vaccine Information Statements (VIS), which are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization.

Instruct the parent or guardian to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or https://vaers.hhs.gov.

Manufactured by:

Sanofi Vaccines Canada Ltd.
Toronto Ontario Canada

Distributed by:

Sanofi Vaccines US Inc.
Swiftwater PA 18370 USA

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