FOLIO 1065

Route of administration

MMR vaccine should be administered subcutaneously; MMRV can be administered subcutaneously or intramuscularly. Refer to Vaccine Administration Practices in Part 1 for additional information.

Schedule

Children (12 months to 12 years of age)

For routine immunization of children aged 12 months to 12 years, two doses of mumps-containing vaccine (MMR or MMRV) should be administered. The first dose of mumps-containing vaccine should be administered at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter, typically before school entry.

The recommended minimum interval between doses of MMR vaccine is 4 weeks. Children who previously received a single dose of MMR vaccine should receive a second dose at least 4 weeks after the first dose. The recommended interval between two doses of MMRV vaccine is at least 3 months; a minimum interval of 6 weeks between doses may be used if rapid, complete protection is required.

Adolescents (13 to 17 years of age)

Mumps-susceptible adolescents should receive two doses of MMR vaccine given at least 4 weeks apart.

Adults (18 years of age and older)

Mumps-susceptible adults should receive one or two doses of MMR vaccine as appropriate for age and risk factors (refer to Table 1). If two doses are needed, MMR vaccine is administered with a minimum interval of 4 weeks between doses.

BOOSTER DOSES AND RE-IMMUNIZATION

Re-immunization with mumps-containing vaccine after age and risk appropriate vaccination is not necessary.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving mumps-containing vaccine. Although generally used as criteria for immunity, the presence of mumps-specific IgG, as determined by enzyme immunoassay (EIA), does not necessarily predict the presence of neutralizing antibodies and, thus, immunity. Conversely, the absence of detectable mumps-specific IgG does not mean the person is susceptible. For further information regarding mumps serology refer to the PHAC Supplement: Guidelines for the Prevention and Control of Mumps Outbreaks in Canada. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10pdf/36s1-eng.pdf)

STORAGE REQUIREMENTS

M-M-R® II: Maintain vaccine at +10°C or colder during shipment. Freezing during shipment will not affect potency of the vaccine. Protect the vaccine from light. Before reconstitution, store the vial of vaccine at +2°C to +8°C or colder. The diluent may be stored in the refrigerator or at room temperature and must not be frozen.

PRIORIX®: Store in a refrigerator at +2°C to +8°C. The diluent may be stored separately at room temperature. Protect from light.

PRIORIX-TETRA®: Store the vaccine and diluent in a refrigerator at +2°C to +8°C and do not freeze. Protect the vaccine from light.

Refer to Storage and Handling of Immunizing Agents in Part 1 for additional general information.

CAIF S.A.
María Bernarda Belay
Farmacéutica

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Live vaccines given by the parenteral route may be administered concomitantly with all other vaccines during the same visit using different injection sites and separate needles and syringes. In general, if two live parenteral vaccines are not administered concomitantly, there should be a period of at least 4 weeks before the second live parenteral vaccine is given. Exceptions are varicella-containing vaccines, such as MMRV vaccine:

- administer doses of varicella-containing vaccine at least 3 months apart for children 1 to 12 years of age. If rapid, complete protection against varicella is required, a minimum interval of 6 weeks between 2 doses may be used for children 1 to 12 years of age.
- do not concomitantly administer varicella-containing vaccines with smallpox vaccine; administer varicella-containing vaccine and smallpox vaccine at least 4 weeks apart.

Oral and intranasal vaccines can be given at the same time as, or any time before or after any other live vaccine, regardless of the route of administration of the other live vaccine.

Refer to Timing of Vaccine Administration in Part 1 for additional general information.

VACCINE SAFETY AND ADVERSE EVENTS

Refer to Vaccine Safety Part 2 for additional general information.

COMMON AND LOCAL ADVERSE EVENTS

MMR vaccine

Adverse events following MMR immunization occur less frequently and are less severe than those associated with natural disease. Adverse reactions are less frequent after the second dose of vaccine and tend to occur only in those not protected by the first dose. Six to 23 days after MMR immunization, approximately 5% of immunized children experience malaise and fever (with or without rash) lasting up to 3 days. Parotitis, rash, lymphadenophy, and joint symptoms also occur occasionally after MMR immunization.

MMRV vaccine

Pain and redness at the injection site or low-grade fever or both occur in 10% or more of vaccinees. Rash, including measles-like, rubella-like and varicella-like rash, as well as swelling at the injection site and moderate fever (greater than 39°C) occur in 1% to less than 10% of vaccinees. As varicella-like rashes that occur within the first two weeks after immunization may be caused by wild-type virus, health care providers should obtain specimens using viral transport media from a lesion of the vaccinee to ensure varicella disease is not confused with a reaction to vaccination.

Rubella-containing vaccines

Acute transient arthritis or arthralgia may occur 1 to 3 weeks after immunization with rubella-containing vaccine; it lasts for about 1 to 3 weeks, and rarely recurs. This is more common in post-pubertal females, among whom arthralgia develops in 25% and arthritis in 10% after immunization with rubella-containing vaccine. There is no evidence of increased risk of new onset, chronic arthropathies or neurologic conditions.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

MMR and MMRV vaccines

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. As with other vaccines, anaphylaxis following vaccination with MMR or MMRV vaccine may occur but is very rare.

FOLIO 1066

Immune Thrombocytopenic Purpura (ITP)

Rarely, ITP occurs within 6 weeks after immunization with MMR or MMRV vaccine. In most children, post-immunization thrombocytopenia resolves within three months without serious complications. In individuals who experienced ITP with the first dose of MMR or MMRV vaccine, serologic status may be evaluated to determine whether an additional dose of vaccine is needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases.

Encephalitis

Encephalitis has been reported in association with administration of measles vaccine in approximately 1 per million doses distributed in North America which is much lower than that observed with natural measles disease (1 per 1,000 cases).

Febrile seizures

Recent studies have found a higher risk of febrile seizures with the first dose of a MMRV vaccine (ProQuad®, not authorized for use in Canada) when compared to the concomitant administration of MMR and univalent varicella vaccine. Data from the US estimated that the risk of febrile seizures in the 5 to 12 days following the first dose of this MMRV vaccine is 1 for every 2,600 vaccinated children aged 12 to 23 months. Experience with the MMRV vaccine available in Canada is more limited; however, one study showed an additional risk of febrile seizures with MMRV vaccine compared to MMR and univalent varicella vaccines given as two separate products administered concomitantly. The risk with the Canadian vaccine was smaller than the risk found with the US product. Close surveillance and further investigation are underway.

OTHER REPORTED ADVERSE EVENTS AND CONDITIONS

In the mid to late 1990s, researchers from the UK reported an association between MMR vaccine and inflammatory bowel disease, and MMR vaccine and autism. Rigorous scientific studies and reviews of the evidence have been done worldwide, and there is now considerable evidence to refute those claims. In 2010, the original study suggesting a link between the MMR vaccine and autism was retracted.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report the following AEFI in particular, through local public health officials:

- Febrile seizures within 30 days after vaccination with MMR or MMRV vaccine.
- Varicella that is moderate (50 to 500 lesions) or severe (more than 500 vesicular lesions or associated complications or hospital admission) and occurs 7 to 21 days after vaccination with MMRV vaccine.
- Any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI.

Refer to Reporting Adverse Events Following Immunization (AEFI) in Canada (http://www.phac-aspc.gc.ca/im/aefi-essi_guide/index-eng.php) and *Vaccine Safety* in Part 2 for additional information about AEFI reporting.

CONTRAINDICATIONS AND PRECAUTIONS

MMR and MMRV vaccines are contraindicated in persons with a history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine (with the exception of egg allergy [refer below]) or its container. Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of vaccines available for use in Canada and their contents. For mumps-containing vaccines, potential allergens include:

CMF S.A.
María Bernarda Delay

- M-M-R®II: neomycin, phenol red, porcine gelatin, residual components of chick embryo cell cultures
- PRIORIX®: egg protein, neomycin
- PRIORIX-TETRA®: neomycin

In situations of suspected hypersensitivity or non-anaphylactic allergy to vaccine components, investigation is indicated which may involve immunization in a controlled setting. Consultation with an allergist is advised.

The measles and mumps components of MMR and MMRV vaccines are produced in chick embryo cell culture and may contain traces of residual egg and chicken protein. The trace amount of egg protein in the vaccine appears to be insufficient to cause an allergic reaction in egg-allergic individuals. Skin testing is not recommended prior to vaccination as it does not predict reaction to the vaccine. MMR or MMRV vaccine can be administered in the routine manner to people who have a history of anaphylactic hypersensitivity to hens' eggs. Prior egg ingestion is not a prerequisite for immunization with egg protein-containing vaccine. For all vaccines, immunization should always be performed by personnel with the capability and facilities to manage adverse events post-vaccination. Refer to Anaphylactic Hypersensitivity to Egg and Egg-Related Antigens in Part 2 for additional information.

Children with a known or suspected family history of congenital or hereditary immunodeficiency that is a contraindication to vaccination with live vaccine should not receive live vaccines unless their immune competence has been established.

MMRV vaccine is contraindicated in persons with impaired immune function, including primary or secondary immunodeficiency disorders. Refer to Immunocompromised persons.

MMR and MMRV vaccines are contraindicated during pregnancy. Refer to Pregnancy and breastfeeding.

MMR vaccine is contraindicated in individuals with active, untreated tuberculosis. While tuberculosis may be exacerbated by natural measles infection, there is no evidence that measles-containing vaccines, such as MMR or MMRV have such an effect.

A history of febrile convulsions or a family history of convulsions is not a contraindication for the use of MMRV vaccine.

Administration of MMR or MMRV vaccine should be postponed in persons with a severe acute illness. Persons with a minor acute illness (with or without fever) may be vaccinated.

It is recommended to avoid the use of salicylates (e.g., acetylsalicylic acid [ASA]) for 6 weeks after immunization with MMRV vaccine because of an association between wild-type varicella, salicylate therapy and Reye's syndrome.

Refer to Contraindications, Precautions and Concerns in Part 2 for additional general information.

DRUG INTERACTIONS

Systemic antiviral therapy (such as acyclovir, valacyclovir, famciclovir) should be avoided in the peri-immunization period, as it may reduce the efficacy of varicella-containing vaccine such as MMRV. On the basis of expert opinion, it is recommended that people taking long-term antiviral therapy should discontinue these drugs, if possible from at least 24 hours before administration of MMRV vaccine and should not restart antiviral therapy until 14 days after.

The measles component in measles-containing vaccines can temporarily suppress tuberculin reactivity, resulting in false-negative results. If tuberculin skin testing or an Interferon Gamma Release Assay (IGRA) test is required, it should be done on the same day as immunization or delayed for at least 4 weeks after measles vaccination. Vaccination with measles-containing vaccine may take place at any time after tuberculin skin testing has been performed and/or read.

FOLIO 1067

Passive immunization with human immune globulin (Ig) or receipt of most blood products can interfere with the immune response to MMR and MMRV vaccines. These vaccines should be given at least 14 days prior to administration of an Ig preparation or blood product, or delayed until the antibodies in the Ig preparation or blood product have degraded. If the interval between administration of vaccine and subsequent administration of an Ig preparation or blood product is less than 14 days or before the antibody has degraded, repeat the vaccine dose after the recommended interval. The recommended interval between administration of an Ig preparation or blood product and subsequent immunization varies, depending on the Ig preparation or blood product. Palivizumab (RSVAb) and washed red blood cell transfusion do not interfere with the antibody response to MMR or MMRV vaccines. Refer to Blood Products, Human Immune Globulin and Timing of Immunization in Part 1 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

On the basis of expert opinion, the MMR vaccines authorized in Canada may be used interchangeably. Refer to Principles of Vaccine Interchangeability in Part 1 for additional general information.

SELECTED REFERENCES

American Academy of Pediatrics. In: Pickering LK, Baker CJ, Kimberlin DW, et al. (editors). *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.

Boulianne N, De Serres G, Ratnam S et al. *Measles, mumps and rubella antibodies in children 5-6 years after immunization: effect of vaccine type and age at vaccination*. Vaccine 1995;13(16):1611-6.

Caplan CE. *Mumps in the era of vaccines*. CMAJ 1999;160(6):865-6.

Centers for Disease Control and Prevention. *Advisory Committee on Immunization Practices Provisional Recommendations for Measles-Mumps-Rubella (MMR) 'Evidence of Immunity' Requirements for Healthcare Personnel*. 2009. Accessed October 2010 at: http://www.cdc.gov/vaccines/recs/provisional/downloads/mmr-evidence-immunity-Aug2009-508.pdf

Centers for Disease Control and Prevention. *Use of Combination Measles, Mumps, Rubella and Varicella Vaccine. Recommendations of the Advisory Committee on Immunization Practices*. MMWR Morb Mortal Wkly Rep 2010;59(03):1-12.

