Part 1

General Guidelines

General Considerations

The goal of those concerned with immunization is the elimination of vaccine-preventable diseases. Eradication of smallpox has been achieved. Currently, global efforts are directed at the eradication of polio and the elimination of measles. Ongoing immunization programs with high vaccine coverage are needed to maintain low levels of other vaccine-preventable diseases. When the incidence of a communicable disease decreases to low levels because of successful vaccination programs, there is a potential for people to question the need to continue the programs, and this may lead to lower vaccine coverage and, inevitably, resurgence of the disease. Therefore, immunization providers must advocate for the continuation of successful programs.

An ideal vaccine would confer lifelong protection against a disease after a single dose. It would be inexpensive, stable during shipping and storage, easy to administer and without adverse effects. Researchers and vaccine manufacturers continue to work to improve vaccines; in the meantime, our existing vaccines save lives. The diseases against which vaccines protect may also change over time for reasons unrelated to vaccine programs. These factors mean that the efficacy, effectiveness and safety of vaccines and vaccination programs must be evaluated continually to ensure that Canadians achieve the greatest possible benefit.

In this *Guide*, information is presented on the immunizing agents available in Canada and their use in the prevention of communicable diseases. Recommendations on routine immunizations are discussed in some detail, and an attempt is made to answer most of the day-to-day queries from providers regarding immunization.

Because of variation in manufacturers' products, precise details of the dosage and route of administration of individual products are not usually given. Readers are referred to manufacturers' labelling and package inserts for this information. As well, the manufacturer has sought approval of the vaccine and provided evidence as to its safety and efficacy only when it is used in accordance with the product monograph. Some information in the *Guide* may differ from that in product monograph(s) and package inserts. Information in the *Guide* is based upon the best and most current publicly available scientific knowledge.

What's in a vaccine?

Vaccines are highly regulated, complex biologic products designed to induce a protective immune response both effectively and safely. The main vaccine types as well as the derivation, purpose and potential risk of vaccine constituents are summarized below. See Table 1 (page 7) for specific information on the type and key constituents of each vaccine marketed in Canada.

Immunogen: The part of the vaccine that stimulates an immune response is also the basis for classification of vaccine type, as follows:

- *Live attenuated:* The vaccine contains whole, living bacteria or viruses that induce immunity by actively replicating within the host. Since the agent replicates within the recipient, the stimulus more closely resembles that associated with natural infection, resulting in longer lasting and broader immunity than can be achieved with other vaccine types. Attenuated means the vaccine strains are weakened so that infection is usually inapparent or very mild, in marked contrast to the natural infection (see inside back cover). Live vaccines require careful storage and handling to avoid inadvertent inactivation and are contraindicated for pregnant women and people with immunodeficiencies.
- *Inactivated:* The vaccine contains killed bacteria or virus. Such vaccines pose no risk for immunocompromised persons and may induce a broad immunity since multiple antigens are present. Disadvantages include the usual need for multiple doses because the response may be weaker than that induced by live organisms and potential toxicity associated with unwanted portions of the killed organism (as was true for the whole-cell pertussis vaccine).
- *Subunit:* The vaccine contains purified products that usually come from the bacteria or virus that causes natural infection but may also be synthesized in the laboratory using recombinant technology (e.g., hepatitis B surface antigen). These products may require inactivation to prevent toxic side effects, and all are purified through a variety of steps in the manufacturing process. The end products include proteins, polysaccharides and protein-polysaccharide conjugates. Subunit vaccines have excellent safety profiles and facilitate the preparation of a variety of combination products. Disadvantages include lower immunogenicity, which sometimes requires the presence of an adjuvant and/or multiple doses.

Adjuvant: A substance added to a vaccine to enhance the immune response by degree and/or duration, making it possible to reduce the amount of immunogen per dose or the total number of doses needed to achieve immunity. The only adjuvants used in vaccines currently marketed in Canada are aluminum salts (aluminum hydroxide, aluminum phosphate or potassium aluminum sulfate), which primarily enhance the immune response to proteins. They have been shown to be safe over seven decades of use. Rarely, they may cause injection site reactions, including subcutaneous nodules, granulomatous inflammation or contact hypersensitivity. Subcutaneous rather than intramuscular deposition, as occurs when using too short a needle, may increase the risk of such reactions. After oxygen and silicon, aluminum is the third most abundant element in the environment and daily exposure occurs, primarily through food. Infant formula contains from 0.2 to 1.1 mg aluminum/litre whereas vaccines contain from 0.2 to 0.85 mg per dose. Both exposures are considered to be within the limits of safety (see Keith et al. for a more detailed discussion).

Preservatives: Chemicals (e.g., thimerosal, phenol, 2 phenoxyethanol) added to multidose, killed or subunit vaccines in order to prevent serious secondary infections as a result of bacterial or fungal contamination. In recent years there has been a great deal of opposition to the use of thimerosal, an ethyl mercury derivative, because of a theoretical risk of brain damage. Scientific evidence has refuted this risk, and it is no longer necessary for health care providers to raise this as a concern before administering influenza or hepatitis B vaccines, which may contain thimerosal. Thimerosal-free versions of both vaccines are available for use in select circumstances (see the relevant chapters in this *Guide*).

Additives: Substances other than those already mentioned may be added to vaccines for two different purposes:

- **to support the growth and purification of specific immunogens and/or the inactivation of toxins.** These include antibiotics added to prevent contamination during viral cell culture; substances needed for the growth of viruses, such as egg or yeast proteins, glycerol, serum, amino acids and enzymes; and formaldehyde used to inactivate viruses and protein toxins. Most of these reagents are removed in subsequent manufacturing steps, but minute "trace" amounts may remain in the final product. The amounts present are only of consequence for individuals who are allergic to them (see Table 1 for a listing of potential allergens in vaccines authorized for marketing in Canada). Concern has been expressed about formaldehyde because of its use as an embalming agent. However formaldehyde is also an intermediate in human metabolism, and the amount normally found in blood, even of a young infant, exceeds by 10 fold or more what is found in a dose of vaccine.
- **to confirm product quality or stability.** Compounds may be added to vaccines for a variety of manufacture-related issues: controlling acidity (pH); stabilizing immunogens through necessary steps in the manufacturing process, such as freeze drying; and preventing immunogens from adhering to the sides of glass vials with a resultant loss in immunogenicity. Examples of such additives include potassium or sodium salts, lactose, polysorbate 20 or 80, human serum albumin and a variety of animal proteins, such as gelatin and bovine serum albumin. Concerns have been expressed regarding the following:
  - Human serum albumin: There is a theoretical risk of infectious agents being present in products made from human blood. However, steps in the manufacturing process of both human albumin and vaccines that contain it greatly reduce the possibility of transmission of these agents. To date, there have been no documented cases of transmission of infectious agents by human serum albumin.
  - Gelatin: This protein may be the cause of rare hypersensitivity reactions to gelatin-containing vaccines (approximately 1 event per 2 million doses). Table 1 identifies which of the vaccines currently marketed in Canada contain gelatin. All individuals who have had an

anaphylactic reaction to one of these products should be referred to an allergist, as should individuals with a history of immediate allergic reactions to foods containing gelatin.

- Bovine reagents: 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 (see http://www.fda.gov/cber/BSE/risk.htm). In Canada, the bovine-derived reagents commonly added to vaccines included in the routine schedule are manufactured from animals considered to be free of bovine spongiform encephalopathy.

Selected references

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Offit PA, Jew RK. *Addressing parents' concerns: Do vaccines contain harmful preservatives, adjuvants, additives, or residuals?* Pediatrics 2003;112:1394-1397. URL: <www.pediatrics.org/cgi/content/full/112/6/1394>.

Table 1. Type and Contents of Vaccines Currently Approved for Use in Canada

Brand name	Mfr/ distr.	Route	Vaccine type			Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
			Vaccine type	Immunogen+	Products				
Act-HIB®	SP	IM	Subunit	Hib	Conjugate				
Actacel™*	SP	IM	Subunit	D, T, aP + (Hib)	Proteins + conjugate	Alum	PE		
Adacel®	SP	IM	Subunit	T, d, ap	Proteins	Alum	PE		
Avaxim®	SP	IM	Inactivated	HA	Killed virus	Alum	PE	Neomycin	Formaldehyde
Avaxim® – Pediatric	SP	IM	Inactivated	HA	Killed virus	Alum	PE	Neomycin	Formaldehyde
BCG Vaccine (Freeze-Dried)	SP	Intra-dermal	Live attenuated	BCG	Live bacteria				Polysorbate 80
Boostrix®*	GSK	IM	Subunit	D, T, aP	Proteins	Alum	PE		Formaldehyde
DT Polio Adsorbed	SP	IM	Subunit + inactivated	D, T, IPV	Proteins + killed virus	Alum	PE	Polymyxin B, Neomycin	Formaldehyde
Dukoral™	SBL/SP	Oral	Subunit + inactivated	Chol-Ecol-O	Proteins + killed bacteria				Saccharin
Multi dose vial Engerix®-B Single dose vial	GSK	IM	Subunit	HB	Recombinant protein	Alum	PE None	Trace thimerosal	Yeast proteins

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Eolarix™ *	GSK	SC	Live	M,R	Live virus			Neomycin	Human albumin Lactose, Dextran
Epaxal®**	BERN	IM	Inactivated	HA in Inf virosome	Killed virus		Tm		Formaldehyde
Fluviral® S/F	IDB	IM	Inactivated	Inf	Killed virus		Tm	Egg proteins	Formaldehyde
FSME - IMMUN	BAX	IM	Inactivated	TBE	Inactivated whole virus	Alum		Neomycin Gentamycin Egg Protamine sulfate Chick protein	Formaldehyde Human serum albumin Sucrose
Havrix®	GSK	IM	Inactivated	HA	Killed virus	Alum	PE	Neomycin Latex in stopper pre-filled syringes	Formaldehyde Polysorbate 20
Hiberix®*	GSK	IM	Subunit	Hib	Conjugate				Lactose
Imovax® Polio*	SP	SC	Inactivated	IPV	Killed virus		PE	Polymyxin B Neomycin, Streptomycin	Bovine serum Formaldehyde Polysorbate 80
Imovax® Rabies	SP	IM	Inactivated	Rab	Killed virus			Neomycin	Human albumin

