CANADIAN IMMUNIZATION GUIDE

PART 1

PROTECTING CANADIANS FROM ILLNESS

Public Health Agency of Canada
Agence de la santé publique du Canada

Canada

TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

—Public Health Agency of Canada

Également disponible en français sous le titre :

Guide canadien d'immunisation Partie 1

Publication date: April 2014

Cat.: HP40-3/2014E-PDF
ISBN: 978-1-100-23215-7
Pub.: 130578

PART 1
TABLE OF CONTENTS

PART 1

IMMUNIZATION IN CANADA

This chapter provides the objectives of immunization programs in Canada, an overview of immunization policy and program development, and a description of national advisory bodies on immunization.

OBJECTIVES OF IMMUNIZATION

The objectives of immunization programs are to prevent, control, eliminate or eradicate vaccine-preventable diseases (depending on the epidemiology of the diseases, efficacy of available vaccines, and the ability to reach the target populations). Over the past 50 years, in countries with effective immunization programs, important reductions have been achieved in the incidence of vaccine-preventable diseases. Globally, smallpox has been eradicated and efforts are currently directed at the eradication of polio and elimination of measles. Universally recommended vaccination has been hailed as one of the ten greatest public health achievements of the 20th century and is credited with saving more lives than any other health intervention. Moreover, immunization programs, particularly those with standardized immunization schedules, have proven to be highly cost-effective and, in some cases, cost-saving. Refer to the Benefits of Immunization in Part 1 for more information.

As the incidence of vaccine-preventable diseases is decreasing, the attention of some of the public may shift from the disease and its sequelae to potential adverse events following immunization. This shift in focus has resulted, in some cases, in individuals questioning the need for immunization, leading to lower vaccine coverage and resurgence of some diseases. In Canada, the resurgence of measles, mumps, and pertussis in particular in 2010 to 2013 has highlighted the need for the continuation of immunization programs that achieve high immunization coverage.

The low incidence of vaccine-preventable diseases and their associated morbidity and mortality in Canada is a result of successful vaccination programs. In addition to achieving high rates of immunization coverage, for Canadians to receive the greatest possible benefit from immunization, it is essential that vaccines and vaccination programs continue to be monitored and evaluated on an ongoing basis. This will ensure the direct protection of vaccinated individuals, as well as help indirectly to protect vulnerable individuals who may not respond to vaccines or for whom vaccines may be contraindicated (e.g., measles vaccine in an immunocompromised child).

IMMUNIZATION POLICY AND PROGRAM DEVELOPMENT

In Canada, the responsibility for health care, including immunization, is shared by the federal, provincial and territorial (F/P/T) governments. While each jurisdiction has a distinct mandate and unique operating context, their activities are complementary and collaborative.

THE NATIONAL IMMUNIZATION STRATEGY

Since its adoption in 2003, the National Immunization Strategy (NIS) (http://www.phac-aspc.gc.ca/im/nis-sni/) has been a platform for collaboration between F/P/T stakeholders and has facilitated the development of consistent and equitable approaches to immunization planning, vaccine purchasing,

program delivery and education. The NIS provides mechanisms for enhanced collaboration on issues such as vaccine safety, surveillance, immunization registries, research, vaccine supply and immunization program planning, and enables bridging of policy recommendations made at the national level with immunization program development at the provincial/territorial (P/T) level. In 2011, F/P/T governments initiated a review of the NIS with a goal to further strengthen the collaboration and coordination of immunization efforts in Canada.

THE NATIONAL IMMUNIZATION

Through their health departments, advisory bodies and other public authorities, all F/P/T governments engage in different aspects of immunization program planning, delivery and evaluation. Some of these stakeholders are described below.

The Federal Government

The Public Health Agency of Canada (PHAC) is the principal federal government agency responsible for immunization. Its mandate is to provide leadership, advice and support for timely vaccine recommendations and sustainable immunization programs. PHAC is supported by two advisory committees that provide the federal government with medical and scientific advice for the prevention and management of vaccine preventable diseases in Canada:

- National Advisory Committee on Immunization *(NACI)*
  NACI is a scientific advisory committee with members who are recognized experts in the fields of paediatrics, infectious diseases, immunology, medical microbiology, internal medicine and public health. NACI makes expert and evidence-based recommendations regarding the use of vaccines authorized for use in Canada, advises on the need for national vaccination strategies, and makes recommendations for vaccine development research. NACI is also responsible for producing the *Canadian Immunization Guide*. Created in 1964 and originally reporting to the predecessor of Health Canada, the Department of National Health and Welfare, and later to Health Canada, NACI has reported to PHAC since the agency was created in 2004. More information about the national immunization guideline development process can be found below. (http://www.phac-aspc.gc.ca/naci-ccni/index-eng.php)

- Committee to Advise on Tropical Medicine and Travel *(CATMAT)*
  CATMAT makes evidence-based recommendations relating to tropical infectious diseases and health risks associated with international travel, suggests mechanisms for the widespread dissemination and utilization of such information, and advises on priorities for epidemiological research and other activities related to travel or tropical medicine. Some CATMAT recommendations for the use of authorized immunization products for travellers may extend beyond recommendations developed by NACI for Canada due to differences in disease prevalence internationally. CATMAT recommendations are available on the PHAC website (http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/index-eng.php).

Health Canada (HC) is the federal authority responsible for regulation of vaccines for human use under the Food and Drugs Act (http://laws-lois.justice.gc.ca/eng/acts/F-27/index.html) and Food and Drugs Regulations (http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.%2C_c._870/). HC reviews the clinical and manufacturing information of vaccine submissions and authorizes the sale of vaccines in Canada. Together with PHAC, it is responsible for monitoring vaccine safety and effectiveness throughout the life cycle of the product. HC also promotes immunization initiatives and ensures that First Nations, Inuit and Métis receive appropriate immunization services.

Other federal departments and bodies with immunization-related interests and activities (i.e. research, policy and operational considerations) include Citizenship and Immigration Canada, Correctional Service of Canada, Department of National Defence, Canada Border Services Agency, Public Works and Governments Services Canada, Department of Foreign Affairs and International Trade, Statistics Canada, Veterans Affairs Canada, Aboriginal Affairs and Northern Development Canada, Patented

Medicine Prices Review Board, Canadian Institutes of Health Research, National Research Council and Industry Canada.

Previously, the federal government has also supported the introduction of new immunization programs by provinces and territories.

Provincial and Territorial Governments

The P/T governments are responsible constitutionally for the administration and delivery of health care services, including immunization-related programs. Immunization policies and schedules are developed by P/T governments and their expert immunization advisory committees based on jurisdiction-specific needs, other vaccine recommendations (i.e. NACI), program resource availability and constraints, and identified priorities. In addition, P/T governments are responsible for: purchasing vaccines for publicly funded programs; the design and maintenance of immunization registries; disease and safety surveillance and program monitoring; and public and professional education and engagement (e.g., immunization campaigns, information services, and professional training, education and guidance). Each P/T has its own process and mechanism for setting immunization targets and planning, designing, implementing and evaluating immunization programs. Typically, P/T governments initiate their vaccine and immunization program assessment processes following, or in tandem with NACI and, where applicable, the Canadian Immunization Committee (CIC). (http://www.phac-aspc.gc.ca/naci-ccni/)

The Pan-Canadian Public Health Network

The Pan-Canadian Public Health Network (PHN) (http://www.phn-rsp.ca/index-eng.php) was established by Canada's F/P/T Ministers of Health in 2005 as a key intergovernmental mechanism to:

- strengthen and enhance Canada's public health capacity,
- enable F/P/T governments to enhance day-to-day business of public health, and
- anticipate, prepare for, and respond to public health events and threats.

The work of the PHN is governed by a 17-member Pan-Canadian Public Health Network Council (PHNC) composed of senior F/P/T government officials responsible for public health, including the Chief Public Health Officer of Canada (http://www.phac-aspc.gc.ca/cpho-acsp/). The PHNC is accountable to the Conference of F/P/T Deputy Ministers of Health. The F/P/T Deputy Ministers of Health provide direction and approve common public health policy and program priorities including the implementation of vaccine recommendations proposed by PHNC.

The Canadian Immunization Committee

The Canadian Immunization Committee (CIC) consists of F/P/T government representatives who review and provide recommendations on immunization program planning, including cost-effectiveness assessment. These recommendations are provided to the F/P/T Deputy Ministers of Health through the PHN.

Council of Chief Medical Officers of Health

The Council of Chief Medical Officers of Health (CCMOH) membership includes the Chief Medical Officer of Health from each P/T, the most senior public health physician of the First Nations and Inuit Health Branch of HC (http://www.hc-sc.gc.ca/fniah-spnia/index-eng.php), and the Chief Public Health Officer of Canada. The CCMOH provides guidance and recommendations on technical issues relating to PHN. The CCMOH reports to the Conference of F/P/T Deputy Ministers of Health through PHNC.

NACI RECOMMENDATION DEVELOPMENT

In developing recommendations, NACI relies on working groups to define issues and to establish the scope and requirements for the evidence review. The working groups consist of NACI members, liaison members and other vaccine experts who review the scientific literature on the burden of disease (epidemiology, morbidity, mortality) in the general population and specific risk groups; vaccine characteristics (e.g., safety, immunogenicity, efficacy, effectiveness); product monograph and other relevant scientific and technical information. Recommendations from other groups (e.g., World Health Organization [WHO], Canadian Paediatric Society, Advisory Committee on Immunization Practices [United States]) are also considered. At present, NACI does not review cost-effectiveness data or make program implementation recommendations.

When the knowledge synthesis is completed, the working group presents a draft NACI Statement with recommendations to the full NACI committee for review, discussion and adoption. Once adopted, NACI statements and updates are published in the Canada Communicable Disease Report (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/) and posted in both official languages on the NACI website (http://www.phac-aspc.gc.ca/naci-ccni/). NACI recommendations are summarized and provided for easy use by vaccine providers, policy makers and the general public in the Canadian Immunization Guide.

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PART 1

BENEFITS OF IMMUNIZATION

BENEFITS OF IMMUNIZATION

Immunization is one of the most important advances in public health and is estimated to have saved more lives in Canada over the past 50 years than any other health intervention. Before vaccines became available, many Canadian children died from diseases such as diphtheria, measles and polio that are now preventable by immunization. Immunization programs are responsible for the elimination, containment or control of infectious diseases that were once common in Canada; however, the viruses and bacteria that cause vaccine preventable diseases still exist globally, can be imported to Canada through travel, and can be transmitted to people who are not protected by immunization. If immunization programs were reduced or stopped, diseases that are now rarely seen in Canada because they are controlled through immunization would re-appear, resulting in epidemics of diseases causing sickness and death. This phenomenon has been seen in other countries; for example, large epidemics of diphtheria and measles have occurred in Europe in recent decades after immunization rates declined.

Immunization is important in all stages of life. Infants and young children are particularly susceptible to vaccine preventable diseases because their immune systems are not mature enough to fight infection; as a result, they require timely immunization. Older children and adults also require immunization to restore waning immunity and to build new immunity against diseases that are more common in adults.

Immunization directly protects individuals who receive vaccines. Through herd immunity, immunization against many diseases also prevents the spread of infection in the community and indirectly protects:

- infants who are too young to be vaccinated,
- people who cannot be vaccinated for medical reasons (e.g., certain immunosuppressed people who cannot receive live vaccines),
- people who may not adequately respond to immunization (e.g.the elderly).

IMPACTS OF VACCINES ON VACCINE PREVENTABLE DISEASES

Table 1, Figures 1, 2, and 3 illustrate the impact of vaccines on infectious diseases in Canada. Refer to Part 4 chapters for additional information about the success of immunization programs against specific vaccine preventable diseases.

Table 1: incidence of select vaccine preventable diseases in Canada – pre-vaccine era compared with 2007-2011

Disease and impact	Vaccine introduction & Disease reporting	Pre-vaccine era			2007-2011[1]	
		Pre-vaccine period	5 year average annual incidence/ 100,000	Peak annual number of cases*	5 year average annual incidence/ 100,000	Peak annual number of cases
Diphtheria Infection of the throat causes severe breathing difficulty which may result in asphyxia. Infection also results in the dissemination of diphtheria toxin, which damages the heart and central nervous system. In the pre-vaccine era case fatality was about 5% to 10%, with highest death rates occurring in the very young and the elderly.	• Diphtheria toxoid introduced in 1926 • Routine infant immunization since 1930 • National notifiable diseases reporting began in 1924	1925-1929	84.2	9,010	0.006	4
***Haemophilus influenzae* type b (Hib) invasive disease** (children less than 5 years of age) Infection can cause meningitis, epiglottitis, bacteremia, cellulitis, pneumonia or septic arthritis in young children. Case fatality rate of meningitis is about 5%. Severe neurologic sequelae occur in 10% to 15% of survivors and deafness in 15% to 20%	• Vaccines first introduced in 1986 • Conjugate vaccine introduced in 1988 • Routine infant immunization since 1988-89 • National notifiable disease reporting of all invasive Hib disease began in 1986	1986-1990	30.1[2]	671	0.49[2]	18
Hepatitis B (HB) Infection in approximately 10% of adults results in chronic infection leading to a chronic carrier state that may result in cirrhosis, liver cancer, and death.	• Universal HB immunization for adolescents implemented in the early- to mid-1990s • National notifiable disease reporting of HB infection began in 1969	1989-1993	9.1[3]	3,378[4]	5.3[5]	2,011[6]
Measles Bronchopneumonia and otitis media occur in about 1/10 cases and encephalitis occurs in 1/1,000 cases (fatal in 15% and neurologic sequelae in 25%). Case fatality rate is 1-2 per 1000. Subacute sclerosing panencephalitis is a rare but fatal complication.	• Live vaccine authorized in 1963 • Universal immunization program implemented in 1983 • 2-dose measles-containing vaccine schedule introduced 1996/97 • National notifiable diseases reporting began in 1924 (no	1950-1954	372.7	61,370	0.60[7]	752[7]

Disease and impact	Vaccine introduction & Disease reporting	Pre-vaccine era			2007-2011[1]	
		Pre-vaccine period	5 year average annual incidence/ 100,000	Peak annual number of cases*	5 year average annual incidence/ 100,000	Peak annual number of cases
	reporting from 1959 to 1968)					
Meningococcal serogroup C invasive disease Invasive meningococcal disease most often results in meningitis or septicemia. Severe cases can result in delirium and coma and, if untreated, shock and death. Case fatality rate is 10%, and 10-20% of survivors have severe sequelae such as limb amputations and deafness.	• Polysaccharide vaccines first introduced in Canada in 1981 • Routine infant or toddler immunization programs using conjugate vaccine introduced across Canada between 2002 and 2006 • National notifiable disease reporting began in 1924	1997-2001	0.30	186	0.06	30
Mumps Acute parotitis develops in 40%, of which 25% are unilateral. Complications include orchitis (20% to 30% of post-pubertal males), oophoritis (5% of post-pubertal females), meningitis (<10% of cases), deafness (0.5 to 5/100,000 cases) and encephalitis (less than 1/50,000 cases). Occasionally mumps can cause permanent infertility or deafness.	• Vaccine authorized in 1969 • Universal immunization program implemented in 1983 • National notifiable disease reporting began in 1924 (no reporting from 1960 to 1985)	1950-1954	251.2	43,671	1.84	1,110
Pertussis Young infants may experience complications, such as vomiting after a coughing spell, weight loss, breathing problems, choking spells, pneumonia, convulsions, brain damage, and in rare cases, death. Older children and adults develop persistent cough lasting for up to 6 weeks.	• Whole cell pertussis vaccine authorized in 1943 • Acellular pertussis vaccine replaced whole cell in 1997-1998 • Adolescent and adult acellular vaccine formulation authorized in 1999 • National notifiable disease reporting began in 1924	1938-1942	156.0	19,878	3.88	1,961
Poliomyelitis Paralysis occurs in less than 1% of infections but among those paralyzed, about 2 - 5% of children	• Inactivated polio vaccine (IPV) authorized in 1955 • Oral polio vaccine	1950-1954	17.5	5,384	0	0

Disease and impact	Vaccine introduction & Disease reporting	Pre-vaccine era			2007-2011[1]	
		Pre-vaccine period	5 year average annual incidence/ 100,000	Peak annual number of cases*	5 year average annual incidence/ 100,000	Peak annual number of cases
and 15-30% of adults die.	authorized in 1962 and in use in Canada until 1996 • IPV used primarily from 1996-present					
Rubella and congenital rubella syndrome (CRS) Although rubella is generally a mild disease, encephalitis occurs in 1/6,000 cases. However, rubella infection in pregnancy can cause **congenital rubella syndrome (CRS)**. Infection in the first 10 weeks of pregnancy has an 85% risk of leading to CRS. CRS can result in miscarriage, stillbirth and fetal malformations (congenital heart disease, cataracts, deafness and mental retardation).	• Rubella vaccine introduced 1969 • Universal immunization program implemented in 1983 • National notifiable disease reporting began in 1924 • National notifiable diseases reporting of CRS began in 1979	Rubella: 1950-1954 CRS: 1979-1983	Rubella: 106.3 CRS: 3.0[8]	Rubella: 37,917 CRS: 29	Rubella: 0.01 CRS: 0.11[8]	Rubella:10 CRS: 1
Tetanus Infection leads to general rigidity, and convulsive spasms, with death in about 10% of cases. Higher rates of death occur among infants.	• Tetanus toxoid introduced in 1940 • National notifiable diseases reporting began in 1957	1935-1939	0.13	25	0.01	6

* Five years preceding vaccine introduction

1 Provisional numbers for measles and rubella from the Canadian Measles and Rubella Surveillance System. All other data from the Canadian Notifiable Disease Surveillance System.

2 Children less than 5 years of age

3 Reported cases of newly diagnosed HBV infection per 100,000 population. Combines acute, chronic and unspecified HBV infections

4 Reported cases of newly diagnosed HBV infection in 1989

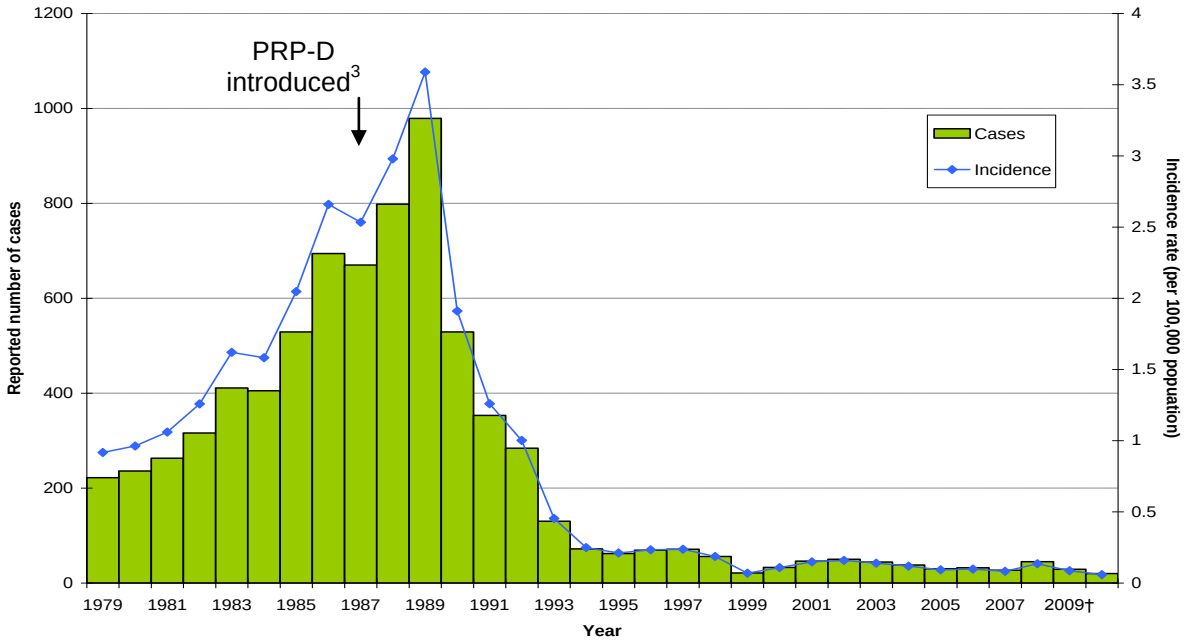
5 Reported cases of newly diagnosed HBV infection per 100,000 population. Combines acute, chronic and unspecified HBV infections

6 Reported cases of newly diagnosed HBV infection in 2008

7 In 2011, a large outbreak of measles occurred in Quebec; a total of 752 cases were reported in Canada. Excluding 2011, the peak number of cases was 102 (2007), and the average annual incidence for this time period (i.e. 2007 – 2010) was 0.21 cases per 100,000 population

8 Per 100,000 live births

Figure 1: *Haemophilus influenzae* type b disease – reported number of cases[1] and incidence rates, Canada, 1979-2010[2]

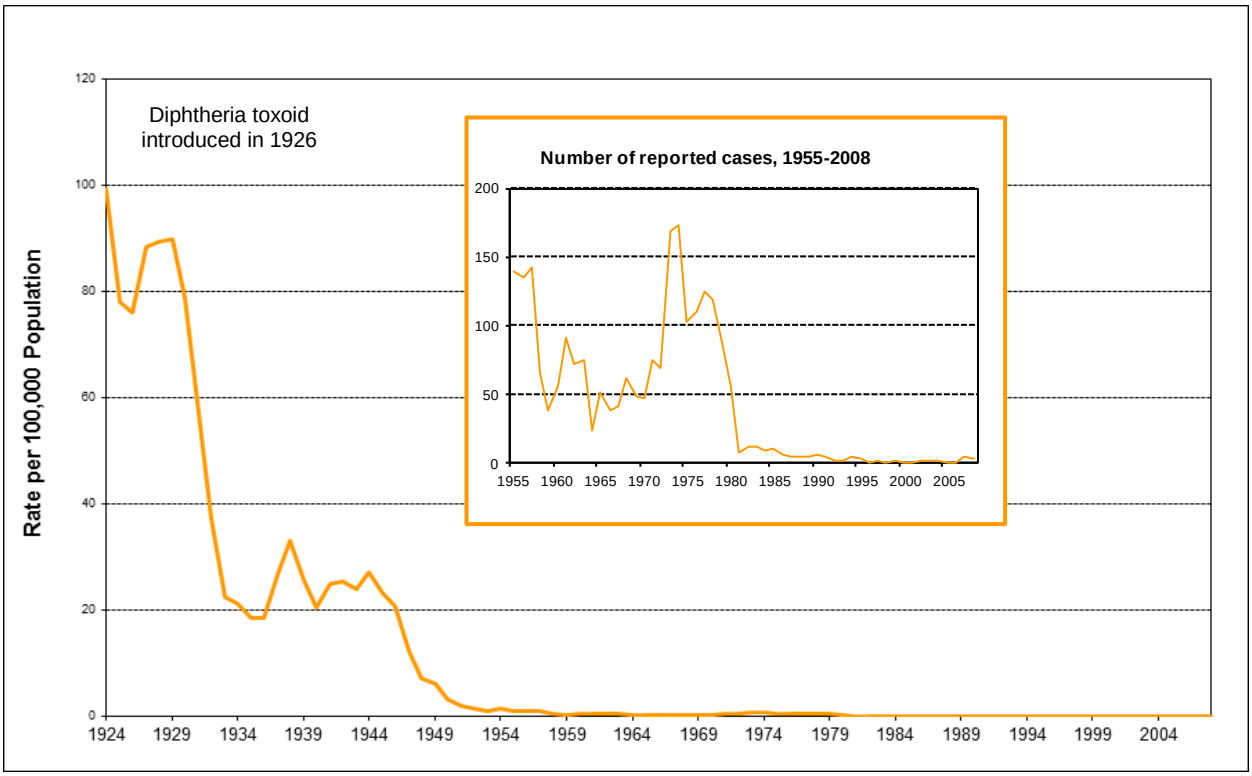


1 Case data obtained from the Canadian Notifiable Disease Surveillance System. Population data obtained from Statistics Canada July 1st annual estimates. Data for 2009 and 2010 are preliminary.

2 Only Hib meningitis was reportable from 1979 to 1985. After this, all invasive disease caused by Hib became reportable.

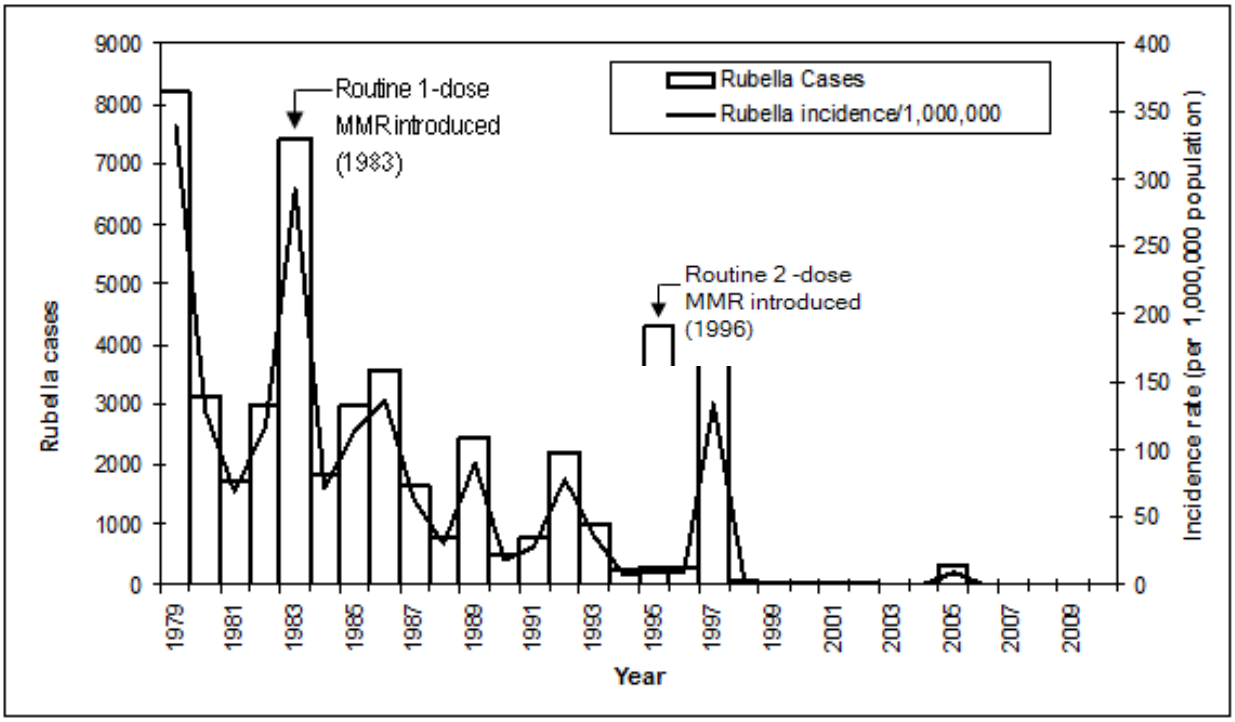
3 PRP-D: Hib conjugate vaccine containing purified polyribosylribitol phosphate capsular polysaccharide of Hib covalently bound to diphtheria protein. The vaccine was licensed in 1986 and in 1988 introduced into the majority of provincial vaccination programs.

Figure 2: Diphtheria – reported number of cases and incidence rates, Canada, 1924-2008



Population data sources: Statistics Canada, Population by Sex and Age, 1921-1971, revised annual estimates of population, Canada and the provinces, (Catalogue 91-512)
Statistics Canada, Population estimates 0-90+ July Canada - Provinces 1971-2008.xls

Figure 3: Rubella - reported number of cases and incidence rates, Canada, 1979 to 2010



COST BENEFIT OF VACCINES

Vaccine preventable diseases result in significant costs to individuals, the health care system, and society, including costs associated with visits to health care providers, hospitalizations, and premature deaths. Parents may lose time from work to care for sick children and sick children lose time at school. For example, the societal cost for each case of rotavirus requiring a visit to the emergency room is estimated to be $675.