Centers for Disease Control and Prevention. *The Pink Book: Epidemiology and Prevention of Vaccine Preventable Diseases*. Updated 11th ed.; May 2009. Accessed October 2010 at: http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm

Centers for Disease Control and Prevention. *Update: recommendations from the Advisory Committee on Immunization Practices (ACIP) regarding administration of combination MMRV vaccine*. MMWR Morb Mortal Wkly Rep 2008;57:258-60.

Centers for Disease Control and Prevention. *Measles, Mumps, and Rubella -- Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP)*. MMWR Recomm Rep 1998; 47(RR-8):1-57.

Cooney MK, Fox JP, Hall CE. *The Seattle Virus Watch, VI. Observations of infections with and illness due to parainfluenza, mumps, and respiratory syncytial viruses and Mycoplasma pneumoniae*. Am J Epidemiol 1975;101(6):532-51.

María Bernarda Belay
Farmacéutica

Davidkin I, Valle M, Julkunen I. *Persistence of anti-mumps virus antibodies after a two-dose MMR vaccination at nine-year follow-up*. Vaccine 1995;13(16):1617-22.

Duclos P, Ward BJ. *Measles vaccines: a review of adverse events*. Drug Saf 1998;19(6):435-54.

Falk WA, Buchan K, Dow M et al. *The epidemiology of mumps in Southern Alberta, 1980-1982*. Am J Epidemiol 1989;130(4):736-49.

GlaxoSmithKline Inc. *Product Monograph – PRIORIX-TETRA™*. May 2010.

GlaxoSmithKline Inc. *Product Monograph - PRIORIX®*. November 2008.

Griffin MR, Ray WA, Mortimer EA et al. *Risk of seizures after measles-mumps-rubella immunization*. Pediatrics 1991;88(5):881-5.

Health Protection Agency, U.K. *Confirmed cases of mumps by age and region: 1996-2005*. Accessed October 2010 at: www.hpa.org.uk/Infections/topics_az/mumps/data_reg_age.htm.

Jadavji T, Scheifele D, Halperin S. *Thrombocytopenia after immunization of Canadian children, 1992 to 2001*. Pediatr Infect Dis J 2003;22(2):119-22.

James JM, Burks AW, Roberson PK et al. *Safe administration of the measles vaccine to children allergic to eggs*. N Engl J Med 1995;332(19):1262-6.

Merck Frosst Canada Ltd. *Product Monograph - M-M-R® II*. February 2009.

Miller E, Goldacre M, Pugh S et al. *Risk of aseptic meningitis after measles, mumps and rubella vaccine in U.K. children*. Lancet 1993;341(8851):979-82.

National Advisory Committee on Immunization. *Updated recommendations for the use of varicella and MMR vaccines in HIV-infected individuals*. Can Commun Dis Rep 2010;36(ACS-7):1-19.

National Advisory Committee on Immunization. *Statement on measles-mumps-rubella-varicella vaccine*. Can Commun Dis Rep 2010;36(ACS-9):1-22.

National Advisory Committee on Immunization. *Statement on mumps vaccine*. Can Commun Dis Rep 2007;33(ACS-8):1-10.

Peltola H, Heinonen OP, Valle M et al. *The elimination of indigenous measles, mumps and rubella from Finland by a 12 year two-dose vaccination program*. N Engl J Med 1994;331(21):1397-1402.

Public Health Agency of Canada. *Supplement: Guidelines for the Prevention and Control of Mumps Outbreaks in Canada*. Can Commun Dis Rep 2010;36(S1):1-46.

West R, Roberts PM. *Measles, mumps and rubella vaccine: current safety issues*. BioDrugs 1999;12(6):423-9.

FOLIO 1068

PART 4

PERTUSSIS VACCINE

KEY INFORMATION (refer to text for details)

What	• Pertussis (whooping cough) is a highly communicable bacterial illness. • Its severity is greatest among infants who are too young to be protected by a complete vaccine series. • Acellular pertussis vaccines have an estimated effectiveness of 80% to 85% following 3 doses. • Acellular pertussis vaccine is only available as a combination vaccine. • Redness, swelling and pain at the injection site are the most common adverse reactions to acellular pertussis-containing vaccines.
Who	• Acellular pertussis-containing vaccine is recommended for: o routine immunization of infants and children, including an adolescent booster dose o immunization of children who missed pertussis immunization on the routine schedule o adults who have not previously received a dose of pertussis-containing vaccine in adulthood
How	• **Routine pertussis immunization of infants, children and adolescents:** administer DTaP-IPV-Hib vaccine at 2, 4, 6 and 12 to 23 months of age (generally given at 18 months of age). If infant immunization for hepatitis B is undertaken, DTaP-HB-IPV-Hib vaccine may be used. Subsequently, administer a booster dose of either DTaP-IPV or Tdap-IPV vaccine at 4 to 6 years of age (school entry) and a booster dose of Tdap vaccine 10 years later at 14 to 16 years of age. • **Adults:** administer one dose of Tdap vaccine if not previously received in adulthood (18 years of age and older). Adults of any age, who have not received a dose of Tdap vaccine in adulthood and who are in contact or anticipate contact with infants (e.g., parents, grandparents, childcare providers) should be prioritized for pertussis vaccination. • Acellular pertussis-containing vaccines may be administered concomitantly with routine vaccines at different injection sites using separate needles and syringes.

CAIF S.A.
María Bernarda Belay
Farmacéutica

Why	• One to three deaths related to pertussis occur each year in Canada, particularly in infants who are too young to be immunized, or unimmunized or partially immunized children. • Adolescents and adults who have not received a booster vaccination are at risk of infection and are often the source of infection in infants.

Significant revisions since the last chapter update are highlighted in the CIG Summary Table of Changes available on the PHAC website. (http://www.phac-aspc.gc.ca/publicat/cig-gci/errarta-eng.php)

For additional information, refer to the National Advisory Committee on Immunization (NACI) *Statement on the recommended use of pentavalent and hexavalent vaccines* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-01/index-eng.php), *Statement on the booster for 4-6 year-olds for protection against pertussis* (http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2014/bpap-drcc_0314-eng.php) and *Update on pertussis vaccination in pregnancy*. (http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2014/pvip-vcpg_0214-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Pertussis (whooping cough) is caused by the bacterium *Bordetella pertussis*.

Reservoir

Humans. Adolescents and adults are often the source of infection in infants.

Transmission

Pertussis is highly communicable with studies showing 80% secondary attack rates among susceptible household contacts. Transmission is less likely from vaccinated cases and to vaccinated contacts. Pertussis is usually transmitted by the respiratory route through contact with respiratory droplets; indirect spread through contaminated objects occurs rarely, if at all. The incubation period is 9 to 10 days (range, 6 to 20 days), and may rarely be as long as 42 days. Infectiousness is greatest during the catarrhal period and during the first 2 weeks after cough onset. Patients are no longer contagious after 5 days of appropriate antibiotic treatment.

Risk factors

Pertussis can affect individuals of any age; however, severity is greatest among infants who are too young to be protected by a complete vaccine series. Young infants are also at highest risk of pertussis-associated complications. Immunity to pertussis from childhood vaccination and natural disease wanes with time; therefore, adolescents and adults who have not received a booster vaccination are at risk of infection and its consequent transmission to others.

Seasonal/temporal patterns

Pertussis is an endemic disease common to children (especially young children) everywhere, regardless of ethnicity, climate or geographic location.

Spectrum of clinical illness

The clinical course of pertussis is divided into three stages. The initial catarrhal stage is characterized by runny nose, sneezing, low-grade fever, and a mild cough, similar to a cold. After 1 to 2 weeks of gradually worsening cough, the paroxysmal stage begins. The paroxysmal stage is characterized by bursts of rapid coughing, ending with a inspiratory whoop and sometimes post-tussive vomiting. This

stage lasts from 1 to 6 weeks but may persist for up to 10 weeks. In the convalescent stage, recovery is gradual and may take weeks to months.

The clinical course varies with age. In young infants, who are at the highest risk, clinical symptoms are frequently atypical. Whoop and post-tussive vomiting may be absent. The presentation may be characterized solely by episodes of apnea. Serious complications occur mainly in infants and may include pneumonia, atelectasis, seizures, encephalopathy, hernias and death.

Pertussis may be milder in adolescents and adults but symptoms can range from asymptomatic infection to a very prolonged, debilitating cough. Pertussis is a common and often unrecognized cause of cough persisting for over 2 weeks in adolescents and adults. Complications in adolescents and adults include sleep disturbance, rib fractures, subconjuctival haemorrhages, rectal prolapse, and urinary incontinence, all from intense and persistent coughing. Adolescents and adults with a cough, and less so in those who are asymptomatic, are a source of infection for those most at risk, namely infants.

Mortality is rare in industrialized countries. Pneumonia is the most common cause of death, typically in infants less than 6 months of age. One to three deaths related to pertussis occur each year in Canada, particularly in infants who are too young to be immunized or unimmunized or partially immunized children.

DISEASE DISTRIBUTION

Pertussis is endemic worldwide, even in regions with high vaccination coverage. In Canada, pertussis incidence is highest in infants and children, and decreases sharply in those older than 14 years of age with peaks in activity occurring in two to five year cycles. For more information about pertussis distribution (http://www.phac-aspc.gc.ca/im/vpd-mev/pertussis-professionals-professionnels-eng.php) in Canada refer to the Public Health Agency of Canada pertussis web page. Comprehensive updates on the epidemiology of pertussis (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-03/dr-rm40-03-per-eng.php) in Canada are published periodically in the Canada Communicable Disease Report (CCDR). (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/index-eng.php)

PREPARATIONS AVAILABLE FOR USE IN CANADA

PERTUSSIS-CONTAINING VACCINES

- **ADACEL®** (adsorbed vaccine containing tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis vaccine), sanofi pasteur Ltd. (Tdap)
- **ADACEL®-POLIO** (adsorbed vaccine containing tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis vaccine combined with inactivated poliomyelitis vaccine), sanofi pasteur Ltd. (Tdap-IPV)
- **BOOSTRIX®** (adsorbed vaccine containing tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis vaccine), GlaxoSmithKline Inc. (Tdap)
- **BOOSTRIX®-POLIO** (adsorbed vaccine containing tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis vaccine combined with inactivated poliomyelitis vaccine), GlaxoSmithKline Inc. (Tdap-IPV)
- **INFANRIX hexa™** (adsorbed vaccine containing combined diphtheria and tetanus toxoids, acellular pertussis, hepatitis B [recombinant], inactivated poliomyelitis and conjugated *Haemophilus influenzae* type b vaccine), GlaxoSmithKline Inc. (DTaP-HB-IPV-Hib)
- **PEDIACEL®** (adsorbed vaccine containing diphtheria and tetanus toxoids and acellular pertussis vaccine combined with inactivated poliomyelitis vaccine and *Haemophilus influenzae* type b conjugate vaccine), sanofi pasteur Ltd. (DTaP-IPV-Hib)
- **QUADRACEL®** (adsorbed vaccine containing diphtheria and tetanus toxoids and acellular pertussis vaccine combined with inactivated poliomyelitis vaccine), sanofi pasteur Ltd. (DTaP-IPV)

Maria Bernarda Belay
Farmacéutica

Pertussis vaccine is only available as an acellular preparation in a combination vaccine. The amount of acellular pertussis antigen present varies by product. Preparations containing higher concentrations of acellular pertussis antigen (designated as "aP") are administered for primary immunization of infants and young children less than 7 years of age (pediatric formulation) and may be administered as a booster for children 4 years to less than 7 years of age. Preparations containing a lower concentration (designated as "ap" and referred to as "reduced") may also be administered as a booster dose to children 4 years to less than 7 years of age and are the recommended product for older children, adolescents and adults (adolescent/adult formulation).

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the *Drug Product Database*. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to Table 1 Contents of Immunizing Agents Available in Canada in Part 1 for a list of all vaccines available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

The vaccine efficacy following the primary series with acellular pertussis vaccines is estimated to be about 85%, and approximately 90% following booster immunization. Although the duration of protection afforded by acellular pertussis vaccine is unknown, available data suggests that protection does not significantly decline between the first booster (18 months) and second booster (4-6 years) with an acellular pertussis vaccine. However, a progressive decline in protection has been observed following the second booster dose. NACI will be assessing the implications of this finding.

IMMUNOGENICITY

Immunologic correlates of protection against pertussis are not well-defined, but higher levels of anti-pertussis antibodies seem to be associated with greater protection. In general, acellular pertussis-containing combination vaccines have demonstrated good immunogenicity of their component antigens. Consistently high response to pertussis vaccine has been observed after booster vaccination.