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			Vaccine type	Immunogen+	Products				
Inactived Poliomyelitis Vaccine – IPV	SP	SC	Inactivated	IPV	Killed virus		PE	Polymyxin B Neomycin	Bovine serum Formaldehyde Polysorbate 80
Infanrix™*	GSK	IM	Subunit	D, T, aP	Proteins	Alum	PE		Formaldehyde Polysorbate 80
Infanrix™-hexa*	GSK	IM	Subunit + inactivated	D, T, aP, HB IPV + (Hib)	Proteins + killed viruses + conjugate	Alum	PE	Polymyxin B Neomycin Trace thimerosal	Yeast protein Formaldehyde Lactose Polysorbate 20 and 80 Bovine serum albumin
Infanrix™/Hib*	GSK	IM	Subunit	D, T, aP + (Hib)	Proteins + conjugate	Alum	PE		Formaldehyde Lactose Polysorbate 80
Infanrix™-IPV*	GSK	IM	Subunit + inactivated	D, T, aP IPV	Proteins + killed virus	Alum	PE	Polymyxin B Neomycin	Bovine serum Formaldehyde Polysorbate 80

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Brand name	Mfr/ distr.	Route	Vaccine type			Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
			Vaccine type	Immunogen+	Products				
Infanrix™ - IPV/Hib*	GSK	IM	Subunit + inactivated	D, T, aP, IPV + (Hib)	Protein + killed virus + conjugate	Alum	PE	Polymyxin B Neomycin	Formaldehyde Polysorbate 80 Lactose Bovine serum albumin
Influvac™	SOLV	IM/SC	Inactivated	Inf	Killed virus			Gentamicin Egg protein	Chicken protein Formaldehyde Polysorbate 80
JE-VAX®	BIKEN/ SP	SC	Inactivated	JE	Killed virus		Tm	Gelatin	Mouse serum Protein Formaldehyde
Liquid Pedvax HIB®	MF	IM	Subunit	Hib	Conjugate	Alum		Latex in stopper	
Meningitec™	BERN/ WA	IM	Subunit	Men	Conjugate	Alum			
Meningococcal Polysaccharide Vaccine, Groups A and C, Menomune® A/C	SP	SC	Subunit	Men	Polysaccharide				Lactose
Menjugate®	CHIR	IM	Subunit	Men	Conjugate	Alum			

Table 1. Type and Contents of Vaccines Currently Approved for Use in Canada

Brand name	Mfr/ distr.	Route	Vaccine type			Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
			Vaccine type	Immunogen+	Products				
Multidose vial Menomune® A/C/Y/W-135 Single dose vial	SP	SC	Subunit	Men	Polysaccharide		Tm† None	Latex in stopper	Lactose
M-M-R® II	MF	SC	Live	M, M, R	Live virus			Gelatine Neomycin Residual components of chick embryo cell cultures	Bovine Serum Glutamate Human albumin Residual protein from cell culture Sorbitol Sucrose
Mutacol™**	BERN	Oral	Live	Chol	Live bacteria				Yeast extract Lactose Aspartame
Neisvac-C™	BAX/ GSK	IM	Subunit	Men	Conjugate	Alum			
Pediacel®*	SP	IM	Subunit + inactivated	D, T, aP, IPV, Hib	Protein, killed virus + conjugate	Alum	PE	Neomycin Polymyxin B Streptomycin Latex in stopper	Bovine serum Formaldehyde Polysorbate 80

Table 1. Type and Contents of Vaccines Currently Approved for Use in Canada

Brand name	Mfr/ distr.	Route	Vaccine type	Immunogen +	Products	Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
Pediarix™*	GSK	IM	Subunit + inactivated	D, T, aP, HB, IPV	Protein + killed virus	Alum	PE	Polymyxin B Neomycin	Yeast protein Formaldehyde Polysorbate 80 Bovine serum albumin
Pentacel®	SP	IM	Subunit + inactivated	D, T, aP, IPV + (Hib)	Protein + killed virus + (conjugate)	Alum	PE	Polymyxin B Neomycin Latex in stopper	Bovine albumin Formaldehyde Polysorbate 80
Pneumo 23®	SP	IM/SC	Subunit	Pneu	Polysaccharide		P		
Multidose vial* Pneumovax® 23 Single dose vial	MF	IM/SC	Subunit	Pneu	Polysaccharide		P		
Prevnar®	WA	IM	Subunit	Pneu	Conjugate	Alum		Latex in stopper	
Priorix®	GSK	SC	Live	M, M, R	Live virus			Neomycin	Lactose
Quadracel®	SP	IM	Subunit + inactivated	D, T, aP, IPV	Protein + killed virus	Alum	PE	Polymyxin B Neomycin Latex in stopper	Bovine albumin Formaldehyde Polysorbate 80

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			Vaccine type	Immunogen+	Products				
RabAvert®	CHIR/ MF	IM	Inactivated	Rab	Killed virus			Neomycin Chlortetracycline Amphotericin B Processed gelatin	Human albumin Ovalbumin Bovine serum
Multidose vial Recombivax HB® Single dose vials	MF	IM	Subunit	HB	Recombinant protein	Alum	Tm† None	Latex in stopper	Yeast proteins Formaldehyde
Td Adsorbed	SP	IM	Subunit	T, d	Protein	Alum			Formaldehyde
Td Polio Adsorbed	SP	IM	Subunit + inactivated	T, d, IPV	Protein + killed virus	Alum	PE	Polymyxin B Neomycin	Bovine albumin Formaldehyde Polysorbate 80
Tetanus Toxoid Adsorbed	SP	IM	Subunit	T	Protein	Alum	Tm		
Tripacel®	SP	IM	Subunit	D, T, aP	Protein	Alum	PE	Latex instopper	Formaldehyde Glutaraldehyde
Twinrix®	GSK	IM	Subunit + inactivated	HB, HA	Recombinant protein + killed virus		PE	Neomycin Trace thimerosal Latex in stopper pre-filled syringes	Yeast proteins Formaldehyde Polysorbate 20

Table 1. Type and Contents of Vaccines Currently Approved for Use in Canada

Brand name	Mfr/ distr.	Route	Vaccine type	Immunogen +	Products	Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
Twinrix® Junior	GSK	IM	Subunit + inactivated	HB, HA	Recombinant protein + killed virus		PE	Neomycin Trace thimerosal Latex in stopper pre-filled syringes	Yeast proteins Formaldehyde Polysorbate 20
Typherix®	GSK	IM	Subunit	Typh-I	Polysaccharide		P	Latex in stopper pre-filled syringes	
Typhim Vi®	SP	IM	Subunit	Typh-I	Polysaccharide		P		
Vaqta®	MF	IM	Inactivated	HA	Killed virus	Alum		Neomycin Latex in stopper	Bovine albumin Formaldehyde Residual protein from cell culture
Varilrix®	GSK	SC	Live	Var	Live virus			Neomycin Latex in stopper pre-filled syringes for diluent	Human albumin Lactose
Varivax® III	MF	SC	Live	Var	Live virus			Gelatin Neomycin	Bovine serum Glutamate Residual protein from cell culture Sucrose Urea

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Brand name	Mfr/ distr.	Route	Vaccine type			Adjuvant	Preservative	Potentiel allergens (egg, antibiotic, gelatin, latex, trace of thimerosal)	Other materials
			Vaccine type	Immunogen+	Products				
Multidose vial Vaxigrip® Single dose vial	SP	IM	Inactivated	Inf	Killed virus		Tm†	Neomycin Egg protein	Formaldehyde
ViVaxim™	SP	IM	Subunit + inactivated	Typh-I + (HA)	Polysaccharide + killed virus	Alum	PE	Neomycin	Formaldehyde
Vivotif® L	BERN	Oral	Live	Typh-O	Live virus				Lactose Aspartame
Vivotif®	BERN	Oral	Live	Typh-I	Live virus			Gelatin	Lactose
YF-VAX®	SP	SC	Live	YF	Live virus			Gelatin Egg protein Latex in stopper	Chicken protein

Empty boxes indicate a lack of the specified component.

* Drug Identification Number assigned (approved for use but not currently marketed)

** Product is on the market but not currently available

† Thimerosal in multidose vial only

Notes and Abbreviations

The information in this table is based on the product's availability as of May 2006. Please consult the manufacturer for complete and up-to-date information. The National Advisory Committee on Immunization (NACI) will publish updated information as required, which will be available at www.naci.gc.ca.

Manufacturer (Mfr) and Distributor (Distr.): For some products, the distributor could be different from the manufacturer.

BAX, Baxter Healthcare Corporation; *BERN*, Berna Biotech; *BIKEN*, Biken; *CHIR*, Chiron; *GSK*, GlaxoSmithKline; *IDB*, ID Biomedical Corporation; *MF*, Merck Frosst; *SBL*, SBL Vaccine; *SP*, Sanofi Pasteur Ltd; *SOLV*, Solvay; *WA*, Wyeth Canada

Route: IM - intramuscular; SC - subcutaneous

Immunogen:

+ For products in which the immunogens of two different vials or chambers are combined, the contents of the second vial or chamber are noted as + (immunogen)

The following abbreviations are the agreed upon standards for use in Canada:

DTaP-IPV-Hib: diphtheria toxoid, tetanus toxoid, acellular pertussis, polio, *Haemophilus influenzae* type b, pediatric formulation; Tdap: tetanus toxoid, diphtheria toxoid, acellular pertussis, adult formulation; Men – meningococcus; Pneu – pneumococcus; HB: hepatitis B; Chol-Ecol-O: cholera – E.coli

IPV – poliomyelitis vaccine; Inf: influenza; HA: hepatitis A; Rab: rabies; JE: Japanese encephalitis; Typh-I : typhoid – injection; Typh-O: Typhoid – Oral; TBE; tickborne encephalitis

MMR: measles, mumps, rubella; Var: varicella; YF: yellow fever; BCG: Bacilles Calmette-Guérin

Adjuvant: Alum – aluminum-containing adjuvant

Preservative:

P – phenol; PE – 2 phenoxy ethanol; Tm – thimerosal. For the Sanofi Pasteur products, PE is not considered a preservative

The Benefits of Vaccines

Vaccines have improved the lives of every Canadian. For instance, before tetanus immunization was available, the fear of tetanus hovered over every cut and puncture wound. Older adults will easily recall the vigour with which every childhood scrape was disinfected to protect against lockjaw and memories of family or friends paralyzed by polio and summers spent in fear. In the last 50 years, immunization has saved more lives in Canada than any other health intervention. Table 2 and Figures 1 and 2 illustrate the impact of childhood vaccines on infectious diseases in Canada. Please refer to the epidemiology sections in the chapters on *Hepatitis B Vaccine* (page 189) and *Pertussis Vaccine* (page 257) for additional data and charts documenting the recent successes of immunization programs against these two vaccine-preventable diseases.