The cost-benefit of vaccine is strongly influenced by the price of the vaccines used. Many vaccines, such as measles-mumps-rubella vaccine for children, provide both health benefits and savings in health care costs (refer to Table 2). This means that the cost of implementing the immunization program is less than the cost of treating the illness or injury that would occur if the program had not been not implemented. Because immunization with these vaccines improves health and results in cost savings, the decision to include these vaccines in publicly funded immunization programs is straightforward. In developing public health programs, international organizations such as the World Health Organization, United Nations Children's Fund and the World Bank recommend that immunization be given high priority because of its high cost-effectiveness.

Table 2: Cost savings achieved through selected immunization programs

Immunization program	Cost saving per $1 spent
Influenza for adults 65 years of age and older	$45
Measles, mumps, rubella for children	$16
Pneumococcal polysaccharide for adults 65 years of age and older	$8
Diphtheria, pertussis, tetanus for children	$6

Newer vaccines tend to be costlier and may not be cost-saving, so the decision to introduce them into publicly funded immunization programs is determined by society's willingness to pay for their anticipated health benefits. In general, such programs compare very favourably to other public health interventions in terms of cost per life year saved (refer to Table 3). In Canada, evaluation of benefits and costs of new immunization programs is done by Provinces and Territories. Refer to Immunization in Canada for more information.

Table 3: Cost per life year saved for selected immunization programs and other public health interventions (ADAPTED FROM REFERENCES)

Public health intervention	Cost per life year saved[1]
Vaccines	
Hepatitis B screening in pregnancy and immunization of children of carriers	$164
Human papillomavirus vaccine for 12 year old girls in a school-based immunization program	$12,921
Varicella vaccine for children	$16,000
Pneumococcal conjugate vaccine for children	$125,000
Other interventions	
Mandatory seat belt law	$69
Chlorination of drinking water	$3,100
Smoking cessation counseling	$1,000 to $10,000
Annual screening for cervical cancer	$40,000
Driver and passenger air bags/manual lap belts (vs. airbag for driver only and belts)	$61,000
Smoke detectors in homes	$210,000
Crossing control arm for school buses	$410,000
Radiation emission standard for nuclear power plants	$100,000,000

[1]monetary resources required to save one year of ‘‘statistical ’’ life

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PART 1

NATIONAL GUIDELINES FOR IMMUNIZATION PRACTICES

To ensure continued success in preventing and controlling vaccine preventable diseases in Canada, proactive collaboration to plan, conduct, review, and evaluate immunization practices is essential.

Ongoing challenges to the success of immunization practices include:

- absence of a national immunization registry
- occurrences of “missed opportunities for immunization”
- groups of persons with less than optimal vaccine coverage
- incorrect handling and storage of vaccine by vaccine providers
- inconsistencies in the reporting of adverse events following immunization (AEFI)
- ineffective, insufficient and conflicting sources of information on the risks and benefits of vaccines
- individual beliefs regarding the risks of vaccine that are not supported by scientific evidence

To address these challenges, the National Advisory Committee on Immunization (NACI) developed National Guidelines for Immunization Practices. The original guidelines were published in the 6th edition of the *Canadian Immunization Guide* and have subsequently undergone revision and modification for the evergreen edition of the *Guide*. The order in which the guidelines are presented does not reflect priorities.

These guidelines define optimal immunization practices and are recommended for use by all health professionals who administer vaccines or manage immunization services. The guidelines can also be used for evaluating immunization practices to identify deficiencies, areas of excellence, and resources needed to achieve immunization goals and targets. The competencies contained in the Public Health Agency of Canada’s Immunization Competencies for Health Professionals were developed to support the application of these guidelines. (http://www.phac-aspc.gc.ca/im/pdf/ichp-cips-eng.pdf)

The following terms are used in the National Guidelines for Immunization Practices:

- *Vaccine provider:* individual qualified to give a vaccine
- *Regular vaccine provider*: individual usually responsible for immunization
- *Child or children:* individuals from birth to adolescence
- *Vaccine recipient:* individual being considered for immunization or who has been vaccinated
- *Parent:* individual(s) legally responsible for a child

GUIDELINE 1

Immunization services should be readily available.

Immunization services should be responsive to the needs of vaccine recipients. When feasible, vaccine providers should schedule immunization appointments in conjunction with appointments for other health services. Newborn infants should have the first immunization appointment arranged as soon as possible after birth. Immunization services should be available during regular business hours as well as during hours that are convenient for working vaccine recipients and parents (e.g., weekends, evenings, early mornings or lunch hours).

GUIDELINE 2

Vaccine providers should facilitate timely receipt of vaccine and eliminate unnecessary prerequisites to the receipt of vaccines.

While appointment systems facilitate clinic planning and avoid long wait times, appointment-only systems may act as barriers to the receipt of vaccines. People who present for vaccination without an appointment, particularly those in hard-to-reach populations, should be accommodated whenever possible.

The administration of vaccine in a clinic setting should not depend on individual written orders or on a referral from a primary health care provider.

GUIDELINE 3

Vaccine providers should use all clinical opportunities to screen for needed vaccines and administer all vaccine doses for which a vaccine recipient is eligible at the time of each visit.

Each encounter with a health care provider, including hospitalization, a visit to an outpatient clinic, or a visit to the emergency department, is an opportunity to review the immunization status and offer vaccination to persons of all ages. Health care providers should review the immunization status at every visit and either offer immunization service as a part of routine care, or encourage attendance at an immunization clinic. At each hospital admission, the vaccination record should be reviewed and needed vaccines should be administered before discharge. The vaccine recipient's regular vaccine provider should be informed about the vaccines administered in hospital. Refer to Immunization of Persons/Residents in Health Care Institutions in Part 3 for additional information.

Home care and public health nurses should use home visits as an opportunity to immunize adults and children who are homebound or otherwise unable to access immunization services.

Most routine vaccines can be safely and effectively administered at the same visit. Refer to Timing of Vaccine Administration and Vaccine Administration Practices in Part 1 information about simultaneous administration of vaccines and administration of multiple injections.

GUIDELINE 4

Vaccine providers should communicate current knowledge about immunization using an evidence-based approach.

Vaccine providers should educate people in a culturally sensitive way, preferably in their own language, about the:

- importance of vaccination
- diseases that vaccines prevent
- recommended immunization schedules
- need to receive vaccines at recommended ages
- importance of bringing the immunization record to every health care visit

Vaccine providers should answer the vaccine recipient's or parent's questions and provide educational materials at suitable reading levels, preferably in the vaccine recipient's or parent's own language. Refer to The Benefits of Immunization, Communicating Effectively about Immunization and Vaccine Administration Practices in Part 1 for additional information about pre-vaccination and post-vaccination counselling.

Parents and adult vaccine recipients should be encouraged to take responsibility for ensuring completion of the vaccine series. Refer to Recommended Immunization Schedules in Part 1 for information about immunization schedules.

GUIDELINE 5

Vaccine providers should inform vaccine recipients and parents in specific terms about the risks and benefits of vaccines that they or their child are to receive.

Information pamphlets about routine vaccines are available from health authorities in many jurisdictions and from the Canadian Paediatric Society. (www.caringforkids.cps.ca/handouts/immunization-index) Information pamphlets facilitate informed consent and are helpful in answering questions that vaccine recipients/parents may have about immunization. Vaccine providers should document in the medical record that they have asked vaccine recipients/parents if they have any questions and should ensure that satisfactory answers to questions were given. Refer to The Benefits of Immunization, Communicating Effectively about Immunization and Immunization Records in Part 1 for additional information.

GUIDELINE 6

Vaccine providers should recommend deferral or withholding of vaccines for true contraindications only.

There are very few true contraindications to vaccination. Vaccine providers must be aware of the true contraindications to vaccination and should not defer administration of indicated vaccines because of conditions or circumstances that are not true contraindications. Withholding vaccines for conditions that are not true contraindications often results in the needless deferral of indicated vaccines. Screening procedures for precautions and contraindications include, at a minimum, asking questions to elicit a history of possible adverse events following prior vaccinations and determining any existing precautions or contraindications. Refer to Contraindications, Precautions and Concerns in Part 2 for additional information about pre-immunization screening for contraindications and precautions.

GUIDELINE 7

Vaccine providers should ensure that all vaccinations are accurately and completely recorded.

Vaccine care providers must maintain a record of all vaccinations administered and must ensure that information is accurately and completely recorded in their files. All vaccine providers should encourage vaccine recipients/parents to keep the personal immunization record and present it at each health care visit so that it can be updated. If the personal immunization record is not available at the time of vaccination, the vaccine provider should ensure that adequate information is given so that the vaccine recipient/parent can update the personal immunization record. Refer to Immunization Records in Part 1 for additional information.

Comprehensive national and provincial/territorial immunization registries enable timely and efficient evaluation and planning of immunization programs by ensuring the availability of accurate and readily accessible information on immunization. Refer to Immunization Records in Part 1 for additional information about immunization registries.

GUIDELINE 8

Vaccine providers should maintain easily retrievable summaries of immunization records to facilitate age-appropriate vaccination.

Vaccine providers should maintain easily retrievable summaries of vaccination records to permit regular checking and updating of the individual's immunization status, as well as the identification and recall of vaccine recipients, especially children, who are delayed in the recommended immunization schedule. Electronic immunization records enable more efficient storage and retrieval of information, including the generation of notices (e.g. recall reminders). Refer to Immunization Records in Part 1 for additional information.

GUIDELINE 9

Vaccine providers should report clinically significant adverse events following immunization (AEFI) promptly, accurately and completely.

All vaccine recipients/parents should receive instructions for post-immunization care.

Prompt reporting of AEFI is essential to ensure vaccine safety, to allow timely corrective action when needed, and to update information regarding vaccine risk-benefit ratios and contraindications. Vaccine providers should instruct vaccine recipients/parents to inform them promptly of AEFI. In addition, at each immunization visit, vaccine providers should ask vaccine recipients/parents about adverse events that may have occurred following previous vaccinations. Vaccine providers should fully document the adverse event in the medical record as soon as possible after they become aware of the event. Vaccine providers should report, without delay, all serious or unexpected AEFI to public health officials according to jurisdictional guidelines.

Refer to Vaccine Safety in Part 2 for additional information about AEFI reporting. Refer to Vaccine Administration Practices in Part 1 for information about pre-immunization and post-immunization counselling.

GUIDELINE 10

Vaccine providers should report all cases of vaccine preventable diseases as required under provincial or territorial legislation.

Vaccine providers should comply with provincial/territorial requirements for communicable disease reporting. Reporting of vaccine preventable diseases is essential for public health management of the disease to limit transmission, ongoing evaluation of the effectiveness of immunization programs, as well as public health and medical investigation of vaccine failures.

GUIDELINE 11

Vaccine providers should adhere to appropriate procedures for the storage and handling of immunizing products.

Vaccines must be handled and stored as recommended in manufacturers' product monographs or leaflets, and jurisdictional or national guidelines. The temperatures at which vaccines are transported and stored should be monitored according to jurisdictional or national guidelines. Vaccines must not be administered after their expiry date, and vaccines that have undergone a breach in the cold chain should not be used without appropriate consultation such as the local public health agency. Vaccine providers should report product usage, wastage, loss and inventory as required by provincial/territorial or local public health officials.

Vaccine providers should be familiar with national and jurisdictional guidelines for vaccine storage and handling and must ensure that staff members designated to handle vaccines are also familiar with the guidelines. Refer to Storage and Handling of Immunizing Agents in Part 1 for additional information.

GUIDELINE 12

Vaccine providers should maintain up-to-date, easily retrievable immunization protocols at all locations where vaccines are administered.

Vaccine providers should maintain protocols that, at a minimum, outline: appropriate vaccine dosage; vaccine contraindications; recommended injection sites and techniques of vaccine administration; and possible adverse events and their emergency management. The *Canadian Immunization Guide* and updates, along with product monographs and product leaflets, can serve as references for the

development of protocols. Adverse event management protocols should specify the necessary emergency equipment, drugs (including dosage), and personnel to manage safely and competently any medical emergencies arising after administration of a vaccine. All vaccine providers should be familiar with the location and content of these protocols, and how to follow them.

Refer to Early Vaccine Reactions Including Anaphylaxis in Part 2 for additional information about possible AEFI and their emergency management. Refer to Vaccine Administration Practices in Part 1 for information about sites and techniques of vaccine administration. Refer to vaccine-specific chapters in Part 4 for vaccine dosage and contraindications.

GUIDELINE 13

Vaccine providers should be properly trained and maintain ongoing education regarding current immunization recommendations.

Vaccines must be administered only by trained persons who are recognized as qualified to administer vaccines in their jurisdiction. Training and ongoing education should be based on current professional guidelines; NACI and provincial/territorial health authority recommendations; and the National Guidelines for Immunization Practices. Vaccine providers should be familiar with immunization information provided by public health officials and other appropriate sources such as the Immunization Competencies for Health Professionals. (http://www.phac-aspc.gc.ca/im/ic-ci/index-eng.php#toc)

GUIDELINE 14

Immunization errors and immunization-related incidents should be reported by vaccine providers to their local jurisdiction.

Immunization errors and immunization-related incidents should be monitored as patient safety issues and reported by the vaccine provider in accordance with provincial/territorial regulation or for advice, if needed.

Common immunization errors include errors in vaccine type, dose, site, route, person, time or schedule. Immunization-related incidents include a range of events, such as a needle injury caused by failed positioning of a child, immunization without consent, or fainting with a fall resulting in injury. Methods to detect immunization errors or incidents may include vaccine provider self-reporting, direct observation or record audits.

Decreasing immunization errors requires an accurate system of error reporting in an open environment that focuses on positive reinforcement rather than punitive action. Activities to prevent immunization error in an organization are a better barometer of quality than the error rate alone. Publishing or sharing information about immunization errors is a first step towards an immunization quality improvement program that strives to reduce the incidence of errors. Immunization errors can be effectively reduced by systematically identifying, eliminating or minimizing both human and system related factors.

Refer to Vaccine Safety in Part 2 for additional information.

GUIDELINE 15

Vaccine providers should operate an immunization tracking system.

A tracking system should generate reminders of upcoming vaccinations as well as recalls for individuals who are overdue for their vaccinations. A system may be manual or automated, and may include electronic (e.g., email, text message), mailed or telephone messages. All vaccine providers should identify, for additional intensive tracking efforts, vaccine recipients considered at high risk of failing to complete the immunization series on schedule (e.g., infants who start their vaccine series late or children who fall behind in their immunization schedule). Refer to Immunization Records in Part 1 for additional

information about health care provider records.

GUIDELINE 16

Audits should be conducted in all immunization services to assess the quality of immunization records and the degree of immunization coverage.

An audit of immunization services should include assessment of all or a random sample of immunization records to assess the quality of documentation and to determine the immunization coverage level (e.g., the percentage of 2-year-old children with up-to-date immunization). The results of the audit should be discussed by vaccine providers as part of ongoing quality assurance reviews and used to develop solutions to the problems identified.

PART 1

COMMUNICATING EFFECTIVELY ABOUT IMMUNIZATION

Immunization is one of the safest and most effective interventions to prevent disease, morbidity and early death. Yet a portion of the population has concerns about vaccines and hesitates to get vaccinated or get their children vaccinated. Lower vaccination rates reduce the level of protection against a vaccine-preventable disease at a population level (i.e. herd immunity), potentially resulting in resurgence of vaccine-preventable diseases and associated complications. Most importantly, unvaccinated children are themselves at significantly higher risk of developing a vaccine preventable disease.

Over the past few years, there has been intense interest in understanding why people are unwilling to receive vaccines and how their concerns can be addressed to allow everyone to take part in vaccination programs. Effective communication by health care providers has an important influence on people's decisions about whether or not to proceed with immunization.

This chapter reviews what is known about vaccine hesitancy, describes basic principles of effective communication, and provides examples of immunization facts.

VACCINE HESITANCY

Vaccine hesitancy is a term used to describe refusal or delay in regular immunization schedules due to concerns about immunization. Vaccines evoke concerns different from other health interventions because they are largely intended for individuals who are healthy, as opposed to other health interventions that are predominantly intended for individuals with a disease. Vaccine hesitancy is a complex issue with multiple determinants, the most important being:

- lack of information about the vaccine being given and about immunizations in general;
- conflicting information from a variety of sources (e.g., alternative medicine practitioners, anti-vaccination websites);
- mistrust of the source of information (e.g., perceptions of business and financial motives of the vaccine industry);
- perceived risk of serious adverse events and concerns regarding injections (e.g., pain and anxiety associated with immunization; coincidental rather than causal adverse events that are perceived as vaccine-related);
- lack of appreciation of the severity and incidence of vaccine-preventable diseases;
- sociocultural beliefs (e.g. religious beliefs)

Loss of public confidence in immunization can reduce the number of people who are immunized and result in resurgence of vaccine-preventable diseases and associated complications. Evidence about the effects of misinformation, rumours, and anti-vaccine groups on vaccine coverage and consequent disease outbreaks in many countries is well documented.

The decision to immunize is a result of personal perceptions of complex vaccine and disease related information and the trust in individuals and institutions that produce, legislate, and deliver vaccines. Research identifies a number of factors that affect the extent to which an individual is trusted: perceptions

of knowledge and expertise, openness and honesty, and concern and caring. Regular health care providers, such as vaccine providers, are perceived as trusted individuals and have a vital role in ensuring continued success of immunization programs and in maintaining confidence in the effectiveness and safety of vaccines. Besides demonstrating skills and expertise in the principles and practices of immunization, vaccine providers need to know how to counsel effectively and how to help vaccine recipients or parents knowledgeably assess the benefits and risks of immunization, as well as the risks associated with being unvaccinated.

PRINCIPLES OF EFFECTIVE COMMUNICATION

The majority of Canadians feel that they are well-equipped to make informed decisions about immunization. However, there are individuals who remain concerned about possible side effects of immunization and who require additional information to make evidence-based decisions. Vaccine providers should make the most of each opportunity to encourage questions, address misinformation, and provide valid and appropriate messages and resources, including websites that provide reliable information. The following principles can be used by vaccine providers to communicate immunization facts effectively (refer to Immunization Facts) to vaccine recipients or parents:

- **Adopt a vaccine recipient-centred approach.**
  Vaccine recipients and parents should have input into the decision to immunize. Effective decision making is best done in a partnership between the vaccine provider, and the vaccine recipient or parent. Building these partnerships takes time and should ideally be established prior to the immunization visit. Vaccine providers should be transparent about the decision-making process, as well as honest and open about uncertainty and risks.

  Engaging and motivating vaccine recipients and parents are best accomplished through dialogue. Motivational interviewing is a semi-directive method aimed at changing behaviour. Additional information about motivational interviewing is available from the Public Health Agency of Canada - Motivational Interviewing – Motivating Patients to Adopt a Healthier Lifestyle. (http://www.phac-aspc.gc.ca/cd-mc/videos/tech-eng.php)

- **Respect differences of opinion about immunization.**
  Democratisation movements and the advent of the internet have changed the environment around immunization from top-down, expert-to-consumer communication, to non-hierarchical, dialogue-based communication. With the public increasingly questioning recommendations of experts and public institutions on the basis of their own, often web-based, research, vaccine providers should anticipate that individuals will question the need for, or the safety of, immunization. The majority of such individuals are not against immunization, but are seeking answers to questions about vaccine safety, immunization schedules, changing policies, and the relevance of some vaccines.

  In general, events that are unfamiliar, involve a man-made process, involve loss of control, are mandatory, or involve a decision to do something rather than avoid something, are perceived as *risky*. Immunization, therefore, is perceived by some individuals as a potential concern, particularly when it comes to immunizing children.

  Vaccine providers should determine the origins of vaccine hesitancy and take time to listen. Asking vaccine recipients or parents about their perceptions and discussing the benefits of immunization should be done using a non-judgemental and non-confrontational tone. Vaccine providers should clarify why a specific belief about a vaccine is held, especially if it is based on misinformation or misunderstanding. Demonstrating patience and respect builds trust and support for deciding to immunize. It is also important to recognize that, despite all the efforts taken, some individuals will not be persuaded into accepting vaccines.

- **Represent the risks and benefits of vaccines fairly and openly.**
  Candidly communicating information about the safety of vaccines and their benefit–risk ratios is essential. For most individuals, vaccine safety is of primary concern and few are aware of Canada's

robust vaccine safety system or that vaccines are held to a higher safety standard than medications. This process includes comprehensive reviews of efficacy and safety data before approval, oversight over good manufacturing practices and quality before product release, expert review of vaccine recommendations, post-marketing surveillance and rapid response to vaccine performance concerns, and international collaboration. Vaccine providers need to outline the work that is done to assess vaccine safety during development, regulatory review, and on an ongoing basis following use of a vaccine. Refer to Vaccine Safety in Part 2 for additional information.

Through direct dialogue and using language that is appropriate, vaccine providers should contrast the known and theoretical risks of vaccines with the known risks associated with the vaccine preventable diseases. Potential risks of any vaccine should not be considered in isolation but in comparison with risks to the individual and community should an individual remain unimmunized.

Vaccine providers have a vested interest in the health of vaccine recipients. In addition to providing information, vaccine providers should provide immunization recommendations in accordance with their patients' best interest. It is honest to express concern about the risks of vaccine preventable diseases should a person remain not vaccinated. It is also important to emphasize that, should vaccine preventable diseases occur, complications may not be correctable, even with the very best medical care. Refer to The Benefits of Vaccines in Part 1 for additional information.

- **Clearly communicate current knowledge using an evidence-based approach**
  Vaccine providers should:

  - Assess the level and type of information that an individual wants and adapt the information provided accordingly; for example, some people will appreciate scientific evidence while others will prefer anecdotal information and stories from personal experience.
  - Present evidence in an understandable way; for example, concepts such as single event probability or relative risk may not be understandable for most vaccine recipients or parents; scientific jargon and acronyms should be avoided.
  - Frame immunization in terms of positive gains; for example, "A vaccine is 99% safe" is more effective than, "There is a 1% chance of side effects." Similarly, "If you decide not to get the vaccine, you increase your chances of getting a disease," is more effective than, "If you decide to get the vaccine, you decrease your chances of getting or transmitting a disease."
  - Use and have available varied information formats (visual, audio, printed material, websites), tailored to a range of socio-cultural groups (i.e., educational level, language, ethnic and cultural background). It is estimated that 60% of adults and 88% of seniors in Canada are not health literate and have difficulty using the everyday health information that is routinely available. Additional information and resources about health literacy are available from the Public Health Agency of Canada (http://www.phac-aspc.gc.ca/cd-mc/hl-ls/index-eng.php#tabs-3) and the Canadian Public Health Association. (http://www.cpha.ca/en/portals/h-l.aspx)
  - Inform vaccine recipients and parents about ways that they can make immunization less stressful (i.e., using combination vaccines and appropriate pain management strategies); pain and anxiety related to immunization are important factors in vaccine hesitancy. Refer to Vaccine Administration Practices in Part 1 for additional information about effective discomfort and anxiety reduction strategies.

Providing information does not need to be time-consuming, particularly given the volume and accessibility of material available on the internet. Refer to Guidance for parents on how to evaluate the accuracy of immunization information (http://www.immunizationinfo.org/parents/evaluating-information-web) for more information regarding credible online sources for information about vaccines and immunization. Refer to Immunize Canada (http://immunize.ca/en/publications-resources/personal.aspx) and Immunization Action Coalition (http://www.immunize.org/reports/) for useful vignettes and personal stories concerning immunization.

IMMUNIZATION FACTS

Vaccines work - immunization is the most effective way to protect against vaccine preventable diseases.

- Vaccines are safe and effective; serious disease can occur if a person, their child and family are not immunized.
- Immunization is one of the most important ways to promote health.
- Over the past 50 years, immunization has saved more lives in Canada than any other health intervention.
- Immunization protects both individuals who receive the vaccine and those with whom they come in contact, especially people who cannot be or are incompletely vaccinated due to medical conditions or age.
- The World Health Organization estimates that every year, more than two million deaths are prevented worldwide due to immunization.
- Immunization provides cost-savings to the individual and to the society.
- Refer to The Benefits of Vaccines in Part 1 for additional information.

Vaccines strengthen the immune system.

- Vaccines stimulate and strengthen the immune system. They train the immune system to defend rapidly against vaccine preventable infections before illness can occur.
- The human immune system is continually challenged and has an enormous capacity to respond to antigens; infants can respond to about 10,000 different antigens at any one time. The few antigens in vaccines are tiny in comparison.
- Children are naturally exposed to multiple antigens on a routine basis and they respond well to these ongoing exposures with no untoward effects on their immune system.
- Immunization does not significantly add to the body's daily exposure to antigens.

Vaccines are safe.

- The vaccines used in Canada are highly effective and extremely safe. Vaccines are among the safest medical products available. Serious side effects, such as severe allergic reactions, are very rare.
- Prior to authorization for use in Canada, vaccines are extensively tested and the manufacturer must submit scientific and clinical evidence that demonstrates the safety and efficacy of the vaccine.
- Health Canada supervises all aspects of vaccine production by manufacturers to ensure safety, efficacy and quality. Vaccine safety continues to be rigorously monitored and evaluated after the vaccine is on the market.
- Even after a vaccine has been authorized for marketing in Canada, every batch is laboratory tested for safety and quality.
- Canada's comprehensive vaccine safety monitoring system helps to alert public health authorities to trends in reported adverse events or any unusual adverse events not previously reported. Once a vaccine is in use, experts in vaccine safety conduct ongoing quality and safety monitoring, and investigate and respond to reports of serious adverse events following immunization. This system detects possible safety concerns associated with a vaccine so that appropriate action can be taken should such a concern arise.
- Refer to Vaccine Safety in Part 2 for additional information.

The risks of vaccine preventable diseases are many times greater than the risk of a serious adverse reaction to a vaccine.

- Serious adverse reactions are rare. The dangers of vaccine-preventable diseases are many times greater than the risks of a serious adverse reaction to the vaccine.
- Diseases like polio, diphtheria, measles and pertussis (whooping cough) can lead to paralysis, meningitis, pneumonia, choking, brain damage, heart problems, and even death. Although today

these diseases are non-existent or rare in Canada, if immunization programs were reduced or stopped, they would re-appear in epidemics causing sickness and death.
- Effective treatments do not exist for many vaccine-preventable diseases.
- In most cases, it is not possible to know in advance if an unvaccinated person will experience mild or severe complications from a vaccine-preventable disease.
- The vast majority of vaccine adverse reactions are minor and resolve quickly.
- Serious adverse reactions to vaccines are very rare and it is often very difficult to determine if a reaction was directly linked to a vaccine or was an unrelated event which only occurred by coincidence after the vaccine was administered.
- Pre-vaccination screening is used to identify individual contraindications to administration of a vaccine and to reduce the risk of serious adverse reactions to a vaccine.
- Vaccinees are observed post-vaccination for signs and symptoms of adverse reactions to a vaccine. Vaccine providers are familiar with the signs and symptoms of serious immediate allergic reactions to vaccines and are prepared to initiate management of the allergic reaction and administer appropriate medications.
- Refer to The Benefits of Vaccines in Part 1 for additional information.

Vaccines are not linked to chronic diseases like autism, multiple sclerosis (MS), asthma, or sudden infant death syndrome.

- Research using rigorous scientific methods has shown that:
  - Measles-mumps-rubella (MMR) vaccine does not cause autism
  - Thimerosal-containing vaccines do not cause autism
  - Hepatitis B vaccine does not cause multiple sclerosis (MS) or relapses of pre-existing MS
  - Pertussis vaccine does not cause brain damage
  - Vaccines do not cause sudden infant death syndrome
  - Childhood vaccines do not increase the risk of developing asthma
- There is no evidence that any vaccine causes chronic diseases, autism or sudden infant death syndrome. Alleged links - for example between hepatitis B vaccine and multiple sclerosis - have been disproved by rigorous scientific study.
- Refer to Vaccine Safety in Part 2 for additional information.

Multiple injections are an effective way of ensuring up to date immunization.