RECOMMENDATIONS FOR USE

INFANTS AND CHILDREN (2 months to 17 years of age)

Acellular pertussis vaccine is recommended for routine infant immunization beginning at 2 months of age. DTaP-IPV (with or without Hib) vaccine is authorized for use in children less than 7 years of age. DTaP-HB-IPV-Hib vaccine is authorized for use in children 6 weeks to 23 months of age and may be given to children aged 24 months to less than 7 years, if necessary. DTaP-IPV or Tdap-IPV vaccine should be used as the booster dose for children at 4 to 6 years of age. Children 7 years of age and older should receive the adolescent/adult formulation of diphtheria-tetanus-pertussis-containing vaccine with or without polio (Tdap or Tdap-IPV) for primary immunization or booster doses as it contains less diphtheria toxoid than preparations given to younger children and is less likely to cause reactions in older children. Tdap vaccine should be administered to adolescents at 14 to 16 years of age as the first 10-year booster dose; Tdap-IPV vaccine should be used if IPV vaccine is also indicated.

ADULTS (18 years of age and older)

All adults should receive one dose of Tdap vaccine if they have not previously received pertussis-containing vaccines in adulthood. In particular, adults who have not previously received pertussis-containing vaccines in adulthood, and who anticipate having regular contact with an infant, should be prioritized to receive a dose of Tdap vaccine, ideally administered at least 2 weeks before contact with the infant.

Persons who have had pertussis infection should receive pertussis-containing vaccines as recommended

because infection does not confer long term immunity.

Refer to *Schedule* and *Booster doses and re-immunization*. Refer to *Diphtheria Toxoid*, *Tetanus Toxoid*, *Poliomyelitis Vaccine*, *Haemophilus influenzae type b Vaccine*, and *Hepatitis B Vaccine* in Part 4 for additional information.

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults lacking adequate documentation of immunization should be considered unimmunized and started on an immunization schedule appropriate for their age and risk factors. There are no established serologic correlates for protection against pertussis. Refer to Immunization of Persons with Inadequate Immunization Records in Part 3 for additional general information.

PREGNANCY AND BREASTFEEDING

Immunization with Tdap to date has been shown to be safe in pregnant women and allows high levels of antibody to be transferred to newborns during the first two months of life when the morbidity and mortality from pertussis infection is the highest. All pregnant women following 26 weeks of pregnancy who have not received a dose of a pertussis-containing vaccine in adulthood should be encouraged to receive Tdap vaccination. In special circumstances, such as an outbreak situation, all pregnant women who are 26 weeks gestation or greater may be offered Tdap vaccination irrespective of their immunization history. Refer to Immunization in Pregnancy and Breastfeeding in Part 3 for additional general information.

INFANTS BORN PREMATURELY

Premature infants in stable clinical condition should be immunized with pertussis-containing vaccine at the same chronological age and according to the same schedule as full-term infants. Infants born prematurely (especially those weighing less than 1,500 grams at birth) are at higher risk of apnea and bradycardia following vaccination. Hospitalized premature infants should have continuous cardiac and respiratory monitoring for 48 hours after their first immunization. Refer to Immunization of Infants Born Prematurely in Part 3 for additional general information.

PATIENTS/RESIDENTS IN HEATH CARE INSTITUTIONS

Residents of long-term care facilities should receive all routine immunizations appropriate for their age and risk factors, including acellular pertussis-containing vaccine. Refer to Immunization of Patients in Health Care Institutions in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

Diphtheria-tetanus-pertussis-polio-Hib-containing vaccines may be administered to immunocompromised persons. When considering immunization of an immunocompromised person, consultation with the individual's attending physician may be of assistance in addition to the guidance provided in Immunocompromised persons in Diphtheria Toxoid in Part 4. For complex cases, referral to a physician with expertise in immunization and/or immunodeficiency is advised.

Refer to Haemophilus influenza type b Vaccine in Part 4 for additional information. Refer to Immunization of Immunocompromised Persons in Part 3 for additional general information.

PERSONS WITH CHRONIC DISEASES

Neurologic disorders

People with neurological disorders are at risk of added morbidity and mortality from pertussis disease. Persons with neurological disorders with onset preceding immunization should receive all routinely recommended immunizations, including pertussis-containing vaccine.

Cases of Guillain Barré Syndrome (GBS) have been reported very rarely following administration of a tetanus toxoid-containing vaccine. Refer to Contraindications and Precautions for additional information. Refer to Tetanus Toxoid in Part 4 for additional information.

María Bernarda Belay
Farmacéutica
Co - Directora Técnica

Refer to Immunization of Persons with Chronic Diseases in Part 3 for additional general information.

TRAVELLERS

Unimmunized or incompletely immunized travellers should receive diphtheria-tetanus-pertussis-polio-Hib-containing vaccine as appropriate for age. Refer to Diphtheria Toxoid and Poliomyelitis Vaccine in Part 4 for information regarding other components in acellular pertussis-containing combination vaccines. Refer to Immunization of Travellers in Part 3 for additional general information.

PERSONS NEW TO CANADA

Health care providers who see people newly arrived in Canada should review the immunization status and update immunization for these individuals. Children who have received one or more doses of diphtheria-tetanus-whole cell pertussis (DPT) vaccine before arriving in Canada should have their vaccine series completed with acellular pertussis- containing vaccine (DTaP or Tdap) as appropriate for age. Refer to Immunization of Persons New to Canada in Part 3 for additional general information.

WORKERS

All health care and child care workers, regardless of age, should receive a single dose of Tdap vaccine for pertussis protection if not previously received in adulthood, even if not due for a tetanus and diphtheria booster. Refer to Immunization of Workers in Part 3 for additional general information.

OUTBREAK CONTROL

Acellular pertussis vaccine has been used for the control of pertussis outbreaks in defined populations, such as in schools or hospitals, although data supporting its effectiveness are lacking. Children exposed to a case of pertussis should have their immunization status reviewed and updated as required. In an outbreak, public health officials may recommend that pregnant women be offered Tdap vaccination after 26 weeks of gestation irrespective of their immunization history.

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose of pertussis-containing vaccine is 0.5 mL

Route of administration

Pertussis-containing vaccines must be administered intramuscularly. Refer to Vaccine Administration Practices in Part 1 for additional information.

Schedule

Infants and children (2 months to 6 years of age)

Routine pertussis immunization of infants: DTaP-IPV-Hib vaccine should be given at 2, 4, 6 and 12 to 23 months of age (generally given at 18 months of age).

If infant immunization for hepatitis B is undertaken, DTaP-HB-IPV-Hib vaccine may be used as an alternative to separately administered hepatitis B and DTaP-IPV-Hib vaccines. DTaP-HB-IPV-Hib vaccine is authorized for use in children 6 weeks to 23 months of age and may be given to children aged 24 months to less than 7 years, if necessary. DTaP-HB-IPV-Hib vaccine may be given at 2, 4, 6 and 12 to 23 months of age but the fourth dose is unlikely to provide significant additional hepatitis B protection and will increase cost; DTaP-IPV-Hib vaccine provided at 12 to 23 months of age may be used to complete the primary series of DTaP-HB-IPV-Hib vaccine administered at 2, 4 and 6 months of age.

If rapid protection is required for an infant, the first dose of DTaP-IPV-Hib or DTaP-HB-IPV-Hib vaccine can be given at 6 weeks of age. The first three doses may be administered at intervals of 4 weeks and, optimally, the fourth dose given 12 months after the third dose. The fourth dose may be given at a minimum interval of 6 months after the third dose in certain situations (e.g., travel) but must be administered on or after 12 months of age for sustained immunity.

Children less than 7 years of age not immunized in infancy: should receive three doses of DTaP-IPV (with or without Hib) vaccine with an interval of 8 weeks between doses, followed by a dose of DTaP-IPV vaccine 6 to 12 months after the third dose. A booster dose of either DTaP-IPV or Tdap-IPV vaccine should be administered at 4 to 6 years of age (school entry). The booster dose at 4 to 6 years of age is not required if the fourth dose of tetanus-toxoid containing vaccine was administered after the fourth birthday.

If rapid protection is required for a child less than 7 years of age not immunized in infancy, the first three doses of vaccine may be administered at intervals of 4 weeks and, optimally the fourth dose given 12 months after the third dose. The fourth dose may be given at a minimum interval of 6 months after the third dose in certain situations (e.g., travel).

Children who received a primary series of acellular pertussis-containing vaccine and a booster dose 6-12 months later as outlined above should receive a booster dose of either DTaP-IPV or Tdap-IPV vaccine at 4 to 6 years of age (school entry); and, 10 years later, a booster dose of Tdap vaccine at 14 to 16 years of age. The booster dose at 4 to 6 years of age is not required if the fourth dose of acellular pertussis-containing vaccine was administered after the fourth birthday.

Children and adolescents (7 years to 17 years of age)

Children 7 years of age and older not previously immunized should receive three doses of Tdap-IPV vaccine with an interval of 8 weeks between the first two doses followed by a third dose administered 6 to 12 months after the second dose. A booster dose of Tdap vaccine should be administered 10 years after the last dose.

Adults (18 years of age and older)

Adults who have not previously received Tdap vaccine in adulthood should receive one dose of Tdap vaccine, which can be administered regardless of the interval since the last dose of tetanus and diphtheria toxoid-containing vaccine.

BOOSTER DOSES AND RE-IMMUNIZATION

The preschool booster dose of either DTaP-IPV or Tdap-IPV vaccine should be administered at 4 to 6 years of age. Adolescents should routinely receive a booster dose of Tdap vaccine at 14 to 16 years of age. Adults who have not previously received Tdap vaccine in adulthood, should receive one dose of Tdap vaccine regardless of the interval since the last dose of tetanus or diphtheria toxoid-containing vaccine.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving pertussis vaccine.

STORAGE REQUIREMENTS

Store pertussis-containing vaccines in a refrigerator at +2°C to +8°C and do not freeze.
Refer to Storage and Handling of Immunizing Agents in Part 1 for additional general information.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Pertussis-containing vaccines may be administered concomitantly with routine vaccines at different injection sites using separate needles and syringes. Refer to Timing of Vaccine Administration in Part 1 for additional general information.

CAIF S.A.
Marla Bernarda Belay

VACCINE AND IMMUNE GLOBULIN SAFETY AND ADVERSE EVENTS

Refer to Vaccine Safety in Part 2 for additional general information. Refer to Diphtheria Toxoid, Tetanus Toxoid, Poliomyelitis Vaccine, Haemophilus influenzae type b Vaccine and Hepatitis B Vaccine in Part 4 for additional information regarding other components in pertussis-containing combination vaccines.

COMMON AND LOCAL ADVERSE EVENTS

Redness, swelling and pain at the injection site are the most common adverse reactions to childhood pertussis-containing combination vaccines. A nodule may be palpable at the injection site and persist for several weeks. Abscess at the injection site has been reported.

In clinical trials, injection site adverse reactions, including tenderness, erythema, and/or swelling were reported in 10% to 40% of children after each of the first 3 doses of pertussis-containing vaccine. Mild systemic reactions such as fever, irritability and/or fussiness were commonly reported (8% to 29%), as well as drowsiness (40% to 52%).

In two clinical studies, swelling (greater than 5 cm) and erythema were reported in 15 % to 20% of vaccinees after the fourth or fifth doses of DTaP vaccines. Extensive limb swelling (greater than 10 cm in diameter) possibly involving the entire proximal limb may occur in 2% to 6% of children. While these injection site reactions produce significant swelling, pain is generally limited. There is some evidence that children with extensive limb swelling following the fourth dose of a DTaP vaccine are at increased risk of such an event following the fifth dose. The presence of a large injection site reaction to a previous dose is not a contraindication to continuing the recommended schedule.

Among adults given a booster dose of Tdap vaccine, very common reactions include pain, redness and swelling at the injection site, headache, and fatigue. Fever and chills are common reactions. Overall, adverse reactions are less common in adults than adolescents. The interval between the childhood DTaP vaccine series or a dose of Td vaccine, and a dose of Tdap vaccine does not affect the rate of injection site or systemic adverse events.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. Anaphylaxis following vaccination with pertussis-containing vaccine may occur but is very rare.

Hypotonic hyporesponsive episodes (HHE) and seizures may occur following immunization with pertussis-containing vaccine. The WHO case definition of HHE includes sudden onset of hypotonia (muscle limpness), hyporesponsiveness (reduced responsiveness or unresponsiveness), and pallor or cyanosis. However, there is evidence that there are no adverse consequences to these events and the adverse consequences of being incompletely immunized have been well documented. HHE occur less frequently following receipt of acellular pertussis-containing vaccine than following whole cell pertussis-containing vaccines which are no longer in use in Canada. High fever and convulsions, both febrile and afebrile, are rarely reported and are not contraindications to further immunization with acellular pertussis-containing vaccine. Encephalopathy with onset temporally related to pertussis immunization is very rare and an alternative etiology is usually established. Encephalopathy itself, from whatever cause, is not a contraindication to pertussis immunization. Refer to Immunization of Persons with Chronic Diseases in Part 3 for additional information.