Many vaccines (and some other public health interventions) result in both a benefit to health and savings in direct medical care costs. For these vaccines, the establishment of publicly funded vaccination programs improves health and results in monetary savings. Therefore, the decision to vaccinate is straightforward. Some newer vaccines result in health benefits but do not save costs. The decision to include these vaccines in vaccination programs then depends on the willingness of society to pay for the health benefits. In general, vaccination programs compare very favourably with other health interventions (Table 3). However, it is important that new vaccination programs be evaluated carefully, and that vaccine researchers and policy makers work together to identify programs that deliver the greatest benefit for the least cost.

Selected references

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Tengs TO, Adams ME, Pliskin JS et al. *Five hundred live-saving interventions and their cost-effectiveness.* Risk Analysis 1995;15:369-90.

US National Immunization Program, Centers for Disease Control and Prevention. *Guide to contraindications to vaccinations.* URL: <http://www.cdc.gov/nip/recs/contraindications.htm#micro>.

Table 2. Incidence of Select Vaccine-Preventable Diseases in Canada – Pre-vaccine Era Compared with Five Most Recent Years

Disease	Details	Pre-vaccine era*		2000-2004**	
		5-year average annual incidence per 100,000	Peak annual number of cases	5-year average annual incidence per 100,000	Peak annual number of cases
Diphtheria	Diphtheria toxoid introduced in 1926, routine infant immunization since 1930, national notifiable diseases reporting began in 1924	1925-29 84.2	1925-29 9,010	0.0	1
Invasive *Haemophilus influenzae* type b (Hib) in children < 5 years of age	PRP vaccine introduced in 1986, currently approved Hib PRP-T and PRP-OMP conjugate vaccines introduced in 1991/92, national notifiable diseases reporting of invasive Hib disease began in 1986	1986-90 22.7	1986-90 526	0.9	17
Measles	Live vaccine approved in 1963, MMR universal infant program implemented in 1983, 2 dose MMR introduced 1996/97, no notifiable diseases reporting from 1959-68	1950-54 369.1	1950-54 61,370	0.2	199
Mumps	Vaccine approved in 1969, MMR universal infant program implemented in 1983, 2 dose MMR introduced 1996/97, no notifiable diseases reporting from 1960-85	1950-54 248.9	1950-54 43,671	0.3	202
Pertussis	Whole cell pertussis vaccine approved in 1943, acellular pertussis vaccine replaced whole cell in 1997-98, adolescent/adult acellular formulation approved in 1999	1938-42 156.0	1938-42 19,878	10.4	4,751
Paralytic poliomyelitis	IPV approved in 1955, OPV approved in 1962 and in use in Canada until 1997, IPV used exclusively from 1998-present	1950-54 17.3	1950-54 1,584	0	0

Table 2. Incidence of Select Vaccine-Preventable Diseases in Canada – Pre-vaccine Era Compared with Five Most Recent Years

Disease	Details	Pre-vaccine era*		2000-2004**	
		5-year average annual incidence per 100,000	Peak annual number of cases	5-year average annual incidence per 100,000	Peak annual number of cases
Rubella	Rubella vaccine introduced 1969, MMR universal infant program implemented in 1983, 2 dose MMR introduced 1996/97	1950-54 105.4	1950-54 37,917	0.1	29
Congenital rubella syndrome (CRS)	See Rubella above. National notifiable diseases reporting of CRS began in 1979	1979-83 2.4†	1979-83 29	0.5†	3

* Five years preceding vaccine introduction

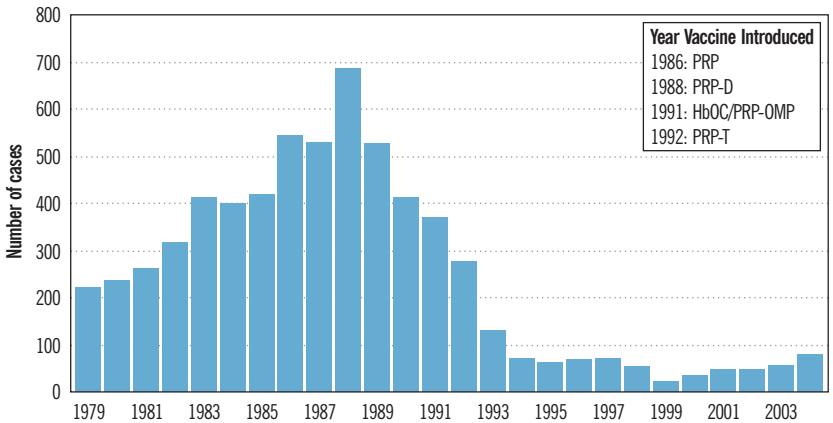
** Provisional numbers from National Disease Reporting System 2002-04

† per 100,000 live births

Table 3. Cost per Life Year Saved for Selected Vaccine Programs and Other Public Health Interventions (adapted from references)

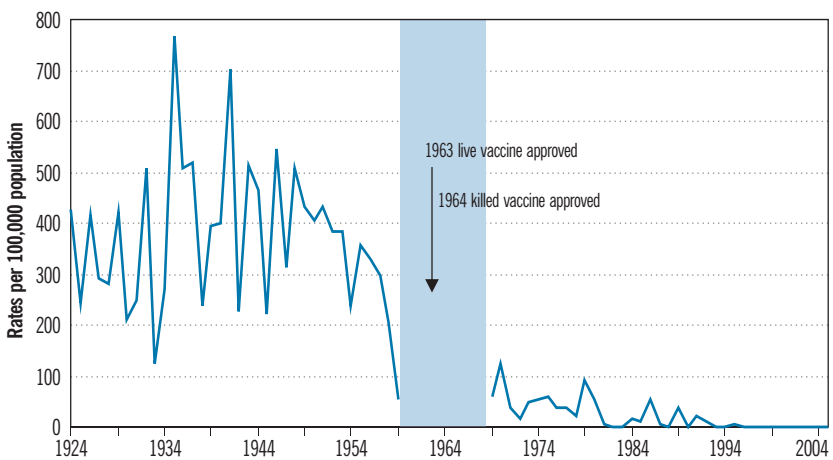
	Cost per life year saved
Vaccines	
Measles, mumps, rubella for children	< 0 ($16 saved per $ spent)
DPT for children	< 0 ($6 saved per $ spent)
Influenza for adults aged ≥ 65 years of age	< 0 ($45 saved per $ spent)
Pneumococcal polysaccharide for adults aged ≥ 65 years	< 0 ($8 saved per $ spent)
Hepatitis B screening in pregnancy and vaccination of children of carriers	$164
Varicella vaccine for children	$16,000
Conjugate pneumococcal vaccine for children	$125,000
Other interventions	
Mandatory seat belt law	$69
Chlorination of drinking water	$3,100
Smoking cessation counseling	$1,000-10,000
Bicycle helmet law	$39,000
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
Low cholesterol diet for men over age 20 and cholesterol over 4.65 mmol/L (180 mg/dL)	$360,000
Crossing control arm for school buses	$410,000
Radiation emission standard for nuclear power plants	$100,000,000

Figure 1. *Haemophilus influenzae* type b (Hib) Disease — Reported Cases, Canada, 1979-2004*



* 1979–1985: reported Hib meningitis only
1986–2004: all invasive forms (meningitis and septicemia)

Figure 2. Measles — Reported Incidence, Canada, 1924-2005



Note: measles was not nationally reportable from 1959 to 1968

National Guidelines for Immunization Practices

Preamble

The current edition of the *Guide* contains many examples of the effectiveness of provincial/territorial childhood immunization programs in Canada as carried out by both private and public providers. These include elimination of wild-type poliovirus and a decrease of over 95% in the incidence of *Haemophilus influenzae* type b and measles infections. To guarantee continued success it is essential that policy makers, program administrators and providers work together, proactively, to plan, conduct and regularly review immunization programs. Furthermore, several challenges remain, such as continued documented occurrences of "missed opportunities for immunization"; subgroups of Canadians with lower than optimal vaccine coverage; evidence of incorrect handling and storage of vaccine by providers; wide variations in the reporting of adverse events following immunization; and evidence that there is insufficient communication regarding the risks and benefits of vaccines.

Accordingly, the National Advisory Committee on Immunization (NACI) has developed guidelines for immunization practices applicable to both public and private systems of vaccine delivery. The guidelines that follow resulted from extensive consultation with provincial/territorial health authorities; medical, nursing, public health and hospital organizations; and individual providers and child advocacy groups. The original guidelines (*Canadian Immunization Guide*, 6th edition) were officially endorsed by the Canadian Paediatric Society, Advisory Committee on Epidemiology, College of Family Physicians of Canada, Canadian Medical Association, Canadian Nurses Association, Aboriginal Nurses Association of Canada, Society of Obstetricians and Gynaecologists of Canada and the Canadian Public Health Association. They have been slightly modified for this edition.

