PRODUCT MONOGRAPH

ACTacel® Hybrid

Act-HIB® Reconstituted with TRIPACEL® Hybrid

**Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate)
Reconstituted with Diphtheria and Tetanus Toxoids
and Acellular Pertussis Vaccine Adsorbed**

Reconstituted product for injection

(For active immunization against
(*Haemophilus influenzae* type b disease, Diphtheria, Tetanus and Pertussis)

ATC Code: J07AG52

Sanofi Pasteur Limited
Toronto, Ontario, Canada

and

Sanofi Pasteur SA
Lyon, France

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration

Intramuscular injection

Dosage Form / Strength

Reconstituted product for injection

Each single dose (approximately 0.5 mL) after reconstitution contains:

Active Ingredients:

Purified polyribosylribitol phosphate capsular polysaccharide (PRP) of *Haemophilus influenzae* type b covalently bound to tetanus protein, diphtheria toxoid, tetanus toxoid and acellular pertussis [pertussis toxoid (PT), filamentous haemagglutinin (FHA), pertactin (PRN), fimbriae types 2 and 3 (FIM)].

Clinically Relevant Non-medicinal Ingredients

Excipients: Aluminum phosphate (adjuvant), 2-phenoxyethanol, Tris (hydroxymethyl amino methane), sucrose

Manufacturing process residuals: Formaldehyde and glutaraldehyde are present in trace amounts.

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

DESCRIPTION

ACTacel® Hybrid [Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed] is supplied in two vials: one vial containing lyophilized Haemophilus b conjugate vaccine consisting of the *Haemophilus influenzae* type b capsular polysaccharide PRP covalently bound to tetanus protein, and one vial containing a suspension of diphtheria and tetanus toxoids adsorbed on aluminum phosphate and 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). After reconstitution, the vaccine is a sterile, uniform, cloudy, white to off-white suspension.

INDICATIONS AND CLINICAL USE

ACTacel® Hybrid is indicated for the primary immunization of infants from the age of 2 months and in children up to 6 years of age (prior to their 7th birthday) against invasive *H. influenzae* type b disease, diphtheria, tetanus and pertussis (whooping cough). (See DOSAGE AND ADMINISTRATION.)

Currently, Haemophilus b conjugate vaccines are not recommended for infants younger than 2 months of age.

According to the National Advisory Committee on Immunization (NACI), children who have had invasive *H. influenzae* type b (Hib) infection, diphtheria, tetanus, or pertussis, should still be immunized since these clinical infections do not always confer immunity. (1) For persons who have been exposed to invasive Hib and who are incompletely immunized, refer to the guidelines in the Canadian Immunization Guide.

NACI recommends that Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against *H. influenzae* type b, diphtheria, tetanus and pertussis according to standard schedules. (1)

ACTacel® Hybrid is not to be used for the treatment of diseases caused by *H. influenzae* type b, *Corynebacterium diphtheriae, Clostridium tetani,* or *Bordetella pertussis* infections.

Pediatrics

ACTacel® Hybrid is not indicated for persons less than 2 months of age or persons 7 years of age or older.

Geriatrics

ACTacel® Hybrid is not indicated for use in adult and elderly populations.

CONTRAINDICATIONS

Hypersensitivity

NACI recommends that known systemic hypersensitivity reaction to any component of ACTacel® Hybrid 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. (1) (2) (3) (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.

Neurological Disorders

According to the Advisory Committee on Immunization Practices (ACIP), the following events are contraindications to administration of any pertussis-containing vaccine, (2) including ACTacel® Hybrid:

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.

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy. Pertussis vaccine should not be administered to persons with such conditions until a treatment regimen has been established and the condition has stabilized.

WARNINGS AND PRECAUTIONS

General

Before administration of ACTacel® Hybrid, health-care providers should inform the parent or guardian of the recipient to be immunized 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 with respect to information to be provided to the parent or guardian before immunization and the importance of completing the immunization series.

It is extremely important that the 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. (3)

Very rarely, large injection site reactions (>50 mm), including limb swelling which may extend from the injection site beyond one or both joints have been reported in children following d/DTaP administration. 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, with a greater risk following the 4th and 5th doses.

Vaccines that contain Hib antigen do not provide protection against infections with other types of *H. influenzae*, or against meningitis of other origin.

Under no circumstances can the tetanus protein contained in conjugate vaccines containing tetanus toxoid as protein carrier be used to replace the usual tetanus vaccination.

Edematous reaction affecting one or both lower limbs has occurred following vaccination with *H. influenzae* type b-containing vaccines. When this reaction occurs, it does so mainly after primary injections and is observed within the first few hours following vaccination. Associated symptoms may include cyanosis, redness, transient purpura and severe crying. In reported cases, all events resolved spontaneously without sequelae within 24 hours.

As with any vaccine, ACTacel® Hybrid may not protect 100% of susceptible individuals.

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

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

ACTacel® Hybrid should not be administered into the buttocks.

Febrile or Acute Disease: ACIP recommends that vaccination should be postponed in cases of an acute or febrile disease. (2) (3). However, a disease with low-grade fever should not usually be a reason to postpone vaccination.