- Multiple injections of vaccines do not overwhelm the immune system.
- Generally, infants and children have similar immune responses whether vaccines are given at the same time or at different visits.
- Giving several routine vaccines at the same visit does not result in increased rates of adverse reaction, compared to giving the vaccines at different visits.
- Giving multiple vaccines at one visit helps to ensure that people are up to date with the vaccines required for their age and risk factors.
- Delaying vaccines may leave a child or adult vulnerable to vaccine-preventable diseases.
- Evidence has shown that multiple injections at one visit cause less pain than waiting a few days between administration.
- Giving more than one vaccine at the same visit is critical when preparing for international travel or if there is uncertainty that a person will return for additional doses of vaccine.
- Refer to Vaccine Administration Practices in Part 1 for additional information.

Vaccine preventable diseases can occur at any time because the bacteria and viruses that cause these infections have not been eliminated.

- Bacteria and viruses that cause pneumonia, meningitis, diphtheria, pertussis, polio, measles, mumps, rubella, varicella, hepatitis A and hepatitis B are present in Canada or other parts of the world.
- Even if a disease is uncommon in Canada, travellers can carry diseases from other countries to Canada. Outbreaks of measles in Canada have resulted from cases being imported.

- Unless a disease has completely disappeared worldwide, there is a real risk that small outbreaks can turn into large epidemics if most of the community is not protected.
- For some vaccine-preventable diseases, such as measles, one case in a community is a concern, because the disease spreads very quickly and easily among people who are not immune.
- *Clostridium tetani* (tetanus or lockjaw) is widely distributed in soil – it will never be eliminated - so the risk of getting tetanus continues to exist for all people who are not immunized.
- *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (pneumococcal disease) and *Neisseria meningitidis* (meningococcal disease) are carried in the nose and throat of some healthy people, so these diseases continue to be a threat.

Unvaccinated individuals have a much greater chance of getting a vaccine-preventable disease than people who have been vaccinated, even in countries with high levels of immunization.

- It may not be possible to avoid exposure to a vaccine-preventable disease. For example, an unvaccinated person can get measles by breathing the air in a room that was occupied hours before by a measles-infected person.
- When disease is spreading in a community, a small percentage of vaccinated people may get sick; that is because no vaccine is 100% effective; however, a much larger percentage of unimmunized people exposed to the disease can become ill. In Canada in 2011, measles importations led to a large outbreak involving more than 700 people, largely in Quebec. Where immunization status was known, approximately 80% were not adequately immunized for their age.
- Immunization can reduce the risk of severe disease if you do happen to get infected.
- Refer to The Benefits of Vaccines in Part 1 for additional information.

Vaccine-preventable diseases re-appear quickly if immunization coverage drops.

- In Japan, pertussis immunization coverage dropped from 90% to less than 40% because of public concern over two infant deaths following vaccination in 1975 (later found not to be caused by the vaccination). Prior to the drop in immunization, there were 200 to 400 cases of pertussis each year. Following the drop in immunization, surveillance data collected over a three year period showed that during this time the number of pertussis cases increased to approximately 13,000 and the number of deaths to over 100 per year.
- In Ireland, measles immunization coverage dropped to 76%, following false allegations of a link with autism. In 2000, the number of measles cases increased from 148 to 1,200, and several children died due to the complications of measles.
- The potential for re-emergence of diphtheria if immunization levels decline was demonstrated during the 1990s in the Commonwealth of Independent States (former Soviet Union) when over 140,000 cases and 4,000 deaths were reported.

Vaccines may contain additional substances to ensure effectiveness and safety – these substances are safe.

- The main ingredients of vaccines are killed or weakened viruses or bacteria or their parts. These are called antigens and they train the immune system to recognize and prevent disease.
- Additional substances may be required in the vaccine to ensure effectiveness and safety:
  - Very small amounts of preservatives, such as phenol, 2-phenoxyethanol or thimerosal, may be added to a vaccine to prevent the growth of microbes in the vaccine when it is used.
    - *Thimerosal* contains a minute amount of one form of mercury which does not accumulate in the body as other forms of mercury can. Current routine childhood vaccines in Canada do not contain thimerosal (with the exception of certain influenza and hepatitis B vaccines).
    - Vaccines do not contain anti-freeze, despite allegations by some opposed to immunisation.
  - Adjuvants, such as aluminum salts and squalene, may be added to strengthen the immune response to the vaccine. Without an adjuvant, people might require more frequent or higher doses of vaccines to be protected.
    - *Aluminum* is found in air, food and water and is present in breast milk and infant formula in similar amounts as in vaccines. Hundreds of millions of people have been safely vaccinated with aluminum-containing vaccines.

        - *Squalene* is a naturally occurring substance often found in plants, animals and humans, as well as foods and cosmetics. It is a compound produced by the liver and circulates throughout the bloodstream.
    - Additives, such as gelatin, human serum albumin or bovine reagents, are added to vaccines to help vaccines remain effective while being stored.
        - *Gelatin* in vaccines very rarely causes severe hypersensitivity reactions (approximately 1 case per 2 million doses). Individuals with a history of immediate allergic reactions to foods containing gelatin or who have had an anaphylactic reaction to any of the products containing gelatin should be referred to an allergist prior to vaccination.
        - *Human serum albumin:* there is an extremely small theoretical risk of infectious agents being present in products made from human blood. However, steps in the manufacturing process of both human albumin and human albumin-containing vaccines eliminate the risk of transmission of these agents. There have been no documented cases of vaccine-related transmission of infectious agents by human serum albumin.
        - In Canada, the *bovine-derived reagents* added to vaccines included in the routine immunization schedule are manufactured from animals known to be free of bovine spongiform encephalopathy. The risk of transmitting variant Creutzfeld Jakob disease from vaccines containing bovine-derived material is theoretical, estimated to be 1 in 40 billion or less.
    - Substances, such as formaldehyde, antibiotics, egg proteins or yeast proteins, may be needed for the vaccine manufacturing process.
        - *Formaldehyde* may be used to kill or weaken the virus or bacterium used to make a vaccine and is removed during the manufacturing process. Any trace amounts that may remain in the vaccine are safe. Formaldehyde is produced naturally in the body and helps with metabolism. There is approximately ten times the amount of formaldehyde in an infant's body at any time than there is in a vaccine.
        - *Antibiotics* are used in some vaccines to prevent bacterial contamination during the manufacturing process. The types of antibiotics that are most likely to cause immediate hypersensitivity reactions (such as penicillin) are not contained in vaccines.
        - *Egg proteins* may be used for the growth of viruses used in some vaccines. Most of the egg protein is removed in the manufacturing process but very small amounts may remain in the final product. Refer to Anaphylactic Hypersensitivity to Egg and Egg-Related Antigens in Part 2 for additional information.
        - *Yeast protein* is used in the manufacture of some vaccines. Hypersensitivity to yeast is very rare and a personal history of yeast allergy is not generally reliable.
        - Vaccines do not contain cells from aborted fetuses or other human cells.
        - Human cell lines are used in the early stages of production of some vaccines; however, all cells are removed during purification of the vaccine.

Refer to Contents of Immunizing Agents in Part 1 for additional information.

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PART 1

PRINCIPLES OF COMBINATION VACCINES

WHAT IS A COMBINATION VACCINE?

There are three different types of vaccine preparations based on how many and what types of immunizing antigens are contained in the vaccine:

- vaccines containing only one immunizing antigen against one disease (e.g., hepatitis A vaccine)
- vaccines containing immunizing antigens against more than one serogroup or serotype of the same disease (e.g., quadrivalent meningococcal vaccine, pneumococcal vaccines)
- vaccines containing immunizing antigen against more than one vaccine preventable disease (e.g., measles-mumps-rubella vaccine)

The nomenclature to describe these types of vaccines is used inconsistently. The term *combination vaccine* is often used to refer to a single vaccine that includes antigens for the prevention of more than one vaccine preventable disease, and is used in that context in this chapter. The term *combined vaccines* may also be used to describe the prescribed mixture of two separate vaccines in a single vial prior to administration or vaccines that are separately manufactured but combined by the manufacturer into one product during the final packaging stages. Vaccination providers should not combine separate vaccines into the same syringe to administer together unless mixing is explicitly specified in the Health Canada approved product monograph. The safety, immunogenicity, and effectiveness of unlicensed combinations are unknown.

There are many combination vaccine products available (refer to Table 1). Diphtheria, tetanus and pertussis vaccines have been available as a combination product for more than 30 years, and infants in Canada have been vaccinated against diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b (Hib) with a product containing all five antigens (DTaP-IPV-Hib) since 1996. In recent years, additional combination vaccine products have become available and new combination vaccines have been added to the routine immunization schedule. For details on specific combination vaccines, refer to the vaccine-specific chapters in Part 4.

Table 1: combination vaccines authorized and available for use in Canada

Antigens in vaccine	Vaccine abbreviation	Brand name
Diphtheria, tetanus, acellular pertussis, inactivated polio (pediatric)	DTaP-IPV	QUADRACEL®
Diphtheria, tetanus, acellular pertussis, inactivated polio, *Haemophilus influenzae* type b (pediatric)	DTaP-IPV-Hib	PEDIACEL®
Diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio, *Haemophilus influenzae* type b (pediatric)	DTaP-HB-IPV-Hib	INFANRIX hexa™
Hepatitis A, hepatitis B	HAHB	TWINRIX® TWINRIX® Junior
Hepatitis A, typhoid (injection)	HA-Typh-I	ViVAXIM®
Measles, mumps, rubella	MMR	M-M-R® II PRIORIX®
Measles, mumps, rubella, varicella	MMRV	PRIORIX-TETRA®
Tetanus, diphtheria (reduced)	Td	Td ADSORBED
Tetanus, diphtheria (reduced), inactivated polio	Td-IPV	Td POLIO ADSORBED
Tetanus, diphtheria (reduced), acellular pertussis (reduced)	Tdap	ADACEL® BOOSTRIX®
Tetanus, diphtheria (reduced), acellular pertussis (reduced), inactivated polio	Tdap-IPV	ADACEL®-POLIO BOOSTRIX®-POLIO

GENERAL PRINCIPLES OF COMBINATION VACCINES

- Combination vaccines are rigorously evaluated before authorization for use in Canada. Only those combinations that have been demonstrated to be safe and efficacious are authorized for use.
- In general, combination vaccines are preferred over separate injections of the single component vaccines to keep the number of injections to a minimum.
- Combination vaccines should fit the recommended immunization schedule, be easily stored, and be easy to administer.
- Vaccines that are intended for separate administration should never be combined by vaccine providers.

EFFICACY OF COMBINATION VACCINES

The efficacy of each component in a combination vaccine is compared with established parameters of protection before the combination vaccine is authorized for use in Canada. Antibody responses to specific antigens in combination products may be either stronger or weaker than responses to separately administered single antigens, but these differences are not considered to have any clinical impact.

SAFETY OF COMBINATION VACCINES

The combination products available in Canada have excellent safety records. The safety of a new combination product is rigorously evaluated and compared against the safety of single antigen products or existing combination vaccines prior to authorization for use in Canada; there may be differences in

minor adverse events associated with combination compared to single component vaccines, but they are not considered to be clinically significant. In case of an adverse event following immunization, determining which component of a combination vaccine is responsible may be more challenging than in single component vaccines.

With the refinement of vaccine development and production, children today are exposed to far fewer vaccine antigens than in the past, even though they are immunized against more infections with more combination vaccines. Refer to Vaccine Safety in Part 2 for additional information about the safety of combination vaccine products.

BENEFITS OF COMBINATION VACCINES

The benefits of combination vaccines include:

- improved adherence to immunization schedules because of a reduction in the number of immunization visits and injections required, leading to improved vaccine coverage rates
- facilitation of uptake of a new vaccine when combined with an older vaccine (e.g., measles-mumps-rubella-varicella vaccine)
- increased opportunity for administration of catch-up or booster doses (e.g., timely vaccination coverage for children who are behind in their routine immunization schedule)
- reduced risk of injury to vaccine providers related to multiple injections of separate vaccines
- reduced time required for an immunization visit when one injection rather than multiple injections are given
- reduced vaccine administration, shipping, handling, wastage and storage costs
- reduced costs for extra immunization visits
- reduced stress for vaccinees and vaccine providers related to multiple injections of separate vaccines

Refer to Benefits of vaccines in Part 1 for additional information about the benefits of immunization.

COMPLEXITIES OF COMBINATION VACCINES

Complexities associated with combination vaccines include:

- Combination products may be more expensive than separate vaccines; however, combination vaccines may be more cost effective if the costs of extra injections, health care provider time and additional handling and storage are taken into consideration.
- It can be difficult to determine which component of a combination vaccine is responsible for an allergic reaction or other adverse event following immunization.
- The use of a combination product may result in administration of extra doses of certain antigens (e.g., a booster dose of pertussis (Tdap) will also give an extra dose of tetanus and diphtheria toxoids). An extra dose of a live-virus vaccine component, or Hib or hepatitis B vaccine, has not been found to be harmful. However, the risk for an adverse event might increase when the extra antigen dose is administered at an earlier time than it would have been given if it had not been part of a combination product (e.g. when tetanus-containing vaccines are given earlier in order to provide pertussis protection). Before administering a combination vaccine with an unneeded antigen or antigens, the benefits and risks of administering this combination vaccine should be carefully considered and discussed with the patient or parent. Using combination vaccines containing unneeded antigens might be justified when 1) the extra antigen is not contraindicated, 2) products that contain only the needed antigens are not readily available, and 3) potential benefits to the patient outweigh the potential risk for adverse events associated with the extra antigen dose.

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PART 1

PRINCIPLES OF VACCINE INTERCHANGEABILITY

Similar vaccines from different manufacturers are routinely authorized for use in Canada. Circumstances such as vaccine shortages, contraindication to a specific vaccine, changes in product availability, or migration across jurisdictions may necessitate giving vaccines from different manufacturers to the same individual over time. Because immunization schedules and specific products used may vary across provinces and territories and between countries, questions about vaccine interchangeability may arise when evaluating the immunization status of persons new to Canada or people who have moved between jurisdictions.

GENERAL PRINCIPLES OF VACCINE INTERCHANGEABILITY

- In general, use the same manufacturer's product for all doses in a vaccine series. However, routine immunization should not be deferred because of the lack of availability of a specific product.
- To be considered interchangeable, the vaccines should:
  - be authorized with the same indications and with equally acceptable schedules, and
  - be authorized for the same population, and
  - contain comparable antigens, and
  - be similar in terms of safety, reactogenicity, immunogenicity and efficacy.
- Even when vaccines from different manufacturers are authorized for the same indications, the manufacturers may use differing production methods, antigens or antigen concentrations, adjuvants, conjugating proteins, stabilizers and preservatives. Each of these factors could affect the vaccine's potential for interchangeability.
- In general, vaccine diluents are not interchangeable. Lyophilized vaccines should be reconstituted only with the diluent provided for that purpose, unless otherwise permitted by the manufacturer.

VACCINE INTERCHANGEABILITY RECOMMENDATIONS

The following recommendations for vaccine interchangeability are applicable only to vaccines with the same indications and authorization for use in the same populations.

DIPHTHERIA, TETANUS, PERTUSSIS, POLIO, *HAEMOPHILUS INFLUENZAE* TYPE B VACCINES

Complete the primary series of three doses of diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b-containing vaccine with the same combination vaccine whenever possible. However, if the original vaccine is unknown or unavailable, an alternative combination vaccine 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.

HEPATITIS A VACCINES

Monovalent hepatitis A vaccines may be used interchangeably. Any hepatitis A vaccine indicated for the age of the vaccine will provide an effective booster dose after a first dose of vaccine from a different manufacturer.

HEPATITIS B VACCINES

Monovalent hepatitis B vaccines may be used interchangeably, using the dosage and schedules recommended by the manufacturer for the age group. Combined hepatitis A and hepatitis B vaccine can be used to complete the hepatitis B primary series. Refer to Hepatitis A Vaccine and Hepatitis B Vaccine in Part 4 for appropriate schedules.

HUMAN PAPILLOMAVIRUS (HPV) VACCINES

Whenever possible, use one manufacturer's brand of HPV vaccine to complete the vaccine series. If the brand of the previously received doses is not known, either brand of HPV vaccine may be used to complete the vaccine series. Both HPV4 and HPV2 vaccines provide protection against HPV types 16 and18, and will likely achieve protective antibody levels against these HPV types. If fewer than three doses of HPV4 vaccine are administered, protection against HPV types 6 and 11 cannot be ensured. HPV2 vaccine is not recommended for boys and men. Refer to Human Papillomavirus Vaccine in Part 4 for additional information.

INFLUENZA VACCINES

If a child (aged less than 9 years) requires 2 doses of influenza vaccine in the same season, it is preferable to use the same type of vaccine (trivalent inactivated [TIV] or live attenuated influenza [LAIV]) for both doses. However, if the child is eligible for either TIV or LAIV, and the type of vaccine used for the first dose is not available, use either type of vaccine for the second dose. If using TIV for both doses, vaccines from different manufacturers can be used for the first and second dose.

MEASLES, MUMPS AND RUBELLA VACCINES

On the basis of expert opinion, the measles-mumps-rubella (MMR) vaccines authorized in Canada may be used interchangeably.

VARICELLA VACCINES

If the child has received only one dose of MMR and one dose of varicella vaccine, or one dose of measles-mumps-rubella-varicella (MMRV) vaccine, then the second dose can be provided as MMRV, **or** as MMR and varicella vaccine separately. It is recommended that the same manufacturer's univalent varicella or MMRV vaccine be used to complete the schedule unless the vaccine used for the first dose is unknown or unavailable.

MENINGOCOCCAL CONJUGATE VACCINES

There are no published data regarding the interchangeability of monovalent conjugate meningococcal vaccines, but the vaccines have been safely interchanged without a noticeable decrease in efficacy. When possible, the infant series should be completed with the same vaccine. Either of the quadrivalent conjugate meningococcal vaccines may be used for re-vaccination when indicated, regardless of which meningococcal vaccine was used for initial vaccination.

PNEUMOCOCCAL CONJUGATE VACCINES

Infants who have started an immunization schedule with one conjugate pneumococcal vaccine should continue their immunization schedule with a conjugate pneumococcal vaccine that contains the largest number of pneumococcal serotypes. For example, infants who have started a vaccine series with pneumococcal conjugate 7-valent or pneumococcal conjugate 10-valent vaccine, should have their series completed with pneumococcal conjugate 13-valent vaccine.

RABIES VACCINES

Wherever possible, complete a rabies immunization series with the same product. However, if this is not feasible, rabies vaccines are considered interchangeable. People who require a booster dose of rabies vaccine for pre-exposure prophylaxis can be given either vaccine, regardless of the vaccine used for the initial vaccination series.

ROTAVIRUS VACCINES

There are no data on safety, immunogenicity, or efficacy when ROTARIX™ (GlaxoSmithKline Inc.) is administered as the first dose and RotaTeq® (Merck Canada Inc.) is used as the second dose or vice versa. Given that the two vaccines differ in composition and schedule, complete the vaccine series with the same product whenever possible. However, in the event that the product used for a previous dose(s) is unknown, complete the series with the available product. If any dose in the series was RotaTeq®, administer a total of 3 doses of vaccine.

TYPHOID VACCINES

There are no data regarding the interchangeability of oral typhoid vaccines.

EVIDENCE-BASE FOR VACCINE INTERCHANGEABILITY RECOMMENDATIONS

Ideally, as new vaccines become available, clinical trials should be conducted evaluating interchangeability with existing products. To date, the majority of information regarding interchangeability has been gathered as a result of situations of vaccine shortages and new product purchases with the negotiation of new contracts. Given the importance of this issue and the limited data available regarding the interchangeability of vaccines, further research in this area is encouraged.

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PART 1

VACCINE ADMINISTRATION PRACTICES

GENERAL CONSIDERATIONS

Appropriate vaccine administration is essential to the optimal safety and efficacy of vaccines. Vaccine administration practices are based on clinical trials that determine the dose, route and schedule for each vaccine. Professional standards for medication and vaccine administration, and jurisdictional policies and procedures (if available) also guide vaccination practices.

All vaccine providers should receive education and competency-based training on vaccine administration before providing vaccines to the public. Programs should be in place to monitor the quality of immunization services. For detailed information about the required immunization competencies, refer to the Public Health Agency of Canada's Immunization Competencies for Health Professionals. (http://www.phac-aspc.gc.ca/im/pdf/ichp-cips-eng.pdf)

The following information provides general guidance regarding vaccine administration practices for use in conjunction with vaccine manufacturers' instructions outlined in product leaflets and product monographs; professional standards of practice; and jurisdictional policies and procedures.

PRE-VACCINATION COUNSELLING

Prior to vaccination, the vaccine provider should:

- assess that the vaccine recipient is capable of consenting to the procedure or that, when required, an appropriate guardian or substitute decision-maker gives consent;
- provide information regarding the risks and benefits of receiving or not receiving the vaccine;
- assess the vaccine recipient's current state of health;
- assess contraindications and precautions to receiving the vaccine, including any history of potential immediate or anaphylactic hypersensitivity to a previous dose of the vaccine or to any of the vaccine components; refer to Contraindications, Precautions and Concerns in Part 2 for additional information;
- evaluate reactions to previous vaccinations;
- discuss frequently occurring minor adverse events and potential rare severe adverse events;
- provide an opportunity for the vaccine recipient or guardian to ask questions;

After informed consent is obtained, the vaccine provider should outline the process of vaccine administration and explain positioning procedures. The parent or guardian should hold a child in a position as instructed by the vaccine provider. Failed positioning can result in inaccurate dose, inappropriate depth of injection, or injury to the vaccine recipient or vaccine provider. Refer to Table 4 for additional information. Table 1 provides an example pre-vaccine administration checklist.

Table 1: pre-vaccine administration check list

(This is not an exhaustive checklist. Refer to vaccine-specific chapters in Part 4 for additional information.)

Screening questions for all vaccines	Yes	No
1. Is the vaccine indicated according to the recommended immunization schedules[1] and the vaccine recipient's immunization history?		
2. Has information regarding administration of the vaccine as well as the risks and benefits of receiving or not receiving the vaccine been provided?		
3. Has the vaccine recipient or appropriate guardian or substitute decision-maker been offered an opportunity to ask questions and consent to vaccination?		
4. Has the vaccine recipient ever had a serious reaction (e.g. anaphylactic reaction) after receiving a vaccine or is the recipient aware of any allergies to medications, a component of the vaccine, or latex?		
Additional screening questions if immunizing with live vaccines	**Yes[2]**	**No**
5. Does the vaccine recipient have any acute or chronic immunocompromising disease or have they taken any immunocompromising medications in the past three months? *If giving a live vaccine to infant consider:* *a. Any known or suspected family history of congenital immunodeficiency disorder or HIV infection, or history of failure to thrive and recurrent infections.* b. *If mother has taken any immunomocompromising drugs in the past three months.*		
6. If the vaccine recipient is a woman, is she pregnant or is there a chance that she may be pregnant?		
7. Has the vaccine recipient received any vaccinations in the past 4 weeks?		
8. Has the vaccine recipient received any transfusions of blood or blood products in the last year?		

[1] vaccines may also be recommended based on occupational or travel-related risks or for post-exposure prophylaxis. Refer to Immunization of Workers or Immunization of Travellers in Part 3.

[2] if yes, refer to vaccine specific chapters in Part 4 for further information

VACCINE ADMINISTRATION

Administer vaccines to the right client using the correct vaccine, correct dose, correct route of administration, correct injection site (if applicable) and correct time (schedule) to optimize vaccine effectiveness and to reduce the risk of local reactions or other adverse events. Table 2 provides an example of a checklist for vaccine administration. Refer to Storage and Handling of Immunizing Agents in Part 1 and vaccine specific chapters in Part 4 for additional information.

Table 2: Vaccine provider administration check list

Vaccine administration	Yes	No
1. Has the vaccine provider washed his or her hands or used an alcohol-based hand sanitizer?		
2. Has the correct vaccine been selected and expiry date been checked? .		
3. Has the vaccine been appropriately reconstituted or mixed if necessary?		
4. Is the appropriate needle length being used?		
5. Are the dose and method of administration correct?		

VACCINE PREPARATION

Vaccine inspection

Before vaccine administration, check the vaccine identification label to ensure that the correct vaccine selection of the correct vaccine and check the expiry date on the vaccine vial and vaccine diluent (if applicable) to ensure that they have not been expired. Do not use vaccines or diluents beyond their expiration date. Before use, inspect vaccine vials for any irregularities, such as particulate matter, damage or contamination. Vaccines should be mixed with a careful swirling motion until a uniform suspension is achieved prior to administration. Unless otherwise instructed by the manufacturer, do not shake the vaccine before use. Refer to Storage and Handling of Immunizing Agents in Part 1 for additional information about expiration dates and multi-dose vials.

Vaccine reconstitution

Reconstitute vaccines according to the manufacturers' guidelines using only the diluent provided by the manufacturer for that purpose and adhering to local policies and procedures. Inject the diluent down the side of the vaccine vial and not directly into the vaccine powder to avoid foaming or denaturing of the vaccine protein. Mix the reconstituted vaccine with a careful swirling motion until a uniform suspension is achieved prior to administration, unless otherwise instructed by the manufacturer. Once reconstituted, administer the vaccine within the time frame specified in the manufacturer's product information. Refer to Storage and Handling of Immunizing Agents in Part 1 for additional information about vaccine reconstitution.

Filling syringes

In immunization clinics in which only a single vaccine is being distributed, the contents of more than one multi-dose vial may be combined to prevent wastage if the vials have the same lot number**.** Vaccine providers should observe strict aseptic technique when using multi-dose vials. Injecting air into a multi-dose vial prior to withdrawing a vaccine dose is not necessary.

Pre-loading vaccine in syringes

Ideally, a vaccine should be withdrawn from the vial by the vaccine provider administering the vaccine. Pre-loading syringes with vaccine is strongly discouraged because of the uncertainty of vaccine stability in syringes, risk of contamination, increased potential for vaccine administration errors and vaccine wastage. Pre-loading of syringes may be considered in the hospital setting if vaccines are drawn up and labelled in the pharmacy or in an immunization clinic to facilitate timely and efficient administration of a single vaccine to a large number of people. If the practice of pre-loading of syringes is implemented, it should be limited to hospital or immunization clinics and should include:

- prior agreement on professional accountability if different people pre-load and administer the vaccine,
- data on stability of pre-loaded product for a specified time period, and

- maintenance of the cold chain.

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

Syringe and needle selection for parenteral vaccines

Use a separate, sterile needle and syringe for each injection. Do not mix different vaccines in the same syringe unless specified by the manufacturer. The use of safety-engineered needles and syringes is preferred and in many places mandated by law to reduce risk of injury. However, vaccines packaged by the manufacturer in pre-filled syringes should not be transferred to safety-engineered injection devices.

Syringe selection

Use a 1 mL or 3 mL syringe, depending on the volume of the vaccine dose.

Needle selection

Appropriate needle selection is important because the immunizing agent must reach the appropriate tissue site (dermis, subcutaneous tissue or muscle) to optimize immune response and to reduce the risk of injection site reactions.

When considering needle length, select a needle that is long enough to reach the tissue site but not so long as to hit underlying nerves, blood vessels, or bone. The use of longer needles for intramuscular injection of vaccine is associated with less injection site redness and swelling than occurs with shorter needles. When needles are too short to reach muscle, vaccine may be inadvertently injected into more superficial tissue (i.e., dermis and subcutaneous tissue), resulting in increased inflammation, induration or granuloma formation. Base needle selection on the: route of administration, vaccine recipient's age and size of muscle mass, and viscosity of the vaccine or passive immunizing agent. Table 3 provides guidelines for needle selection.

Table 3: needle selection guidelines

Route of administration	Age of vaccine recipient	Recommended needle gauge	Recommended needle length
Intradermal (ID)	All ages	26-27	1.0 cm
Subcutaneous (SC)	All ages	25	1.6 cm (⅝ inch)
Intramuscular (IM)[1]	Infants, toddlers and older children	22-25[2]	2.2 cm - 2.5 cm (⅞ inch – 1 inch)
	Adolescents and adults	22-25[2]	2.5 cm - 3.8 cm (1 inch - 1½ inch)

[1] For IM injections, the needle must be long enough to reach muscle but not involve underlying nerves, blood vessels, or bone; insert the needle as far as possible into the muscle

[2] A larger gauge needle (e.g., 22 gauge) may be required when administering viscous or larger volume products such as immune globulin.