OTHER REPORTED ADVERSE EVENTS AND CONDITIONS

Epidemiological studies do not support allegations of a causal relationship between pertussis-containing vaccines and permanent neurological injury.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report, through local public health officials, any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI. Refer to Reporting Adverse Events Following Immunization (AEFI) (http://www.phac-aspc.gc.ca/im/aefi_guide/index-eng.php) in Canada in Vaccine Safety Part 2 for additional information about AEFI reporting.

CONTRAINDICATIONS AND PRECAUTIONS

Pertussis-containing vaccines are contraindicated in persons with a history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its container. Refer to Table 1 in Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of all vaccines available for use in Canada and their contents. For pertussis-containing vaccines, potential allergens include:

- ADACEL®-POLIO: neomycin, polymyxin B, streptomycin
- BOOSTRIX®: latex in plunger stopper of pre-filled syringe
- BOOSTRIX®-POLIO: latex in plunger stopper of pre-filled syringe, neomycin, polymyxin B
- INFANRIX hexa™: latex in plunger stopper of pre-filled syringe, neomycin, polymyxin B, yeast
- PEDIACEL®: neomycin, polymyxin B, streptomycin
- QUADRACEL®: neomycin, polymyxin B

There are no currently known potential allergens in ADACEL® vaccine.

With respect to Infanrix hexa™, hypersensitivity to yeast is very rare and a personal history of yeast allergy is not generally reliable. In situations of suspected hypersensitivity or non-anaphylactic allergy to vaccine components, investigation is indicated which may involve immunization in a controlled setting. Consultation with an allergist is advised.

It is prudent to not administer further doses of tetanus-toxoid containing vaccine to persons who develop Guillain-Barre Syndrome (GBS) within 6 weeks of receiving such vaccine. Those who develop GBS outside the 6 week interval may receive subsequent doses of tetanus toxoid-containing vaccine. If there is a history of both *Campylobacter* infection (which has been associated with GBS) and receipt of a tetanus and diphtheria toxoid-containing vaccine within the 6 weeks before the onset of GBS, consultation with an infectious disease specialist is advised. Refer to Tetanus Toxoid in Part 4 for additional information.

Administration of pertussis-containing vaccine should be postponed in persons suffering from severe acute illness. Immunization should not be delayed because of minor acute illness, with or without fever. Refer to General Contraindications and Precautions in Part 2 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

The primary series of three doses of pertussis-containing vaccine should be completed with an appropriate vaccine from the same manufacturer whenever possible. However, if the original vaccine is unknown or unavailable, an alternative combination vaccine from a different manufacturer may be used to complete the primary series. On the basis of expert opinion, an appropriate product from any manufacturer can be used for all booster doses. Refer to Principles of Vaccine Interchangeability in Part 1 for additional general information.

CAIF S.A.
María Bernarda Belay
Farmacéutica
Co - Directora Técnica

SELECTED REFERENCES

Advisory Committee on Immunization Practices. *Resolution No. 6/11-2, Vaccines for Children Program, Vaccines to prevent Diphtheria, Tetanus and Pertussis.* Accessed July 2011 at: http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/0611dtap.pdf

Centers for Disease Control and Prevention. *ACIP Provisional Recommendations for Health Care Personnel on use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (Tdap) and use of Postexposure Antimicrobial Prophylaxis.* Accessed May 2011 at: http://www.cdc.gov/vaccines/recs/provisional/default.htm

Centers for Disease Control and Prevention. *Notice to Readers: FDA Approval of Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, (INFANRIX®) for Fifth Consecutive DTaP Vaccine Dose.* MMWR Morb Mortal Wkly Rep. 2003 Sep 26;52(38):921.

Centers for Disease Control and Prevention. *Prevention of Pertussis, Tetanus, and Diphtheria Among Pregnant and Postpartum Women and Their Infants. Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR Morb Mortal Wkly Rep. 2008;57(RR-4):1-49.

Centers for Disease Control and Prevention. *The Pink Book: Epidemiology and Prevention of Vaccine Preventable Diseases.* Updated 11th ed.; May 2009. Accessed October 2010 at: http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm

Centers for Disease Control and Prevention. *Health Information for International Travel 2010. The Yellow Book.* Accessed October 2010 at: http://wwwnc.cdc.gov/travel/content/yellowbook/home-2010.aspx

Centers for Disease Control and Prevention. *Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccine from the Advisory Committee on Immunization Practices, 2010.* MMWR Morb Mortal Wkly Rep. 2011;60(1):13-15.

Centers for Disease Control and Prevention. *Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Vaccine in Adults Aged 65 Years and Older — Advisory Committee on Immunization Practices (ACIP), 2012.* Accessed October 2012 at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6125a4.htm

David S, Hemsley C, Pasquali P et al. *Enhanced surveillance for vaccine-associated adverse events: dTap catch-up of high school students in Yukon.* Can Commun Dis Rep 2005;31(11):117-26.

Decker M, Edwards K, Steinhoff M et al. *Comparison of 13 acellular pertussis vaccines: adverse reactions.* Pediatrics 1995;96(3 Pt 2):557-66.

De Serres G, Shadmani R, Boulianne N et al. *Effectiveness of a single dose of acellular pertussis vaccine to prevent pertussis in children primed with pertussis whole cell vaccine.* Vaccine 2001;19(20-22):3004-8.

Edwards KM, Decker MD. *Acellular pertussis vaccines for infants.* N Engl J Med 1996;334(6):391-92.

Edwards KM, Meade BD, Decker MD et al. *Comparison of 13 acellular pertussis vaccines: overview and serologic response.* Pediatrics 1995;96(3 Pt 2):548-57.

Gautret P, Wilder-Smith A. *Vaccination against tetanus, diphtheria, pertussis and poliomyelitis in adult travellers.* Travel Med Infect Dis 2010;8:155-60.

GlaxoSmithKline Inc. *Product Monograph - BOOSTRIX®,* October 2009.

GlaxoSmithKline Inc. *Product Monograph - BOOSTRIX®-POLIO,* June 2008.

GlaxoSmithKline Inc. *Product Monograph - INFANRIX hexa™*. July 2008.

Greco D, Salmaso S, Mastrantonio P et al. *A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis.* N Engl J Med 1996;334(6):341-48.

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

Halperin S, McNeil S, Langley J et al. *Tolerability and antibody response in adolescents and adults revaccinated withtetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed (Tdap) 4–5 years after a previous dose.* Vaccine 2011;29: 8459–65.

Halperin S, Smith B, Russell M et al. *An adult formulation of a five component acellular pertussis vaccine combined with diphtheria and tetanus toxoids is safe and immunogenic in adolescents and adults. Pediatr Infect Dis J* 2000;19(4):276-83.

Health Canada. *National Consensus Conference on Pertussis.* Can Commun Dis Rep 2003;29(S3):1-39.

Le Saux N, Barrowman NJ, Moore DL et al. Canadian Paediatric Society/ Health Canada Immunization Monitoring Program-Active (IMPACT). *Decrease in hospital admissions for febrile seizures and reports of hypotonic-hyporesponsive episodes presenting to hospital emergency departments since switching to acellular pertussis vaccine in Canada: a report from IMPACT. Pediatrics.* 2003 Nov;112(5):e348.

Mikelova L, Halperin S, Scheifele D et al. *Predictors of death in infants hospitalized with pertussis: a case-control study of 16 pertussis deaths in Canada.* J Pediatr 2003;143:576-81.

Moore DL, Le Saux N, Scheifele D, et al. *Lack of evidence of encephalopathy related to pertussis vaccine: active surveillance by IMPACT, Canada, 1993–2002.* Pediatr Infect Dis J 2004;23:568–71.

Murphy TV, Slade BA, Broder KR et al. *Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Prevention of pertussis, tetanus, and diphtheria among pregnant and postpartum women and their infants recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR Recomm Rep. 2008 May 30;57(RR-4):1-51. Review. Erratum in: MMWR Morb Mortal Wkly Rep. 2008 Jul 4;57(26):723.

National Advisory Committee on Immunization. *Prevention of pertussis in adolescents and adults.* Can Commun Dis Rep 2003;29(ACS-5):1-9.

National Advisory Committee on Immunization. *Statement on adult/adolescent formulation of combined acellular pertussis, tetanus, and diphtheria vaccine.* Can Commun Dis Rep 2000;26(ACS-1):1-8.

National Advisory Committee on Immunization. *Statement on the booster for 4-6 year-olds for protection against pertussis* Can Commun Dis Rep 2014; 40

National Advisory Committee on Immunization. *Statement on the recommended use of pentavalent and hexavalent vaccines.* Can Comm Dis Rep 2007;33(ACS-1):1-15.

National Advisory Committee on Immunization. *Statement on pertussis vaccine.* Can Commun Dis Rep 1997;23(ACS-3):1-16.

National Advisory Committee on Immunization. *Update on pertussis vaccination in pregnancy.* Can Commun Dis Rep 2014; 40

Ntezayabo B, De Serres G, Duval B. *Pertussis resurgence in Canada largely caused by a cohort effect.* Pediatr Infect Dis J 2003;22(1):22-7.

CAIEIRO
Maria Bernarda Belay
Farmacêutica
Co - Directora Técnica

Ray P, Hayward J, Michelson D, et al. *Encephalopathy after whole cell pertussis or measles vaccination: lack of evidence for a causal association in a retrospective case-control study.* Pediatr Infect Dis J 2006;25:768–73.

Rennels MB. *Extensive swelling reactions occurring after booster doses of diphtheria-tetanus-acellular pertussis vaccines.* Semin Pediatr Infect Dis. 2003;14(3):196-8.

Rennels MB, Black S, Woo EJ et al. *Safety of a fifth dose of diphtheria and tetanus toxoid and acellular pertussis vaccine in children experiencing extensive, local reactions to the fourth dose.* Pediatr Infect Dis J 2008;27(5):464-5.

Sanofi Pasteur Ltd. *Product Monograph - ADACEL®*, August 2009.

Sanofi Pasteur Ltd. *Product Monograph - ADACEL®-POLIO*, October 2010.

Sanofi Pasteur Ltd. *Product Monograph – PEDIACEL®*, January 2009.

Sanofi Pasteur Ltd. *Product Monograph - QUADRACEL®*, July 2008.

Schmitt H, von Konig C, Neiss A et al. *Efficacy of acellular pertussis vaccine in early childhood after household exposure.* JAMA1996;275(1):37-41.

Stehr K, Cherry J, Heininger U et al. *A comparative efficacy trial in Germany in infants who received either the Lederle-Takeda acellular pertussis component DTP (DTap) vaccine, the Lederle whole-cell component DTP vaccine, or DT vaccine.* Pediatrics 1998;101(1 Pt 1):1-11.

Trollfors B, Taranger J, Lagergard T et al. *A placebo-controlled trial of a pertussis-toxoid vaccine.* N Engl J Med 1995;333(16):1045-50.

Ward J, Cherry J, Chang S et al. *Efficacy of an acellular pertussis vaccine among adolescents and adults.* N Engl J Med 2005;353(15):1555-63.

Waters V, Jamieson F, Richardson S et al. *Outbreak of atypical pertussis detected by polymerase chain reaction in immunized preschool-aged children.* Pediatr Infect Dis J 2009;28(7):582-7.

FOLIO 1074

PART 4

PNEUMOCOCCAL VACCINE

KEY INFORMATION (refer to text for details)

What	• *Streptococcus pneumoniae* infections are a major cause of illness and death worldwide. • Invasive pneumococcal disease (IPD) is most common in the very young, the elderly and persons at high risk (such as those with functional or anatomic asplenia; congenital or acquired immunodeficiency). • In children, efficacy of pneumococcal conjugate 7-valent (Pneu-C-7) vaccine against IPD due to serotypes contained in the vaccine is estimated to range from 89% to 97%. There are no efficacy data available for other pneumococcal conjugate vaccines. • Pneu-P-23 vaccine efficacy against IPD is estimated to be 50% to 80% among the elderly and in specific groups. • There may be redness, swelling and soreness at the injection site following pneumococcal immunization.
Who	• Routine pneumococcal immunization is recommended for all children • Adults and children considered to be at increased risk from IPD should be vaccinated using the pneumococcal vaccine and schedule recommended for their age group and specific risk condition.