ACIP recommends that if any of the following events occur within the specified period after administration of a whole-cell pertussis vaccine or a vaccine containing an acellular pertussis component, the decision to administer ACTacel® Hybrid should be based on careful consideration of potential benefits and possible risks. (2)

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

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 ACTacel® Hybrid 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 ACTacel® Hybrid even in persons with no prior history of hypersensitivity to the product components. Cases of allergic or anaphylactic reaction have been reported after receiving some preparations containing diphtheria and tetanus toxoids and/or pertussis antigens. (4)

As recommended by NACI and 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.

According to NACI immunocompromised persons (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. (1) Nevertheless, ACIP advises that vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited. (2)

Neurologic

A review by the US Institute of Medicine (IOM) found evidence for a causal relationship between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome (GBS). (5) ACIP recommends that if GBS occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give ACTacel® Hybrid or any vaccine containing tetanus toxoid should be based on careful consideration of potential benefits and possible risks. (2)

ACIP recommends that for infants or children at higher risk for seizures than the general population that an appropriate antipyretic may be administered (in the dosage recommended in its prescribing information) at the time of vaccination with a vaccine containing an acellular pertussis component (including ACTacel® Hybrid) and for the following 24 hours, to reduce the possibility of post-vaccination fever. (2)

Hypotonic-hyporesponsive episodes (HHEs) rarely follow vaccination with whole-cell pertussis-containing DTP vaccines and occur even less commonly after acellular pertussis-containing DTP vaccines and DT vaccines. NACI states that a history of HHEs is not a contraindication to the use of acellular pertussis vaccines but recommends caution in these cases. (1)

Pregnant Women:

This vaccine is not indicated for persons 7 years of age and older.

Nursing Women:

This vaccine is not indicated for persons 7 years of age and older.

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.

In a randomized controlled clinical study conducted in Taiwan, 68 infants were vaccinated with TRIPACEL® Hybrid used to reconstitute Act-HIB® [Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate)], at 2, 4 and 6 months of age. A fourth dose was administered to 62 of these children at 18 months of age. Table 1 below presents the rates of solicited adverse reactions observed in this study. Injection site reactions were reported in up to 38.8% of children. A systemic reaction was reported in up to 47.8% of children. Injection site reactions tended to be

reported as being mild or moderate, and systemic reactions, if present, were usually mild. Reactions tended to be reported at lower rates with each subsequent dose, with the most marked decrease of the 18 months dose. No seizure, HHE or Sudden Infant Death Syndrome (SIDS) was reported in this study. (6) (7)

Table 1: Frequency (%) of Solicited Reactions Observed Within 48 Hours Following a Single Dose of ACTacel® Hybrid Administered at 2,4, 6 and 18 Months of Age. (6) (7)

Solicited Reaction	2 Months	4 Months	6 Months	18 Months
Injection Site Reactions				
Redness	19.4	10.6	15.6	0.0
Swelling	22.4	16.7	17.2	0.0
Tenderness	28.4	13.6	15.6	0.0
Systemic Reactions				
Fever	8.7	9.8	5.1	0.0
Fussiness	35.8	24.2	18.8	3.3
Crying	22.4	13.6	1.6	0.0
Eating Less	20.9	10.6	10.9	1.6
Less Active	6.0	3.0	1.6	0.0
Vomiting	4.5	3.0	0.0	0.0
Diarrhea	4.5	0.0	1.6	1.6

In another clinical trial conducted in Sweden comparing 3 acellular pertussis vaccines and 1 whole-cell DTP vaccine, 20,745 infants received the TRIPACEL® Hybrid component of ACTacel® Hybrid at 2, 4 and 6 or 3, 5 and 12 months of age. Rates of adverse events were less than or comparable to the rates in the other acellular pertussis vaccine and whole-cell DTP groups in this study. The rates of reports of fever >40.5°C and seizures or suspected seizures were significantly higher following whole-cell DTP than following acellular pertussis vaccines. (8)

Hypotonic-hyporesponsive episodes (HHEs) were observed in all vaccine groups and rates were comparable. No deaths or cases of encephalitis or acute encephalopathy, invasive bacterial infection, infantile spasms or anaphylactic reactions were reported within 48 hours of vaccination. (8) (9)

Data from Post-Marketing Experience

No data available.

Physicians, nurses and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and report to the Global Pharmacovigilance Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4, Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

DRUG INTERACTIONS

Vaccine-Drug Interactions

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

Concomitant Vaccine Administration

NACI states that 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) NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites. (1) (2) Simultaneous administration is suggested, particularly when there is concern that a person may not return for subsequent vaccination. Simultaneous administration of childhood vaccines such as ACTacel® Hybrid, MMR, varicella, pneumococcal conjugate and hepatitis B vaccines, is encouraged for children who are at the recommended age to receive these vaccines and for whom no contraindications exist.

Clinical trials with PENTACEL® suggest that ACTacel® Hybrid may be safely administered at the same time as other vaccines (including meningococcal C conjugate vaccine (10) and hepatitis B vaccine).

Once reconstituted, ACTacel® Hybrid should not be mixed in the same syringe with other parenterals.

Vaccine-Laboratory Test Interactions

Antigenuria has been detected in some instances following administration of a vaccine containing Hib antigen. Therefore, urine antigen detection may not have definite diagnostic value in suspected *H. influenzae* type b disease within two weeks of immunization. (11)

DOSAGE AND ADMINISTRATION

Recommended Dose

For routine immunization, ACTacel® Hybrid is recommended as a 4-dose series, with a single dose of ACTacel® Hybrid at 2, 4, 6 and 18 months of age.