ROUTE, SITE AND TECHNIQUE FOR VACCINE ADMINISTRATION

Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for information about the recommended route of administration for vaccines and passive immunizing agents authorized and available for use in Canada.

Parenteral vaccines

Vaccines are injected via the intradermal (ID), subcutaneous (SC), or intramuscular (IM) routes.

Intradermal (ID) injections

Intradermal vaccine administration technique is product-specific and should be applied according to the vaccine's product monograph. ID vaccines available in Canada include:

- Bacillus Calmette-Guérin (BCG) vaccine
- Trivalent inactivated influenza vaccine, Intanza®.
- Smallpox vaccine.
- Rabies vaccine for pre-exposure immunization protection only.

Subcutaneous (SC) injections

For infants younger than 12 months of age, the usual site for SC administration of vaccine is the subcutaneous tissue of the anterolateral thigh; if necessary, the upper triceps area of the arm may be used. SC injections for vaccine recipients 12 months of age and older are usually given into the subcutaneous tissue of the upper triceps area of the arm. SC injections should be administered at a 45^{o} angle.

Intramuscular (IM) injections

IM injections of vaccine are administered at a 90^{o} angle into the vastus lateralis muscle (anterolateral thigh) in infants less than 12 months of age and into the deltoid muscle of persons 12 months of age and older (unless the muscle mass is not adequate, in which case the anterolateral thigh can be used). For the injection of diphtheria, tetanus, acellular pertussis (DTaP) vaccine in children 12 to 35 months of age, the deltoid muscle or anterolateral thigh can be used. A large retrospective cohort study of children 12 to 35 months of age demonstrated a lower risk of medically- attended local reactions when DTaP vaccine was given into the thigh compared to vaccination into the arm.
Appropriate site selection is important to avoid inadvertent injection into a blood vessel or injury to a nerve. Vaccines containing adjuvants must be injected intramuscularly. If a vaccines containing an adjuvant is inadvertently injected subcutaneously or intradermally, increased inflammation, induration or granuloma formation may occur. Refer to Immunization of Persons with Chronic Diseases in Part 3 for additional information about IM administration of vaccines to people with bleeding disorders.

Active immunizing agents should not be administered into the buttock (gluteal muscle). Immunogenicity is lower to hepatitis B and rabies vaccines if given in the buttock, probably because of injection into adipose tissue where the vaccine is not well absorbed. The buttock is an acceptable site for administration of immune globulin when large volumes are administered, but appropriate site selection of the gluteal muscle is necessary to avoid injury to the sciatic nerve.

Multiple injections

All opportunities to immunize should be used and giving multiple vaccines at the same clinic visit is encouraged. Giving multiple injections at one visit helps to ensure that individuals are up to date with the vaccines required for their age and risk factors. Generally, infants and children have similar immune responses whether vaccines are given at the same time or at different visits. Although children are now receiving more vaccines, they are exposed to fewer antigenic proteins in today's vaccines than in the past because of changes in the vaccine products.

Practice considerations for multiple injections include the following:

- Label syringes to identify which vaccine each syringe contains.
- Record the site of administration of each vaccine so that if an injection site reaction occurs, the associated vaccine can be identified.
- Use separate limbs if two IM injections are required. If more than two injections in the same limb are required, administer the two injections into the same muscle separated by at least 2.5 cm (1 inch). In cases where there is insufficient deltoid muscle mass, the anterolateral thigh can be used in children to 35 months of age.
- Administer vaccines that are known to cause more stinging or pain last (e.g., Prevnar®13; M-M-R®II, human papillomavirus vaccines (HPV)).
- If a vaccine and an immune globulin preparation are administered simultaneously (e.g., tetanus toxoid-containing vaccine and tetanus immune globulin), use separate anatomic sites (different limbs) for each injection.

Techniques to decrease immunization injection pain

Vaccine injections can be a source of distress for individuals of any age as well as for the immunization provider. If not addressed, the pain and anxiety associated with immunization can be related to fears of future procedures, medical fears, and avoidance behaviours, including non-adherence with immunization schedules. It is estimated that up to 25% of adults have needle fears and 10% have needle phobias. The majority of people with needle fears develop them in childhood. Efforts aimed at minimizing pain in childhood have the potential to prevent the development of needle fears and to promote satisfaction and trust in health care providers because of more positive experiences for children and their families.

Research has shown that there are many effective pharmacologic, physical, and psychological interventions available for use during the immunization procedure. Combining strategies has been shown to improve pain relief. The most effective strategies for infants, in order of effectiveness, are breastfeeding or administration of a sucrose solution, topical anesthetics, and distraction. The most effective strategies for older children, in order of effectiveness, are topical anesthetics and distraction.
Refer to Table 4 for a listing of pain management strategies for children by age groups.

Table 4: Immunization pain management strategies for children, by age groups

Age of child	Pain management strategies[1]
2 to 12 months	• Breastfeeding • Administration of a sucrose solution • Topical anesthetics • Clinician led distraction (e.g., toys, bubbles, singing, re-directing infant's attention) • Seated upright in adult's lap using comforting positioning • Rapid injection of the vaccine without aspiration • Injecting the most painful vaccine last (e.g., Prevnar®13)
12 months to 2 years	• Breastfeeding • Topical anesthetics • Clinician led distraction (e.g., toys, bubbles, singing, books, kaleidoscopes, party blowers, re-directing child's attention) • Seated upright in adult's lap using comforting positioning • Rapid injection of the vaccine without aspiration • Injecting the most painful vaccine last (e.g., M-M-R®II) • Do not tell children, "it won't hurt"
3 to 6 years	• Topical anesthetics • Clinician led or parent led distraction (e.g., toys, books, counting, re-directing child's attention) • Child led distraction (e.g., hand held video games, music with personal headphones) • Slow deep breathing or blowing (e.g., pinwheels, bubbles) • Seated upright in adult's lap using comforting positioning • Rapid injection of the vaccine without aspiration • Injecting the most painful vaccine last (e.g., M-M-R®II) • If child is 4 years of age and older, rubbing or stroking at immunization site before injection • Do not tell children, "it won't hurt."
Age of child	**Pain management strategies[1]**
School age	• Topical anesthetics • Child led distraction (e.g., toys, stories, videos, music) • Clinician led or parent led distraction (e.g., non-procedural talk, re-directing child's attention) • Slow deep breathing • Comfortable seated position • Rapid injection of the vaccine without aspiration • Injecting the most painful vaccine last (e.g., HPV vaccine) • Rubbing or stroking immunization site before injection • Do not tell children, "it won't hurt"

[1] For further information on pain management strategies refer to: Taddio, A, Appleton M, Bortolussi R et al. *Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline*. Can Med Assoc J 2010;182(18):E843-55.

Breastfeeding

Encourage lactating mothers to breastfeed their infants before, during, and after the immunization. Research indicates that breastfeeding during immunization may reduce pain and distress through:

- presence of a comforting person
- diversion of attention (sucking and distraction)
- physical sensation of skin to skin contact with mother
- sweet taste of breast milk and other chemicals in the milk (e.g., tryptophan [a precursor of melatonin] which has been reported to increase the concentration of ß-endorphins, thereby producing analgesia and relaxation).

Administration of a sucrose solution

For infants up to and including 12 months of age who cannot be breastfed during immunizations, a sucrose solution may be administered to the infant one to two minutes before the immunization. By activating the sweet taste receptors, a sucrose solution stimulates the release of endogenous opioids and acts as a distraction.

The analgesic effect of a sucrose solution has been demonstrated to last for up to10 minutes following its administration. Due to the duration of its effect, it is expected to mitigate immunization injection pain when multiple injections are administered. The analgesic effect may be enhanced by having the infant suck on a pacifier following administration of the sucrose solution.

Inform parents that sucrose solutions should not be used at home as a comfort measure for their infant. A sucrose solution is specifically recommended for the management of painful medical interventions.

Application of topical local anesthetics

Topical local anesthetics act by inhibiting the generation and transmission of pain impulses across nerve endings located in the dermis. They decrease the pain as the needle penetrates the skin and reduce the underlying muscle spasm associated with this pain. Given that there is a cumulative effect when infants or children are exposed to sequential painful stimuli, prevention of the initial painful stimulus (needle puncture through the skin) decreases the overall pain experience.

Topical anesthetics are effective in reducing vaccine injection pain in individuals of all ages and are available without prescription. There is no evidence that the application of a topical local anesthetic poses a risk of decreased immune response to vaccines if the topical anesthetic is used as directed in the product leaflet and only for the ages recommended by the manufacturer. There have been reports of serious adverse events with excessive topical application of local anesthetics in adults and children. Observe children during and after use of topical anesthetics, as they may be at greater risk than adults for serious adverse events. For additional information refer to Health Canada's advisory Safety information regarding topical anesthetics and serious adverse events - For Health Professionals. (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/index-eng.php)

Oral analgesics

There is no demonstrated benefit of administering oral analgesics (such as acetaminophen or ibuprofen) to children to reduce pain at the time of injection.

Seated position

Studies have demonstrated that parental holding in a seated or semi-seated position (for infants) and sitting up (for all other ages) are associated with reduced pain during immunization when compared to a supine position. This may be because parental holding and sitting up are associated

with a greater sense of personal control and reduced anxiety which in turn reduces the perception of pain.

Rapid injection without aspiration

Perform injections using rapid injection without aspiration technique. Aspiration is not recommended as there are no data to document its necessity prior to IM or SC injection of vaccines. There are no large blood vessels at the recommended immunization sites. Not aspirating before injection has been demonstrated to reduce pain at the injection site because there is less contact time between the needle and tissue and less lateral movement of the needle.

Inject the most painful vaccine last

When administering multiple vaccine injections sequentially, the most painful vaccine should be injected last. Studies have indicated that when two vaccines were injected sequentially, injection of the least painful vaccine first not only reduced pain from the first injection but also reduced pain from the second injection. This finding is consistent with other pain research which has found a relationship between increased pain perception and repeated painful stimulation.

Rubbing or stroking the skin near the injection site

Rubbing the area near the injection site prior to and during immunization may decrease pain perception by stimulating large diameter (touch) neurons that compete with small diameter (pain) neurons activated during painful procedures, resulting in reduced “pain” input transmission to the brain. This pain management strategy has only been studied in children 4 years of age and older. Rubbing should be tailored according to the request and comfort level of the individual child. In adults, pressure applied to the injection site prior to injection has been demonstrated to reduce pain during injections. Rubbing the injection site after immunization is not recommended.

Distraction

Distraction during immunization can be used as a pain management strategy with all age groups. There are many theories about why distraction is effective (e.g., the parts of the brain that process painful stimuli are less active when the person is distracted; or when attention is directed to a distracting task, there are fewer resources available within the brain to pay attention to the pain).

Studies have demonstrated that distraction is most effective when it is interactive and when the individual is actively engaged in the distraction strategy. Parents can be engaged in selecting a distraction strategy for their child. Distraction led by a parent has been found to be less effective than distraction led by the immunization provider or the child. This may be because the parent finds it difficult to provide distraction when he or she is also concerned about the immunization.

Examples of distraction include the use of toys, stories, bubbles, singing, pinwheels, pop-up books, non-procedural talk, hand-held games, and directing the individual’s attention to something in the environment. Most children (3 years of age and older) are able to participate in distraction activities without adult assistance. For example, children in this age group can engage in slow deep breathing or blowing out during immunizations. Simple breathing exercises are effective at significantly reducing immunization pain and distress.

Do not tell children that “it won’t hurt”

Telling a child that the immunization won’t hurt has been found to be ineffective at reducing pain during immunization and may lead to a relationship of distrust between the child and health care provider. Honest statements such as “you may feel it a bit, but I think you can handle it” should be used, as well as words that are explanatory without evoking anxiety (e.g., use words such as pressure and squeezing, and avoid words such as shot, pain, and hurt).

Preventing anxiety and fainting

Techniques to decrease anxiety in adolescents and adults are important to minimize the risk of fainting. These techniques include ensuring comfortable room temperature and short waiting times, preparation of vaccines out of view of recipients, providing privacy during the procedure, and administering the vaccine while the person is seated. Pain reduction techniques such as applying topical local anesthetics and tactile stimulation will also help reduce anxiety. People who appear very anxious should be observed while seated until anxiety has resolved post-immunization.

Oral vaccines

In Canada, oral vaccines include rotavirus, oral typhoid capsules, and oral vaccine for cholera and travellers' diarrhea. Oral vaccines should be administered as directed in the product leaflet. In general, oral vaccines should be given prior to injectable vaccines.

All doses of rotavirus vaccine should be given in a clinic or office setting under the direction of a health care provider. If an infant spits or regurgitates the vaccine, a replacement dose should not be administered.

Intranasal vaccine

Live attenuated influenza vaccine (LAIV) is the only vaccine in Canada administered by the intranasal route. LAIV should be administered by a health care provider following the instructions in the product leaflet. If the vaccine recipient sneezes immediately after administration, there is no need to repeat the dose.

POST-VACCINATION COUNSELLING AND OBSERVATION

Vaccine recipients should be counselled about the reporting and management of common adverse events following immunization. Individuals who are particularly anxious about receiving the vaccine should be identified and observed. Syncope can occur after immunization and is most common among adolescents and young adults. Individuals with pre-syncopal symptoms, such as pallor or sweating, should sit or lie down until symptoms resolve. Care should be taken to ensure they do not faint if they need to stand up and that they are supported and injury prevented if they do faint.

Vaccinees should remain in the clinic, or be advised to stay with someone else if outside of the clinic area, for at least 15 minutes post-immunization, as most syncopal events occur within 15 minutes of vaccination (63% within 5 minutes of vaccination and 89% within 15 minutes). They should be advised to avoid stairs so that injury does not occur if they faint.

Vaccine recipients should be kept under observation for at least 15 minutes when there is a specific concern about possible vaccine allergy; 30 minutes is a safer interval since the majority of cases of anaphylaxis will occur within 30 minutes following vaccine administration. In low-risk situations, observation can include having vaccinees remain within a short distance of the vaccinator (e.g., within a school where an immunization clinic is being held) in the company of another person and return immediately for assessment if they feel unwell. Every vaccine provider should be familiar with the signs and symptoms of anaphylaxis and be prepared to act quickly. Refer to Early Vaccine Reactions Including Anaphylaxis in Part 2. Refer to Immunization Records in Part 1 for information which is to be recorded post-vaccine administration.

Oral analgesics and antipyretics

Oral analgesics and antipyretics (such as acetaminophen or ibuprofen) can be used for treatment of minor adverse reactions such as fever or injection site discomfort that might occur following vaccination. There is no evidence that antipyretics prevent febrile seizures.

INFECTION PREVENTION AND CONTROL

Immunization providers should incorporate routine infection control practices into all immunization procedures as follows:

- Prior to withdrawal of vaccine into the syringe, uncap the vaccine vial, wipe the stopper with a suitable disinfectant (e.g., isopropyl alcohol) and allow the stopper to dry.
- Before injection, cleanse the skin with a suitable antiseptic and allow to dry. Skin cleaning prior to vaccination is under review by NACI.
- Use a separate, sterile needle and syringe for each injection.
- Perform hand hygiene before vaccine preparation, between vaccine recipients, and whenever the hands are soiled. Alcohol-based hand sanitizers are an alternative to hand washing with soap and water when hands are not visibly soiled. Perform hand hygiene after removing gloves.
- Glove use during immunization is not routinely recommended unless the skin on the vaccine provider's hands is not intact or when administering BCG or smallpox vaccine. If gloves are worn, they should be changed between clients.
- Develop and implement policies and procedures regarding accidental exposure to blood or body fluids, including needle stick injuries, and educate vaccine providers about these policies and procedures. Refer to Immunization of workers in Part 3 for more information about recommended immunization schedules for vaccine providers.

In addition to the above, the following practices should be observed:

- Do not change the needle between withdrawing vaccine from the vial and administering the vaccine, unless the needle is contaminated or damaged.
- Do not recap needles after use.
- Immediately and carefully dispose of used syringes and needles in a container designed for this purpose; used syringes and needles should never be placed on the work surface.
- Dispose empty or expired vaccine vials according to local waste management legislation or guidelines.

Additional information on infection prevention and control guidelines is available in Infection Prevention and Control Best Practices for Long Term Care, Home and Community Care including Health Care Offices and Ambulatory Clinics. (http://www.phac-aspc.gc.ca/amr-ram/ipcbp-pepci/index-eng.php)

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PART 1

STORAGE AND HANDLING OF IMMUNIZING AGENTS

GENERAL CONSIDERATIONS

Immunizing agents are biologic materials that are subject to gradual loss of potency from deterioration and denaturation. Loss of potency can be accelerated under certain conditions of transport, storage and handling and may result in failure to stimulate an adequate immunologic response, leading to lower levels of protection against disease. Conditions that result in loss of potency vary among products.

Maintaining the potency of vaccines is important for several reasons:

- There is a need to ensure that an effective product is being used. Vaccine failures caused by administration of compromised vaccine may result in the occurrence and possible transmission of a vaccine preventable disease.
- Vaccine losses are expensive and may exacerbate existing supply problems. Loss of vaccines may result in the cancellation of immunization clinics, resulting in lost opportunities to immunize.
- The recommendation for revaccination of people who have received a potentially ineffective vaccine may cause a loss of public confidence in vaccines and the health care system, as well as inconvenience for the vaccine recipient and the provider.

A detailed discussion of storage and handling recommendations for immunizing agents is beyond the scope of the *Canadian Immunization Guide*. Detailed information for vaccine providers regarding vaccine storage and handling is available in the Public Health Agency of Canada's (PHAC) National Vaccine Storage and Handling Guidelines for Immunization Providers (2007). Recommendations for vaccine storage and handling procedures may vary across jurisdictions. (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

HANDLING OF VACCINES

Vaccines are biological products which may become less effective, or even be destroyed, if exposed to light or temperatures outside the recommended range.

VACCINE "COLD CHAIN"

"Cold chain" refers to the process used to maintain optimal conditions, particularly temperature, during the transport, storage and handling of vaccines, beginning at the manufacturer and ending with administration of the vaccine to the vaccine recipient. Monitoring of vaccines' cold chain is required to ensure that these products have been stored and transported at recommended temperatures. Exposure of a vaccine to

environmental conditions outside those recommended for the product is called a cold chain break, breach or failure, or temperature excursion. Refer to *the list of steps in handling vaccines exposed to inappropriate vaccine storage conditions* for product specific storage recommendations.

There are several negative consequences of breaks in the cold chain. Vaccines exposed to temperatures above the recommended temperature range may experience some loss of potency with each episode of exposure. Repetitive exposure to increased temperature can result in protein denaturation and a cumulative loss of potency that is not reversible. Some vaccines, such as those containing an aluminum adjuvant, experience a permanent loss of potency due to adjuvant clustering when subjected to freezing and thawing. Freezing of a vaccine or diluent may cause cracks in the container which may lead to contamination of the contents.

It can be difficult to assess the potency of a mishandled vaccine because there is little information about vaccine degradation; multipoint stability studies on vaccines are challenging to perform and information from manufacturers is not always available. Data are available to indicate that some products remain stable at temperatures outside of the recommended range for specified periods of time, but mechanisms rarely exist for monitoring the effect of cumulative exposures. Products that have been exposed to adverse environmental conditions should be managed in accordance with specific instructions from public health officials or the vaccine supplier.

Ongoing cold chain monitoring is an integral part of immunization practices. PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007) provides detailed information on establishing standards for cold chain monitoring (i.e., temperature monitors in packages or on vaccine vials, freeze indicators) and evaluating awareness, equipment, practices and potential administrative errors during vaccine transportation and storage. (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

SINGLE-DOSE VIALS

Single-dose vaccines should be reconstituted or drawn up immediately before administration. They should be discarded if the vaccine has been drawn up or reconstituted and subsequently not used within the time frame specified by the manufacturer or jurisdictional guidelines. If the protective cap on a single-dose vial is removed, or if a manufacturer's pre-filled syringe is opened (e.g., syringe cap removed), the vaccine should be used on that clinic day or discarded.

MULTI-DOSE VIALS

Once punctured, multi-dose vials should be marked with the date of initial entry into the vial and, if reconstituted, marked with the date and time of reconstitution. Some vaccines provided in multi-dose vials must be used within a specified time after initial puncturing of the vial or after reconstitution. This date will be different than the expiration date printed on the vial by the manufacturer. The new "use by" date should be written on the vial once it has been punctured.

Multi-dose vials must be maintained under appropriate storage conditions (+2°C to +8°C in a secure site to prevent tampering) and removed from the refrigerator (or cooler in community immunization clinics) only to withdraw the required dose from the vial. Vaccine providers should observe strict aseptic technique when using multi-dose vials.

In immunization clinic sessions in which only a single vaccine is being administered, the contents of more than one multi-dose vial may be combined to prevent wastage if the vials have the same lot number**.**

Manufacturer's recommendations or jurisdictional guidelines for use of multi-dose vials should be followed. Available information from the product monographs has been summarized in Annex 1.

RECONSTITUTION OF LYOPHILIZED VACCINES

For optimal potency, lyophilized (freeze-dried) vaccines (refer to *Appendix 1*) should be reconstituted immediately before use with the diluent provided by the manufacturer for that purpose. Refer to the

product leaflet, product monograph, or jurisdictional guidelines for vaccine-specific recommendations regarding storage requirements for lyophilized vaccines and diluents, and the time frame for use following reconstitution. If not otherwise instructed by the manufacturer or jurisdictional guidelines, diluents that do not contain vaccine components and that are packaged separately from the vaccine may be stored at room temperature to conserve refrigerator space. The vaccine for which the diluent should be used must be marked clearly to avoid using the wrong diluent.

Reconstituted vaccines should be discarded if not used within the time frame specified for use by the manufacturer or jurisdictional guidelines.

PRE-LOADING VACCINES IN SYRINGES

Many vaccines are now provided by manufacturers in pre-loaded syringes. If a vaccine is not provided in a pre-loaded syringe, it should ideally be drawn into the syringe immediately before use. If pre-loading vaccines in syringes is undertaken in an office setting, vaccine providers should prepare only the number of vaccine doses that are expected to be administered during the consultation. If pre-loading vaccines in syringes is undertaken in an immunization clinic setting, vaccine providers should prepare only the number of doses required to keep the clinic running efficiently and doses should be used as soon as possible. If syringes are pre-loaded by a hospital pharmacy, labels should indicate the time by which the vaccine should be used. Vaccine administrators need to consider: the length of time the vaccine will be stored in the pre-loaded syringe; the type of vaccine (i.e., live vs. inactivated vaccine); the potential of exposure to light; the potential for interaction between the vaccine and the material used in the syringe; and the manufacturers' specifications for vaccine storage. Refer to Vaccine Administration Practices in Part 1 for additional information.

VACCINE-SPECIFIC STORAGE AND HANDLING INFORMATION

Appendix 1 provides vaccine-specific storage and handling information. For additional storage and handling information consult the product leaflet or information contained within the product monograph available through Health Canada's Drug Product Database. (http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp)

SOTRAGE AND VACCINES

PACKAGING

Store vaccines in their original packaging; the packaging provides protection from light and physical damage.

REFRIGERATED VACCINES

The storage temperature for refrigerated vaccines is between +2°C and +8°C.

FROZEN VACCINES

Store frozen vaccines at a temperature between -15°C to -50°C or as specified by the product monograph. It should be noted that the use of dry ice may subject vaccines to temperatures colder than -50°C. In general vaccines that have thawed should not be refrozen.

EXPOSURE TO FREEZING

Vaccines that should be stored at +2°C to +8°C should not be used if they have been frozen. Diluent that has been frozen should not be used. Before use, vaccines should be inspected and not used if the usual appearance is altered or a temperature recording device shows that the vaccine was exposed to temperatures below 0ºC. If a vaccine has been exposed to freezing, refer to *The list of steps in handling vaccines exposed to inappropriate vaccine storage conditions* and *Appendix 1* and consult public health officials for advice. Additional information regarding stability of vaccines is available from the World Health Organization. (http://www.who.int/biologicals/vaccines/stability_of_vaccines_ref_mats/en/index.html)

EXPOSURE TO HEAT

Refer to the section on cold chain break management below.

EXPOSURE TO LIGHT

Vaccines should be stored in their original packaging and protected from light, as exposure to light may cause loss of potency in some vaccines. Some vaccines (such as measles-mumps-rubella (MMR), varicella, and Bacille Calmette-Guérin [BCG] vaccines) should be protected from light exposure at all times. Exposure to light should be limited when pre-loading syringes.

EXPIRATION DATES

All vaccines and diluents have expiration dates beyond which the product must not be used. Expiration dates are labelled on product containers (e.g., vials, syringes) and package boxes. When the expiration date is marked with only a month and year, the vaccine or diluent may be used up to and including the last day of the month indicated on the vial. If vaccine has been inappropriately exposed to excessive heat, cold, or light, its potency may be reduced before the expiration date is reached. If an expired vaccine has been inadvertently administered, it should not be counted as a valid dose and should be repeated, respecting the appropriate interval between live parenteral vaccines.

VACCINE DISPOSAL

Vaccines that cannot be used because of expiry or breach of the cold chain should either be returned to the supplier for disposal or appropriately disposed of according to jurisdictional standards. Live vaccines and their containers must be disposed of according to standards for biologic products.

REFRIGERATORS AND FREEZERS FOR VACCINE STORAGE

GENERAL REQUIREMENTS

Any refrigerator or freezer used for vaccine storage must:

- maintain required vaccine storage temperatures; under-counter bar or dormitory refrigerators should not be used because they do not reliably maintain temperature.
- hold sufficient inventory, including vaccine for the influenza season, and should not be an under-counter bar or dormitory type refrigerator
- have a minimum/maximum thermometer or calibrated temperature data logger inside each storage compartment
- be dedicated to the storage of vaccines only
- be placed in a secure location away from unauthorized and public access

Central vaccine depots should be equipped with auxiliary generators for refrigerators in case of power failures.

Refer to Section 3 of PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007) for detailed information on vaccine storage equipment, including guidelines for purchase of vaccine refrigerators. (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

TEMPERATURE MONITORING

The temperature in frost-free refrigerators may vary widely; temperature should be monitored to ensure that temperature cycling is within the acceptable range of +2ºC to +8ºC. Maximum/minimum thermometers are commercially available and are useful for refrigerators used to store vaccines in offices. Constant chart-recording thermometers with alarms are appropriate for larger vaccine storage depots.

Current, maximum and minimum refrigerator temperatures should be recorded twice daily and local public health officials or the vaccine supplier should be contacted if vaccines are exposed to temperatures outside the recommended range. Refer to *Cold chain break management* for additional information.

DOMESTIC REFRIGERATORS

Domestic refrigerators are not designed to meet the requirements for vaccine storage; therefore, precautions and modifications are needed if vaccines are stored in such refrigerators. Refrigerators older than 10 years are more likely to malfunction and to have breaks in the seal around the door, leading to temperature instability. The use of such refrigerators for vaccine storage is a leading cause of cold chain breaks.

PURPOSE-BUILT VACCINE REFRIGERATORS

A purpose-built vaccine refrigerator (pharmacy, lab-style or laboratory grade refrigerator) is the standard for storing large inventories of vaccines. Under-counter purpose-built vaccine refrigerators are acceptable for vaccine storage.

RECOMMENDED OFFICE PROCEDURES

Refer to PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007) for detailed information on vaccine inventory management and storage practices. The following procedures are recommended to ensure that storage of vaccines in vaccine provider offices is optimized. (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

INVENTORY MANAGEMENT

An adequate supply of vaccines should be maintained to meet the monthly needs of the served population. Do not over order vaccines since this increases the risk of wastage (e.g. cold chain break as a result of power failure, or expiry of unused vaccines). To ensure good management of inventory:

- Designate and train one staff member to be responsible for managing vaccines and another staff member as a backup.
- Limit access to the vaccine supply to authorized personnel only. This will help to protect the vaccine supply by avoiding inappropriate removal of vaccine or inappropriate handling of vaccine and vaccine storage units by untrained personnel. All staff handling vaccines should be familiar with policies and procedures for vaccine storage and handling.
- Place vaccines into the designated refrigerator immediately upon delivery to the office.
- Rotate stock so that vaccines with the earliest expiration date are at the front of the shelf.
- Check inventory and expiry dates monthly.
- Store vaccine products that have similar packaging in different locations that are clearly marked in order to avoid confusion and administration errors.
- Place expired vaccine into a marked box and remove from the refrigerator for appropriate disposal.
- Establish at least one alternate storage facility where vaccine can be appropriately stored and monitored in case of failure of the designated refrigerator.