CAIF S.A.
María Bernarda Belay
Farmacéutica
Co - Directora Técnica

How	**Pneu-C-13 vaccine** • **Routine infant immunization:** administer three doses of Pneu-C-13 vaccine at minimum 8-week intervals beginning at 2 months of age, followed by a fourth dose at 12 to 15 months of age. For healthy infants, a three-dose schedule may be used with doses at 2 months, 4 months, and 12 months of age. • **12 to 23 months of age:** administer two doses of Pneu-C-13 vaccine at least 8 weeks apart to children not previously vaccinated with a conjugate pneumococcal vaccine or who received only 1 dose before 12 months of age • **24 to 35 months of age:** administer one dose of Pneu-C-13 vaccine to children with no or incomplete vaccination schedules with any conjugate pneumococcal vaccine. • **36 to 59 months of age** - administer one dose of Pneu-C-13 vaccine to: o Healthy children who are of aboriginal origin or who attend group child care who have received age-appropriate pneumococcal conjugate vaccination but have not received Pneu-C-13 vaccine. Consider one dose of Pneu-C-13 vaccine for other healthy children. o Children at high risk of IPD who have received age-appropriate pneumococcal conjugate vaccination but have not received Pneu-C-13 vaccine. o Children with no or incomplete vaccination schedules with any conjugate pneumococcal vaccine. • **60 months to 17 years of age:** administer one dose of Pneu-C-13 vaccine to children and adolescents at high risk of IPD who have not previously received Pneu-C-13 vaccine. • **Adults with immunocompromising conditions (except hematopoietic stem cell transplant (HSCT)):** administer one dose of Pneu-C-13 followed 8 weeks later by one dose of Pneu-P-23 (if not previously immunized with Pneu-P-23). The Pneu-C-13 dose should be administered at least one year after any previous dose of Pneu-P-23. A single re-immunization with Pneu-P-23 is recommended. • **Adults with hematopoietic stem cell transplantation (HSCT):** administer three doses of Pneu-C-13 starting 3-9 months after transplant. These doses should be administered at least 4 weeks apart, followed by a dose of Pneu-P-23 12 to 18 months post transplant (6 to 12 months after the last dose of Pneu-C-13). A single re-immunization with Pneu-P-23 is recommended. **Pneu-P-23 vaccine** • Administer one dose of Pneu-P-23 vaccine after pneumococcal conjugate vaccine to children 24 months of age and older, adolescents and adults who are at high risk of IPD. • Administer one dose of Pneu-P-23 vaccine to immunocompetent adults 65 years of age and older and to immunocompetent residents of long-term care facilities without contraindications. Immunocompromised adults should be immunized with Pneu-C-13 and Pneu-P-23 as indicated above. • One lifetime re-immunization with Pneu-P-23 vaccine is recommended for those at highest risk of IPD.
Why	• *S. pneumoniae* is a common cause of invasive disease, such as pneumonia, bacteremia, and meningitis. • The case fatality rate of bacteremic pneumococcal pneumonia is 5% to 7% and is higher among elderly persons.

For additional information, refer to the National Advisory Committee on Immunization (NACI) Statements: *Statement on the recommended use of pneumococcal 23-valent polysaccharide vaccine in homeless persons and injection drug users* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/08vol34/acs-5/index-eng.php); *Update on pediatric invasive pneumococcal disease and recommended use of conjugate pneumococcal vaccines* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-3/index-eng.php); *Update on the use of conjugate pneumococcal vaccines in childhood* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-12/index-eng.php); *Statement on the Use of Conjugate*

Pneumococcal Vaccine – 13 valent in Adults (Pneu-C-13) (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-5/index-eng.php); and *Update on the Use of Pneumococcal Vaccines: Addition of Asthma as a High-Risk Condition* (http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2014/pvaa-vaaa_0414-eng.php).

Significant revisions since the last chapter update are highlighted in the CIG Summary Table of Changes available on the PHAC website. (http://www.phac-aspc.gc.ca/publicat/cig-gci/errata-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Pneumococcal disease is caused by a bacterium, *Streptococcus pneumoniae* (*S. pneumoniae* or pneumococcus) of which 15 serotypes cause the majority of disease.

Reservoir

Humans carry *S.pneumoniae* in their nasopharynx.

Transmission

S. pneumoniae is transmitted by direct oral contact, respiratory droplets, or indirect contact with respiratory secretions of infected or colonized persons. A person can transmit the infection as long as nasal and throat secretions contain pneumococci in large numbers; usually until 24 hours following appropriate antibiotic treatment. The incubation period has not been clearly defined and may be as short as 1 to 3 days.

Risk factors

IPD is most common in the very young, the elderly and groups at high risk (*Table 1*). Persons with a cochlear implant appear to be at increased risk of pneumococcal meningitis. Attendance at a child care center has been shown to increase the risk of IPD and acute otitis media (AOM) 2-fold to 3-fold among children under 5 years of age. Homeless populations have high rates of respiratory infections, including those caused by *S. pneumoniae*.

CAIF S.A.
María Bernarda Belay
Farmacéutica
Co - Directora Técnica
M.P. 15.148

Table 1: Conditions resulting in high risk of IPD

Conditions without immunocompromising conditions
Chronic cerebral spinal fluid (CSF) leak
Chronic neurologic condition that may impair clearance of oral secretions
Cochlear implants (including those children who are to receive implants)
Chronic cardiac or pulmonary disease
Diabetes mellitus
Chronic kidney disease
Nephrotic syndrome
Chronic liver disease (including hepatic cirrhosis due to any cause)
Asthma that required medical care in the preceding 12 months
Conditions with immunocompromising conditions
Sickle cell disease or other hemoglobinopathies*
Congenital immunodeficiencies involving any part of the immune system, including B-lymphocyte (humoral) immunity, T-lymphocyte (cell) mediated immunity, complement system (properdin, or factor D deficiencies), or phagocytic functions
Asplenia (functional or anatomic)*
Immunocompromising therapy including use of long-term corticosteroids, chemotherapy, radiation therapy, post-organ transplant therapy, and certain anti-rheumatic drugs
HIV infection
Hematopoietic stem cell transplant (recipient)
Malignant neoplasms including leukemia and lymphoma
Solid organ or islet transplant (candidate or recipient)

* Generally asplenia (functional or anatomic), sickle cell disease and other hemoglobinopathies are not considered immunocompromising conditions, but for the purposes of pneumococcal vaccine recommendations they are included in this category.

Seasonal/temporal pattern

IPD is more common in the winter and spring in temperate climates.

Spectrum of clinical illness

Pneumonia with secondary bacteremia, bacteremia, and meningitis are the most common IPDs. Bacteremia is the most common manifestation of IPD among children 2 years of age and younger. Bacteremic pneumococcal pneumonia is the most common presentation among adults and is a common complication following influenza. The case fatality rate of bacteremic pneumococcal pneumonia is 5% to 7% and is higher among elderly persons. Bacterial spread within the respiratory tract may result in AOM, sinusitis or recurrent bronchitis.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

Pneumococcal infections are a major cause of morbidity and mortality worldwide and pneumonia is the most common cause of pneumococcal-attributed death. Each year, an estimated 1 million children under five years of age die due to S. *pneumoniae* respiratory infections, most in developing countries. In Europe and the United States (US), pneumococcal pneumonia is the most common community-

acquired bacterial pneumonia, estimated to affect approximately 100 of every 100,000 adults each year. Bacteremia affects approximately 15 to 19 of every 100,000 adults and meningitis affects about 1 to 2 of every 100,000 adults each year.

National

IPD has been nationally notifiable since 2000. In Canada between 2005 to 2008, incidence rates per 100,000 population per year of IPD were 26.6 among infants less than 1 year of age, 16.9 among children 1 to 4 years, and 20.4 among adults 60 years of age and older. Children under 1 year of age accounted for 3% of cases, those aged 1 to 4 years accounted for 8%, and adults 60 years of age and older accounted for 40% of IPD cases.

Pneu-C-7 vaccine was incorporated into routine childhood immunization schedules in all Canadian jurisdictions by 2006. Pneu-C-10 came on the market in 2009 and Pneu-C-13 replaced Pneu-C-7 vaccine in 2010. A population-based study has shown a greater than 80% decline in the incidence of pediatric IPD following Pneu-C-7 vaccine implementation. However, the incidence of IPD caused by serotypes not protected by Pneu-C-7 increased, resulting in a decreased impact of the vaccination program.

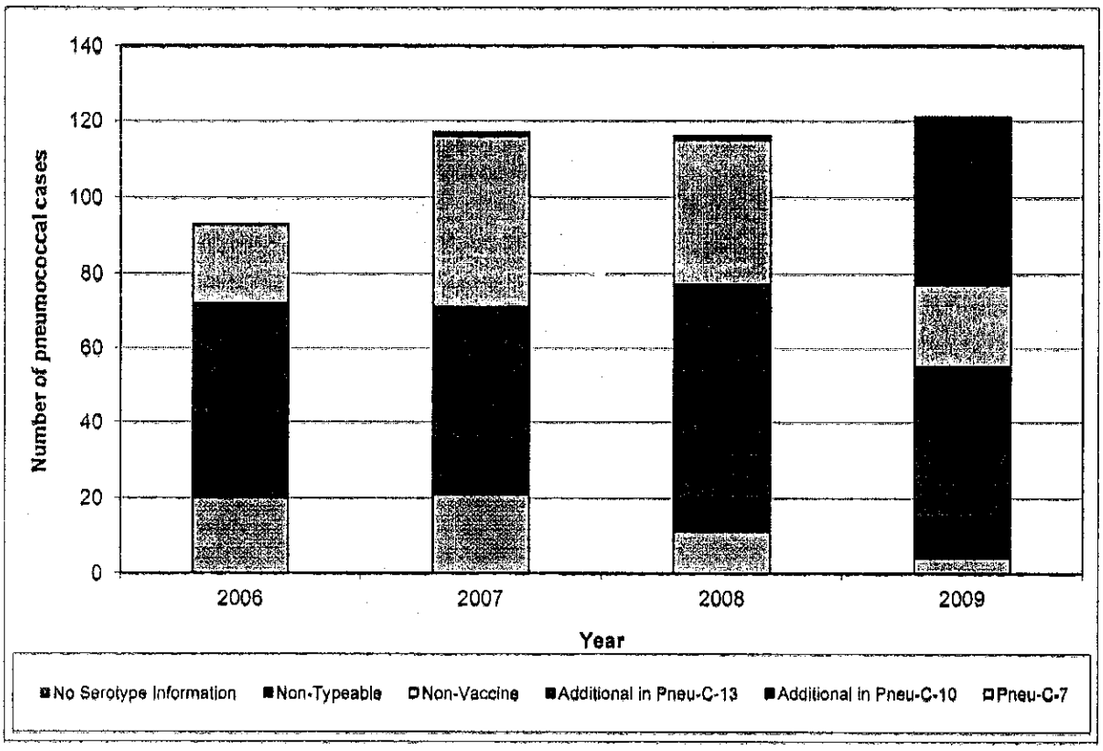
Canada does not currently have a national surveillance system that links epidemiological and serological data. However, data from regional surveillance systems in British Columbia, Alberta, Quebec, Ontario and Northern Canada provide information on IPD incidence rates by serotype. In 2008, among children under 5 years of age, the incidence of IPD varied by serotype grouping and by surveillance system. The incidence rate of IPD caused by serotypes covered by Pneu-C-7 vaccine was estimated to range from 0.0 to 7.8 per 100,000. Compared to Pneu-C-7 vaccine, the incidence rate of IPD additionally covered by Pneu-C-10 vaccine ranged from 0.0 to 2.1 cases per 100,000 and the incidence rate of IPD additionally covered by Pneu-C-13 vaccine ranged from 3.7 to 31.2 per 100,000 individuals.

From 2006 to 2009, Immunization Monitoring Program, ACTive (IMPACT) data suggest that the number of IPD cases due to serotypes contained in Pneu-C-7 vaccine decreased, but the number of cases due to other serotypes increased in children aged 0 to 4 years. Refer to *Figure 1* and *Table 2*. Other studies have shown that there was also a decline in the incidence of IPD caused by serotypes contained in Pneu-C-7 vaccine among adults 65 years of age and older, likely due to the indirect effect of conjugate pneumococcal vaccines decreasing carriage in children and subsequent transmission to older adults, rather than a direct effect of Pneu-P-23 vaccine.

In particular, the incidence of disease due to strains of *S. pneumoniae* serotype 19A has increased in Canada and other countries (refer to *Figure 1*). Data on the effectiveness of the new Pneu-C-13 vaccine that covers this serotype are pending.

CAIF S.A.
María Bernarda Bolay
Farmacéutica
Co - Directora Técnica
M.P. 15.148

Figure 1: Number of pneumococcal cases among children less than 5 years of age by year and serotype category, Canada, 2006-2009



Data from the Immunization Monitoring Program ACTive (IMPACT) hospital-based surveillance network.
Pneu-C-7: cases of pneumococcal disease caused by serotypes contained in Pneu-C-7 vaccine
Additional in Pneu-C-10: cases of pneumococcal disease caused by the three additional serotypes contained in Pneu-C-10 vaccine, compared to Pneu-C-7 vaccine
Additional in Pneu-C-13: cases of pneumococcal disease caused by the three additional serotypes contained in Pneu-C-13 vaccine, compared to Pneu-C-10 vaccine
Non-vaccine: cases of pneumococcal disease caused by serotypes that are not contained in a conjugate pneumococcal vaccine.
Cases of IPD: patients with clinical evidence of invasive disease with isolation of *S. pneumoniae*, or demonstration of *S. pneumoniae* DNA from a normally sterile site (excluding the middle ear [mastoiditis] and pleural cavity [pneumonia, pleural effusion or empyema]).