If for any reason this schedule is delayed, it is recommended that 3 doses be administered with an interval of 2 months between each dose, followed by a fourth dose administered approximately 6 to 12 months after the third dose.

Whenever feasible, ACTacel® Hybrid should be used for all 4 doses in the vaccination series as there are no clinical data to support the use of ACTacel® Hybrid with any other licensed acellular pertussis combination vaccine in a mixed sequence. For situations where a different brand of DTaP, DTaP-IPV or DTaP-IPV/Hib vaccine was originally used, or where the brand is unknown, please refer to the latest edition of the Canadian Immunization Guide.

NACI recommends that premature infants whose clinical condition is satisfactory should be immunized with full doses of vaccine at the same chronological age and according to the same schedule as full-term infants, regardless of birth weight. (1)

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

In compliance with NACI's recommended immunization schedule, the childhood immunization series should be completed with a single 0.5 mL dose of Sanofi Pasteur Limited's QUADRACEL® between 4 and 6 years of age (i.e., at the time of school entry). Alternatively, ADACEL® [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed] and IPV may be administered at separate sites for this booster at 4 to 6 years of age. This booster dose is unnecessary if the fourth dose of ACTacel® Hybrid was administered after the child's fourth birthday. (1)

ACTacel® Hybrid should not be administered to persons less than 2 months or to persons 7 years of age or older. (See INDICATIONS AND CLINICAL USE.)

Administration

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

Reconstitution of Freeze-Dried Product and Withdrawal from Stoppered Vial

Reconstitute Act-HIB® with the TRIPACEL® Hybrid vaccine provided. Cleanse the Act-HIB® and TRIPACEL® Hybrid vial stoppers with a suitable germicide before reconstitution. Do not remove from either vial the stoppers or the metal seals holding them in place. Thoroughly but gently shake the vial of TRIPACEL® Hybrid, withdraw the entire contents of the liquid vaccine and inject slowly into the vial of lyophilized Act-HIB®. Shake the vial now containing ACTacel® Hybrid thoroughly until a uniform, cloudy, white to off-white suspension results. Withdraw the total volume of reconstituted combined vaccine. ACTacel® Hybrid should be used immediately after reconstitution. (1) Refer to Figures 1, 2, 3, 4 and 5.

INSTRUCTIONS FOR RECONSTITUTION OF TRIPACEL® HYBRID WITH Act-HIB®

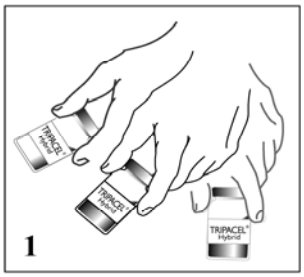

Figure 1
Cleanse stopper and gently shake the vial of TRIPACEL® Hybrid liquid vaccine to reconstitute ActHIB®.

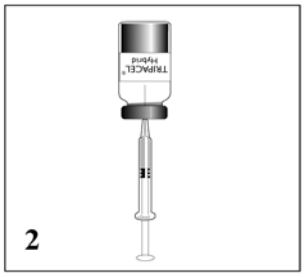

Figure 2
Withdraw the entire contents of the liquid vaccine as indicated.

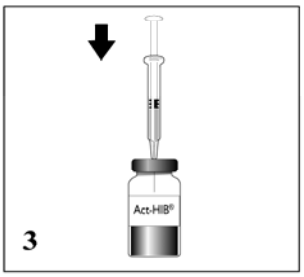

Figure 3
Cleanse the Act-HIB® vaccine stopper, insert syringe needle through the stopper and inject volume slowly as directed.

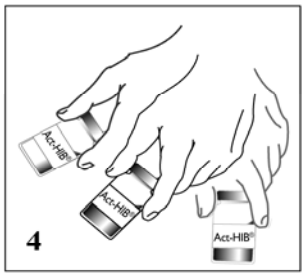

Figure 4
Shake vial thoroughly.

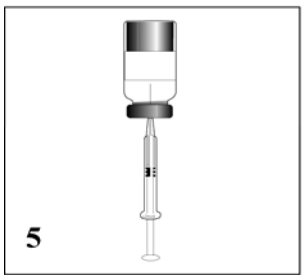

Figure 5
After reconstitution with the liquid vaccine, withdraw the total volume of ACTacel® Hybrid reconstituted combined vaccine and administer **intramuscularly**

Aseptic technique must be used. 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 reconstituted vaccine (I.M.). In infants younger than 1 year, the anterolateral aspect of the thigh provides the largest muscle and is the preferred site of injection. In older children, the deltoid muscle is usually large enough for injection.

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.

ACTION AND CLINICAL PHARMACOLOGY

Diphtheria and Tetanus: 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. 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. (2) (3) Levels of 1.0 IU/mL have been associated with long-term protection. (3)

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. (2) (3) A tetanus antitoxin level of at least 0.1 IU/mL as measured by the ELISA used in clinical studies of ACTacel® Hybrid is considered protective for tetanus. Levels of 1.0 IU/mL have been associated with long-term protection.