REFIGERATORS

- Post storage and handling guidelines on the refrigerator.
- Place full, plastic water bottles in the lower compartment and door shelves of the refrigerator and ice packs in the freezer compartment to help stabilize temperatures, especially in the event of a power failure.
- Store vaccines in the middle of the refrigerator to avoid the coldest and warmest parts of the refrigerator; do not store vaccines on the door shelves or in the vegetable and fruit bins i.e. crispers of domestic refrigerators.
- Ideally, store frozen vaccines in a separate designated freezer unit. However, for domestic refrigerators having a separate freezer compartment, frozen vaccine may be stored at -15° C or

colder in the middle of the freezer compartment away from the walls and coils. Do not store vaccines in the freezer door.

- Place a maximum/minimum thermometer on the middle shelf of the fridge and another in the freezer compartment.
- Read, record and re-set the thermometer inside each compartment of the vaccine storage unit at least twice during each work day – once at the beginning of the day and once at the end of the day just before the door is closed for the last time.
- Check the thermometer function annually (refer to PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007) for instructions). (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)
- Secure the electrical cord from the fridge to the wall outlet to prevent the plug from being removed from the electrical socket. Place a warning near the outlet stating that the plug must not be disconnected.
- Ensure that the refrigerator door does not inadvertently open by installing a fail-safe closing mechanism (e.g., hook and ladder fastener). Keyed door locks to the room storing the refrigerator contribute to vaccine inventory security.
- Do not store food or biologic specimens in the same refrigerator as vaccines.
- If refrigerator malfunction is suspected on the basis of temperature readings, obtain servicing immediately, move the vaccine to an alternative refrigerator and refer to the section on cold chain break management below.
- In the event of a power failure, move the vaccine to an alternative refrigerator and refer to the section on cold chain break management below.
- Defrost non-frost-free refrigerators regularly; defrost when frost has accumulated to a thickness of more than 1 cm; move vaccines to a functioning refrigerator with the proper temperature during the defrosting process.
- Avoid unnecessarily opening the refrigerator door.
- Remove the vaccine from the refrigerator only immediately prior to administration.

REFIGERATORS

- Use insulated storage containers with ice packs for transport of vaccines out of the office (e.g., to vaccinate people in their homes or in off-site clinics); to avoid freezing, do not place vaccine packages in direct contact with ice packs.
- Maintain vaccine between +2°C and +8°C during off-site clinics; store in an insulated container with ice packs. Keep the container closed as much as possible. Keep a thermometer in the container with the vaccines, and check and record temperatures periodically to ensure that the cold chain is maintained.
- When transporting vaccines, keep a log of pre- and post-transport vaccine temperatures and the vaccine lots transported.

COLD CHAIN BREAK MANAGEMENT

If vaccines are exposed to temperatures outside the recommended range (refer to Appendix 1) or other inappropriate storage conditions, immediate action should be taken in order to avoid product loss (refer to The list of steps in handling vaccines exposed to inappropriate vaccine storage conditions). It should not be assumed that vaccine inappropriately exposed to light or to temperatures outside the recommended range cannot be salvaged.

List of Steps in handling vaccines exposed to inappropriate vaccine storage conditions.

1. Separate the affected vaccine from other vaccine supplies and label it as "DO NOT USE" to ensure that the vaccine is not administered. Store the affected vaccine under appropriate cold chain conditions until its integrity is determined.
2. Record the following information:
   a. Vaccine name, lot number, expiry date
   b. Date and time of incident

   c. The issue (e.g., exposure to inappropriate temperature or exposure to light)
   d. Length of time the vaccine may have been exposed to inappropriate conditions
   e. The room temperature where the vaccine storage unit is located
   f. Current temperature inside the vaccine storage unit (and freezer)
   g. Minimum and maximum temperature readings inside the vaccine storage unit (and freezer)
   h. Presence of water bottles in the refrigerator
   i. Presence of frozen packs in the freezer
3. Contact local public health officials or the vaccine supplier to seek advice regarding use of the vaccine. Provide the information outlined in step 2.
4. Follow directions provided by local public health officials or the vaccine supplier regarding use or disposal of affected vaccines.

Adapted from PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007). (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

In general, live attenuated vaccines, even in their lyophilised form, are more sensitive to heat exposure than inactivated vaccines. High ambient temperatures (up to +37°C) may not cause an immediate loss of potency but can shorten the shelf life of a vaccine. Evidence on the thermostability of vaccines suggests that an increase in temperature to above +8°C for a short period of time is unlikely to affect the potency of most vaccines significantly, particularly if the vaccines are used relatively quickly.

When a cold chain break is identified after an affected vaccine has been administered, consult local public health officials or the vaccine supplier for advice. The type of vaccine, as well as the duration and temperature of the exposure, need to be taken into account when assessing the situation. Serological testing or revaccination may be suggested.

Refer to Section 6 of PHAC's National Vaccine Storage and Handling Guidelines for Immunization Providers (2007) for detailed information on handling vaccines that have been exposed to inappropriate storage conditions. (http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/)

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Appendix 1: Vaccine storage recommendations

Cold chain should always be maintained

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations**' (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
Act-HIB®	L	V		*	*	Use immediately			y	Use immediately after reconstitution	Diluent: sterile saline in a vial
ADACEL®	S	V		*					Y	NI	Stable at above +8° and up to +25° for maximum of 72 hr, before opening[4]
ADACEL® - POLIO	S	V *or* S		*					Y	NI	Stable at above +8° and up to +25°for maximum of 72 hr, before opening[4]
AGRIFLU®	S	S		*				Y	Y	NI	Can be used after 2 hr exposure at +8° to +25° before opening[4]
AVAXIM®	S	S		*					Y	NI	
BCG vaccine (live)	L		N	*	*	*	*	Y	Y	Discard if not used within 8 hr after first puncture	• Diluent: sterile phosphate-buffered saline containing 0.025% polysorbate 80 in a vial • Store in the dark except when doses are being withdrawn from vial
BOOSTRIX®	S	S		*				Y	Y	NI	Stable at 21° for 8 hr, before opening[4]

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
BOOSTRIX® - POLIO	S	V *or* S		*				Y	Y	NI	
CERVARIX®	S	V *or* S		*				Y	Y	NI	• Stable at +8° to +25° for maximum of 3 days, before opening[4] • Stable at between +25° to +37° for up to 1 day, before opening[4] • Discard is exposed to +37° or higher
DUKORAL®	S	V		*	Room temp (up to 25°)	Room temp			Y	2 hr after opening	• Store buffer sachet at room temperature • Vaccine can be stored at room temperature (up to +25°) for up to 2 weeks on one occasion only, before opening
ENGERIX®-B (multi-dose)	S		Y	*			*	Y	Y	24 hr after first puncture	
ENGERIX®-B (single-dose)	S	V		*				Y	Y	Use immediately after withdrawal	
FLUAD®	S	S		*				Y	Y	NI	Can be used after 2 hr exposure at temperatures between +8° to +25°, before opening[4]
FLUMIST® (live)	Intranasal spray	Nasal spraye		*					Y	NI	

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative								
		r									
FLUVIRAL® (multi-dose)	S		Y	*			*		Y	28 days after first puncture	
FLUZONE® (multi-dose)	S		Y	*			*	Y	Y	28 days after first puncture	
FLUZONE® (single-dose)	S	V *or* S		*				Y	Y	NI	
FSME – IMMUN™	S	S		*					Y	NI	
GARDASIL®	S	V *or* S		*				Y	Y	NI	• Can be used if total cumulative time out of refrigeration (between +8° to +25°) does not exceed 72 hr, before opening[4] • Can be used if total cumulative time between +0° to +2° does not exceed 72 hr, before opening[4]
HAVRIX®	S	V *or* S		*				Y	Y	NI	
HIBERIX®	L	V		*	• * *or* ambient temps (up to 25°) • Do not freeze	Use immediately		Y	Y	Use immediately after reconstitution	• Diluent: sterile saline in vial or pre-filled syringe

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
IMOVAX® Polio	S	S		*					Y	NI	
IMOVAX® Rabies	L	V		*	*	Use immediately			Y	Use immediately after reconstitution	Diluent: sterile water in syringe
INFANRIX hexa®	L & S	V & S		*	*	• Use promptly • Stable for 8 hr at 21°			Y	• Use promptly • Stable for 8 hr at 21°	• PEDIARIX™ suspension in pre-filled syringe • Lyophilized Haemophilus influenza type b vaccine in vial
INFLUVAC®	S	S		*				Y	Y	NI	
INTANZA	S	S		*					Y	NI	Microinjection system
IXIARO®	S	S		*				Y	Y	NI	
Menactra®	LS	V		*					Y	NI	
Meningitec®	S	S		*					Y	NI	
Menjugate®	L	V		*	*	Use immediately		Y	Y	Use immediately after reconstitution	• Diluent: aluminum hydroxide in vial or syringe • ¶ Alternatively, vaccine can be stored for up to 6 months at +8° to +25°, if unopened
MENOMUNE® (multi-dose)	L		Y	*	*	*	*		Y	35 days after first puncture	Diluent: sterile saline with lactose and thimerosal in vial

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
MENOMUNE® (single-dose)	L	V		*	*	*			Y	24 hr after reconstitution	Diluent: sterile saline with lactose in vial
Menveo™	L & LS	V		*	*	• Stable for up to 2 hr at or below 25°		Y	Y	• Stable for up to 2 hr at or below 25° after reconstitution	• Lyophilized Men A conjugate in 1 vial • Liquid MenCWY conjugate in 1 vial
M-M-R® II Live	L	V		* or frozen at temperature above –50°	• *or room temp • Do not freeze	*		Y	Y	• Maximum 8 hr at +2° to +8° after reconstitution	• Diluent: sterile water in vial • Maintain vaccine at 10° or colder during shipment. • Protect vaccine from light at all times • Prior to reconstitution, can be used if total cumulative time out of refrigeration, at +8°C to +25°C does not exceed 6 hours. These are not, however, recommendations for storage
NeisVac-C®	S	S		*					Y	NI	Alternatively, can be stored for a single period not exceeding 9 months at room temperature (up to +25°), if unopened

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
PEDIACEL®	S	V		*					Y	NI	• Discard if exposed to 0° or lower • Stable at +8° to +25° for a maximum of 72 hr, if unopened4
PNEUMO 23®	LS	S		*					Y	NI	
PNEUMOVAX ® 23 (multi-dose)	LS		Y	*			*			48 hr after first puncture	
PNEUMOVAX ® 23 (single-dose)	LS	V		*						NI	
Prevnar® 13	S	S		*					Y	NI	Prevnar 13 has been shown to be stable at temperatures of up to 25°C for 4 days. Cumulative multiple temperature excursions between 8°C and 25°C are permitted, as long as the total time does not exceed 4 days (96 hours). These data are not recommendations for shipping or storage, but may guide decisions for use in case of temporary temperature excursions 4

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
PRIORIX® (live)	L	V		*	Room temp	*		Y		• Use as soon as possible • Maximum 8 hr at +2° to +8° after reconstitution	Diluent: sterile water in ampoule
PRIORIX-TETRA® (live)	L	V		*	*	*		Y	Y	• Use as soon as possible • Maximum 8 hr at +2° to +8° after reconstitution	Diluent: sterile water in pre-filled syringe or ampoule
QUADRACEL®	S	V		*					Y	NI	• Discard if exposed to 0°C or lower • Stable at above +8°C and up to +25°C for a maximum of 72 hr, if unopened4
RabAvert®	L	V		*	*	Use immediately		Y		Use immediately after reconstitution	• Diluent: sterile water in vial

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
RECOMBIVAX HB® (single-dose)	S	V		*					Y	NI	• Can be used if total cumulative time out of refrigeration (between +8° to +25°) before opening does not exceed 72 hr4 • Can be used if total cumulative time between +0° to +2° before opening does not exceed 72 hr4
ROTARIX™ (live)	LS	Oral applicator		*				Y	Y	NI	
RotaTeq® (live)	LS	Oral applicator		*				Y	Y	• Administer as soon as possible • Stable for up to 4 hr at +25° after opening	
Smallpox Vaccine (live)	L		N	° Frozen at -15°C to -25°C	Do not freeze+15°C to+30°C	* Do not freeze	* Do not freeze			Preferably use at once Stable for 6-8 hr at 20-25°C and 30 days at +2° to +8° C after reconstitutions	Supplied with bifurcated needles for percutaneous scarification Diluent: glycerol in McIlvaine buffer with 0.2% v/v phenol

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**							NI = no information	
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**		
SYNFLORIX® (multi-dose)	S		N	*			*	Y	Y	• Use immediately • Discard if not used within 6 hr after first puncture	Can be administered when vaccine has been at +8°C to +25°C for up to 72 hours before opening. These data are not recommendations for storage.
SYNFLORIX® (single-dose)	S	V or S		*				Y	Y	NI	
Td ADSORBED	S	V		*					Y	NI	
Td POLIO ADSORBED	S	V		*					Y	NI	
TWINRIX®	S	V or S		*				Y	Y	NI	
TYPHERIX®	LS	S		*				Y	Y	NI	
TYPHIM Vi® (multi-dose)	LS		Y	*			* Do not freeze		Y	6h after first puncture	
TYPHIM Vi® (single-dose)	LS	S		*					Y	NI	

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
VAQTA®	S	V		*					Y	NI	• Can be used if total cumulative time out of refrigeration (between +8° to +25°) before opening does not exceed 72 hr4 • Can be used if total cumulative time between +0° to +2° before opening does not exceed 72 hr4
VARILRIX® (live)	L	V		*	* or +8° to +25°	*				Up to 8 hr at +2° to +8°C or Up to 90 min at +25°C after reconstitution	• Lyophilized vaccine not affected by freezing • Diluent: sterile water in pre-filled syringe or ampoule
VARIVAX® III (live)	L	V		*or Frozen at above -50°	• * or +8° to +25° • Do not freeze	Do not freeze		Y		Up to 90 min at +20° to +25°C after reconstitution	• Prior to reconstitution, can be used if total cumulative time out of refrigeration, at +8° to +25°, does not exceed 6hr4
VAXIGRIP® (multi-dose)	S		Y	*			*	Y	Y	7 days after first puncture	
VAXIGRIP® (single-dose)	S	Ampoule or S		*				Y	Y	NI	

Vaccine (brand name)	**Vaccine form**	**Vaccine presentation**		**Storage temperature**[1] (°C) (* = +2° to +8°C)		**Handling recommendations** (°C) (* = +2° to +8°C)		**Other (y=yes)**		**Time frame for use**	**Additional recommendations and information**
	L = Lyophilized powder LS = Liquid or solution S = Suspension	**Single-dose**	**Multi-dose vial**								
		V = vial S = pre-filled syringe	Y = with preservative N = no preservative	**Vaccine**	**Diluent** NI = no information	**Reconstituted vaccine**[2]	**Multi-dose vial after entry**[3]	**Protect from light**	**Do not freeze**	NI = no information	
ViVAXIM®	S & LS	S		*		Use immediately after mixing			Y	Use immediately after mixing	• Syringe contains 2 components in separate chambers: hepatitis A vaccine suspension and typhoid vaccine solution • Mix contents of double chamber syringe just before administration
Vivotif® (live)	L	Oral capsule		*				Y	Y	NI	• May be out of refrigeration during a reasonable transit time from clinic to home • Can be used if out of refrigeration at 25° for up to 12 hr on one occasion only • Protect from moisture or high humidity
YF-VAX® (live, multi-dose)	L		N	*	* Do not freeze	*	*		Y	60 min after reconstitution	Diluent: sterile saline in vial
YF-VAX® (live, single-dose)	L	V		*	* Do not freeze	*			Y	60 min after reconstitution	Diluent: sterile saline in vial
ZOSTAVAX® (live)	L	V		Frozen at -15° to -50°	• * or +20° to +25° • Do not freeze	• 30 min at room temp • Do not freeze		Y		30 min after reconstitution	Diluent: sterile water in vial

Table developed from information contained in manufacturer's product monographs accessed April 2013 at Health Canada's *Drug Product Database*. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Product monographs are continually updated; it is a best practice to consult the current product monographs available at Health Canada's *Drug Product Database*. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Additional information regarding stability of vaccines is available from the *World Health Organization*. (http://www.who.int/biologicals/vaccines/stability_of_vaccines_ref_mats/en/index.html)

[1] In general, do not use vaccines that should be stored at +2°C to +8°C if they have been frozen. Do not use diluent which has been frozen.
[2] Reconstitute or withdraw single-dose vaccines immediately before administration. Discard single-dose vaccines if the vaccine has been withdrawn or reconstituted and subsequently not used within the time frame specified by the manufacturer or jurisdictional guidelines.
[3] Maintain multi-dose vials under appropriate storage conditions and remove from the refrigerator only to withdraw the required dose. Observe strict aseptic technique when using multi-dose vials.
[4] In cases of temporary temperature excursions only; not a storage or shipping recommendation

= not applicable
hr = hours

PART 1

TIMING OF VACCINE ADMINISTRATION

GENERAL CONSIDERATION

To provide optimal protection, recommended immunization schedules should be followed as closely as possible. However, it is not always possible to keep to the immunization schedule. People may not come for their scheduled appointment, or people may come just before a vaccine is needed or may not be available when a vaccination is due. This chapter identifies the considerations that need to be taken into account in situations in which a vaccine provider may want to give a vaccine either sooner or later than the recommended interval, or before the recommended age of vaccination.

DELAYED IMMUNIZATION SCHEDULES

One of the most common breaches of the immunization schedule occurs when people miss an appointment, resulting in a longer than recommended interval between doses of a vaccine. Delays generally do not result in a reduction in final antibody concentrations for most multi-dose products. However, maximum protection may not be attained until the complete vaccine series has been administered.

In general, interruption of a vaccine series does not require restarting the series, regardless of the time between doses. Exceptions include the vaccine for oral cholera and travellers' diarrhea. The vaccine dose should be repeated if more than 6 weeks elapses between doses of the primary series or if more than 5 years have passed since the primary series or last booster dose.

The vaccination schedule for rabies post-exposure prophylaxis should be adhered to as closely as possible and it is essential that all recommended doses of vaccine be administered. If a dose of vaccine is delayed, it should be given as soon as possible and the schedule resumed. If the vaccination schedule has been altered creating doubt about an appropriate immune response, post-vaccination serology should be obtained 7 to 14 days after completing the rabies vaccination series.

Table 1 provides recommended and minimum dose intervals for routine childhood vaccines.
Refer to Immunization of Immunocompromised Persons in Part 3 for dosing interval recommendations for immunocompromised persons.

ACCELERATED IMMUNIZATION SCHEDULES

When people get behind in a multi-dose series, consideration is generally given on how quickly the subsequent doses can be given as "catch-up". When considering this issue, it is important to know the minimum interval between doses, which may be less than the recommended interval. For example, the first two doses of the childhood immunization series of diphtheria, tetanus, acellular pertussis and inactivated polio has a recommended interval of 8 weeks, but has a minimum interval of 4 weeks, allowing for more rapid catch-up if needed.

In other circumstances, such as immunisation for travel or for rapid protection, shorter than recommended intervals between doses of vaccine may be required or vaccine may be administered at an age younger than usually recommended. When considering this issue, it is important to know the minimum age of each dose, which may be less than the recommended age.

DOSES GIVEN BEFORE THE RECOMMENDED MINIMUM AGE

Minimum age recommendations for receipt of vaccines are based on the youngest age group at risk for the disease and for which vaccine safety and efficacy have been demonstrated, Doses given before the recommended minimum age may lead to a less than optimal immune response (e.g. the minimum age for influenza vaccine is six months, and the vaccine works poorly in infants who are younger)..

There may be circumstances in which receiving a vaccine a few days early may be appropriate to avoid missing an opportunity for vaccination (e.g., administering a vaccine a few days early to a child who reaches the minimum age for the vaccine on the upcoming weekend). A vaccine may also be given earlier if needed for international travel or if there is an imminent risk of disease such as during an outbreak.

However, generally, if a vaccine dose is given before the minimum age, the dose should be repeated on or after the date when the person reaches the minimum age in accordance with the vaccine specific minimum recommended interval between doses. For example, MMR vaccine may be given as early as 6 months of age for children travelling outside of North America; however, two additional doses of measles-containing vaccine must be administered after the child is 12 months old to ensure long lasting immunity to measles.

Table 1 provides the recommended, minimum and maximum ages for routine childhood vaccines. Refer to vaccine specific chapters in Part 4 for additional information on recommended ages and intervals for vaccine administration. Refer to Immunization of Travellers chapter in Part 3 for detailed information about accelerated immunization schedules.

Table 1: Routine childhood vaccines (except influenza), primary series, healthy children – recommended, minimum, and maximum ages for vaccine doses; recommended and minimum intervals between vaccine doses

Vaccine(s) (brand name)	Recommended age for this dose	Recommended time[1] for this dose	Minimum age for this dose	Maximum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Diphtheria, tetanus, acellular pertussis, inactivated polio, *Haemophilus influenzae* type b (PEDIACEL®) **Diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio, *Haemophilus influenzae* type b** (INFANRIX hexa®)	2 months of age		6 weeks	Less than 7 years	8 weeks	4 weeks
	4 months of age		10 weeks		8 weeks	4 weeks
	6 months of age		14 weeks		6 - 12 months	6 months[2]
	12 - 23 months of age[3,4]		12 months		-	-
Hepatitis B (ENGERIX®-B, RECOMBIVAX HB®)		Month 0[7]	birth[5,6]	-	4 weeks	4 weeks
		Month 1	4 weeks		20 weeks	8 weeks[5,6]
		Month 6	16 weeks		-	-
Human papillomavirus bivalent (CERVARIX®)		Month 0	9 years[8]	-	4 weeks	4 weeks
		Month 1			20 weeks	20 weeks
		Month 6			-	-
Human papillomavirus quadrivalent (GARDASIL®)		Month 0	9 years[8]	-	8 weeks	4 weeks
		Month 2			16 weeks	12 weeks
		Month 6			-	-
Meningococcal conjugate monovalent (Meningitec®, Menjugate®, NeisVac-C®)	12 months of age[9]		2 months	Less than 24 years	-	-

Vaccine(s) (brand name)	Recommended age for this dose	Recommended time[1] for this dose	Minimum age for this dose	Maximum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Meningococcal conjugate quadrivalent (Menactra®)	12 years		24 months	Less than 24 years	-	-
Meningococcal conjugate quadrivalent (Menveo™)	12 years		2 months[10]	Less than 24 years	-[10]	-[10]
Measles, mumps, rubella (M-M-R® II, PRIORIX®)	12 - 15 months of age		6 months[11]	-	3 – 6 months	4 weeks
	18 months of age or older[12]		13 months		-	-
Measles, mumps, rubella, varicella (PRIORIX-TETRA®)	12 - 15 months of age		12 months	Less than 13 years	3 months	6 weeks
	18 months of age or older[12]		13.5 months		-	-
Pneumococcal conjugate 13-valent[13] (Prevnar® 13)	2 months of age		6 weeks of age	Less than 5 years	8 weeks	8 weeks
	4 months of age		14 weeks of age		8 weeks	8 weeks
	6 months of age[14]		22 weeks of age[14]		6 months	8 weeks[15]
	12 months of age[14, 15]		12 months of age[15]		-	-
Rotavirus monovalent (ROTARIX™)	2 months of age		6 weeks	Less than 14 weeks and 6 days[16]	8 weeks	4 weeks
	4 months of age		10 weeks	Less than 8 months	-	-
Rotavirus pentavalent (RotaTeq®)	2 months of age		6 weeks	Less than 14 weeks and 6 days	8 weeks	4 weeks
	4 months of age		10 weeks	Less than 7 months	8 weeks	4 weeks
	6 months of age		14 weeks	Less than 8 months	-	-
Tetanus, diphtheria (reduced),		Month 0	7 years[17]	-	8 weeks	8 weeks
		Month 2			6 - 12 months	6 months

Vaccine(s) (brand name)	Recommended age for this dose	Recommended time[1] for this dose	Minimum age for this dose	Maximum age for this dose	Recommended interval to next dose	Minimum interval to next dose
acellular pertussis (reduced), inactivated polio (ADACEL® - POLIO, BOOSTRIX® - POLIO)		Month 8 - 14			-	-
Varicella (chickenpox) (VARILRIX®, VARIVAX® III)	12 - 15 months of age		12 months	Less than 13 years	3 months	6 weeks
	18 months of age or older[12]		13.5 months		-	-
		Month 0	13 years	-	6 weeks	6 weeks
		Week 6			-	-

1 first dose = month 0; recommended time is calculated from first dose

2 must be administered at or after 12 months of age for sustained immunity

3 generally given at 18 months of age

4 INFANRIX hexa® may be given at 2, 4, 6 and 12 - 23 months of age but the fourth dose is unlikely to provide significant additional hepatitis B protection and will increase cost. Alternative schedules may be used. Refer to Diphtheria Toxoid in Part 4 for additional information.

5 if accelerated schedule for ENGERIX®-B vaccine is used (day 0, 7 and 21), a fourth dose (booster dose) is required at 12 months after first dose (month 12)

6 interval of at least 4 weeks between the first and second dose, 2 months between the second and third dose and 4 months between the first and the third dose

7 a 2-dose schedule (months 0 and 6 for ENGERIX®-B; months 0 and 4-6 for RECOMBIVAX HB®) may be used for adolescents 11 - 15 years of age

8 HPV vaccine may be considered in children less than 9 years of age who are at risk of exposure to HPV (e.g., those who are sexually active, have a history of sexual abuse or have been diagnosed with a sexually transmitted infection)

9 may begin meningococcal immunization earlier depending on provincial/territorial schedules

10 for infants and children (2 - 23 months of age) receiving Menveo™ for non-routine reasons (such as travel or specific medical conditions) refer to Meningococcal Vaccine in Part 4 for schedule information. Additional dose(s) of vaccine are recommended.

11 MMR may be given as early as 6 months of age; however, two additional doses of measles-containing vaccine must be administered after the child is 12 months old to ensure long lasting immunity to measles

12 generally 4 - 6 years of age before school entry

13 the number of doses pneumococcal conjugate 13-valent (Pneu-C-13) vaccine required varies with age at first dose: 12 - 23 months of age at first dose – 2 doses, at least 8 weeks apart. 24 - 59 months of age (fifth birthday) at first dose – 1 dose. Pneu-C-13 vaccine is not recommended for healthy children 5 years of age and older.

14 a 2-dose schedule and a booster (2, 4 and 12 months of age) of Pneu-C-13 may be considered for healthy infants

15 for infants receiving a three dose schedule (2, 4 and 6 months of age) of Pneu-C-13, a fourth dose (booster) should be administered at least 8 weeks after the third dose at 12 - 15 months of age

16 if catch-up is needed, the first dose of ROTARIX™ may be given up to 20 weeks of age

17 Tdap-IPV may be used as a primary series for previously unimmunized children 7 years of age and older and as booster dose for previously immunized children 4 years of age and older

SIMULTANEOUS ADMINISTRATION OF VACCINES

When someone is behind in their immunization schedule, simultaneous administration of vaccine may be a catch up strategy. In general, all vaccine doses for which a recipient is eligible should be administered at a single visit to increase the probability that the person will be fully immunized. Simultaneous administration of vaccines is particularly important for persons preparing for travel or if it is uncertain that the person will return for additional immunization. Most routine vaccines can be safely and effectively administered at the same visit.

Some vaccines are provided as a combination product, allowing more than one vaccine to be given in a single injection. In general, oral, intranasal and parenteral vaccines may be administered at the same visit with consideration of the minimum age and interval between doses.