RECENT OUTBREAKS

Between 2004 and 2008, a widespread community-based outbreak of S. pneumoniae serotype 5 occurred, principally in homeless adults and intravenous drug users, in British Columbia, Alberta, Saskatchewan and Manitoba, with 1,002 cases reported as of December 31, 2008.

PREPARATIONS AUTHORIZED FOR USE IN CANADA

PNEUMOCOCCAL VACCINES

Conjugate pneumococcal vaccines

- **Prevnar®13** (pneumococcal 13-valent conjugate vaccine, CRM197 protein), Pfizer Canada Inc. (licensee) (Pneu-C-13)
- **SYNFLORIX™** (pneumococcal 10-valent conjugate vaccine, non-typeable *Haemophilus influenzae* protein D, diphtheria or tetanus toxoid conjugates adsorbed), GlaxoSmithKline Inc. (Pneu-C-10).

The tetanus, diphtheria and non-typeable *Haemophilus influenzae* carrier proteins used in conjugate pneumococcal vaccines do not confer protection against diphtheria, tetanus or *Haemophilus influenzae* type b disease.

Pneumococcal 23-valent polysaccharide vaccines

- **PNEUMOVAX® 23** (pneumococcal 23-valent polysaccharide vaccine), Merck Canada Inc. (Pneu-P-23)
- **PNEUMO 23®** (pneumococcal 23-valent polysaccharide vaccine), Sanofi Pasteur SA (manufacturer), sanofi pasteur Ltd. (distributor) (Pneu-P-23)

Table 2: *S. pneumoniae* serotypes included in pneumococcal vaccines

Vaccine	Serotypes in Pneumococcal Vaccines																							
	4	9V	6B	14	18C	19F	23F	1	5	7F	3	6A	19A	2	8	9N	10A	11A	12F	15B	17F	20	22F	33F
Pneu-C-7*	■	■	■	■	■	■	■																	
Pneu-C-10	■	■	■	■	■	■	■	■	■	■														
Pneu-C-13	■	■	■	■	■	■	■	■	■	■	■	■	■											
Pneu-P-23	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	■

*Pneu-C-7 vaccine is no longer available.

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monograph available through the Drug Product Database. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of all vaccines available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

Conjugate pneumococcal vaccines

In children, the efficacy of Pneu-C-7 vaccine is 89% to 97% against IPD serotypes whose antigens are contained in the vaccine. Pneu-C-7 vaccine provides a 54% reduction in AOM and a 20% reduction in tympanostomy tube placement due to vaccine serotypes. There are no efficacy data available for Pneu-C-13 vaccine for any indication and no efficacy data available for Pneu-C-10 vaccine for its primary indication against IPD. However, preliminary estimates from an unpublished case control study that was conducted in the US suggest 79% to 95% vaccine effectiveness among 2-59 month old children against Pneu-C-13 serotype IPD.

CAIF S.A.
María Bernarda Belay
Farmacéutica

Pneumococcal polysaccharide vaccines

Pneu-P-23 vaccine efficacy is more than 80% against IPD among healthy young adults and ranges from 50% to 80% among the elderly and in high-risk groups. Effectiveness in preventing community-acquired pneumonia in the elderly remains a challenge. Immunogenicity and efficacy are decreased in certain groups at particularly high risk of pneumococcal infection, such as persons with renal failure, sickle cell anemia, or impaired immune responsiveness, including HIV infection. Following immunization with Pneu-P-23 vaccine, antibody levels decline after 5 to 10 years and decrease more rapidly in some groups than others. The duration of immunity is not known.

IMMUNOGENICITY

Conjugate pneumococcal vaccines

Infants immunized with Pneu-C-7 vaccine develop a 3.4-fold to 20-fold increase in serum antibodies against vaccine serotypes. Anamnestic responses are induced upon boosting with either conjugate pneumococcal or Pneu-P-23 vaccines. The immunogenicity of Pneu-C-7 vaccine has been demonstrated in children with immunodeficiency.

New conjugate pneumococcal vaccines Pneu-C-10 and Pneu-C-13 were authorized based on identifying an immune response to all serotypes in the vaccine and demonstrating non-inferiority to each of the 7 serotypes common to the new vaccine and Pneu-C-7 vaccine. Studies on Pneu-C-10 vaccine demonstrated an antibody response to all 10 serotypes. Studies on Pneu-C-13 vaccine demonstrated an antibody response to all 13 serotypes. There are no studies comparing the immunogenicity of Pneu-C-10 and Pneu-C-13 vaccines.

Pneumococcal polysaccharide vaccines

In healthy young adults, a single dose of pneumococcal polysaccharide vaccine stimulates an antibody response to each of the serotypes in the vaccine. Polysaccharide vaccine is less immunogenic in children than the conjugate pneumococcal vaccine.

RECOMMENDATIONS FOR USE

INFANTS AND CHILDREN (2 months to 17 years of age)

Routine infant immunization (2 to 11 months of age)

Conjugate pneumococcal vaccine is recommended for routine infant immunization. Pneu-C-13 vaccine is recommended as the product of choice.

Children (12 to 23 months of age)

Assess children with no pneumococcal vaccinations or interrupted or incomplete vaccination schedules to determine the number of doses required to complete the series; children who have received complete, age-appropriate pneumococcal vaccination but have not received Pneu-C-13 vaccine should receive one dose of Pneu-C-13 vaccine (refer to *Table 3*). Children at high risk of IPD (refer to *Table 1*) should also receive one dose of Pneu-P-23 vaccine when they reach 24 months of age.

Children (24 to 35 months of age)

One dose of Pneu-C-13 vaccine is recommended for:

- Children with no pneumococcal vaccinations or incomplete vaccination schedules with any conjugate pneumococcal vaccine product.
- Children who have received complete, age-appropriate pneumococcal vaccination but have not received Pneu-C-13 vaccine.

Children at high risk of IPD (refer to *Table 1*) should also receive one dose of Pneu-P-23 vaccine, at least 8 weeks after Pneu-C-13 vaccine.

Children (36 to 59 months of age)

One dose of Pneu-C-13 vaccine is recommended for:

- Healthy children who have received age-appropriate pneumococcal vaccination but have not received Pneu-C-13 vaccine and who are of aboriginal origin or who attend group child care.
- Children at high risk of IPD (refer to *Table 1*) who have received age-appropriate pneumococcal vaccination but have not received Pneu-C-13 vaccine.
- Children with no or incomplete vaccination schedules with any conjugate pneumococcal vaccine product (refer to *Table 3*).
- Other healthy children who have received age-appropriate pneumococcal vaccination but have not received Pneu-C-13 vaccine, one dose of Pneu-C-13 vaccine may be considered. The age of the child (incidence of IPD declines from 24 to 59 months of age), the degree of exposure to other young children, and the local epidemiology of IPD need to be considered.

If a child at high risk of IPD has not previously received Pneu-P-23 vaccine, one dose of Pneu-P-23 vaccine should also be administered 8 weeks after Pneu-C-13 vaccine. Refer to *Booster doses and re-immunization* for re-immunization recommendations.

Children (60 months to 17 years of age)

Children and adolescents at high risk of IPD (refer to *Table 1*) who have not previously received Pneu-C-13 vaccine should receive one dose of Pneu-C-13 vaccine. If a child or adolescent at high risk of IPD has not previously received Pneu-P-23 vaccine, one dose of Pneu-P-23 vaccine should also be administered, at least 8 weeks after the Pneu-C-13 vaccine. Refer to *Schedule* and *Booster doses and re-immunization*.

HEALTHY CHILDREN AND ADOLESCENTS IN THIS AGE GROUP DO NOT NEED PNEUMOCOCCAL VACCINE

Adults (18 years of age and older)

One dose of Pneu-P-23 vaccine is recommended for all immunocompetent adults 65 years of age and older, and for immunocompetent adults less than 65 years of age in long-term care facilities or who have conditions putting them at increased risk of pneumococcal disease (*Table 1*). In addition, the following adults who are immunocompetent are recommended for vaccination with Pneu-P-23 vaccine:

- Persons with alcoholism,
- Smokers,
- Persons who are homeless, and
- Individuals who use illicit drugs should also be considered for vaccination.

Immunization with Pneu-C-13 vaccine is recommended for adults with immunocompromising conditions (*Table 1*). Adults with immunocompromising conditions (except HSCT) should receive one dose of Pneu-C-13 followed 8 weeks later by one dose of Pneu-P-23 (if not previously immunized with Pneu-P-23). The Pneu-C-13 dose should be administered at least one year after any previous dose of Pneu-P-23. Adults with HSCT should receive three doses of Pneu-C-13 starting 3-9 months after transplant. These doses should be administered at least 4 weeks apart, followed by a booster dose of Pneu-P-23 12 to 18 months post-transplant (6 to 12 months after the last dose of Pneu-C-13).

There is currently no evidence that a Pneu-C-13 booster dose adds any benefit. Refer to *Booster doses and re-immunization* for re-immunization recommendations for Pneu-P-23. Individuals who have previously received Pneu-P-23 vaccine and require re-immunization following immunization with Pneu-C-13 vaccine, should receive Pneu-P-23 no sooner than 8 weeks after Pneu-C-13 vaccine and no sooner than 3 to 5 years after the initial dose of Pneu-P-23, depending on the age of the initial Pneu-P-23.

CAIF S.A.
Maria Bernarda Belay

Some experts suggest that a conjugate pneumococcal vaccine may be given as the initial dose, followed by the Pneu-P-23 vaccine for immunocompetent adults at increased risk of IPD, as this may theoretically improve antibody response and immunologic memory. If this strategy is chosen, Pneu-C-13 vaccine should be administered first, followed at least 8 weeks later by Pneu-P-23 vaccine. However, Pneu-P-23 vaccine is the vaccine of choice for these individuals, and if only one vaccine can be provided, it should be Pneu-P-23 vaccine, because of the greater number of serotypes prevented by the vaccine. Refer to *Booster doses and re-immunization*.

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults lacking adequate documentation of immunization should be considered unimmunized and started on an immunization schedule appropriate for their age and risk factors. Conjugate and polysaccharide pneumococcal vaccine, as appropriate for age and risk condition, may be given, regardless of possible previous receipt of the vaccine, as adverse events associated with repeated immunization have not been demonstrated. Refer to *Immunization of Persons with Inadequate Immunization Records* in Part 3 for additional general information.

PREGNANCY AND BREASTFEEDING

Pneu-P-23 and/or Pneu-C-13 vaccines are recommended for pregnant women who are at high risk of IPD (refer to *Recommendations for Use - Adults*). There is no evidence to suggest a risk to the fetus or to the pregnancy from maternal immunization with inactivated vaccines. Women who are breastfeeding can be vaccinated with Pneu-P-23 or Pneu-C-13 vaccine. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional general information.

INFANTS BORN PREMATURELY

Premature infants in stable clinical condition should be immunized with conjugate pneumococcal vaccine at the same chronological age and according to the same schedule as full-term infants. Infants born prematurely (especially those weighing less than 1,500 grams at birth) are at higher risk of apnea and bradycardia following vaccination. Hospitalized premature infants should have continuous cardiac and respiratory monitoring for 48 hours after their first immunization. Refer to *Immunization of Infants Born Prematurely* in Part 3 for additional general information.

PERSONS/RESIDENTS IN HEALTH CARE INSTITUTIONS

Residents of long-term care facilities should receive Pneu-P-23 vaccine. For adults with immunocompromising conditions, Pneu-C-13 is also recommended with the Pneu-C-13 administered first, if possible. A single re-immunization of Pneu-P-23 is recommended for some conditions. Refer to *Booster doses and re-immunization*.

Refer to *Immunization of Patients in Health Care Institutions* in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

Conjugate pneumococcal vaccine (Pneu-C-13) followed by polysaccharide pneumococcal vaccine (Pneu-P-23) is recommended for individuals aged 2 years and over with immunocompromising conditions due to underlying disease or therapy (refer to *Table 1*). Immunologic abnormalities may decrease the protection provided by either type of pneumococcal vaccine and those at highest risk should be counselled regarding the risk of fulminant pneumococcal sepsis, which may occur despite immunization. When considering immunization of an immunocompromised person, consultation with the individual's attending physicians may be of assistance in addition to the guidance provided below. For complex cases, referral to a physician with expertise in immunization or immunodeficiency is advised.

Congenital (primary) immunodeficiency

Individuals with congenital immunodeficiencies involving any part of the immune system should be immunized against pneumococcal disease. Both Pneu-C-13 and Pneu-P-23 vaccines are recommended along with a single re-immunization with Pneu-P-23 (refer to *Table 3* and *Table 4*).