In a clinical trial in Taiwan, after 4 doses of ACTacel® Hybrid, 100% (N = 61) of immunized children achieved serum diphtheria and tetanus antitoxin levels of at least 0.1 IU/mL. (6) (7)

After completion of the childhood immunization series, circulating antibodies to diphtheria and tetanus toxoids gradually decline but are thought to persist at protective levels for up to 10 years. NACI recommends diphtheria and tetanus toxoids boosters every 10 years. (1)

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), pertussis components in ACTacel® Hybrid (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%.

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. (12) (13) (14) (15) (16) (17) In a controlled clinical trial in Sweden (Sweden II Trial), the efficacy of a DTaP vaccine with the same formulation of five pertussis antigens as ACTacel® Hybrid was demonstrated to provide a two-fold to three-fold higher protection against pertussis with any cough compared to the vaccine containing three pertussis antigens. The observed difference supports the role of FIM in the protection against colonization of *B. pertussis* and mild disease. (18)

PENTACEL®, a combination vaccine containing the same antigens at the same concentration as ACTacel® Hybrid, with the addition of Inactivated Poliomyelitis Vaccine, has been used for childhood vaccinations in Canada since 1999. In a recent publication, Bettinger *et al* reviewed

pertussis cases during 1991-2004 using surveillance data from the Canadian Immunization Monitoring Program, Active (IMPACT), an active surveillance network based in 12 pediatric tertiary-care hospitals across Canada. (19) Overall, the data show declining rates of pertussis during the years in which PENTACEL® has been used (1999-2004) compared to the period when whole-cell pertussis vaccine was used (1991-1996). Among children 1-4 years of age, incidence of pertussis declined 85%. Data from the Northwest Territories, (20) Newfoundland and Labrador (21) and British Columbia (22) support national and IMPACT data demonstrating a progressive decline of pertussis cases among infants and children through 9 years of age.

***Haemophilus influenzae* type b:** The response to the Act-HIB® component of the vaccine is typical of a T-dependent immune response with induction of immunologic priming and memory. (3) Bactericidal activity against Hib is demonstrated in serum after immunization and correlates with the anti-PRP antibody response induced by Hib conjugate vaccine. In children aged ≥24 months, antibody titres to *H. influenzae* capsular polysaccharide (anti-PRP) of ≥0.15 μg/mL following vaccination with unconjugated PRP vaccine correlated with protection against invasive *H. influenzae* type b disease immediately after immunization, whereas titres ≥1.0 μg/mL correlated with protection for at least 1 year. (23) Although the relevance of the 0.15 μg/mL and 1.0 μg/mL thresholds to clinical protection after immunization with conjugate vaccines is not known, these levels have been used to gauge antibody response to vaccination. In a clinical study in Taiwan, after 4 doses of ACTacel® Hybrid, 100% of children achieved protective antibody levels ≥1.0 μg/mL.

Duration of Effect

To ensure optimal protection during childhood, 4 consecutive doses should be given at 2, 4, 6 and 18 months of age. A booster with a vaccine containing diphtheria, tetanus and acellular pertussis with or without IPV is required at 4 to 6 years.

STORAGE AND STABILITY

Store at 2° to 8°C (35° to 46°F). **Do not freeze**. Discard product if exposed to freezing.

The vaccine should be used immediately after reconstitution.

Do not use vaccine after expiration date.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

After reconstitution, ACTacel® Hybrid (Act-HIB® reconstituted with TRIPACEL® Hybrid) is supplied as a sterile, uniform, cloudy, white to off-white suspension. Each component is supplied in a monodose vial.

Composition

Each single dose (approximately 0.5 mL) after reconstitution contains:

Active Ingredients

Purified Polyribosylribitol Phosphate Capsular Polysaccharide (PRP) of *Haemophilus influenzae* type b covalently bound to 20 µg of Tetanus Protein	10 µg
Diphtheria Toxoid	15 Lf
Tetanus Toxoid	5 Lf
Acellular Pertussis	
Pertussis Toxoid (PT)	20 µg
Filamentous Haemagglutinin (FHA)	20 µg
Pertactin (PRN)	3 µg
Fimbriae Types 2 and 3 (FIM)	5 µg

Other Ingredients

Excipients:

Aluminum Phosphate (adjuvant) (aluminum 0.33 mg)	1.5 mg
2-phenoxyethanol	0.6% v/v
Tris (hydroxymethyl aminomethane)	0.6 mg
Sucrose	42.5 mg

Manufacturing Process Residuals:

Formaldehyde and glutaraldehyde are present in trace amounts.

Packaging

Both components of ACTacel® Hybrid (TRIPACEL® Hybrid and Act-HIB®) are supplied in single dose vials.

The vials are made of Type 1 glass. The vial stoppers for this product do not contain latex (natural rubber).

ACTacel® Hybrid is supplied in a package of:

1 x 0.5 mL (single dose) vial of TRIPACEL® Hybrid for reconstituting 1 x 1 dose of Act-HIB®

5 x 0.5 mL (single dose) vials of TRIPACEL® Hybrid for reconstituting 5 x 1 dose of Act-HIB®

Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.
Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of May 2009

Manufactured by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

and

Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R2-0509 Canada

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed

Product Characteristics

ACTacel® Hybrid [Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed] is supplied in two vials: one vial containing lyophilized Haemophilus b conjugate vaccine consisting of the *H. influenzae* type b capsular polysaccharide PRP covalently bound to tetanus protein, and one vial containing a suspension of diphtheria and tetanus toxoids adsorbed on aluminum phosphate and 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). After reconstitution, the vaccine is a sterile, uniform, cloudy, white to off-white suspension.