The guidelines are deliberately broad, far-reaching and rigorous. They define the most desirable immunization practices that health care providers can use to assess their own current practices and identify areas of excellence as well as deficiency. It is recognized that some of the guidelines require involvement of the provinces and territories (e.g., regarding the need to track immunizations and audit coverage levels). Furthermore, some providers/programs may not have the funds necessary to fully implement the guidelines immediately. In such cases the guidelines can act as a tool to clarify immunization needs and to facilitate obtaining additional resources in order to achieve national goals and targets.

The following terms have been used throughout:

- *Provider*: any individual, nurse or physician qualified to give a vaccine

- *Regular provider*: individual usually responsible for a given child's vaccinations
- *Child/children*: the individuals (infancy to adolescence) being considered for immunization
- *Recipient*: the individual being considered for immunization
- *Parent*: the individual(s) legally responsible for the child

These guidelines are recommended for use by all health professionals in the public and private sector who administer vaccines to or manage immunization services for Canadians. Although some guidelines will be more directly applicable to one or other setting, all providers and local health officials should collaborate in their efforts to ensure that there are high coverage rates throughout the community and thus achieve and maintain the highest possible degree of community protection against **vaccine-preventable diseases.**

Guideline 1

Immunization services should be readily available.

Immunization services should be responsive to the needs of vaccine recipients. When feasible, 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, whether public health clinics or physicians' offices, should be available during the week and at hours that are convenient for working parents. Public sector services should be available on working days, as well as during some other hours (e.g., weekends, evenings, early mornings or lunch hours).

Guideline 2

There should be no barriers or unnecessary prerequisites to the receipt of vaccines.

While appointment systems facilitate clinic planning and avoid unnecessarily long waits, appointment-only systems may act as barriers to the receipt of vaccines. People who appear on an unscheduled basis for vaccination, particularly those in hard-to-reach populations, should be accommodated when possible. Such recipients should be rapidly and efficiently screened without requiring other comprehensive health services.

A reliable decision to vaccinate an adult or a child can be based exclusively on the information elicited from the recipient or from the child's parent, and on the provider's observations and judgment about the health of the potential vaccine recipient at the time. At a minimum, this includes questioning the patient or the child's parent about:

- the recipient's current state of health;
- potential contraindications;
- reactions to previous vaccinations.

Policies and protocols should be developed and implemented so that the administration of vaccine does not depend on individual written orders or on a referral from a primary care provider.

Guideline 3

Providers should use all clinical opportunities to screen for needed vaccines and, when indicated, to vaccinate.

Each encounter with a health care provider, including those encounters that occur during hospitalization, is an opportunity to review the immunization status and, if indicated, administer needed vaccines. Physicians should consider the immunization status at every visit and offer immunization service as a routine part of that care or encourage attendance at the appropriate public health or physician clinic. At each hospital admission the vaccination record should be reviewed and, before discharge from the hospital, patients should receive the vaccines for which they are eligible by age or health status. The patient's current immunization provider should be informed about the vaccines administered in hospital. However, successful implementation requires significant improvements in record-keeping of immunization histories (see Guideline 8).

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

Guideline 4

Providers should educate parents and adult vaccine recipients in general terms about immunization.

Providers should educate people in a culturally sensitive way, preferably in their own language, about the importance of vaccination, the diseases that vaccines prevent, the recommended immunization schedules, the need to receive vaccines at recommended ages and the importance of them bringing their or their child's vaccination record to every health care visit. Parents and adult recipients should be encouraged to take responsibility for ensuring that they or their child complete the full series. Providers should answer all questions recipients may have and provide appropriate educational materials at suitable reading levels, preferably in the patient's preferred language. Providers should familiarize themselves with information on immunization provided by the appropriate health departments as well as by other sources.

Guideline 5

Providers should inform patients 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 ministries of health in many provinces and territories, and also from the Canadian Paediatric Society. Such pamphlets are helpful in answering many questions

that patients and parents may have about immunization, and they facilitate informed consent. Providers should document in the medical record that they have asked the patients and parents if they have any questions and should ensure that satisfactory answers to any questions were given.

Guideline 6

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

There are very few true contraindications to vaccination according to current Canadian guidelines, and providers must be aware of them. Accepting conditions that are not true contraindications often results in the needless deferral of indicated vaccines. Minimal acceptable screening procedures for precautions and contraindications include asking questions to elicit a history of possible adverse events following prior vaccinations and determining any existing precautions or contraindications.

Guideline 7

Providers should administer all vaccine doses for which a recipient is eligible at the time of each visit.

Available evidence indicates that most routine vaccines can be administered at the same visit, safely and effectively, including multiple injections. Some vaccines are provided in a combination format whereby more than one is given in a single injection, and others require separate injections. Unless the package insert specifically allows, vaccines should never be mixed in the same syringe.

Guideline 8

Providers should ensure that all vaccinations are accurately and completely recorded.

8.1 Data to be recorded in the patient's record at the time of vaccination

For each vaccine administered the minimum data to be recorded in the patient's record should include the name of the vaccine, the date (day, month and year) and route of administration, the anatomical site, the name of the vaccine manufacturer, the lot number, and the name and title of the person administering the vaccine.

8.2 Updating and maintaining the personal vaccination record

All providers should encourage recipients or parents to maintain a copy of their own or their child's personal vaccination record card and present it at each health care visit so that it can be updated. If a patient or parent fails to bring the card, the provider should ensure that adequate information is given so that the recipient/parent can update the card with the name(s) of the vaccine(s), the date, the provider and the facility.

8.3 Documentation for vaccines given by other providers

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

8.4 All provinces/territories should develop and maintain electronic immunization registries.

Guideline 9

Providers should maintain easily retrievable summaries of the vaccination records to facilitate age-appropriate vaccination.

Providers should maintain separate or easily retrievable summaries of vaccination records to facilitate assessment of coverage as well as the identification and recall of patients, especially children, who are delayed in the recommended immunization schedule. In addition, immunization files should be sorted periodically and inactive records placed into a separate file. Providers should indicate in their records, or in an appropriately identified place, all primary care services that each patient receives in order to facilitate scheduling with other services.

Guideline 10

Providers should report clinically significant adverse events following vaccination – promptly, accurately and completely.

All individuals who are immunized should be given instructions for post-immunization care. Prompt reporting of adverse events following vaccination is essential to guarantee vaccine safety, allowing for timely corrective action when needed, and to keep information regarding vaccine risk-benefit and contraindications up to date.

Providers should instruct parents to inform them of adverse events following vaccination. Providers should report all clinically significant events to the local public health authority, regardless of whether they believe the events are caused by the vaccine or not. Providers should fully document the adverse event in the medical record at the time of the event or as soon as possible thereafter. At each immunization visit, information should be sought regarding serious adverse events that may have occurred following previous vaccinations.

Guideline 11

Providers should report all cases of vaccine-preventable diseases as required under provincial and territorial legislation.

Providers should know the provincial/territorial requirements for communicable disease reporting. Reporting of vaccine-preventable diseases (VPD) is essential for the ongoing evaluation of the effectiveness of immunization

programs, to facilitate public health investigation of vaccine failure and to facilitate appropriate medical investigation of a patient's failure to respond to a vaccine that has been appropriately administered. Provincial data systems for VPD should be linked to electronic immunization registries.

Guideline 12

Providers should adhere to appropriate procedures for vaccine management.

Vaccines must be handled and stored as recommended in manufacturers' package inserts. The temperatures at which vaccines are transported and stored should be monitored according to provincial/territorial 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.

Providers should report usage, wastage, loss and inventory as required by provincial, territorial or local public health authorities.

Providers should be familiar with published national and local guidelines for vaccine storage and handling. Providers must ensure that any office staff designated to handle vaccines are also familiar with the guidelines.

Guideline 13

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

Providers administering vaccines should maintain a protocol that, at a minimum, discusses the appropriate vaccine dosage, vaccine contraindications, the recommended sites and techniques of vaccine administration, as well as possible adverse events and their emergency management. The *Canadian Immunization Guide* and updates, along with package inserts, can serve as references for the development of protocols. Such protocols should specify the necessary emergency equipment, drugs (including dosage), and personnel to manage safely and competently any medical emergency arising after administration of a vaccine. All providers should be familiar with the content of these protocols, their location, and how to follow them.

Guideline 14

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

Vaccines must be administered only by properly trained persons who are recognized as qualified in their specific jurisdiction. Training and ongoing education should be based on current guidelines and the recommendations of NACI and provincial and territorial ministries of health, the National Guidelines for Immunization Practices, and other sources of information on immunization.

Guideline 15

Immunization errors should be reported by providers to their local jurisdiction.

Immunization errors and related incidents should be monitored as a patient safety issue. All immunization errors should be reported by the vaccine provider to the agency or local sector that assumes accountability for the quality of immunization programs. Immunization errors commonly include an error in vaccine type, dose, site, route, person, time or schedule. Immunization-related incidents include a range of events, such as needle injury caused by failed restraint of children, immunization without consent, or fainting with a fall resulting in injury. Methods to detect immunization errors or incidents may include 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 agency or 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.

Guideline 16

Providers should operate a 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 mailed or telephone messages. All providers should identify, for additional intensive tracking efforts, patients considered at high risk of failing to complete the immunization series on schedule (e.g., children who start their series late or children who fall behind schedule).

Guideline 17

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

In both public and private sectors, 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 who are up to date). The results of the audit should be discussed by providers as part of their ongoing quality assurance reviews and used to develop solutions to the problems identified.

Communicating Effectively about Immunization

Public concern regarding vaccine safety can reduce vaccine coverage and result in resurgence of vaccine-preventable diseases. As trusted information sources, health care providers have a vital role in the continued success of immunization programs. To be most effective, providers must have skill and expertise, not only in the principles and practices of immunization but also in risk communication. This section outlines the general principles of risk communication and identifies additional resources for providers and the public.

Principles of risk communication

The goal of effective risk communication is the development of an informed decision-making partnership. The process involves both education and advocacy, and is facilitated through advance preparation by all participants, clear messaging, and an open and respectful atmosphere. An individual's perception of risk is influenced by experience as well as personal, religious and cultural contexts. Furthermore, events that are familiar, involve a natural process, seem to be under an individual's control, are of a voluntary nature or involve a decision to forgo something are generally perceived as less risky than those 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. A decision to become immunized or immunize a child clearly falls into the latter "high risk" category regardless of the true odds. Framing the risks in the right context is very important. Countering an individual's concerns by citing the greater dangers of a familiar event, like driving a car, while true, may be counterproductive.