FOLIO 1079

Acquired (secondary) Immunodeficiency

Hematopoietic stem cell transplantation (HSCT-autologous or allogeneic)

Hematopoietic stem cell transplant recipients are at increased risk of pneumococcal diseases and pneumococcal vaccine is recommended for all persons. Regardless of age, pneumococcal vaccination should be started at 3 to 9 months after HSCT with three doses of Pneu-C-13 vaccine provided at least 4 weeks apart, followed by a dose of Pneu-P-23 vaccine 6 to 12 months later or when recipient reaches age 2 years. Because antibody response to pneumococcal vaccination is known to be poor in these persons, some experts recommend that all transplant recipients over 2 years of age receive a booster dose of Pneu-P-23 vaccine 1 year after their initial Pneu-P-23 immunization.

Solid organ transplantation

If possible, individuals being considered for solid organ transplantation should receive age-appropriate pneumococcal vaccines at least 2 weeks before transplantation. If the vaccination was not completed prior to transplant, in general, it should not be re-initiated until at least 3 to 6 months after transplantation. Both Pneu-C-13 and Pneu-P-23 vaccines are recommended along with a single re-immunization with Pneu-P-23 (refer to *Table 3* and *Table 4*).

Immunocompromising therapy

Vaccination status for pneumococcal disease should be reviewed for immunocompetent persons who might be anticipating initiation of immunocompromising treatments or who have diseases that might lead to immunodeficiency. Although pneumococcal vaccine can be safely administered at any time before, during or after immunosuppression, all attempts should be made to time vaccination so that optimal immunogenicity is achieved.

If indicated, pneumococcal vaccine should be administered at least 14 days before the initiation of immunocompromising therapy including use of long-term corticosteroids (e.g., high-dose systemic corticosteroids [≥2 mg/kg per day for a child or ≥20 mg/day for an adult of prednisone or its equivalent] for 14 days or more), chemotherapy, radiation therapy, post-organ-transplant therapy, biologic and non-biologic immunocompromising therapies for rheumatologic and other inflammatory diseases. If this process cannot be completed, a period of 3 months should elapse after immunocompromising drugs (except high-dose systemic corticosteroids) have been stopped before administration of pneumococcal vaccine to ensure immunogenicity. A period of at least 4 weeks should elapse between discontinuation of high-dose systemic steroids and administration of pneumococcal vaccines. The interval between discontinuation of immunocompromising drugs and pneumococcal vaccine may vary with the intensity of the immunocompromising therapy, underlying disease and other factors.

If immunocompromising therapy cannot be stopped, pneumococcal vaccine should be given when the person is least immunosuppressed. Both Pneu-C-13 and Pneu-P-23 vaccines are recommended along with a single re-immunization with Pneu-P-23 (refer to *Table 3* and *Table 4*).

HIV-infected

When possible, pneumococcal vaccine should be given early in the course of HIV infection; however, there is no contraindication to the use of pneumococcal vaccines at any time. Both Pneu-C-13 and Pneu-P-23 vaccines are recommended along with a single re-immunization with Pneu-P-23 (refer to *Table 3* and *Table 4*).

Refer to *Booster doses and re-immunization* for reason and schedule for re-vaccination. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional general information.

CAIF S.A.
María Bernarda Belay
Farmacéutica

PERSONS WITH CHRONIC DISEASES

Hyposplenism or asplenia

Hyposplenic or asplenic individuals should receive pneumococcal vaccine as they are at risk of serious pneumococcal infections. When elective splenectomy is planned, all recommended vaccines should ideally be administered at least 2 weeks before surgery. In the case of an emergency splenectomy, vaccines should be given 2 weeks after surgery or before discharge (if the person might not return for vaccination after discharge). Both Pneu-C-13 and Pneu-P-23 vaccines are recommended along with a single re-immunization with Pneu-P-23 (refer to *Table 3* and *Table 4*).

Chronic renal disease/dialysis

Individuals with chronic renal disease or on dialysis should be vaccinated using the pneumococcal vaccine (conjugate vs. polysaccharide) and schedule recommended for their age. Children and adolescents less than 18 years of age should receive both Pneu-C-13 and Pneu-P-23. For adults, only Pneu-P-23 is generally recommended. Due to the decreased immunogenicity and efficacy of polysaccharide vaccine in people with chronic renal failure, a single re-immunization is recommended. Refer to *Booster doses and re-immunization* for schedule for re-vaccination.

Asthma

Individuals who required medical attention for asthma in the past 12 months should be vaccinated using the pneumococcal vaccine (conjugate vs. polysaccharide) and schedule recommended for their age group. Children and adolescents less than 18 years of age should receive both Pneu-C-13 and Pneu-P-23. For adults, only Pneu-P-23 is generally recommended. No re-immunization is recommended.

Neurologic disorders

Persons with chronic CSF leak or chronic neurologic conditions that may impair clearance of oral secretions should be vaccinated using the pneumococcal vaccine (conjugate vs. polysaccharide) and schedule recommended for their age group. Children and adolescents less than 18 years of age should receive both Pneu-C-13 and Pneu-P-23. For adults, only Pneu-P-23 is generally recommended. No re-immunization is recommended.

Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for additional general information.

TRAVELLERS

The primary series of conjugate pneumococcal vaccine may be started at 6 weeks of age for infants who will be travelling. Refer to *Immunization of Travellers* in Part 3 for additional general information.

PERSONS NEW TO CANADA

Health care providers who see persons newly arrived in Canada should review the immunization status and update immunization for these individuals. Review of pneumococcal vaccination status is particularly important for persons from areas of the world where sickle cell disease is present as persons with sickle cell disease are at risk of serious pneumococcal infections. Information on vaccination schedules in other countries is available at: http://www.who.int/vaccines/GlobalSummary/Immunization/ScheduleSelect.cfm.

Refer to *Immunization of Persons New to Canada* in Part 3 for additional general information.

OUTBREAK CONTROL

During outbreaks of pneumococcal infection due to Pneu-C-13 vaccine serotypes, immunization with Pneu-C-13 vaccine is recommended for children who have not previously received adequate vaccination with Pneu-C-13. Pneu-P-23 vaccine has also been used to control outbreaks of pneumococcal infection due to Pneu-P-23 vaccine serotypes in adults. Pneu-C-10 or Pneu-13 vaccine could be used in adults if the serotype of the outbreak is covered by the vaccine.

FOLIO 1080

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose of pneumococcal vaccine is 0.5 mL.

Route of administration

Conjugate pneumococcal vaccine should be administered intramuscularly (IM). Pneu-P-23 vaccine may be given either IM or subcutaneously (SC). Refer to *Vaccine Administration Practices* in Part 1 for additional information.

Schedule

Infants and children: For routine infant immunization, three doses of conjugate pneumococcal vaccine with a minimum of 8 weeks intervals beginning at 2 months of age, followed by a fourth dose (booster) at 12 to 15 months of age should be administered. Pneu-C-13 vaccine is recommended as the product of choice. For healthy infants, a 3-dose schedule may be used, with doses given at 2, 4, and 12 months of age. A 4-dose schedule is recommended for immunization of infants at high risk of IPD.

Infants 7 to 11 months of age who have not been previously immunized against IPD should receive two doses of conjugate pneumococcal vaccine at least 8 weeks apart followed by a third dose after 12 months of age, at least 8 weeks after the second dose.

Children between 12 and 23 months require two doses of Pneu-C-13 at least 8 weeks apart. Older children who are recommended to receive pneumococcal vaccine (see *Recommendations for Use*) require only one dose Pneu-C-13.

The number of doses required to complete a vaccination series for children with interrupted or incomplete schedules varies with the age of the child. Infants who are less than 12 months of age when they re-present should complete their immunization schedule as if no interruption had occurred. Older children with interrupted or incomplete vaccination schedules should be assessed to determine the number of doses required to complete the series (refer to *Table 3*).

Children who are at high risk of IPD should also receive one dose of Pneu-P-23 vaccine at 24 months of age with possible re-immunization depending on the condition (refer to *Booster doses and re-immunization*). Refer to *Table 3* and *Recommendations for Use*.

CAIP S.A.
María Bernarda Belay
Farmacéutica
Co - Directora Técnica
M.P. 15.148

Table 3: Recommended schedules for conjugate pneumococcal vaccine for children 2 months up to and including 17 years of age, by conjugate pneumococcal vaccination history

Age at presentation for immunization	Number of doses of Pneu-C-7, Pneu-C-10 or Pneu-C-13 previously received	Recommended schedule for Pneu-C-13*
2-6 months	0 dose	2 or 3 doses† + booster at 12[0]-15 months of age
	1 dose	1 or 2 doses† + booster at 12[0]-15 months of age
	2 doses	0 or 1 dose† + booster at 12[0]-15 months of age
7-11 months	0 doses	2 doses + booster at 12-15 months of age
	1 dose	1 dose at 7-11 months + booster at 12-15 months of age
	2 doses	booster at 12-15 months of age
12-23 months, healthy or high risk of IPD	0 dose	2 doses
	1 dose at less than 12 months of age	
	2 or more doses at less than 12 months of age	1 dose
	1 dose at 12 months of age or older	
	Complete, age-appropriate vaccination with Pneu-C-7 or Pneu-C-10 (0 doses Pneu-C-13)	
24-35 months, healthy or high risk of IPD	0 dose or incomplete vaccination schedule with any product	1 dose
	Complete, age-appropriate vaccination with Pneu-C-7 or Pneu-C-10 (0 doses Pneu-C-13)	
36-59 months, healthy	0 dose or incomplete vaccination schedule with any product	1 dose
	Complete, age-appropriate vaccination with Pneu-C-7 or Pneu-C-10 (0 doses Pneu-C-13)	• If of aboriginal origin or attending group child care, 1 dose • All other children, consider 1 dose
36-59 months, high risk of IPD‡	0 dose or incomplete vaccination schedule with any product	1 dose
	Complete, age-appropriate vaccination with Pneu-C-7 or Pneu-C-10 (0 doses Pneu-C-13)	
60 months – 17 years, high risk of IPD‡	0 dose Pneu-C-13	1 dose.

* The minimum interval between doses of conjugate pneumococcal vaccine is 8 weeks.
** Children at high risk of IPD should follow the 4-dose schedule and also receive one dose of Pneu-P-23 at 24 months of age. A single re-immunization with Pneu-P-23 is recommended for some conditions (refer Booster doses and re-immunization),
† Follow relevant provincial/territorial schedule.
ü Programs using a 3-dose schedule should offer the third dose early in the second year of life (at 12 months of age) to allow for early complete protection.
¥ Children at high risk of IPD should also receive one dose of Pneu-P-23 at 24 months of age. When both Pneu-C-13 and Pneu-P-23 need to be given, the conjugate vaccine should be given first. A single re-immunization with Pneu-P-23 is recommended for some conditions (refer to Booster doses and re-immunization),

Adults: Immunocompetent adults who are at high risk of IPD (refer to *Table 1*), immunocompetent residents of long-term care facilities and all adults 65 years of age and older without contraindications should receive one dose of Pneu-P-23 vaccine. Adults with immunocompromising conditions require Pneu-C-13 and Pneu-P-23 with the Pneu-C-13 given first (refer to *Table 4*). A single re-immunization with Pneu-P-23 is recommended for some conditions (refer to *Booster doses and re-immunization*)

Table 4: Recommended schedules for adult (18 years of age and over) immunization with pneumococcal vaccine

Age/underlying condition	Type of vaccine	Number of doses and recommended schedule
At high risk of IPD and without immunocompromising conditions	Pneu-P-23*	1 dose - a single re-immunization with Pneu-P-23 recommended 5 years later for some conditions
Resident of long-term care facility and without immunocompromising conditions and without conditions that increase the risk of IPD	Pneu-P-23	1 dose
65 years or greater without immunocompromising conditions and without conditions that increase the risk of IPD	Pneu-P-23	1 dose
Immunocompromising condition (other than HSCT)	Pneu-C-13; Pneu-P-23	- 1 dose of Pneu-C-13** - 1 dose of Pneu-P-23 at least 8 weeks after Pneu-C-13 - a single re-immunization with Pneu-P-23 recommended 5 years later
Hematopoietic stem cell transplant (HSCT)	Pneu-C-13; Pneu-P-23	- 3 doses of Pneu-C-13 starting 3-9 months after transplant, administered at least 4 weeks apart - 1 dose of Pneu-P-23 12 to 18 months post-transplant (6 to 12 months after the last dose of Pneu-C-13) - a single re-immunization with Pneu-P-23 recommended as early as 1 year later by some experts

CAIF S.A.
María Bernarda Belay

* Some experts suggest that a conjugate pneumococcal vaccine may be given as the initial dose followed by the Pneu-P-23 vaccine for immunocompetent adults at increased risk of IPD, as this may theoretically improve antibody response and immunologic memory. If this strategy is chosen, Pneu-C-13 vaccine should be administered first, followed at least 8 weeks later by Pneu-P-23 vaccine. However, Pneu-P-23 vaccine is the vaccine of choice for these individuals, and if only one vaccine can be provided, it should be Pneu-P-23 vaccine

** The Pneu-C-13 dose should be administered at least one year after any previous dose of Pneu-P-23

BOOSTER DOSES AND RE-IMMUNIZATION

Conjugate Pneumococcal Vaccine

Re-immunization with conjugate pneumococcal vaccine after age and risk appropriate childhood vaccination is not necessary.