C. diphtheriae is grown in modified Mueller's growth medium. (24) After purification by ammonium sulphate fractionation, the diphtheria toxin is detoxified with formaldehyde and diafiltered. *C. tetani* is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (25) 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 produced from *B. pertussis* cultures grown in Stainer-Scholte medium (26) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. PT, FHA and PRN are isolated separately from the supernatant culture medium. The FIM components 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. The residual aldehydes are removed by diafiltration. The individual antigens are adsorbed separately onto aluminum phosphate.

Both diphtheria and tetanus toxoids induce at least 2 neutralizing units per mL in the guinea pig potency test. The potency of the acellular pertussis vaccine components is evaluated by the antibody response of immunized guinea pigs to PT, FHA, PRN and FIM as measured by enzyme-linked immunosorbent assay (ELISA).

Act-HIB® is a sterile, lyophilized vaccine that is reconstituted at the time of use with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed. Act-HIB® consists of the Haemophilus b capsular polysaccharide PRP, a high molecular weight polymer prepared from the *H. influenzae* type b strain 1482 grown in a semi-synthetic medium, covalently bound to tetanus protein. (27) Act-HIB® contains no preservative. The tetanus protein is prepared by ammonium sulphate purification, and formalin inactivation of the toxin from cultures of *C. tetani* (Harvard

strain) grown in a modified Mueller and Miller medium. (28) The toxoid is filter sterilized before the conjugation process. Potency of Act-HIB® is specified on each lot by limits on the content of PRP polysaccharide and protein in each dose and the proportion of polysaccharide and protein that is characterized as high molecular weight conjugate.

CLINICAL TRIALS

Three pivotal clinical studies (Sweden Trial I, Sweden Trial II and Taiwan Trial) provide the clinical basis for the licensure of ACTacel® Hybrid in Canada. (See Table 2.)

Table 2: Summary of Demographics and Study Design of the Trials with ACTacel® Hybrid

Study	Study Design	Dosage and Route of Administration	Vaccination Schedule/ Study Population*	Gender
Sweden I (29) (30)	Randomized, placebo-controlled, double-blind, efficacy and safety trial with one whole cell DTP, two DTaP vaccines (2 and 5-component).	0.5 mL I.M.	2, 4, 6 months of age N = 2,587	Males N = 1,330 Females N = 1,257
Sweden II (18)	Randomized, controlled, double blind, multicentre efficacy trial with one whole cell DTP and three DTaP vaccines (2, 3 and 5-component).	0.5 mL I.M.	2, 4, 6 months of age N = 2,551 and 3, 5, 12 months of age N = 18,196	Males N = 10,590 Females N = 10,157
Trial P3T02393 (6) (7)	Randomized, controlled safety and immunogenicity trial with ACTacel® Hybrid.	0.5 mL I.M.	2, 4, 6 and 18 months of age N = 68	Males N = 34 Females N = 34

* Number enrolled.

Sweden I Efficacy Trial

A randomized, double-blinded, placebo-controlled efficacy and safety study was conducted in Sweden from 1992 - 1995 (Sweden I Efficacy Trial) under the sponsorship of the National Institute of Allergy and Infectious Diseases (NIAID). (30) A total of 9,829 infants received 1 of 4 vaccines: TRIPACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed], the five-component DTaP vaccine that contains the same antigens (but with a lower content of PT and FHA per dose) present in ACTacel® Hybrid (N = 2,587); a two-component DTaP vaccine (N = 2,566); a whole-cell pertussis DTP vaccine from the U.S. (N = 2,102); or DT vaccine (Swedish National Bacteriological Laboratory) as placebo (N = 2,574). Infants were immunized at 2, 4 and 6 months of age. The mean length of follow-up was 2 years after the third dose of vaccine. The protective efficacy of TRIPACEL® against pertussis after 3 doses of vaccine using the World Health Organization (WHO) case definition (≥21 consecutive days of paroxysmal cough with culture or serologic confirmation or epidemiologic link to a confirmed case) was 85.2% (95% confidence interval [CI] 80.6 to 88.8). (30) The protective efficacy of TRIPACEL® against mild pertussis (≥1 day of cough with laboratory confirmation) was 77.9% (95% CI 72.6 to 82.2). (Table 3) Protection against pertussis by TRIPACEL® was sustained for the 2-year follow-up period. (30) (Table 4)

Table 3: Vaccine Efficacy Against Pertussis Infection of Varying Clinical Severity (30) (31)

Clinical Severity of Pertussis	Vaccine Efficacy (%) of TRIPACEL® (n = 2,551) Compared to DT Control (n = 2,539)
cough ≥1 day	77.9
cough >7 days	78.4
cough ≥21 days	81.4
cough ≥30 days	87.3
paroxysmal cough ≥14 days	82.3
paroxysmal cough ≥21 days	85.1

Another arm of the trial (30) (31) looked at the persistence of the protection provided by this TRIPACEL® formulation compared to a placebo. High levels of protection were sustained for TRIPACEL® over the entire 2-year follow-up period.