For effective risk communication, physicians and other health care providers should attempt to do the following:

1. **Communicate current knowledge**, taking into account what an individual already knows and the level of detail requested. The process need not be time-consuming. It is useful to have varied information formats (visual, audio, printed material, Web sites) tailored to a range of educational levels and languages as appropriate to a given practice/clientele. Given the volume, accessibility and variable quality of material available on the Internet, it is also helpful to provide guidance on how to assess Web site reliability. Several excellent resources are listed at the end of this section.
2. **Respect differences of opinion about immunization.** Some individuals will express reluctance or refusal to accept immunization for themselves or their children. It is important to both gauge the strength of this stance as well as discover its underlying reasons.

3. **Represent the risks and benefits of vaccines fairly and openly.** Contrast the known and theoretical risks of vaccine with the known risks associated with the vaccine-preventable infection (see at the end of this *Guide* for a table on *Comparison of Effects of Diseases and Vaccines*). It is also important to counter the notion that vaccine-preventable diseases are gone (see box).

4. **Adopt a patient-centred approach.** Effective decision making is best done in a partnership between the provider or vaccinator and the parent or patient. Central to this is the acceptance that individuals have input into the decision to immunize and retain responsibility for their own or their child's health. A decision to do something rather than to avoid something may cause greater concern when it comes to immunizing children. It may be helpful to present the facts and then ask those responsible to consider what the child would choose, were he or she old enough to do so.

5. **Make the most of each opportunity to present clear, evidence-based messages regarding vaccines and immunizations (see box)**. Encourage questions, address misinformation, and provide valid and appropriate resources, including authoritative Web sites, for those who want more information.

Conclusion

As long as the diseases that vaccines prevent are rarely seen by the general public today, vaccine safety concerns will continue to have a high profile. Careful and timely counselling can help people to weigh the benefits of vaccines and the risks of the disease that the vaccine will prevent, as well as the small risk posed by the vaccine itself. By providing vaccines in a climate of appropriate informed consent, including discussion of commonly held misconceptions, health care providers can help ensure that immunization will maintain its status as one of the most effective preventive measures in the history of medicine.

Immunization Truths

- Immunization is the best protective strategy against vaccine-preventable diseases.
- The vaccines used in Canada are both effective and safe.
- Health authorities worldwide take vaccine safety very seriously. Expert committees in Canada investigate reports of serious adverse events following immunization.
- Vaccines do not weaken the immune system. Rather, they harness and train it to defend, rapidly, against vaccine-preventable pathogens before illness can occur.
- Vaccine-preventable infections are far more dangerous than vaccines (see the Table on *Comparison of Effects of Diseases and Vaccines* at the end of the Guide).
- The bacteria and viruses that cause vaccine-preventable diseases are not gone.
  - Diphtheria, pertussis, polio, measles, mumps, rubella, varicella, hepatitis A and B are well adapted human pathogens that, to a greater or lesser extent, are contagious and are still occurring in parts of the world.
  - Tetanus is a soil organism – it will never be eliminated.
  - *Haemophilus influenzae* type b, *Streptococcus pneumoniae* and *Neisseria meningitidis* can survive in the nose and throat and will likely never be completely eliminated.
- Unvaccinated individuals have a much greater chance of getting a vaccine-preventable disease than those who have received the vaccine. This is true even in countries where high levels of immunization provide some degree of protection to susceptible individuals (i.e., herd immunity). Three examples:
  - An outbreak of rubella occurred in 2005 among unimmunized individuals in Ontario.
  - Children in the United States who did not receive measles vaccine were 22 to 35 times more likely to get measles than immunized children.
  - Children in the United States who did not receive pertussis vaccine were almost 6 times more likely to get whooping cough than immunized children.
- When vaccine coverage drops, vaccine-preventable diseases return:
  - In Japan, pertussis vaccine coverage dropped from 90% to less than 40% because of public concern over two infant deaths that followed DPT immunization. Prior to the drop in coverage there were 200 to 400 cases of pertussis each year in Japan. From 1976 to 1979, following the marked drop in vaccine coverage, there were 13,000 cases of pertussis, of which over 100 were fatal.
  - In Ireland, measles vaccine coverage dropped to 76% following allegations of a link with autism. The number of measles cases increased from 148 in 1999 to 1200 in 2000, along with several child deaths due to the complications of measles.

References and Web resources for immunization risk communication

A. How to communicate

Spier RE. *Perception of risk of vaccine adverse events: a historical perspective.* Vaccine 2001;20:S78-84.

Stoto MA, Evans G, Bostrom A. *Vaccine risk communication.* American Journal of Preventive Medicine 1998;14(3):237-39.

Summary. Workshop on Vaccine Communication, October 5-6, 2000, Arlington, Virginia. URL: <http://www.dhhs.gov/nvpo/pubs/vcwsummary.pdf>.

Tenrreiro KN. *Time-efficient strategies to ensure vaccine risk/benefit communication.* Journal of Pediatric Nursing 2005;20:469-76.

B. What to communicate

Canadian Coalition for Immunization Awareness and Promotion. *Addressing patient concerns.* URL: <http://www.immunize.cpha.ca/english/links/hlthprv.htm> (English); <http://www.immunize.cpha.ca/francais/hcprovdf/provresf/provparf.htm> (French).

Canadian Paediatric Society. URL: <www.cps.ca>

Children's Hospital of Philadelphia Vaccine Education Center. URL: <http://www.chop.edu/consumer/jsp/microsite/microsite.jsp?id=75918>.

Gold R and Canadian Paediatric Society. *Your child's best shot: a parent's guide to vaccination*, 2nd ed. 2002. URL: <www.cps.ca/english/publications/Bookstore/YourChildsBestShot.htm>.

Immunization Action Coalition. URL: <www.immunize.org>. (Information in several formats, including video.)

National Network for Immunization Information. URL: <www.immunizationinfo.org>. *Communicating with patients about immunization*. URL: <http://www.immunizationinfo.org/healthProfessionals/resource_kit.cfm>.

C. How to evaluate Web site quality and reliability

Centers for Disease Control and Prevention. URL: <http://www.immunizationinfo.org/parents/evaluatingWeb.cfm > (tips on how to assess vaccine Web sites).

World Health Organization. URL: <http://www.who.int/immunization_safety/safety_quality/vaccine_safety_websites/en/>. Vaccine safety net – lists sites with information related to vaccine safety that meet criteria related to credibility, content, accessibility and design.

Principles of Combination Vaccines

Combination vaccine products are already available for many immunizations conducted in Canada. Diphtheria, tetanus and polio vaccines have been available as a combination product for over 30 years. Since 1996, all infants in Canada have been vaccinated against diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b (DTaP-IPV-Hib) with a single, pentavalent vaccine.

Over the past few years, the number of combination vaccine products has grown considerably, and this trend will continue with more vaccines being introduced to the routine immunization schedule for children and adults. As new products are recommended, it is important for the immunization provider to feel comfortable with the principles of combination vaccines. This chapter serves as a general overview of these principles. For details on specific combination vaccines, please refer to the individual chapters in this *Guide*.

What is a combination vaccine?

Combination vaccines are developed to protect against more than one infection. Polyvalent vaccines against multiple strains or serotypes of the same infectious agent are not considered to be combination vaccines. The term "combined vaccines" may also be used to describe the mixture of two separate vaccines in a single vial prior to administration or vaccines that are separately manufactured but combined into one product during the final packaging stages.

General principles of combination vaccines

- Combination vaccines are rigorously evaluated before approval for use in Canada. Only those combinations that are known to be safe and efficacious are recommended for routine use. For an overview of vaccine safety, including that of specific combination products, please refer to the chapter on *Vaccine Safety*, page 59.
- Ideal combination vaccines are as safe and effective as each of their single component counterparts.
- Combination vaccines should fit the currently recommended schedule, be easily stored and easy to administer.
- Combination vaccines facilitate adherence to recommended immunization schedules by reducing the number of immunization visits required as well as the number of injections a person receives.

- Combination products can potentially decrease the amount of adjuvants and preservatives when compared with multiple, single-antigen products.
- Health care providers should never combine products that are intended for separate administration.

Efficacy of combination vaccines

- The efficacy of each component in a combination vaccine is compared with established parameters of protection before approval.
- Antibody responses to specific antigens in combination products may be either stronger or weaker than those to separately administered single antigens.
- The impact of any observed changes in antibody titres is assessed against the known human protective levels of antibodies or other indicators of efficacy.
- Combination vaccines approved to date have an efficacy and safety record similar to that of single-component vaccines.
  - The addition of Hib to the combination vaccine with tetanus, diphtheria, acellular pertussis and polio did not result in diminished immune responses to the tetanus, diphtheria, acellular pertussis and polio components. The response to the Hib antigens was somewhat reduced; however, a significant impact on clinical efficacy when the vaccine was administered according to the Canadian immunization schedule was not demonstrated through post-marketing studies.

Safety of combination vaccines

- The currently available combination products in Canada have had excellent safety records.
- Ideal combination vaccines should have fewer adverse reactions or, at the very least, no more than if administering single-antigen products separately.
- The safety of each new combination product is rigorously evaluated prior to approval and compared against the safety of single-antigen products or existing combination vaccines.
- New combination vaccines help to further our knowledge regarding co-administration of antigens as combination vaccines, as they are all well evaluated before approval.
- The vaccine provider may face questions from parents about their feelings that multiple combination vaccines can weaken the immune system.

- With the refinement of vaccine development and production over past decades, 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.
- Children are naturally exposed to multiple antigens on a routine basis. They respond well to these persistent exposures with no untoward effects on their immune system.
- If multiple antigens posed a problem for the immune system, we would find that infants vaccinated with combination products had less protection against the infection than those vaccinated with single products. This has not been found.