Pneumococcal Polysaccharide Vaccine

Immunity induced by Pneu-P-23 vaccine decreases over time. Routine re-immunization of healthy individuals who have been vaccinated with Pneu-P-23 vaccine is not recommended. However, re-immunization is recommended for those of any age at highest risk of IPD, including those with functional or anatomic asplenia or sickle cell disease; hepatic cirrhosis; chronic renal failure; nephrotic syndrome; HIV infection; and immunosuppression related to disease or therapy. For solid organ transplant recipients, there is evidence that antibody titers decline after 3 years. Experience with re-immunization after solid organ transplant is limited.

If re-immunization is carried out, a single re-immunization after 5 years is recommended in persons who were 11 years of age or over at the time of initial immunization with Pneu-P-23 vaccine. A single re-immunization after 3 years is recommended for those who were 10 years of age or younger at the time of initial immunization with Pneu-P-23 vaccine. Because there are insufficient data to recommend repeated administration of Pneu-P-23 vaccine, re-vaccination following a second dose is not routinely recommended.

Individuals who have previously received Pneu-P-23 vaccine and require re-immunization following immunization with Pneu-C-13 vaccine, should receive Pneu-P-23 no sooner than 8 weeks after Pneu-C-13 vaccine and no sooner than 3 to 5 years after the initial dose of Pneu-P-23, depending on the age of the initial Pneu-P-23.

Refer to *Immunocompromised persons* for considerations for persons undergoing HSCT.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving pneumococcal vaccine.

STORAGE REQUIREMENTS

Pneu-C-13: Store in a refrigerator at +2°C to +8°C. Do not freeze.

Pneu-C-10: Store in a refrigerator at +2°C to +8°C. Protect from light. Do not freeze.

PNEUMOVAX® 23: Store at +2°C to +8°C.

PNEUMO® 23: Store at +2°C to +8°C. Do not freeze.

Refer to *Storage and Handling of Immunizing Agents* in Part 1.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Conjugate pneumococcal vaccine may be administered concomitantly with routine childhood vaccines at different injection sites using separate needles and syringes.

1082

Conjugate pneumococcal vaccine and Pneu-P23 vaccine should be administered at least 8 weeks apart. However, for adults, Pneu-C-13 dose should be administered at least one year after any previous dose of Pneu-P-23. Pneumococcal 23-valent polysaccharide vaccine and HZ vaccine may be administered together.

Refer to *Timing of Vaccine Administration* in Part 1 for additional general information.

VACCINE SAFETY AND ADVERSE EVENTS

Refer to Vaccine Safety Part 2 for additional information.

COMMON AND LOCAL ADVERSE EVENTS

Conjugate pneumococcal vaccine

Clinical trials of Pneu-C-10 vaccine have found that irritability; decreased appetite; drowsiness; pain, swelling and redness at the injection site; or low-grade fever occur in 29% to 37% of vaccinees. Fever above 39°C occurs in 2% to 3% of vaccines. An increase in reactogenicity was reported after booster vaccination compared to the doses of the primary series.

Studies of Pneu-C-13 vaccine indicate that irritability, decreased appetite, increased or decreased sleep, pain, swelling and redness at the injection site (after the toddler dose and in older children), are common adverse events. Low-grade fever occurs in 20% to 30% or more of vaccinees. In adults over 50 years of age, the most commonly reported adverse events include pain at the injection site, fatigue, headache and new onset myalgia, with fever above 38°C occurring in approximately 3% of vaccine recipients.

Pneumococcal polysaccharide vaccine

Reactions to Pneu-P-23 vaccine are usually mild. Soreness, redness and swelling at the injection site occur in 30% to 60% of vaccinees and more commonly follow SC administration than IM administration. Occasionally, low grade fever may occur. Re-immunization of healthy adults less than 2 years after the initial dose is associated with increased local injection site and systemic reactions. Studies have suggested that re-vaccination after an interval of at least 4 years is not associated with an increased incidence of adverse side effects. However, severe local reactions including reports of injection site cellulitis and peripheral edema in the injected extremity have been documented rarely with Pneu-P-23 vaccine in post-marketing surveillance, even with the first dose. Multiple re-vaccinations are not recommended. Refer to *Booster doses and re-immunization*.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. Few serious adverse events were reported in clinical trials with any of the pneumococcal vaccines, and consisted mainly of reports of afebrile and febrile seizure. Arthus-like reactions (causing a local vasculitis from deposition of immune complexes) are very rare and mainly occur in persons with high initial pneumococcal antibody levels. Anaphylaxis following vaccination with pneumococcal vaccine may occur but is very rare. Refer to *Vaccine Safety* in Part 2 for additional general information.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report, through local public health officials, any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI. Refer to Reporting Adverse Events Following Immunization (AEFI) in Canada (http://www.phac-aspc.gc.ca/im/aefi-essi_guide/index-eng.php) or consult *Vaccine Safety* in Part 2 for additional information about AEFI reporting.

CMF S.A.
Maria Bernarda Belay
Farmacéutica

CONTRAINDICATIONS AND PRECAUTIONS

Pneumococcal vaccines are contraindicated in persons with a history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its container. For pneumococcal vaccines, potential allergens include:

- **Prevnar®13:** diphtheria CRM_{197} carrier protein
- **SYNFLORIX™:** latex in plunger stopper of pre-filled syringe, diphtheria toxoid carrier protein, tetanus toxoid carrier protein, non-typeable *Haemophilus influenzae* protein D carrier protein

In situations of suspected hypersensitivity or non-anaphylactic allergy to vaccine components, investigation is indicated, which may involve immunization in a controlled setting. Consultation with an allergist is advised.

Administration of pneumococcal vaccine should be postponed in persons suffering from severe acute illness. Immunization should not be delayed because of minor acute illness, with or without fever.

There are currently no data available regarding safety for children below the age of 6 weeks of age. There are limited safety and immunogenicity data on Pneu-C-13 vaccine for children or adults in groups at higher risk for IPD (e.g., children or adults with splenic dysfunction, HIV infection, malignancy, nephrotic syndrome).

Refer to *General Contraindications and Precautions* in Part 2 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

Infants who have started an immunization schedule with one conjugate pneumococcal vaccine may continue their immunization schedule with a different conjugate pneumococcal vaccine. For example, infants who started a series with Pneu-C-7 or Pneu-C-10 vaccine can complete it with Pneu-C-13 vaccine. Refer to *Principles of Vaccine Interchangeability* in Part 1 for additional general information.

SELECTED REFERENCES

American Academy of Pediatrics. In: Pickering LK, Baker CJ, Kimberlin DW, et al. (editors). *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.

American Academy of Pediatrics. *Technical report: prevention of pneumococcal infections, including the use of pneumococcal conjugate and polysaccharide vaccines and antibiotic prophylaxis.* Pediatrics 2000;106:367-76.

Black S, Shinefield H, Fireman B, et al. *Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children.* Pediatr Infect Dis J. 2000;19:87-95.

Butler JC, Breiman RF, Campbell JF, et al. *Pneumococcal polysaccharide vaccine efficacy: an evaluation of current recommendations.* JAMA;1993;270:1826-31.

Centers for Disease Control and Prevention. *Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease – United States, 1998-2003.* MMWR Morb Mortal Wkly Rep 2005;54(36):893-7.

Centers for Disease Control and Prevention. *Licensure of a 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Recommendations for Use Among Children – Advisory Committee on Immunization Practices (ACIP)*, 2010. MMWR Morb Mortal Wkly Rep 2010;59(09):258-61.

1083

Centers for Disease Control and Prevention. *Updated Recommendations for Prevention of Invasive Pneumococcal Disease Among Adults Using the 23-Valent Pneumococcal Polysaccharide Vaccine.* MMWR Morb Mortal Wkly Rep t 2010;59(34):1102-6.

DeStefano F, Pfeifer D, Nohynek H. *Safety profile of pneumococcal conjugate vaccines: systematic review of pre- and post-licensure data.* Bull World Health Organ 2008;86:373-80.

Eskola J, Anttila M. *Pneumococcal conjugate vaccines.* Pediatr Infect Dis J. 1999;18:543-51.

Eskola J, Kilpi T, Palmu A, et al. *Efficacy of a pneumococcal conjugate vaccine against acute otitis media.* N Engl J Med. 2001;334:403-9.

Esposito S, Tansey S, Thompson A et al. *Safety and Immunogenicity of a 13-Valent Pneumococcal Conjugate Vaccine Compared to Those of a 7-Valent Pneumococcal Conjugate Vaccine Given as a Three-Dose Series with Routine Vaccines in Healthy Infants and Toddlers.* Clin Vaccine Immunol 2010;17(6):1017-26.

Fine MJ, Smith MA, Carson CA, et al. *Efficacy of pneumococcal vaccination in adults: a meta-analysis of randomized clinical trials.* Arch Intern Med. 1994;154:2666-77.

GlaxoSmithKline Inc. *Product Monograph - SYNFLORIX™.* May 2009.

Jackson L et al. *Safety of Revaccination with Pneumococcal Polysaccharide Vaccine.* JAMA. 1999;281:243-48.

Johnstone J, Eurich DT, Minhas JK et al. *Impact of the pneumococcal vaccine on long-term morbidity and mortality of adults at high risk for pneumonia.* Clin Infect Dis 2010;5:15-22.

Kellner JD, Church DL, MacDonald J, et al. *Progress in the prevention of pneumococcal infection.* Can Med Assoc J. 2005;173(10):1149-51.

Merck Frosst Canada Ltd. *Product Monograph - PNEUMOVAX® 23.* January 2011.

National Advisory Committee on Immunization. *Statement on the recommended use of pneumococcal 23-valent polysaccharide vaccine in homeless persons and injection drug users.* Can Commun Dis Rep. 2008;34(ACS-5):1-12.

National Advisory Committee on Immunization. An Advisory Committee Statement (ACS). *National Advisory Committee on Immunization (NACI): Statement on the Use of Conjugate Pneumococcal Vaccine – 13 Valent in Adults (Pneu-C-13).* Can Commun Dis Rep. 2013:39(ACS-5).

National Advisory Committee on Immunization. An Advisory Committee Statement (ACS). *National Advisory Committee on Immunization (NACI): Update on the Use of Pneumococcal Vaccines: Addition of Asthma as a High-Risk Condition.* Public Health Agency of Canada. February 2014 (Catalogue no. HP40-94/2014E-PDF).

National Advisory Committee on Immunization. *Update on pediatric invasive pneumococcal disease and recommended use of conjugate pneumococcal vaccines.* Can Commun Dis Rep. 2010:36(ACS-3):1-30.

National Advisory Committee on Immunization. *Update on the use of conjugate pneumococcal vaccines in childhood.* Can Commun Dis Rep. 2010:36(ACS-12):1-21.

Pfizer Canada Inc. *Product Monograph – Prevnar® 13.* October 2010.

Rodriguez R. *Safety of pneumococcal revaccination.* J Gen Intern Med. 1995;10:511-2.

CMF S.A.
María Bernarda Belay
Farmacéutica
Co - Directora Técnica

Sanofi Pasteur Ltd. *Product Monograph – PNEUMO 23®*. July 2008.

Scheifele D, Halperin S, Pelletier L, et al. *Invasive pneumococcal infection in Canadian children 1991-1998: implications for new vaccination strategies*. Clin Infect Dis. 2000;31:58-64.

Shapiro ED, Berg AT, Austrain R, et al. *The protective effect of polyvalent pneumococcal polysaccharide vaccine*. N Engl J Med. 1991;325:1453-60.

Shinefield HR, Black S, Ray P, et al. *Safety and immunogenicity of heptavalent pneumococcal CRM197 conjugate vaccine in infants and toddlers*. Pediatr Infect Dis J. 1999;18:757-63.

Tseng HF, Smith N, Sy LS et al. *Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine*. Vaccine 2011; 29:3628–32.

van Gils EJ, Veenhoven RH, Hak E et al. *Pneumococcal Conjugate Vaccination and Nasopharyngeal Acquisition of Pneumococcal Serotype 19A Strains*. JAMA 2010;304(10):1099-1106.

World Health Organization. *Pneumococcal conjugate vaccine for childhood immunization – WHO position paper*. Wkly Epidemiol Rec 2007; 12(83): 93-104.

World Health Organization. *23-valent pneumococcal polysaccharide vaccine – WHO position paper*. Wkly Epidemiol Rec 2008; 42(83): 373-84.

Yeh SH, Gurtman A, Hurley DC et al. *Immunogenicity and Safety of 13-Valent Pneumococcal Conjugate Vaccine in Infants and Toddlers*. Pediatrics 2010;126(3):e493-e505.