Table 4: Duration of Vaccine Efficacy for TRIPACEL® Compared to Placebo (30) (31)

Vaccine Efficacy (%) Compared to DT (Placebo n = 2,068)	
Interval Since Third Dose (in days)	**TRIPACEL® (n = 2,069)**
0-89	95
90-179	83.6
180-269	86.7
270-359	84.4
360-449	92.1
450-539	78.3
540-629	86.4
630-719	81.3

The incidence of injection site and systemic reactions after administration of TRIPACEL® was comparable to the DT control group. (30) (31)

A sub-study of this trial looked specifically at immunized children exposed to pertussis from other members of their households. (12) This formulation of TRIPACEL® was more efficacious than any of the other acellular and whole-cell vaccines studied. There was a correlation between clinical protection and the presence of anti-PRN, anti-FIM and anti-PT antibodies respectively in the serum of immunized children.

Sweden II Efficacy Trial

A second NIAID-sponsored, prospective, randomized, double-blinded efficacy trial was conducted in Sweden (Sweden II Efficacy Trial) from 1993 to 1996. Infants (N = 82,892) were randomized to receive one of four vaccines: a two-component acellular DTaP vaccine (N = 20,697); a three-component acellular DTaP vaccine (n = 20,728); TRIPACEL® Hybrid (N = 20,747); or a European whole-cell DTP vaccine (N = 20,720). (18) Vaccination occurred at 3, 5 and 12 months of age (88% of participants) or at 2, 4 and 6 months of age (12% of participants). The relative risk of typical pertussis (culture-confirmed *B. pertussis* infection with at least 21 days of paroxysmal cough) was 0.85 and 1.38 among children given the five-component and three-component vaccines, respectively, as compared with those given the whole-cell vaccine. The relative risk of typical pertussis was 0.62 among children given the five-component vaccine as compared with the three-component vaccine. The absolute efficacy of the three-component vaccine, when tested in an earlier double-blinded randomized placebo-controlled trial in Italy was 84% (95% CI, 76-89). (32) Although the absolute efficacy of the five-component vaccine could not be determined in the Sweden II Efficacy Trial because of the lack of a DT control group, based on the relative risk data, it appears that the five-component vaccine demonstrated improved efficacy compared with the 84% absolute efficacy associated with the three-component vaccine. The observed difference supports the role of fimbriae types 2 and 3 (FIM) in the protection against colonization by *B. pertussis* and mild disease. (See Table 5.) (18)

Table 5: Geometric Mean Titres (GMTs) to Pertussis Antigens Following the Third Dose (Vaccine Administered at 2, 4 and 6 Months) (31)

Pertussis Antigens	TRIPACEL® (n = 80) GMTs (EU/mL)
PT	51.6
FHA	57.0
PRN	134.3
FIM	351.9

Rates of serious adverse events were less than or comparable to the rates in the other acellular pertussis and European whole-cell DTP groups in this study. (8) (18) (31)

Trial P3T02393

In a randomized controlled clinical trial conducted in Taiwan, 67 infants received ACTacel® Hybrid and 67 infants received TRIPACEL® Hybrid and Act-HIB®, given concomitantly at separate injection sites, at 2, 4 and 6 months of age. Respectively, 61 and 66 of these children received a 4th dose of the same vaccines at 18 months of age. OPV was administered concomitantly to all children at each visit.

Immunogenicity

In this study, the immunogenicity of ACTacel® Hybrid antigens did not show any significant difference compared to the separate administration of the vaccines, with the exception of PT after the 3rd dose and tetanus after the 4th dose. Nevertheless, these differences were not considered clinically significant, based on the rigorous immune response obtained for all antigens. After 3 doses of ACTacel® Hybrid, 100% of children achieved protective levels of tetanus antitoxin (≥0.01 EU/mL) and 100% of children achieved protective diphtheria antitoxin levels (≥0.01 IU/mL). 100% of children achieved anti-PRP levels ≥0.15 µg/mL, considered protective. After 4 doses of ACTacel® Hybrid, 100% of children achieved higher protective antibody levels for diphtheria (≥0.1 IU/mL), tetanus (≥0.1 EU/mL) and PRP (≥1.0 µg/mL). In addition, after 4 doses of Act-HIB® the GMTs of antibodies against all pertussis antigens were higher than those observed in Sweden trials, suggesting protection against pertussis disease. (6) (7)

Safety

Reaction rates at the injection site were comparable whether the vaccines were given combined as ACTacel® or given separately as TRIPACEL® and Act-HIB®. No serious adverse events were observed during this study. Systemic adverse events were usually mild. There were no reports of fever ≥40°C. Few systemic reactions were reported after the fourth dose. (See Table 6.) (6) (7)

Table 6: Adverse Event Rates (%) Observed in a Taiwanese Clinical Trial within 48 Hours of Vaccination with ACTacel® at 2, 4, 6 and 18 Months (6) (7)