INACTIVATED VACCINES

In general, inactivated vaccines may be administered concomitantly with or at any time before or after other inactivated vaccines or live vaccines. Exceptions include:

- different formulations of vaccine that protect against the same disease should be separated in time (e.g., pneumococcal conjugate and pneumococcal polysaccharide vaccine or meningococcal conjugate and meningococcal polysaccharide vaccine) at the same visit; a minimum interval should elapse between administration of the two types of vaccines. Refer to vaccine specific chapters in Part 4 for additional information.
- oral cholera vaccine (inactivated) and oral typhoid vaccine (live) should be administered at least 8 hours apart.

Different injection sites and separate needles and syringes should be used for concomitant parenteral injections.

LIVE VACCIN

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:

- doses of varicella-containing vaccine should be administered 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.
- doses of varicella-containing vaccine should be administered at least 6 weeks apart for adolescents and adults 13 years of age and older.
- doses of univalent varicella vaccine should be administered at least 3 months apart for vaccine-eligible groups of immunocompromised persons.
- varicella-containing vaccines should be not administered with smallpox vaccine; varicella-containing vaccine or herpes zoster vaccine should be administered at least 4 weeks before or after.

If live parenteral vaccines are given too close together, the immune response to the second dose may be affected by the first dose and is considered invalid; it should be repeated at the recommended interval.

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

Refer to Varicella Vaccine and Herpes Zoster (Shingles) Vaccine in Part 4 for additional information.

Refer to Vaccine Administration Practices in Part 1 for additional information about administration of multiple injections.

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PART 1

BLOOD PRODUCTS, HUMAN IMMUNE GLOBULIN AND TIMING OF IMMUNIZATION

This chapter provides guidance on the timing of administration of live vaccines and human immune globulin (Ig) preparations and blood products.

GENERAL CONSIDERATIONS

Blood products of human origin contain significant amounts of antibodies to infectious agents that are prevalent in the general population, such as measles virus and varicella zoster virus (VZV); these antibodies are present either because of natural disease or following vaccination. Therefore, administration of Ig preparations and certain blood products can interfere with the immune response to parenteral live virus vaccines if given concomitantly with or shortly before or after the vaccine. The duration of the interference with the immune response to the vaccine is related to the amount of antibody in the Ig preparation or blood product. Exceptions are respiratory syncytial virus monoclonal antibody (RSVAb) and transfusion of washed red blood cells (which is infrequently used). These products do not interfere with live vaccines because RSVAb contains only antibody to respiratory syncytial virus and washed red blood cells contain a negligible amount of antibody.

There is minimal or no interaction between blood products or Ig preparations, and:

- inactivated vaccines
- live oral vaccines (rotavirus, oral typhoid vaccines)
- live intranasal vaccine (live attenuated influenza vaccine)
- Bacille Calmette-Guerin (BCG) vaccine
- yellow fever vaccine

These vaccines may be given concomitantly with, or at any time before or after, an Ig preparation or blood product has been administered. If a parenteral vaccine and intramuscular Ig are given concomitantly, administer the vaccine and Ig preparation at different anatomic injection sites, using separate needles and syringes.

Refer to Passive Immunizing Agents in Part 5 and vaccine specific chapters in Part 4 for additional information.

MEASLES-MUMPS-RUBELLA (MMR), MEASLES-MUMPS-RUBELLA-VARICELLA (MMRV) AND UNIVALENT VARICELLA VACCINS

Guidelines for the interval between administration of Ig preparations or blood products and MMR, MMRV or univalent varicella vaccines have been developed because of the potential for reduced effectiveness of the vaccine if Ig is administered with, or shortly before or after the vaccine; it should be noted that there are no additional safety concerns if Ig is inadvertently administered with, or shortly before or after the vaccine. For an optimum immune response to MMR, MMRV or univalent varicella vaccine, the vaccine should be administered at least 14 days prior to administration of an Ig preparation or blood product, or the vaccine administration delayed until the antibodies in the Ig preparation or blood product have degraded (refer to Table 1). If the interval between the administration of any of these vaccines and subsequent administration of an Ig preparation or blood product is less than 14 days, or if these vaccines are administered before the antibody has degraded, repeat the vaccine dose after the recommended interval. The recommended interval between administration of Ig preparation or blood product and subsequent vaccination varies, depending on the Ig preparation or blood product (refer to Table 1). The recommended intervals between live parenteral vaccines should also be respected when repeating vaccine doses.

Individuals with chronic conditions requiring continuous subcutaneous Ig therapy should not be immunized with MMR, MMRV or univalent varicella vaccine (refer to footnote 1 in Table 1). Individuals who have undergone cardiac surgery with cardiopulmonary bypass would have received packed red blood cells and platelets and may have received frozen plasma. They may have received subsequent blood products in the ICU after their surgery. They should delay receiving MMR, MMRV or univalent varicella vaccine until 7 months after the date they were discharged from the ICU

Table 1: Guidelines for the interval between administration of immune globulin (Ig) preparations or blood products and measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV) or univalent varicella vaccine to maximize immunization effectiveness

Immune globulin or blood product	Dose, route	Interval between receipt of Ig or blood product and subsequent administration of MMR, MMRV or univalent varicella vaccine (months)
Standard immune globulin (human) [1]		
Immune globulin (Ig)	0.02 - 0.06 mL/kg, IM	3
	0.25 mL/kg, IM	5
	0.50 mL/kg, IM	6
Intravenous immune globulin (IVIg)	300 - 400 mg/kg, IV	8
	1,000 mg/kg, IV	10
	2,000 mg/kg, IV	11
Blood transfusion products		
Plasma and platelet products	10 mL/kg, IV	7

Immune globulin or blood product	Dose, route	Interval between receipt of Ig or blood product and subsequent administration of MMR, MMRV or univalent varicella vaccine (months)
Whole blood	10 ml/kg, IV	6
Packed red blood cells	10 mL/kg, IV	5
Reconstituted red blood cells	10 mL/kg, IV	3
Washed red blood cells[2]	10 mL/kg, IV	0
Specific immune globulin (human)		
Cytomegalovirus immune globulin (CMVIg)	150 mg/kg, IV	6
Hepatitis B immune globulin (HBIg)	0.06 mL/kg, IM	3
Rabies immune globulin (RabIg)	20 IU/kg, IM	4
Rh immune globulin (RhIg)	300 mcg, IM	3[3]
Tetanus immune globulin (TIg)	250 units, IM	3
Varicella immune globulin (VarIg)	125 IU/10 kg, IM	5
Specific immune globulin (humanized monoclonal antibody)		
Respiratory syncytial virus monoclonal antibody (palivizumab) (RSVAb)	15 mg/kg/4 weeks, IM	0

[1] Ig can also be administered subcutaneously (SCIg). SCIg is primarily indicated as life-long replacement therapy in patients with primary antibody deficiencies for whom immunization with live vaccines is contraindicated. However, potential alternative indications for SCIg therapy may result in temporary use and discontinuation of therapy. Because pharmacokinetic properties of Ig G following SCIg administration have been shown to resemble those following IVIg administration, the recommended interval between the administration of SCIg and MMR, MMRV or univalent varicella vaccines should be considered equivalent to the recommended interval after the corresponding IVIg monthly dosing.

[2] washed red blood cells are infrequently used

[3] refer to *Rh immune globulin* for additional information

Rh IMMUNE GLOBULIN (RhIg)

A risk-benefit assessment is needed for post-partum women who have received RhIg and require MMR or univalent varicella vaccine. The risk of lowered vaccine efficacy due to potential interference from the RhIg needs to be weighed against the need for protection against the vaccine preventable disease. To optimize response to vaccine, rubella-, measles- or varicella-susceptible women who receive RhIg in the peri-partum period should generally wait 3 months before being vaccinated with MMR or varicella vaccine.

However, if there is a risk of: exposure to rubella, measles, or varicella; recurrent pregnancy in the 3 months post-partum period; or a risk that vaccines may not be received later, either MMR or univalent

varicella vaccine or both may be given prior to discharge. In this context, serologic testing for antibodies to the vaccine antigens should be done 3 months after vaccination and non-immune women should be revaccinated. In the event that a post-partum woman receives either MMR or varicella vaccine or both vaccines in the 14 days prior to receiving RhIg, serologic testing for MMR or varicella should be done 3 months later and the woman revaccinated if non-immune.

HERPES ZOSTER VACCINE

Although no safety or efficacy data are available for the administration of herpes zoster vaccine to individuals who have recently received Ig preparations or other blood products, the vaccine is known to be immunogenic in adults with pre-existing antibody to VZV. In theory, administration of Ig should not interfere with the vaccine response; therefore, some experts do not consider recent administration of Ig or blood products as a reason to delay the administration of herpes zoster vaccine.

YELLOW FEVER VACCINE

The background antibody level for yellow fever is low in North America; therefore, an Ig or blood product produced from blood donated in Canada or the United States is unlikely to interfere with vaccination with yellow fever vaccine.

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PART 1

IMMUNIZATION RECORDS

Immunization records are a crucial component of the immunization process that allow monitoring of provided immunizations and help to optimize protection from vaccine preventable diseases. This chapter provides information and guidance about the use of immunization records and their contents.

GENERAL CONSIDERATIONS

RECORDING IMMUNIZATIONS

Vaccine providers should record vaccines administered to an individual in three locations (either on paper or electronically):

1. the **personal immunization record** held by the vaccinee, or his or her parent or guardian
2. the **record maintained by the health care provider** who administered the vaccine
3. the local or provincial/territorial **immunization registry** (if one has been established)

IMMUNIZATION RECORD CONTENTS

Vaccine providers should include the following information in each of the above locations:

- the trade name of the administered product
- date of administration (time, day, month and year)
- dose administered (by volume, i.e., mL)
- anatomical site of administration
- route of administration
- lot number of the product and expiry date
- name and professional designation of the person administering the product (this information may not be required in provincial/territorial immunization registries)

Vaccine providers should record additional relevant information, such as rubella and hepatitis B serology or tuberculin skin test results, in the personal immunization record, as well as the record maintained by the health care provider.

Product manufacturers are encouraged to provide peel-off labels and to provide bar codes for products to facilitate recording of product information. Pharmacists who dispense vaccines should consider providing peel-off labels if these are not provided by the manufacturer.

PERSONAL IMMUNIZATION RECORDS

Each vaccinee should be provided with a permanent personal immunization record. Vaccine recipients, or their parents or guardians, should be instructed to keep the record in a safe place and to present it at each health care visit so that it can be updated. If the personal immunization record is not available at the time of vaccination, the provider should ensure that adequate information is given so that the recipient or

parent can update the personal immunization record with the information outlined above (see immunization record contents). Parents should maintain these records on behalf of their children and give them to their children at the appropriate time, such as when they are leaving home. An example of an adult personal immunization record is available from Immunize Canada. (http://immunize.ca/en/learn/records.aspx) Initiatives for electronic immunization record keeping that allow online access by vaccinees and health care providers are under development and their use should be encouraged as they become available.

Immunization records may be required for children to attend school or child care centres. Adults may be required to provide immunization records to be able to work in certain professions, such as health care, teaching or occupations requiring foreign travel.

Refer to National Guidelines for Immunization Practices in Part 1 for additional information about personal immunization records.

HEALTH CARE PROVIDER RECORDS

Health care providers must maintain a record of all vaccinations administered and ensure that all vaccinations are accurately and completely recorded and updated. In addition to information about vaccinations given (refer to Immunization record contents), vaccine providers should:

- include all relevant serologic data (e.g., rubella serologic results, hepatitis B surface antibody titres),
- document adverse events following immunization, and
- record contraindications, exemptions, or reasons for deferring vaccination in the health care provider's record.

Electronic medical records used by health care providers should have the capacity to record, collect and easily retrieve all information outlined in immunization record contents, and should permit production of line listings of persons who received a specific vaccine in the event that the vaccine is recalled.

At each immunization visit, information should be sought regarding serious adverse events that may have occurred following previous doses in an immunization series. Health care providers should fully document the adverse event in the medical record at the time of the event or as soon as possible thereafter. Contraindications to vaccinations should be kept up to date.

Providers should maintain easily retrievable summaries of the vaccination records to permit regular checking and updating of the individual's immunization status, as well as the identification and recall of patients, especially children, who are delayed in the recommended immunization schedule. It is useful to record all the information in a single sheet or section of the vaccinee's chart. Immunization information should be readily available and should not be archived in a medical record.

Providers should facilitate the transfer of information in the immunization record to other providers and to appropriate agencies in accordance with requirements, such as compliance with provincial legislation. When a provider who does not routinely vaccinate or provide care to an individual administers a vaccine to that individual, the regular provider should be informed.

Refer to National Guidelines for Immunization Practices in Part 1 for additional information about the use and maintenance of immunization records.

IMMUNIZATION REGISTRIES

Immunization registries are centralized, confidential, electronic information systems that record doses of vaccine administered and maintain vaccination histories to help ensure accurate and timely immunizations. All provinces/territories should develop and maintain electronic immunization registries. A comprehensive local or provincial/territorial immunization registry system contributes to:

- facilitating timely, accurate recording of all relevant immunization information, regardless of where and by whom vaccines are administered
- preventing duplication of immunizations already given by another health care provider
- identifying persons who are overdue for immunizations and generating reminders and recalls for these individuals
- allowing health care providers to review the individual's immunization status at each encounter in a confidential, secure manner
- providing data for public health officials to assess immunization rates and coverage, and to plan and evaluate targeted interventions for populations with less than optimal immunization rates
- assisting with planning upcoming immunization visits
- assisting with inventory management of vaccine products or immunizing agents

Where immunization registries exist, vaccine providers should be aware of legislative or other requirements to report immunization information to these registries because incomplete information can significantly decrease the benefits derived from an immunization registry.

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PART 1

RECOMMENDED IMMUNIZATION SCHEDULES

GENERAL RECOMMENDATIONS

Administration of vaccines in accordance with the immunization schedules summarized in the following tables will provide optimal protection from vaccine-preventable diseases for most individuals. However, modifications of the recommended schedule may be necessary due to missed appointments or illness. **In general, interruption of an immunization series does not require restarting the vaccine series, regardless of the interval between doses. Individuals with interrupted immunization schedules should be vaccinated to complete the appropriate schedule for their *current* age.** Refer to Timing of Vaccine Administration in Part 1 and vaccine-specific chapters in Part 4 for additional information.

Similar, but not identical, vaccines may be available from different manufacturers; therefore; it is useful to review the relevant chapters in the *Canadian Immunization Guide* as well as the manufacturer's product leaflet or product monograph before administering a vaccine. Refer to Principles of Vaccine Interchangeability in Part 1 for information about the interchangeability of similar vaccines from different manufacturers. Product monographs are continually updated; it is a best practice to consult the product monographs for vaccines authorized by Health Canada found in Health Canada's *Drug Product Database* (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php).

TABLE 1: ROUTINE CHILDHOOD IMMUNIZATION SCHEDULE, INFANTS AND CHILDREN (BIRTH TO 17 YEARS OF AGE)

- **For children at-risk due to underlying medical conditions**, refer to *Table 4* for additional recommendations for immunization.
- [ ] = dose(s) may not be required depending upon age of child and/or vaccine used (refer to the relevant vaccine-specific chapter in Part 4 and provincial/territorial schedule).
- Refer to vaccine-specific chapters in Part 4 for additional information.

Vaccine*	Age															
	Birth	2 mos.	4 mos.	6 mos.	12 mos.	15 mos.	18 mos.	23 mos.	2 years	4 years	5 years	6 years	9 years	12 years	14-16 years	17 years
DTaP-IPV-Hib		A	A	A	A Generally at 18 months											
OR																
DTaP-HB-IPV-Hib *followed by* **DTaP-IPV-Hib**		B	B	B	A Generally at 18 months											
DTaP-IPV *or* **Tdap-IPV**										C						
Tdap															D	
Rot		E	E	[E] Complete series by 8 months + 0												

Vaccine*	Age															
	Birth	2 mos.	4 mos.	6 mos.	12 mos.	15 mos.	18 mos.	23 mos.	2 years	4 years	5 years	6 years	9 years	12 years	14-16 years	17 years
				days												
Pneu-C-13		F	F	[F]	F											
Men-C-C		[G]	[G]	[G]	G Generally at 12 months											
Men-C-C														H		
OR																
Men-C-ACYW-135														H		
MMR					I		I Generally at 4-6 years									
Var					J		J Generally at 4-6 years									
OR																
MMRV					K		K Generally at 4-6 years									
HB	L 3 dose schedule Generally at months 0,1 and 6 (1st dose = month 0															

<table>
<tr><th rowspan="2">Vaccine*</th><th colspan="15">Age</th></tr>
<tr><th>Birth</th><th>2 mos.</th><th>4 mos.</th><th>6 mos.</th><th>12 mos.</th><th>15 mos.</th><th>18 mos.</th><th>23 mos.</th><th>2 years</th><th>4 years</th><th>5 years</th><th>6 years</th><th>9 years</th><th>12 years</th><th>14-16 years</th><th>17 years</th></tr>
<tr><td colspan="16">OR</td></tr>
<tr><td>HB</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="3">M
2 or 3 dose schedule</td><td></td></tr>
<tr><td>HPV</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="4">N
3 dose schedule</td></tr>
<tr><td rowspan="2">Inf</td><td rowspan="2"></td><td rowspan="2"></td><td rowspan="2"></td><td colspan="8">O
Recommended annually</td><td colspan="4">O
Encouraged annually</td></tr>
<tr><td colspan="11">1 or 2 dose schedule</td><td colspan="4">1 dose</td></tr>
</table>

* Refer to *Table 8* for abbreviations and brand names for vaccines.
mos. = months

A. **Diphtheria toxoid- tetanus toxoid acellular pertussis inactivated polio *Haemophilus influenzae* type b** (DTaP-IPV-Hib): for infants and children beginning primary immunization at 7 months of age and older, the number of doses of Hib vaccine required varies by age.
B. **Diphtheria toxoid, tetanus toxoid, acellular pertussis, hepatitis B-inactivated polio, *Haemophilus influenzae* type b** (DTaP-HB-IPV-Hib): an alternative schedule may be used at 2, 4 and 12 to 23 months of age with DTaP-IPV-Hib vaccine at 6 months of age.
C. **Diphtheria toxoid, tetanus toxoid, acellular pertussis, inactivated polio** (DTaP-IPV) *or* **tetanus toxoid-reduced diphtheria toxoid-reduced acellular pertussis-inactivated polio** (Tdap-IPV).
D. **Tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis** (Tdap): 10 years after last dose.
E. **Rotavirus**: Rot-5 vaccine - 3 doses, at least 4 weeks apart; Rot-1 vaccine- 2 doses, at least 4 weeks apart. Give first dose between 6 weeks and 14 weeks and 6 days of age. Do not initiate series in infants aged 15 weeks or older. Administer all doses by age 8 months plus 0 days.
F. **Pneumococcal conjugate 13-valent**: healthy infants, consider a 3 dose schedule - 2, 4 and 12 months of age. Infants beginning primary immunization at 7-11 months of age - 2 doses, at least 8 weeks apart followed by a third dose after 12 months of age, at least 8 weeks after the second dose.
G. **Meningococcal conjugate monovalent**: healthy children, 1 dose at 12 months of age. Meningococcal immunization may begin in infancy depending on provincial/territorial schedule; schedule for infants depends on age at first dose and vaccine used. If Men-C-C first received at less than 12 months of age, give a booster dose at 12-23 months of age. If Men-C-C first received at 12 months of age or older, only 1 dose required until adolescence. Refer to *Table 4* for alternate recommended meningococcal immunization for children considered at-risk.
H. **Meningococcal conjugate monovalent or quadrivalent**: early adolescence (around 12 years of age) - 1 dose, even if meningococcal conjugate vaccine received at a younger age. Vaccine chosen depends on local epidemiology and programmatic considerations.

I. **Measles-mumps-rubella**: first dose at 12-15 months of age; second dose at 18 months of age or anytime thereafter, typically before school entry.
J. **Varicella:** first dose at 12-15 months of age; second dose at 18 months of age or anytime thereafter, typically before school entry.
K. **Measles-mumps-rubella-varicella**: first dose at 12-15 months of age; second dose at 18 months of age or anytime thereafter, typically before school entry.
L. **Hepatitis B**: preferred schedule - months 0, 1 and 6 (first dose = month 0) with at least 4 weeks between the first and second dose, 2 months between the second and third dose, and 4 months between the first and third dose. Alternatively, HB may be routinely administered in infancy as DTaP-HB-IPV-Hib vaccine, with first dose at 2 months of age. Refer to *Table 4* for recommended HB immunization for newborns considered at-risk.
M. **Hepatitis B**: 9-17 years of age - preferred 3 dose schedule, months 0, 1 and 6 (first dose = month 0) with at least 4 weeks between the first and second dose, at least 2 months between the second and third dose, and at least 4 months between the first and third dose; 11-15 years of age - 2 dose schedule (months 0 and 4-6, depending on the vaccine product used).
N. **Human papillomavirus**: Girls - HPV2 vaccine – months 0, 1 and 6 (first dose = month 0) *or* HPV4 vaccine – months 0, 2 and 6 (first dose=month 0). Boys - HPV4 vaccine – months 0, 2 and 6 (first dose= month 0).
O. **Influenza**: recommended annually for children 6-59 months of age (fifth birthday) and encouraged for older children. Children (6 months-8 years of age, previously immunized with Inf) and children (9 years of age and older) - 1 dose. Children (6 months-less than 9 years of age, receiving Inf for the first time) - 2 doses, at least 4 weeks apart.

TABLE 2: RECOMMENDED IMMUNIZATION SCHEDULE, CHILDREN (LESS THAN 7 YEARS OF AGE), NOT PREVIOUSLY IMMUNIZED AS INFANTS

- **For children at-risk due to underlying medical conditions**, refer to *Table 4* for additional recommendations for immunization.
- [ ] = dose(s) may not be required depending upon age of child and/or vaccine used (refer to the relevant vaccine-specific chapter in Part 4 and provincial/territorial schedule).
- Refer to vaccine-specific chapters in Part 4 for additional information.

Vaccine*	1st visit+	Time after 1st visit					6-12 months after last dose	4-6 years of age
		4 weeks	8 weeks	3 months	4 months	6 months		
DTaP-IPV-Hib *or* **DTaP-IPV**	A		A		A		A	
DTaP-IPV *or* **Tdap-IPV**								[B]
Pneu-C-13	[C]		[C]					
Men-C-C	D							
MMR	E	E Generally at 4-6 years						
Var	F			F				
OR								
MMRV	G			G Generally at 4-6 years				

Vaccine*	1st visit+	Time after 1st visit					6-12 months after last dose	4-6 years of age
		4 weeks	8 weeks	3 months	4 months	6 months		
[HB]	[H]	[H]				[H]		
Inf	I	[I]						

* Refer to *Table 8* for abbreviations and brand names for vaccines.
+ Refer to Timing of Vaccine Administration and Vaccine Administration Practices in Part 1 regarding administration of multiple injections.

A. **Diphtheria toxoid, tetanus toxoid, acellular pertussis, inactivated polio, *Haemophilus influenzae* type b** (DTaP-IPV-Hib) *or* **diphtheria toxoid, tetanus toxoid, acellular pertussis, inactivated polio combination vaccine** (DTaP-IPV): the number of doses of Hib-containing vaccine required varies by age at first dose. If first visit at 12-14 months of age: 1 dose of Hib-containing vaccine at first visit and booster dose at least 2 months after the previous dose. If first visit at 15 months to less than 5 years of age: 1 dose of Hib-containing vaccine. If first visit at 60 months of age (5 years of age) or older, Hib-containing vaccine is not required.
B. **Diphtheria toxoid, tetanus toxoid, acellular pertussis, inactivated polio** (DTaP-IPV) *or* **tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis, inactivated polio** (Tdap-IPV): omit the dose at 4-6 years of age if the fourth dose of DTaP-IPV vaccine was given after the fourth birthday.
C. **Pneumococcal conjugate 13-valent**: 12-23 months of age at first visit - 2 doses, at least 8 weeks apart. 24-59 months of age (fifth birthday) at first visit - 1 dose.
D. **Meningococcal conjugate monovalent**: 12 months to less than 5 years of age – 1 dose; 5-11 years of age – consider 1 dose. Refer to *Table 4* for alternate recommended meningococcal immunization for children considered at-risk.
E. **Measles-mumps-rubella**: 2 doses, at least 4 weeks apart.
F. **Varicella:** 2 doses, at least 3 months apart. A minimum interval of 6 weeks between doses may be used if rapid, complete protection is required.
G. **Measles-mumps-rubella-varicella**: 2 doses, at least 3 months apart. A minimum interval of 6 weeks between doses may be used if rapid, complete protection is required.
H. **Hepatitis B**: preferred 3-dose schedule - months 0, 1 and 6 (first dose = month 0) with at least 4 weeks between the first and second dose, 2 months between the second and third dose, and 4 months between the first and third dose.
I. **Influenza**: recommended annually for children 6-59 months of age (fifth birthday) and encouraged for older children. Children (6 months to less than 9 years of age receiving Inf for the first time) - 2 doses, at least 4 weeks apart.

TABLE 3: RECOMMENDED IMMUNIZATION SCHEDULE, CHILDREN (7 TO 17 YEARS OF AGE), NOT PREVIOUSLY IMMUNIZED

- **For children at-risk due to underlying medical conditions**, refer to *Table 4* for additional recommendations for immunization.
- [ ] = dose(s) may not be required depending upon age of child and/or vaccine used (refer to the relevant vaccine-specific chapter in Part 4 and provincial/territorial schedule).
- Refer to the vaccine-specific chapters in Part 4 for additional information.

Vaccine*	1st visit+	Time after first visit					6-12 months after last dose	10 years after last dose	9-11 years of age	12 years of age	13-17 years of age
		4 weeks	6 weeks	8 weeks	3 months	6 months					
Tdap-IPV	A			A			A				
Tdap								B			
Men-C-C	[C]										
Men-C-C										D	
OR											
Men-C-ACYW-135										D	
MMR	E	E									
Var	F		F								
OR											
MMRV	G				G						
HB	H	[H]				H					

<table>
<tr><th rowspan="2">Vaccine*</th><th rowspan="2">1st visit+</th><th colspan="5">Time after first visit</th><th rowspan="2">6-12 months after last dose</th><th rowspan="2">10 years after last dose</th><th rowspan="2">9-11 years of age</th><th rowspan="2">12 years of age</th><th rowspan="2">13-17 years of age</th></tr>
<tr><th>4 weeks</th><th>6 weeks</th><th>8 weeks</th><th>3 months</th><th>6 months</th></tr>
<tr><td>HPV</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="3">I
3 dose schedule</td></tr>
<tr><td>Inf</td><td colspan="10">J
Encouraged annually
1 or 2 dose schedule</td></tr>
</table>

* Refer to *Table 8* for abbreviations and brand names for vaccines.
+ Refer to *Timing of Vaccine Administration* and *Vaccine Administration Practices* in Part 1 regarding administration of multiple injections.

A. **Tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis, inactivated polio**: 2 doses, 8 weeks apart; third dose 6-12 months after second dose.
B. **Tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis:** 10 years after last dose.
C. **Meningococcal conjugate monovalent**: 5-11 years of age – consider 1 dose.
D. **Meningococcal conjugate monovalent or quadrivalent**: early adolescence (around 12 years of age) - 1 dose, even if meningococcal conjugate vaccine received at a younger age. Vaccine chosen depends on local epidemiology and programmatic considerations. Refer to *Table 4* for alternate recommended meningococcal immunization for children considered at-risk.
E. **Measles-mumps-rubella**: 2 doses, at least 4 weeks apart**.**
F. **Varicella:** 7-12 years of age - 2 doses, at least 3 months apart. A minimum interval of 6 weeks between doses may be used if rapid, complete protection is required. 13 years of age and older - 2 doses, at least 6 weeks apart; immunity should be evaluated prior to vaccination.
G. **Measles-mumps-rubella-varicella**: 7-12 years of age - 2 doses, at least 3 months apart. A minimum interval of 6 weeks between doses may be used if rapid, complete protection is required.
H. **Hepatitis B**: preferred 3-dose schedule - months 0, 1 and 6 (first dose = month 0) with at least 4 weeks between the first and second dose, 2 months between the second and third dose, and 4 months between the first and third dose. 11-15 years of age - 2 dose schedule (months 0 and 4-6, depending on the vaccine product used).
I. **Human papillomavirus:** Girls, 9 years of age and older - HPV2 vaccine – months 0, 1 and 6 (first dose = month 0) or HPV4 vaccine – months 0, 2 and 6 (first dose=month 0). Boys, 9 years of age and older – HPV4 vaccine – months 0, 2 and 6 (first dose=month 0).
J. **Influenza**: encouraged annually for all children. Children (6 months-8 years of age, previously immunized with Inf) and children (9 years of age and older) - 1 dose. Children (6 months-less than 9 years of age, receiving Inf for the first time) - 2 doses, at least 4 weeks apart.