Complexities of combination vaccines

- The efficacy and safety of each component in a combination must be evaluated separately and in its combined form, thereby increasing the complexity of pre-approval clinical trials.
- Clinically important interference between each component of a combination vaccine must be ruled out. Antibody responses to individual antigens in combination products may be diminished. Given that antibody responses are only a surrogate for clinical efficacy, assessing or estimating the clinical relevance of this is complex. In the development of new combination products, acceptable endpoints and immunization goals should be clearly defined.
- The measurement of potency and antigen content of combination products is more complex and difficult.
- Even a single, transient problem in the production of an individual component of a combination product could lead to a significant shortage in vaccine supply for multiple diseases.
- In the context of combination products, the effects of adjuvants can be difficult to assess.
- It can be difficult to determine which component is responsible for an allergic or other adverse event.
- There are usually increased costs associated with combination product procurement.

Principles of Vaccine Interchangeability

This chapter provides the health care provider with an overview of the general principles of vaccine interchangeability for the currently approved vaccines in Canada.

The principles of interchangeability are only applicable to vaccines with the same indication and specified for the same population (i.e., the same age groups). It has now become routine to have similar vaccines from different manufacturers approved for use in Canada. Several factors may necessitate giving different products to the same individual over time. When faced with vaccine shortages, deferring vaccination is not desirable: one study demonstrated that 25% of children whose vaccination had been deferred never returned for the indicated vaccine.

Factors to consider in determining potential candidate vaccines for interchangeability

- The vaccines should be approved with the same indications, specified for the same population and be equally acceptable in terms of safety, reactogenicity, immunogenicity and efficacy.
- A regularly scheduled primary or booster vaccine should not be deferred because of the lack of availability of a particular product.
- Any new regimen should be equally acceptable from a safety, efficacy and scheduling perspective.
- Even when vaccines are approved for the same indications, different manufacturers often use different production methods, antigen concentrations, stabilizers and preservatives. Each of these could affect the immunogenicity, safety or efficacy profile of the product.

Interchangeability following provincial variations in immunization schedules and products

- At present, the immunization schedules as well as the specific products used may vary across the provinces and territories.
- With immigration and migration of people between provinces and territories, issues of vaccine interchangeability have arisen with specific concern regarding measles, mumps, rubella (MMR), varicella and meningococcal conjugate vaccines.
- For DTaP-IPV-Hib, the primary immunization series of three doses given in infancy should, whenever possible, be completed with a single combination product. However, on the basis of expert opinion, if the

original vaccine is not known or not available, it is recommended that an alternative combination product be used to complete the primary immunization series. According to expert opinion and the limited data available to date, NACI recommends that the DTaP-IPV-Hib and DTaP-IPV combination vaccine products currently approved for sale in Canada may be used interchangeably for the 18 month and 4-6 year booster, respectively.

- On the basis of expert opinion, the MMR products currently available in Canada may be used interchangeably if required.
- On the basis of expert opinion, the varicella products currently available in Canada may be used interchangeably if required

Development of evidence for interchangeability

Ideally, as new combination vaccines become available, there should be randomized controlled clinical trials evaluating their interchangeability with existing products. This has only been done in limited instances to date. Most of our knowledge regarding interchangeability has been gathered as a result of situations of vaccine shortages, immigration to areas where different vaccine products are available, 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 early childhood vaccines, every opportunity should be taken to encourage further research in this area.

Vaccine Administration Practices

Appropriate vaccine administration is a key element to ensuring 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 federal/provincial/territorial policies and procedures, where these exist, also guide vaccination practices. All providers of vaccines 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. The following information provides general guidance for vaccine administration practices.

Pre-vaccination counselling

Prior to vaccination, the vaccine provider should ensure that the vaccine recipient is capable of consenting to the procedure or that, when required, an appropriate guardian or substitute decision maker is present to give consent. Information regarding the risks and benefits of both receiving and not receiving the vaccination should be provided, along with the opportunity to ask questions. Minor side effects that occur frequently and any adverse effects that are severe should be discussed with the individual, guardian or substitute decision maker. This person should be asked about all relevant contraindications and precautions to receiving the vaccine. Care should be taken to determine whether there is a risk of anaphylaxis, such as previous anaphylaxis or severe allergy to any of the vaccine components or latex, if contained in the vaccine products. For more information, please refer to the *General Contraindications and Precautions* chapter, page 73.

Vaccine administration

Vaccines should be administered using the recommended dose, route, site and schedule to optimize vaccine effectiveness and reduce the risk of local reactions or other adverse events.

Vaccine preparation

- Vaccine inspection: The vaccine identification label and expiry date on the vaccine vial or package should be checked by the vaccine provider before administration. Vaccines should not be used beyond their expiry date. If only the month and year are provided for the expiry date, the vaccine can be used to the end of that month. Multi-dose vials should be labelled with the date of first entry into the vial and, unless otherwise specified by the manufacturer, should be discarded after 30 days

of the date of first entry. Before use, vaccine vials should be inspected for any irregularities, e.g., particulate matter, damage or contamination. Vaccines should be mixed with a careful swirling motion until a uniform suspension is achieved prior to administration.

- Vaccine reconstitution: Vaccines requiring reconstitution, i.e., a lyophilized product that is mixed with a diluent, should be mixed only with the diluent supplied for the vaccine unless otherwise permitted by the manufacturer.
- Pre-loading vaccines in syringes: Ideally, a vaccine should be withdrawn from the vial by the vaccine provider administering the vaccine. Pre-loading syringes with vaccine is 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 in the hospital setting where vaccines are drawn up and labeled in the pharmacy may be considered. In addition, to facilitate timely and efficient administration of a single vaccine to a large number of people in an immunization clinic setting, pre-loading of syringes may be considered. However, if implemented, this practice should be limited to these settings and should include the following: 1) prior agreement on how professional accountability can be ensured if different people pre-load and administer the vaccine, 2) data on stability of pre-loaded product for a specified time period and 3) maintenance of the cold chain.

Syringe and needle selection

- Syringe selection: A separate, sterile syringe should be used for each injection, and different vaccines should not be mixed in the same syringe unless specified by the manufacturer as part of the reconstitution and administration procedure. Depending on the dosage, a 3 mL or 1 mL syringe should be selected.
- Needle selection: Needle selection should be based on the route of administration, individual's age, size of the muscle mass and viscosity of the vaccine:
  - For intradermal (ID) injections, a 26-27 gauge needle is recommended.
  - For subcutaneous (SC) injections, a 25 gauge, 1.6 cm (5/8”) needle is recommended.
  - For intramuscular injections (IM) a 22-25 gauge needle that is long enough to reach muscle is recommended:
    - 2.2 cm (7/8”) to 2.5 cm (1”) for infants
    - 2.2 cm (7/8”) to 2.5 cm (1”) for toddlers and older children
    - 2.5 cm (1”) to 3.8 cm (1½”) for adolescents and adults

The needle should be inserted as far as possible into the muscle. A larger bore needle (e.g., 22 gauge) may be required when administering viscous or larger volume products such as immune globulin.

Restraint

After informed consent, the process of vaccine administration should be shared with the individual, and restraint procedures should be explained. The parent or guardian should hold a child with specific instructions on restraint positioning. Failed restraint can result in inaccurate dose, inappropriate depth of injection or injury to the individual being immunized and/or vaccine provider.

Injection site, route and technique

Vaccines and other biologic products are injected via ID, SC or IM routes.

- ID injections:
  - ID injections are usually administered on the flexor surface of the forearm.
  - The bevel of the needle should be turned upwards and at an angle parallel to the forearm.
  - The needle is inserted so that the bevel penetrates the skin. If done correctly, a small bleb should be observed at the injection site upon injection of the vaccine.
- SC injections: SC injections are usually given at a 45° angle into subcutaneous tissue of the upper triceps area of the arm.
- IM injections:
  - IM injections are administered at a 90° angle into the vastus lateralis muscle (anterolateral thigh) in infants < 1 year of age and the deltoid muscle of anyone ≥ 1 year of age (unless the muscle mass is not adequate). Appropriate site selection is important to avoid inadvertent injection into a blood vessel or injury to a nerve. Some vaccine providers prefer to pull back on the plunger (aspiration) to determine whether the needle has entered a blood vessel. There are no studies that have assessed the need for aspiration prior to IM injection of vaccines in relation to vaccine safety. As well, the syringes provided for immunization may not allow aspiration.
  - The buttock should not be used for active immunization. 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 mobilized. The buttock is an acceptable site for administration of immune globulin when large volumes are adminis-

tered, but appropriate site selection of the gluteal muscle is necessary to avoid injury to the sciatic nerve.

- Vaccines containing adjuvants are to be injected intramuscularly. If inadvertently injected subcutaneously or intradermally, increased inflammation, induration or granuloma formation may occur.

Please see Table 1, which outlines the route of administration of all vaccines approved for use in Canada, in the *General Considerations* chapter, page 7.

Multiple injections

There are no contraindications to giving multiple vaccines at the same clinic visit, and all opportunities to immunize should be utilized. Giving multiple injections at one visit helps to ensure that children are up to date with the vaccines required for their age. 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:

- Vaccines prepared in separate syringes should be labelled in order to identify which vaccine each syringe contains. The site of administration of each vaccine should be recorded.
- Separate limbs should be used if two IM injections are required. If more than two injections are required, two injections may be administered into the same muscle separated by at least 2.5 cm (1").
- Vaccines that are known to cause more stinging and/or pain should be given last.

Techniques to decrease pain and anxiety

Pain associated with immunizations is generally described as mild and short-lived, and no specific pain reduction strategies are recommended for routine use. However, the following strategies can be considered for individuals who are particularly concerned about immunization pain.

- Swaddling, holding or sucking on a pacifier.
- Breastfeeding infants or offering sweet-tasting solutions such as oral sucrose or glucose.
- Distraction techniques, such as books, video games, cartoons, movies, bubble and party blowers for older children; children can be instructed to "blow away the pain" using party blowers, windmills or bubbles.