		2 months	4 months	6 months	18 months
Adverse Event	**Severity**	**n = 67**	**n = 66**	**n = 64**	**n = 61**
Redness	Any	19.4	10.6	15.6	0.0
	≥30 mm	6.0	7.6	3.1	0.0
Swelling	Any	22.4	16.7	7.2	0.0
	≥30 mm	10.4	4.5	1.6	0.0
Tenderness	Any	28.4	13.6	15.6	0.0
	Severe	0.0	0.0	0.0	0.0
Fussiness	Any	35.8	24.2	18.8	3.3
	≥3 hours	3.0	0.0	0.0	0.0
Less Active	Any	6.0	3.0	1.6	0.0
	Severe	.5	0.0	0.0	0.0
Eating Less	Any	20.9	10.6	10.9	1.6
	Severe	0.0	0.0	0.0	0.0
Crying	Any	22.4	13.6	1.6	0.0
	≥3 hours	3.0	0.0	0.0	0.0
Vomiting	Any	4.5	3.0	0.0	0.0
	Severe	0.0	0.0	1.5	0.0
Diarrhea	Any	4.5	0.0	1.6	1.6
	Severe	0.0	0.0	0.0	0.0
Fever	Any	8.7	9.8	5.1	0.0
	≥40°C	0.0	0.0	0.0	0.0

ADDITIONAL RELEVANT INFORMATION

Simultaneous vaccination with combination vaccines during early childhood has been the cornerstone of Canada's immunization program for many years. ACTacel® Hybrid combines four childhood vaccines and offers protection against invasive Hib disease, diphtheria, tetanus and pertussis. Immunization with these antigens has been associated with a striking decrease in the incidence of morbidity and mortality caused by these infections. ACTacel® Hybrid has been licensed in Canada since 1997.

Diphtheria and Tetanus: The information provided below is consistent with NACI's guidelines. Diphtheria is an acute communicable disease caused by exotoxin-producing strains of the bacterium *C. diphtheriae*. Symptoms result from local infection of the respiratory tract, which may lead to breathing difficulties, or infection of the skin or mucosal surfaces, or from dissemination of diphtheria toxin, which damages the heart and central nervous system. Routine immunization

against diphtheria in infancy and childhood has been widely practised in Canada since 1930, resulting in a decline in morbidity and mortality. In Canada, there are 0 to 5 isolates reported each year. The case-fatality rate remains at about 5 to 10%, with the highest death rates in the very young and elderly. (1) The disease occurs most frequently in unimmunized or partially immunized persons.

Tetanus is an acute and often-fatal disease caused by an extremely potent neurotoxin produced by *C. 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. Between 1980 and 2004, the number of cases reported annually in Canada ranged from 1 to 10, with an average of 4 cases per year. (1)

Both diphtheria and tetanus toxoids are prepared by detoxification of the respective toxins with formaldehyde. Intramuscular injection of diphtheria and tetanus toxoids results in the production of protective antibodies against the toxins and their lethal effects, but it does not preclude local infections by the bacteria. (1) After completion of a primary series, circulating antibodies to tetanus and diphtheria toxoids gradually decline but are thought to persist at protective levels for up to 10 years. (1) NACI continues to recommend tetanus and diphtheria boosters every 10 years based on concern regarding the decline of antibody levels with age and potential failure of single booster doses to produce protective levels in older individuals. (1)

Pertussis: Pertussis (whooping cough) results from an acute infection of the respiratory tract caused by *B. pertussis*. Severity and mortality are greatest in infancy and even infants born to apparently immune mothers are highly susceptible to infection, particularly if maternal immunity was induced by whole-cell pertussis vaccine.

Whole-cell pertussis vaccine was first introduced in Canada in 1943. NACI states that over the past 64 years, pertussis incidence has declined by over 90%, although outbreaks of pertussis continue to arise. (1) Because of concerns about the frequency and severity of systemic and injection site adverse reactions with whole-cell pertussis vaccines, acellular pertussis vaccines have replaced whole-cell formulations in Canada. Acellular vaccines provoke significantly fewer injection site reactions, lower rates of fever and fewer episodes of unusual or persistent crying. (18) (30) (31) (33)

ACTacel® Hybrid contains a five-component acellular pertussis vaccine stimulating immune response to PT, FHA, PRN and FIM. In an efficacy trial, five-component acellular pertussis vaccines were significantly more efficacious than other acellular pertussis formulations containing fewer antigens. (30) (31) (34)

***H. influenzae* type b:** Before the introduction of Haemophilus b conjugate vaccines in Canada, *H. influenzae* type b (Hib) was the most common cause of bacterial meningitis and a leading cause of other serious infections in young children. Four hundred and eighty-five cases were recorded in 1985 before the first vaccine was available. (35) After 1997 when routine infant immunization with PENTACEL® (same Hib conjugate as ACTacel® Hybrid) began, only 8 - 10 cases a year were reported. Only a single case of Hib infection in a child fully vaccinated with PENTACEL® was reported to Canada's nationwide vaccine surveillance system in 1999. (36) In 2000, case reports of Haemophilus b meningitis reached an historical low with only 4 cases reported, a reduction of 99% from pre-vaccine levels. (35)

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Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

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

Product information as of May 2009

Manufactured by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

and
Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R2-0509 Canada

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

ACTacel® Hybrid

Act-HIB® Reconstituted with TRIPACEL® Hybrid

[Haemophilus b Conjugate Vaccine (Tetanus Protein – Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed]

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

ABOUT THIS VACCINE

What the vaccine is used for:

ACTacel® Hybrid is a vaccine that is used to help prevent against invasive H. influenzae type b (Hib) infections, diphtheria, tetanus (lock jaw) and pertussis (whooping cough). This vaccine may be given to children aged 2 months or older. It may also be given as a booster to children up to age 7.