TABLE 4: ADDITIONAL RECOMMENDED IMMUNIZATIONS, CHILDREN (BIRTH TO 17 YEARS OF AGE), CONSIDERED AT-RISK DUE TO UNDERLYING MEDICAL CONDITIONS

- [ ] = dose(s) may not be required depending upon age of child and/or vaccine used (refer to vaccine-specific chapter in Part 4 and provincial/territorial schedule).
- Refer to Immunization of Travellers and Immunization of Workers in Part 3 for additional information about vaccines recommended for travellers and workers.
- Refer to Immunization of Immunocompromised Persons and Immunization of Persons with Chronic Diseases in Part 3 for additional condition-specific recommendations.

Vaccine*	Age									
	Birth	2 months	6 months	12 months	15 months	18 months	23 months	2 years	3 years	5-17 years
Hib										A 1 dose
Pneu-P-23								B 1 dose + 1 booster dose for highest risk		
Pneu-C-13			C						[C]	
Men-C-ACYW-135		D 2, 3 or 4 dose schedule + booster doses								
HA				E 2 dose schedule						
HB	F 3 or 4 dose schedule									
OR										
HAHB				G 2 or 3 dose schedule						

Vaccine*	Age									
	Birth	2 months	6 months	12 months	15 months	18 months	23 months	2 years	3 years	5-17 years
Inf			H 1 or 2 dose schedule							

* Refer to *Table 8* for abbreviations and brand names for vaccines.

A. ***Haemophilus influenzae* type b**: 5 years of age and older with increased risk of invasive Hib disease -1 dose regardless of prior history of Hib vaccination and at least 1 year after any previous dose.
B. **Pneumococcal polysaccharide 23-valent**: 2 years of age or older, at high risk of invasive pneumococcal disease - 1 dose. If Pneu-C-13 is also required, give Pneu-C-13 first followed by Pneu-P-23, at least 8 weeks later. Re-immunize children at highest risk of IPD – give 1 booster dose after 3 years if first vaccinated with Pneu-P-23 at 10 years of age or younger, give 1 booster dose after 5 years if first vaccinated with Pneu-P-23 at 11 years of age and older.
C. **Pneumococcal conjugate 13-valent**: infants at high risk of invasive pneumococcal disease – in addition to the routine doses at 2, 4, and 12 months of age, give an extra dose at 6 months to make a 4-dose primary series. Children aged 3 and older at high risk of invasive pneumococcal disease who have not previously received Pneu-C-13 - 1 dose.
D. **Meningococcal conjugate quadrivalent**: children at high risk of invasive meningococcal disease: 2-11 months of age - 2 or 3 doses of Menveo™, 8 weeks apart with another dose between 12-23 months of age and at least 8 weeks after the previous dose; 12-23 months of age – 2 doses of Menveo™, 8 weeks apart; 24 months of age and older - 2 doses of either Men-C-ACYW-135 vaccine, 8 weeks apart. Give a booster dose every 3 to 5 years if vaccinated at less than 7 years of age and every 5 years if vaccinated at 7 years of age and older.
E. **Hepatitis A**: 12 months of age and older in high risk groups - 2 doses, given 6-36 months apart (depending on vaccine product used).
F. **Hepatitis B**: higher dose of monovalent HB vaccine recommended for certain immune compromising or chronic conditions. Premature infants weighing less than 2,000 grams at birth vaccinated because born to HB infected mothers - 4 doses.
G. **Hepatitis A-hepatitis B**: combined vaccine preferred for children 12 months of age and older if both HA and standard dosage HB vaccines are recommended – 2 or 3 dose schedule.
H. **Influenza**: recommended annually for children at risk of influenza-related complications. Children (6 months-8 years of age, previously immunized with Inf) and children (9 years of age and older) - 1 dose. Children (6 months-less than 9 years of age, receiving Inf for the first time) - 2 doses, at least 4 weeks apart.

TABLE 5: RECOMMENDED IMMUNIZATION SCHEDULE, ADULTS (18 YEARS OF AGE AND OLDER), NOT PREVIOUSLY IMMUNIZED

- **For adults considered at-risk**, refer to *Table 7* for additional recommendations for immunization.
- Refer to Immunization of Travellers and Immunization of Workers in Part 3 for additional information about vaccines recommended for travellers and workers.
- [ ] = dose(s) may not be required depending upon age of vaccinee and/or vaccine used (refer to vaccine-specific chapter in Part 4 and provincial/territorial schedule).
- Refer to vaccine-specific chapters in Part 4 for further information.

Vaccine*	1st visit	Time after 1st visit				6-12 months after last dose	10 years after last dose
		4 weeks	6 weeks	8 weeks	6 months		
Tdap-IPV *followed by* **Td-IPV**	A			B		B	
Td							C
MMR	[D]						
Var	[E]		[E]				
OR							
Zos	[F]						
Pneu-P-23	[G]						
Men-C-C	[H]						
OR							

Vaccine*	1st visit	Time after 1st visit				6-12 months after last dose	10 years after last dose
		4 weeks	6 weeks	8 weeks	6 months		
Men-C-ACYW-135	[H]						
HPV	I 3 dose schedule						
Inf	J Annually						

* Refer to *Table 8* for abbreviations and brand names for vaccines.

A. **Tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis, inactivated polio** (Tdap-IPV): 1 dose for pertussis protection.
B. **Tetanus toxoid, reduced diphtheria toxoid, inactivated polio** (Td-IPV): first dose, 8 weeks after the dose of Tdap-IPV; second dose, 6-12 months after the previous dose.
C. **Tetanus toxoid, reduced diphtheria toxoid** (Td): 10 years after last dose.
D. **Measles-mumps-rubella**: adults born ***in 1970 or later*** - 1 dose, except - travellers to destinations outside of North America, health care workers, students in post-secondary educational settings, and military personnel - 2 doses, at least 4 weeks apart. Adults born ***before 1970*** can be assumed to have acquired natural immunity to measles and mumps and do not need MMR vaccination except - non-immune military personnel or health care workers (2 doses, at least 4 weeks apart), non-immune travellers (1 dose), non-immune students in post-secondary educational settings (consider 1 dose). Rubella-susceptible adults, regardless of age – 1 dose.
E. **Varicella**: adults 18-49 years of age - 2 doses, at least 6 weeks apart; immunity should be evaluated prior to vaccination. Adults 50 years of age and older are generally presumed to be immune.
F. **Herpes zoster**: adults 50-59 years of age – may receive 1 dose; adults 60 years of age and older – 1 dose.
G. **Pneumococcal polysaccharide 23-valent**: adults 65 years of age and older – 1 dose.
H. **Meningococcal conjugate monovalent or quadrivalent:** adults less than 25 years of age – 1 dose (vaccine chosen depends on local epidemiology). Refer to *Table 7* for alternate recommended meningococcal immunization for adults considered at-risk.
I. **Human papillomavirus**: recommended for women up to 26 years of age, may be given to women 27 years of age and older at ongoing risk of exposure - HPV2 vaccine - months 0, 1 and 6 (first dose = month 0) or HPV4 vaccine - months 0, 2 and 6 (first dose = month 0). Recommended for men to 26 years of age, may be given to men 27 years of age and older at ongoing risk of exposure - HPV4 vaccine – months 0, 2 and 6 (first dose = month 0).
J. **Influenza**: adults at high risk of influenza-related complications (including pregnant women, adults 65 years of age and older); adults capable of transmitting influenza to individuals at high risk; adults who provide essential community services – 1 dose annually. Encouraged for all adults.

TABLE 6: RECOMMENDED IMMUNIZATIONS, ADULTS (18 YEARS OF AGE AND OLDER), PREVIOUSLY IMMUNIZED

- **For adults considered at-risk**, refer to *Table 7* for additional recommendations for immunization.
- Refer to Immunization of Travellers and Immunization of Workers in Part 3 for additional information about vaccines recommended for travellers and workers.
- [ ] = dose may not be required.
- Refer to vaccine-specific chapters in Part 4 for additional information.

<table>
<tr><th rowspan="2">Vaccine*</th><th colspan="5">Age</th></tr>
<tr><th>18-26 years</th><th>27-49 years</th><th>50-59 years</th><th>60 years</th><th>65 years and older</th></tr>
<tr><td>Td</td><td colspan="5">A
1 dose every 10 years</td></tr>
<tr><td>Tdap</td><td colspan="5">B
1 dose</td></tr>
<tr><td>Pneu-P-23</td><td></td><td></td><td></td><td></td><td>C
1 dose</td></tr>
<tr><td>Zos</td><td></td><td></td><td>[D]
1 dose</td><td colspan="2">[D]
1 dose</td></tr>
<tr><td>Inf</td><td colspan="4">E
Annually</td><td>E
Annually</td></tr>
</table>

* Refer to *Table 8* for abbreviations and brand names for vaccines.

A. **Tetanus toxoid, reduced diphtheria toxoid** (Td): 1 booster dose every 10 years.
B. **Tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis** (Tdap): 1 dose in adulthood for pertussis protection regardless of interval from last dose of Td.
C. **Pneumococcal polysaccharide 23-valent**: adults 65 years of age and older – 1 dose.
D. **Herpes zoster**: 50-59 years of age and older – may receive 1 dose; 60 years of age and older – 1 dose. If dose given before 60 years of age, additional dose at 60 years of age or older is not currently recommended.
E. **Influenza**: adults at high risk of influenza-related complications (including pregnant women, adults 65 years of age and older); adults capable of transmitting influenza to individuals at high risk; adults who provide essential community services – 1 dose annually. Encouraged for all adults.

TABLE 7: ADDITIONAL RECOMMENDED IMMUNIZATIONS, ADULTS (18 YEARS OF AGE AND OLDER), CONSIDERED AT-RISK

- Refer to Immunization of Travellers and Immunization of Workers in Part 3 for information about vaccines recommended for travellers and workers.
- Refer to Immunization of Immunocompromised Persons and Immunization of Persons with Chronic Diseases in Part 3 for additional condition-specific immunization recommendations.
- Refer to vaccine-specific chapters in Part 4 for additional information.

Vaccine*	Age
	18 years of age and older
Hib	A 1 dose
IPV	B 1 booster dose
MMR	C Second dose
Pneu-P-23	D 1 dose + 1 booster dose for highest risk
Men-C-ACYW-135	E 2 dose schedule + booster doses
HA	F 2 dose schedule
HB	G 3 or 4 dose schedule

Vaccine*	Age
	18 years of age and older
OR	
HAHB	H 3 or 4 dose schedule
Inf	I Annually
Typh-I	J 1 dose + booster doses if at ongoing risk
OR	
Typh-O	J 4 dose schedule + booster doses if at ongoing risk
BCG	K 1 dose
Rab	L 3 dose schedule + booster doses if required

* Refer to *Table 8* for abbreviations and brand names for vaccines.

A. ***Haemophilus influenzae* type b**: adults with increased risk of invasive Hib disease – 1 dose regardless of prior history of Hib vaccination and at least 1 year after any previous dose.
B. **Inactivated polio**: 1 booster dose for adults at increased risk of exposure to polio.
C. **Measles-mumps-rubella**: adults born in 1970 or later - 1 dose, except - travellers to destinations outside of North America, health care workers, students in post-secondary educational settings, and military personnel - 2 doses, at least 4 weeks apart. Adults born before 1970 can be assumed to have acquired natural immunity to measles and mumps and do not need MMR vaccination except - non-immune military personnel or health care workers (2 doses, at least 4 weeks apart), non-immune travellers (1 dose), non-immune students in post-secondary educational settings (consider 1 dose). Rubella-susceptible adults, regardless of age – 1 dose.
D. **Pneumococcal polysaccharide 23-valent**: adults at high risk of invasive pneumococcal disease - 1 dose. Give 1 booster dose if 5 years from first vaccination with Pneu-P-23.

E. **Meningococcal conjugate quadrivalent**: adults at high risk of invasive meningococcal disease - 2 doses, 8 weeks apart. Re-immunize every 5 years.
F. **Hepatitis A**: adults in high risk groups - 2 doses, 6-36 months apart (depending on vaccine product used).
G. **Hepatitis B**: adults in high risk groups - 3 or 4 dose schedule (depending on vaccine product used). Higher dose of monovalent HB vaccine recommended for certain immune compromising or chronic conditions.
H. **Hepatitis A-hepatitis B**: combined vaccine preferred if both HA and standard dosage HB vaccines are recommended - 3 or 4 dose schedule
I. **Influenza**: adults at high risk of influenza-related complications - 1 dose annually.
J. **Typhoid**: adults with ongoing or intimate exposure to a chronic carrier of *Salmonella typhi* - 1 dose injectable typhoid vaccine or 4 doses oral typhoid vaccine; re-immunization recommended if at continuing risk.
K. **Bacille Calmette-Guérin**: 1 dose may be considered in exceptional circumstances for adults at high risk of repeated exposure to tuberculosis.
L. **Rabies**: adults at high risk of close contact with rabid animals - 3 doses for pre-exposure immunization. Periodic serology testing and booster doses (if required) for those at continuing high risk.

TABLE 8: ABBREVIATIONS AND BRAND NAMES OF VACCINES USED IN IMMUNIZATION SCHEDULES

Abbreviation	Vaccine	Brand names*
BCG	Bacillus Calmette-Guérin	BCG Vaccine
DTaP-HB-IPV-Hib	Diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio, *Haemophilus influenzae* type b (pediatric)	INFANRIX hexa™
DTaP-IPV	Diphtheria, tetanus, acellular pertussis, inactivated polio (pediatric)	QUADRACEL®
DTaP-IPV-Hib	Diphtheria, tetanus, acellular pertussis, inactivated polio, *Haemophilus influenzae* type b (pediatric)	PEDIACEL®
HA	Hepatitis A	AVAXIM® AVAXIM® – Pediatric HAVRIX® 1440 HAVRIX® 720 Junior VAQTA®
HAHB	Hepatitis A, hepatitis B	TWINRIX® TWINRIX® Junior
HB	Hepatitis B	ENGERIX®-B RECOMBIVAX HB®
Hib	*Haemophilus influenzae* type b	Act-HIB®
HPV2	Human papillomavirus	CERVARIX™
HPV4	Human papillomavirus	GARDASIL®

Abbreviation	Vaccine	Brand names*
Inf	Influenza	AGRIFLU® FLUAD® FLUMIST® FLUVIRAL® FLUZONE® INFLUVAC® INTANZA® VAXIGRIP®
IPV	Polio (inactivated)	IMOVAX® Polio
Men-C-ACYW-135	Meningococcal conjugate quadrivalent	Menactra® Menveo™
Men-C-C	Meningococcal conjugate monovalent	Meningitec® Menjugate® NeisVac-C®
MMR	Measles, mumps, rubella	M-M-R® II PRIORIX®
MMRV	Measles, mumps, rubella, varicella	PRIORIX-TETRA®
Pneu-C-13	Pneumococcal conjugate 13-valent	Prevnar® 13
Pneu-P-23	Pneumococcal polysaccharide 23-valent	PNEUMOVAX® 23 PNEUMO 23®
Rab	Rabies	IMOVAX® Rabies RabAvert®
Rot-1	Rotavirus monovalent	ROTARIX™
Rot-5	Rotavirus pentavalent	RotaTeq®
Td	Tetanus, diphtheria (reduced)	Td ADSORBED
Tdap	Tetanus, diphtheria (reduced), acellular pertussis (reduced)	ADACEL® BOOSTRIX®

Abbreviation	Vaccine	Brand names*
Tdap-IPV	Tetanus, diphtheria (reduced), acellular pertussis (reduced), inactivated polio	ADACEL®-POLIO BOOSTRIX®-POLIO
Td-IPV	Tetanus, diphtheria (reduced), inactivated polio	Td POLIO ADSORBED
Typh-I	Typhoid (injection)	TYPHIM Vi® TYPHERIX®
Typh-O	Typhoid (oral)	Vivotif®
Var	Varicella (chickenpox)	VARILRIX® VARIVAX® III
Zos	Herpes zoster (shingles)	ZOSTAVAX®

* Refer to vaccine-specific chapters in Part 4 for brand-specific recommendations.

PART 1

BASIC IMMUNOLOGY AND VACCINOLOGY

Immunology is the study of the structure and function of the immune system. V*accinology* is the science of vaccine development and how the immune system responds to vaccines, but also includes ongoing evaluation of immunization programs and vaccine safety and effectiveness, as well as surveillance of the epidemiology of vaccine-preventable diseases. This chapter provides a brief overview of some of the main concepts of immunology and vaccinology as they relate to immunization. A detailed review of immunology and vaccinology is beyond the scope of the *Canadian Immunization Guide*.

HUMAN IMMUNE SYSTEM

COMPONENT OF THE IMMUNE SYSTEM

An *antigen* is a substance that the body recognizes as foreign and that triggers immune responses. The terms *immunogen* and *antigen* are often used interchangeably.

Antibodies are proteins that are produced in response to antigens introduced into the body. Antibodies protect the body from disease by:

- binding to the surface of the antigen to block its biological activity (*neutralization*)
- binding or coating (*opsonisation*) of the antigen to make it more susceptible to destruction and clearance by phagocytes (*phagocytosis*)
- opsonisation of special receptors on various cells, allowing them to recognise and respond to the antigen
- activation of the complement system to cause disintegration (*lysis*) of the pathogen and to enhance phagocytosis.

IMMUNE REPONSES

Immunity is the ability of the human body to protect itself from infectious diseases. The human immune system is able to react to an enormous number and variety of foreign antigens and provides immunity through two complementary types of responses:

- *Innate immunity* is the body's initial defence mechanism that is not specific to particular antigens and comes into play immediately or within hours of a pathogen's entry into the body. Innate immunity is made up of physical barriers (skin and mucous membranes), physiologic defences (temperature, low pH and chemical mediators), human microbiome (aggregate of microorganisms that reside on and in the human body; these microorganisms may protect from potential pathogens by blocking binding sites and competing for nutrients), as well as phagocytic and humoral inflammatory responses. Innate immunity:
    - does not depend upon previous exposure to the pathogen
    - does not produce immunologic memory
    - does not improve with repeated exposure to the pathogen.

- *Adaptive immunity* is the body's second level of defence, which develops as a result of infection with a pathogen or following immunization. It defends against a specific pathogen and takes several days to become protective. Adaptive immunity:

    - has the capacity for immunologic memory
    - provides long-term immunity which may persist for a lifetime but may wane over time
    - increases in strength and effectiveness each time it encounters a specific pathogen or antigen.

The cells of the adaptive immune system include specialized white blood cells: T cells (T lymphocytes) and B cells (B lymphocytes), which provide *cell-mediated immunity* and *antibody-mediated immunity*, respectively:

- *Cell-mediated immunity* provides protection through activation of specialized T cells to destroy pathogens or to induce the death of cells displaying the foreign antigen on their surface, and stimulation of further immune response.
- *Antibody-mediated (humoral) immunity* is mediated by B cells. The terms *antibody* and *immunoglobulin (Ig)* are often used interchangeably. There are five types of antibodies: IgA, IgD, IgE, IgG and IgM.

Immunologic memory is the immune system's ability to remember its experience with an infectious agent, leading to effective and rapid immune response upon subsequent exposure to the same or similar infectious agents. Development of immunologic memory requires participation of both B and T cells; memory B cell development is dependent on the presentation of antigens by T cells.

IMMUNIZING AGENTS

Immunization refers to the process by which a person becomes protected against a disease with immunizing agents. Immunizing agents are classified as active or passive, depending on the process by which they confer immunity; prevention of disease through the use of immunizing agents is called *immunoprophylaxis. Active immunization* is the production of antibodies against a specific agent after exposure to the antigen through vaccination. Active immunizing agents are typically referred to as vaccines. Refer to Part 4 for information on active vaccines. *Passive immunization* involves the transfer of pre-formed antibodies, generally from one person to another or from an animal product, to provide temporary protection, since transferred antibody degrades over time. It can occur by transplacental transfer of maternal antibodies to the developing foetus, or it can be provided by administration of a passive immunizing agent prepared from the serum of immune individuals or animals. Refer to Passive Immunizing Agents in Part 5 for information on passive immunizing agents.

ACTIVE VACCINES

Vaccines are complex biologic products designed to induce a protective immune response effectively and safely. An ideal vaccine is safe with minimal adverse effects, and effective in providing lifelong protection against disease after a single dose that can be administered at birth. Also ideally, it would be inexpensive, stable during shipment and storage, and easy to administer. Some vaccines come closer to fulfilling these criteria than others. Although each vaccine has its own benefits and risks, and indications and contraindications, all vaccines offer protection against the disease for which they were created.

In addition to the active component (the antigen), which induces the immune response, vaccines may contain additional ingredients such as preservatives, additives, adjuvants and traces of other substances necessary in the production of the vaccine. Vaccine antigens include: inactivated (killed) or attenuated (weakened) live organisms; products secreted by organisms that are modified to remove their pathogenic effects (e.g., tetanus toxoid); and components of the organism, some of which some are made in the laboratory through recombinant technology.

Vaccines are classified according to the type of antigen they contain (refer to Table 1). Most often they are categorized in two groups - live attenuated vaccines and inactivated vaccines:

- *Live attenuated vaccines* contain whole, weakened bacteria or viruses. Since the agent replicates within the vaccine recipient, the stimulus to the immune system more closely resembles that associated with natural infection, resulting in longer lasting and broader immunity than can be achieved with other vaccine types. Because of the strong immunogenic response, live attenuated vaccines, except those administered orally, typically produce immunity in most recipients with one dose; however, a second dose helps to make sure that almost everyone is protected, because some individuals may not respond to the first dose. Live vaccines require careful storage and handling to avoid inadvertent inactivation and are, in general, contraindicated for pregnant women (because of the theoretical risk of effects on the foetus) and for people who are immunocompromised (because of the risk of disease being caused by the live vaccine strains).

- *Inactivated vaccines* contain whole or part of (fractional) killed bacteria or viruses and cannot cause the disease it is designed to prevent, even in an immunocompromised person. Fractional inactivated vaccines can be protein or polysaccharide-based. Antigens of protein-based vaccines include *toxoids* (inactivated bacterial toxin), *subunit* and *split-virus* products.

    - *Subunit* vaccines are highly purified products containing surface antigen only, with most (if not all), of the internal viral or bacterial components removed. Some subunit vaccines are synthesized using *recombinant* technology (e.g. hepatitis B vaccine). Subunit vaccines have excellent safety profiles and are used in a variety of combination products.
    - *Split-virus* vaccines are treated to disrupt the integrity of the virus but contain essentially all viral structural proteins and components.

Polysaccharide vaccines are composed of bacterial capsule and are less immunogenic compared to other vaccines, particularly in children younger than two years of age. However, polysaccharides may be conjugated (chemically joined or linked) to a carrier protein (a protein that is easily recognized by the immune system, such as diphtheria or tetanus) to produce conjugate polysaccharide vaccines that have improved functional activity and are highly immunogenic in young children.

Because the immune response to inactivated vaccines may be less than that induced by live organisms, inactivated vaccines often require multiple doses: the first dose *primes* the immune system and a protective immune response develops after the second or third dose. These initial doses are called *primary vaccination* or *the primary series*. Because protection following primary vaccination may diminish over time, periodic supplemental doses (*booster doses*) may be required to increase or boost antibody levels.

Table 1: Live attenuated vaccines and inactivated vaccines

Live, attenuated vaccines
Live attenuated bacterial vaccines
• BCG vaccine • Typhoid vaccine (oral formulation)
Live attenuated viral vaccines
• Live attenuated influenza vaccine (intranasal formulation) • Measles-mumps-rubella containing vaccines • Rotavirus vaccines • Varicella-containing vaccines, including herpes zoster vaccine • Yellow fever vaccine
Inactivated vaccines
Whole inactivated vaccines
• Viruses (e.g., polio, hepatitis A, rabies vaccines) • Bacteria (e.g., cholera vaccine)
Fractional inactivated vaccines

• Protein-based
  ○ Toxoid (e.g., diphtheria toxoid, tetanus toxoid)
  ○ Subunit (e.g., hepatitis B, acellular pertussis, some influenza vaccines)
  ○ Split-virus (e.g., some influenza vaccines)
• Polysaccharide-based
  ○ Pure polysaccharide (e.g., pneumococcal polysaccharide, parenteral typhoid vaccine)
  ○ Conjugate polysaccharide (e.g., pneumococcal conjugate, meningococcal conjugate, *Haemophilus influenzae* type b [Hib] vaccines)
• Virus-like particle (e.g., human papillomavirus [HPV])

Adjuvants

An adjuvant is a substance that is added to a vaccine to enhance the immune response and to extend the duration of B and T cell activation. An adjuvant allows the reduction of the amount of antigen per dose or the total number of doses needed to achieve immunity and helps to improve the immune response in individuals with some degree of immune suppression (e.g., the elderly). The adjuvants used in vaccines currently marketed in Canada are:

- aluminum salts (aluminum hydroxide, aluminum phosphate, or aluminum hydroxyphosphate sulfate)
- AS04 (3-O-desacyl-4'-monophosphoryl lipid A adsorbed onto aluminum [as hydroxide salt])
- MF59C.1 (oil-in-water emulsion composed of squalene as the oil phase, stabilised with the surfactants polysorbate 80 and sorbitan trioleate, in citrate buffer).

Refer to Contents of immunizing agents available for use in Canada in Part 1 for a list of product specific adjuvants.

Preservatives
Chemicals (e.g., thimerosal, phenol, 2-phenoxyethanol) may be added to vaccines to prevent serious secondary infections as a result of bacterial or fungal contamination of the vaccine. Most vaccines available for use in Canada do not contain thimerosal.

Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of product specific preservatives.

Additives
Additives are substances that may be added to vaccines to:

- support the growth or purification of specific antigens or the inactivation of toxins, or both. They include: antibiotics added to prevent contamination during viral cell culture; substances needed for the growth of viruses, such as egg or yeast proteins, glycerol, serum, amino acids and enzymes; and formaldehyde, used to inactivate viruses and protein toxins. Most of these reagents are removed in subsequent manufacturing steps, but minute amounts may remain in the final product.
- support product quality or stability. Compounds may be added to vaccines for a variety of manufacture-related issues: controlling acidity (pH); stabilizing antigens through the manufacturing process, such as during freeze drying (lyophilizing); and preventing antigens from adhering to the sides of glass vials with a resultant loss in immunogenicity. Examples of such additives include potassium or sodium salts, lactose, polysorbate 20 or 80, and human serum albumin and animal proteins, such as gelatin and bovine serum albumin

Refer to Contents of Immunizing Agents Available for use in Canada in Part 1 for a list of product specific additives.

PASSIVE IMMUNIZING AGENTS – IMMUNE GLOBULINS

Passive immunization with immune globulins provides protection when vaccines for active immunization are unavailable or contraindicated, or in certain instances when unimmunized individuals have been exposed to the infectious agent and rapid protection is required (post-exposure immunoprophylaxis). Passive immunization also has a role in the management of immunocompromised people who may not be able to respond fully to vaccines or for whom live vaccines may be contraindicated. The duration of the beneficial effects provided by passive immunizing agents is relatively short and protection may be incomplete. Refer to Passive Immunizing Agents in Part 5 for additional information on passive immunizing agents.