- Pharmacologic agents such as EMLA (eutectic mixture of local anesthesia, consisting of 2.5% lidocaine and 2.5% prilocaine), Ametop® gel (4% amethocaine) and vapocoolants (e.g., Fluori-Methane). Studies have demonstrated that EMLA does not affect the immunologic response to MMR, DTaP-IPV-Hib (Pentacel®), hepatitis B (Recombivax®) or Bacille Calmett-Guérin (BCG) vaccinations. EMLA needs to be applied approximately 60 minutes before the injection. Ametop® gel produces anesthesia within 30 to 40 minutes and has been shown not to interfere with the immunologic response to MMR vaccine. Vapocoolants are effective immediately after application.

Techniques to decrease anxiety in adolescents and adults are important to minimize the risk of fainting. These techniques include ensuring that the temperature in the room is comfortable, avoiding long line-ups in mass immunization clinics and administering the vaccine while the person is seated. Patients who appear very anxious should be observed while seated until anxiety has resolved after the immunization.

After the vaccination

After vaccination, vaccine recipients should be counselled on common side effects and the reporting and management of these reactions. Vaccine providers should identify and observe individuals who are particularly anxious about receiving the vaccine. Individuals with presyncopal symptoms such as pallor or sweating should sit or lie down until symptoms resolve. A study using the American Vaccine Adverse Reporting System found that 63% of syncopal events occurred within 5 minutes of vaccination, and 89% occurred within 15 minutes. It is therefore prudent to keep the person in the clinic for 15 minutes after vaccination. This will also facilitate the management of the rare anaphylactic event. All vaccination providers should have the necessary training and equipment to manage anaphylactic events Please refer to the *Anaphylaxis: Initial Management in Non-Hospital Settings* chapter, page 80.

Infection prevention and control (IPC)

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

- The vaccine vial should be uncapped, wiped with a suitable disinfectant (e.g., isopropyl alcohol) and allowed to dry prior to withdrawal of vaccine into the syringe.
- Before injection, the skin should be cleansed with a suitable antiseptic and allowed to dry.
- A separate, sterile needle and syringe should be used for each injection.

- Hand hygiene should be performed 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. Glove use during immunization is not routinely recommended, unless the skin on the vaccine provider's hands is not intact. The Health Canada (now the Public Health Agency of Canada) document on Infection Control Guidelines, *Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care,* provides information on IPC precautions.
- Additional practices recommended during immunization include the following:
  - Needles used during immunization should not be recapped after use.
  - Used syringes and needles should be immediately and carefully disposed of in a container designed for this purpose and should never be laid down on the work surface.
  - Used syringes with attached needles and empty or expired vaccine vials should be disposed of according to local waste management legislation or guidelines.

Occupational health

- All vaccine providers should be offered hepatitis B vaccine. Post-immunization serologic testing should be obtained to ensure that there is an adequate antibody response. Please refer to the *Hepatitis B Vaccine* chapter, page 189, for more information.
- Procedures for accidental exposure to blood or body fluids should be in place and understood by vaccine providers.

Vaccine administration check list

- Is the vaccine indicated according to the recommended immunization schedule and the individual's immunization history?
- Has the appropriate consent been obtained?
- Are there any contraindications to vaccination?
- Has the expiry date been checked?
- Has the vaccine provider washed his or her hands or used an alcohol-based hand sanitizer?
- Has the vaccine been appropriately reconstituted and/or mixed?
- Are the dose and route of administration correct?
- Is the appropriate needle gauge and length being used in the correct site?
- Has the appropriate documentation been completed?
- Have post-vaccination instructions been given to the vaccine recipient?

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Storage and Handling of Immunizing Agents

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.

The province or territory should follow Public Health Agency of Canada guidelines to ensure that the manufacturer monitors the cold chain during the shipment of vaccine. Also, the province or territory should have a standard for monitoring shipments to regions, public health units and private offices. Manufacturer and NACI recommendations generally specify that most products should be stored at temperatures from +2° to +8° C. Exceptions exist (e.g., yellow fever) for which the recommended storage conditions are –30° to +5° C, as outlined in the manufacturer's product leaflets.

The term "cold chain" as used in this statement refers to all equipment and procedures used to ensure that vaccines are protected from inappropriate temperatures and light, from the time of transport from the manufacturer to the time of administration.

The effects of exposure to adverse environmental conditions, such as freezing, heat and light, are cumulative. Data are available to indicate that certain products remain stable at temperatures outside of +2° to +8° C for specified periods of time, but mechanisms rarely exist for monitoring the effect of cumulative exposures. Additionally, different products are often transported and stored in the same container. Therefore, it is recommended that all biologics for immunization be maintained at +2° to +8° C at all times, unless otherwise specified in the product leaflet. Management of products that have been exposed to adverse conditions should be guided by specific instructions pertaining to the conditions from the vaccine supplier.

Monitoring of the vaccine cold chain is required to ensure that biologics are being stored and transported at recommended temperatures. Testing of product potency or seroconversion rates as indicators of cold chain integrity are rarely feasible.

Refer to the product leaflet of each immunizing agent for specific instructions related to storage and handling. The following general principles apply.

Multidose vials

Multidose vials should be removed from the refrigerator only to draw up the dose required and should be replaced immediately. Although the practice of drawing vaccines and leaving them in the refrigerator in advance of administration is strongly discouraged (see page 39 in the *Vaccine Administration Practices* chapter), two exceptions are noted:

- Pre-loading of syringes in the hospital setting where vaccines are drawn up and labeled in the pharmacy. Strict adherence to cold chain procedure for transport of the vaccine to the ward and patient bedside is required.
- Pre-loading of syringes in an immunization clinic setting. This may be considered in order to facilitate the flow of the clinic. Proper labeling and adherence to cold chain is required

Vaccine providers should observe strict aseptic technique when using multidose vials. Multidose vials should be dated once entered and used only for the period of time specified in the manufacturer's product leaflet. If no directions are given the vaccine should not be used beyond 30 days after initial entry into the vial.

Lyophilized (freeze-dried) vaccines

For optimal potency, freeze-dried vaccines (e.g., measles, mumps rubella [MMR], varicella, Bacille Calmette-Guérin [BCG], *Haemophilus influenzae* type b) should be reconstituted immediately before use with the diluent provided for that purpose. Reconstituted vaccines, including yellow fever vaccine, should be used within 1 hour of reconstitution; if unused, they should be discarded. There are slight variations in the time intervals recommended by specific manufacturers, and users should refer to the product leaflet to guide timing of reconstitution.

Light exposure

MMR, varicella and BCG vaccines should be protected from light at all times by storage of the vials in the cartons provided. After reconstitution, if vaccines are not used immediately, they **must** be kept at +2º to +8º C, protected from light and used within the time frame recommended in the product leaflet.

Freezing

Vaccine providers are reminded that the maintenance of cold chain also requires that vaccines not be exposed to temperatures lower than those recommended. Liquid inactivated and adsorbed vaccines should not be used if they have been frozen. These include Tdap, DTaP, DT, DTaP-Polio, DT-Polio, Td, Td-Polio, hepatitis A and B vaccines, influenza, pneumo-

coccal and meningococcal vaccines. Before use, liquid vaccines should be inspected and should not be used if the usual appearance is altered or a temperature recording device shows that the vaccine was exposed to temperatures below zero.

Expiry

Vaccines should not be used beyond their expiry date. For expiry dates specified as month/year, products are deemed to expire on the last day of the specified month. The error of administration of expired vaccine should be reported to the local public health authority.

Disposal of spoiled or expired vaccines

All vaccines that cannot be used because of expiry or adverse environmental exposure should be returned to the source for appropriate recording of returns and disposal or should be appropriately disposed of according to local or regional standards.

Refrigerators

The temperature in frost-free refrigerators may cycle widely and should be monitored to ensure that cycling is within the acceptable range. Special maximum-minimum thermometers are commercially available for purchase and are useful for most office storage. Vaccine providers should record daily current maximum and minimum refrigerator temperatures and contact the local public health unit if vaccines are exposed to temperatures outside the recommended range. More expensive, constant chart-recording thermometers with alarms are appropriate for larger vaccine storage depots. Non-frost-free refrigerators should be defrosted regularly and immunizing agents stored in a functioning refrigerator during the defrosting process. Refrigerators older than 10 years are more likely to malfunction and to have breaks in the seal around the door, leading to temperature instability. Half-size/under the counter/bar refrigerators are less reliable than full-size kitchen refrigerators. Vaccine providers in private practice will discover that the cost of replacing ageing bar refrigerators with newer and full-size equipment is offset by the savings in hydroelectric power and staff time dealing with reporting and fixing cold chain breaks.

Placement of full, plastic water bottles in the lower compartment and door shelves of the refrigerator and ice packs in the freezer compartment will help stabilize temperatures, especially in the event of a power failure.

Recommended office procedures

The following office procedures should be implemented to ensure that storage of vaccines is optimized:

- Designate and train a specific staff person to be responsible for managing vaccines.
- Post storage and handling guidelines on the refrigerator.
- Use insulated storage containers with ice packs for transport of vaccines; to avoid freezing, do not place vaccine packages in direct contact with ice packs. Practitioners transporting vaccines out of the office (e.g., to housebound seniors) should observe these cold chain precautions as well.
- When transporting vaccines, keep a log of pre- and post-transport vaccine temperatures and the specific batches transported.
- Place newly delivered vaccines into the refrigerator immediately upon delivery to the office.
- 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.
- Place a maximum-minimum thermometer on the middle shelf of the fridge.
- Read, record and re-set the thermometer at least once daily.
- Secure the electrical cord from the fridge to the wall outlet to prevent accidental power interruptions.
- Ensure that the fridge door does not accidentally swing open by installing a fail-safe (e.g., Velcro™) closing mechanism.
- Do not store food or biologic specimens in the same fridge as vaccines.
- Rotate stock so that vaccines with the earliest expiry date are at the front of the shelf. Place expired vaccine into a marked box in the refrigerator for appropriate disposal, based on consultation with local public health authorities.
- Vaccine should only be removed from the refrigerator immediately prior to administration.
- If refrigerator malfunction is suspected on the basis of temperature readings, obtain servicing immediately and store the vaccine in an alternative refrigerator in the meantime.
- In the event of an identified cold chain break, seek advice from your local public health authority about whether the vaccine(s) may continue to be used; while awaiting advice, keep the vaccines stored in appropri-

ate cold chain conditions and ensure that they are not administered until a determination has been made by the public health authority.