The majority of children who are vaccinated with ACTacel® Hybrid will produce enough antibodies to help protect them against these 4 diseases. However, as with all vaccines, 100% protection cannot be guaranteed.

What the vaccine does:

ACTacel® Hybrid causes the body to produce its own natural protection against invasive Hib infections, diphtheria, tetanus and pertussis (whooping cough). After your child receives the vaccine, the body begins to make substances called antibodies. Antibodies help the 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 the vaccine should not be used:

- Do not give ACTacel® Hybrid to a child who has an allergy to any ingredient in the vaccine or has had an allergic reaction after receiving a vaccine that contained similar ingredients.
- Do not give ACTacel® Hybrid to a person who has had a serious nervous system disorder within 7 days after a previous pertussis vaccine. In case of progressive nervous system disorder or uncontrolled epilepsy, vaccination may be considered only after a treatment has been established and the condition is stabilized.

What the medicinal ingredient is:

Each 0.5 mL dose of ACTacel® Hybrid contains: Hib conjugate vaccine, diphtheria toxoid, tetanus toxoid, acellular pertussis vaccine (pertussis toxoid, filamentous haemagglutinin, pertactin and fimbriae types 2 and 3).

What the important non-medicinal ingredients are:

Aluminum phosphate (adjuvant), 2-phenoxyethanol, Tris (hydroxymethyl aminomethane), sucrose. Residual formaldehyde and glutaraldehyde are present in trace amounts.

For a full listing of non-medicinal ingredients see Part 1 of the product monograph.

What dosage forms the vaccine comes in:

ACTacel® Hybrid is supplied in two vials: one vial of freeze-dried Act-HIB® vaccine and one vial of liquid dose of 0.5 mL TRIPACEL® Hybrid vaccine which are then combined for injection into a muscle.

WARNINGS AND PRECAUTIONS

If your child has any of the following conditions, talk to your doctor, nurse or pharmacist BEFORE the child receives ACTacel® Hybrid:

- **A high fever or serious illness.** Wait until the child is better to give the vaccination.
- **An allergy to any component of the vaccine.**
- **A serious nervous system adverse event following a previous pertussis vaccination.**
- **Diseases of the immune system or taking a medical treatment that affects the immune system.** The vaccine may provide your child with a lower level of protection than it does for people with healthy immune systems. If possible, try to postpone the vaccination until after your child has completed the treatment.
- **A bleeding disorder or taking blood-thinning medications.** Tell the person giving the injection about your child's condition. The injection must be done carefully to prevent excessive bleeding.
- **A higher risk of seizure than the general population.** A fever-reducing medication (AW) may be given to your child.

INTERACTIONS WITH THIS VACCINE

DO NOT mix ACTacel® Hybrid with other vaccines or medicinal products in the same syringe.

ACTacel® Hybrid may be given at the same time but at separate sites with Hepatitis B vaccine, 7-valent pneumococcal conjugate vaccine, MMR and Varicella vaccines.

PROPER USE OF THIS VACCINE

Usual Dose:

A single dose of 0.5 mL is recommended for routine immunization of infants at 2, 4, 6 and 18 months of age and in children up to their 7th birthday.

The vaccination should be given in the muscle, preferably in the thigh for children up to 1 year-old. In children >1 year of age, the shoulder is the preferred site since use of the thigh results in limping due to muscle pain.

Overdose:

Not applicable to this vaccine.

Missed Dose:

If immunization is delayed for any reason, the recommended schedule is:

- 3 single doses of 0.5 mL with 2 months between doses
- a 4th dose given 6 to 12 months after the 3rd dose

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A vaccine, like any medicine, may cause side effects. Up to one third of children who receive ACTacel® Hybrid may have mild side effects such as redness, swelling or tenderness around the injection site. Other common reactions include fever, increased crying, fussiness, being less active and have decreased eating. These side effects are usually mild and last no more than 3 to 4 days. Severe reactions, such as high fever, swelling and redness of the entire arm or leg, or a serious allergic reaction are very rare.

Tell your doctor, nurse or pharmacist as soon as possible if your child is not feeling well after receiving ACTacel® Hybrid.

Serious side effects are extremely rare.

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

HOW TO STORE THE VACCINE

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 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 information on serious and unexpected adverse events following vaccination.

If your child has had a serious or unexpected event following receipt of a vaccine, you may notify the Public Health Agency of Canada:

By toll-free telephone: 613-954-5590
(1-866-844-0018)

By toll-free fax: 613-954-9874
(1-866-844-5931)

By email: caefi@phac-aspc.gc.ca

By regular mail:
Vaccine Safety Section
Centre for Immunization & Respiratory Infectious Diseases
Public Health Agency of Canada
100 Eglantine Driveway
A/L0602C, Bldg #6
Tunney's Pasture
Ottawa, Ontario
K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.

MORE INFORMATION

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

You may also contact the vaccine producer, Sanofi Pasteur Limited, for more information. Telephone: 1-888-621-1146 (no charge) or 416-667-2779 (Toronto area). Business hours: (8 a.m. to 5 p.m. Eastern Time, Monday to Friday).

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