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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840

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).

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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.

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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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842

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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

Antigen 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[2]	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° angle.

Intramuscular (IM) injections

IM injections of vaccine are administered at a 90° 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
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**
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-pepcl/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/nvshgip-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/nvshgip-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 0°C. 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/nvshgip-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 +2°C to +8°C. 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/nvshgip-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

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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/nvshgip-idemv/)

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/nvshgip-idemv/)

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Appendix 1: Vaccine storage recommendations

Cold chain should always be maintained

Vaccine	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 V = vial S = pre-filled syringe	Multi-dose vial 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 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 V = vial S = pre-filled syringe	Multi-dose vial 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 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 V = vial S = pre-filled syringe	Multi-dose vial 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	
		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