- When a cold chain break is identified after vaccine has been administered, consult with the local health department about management of the situation. Information required to assess the circumstances will include the name of the vaccine(s), and the duration and temperatures of exposure. People immunized with vaccines whose potency is likely to have been jeopardized may need to be tested for serologic evidence of immunity or be re-vaccinated.

Ongoing cold chain monitoring should be integrated into immunization practice. Periodic cold chain surveys are worthwhile to evaluate awareness, equipment and practices as well as the frequency of breaks in the cold chain during transport from depots and storage in peripheral offices. These should be undertaken by provincial/territorial and local immunization programs.

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Timing of Vaccine Administration

For most products that require more than one dose or booster doses for full immunization, intervals longer than those recommended between doses do not lead to a reduction in final antibody concentrations. Therefore, as a general rule, *interruption of a series of vaccinations for any reason does not require starting the series over again, regardless of the interval elapsed.* By contrast, doses given at less than the recommended interval may result in less than optimal antibody response and should not be counted as part of a primary series.

There are obvious practical advantages to giving more than one vaccine at the same visit, especially for infant immunization schedules, for travel immunization or when there is doubt that an individual will return for further doses of vaccine. No increase in the frequency or severity of clinically significant side effects has been observed. The immune response to each antigen is generally adequate and comparable to that found in persons receiving these vaccines at separate times.

Simultaneous administration of childhood vaccines (diphtheria, tetanus, acellular pertussis [DTaP]; inactivated poliovirus [IPV]; *Haemophilus influenzae* type b [Hib]; measles, mumps, and rubella [MMR]; varicella; pneumococcal conjugate and hepatitis B vaccine) is encouraged for children who are the recommended age to receive these vaccines and for whom no contraindications exist. If not given during the same visit as other live virus vaccines, administration of two live vaccines should generally be separated by at least 4 weeks. A number of vaccines that deliver protection against more than one disease (i.e., combination vaccines) are available and approved for use in Canada.

Simultaneously administering pneumococcal polysaccharide vaccine and inactivated influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions. Therefore, simultaneous administration is strongly recommended for all persons for whom both vaccines are indicated.

Different formulations of vaccine against the same disease (e.g., pneumococcal conjugate and pneumococcal polysaccharide vaccine or meningococcal conjugate and meningococcal polysaccharide vaccine) cannot be given simultaneously, and a minimum time interval should elapse between the administration of the two formulations.

Vaccines administered simultaneously should be given using separate syringes at separate sites unless otherwise specified by the manufacturer, with consideration being given to the precautions that apply to each individual vaccine.

MMR vaccine can decrease the immunologic response to tuberculin skin testing, resulting in false-negative results. Therefore, tuberculin skin tests should be given either on the same day as MMR immunization or at least 4-6 weeks later. The effect of other live virus vaccines such as varicella and yellow fever vaccines on tuberculin reacitivity is currently unknown, and no recommendations for postponement of tuberculin skin testing can be made at this time.

Please refer to the specific vaccine chapters in this *Guide* for further information.

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Recent Administration of Human Immune Globulin Products

Passive immunization with products of human origin can interfere with the immune response to live viral vaccines. For measles vaccine and varicella vaccine, the recommended interval between immune globulin (Ig) or other blood products and subsequent immunization varies from 3 to 11 months, depending on the specific product and dose given, as shown in Table 4 (page 54).

For an optimum response to rubella or mumps vaccine given as individual components, there should be an interval of at least 3 months between administration of Ig or blood products and immunization. If given as combined measles, mumps and rubella (MMR) vaccine, as is the usual circumstance in Canada, longer intervals, as recommended in Table 4, should be followed to ensure that there is an adequate response to the measles component.

For women susceptible to rubella who are given Rh Ig in the peripartum period, MMR should be administered as soon as possible following delivery to increase the likelihood that these susceptible women get vaccinated. Serologic testing should be done 2 months later and non-immune women should be re-vaccinated. After receipt of an Rh Ig product, an interval of 2 months should elapse before varicella vaccine is administered to varicella-susceptible women.

If administration of an Ig preparation becomes necessary after varicella or MMR or any of the individual MMR component vaccines have been given, interference can also occur. If the interval between administration of any of these vaccines and subsequent administration of an Ig preparation is < 14 days, immunization should be repeated at the interval indicated in Table 4, unless a serologic test conducted after this recommended interval (given in the Table) indicates immunity. If the Ig product is given > 14 days after the vaccine, immunization does not have to be repeated.

Studies have found no evidence that Ig administration interferes with the response to inactivated vaccines, toxoids or the live vaccines for yellow fever or polio. Orally administered polio vaccine is no longer used in Canada. Yellow fever vaccine is not affected by either the simultaneous or previous use of Ig preparations. The background antibody level for typhoid is low in Canada, and therefore an Ig preparation produced in Canada is unlikely to interfere with typhoid immunization. Because there is little interaction between Ig preparations and inactivated vaccines or the live vaccines specified above, these vaccines can be given before, concurrently or after an Ig preparation has been used. The vaccine and Ig preparation should be given at different sites. Dukoral™ (oral, inactivated travellers' diarrhea and cholera vaccine) is the only vaccine currently marketed in Canada for protec-

tion against cholera and, as noted previously for other inactivated vaccines, no interference should be expected when Ig is administered.

A humanized, monoclonal anti-respiratory syncytial virus (RSV) antibody (palivizumab) is available for prevention of respiratory syncytial virus infection in high-risk infants and young children. This product contains only antibody to RSV and therefore will not interfere with the immune response to vaccines; it can be administered at the same time at a separate site.

Table 4. Guidelines for the Interval Between Administration of Immune Globulin Preparation or Blood Products and MMR or Varicella Vaccines*

Product	Dose	Interval (months)
General products†		
Immune globulin (Ig)	0.02-0.06 mL/kg	3
	0.25 mL/kg	5
	0.50 mL/kg	6
Intravenous immune globulin (IVIg)	160 mg/kg	7
	320 mg/kg	8
	640 mg/kg	9
	> 640-1280 mg/kg	10
	> 1280-2000 mg/kg	11
Plasma and platelet products	10 mg/kg	7
Reconstituted RBCs	10 mg/kg	3
Washed RBCs	10 mg/kg	0
Agent-specific products		
Hepatitis B immune globulin (HBIg)	0.06 mL/kg	3
Rabies immune globulin (RabIg)	20 IU/kg	4
RSV Ig (palivizumab)	15 mg/kg/month	0
Rh immune globulin (RhIg)	300 μg	2**
Tetanus immune globulin(TIg)	250 units	3
Varicella immune globulin (VarIg)	12.5 units/kg	5

* This table was originally developed for guidance related to the use of measles vaccines. It has been generalized to include recommendations related to the use of varicella vaccine.

† RBC = red blood cells

** Based on expert opinion: for women susceptible to rubella who are given Rh Ig in the peripartum period, MMR should be administered as soon as possible following delivery and serologic testing done 2 months later to assess the immune response.

Immunization Records

Vaccines administered to an individual should be recorded in three locations:

- the personal immunization record held by the person or his or her parent/guardian;
- the record maintained by the health care provider who gave the immunization; and
- the local or provincial registry.

Each method of recording should include the following:

- trade name of the product;
- disease(s) against which it protects;
- date given (day, month and year);
- dose;
- site and route of administration;
- manufacturer;
- lot number;
- name and title of person administering the vaccine.

Pre-printed, peel-off labels and bar coding of products will facilitate such recording. Manufacturers are encouraged to produce these labels and to bar code products. Immunization registries should have mechanisms that will allow bar coded information about the products to be read into the database.

Personal immunization records: Each person who is immunized should be given a permanent personal immunization record. Individuals should be instructed to keep the record in a safe place and bring it to immunization visits. Parents should maintain these records on behalf of their children and pass them on to their children at the appropriate time, such as when they are leaving home. Immunization records may be required for children to attend school or child-care centres. Adults may be required to produce these records in order to work in certain professions, such as health care, teaching or occupations requiring foreign travel. Relevant information, such as rubella and hepatitis B serology or tuberculin skin test results, can also be recorded in the personal immunization record.

Health care provider records: Health care providers must also maintain a record of all vaccinations provided. In addition to information about vaccinations given, the health care provider's record should include all relevant serologic data (e.g., rubella serologic results, hepatitis B surface antibody titres) and should document adverse events following immunization as well as contraindications, exemptions or reasons for deferring vaccination. It is recommended that a summary of immunizations, serologic results and any significant adverse vaccine reactions be stored in an easily retrievable man-

ner that permits regular checking and updating of the individual's immunization status (i.e., immunization information should not be archived in a medical record). Electronic medical records used by health care providers should have the capacity to collect and easily retrieve all required vaccination information. Vaccine providers should forward the immunization information to other providers and/or to agencies, such as public health, as appropriate or required by legislation.

Immunization registries: There are several advantages to maintaining immunization records in a registry. On an individual level, immunization registries prevent immunizations already given by another health care provider from being duplicated.

A comprehensive immunization registry system will serve the following functions:

- facilitate the timely, accurate recording of all relevant immunization information regardless of where and by whom the vaccines were administered;
- identify children and adults who are overdue for immunizations and generate reminders and recalls for these individuals;
- allow health care providers to review immunization status at each encounter in a confidential, secure manner and produce immunization records for their patients;
- provide data for public health professionals to assess immunization rates, and plan and evaluate targeted interventions for populations with less than optimal immunization rates.

Where immunization registries exist, immunization providers should be aware of legislative or other requirements to report immunization information to these registries. Incomplete information can significantly decrease the benefits derived from an immunization registry. Strategies should be employed to maximize participation by health care providers.

Refer to the *National Guidelines for Immunization Practices,* page 22, for additional information about the use and maintenance of immunization records.

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