VACCINE DEVELOPMENT

HOW VACCINE ARE DEVELOPPED

The first steps in the development of a vaccine include the identification of the microorganism or toxin that causes a significant burden of disease in the population and an understanding of the disease pathogenesis. Once the pathogen and pathogenesis are understood, research is initiated into the possibility of developing a vaccine to reduce the disease incidence, severity or both. New vaccines undergo a very rigorous development process, beginning with pre-clinical laboratory testing to ensure that the candidate vaccine produces the immune response needed to prevent disease and has no toxicities that would prevent its use in people. Clinical trials (human studies) then proceed through several phases involving progressively more study subjects. Vaccine Safety in Part 2 describes pre-clinical and clinical research throughout the vaccine life cycle and the accompanying regulatory requirements to ensure data and product quality.

HOW VACCINES WORK

Vaccines work at an individual level to protect the immunized person against the specific disease, as well as at a population level to reduce the incidence of the disease in the population, thereby reducing exposure of susceptible persons and consequent illness. Although the primary measure of effectiveness occurs at an individual level, there is also interest in decreasing or even eliminating disease at a population level.

HOW VACCINES WORK AT THE INDIVIDUAL LEVEL

The administration of a vaccine antigen triggers an inflammatory reaction that is initially mediated by the innate immune system and subsequently expands to involve the adaptive immune system through the activation of T and B cells. While the majority of vaccines provide protection through the induction of humoral immunity (primarily through B cells), some vaccines such as Bacille Calmette-Guerin (BCG) and herpes zoster act principally by inducing cell-mediated immunity (primarily though T cells).

Long-term immunity requires the persistence of antibodies, and/or the creation and maintenance of antigen-specific memory cells (*priming*), that can rapidly reactivate to produce an effective immune response upon subsequent exposure to the same or similar antigen.

MARKERS OF PROTECTION INDUCED BY VACCINATION

A *correlate* of protection is a specific immune response that is responsible for and statistically linked to protection against infection or disease. Following administration of most vaccines, prevention of infection has been shown to correlate predominantly with the production of antigen-specific antibodies. Serologic markers can be measured using enzyme-linked immunosorbent assays (ELISA), functional antibody activity such as the opsonophagocytic assay (OPA), or both. A *surrogate* of protection is a substitute immune marker, which may not be linked to protection against infection or disease. For example, serum antibodies may be produced for mucosal vaccines against rotavirus. Although serum antibodies against rotavirus serve as surrogates of protection, they are not necessarily directly protective against infection as this may require mucosal antibodies.

Immunogenicity means the vaccine's ability to induce an immune response. Vaccine-induced *seroconversion* is the development of detectable antigen-specific antibodies in the serum as a result of vaccination; *seroprotection* is a predetermined antibody level as a result of vaccination, above which the probability of infection is low. The seroprotective antibody level differs depending on the vaccine.

HOW VACINES WORK AT THE POPULATION-LEVEL

Vaccine efficacy refers to the vaccine's ability to prevent illness in people vaccinated in controlled studies. *Vaccine effectiveness* refers to the vaccine's ability to prevent illness in people vaccinated in broader settings (i.e., the "real world").

Herd immunity refers to the immunity of a population against a specific infectious disease. The resistance of that population to the spread of an infectious disease is based on the percentage of people who are immune and the probability that those who are still susceptible will come into contact with an infected person. The proportion of the population required to be immune to reach herd immunity depends on a number of factors, the most important one being the transmissibility of the infectious agent either from a symptomatically infected person or from an asymptomatically colonized person.

The *reproduction number* (also called the basic reproductive rate) or R_0 is defined as the average number of transmissions expected from a single primary case introduced into a totally susceptible population. Diseases that are highly infectious have a high R_0 (e.g., measles) and require higher vaccine coverage to attain herd immunity than a disease with a lower R_0 (e.g., rubella, Hib).

Immunization (vaccine) coverage refers to the proportion of the population (either overall or for particular risk groups) that has been immunized against a disease. High immunization coverage is especially required for diseases that have a high reproduction number (R_0) to prevent further transmission. To stop

transmission of a given disease, there needs to be at least a specified percentage (1 minus $1/R_0$) of the population immune to the disease. For example, measles has an estimated R_0 of 15; therefore, at least 94% (1 minus 1/15 = 94%) of the population needs to be immune to prevent transmission of measles.

DETERMINANTS OF VACCINE RESPONSE IN INDIVIDUALS

The strength and duration of the immune system's response to a vaccine is determined by a number of factors as outlined in Table 2.

Table 2: Determinants of vaccine response in individuals

Vaccine type	The type of vaccine antigen and its immunogenicity directly influence the nature of the immune response that is induced to provide protection: • Live, attenuated vaccines generally induce a significantly stronger and more sustained antibody response. • Inactivated vaccines often require adjuvants to enhance antibody response, usually require multiple doses to generate high and sustained antibody responses, and induce vaccine antibodies that decline over time to below protective thresholds unless repeat exposure to the antigen reactivates immune memory. Pure polysaccharide vaccines induce limited immune response and do not induce immunologic memory.
Vaccine adjuvants and carrier proteins	• The addition of adjuvants to inactivated vaccines enhances immune response and extends the duration of B and T cell activation. • Conjugating (linking) a polysaccharide with a carrier protein (protein that is easily recognized by the immune system such as diphtheria or tetanus) leads to a significantly higher immune response.
Optimal dose of antigen	• Higher doses of inactivated antigens up to a certain threshold elicit higher antibody responses.
Interval between doses	• The recommended interval between doses allows development of successive waves of antigen-specific immune system responses without interference, as well as the maturation of memory cells
Age of vaccine recipient	• In early life, the immune system is immature, resulting in limited immune responses to vaccines. For example, children less than 2 years of age do not respond to polysaccharide vaccines. • In general, antibody responses to vaccines received early in life decline rapidly for most, but not all (e.g., hepatitis B) vaccines. • In older age, immune responses decline (*immunosenescence)* and can result in an increased incidence and severity of infectious diseases and a reduction in the strength and persistence of antibody responses to vaccines.
Pre-existent antibodies	• The immune response to vaccines received early in life may be influenced by the presence of maternal antibodies transferred across the placenta. • The immune response to live vaccines will be influenced by passively transferred antibodies, such as after blood product transfusion and immune globulins. Refer to Blood products, human immune globulin and timing of immunization in Part 1.
Status of the immune system	• Immune response to vaccines will be modified by the status of vaccine recipient's immune system. . Refer to Immunization of Immunocompromised Persons and Immunization of Persons with Chronic Diseases in Part 3.

EPIDEMIOLOGY AND IMMUNIZATION

Epidemiology provides data on the distribution and determinants of diseases. Epidemiology informs the first steps in vaccine development by describing the diseases caused by a particular pathogen in a particular population and indicating the need for vaccine development. As a vaccine is introduced into the population, epidemiology monitors the effect of the vaccine in the population by describing changes in the disease burden and the pathogens causing that disease. Epidemiology can also provide information regarding immunization coverage and vaccine safety.

Surveillance is the process of systematic collection, orderly analysis, evaluation and reporting of epidemiological data (particularly to public health officials who are in a position to take action), to inform disease control measures or policy decisions or both. Surveillance of vaccine preventable diseases, including immunization coverage and vaccine safety, is needed to:

- identify and quantify risk factors to enable appropriate control of communicable diseases.
- assist in the investigation, containment and management of vaccine preventable disease outbreaks or a signal of adverse events following immunization.
- monitor progress toward the achievement of set goals and targets in disease control programmes.
- provide up-to-date information to assist in the development of evidence-based guidelines.

Determining the *burden of disease* is important in setting immunization priorities. Burden of disease includes: the prevalence (total number of cases of a particular disease in a geographic area); the incidence (number of new cases of a particular disease in a geographic area over a specified period of time); the age or risk group that is most affected (e.g., infants, children, adults, the elderly, immunocompromised persons); the severity of the disease (e.g., as measured by time missed from work, hospitalization, complications or death); and the risk factors for disease that should be considered. These factors are particularly important when making vaccine recommendations regarding:

- groups who are susceptible to the disease and who require the direct protection of a vaccine; and
- groups who require indirect protection (herd immunity) because they may be susceptible to the disease but are not ideal target groups to receive the vaccine.

Evaluation of vaccine programs is the systematic investigation of the structure, activities, or outcomes of public health programs. It explores whether activities are implemented as planned and outcomes have occurred as intended, and why. Evaluation can help to support program implementation, and through its activities, builds on the program monitoring activities that immunization programs currently conduct in assessing whether program objectives have been met.

FUTURE OF VACCINOLOGY

Ongoing scientific advances in biotechnology, genetics and virology are providing new tools for vaccine development. This knowledge provides the basis for improving the effectiveness of existing vaccines, as well as the development of novel vaccines and vaccine delivery systems. These ongoing scientific advances in vaccine development need to be accompanied by scientific advances in epidemiological methods which can continue to inform the development and monitoring of new vaccines.

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PART 1

CONTENTS OF IMMUNIZING AGENTS AVAILABLE IN CANADA

The following tables provide a comprehensive list of contents of immunizing agents available in Canada. *Table 1* identifies all the active vaccines and *Table 2* identifies all passive immunizing agents. Vaccine providers should consult the product label, product leaflet, and/or product monograph for current product information. Manufacturers provide evidence of vaccine safety and efficacy and receive authorization for the immunizing agent only when it is used in accordance with the product monograph. Product monographs are available through Health Canada's Drug Product Database. (http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp)

Table 1: Types and contents of vaccines available for use in Canada

- For up-to-date, complete prescribing information consult the product leaflet or information contained within the product monographs available through Health Canada's Drug Product Database (http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp)
- Any component in a vaccine may be a potential allergen. This table identifies most common allergens; adjuvants and preservatives may be potential allergens, but this is extremely rare.
- Information about the vaccine manufacturer/distributor is available in the Appendix of Vaccine Abbreviations

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
Act-HIB®	IM	Subunit Conjugate	Hib			Tetanus toxoid carrier protein	Sodium chloride Sucrose Trometamol
ADACEL®	IM	Toxoid + Subunit	T d ap	Alum	PE		Formaldehyde Glutaraldehyde
ADACEL®-POLIO	IM	Toxoid + Subunit+ Inactivated	T d ap IPV	Alum	PE	Neomycin Polymyxin B Streptomycin	Bovine serum albumin Formaldehyde Glutaraldehyde Polysorbate 80 Water for injection
AGRIFLU®	IM	Inactivated - subunit	Inf			Egg protein Kanamycin Neomycin	Barium Calcium chloride Cetyltrimethylammonium bromide Citrates Disodium phosphate dihydrate Formaldehyde Magnesium chloride Polysorbate 80 Potassium chloride Potassium dihydrogen phosphate Sodium chloride Water for injection

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
AVAXIM® **AVAXIM® Pediatric**	IM	Inactivated	HA	Alum	PE CH_2O	Neomycin	Medium 199 Hanks Polysorbate 80 Water for injection
BCG Vaccine	ID	Live attenuated	BCG			Latex in vial stopper	Disodium hydrogen phosphate Monosodium glutamate Polysorbate 80 Sodium chloride Sodium dihydrogen phosphate Water for injection
BOOSTRIX®	IM	Toxoid + Subunit	T d ap	Alum		Latex in plunger stopper of pre-filled syringe	Formaldehyde Glycine Polysorbate 80 Sodium chloride Water for injection
BOOSTRIX®-POLIO	IM	Toxoid + Subunit + Inactivated	T d ap IPV	Alum		Latex in plunger stopper of pre-filled syringe Neomycin Polymyxin B	Formaldehyde Medium 199 Sodium chloride Water for injection
CERVARIX™	IM	Recombinant	HPV	AS04		Latex in plunger stopper of pre-filled syringe	Hydrated sodium chloride Sodium dihydrogen phosphate dihydrate Water for injection
DUKORAL®	Oral	Subunit + Inactivated	Chol Ecol				Citric acid Disodium hydrogen phosphate Raspberry flavor Saccharin sodium Sodium carbonate Sodium citrate Sodium chloride Sodium dihydrogen phosphate Sodium hydrogen carbonate Water for injection

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
ENGERIX®-B **ENGERIX®-B Pediatric dose**	IM	Recombinant	HB	Alum	Tm[1] PE[1]	Yeast protein Thimerosal	Disodium phosphate dihydrate Polysorbate 20 Sodium chloride Sodium dihydrogen phosphate dihydrate
FLUAD®	IM	Inactivated - subunit	Inf	MF59		Egg protein Kanamycin Neomycin	Barium Calcium chloride dihydrate Cetyltrimethylammonium bromide Disodium phosphate dihydrate Formaldehyde Magnesium chloride hexahydrate Polysorbate 80 Potassium chloride Potassium dihydrogen phosphate Sodium chloride Water for injection
FLUMIST®	IN	Live attenuated	Inf			Arginine Egg protein Gelatin Gentamicin	Dibasic potassium phosphate Monosodium glutamate Monobasic potassium phosphate Sucrose
FLUVIRAL® (2012-2013)	IM	Inactivated – split virus	Inf		Tm	Egg protein Thimerosal	Disodium hydrogen phosphate heptahydrate Formaldehyde Potassium chloride Potassium dihydrogen phosphate Sodium chloride Sodium deoxycholate Sucrose Water for injection
FLUZONE®	IM	Inactivated – split virus	Inf		Tm[1]	Egg protein Gelatin Neomycin Thimerosal[1]	Formaldehyde Gelatin Sucrose Triton® X-100

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
FSME-IMMUN™	IM	Inactivated	TBE	Alum		Chick protein Egg protein Formaldehyde Gentamicin Latex in container of product Neomycin Protamine sulfate	Disodium hydrogen phosphate dihydrate Human albumin Potassium dihydrogen phosphate Sodium chloride Sucrose Water for injection
GARDASIL®	IM	Recombinant	HPV	Alum		Yeast protein	L-histidine Polysorbate 80 Sodium borate Sodium chloride Water for injection
HAVRIX®	IM	Inactivated	HA	Alum		Latex in plunger stopper of pre-filled syringe Neomycin	Amino acids Disodium phosphate Formaldehyde Monopotassium phosphate Polysorbate 20 Potassium chloride Sodium chloride Water for injection
HAVRIX® 720 JUNIOR							
IMOVAX® Polio	SC	Inactivated	IPV		PE	Neomycin Polymyxin B Streptomycin	Bovine serum Formaldehyde Medium 199 Hanks Polysorbate 80
IMOVAX® Rabies	IM	Inactivated	Rab			Neomycin Phenol red	Human albumin Water for injection
INFANRIX hexa™	IM	Toxoid + Subunit + Recombinant + Inactivated + Conjugate	D T aP HB IPV ++ (Hib)	Alum		Latex in plunger stopper of pre-filled syringe Neomycin Polymyxin B Tetanus toxoid carrier protein Yeast protein	Disodium phosphate Formaldehyde Glycine Lactose M199 Monopotassium phosphate Polysorbate 20 and 80

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
							Potassium chloride Sodium chloride Water for injection
INFLUVAC®	IM	Inactivated - subunit	Inf			Chick protein Egg protein Gentamicin	Calcium chloride dihydrate Cetyltrimethylammonium bromide Disodium phosphate dihydrate Formaldehyde Magnesium chloride hexahydrate Polysorbate 80 Potassium chloride Potassium dihydrogen phosphate Sodium chloride Water for injection
INTANZA®	ID	Inactivated – split virus	Inf			Chick protein Egg protein Neomycin	Disodium phosphate dihydrate Formaldehyde Potassium chloride Potassium dihydrogen phosphate Sodium chloride Triton® X-100
IXIARO®	IM	Inactivated	JE	Alum			Disodium hydrogen phosphate Potassium dihydrogen phosphate Sodium chloride Water for injection
Menactra®	IM	Subunit -conjugate	Men			Diphtheria toxoid carrier protein	Sodium chloride Sodium phosphate dibasic (anhydrous) Sodium phosphate monobasic Water for injection
Meningitec®	IM	Conjugate	Men	Alum		Latex in vial stopper (vial presentation only) Diphtheria CRM_{197} toxoid carrier protein	Sodium chloride Water for injection

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
Menjugate®	IM	Conjugate	Men	Alum		Latex in tip cap of syringe Diphtheria CRM_{197} toxoid carrier protein	Disodium phosphate heptahydrate Mannitol Sodium chloride Sodium dihydrogen phosphate monohydrate Water for injection
MENOMUNE® A/C/Y/W-135	SC	Subunit	Men		Tm[1]	Latex in stopper	Lactose Sodium chloride
Menveo™	IM	Conjugate	Men			Diphtheria CRM_{197} toxoid carrier protein	Disodium hydrogen phosphate bihydrate Potassium dihydrogen phosphate Sodium chloride Sodium dihydrogen phosphate monohydrate Sucrose Water for injection
M-M-R® II	SC	Live attenuated	Meas Mumps R			Neomycin Phenol red Porcine gelatin Residual components of chick embryo cell cultures	Fetal bovine serum Medium 199 with Hank's salts Minimum essential medium (Eagle) Monosodium L-glutamate monohydrate Potassium phosphate dibasic (anhydrous) Potassium phosphate monobasic Recombinant human albumin Sodium bicarbonate Sodium phosphate dibasic (anhydrous) Sodium phosphate monobasic Sorbitol Sucrose Water for injection
NeisVac-C®	IM	Subunit Conjugate	Men	Alum		Tetanus toxoid carrier protein	Sodium chloride

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
NIMERIX™	IM	Conjugate	Men-P-ACYW-135				Sucrose Trometamol Sodium chlorideWater for injection
PEDIACEL®	IM	Toxoid + Subunit + Inactivated + Conjugate	D T aP IPV Hib	Alum	PE	Neomycin Polymyxin B Streptomycin Tetanus toxoid carrier protein	Bovine serum albumin Formaldehyde Glutaraldehyde Polysorbate 80
PNEUMO 23®	IM/ SC	Subunit	Pneu		P		Disodium phosphate Monosodium phosphate Sodium chloride Water for injection
PNEUMOVAX® 23	IM/ SC	Subunit	Pneu		P		Sodium chloride Water for injection
Prevnar® 13	IM	Conjugate	Pneu	Alum		Diphtheria CRM_{197} toxoid carrier protein	Polysorbate 80 Sodium chloride Succinic acid Water for injection
PRIORIX®	SC/ IM	Live attenuated	Meas Mumps R			Egg protein Neomycin	Amino acids Lactose Mannitol Sorbitol Water for injection
PRIORIX-TETRA®	SC/ IM	Live attenuated	Meas Mumps R Var			Egg protein Neomycin	Amino acids Lactose Mannitol Sorbitol Water for injection
QUADRACEL®	IM	Toxoid + Subunit + Inactivated	D T aP IPV	Alum	PE	Neomycin Polymyxin B	Bovine serum albumin Formaldehyde Glutaraldehyde Polysorbate 80

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
RabAvert®	IM	Inactivated	Rab			Amphotericin B Chick protein Chlortetracycline Neomycin Polygeline (gelatin) Egg protein	Human serum albumin
RECOMBIVAX HB®	IM	Recombinant	HB	Alum		Latex in vial stopper Yeast protein	Formaldehyde Sodium borate Sodium chloride Water for injection
ROTARIX™	Oral	Live attenuated	Rot				Disodium adipate DNA fragments from porcine circovirus 1 Dulbecco's Modified Eagle Medium Sterile water Sucrose
RotaTeq®	Oral	Live	Rot				DNA fragments from porcine circoviruses 1 and 2 Fetal bovine serum Polysorbate 80 Residual protein from cell culture Sodium citrate dihydrate Sodium hydroxide Sodium phosphate monobasic monohydrate Sucrose
Smallpox (dried)[2]	ID	Live	Vaccinia			Latex in stopper of vaccine vial Neomycin Streptomycin	Bovine tissue (trace) Glycerol McIlvaine buffer Phenol
SYNFLORIX®	IM	Conjugate	Pneu	Alum		Latex in syringe components Diphtheria toxoid carrier protein	Sodium chloride Water for injection

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
						Tetanus toxoid carrier protein Non-typeable *Haemophilus influenzae* protein D carrier protein	
Td ADSORBED	IM	Toxoid	T d	Alum	PE		Formaldehyde Sodium chloride Water for injection
Td POLIO ADSORBED	IM	Toxoid + Inactivated	T d IPV	Alum	PE	Neomycin Polymyxin B	Bovine serum albumin Formaldehyde Polysorbate 80
TWINRIX®	IM	Inactivated + Recombinant	HA HB	Alum		Latex in plunger stopper of pre-filled syringe Neomycin Yeast protein	Amino acids Formaldehyde Polysorbate 20 Sodium chloride Water for injection
TWINRIX® Junior							
TYPHERIX®	IM	Subunit	Typh		P	Latex in plunger stopper of pre-filled syringe	Disodium phosphate dihydrate Sodium chloride Sodium phosphate dihydrate Water for injection
TYPHIM Vi®	IM	Subunit	Typh		P		Isotonic buffer solution
VAQTA®	IM	Inactivated	HA	Alum		Latex in vial stopper Neomycin	Bovine albumin DNA Formaldehyde Residual protein from cell culture Sodium borate Sodium chloride Water for injection
VARILRIX®	SC	Live attenuated	Var			Neomycin	Amino acids Human albumin Lactose Polyalcohols Water for injection

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
VARIVAX® III	SC	Live attenuated	Var			Neomycin Porcine gelatin	Fetal bovine serum Monosodium L-glutamate Potassium chloride Potassium phosphate monobasic Residual protein from cell culture Sodium chloride Sodium phosphate dibasic Sucrose Urea Water for injection
VAXIGRIP®	IM	Inactivated – split unit	Inf		Tm[1]	Egg protein Neomycin Thimerosal[1]	Disodium phosphate dihydrate Formaldehyde Potassium chloride Potassium dihydrogen phosphate Sodium chloride Sucrose Triton® X-100
ViVAXIM®	IM	Subunit + Inactivated	Typh++ (HA)	Alum	PE CH_2O	Neomycin	Disodium phosphate dihydrate Medium 199 Hanks Polysorbate 80 Sodium chloride Sodium dihydrogen phosphate dihydrate Water for injection
Vivotif®	Oral	Live attenuated	Typh			Gelatin	Amino acid mixture Ascorbic acid Dibutyl phthalate Diethyl phthalate Erythrosine FD+C red 3 Ethylene glycol Hydroxypropylcellulose-phthalate Lactose Magnesium stearate

Brand name	Route	Vaccine type	Immunogen ++	Adjuvant	Preservative	Potential allergens	Other materials
							Red iron oxide Sucrose Titanium dioxide Yellow iron oxide
YF-VAX®	SC	Live attenuated	YF			Chick protein Egg protein Gelatin Latex in stopper of diluent vial	Sodium chloride Sorbitol
ZOSTAVAX®	SC	Live attenuated	Zos			Neomycin Porcine gelatin	Bovine calf serum Monosodium L-glutamate monohydrate Potassium chloride Potassium phosphate monobasic Residual protein from cell culture Sodium chloride Sucrose Sodium phosphate dibasic Water for injection

[1] multi-dose presentation only
[2] Smallpox vaccine (dried) is not available for general use. Smallpox vaccine (frozen liquid) is not a Health Canada authorized product but will be released under Health Canada's Special Access Program if required.

- The information in this table is based on the product information available as of January 2013.
- Empty boxes indicate that there are no materials of relevance in the product.

ABBREVIATIONS (TABLE 1)

Route	
ID	intradermal
IM	intramuscular
IN	intranasal
SC	subcutaneous
Immunogen: ++ For products in which the immunogens of two different vials or chambers are combined, the contents of the second vial or chamber are noted as ++(immunogen)	
aP	acellular pertussis
ap	acellular pertussis (reduced)
BCG	Bacillus Calmette-Guérin
Chol	cholera
D	diphtheria
d	diphtheria (reduced)
Ecol	enterotoxigenic *Escherichia coli*
Hib	*Haemophilus influenzae* type b
HA	hepatitis A
HB	hepatitis B
HPV	human papillomavirus
Inf	influenza
IPV	inactivated poliomyelitis
JE	Japanese encephalitis
Men	meningococcus
Meas	measles
Mumps	mumps
Pneu	pneumococcus
Rab	rabies
Rot	rotavirus
R	rubella
TBE	tick-borne encephalitis
T	tetanus
Typh	typhoid
Var	varicella
YF	yellow fever
Zos	herpes zoster
Adjuvant	
Alum	aluminum-containing adjuvant
AS04	3-O-desacyl-4’-monophosphoryl lipid A adsorbed onto aluminum (as hydroxide salt)
MF59	squalene, polysorbate 80, sorbitan trioleate, sodium citrate, citric acid, water for inje
Preservative	
CH2O	formaldehyde
P	phenol
PE	2-phenoxyethanol
Tm	thimerosal

Products with active drug identification numbers (DIN):
The following vaccines are authorized for marketing in Canada but are not generally available:

- Epaxal® (Berna Biotech Ltd.)
- Inactivated Poliomyelitis Vaccine – IPV (Sanofi Pasteur Ltd.)
- Infanrix™- IPV/Hib (GlaxoSmithKline)
- Infanrix™-IPV (GlaxoSmithKline)
- Liquid Pedvax HIB® (Merck Canada Inc.)
- Pentacel® (Sanofi Pasteur Ltd.)
- Prevnar® (Pfizer Canada Inc.)
- Tripacel® Hybrid (Sanofi Pasteur Ltd.)
- Vivotif® L (Berna Biotech Ltd.)
- Zostavax® II (Merck Canada Inc.)

Table 2: Types and contents of passive immunizing agents available for use in Canada

- For up-to-date, complete prescribing information consult the product leaflet or information contained within the authorized product monographs available through Health Canada's Drug Product Database (http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp)
- Information about the passive immunizing agent manufacturer/distributor is available in the Appendix of Vaccine Abbreviations

Brand name	Route	Passive immunizing agent type	Protects against or treats	Preservative	Potential allergens	Other materials
Botulism Antitoxin-Behring	IV	Antitoxin	Bot	P	Equine protein	Sodium chloride Water for injection
ANTIDIPHTHERIA SERUM	IV	Antitoxin	D	P	Equine protein	Sodium chloride
GamaSTAN® S/D	IM	Immune globulin	HA Meas Var R			Glycine Human plasma protein Sodium chloride Water for injection
HepaGam B™	IM	Immune globulin	HB			Human plasma protein Maltose Polysorbate 80 Tri-n-butyl phosphate Triton® X-100
HyperHEP B® S/D	IM	Immune globulin	HB			Glycine Human plasma protein Sodium chloride Water for injection
HYPERRAB™ S/D	IM/ local	Immune globulin	Rab			Glycine Human plasma protein Sodium chloride Water for injection
HYPERTET® S/D	IM	Immune globulin	Tet			Glycine Human plasma protein Sodium chloride Water for injection

Brand name	Route	Passive immunizing agent type	Protects against or treats	Preservative	Potential allergens	Other materials
IMOGAM® Rabies Pasteurized	IM/ local	Immune globulin	Rab		Latex in vial stopper	Glycine Human plasma protein Hydrochloric acid Sodium hydroxide Sodium chloride
SYNAGIS® (palivizumab)	IM	Humanized monoclonal antibody	RSV			Glycine Histidine Mannitol Water for injection
CNJ-016™	IV	Immune globulin	Vaccinia			Maltose Polysorbate 80 Water for injection
VariZIG™	IV/ IM	Immune globulin	Var			Glycine Human plasma protein Polysorbate 80 Sodium chloride Sodium phosphate Tri-n-butyl phosphate Triton® X-100

- The information in this table is based on the product information available as of January 2013.
- Empty boxes indicate that there are no materials of relevance in the product.

ABBREVIATIONS (TABLE 2)

Route	
IM	intramuscular
IV	intravenous
Protects against or treats	
Bot	botulism
D	diphtheria
HA	hepatitis A
HB	hepatitis B
Meas	measles
R	rubella
Rab	rabies
RSV	Respiratory Syncytial Virus
T	tetanus
Var	varicella
Preservative	
P	phenol

Products with active drug identification numbers (DIN):
The following passive immunizing agent is authorized in Canada but is not generally available:

- Immune Serum Globulin (Human) (Grifols Therapeutics Inc.)

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Cat.: HP40-3/2014E-PDF ISBN: 978-1-100-23215-7 Pub.: 130578