Influenza Immunization Pocket Guide

For Health Care Providers

2022-2023

The purpose of this pocket guide is to serve as a tool for health care providers to learn more about seasonal influenza vaccines in Canada and make strong recommendations to their patients.

Vaccination is an important component to help manage healthcare capacity during the influenza season in the fall and winter months, especially in the context of ongoing COVID-19 activity and community transmission of other respiratory viruses.

This pocket guide references recommendations made in the Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023 from the National Advisory Committee on Immunization (NACI).

This pocket guide will include information on who should and should not receive the influenza vaccine, vaccine co-administration, recommended doses, and available vaccine products.

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Who should receive the influenza vaccine?

All individuals 6 months of age and older who do not have contraindications, should receive the annual influenza vaccine. According to NACI, particular focus should be placed on the following groups of people:

People at high risk of severe disease, influenza-related complications, or hospitalization

- All children 6–59 months of age
- Adults and children with the following chronic health conditions:
  - cardiac or pulmonary disorders (includes bronchopulmonary dysplasia, cystic fibrosis, and asthma);
  - diabetes mellitus and other metabolic diseases;
  - cancer, immune-compromising conditions (due to underlying disease, therapy, or both, such as solid organ transplant or hematopoietic stem cell transplant recipients);
  - renal disease
  - anemia or hemoglobinopathy
  - neurologic or neurodevelopment conditions (includes neuromuscular, neurovascular, neurodegenerative, neurodevelopmental conditions, and seizure disorders [and, for children, includes febrile seizures and isolated developmental delay], but excludes migraines and psychiatric conditions without neurological conditions);
  - morbid obesity (body mass index [BMI] of 40kg/m^2 and over); and
  - children 6 months to 18 years of age undergoing treatment for long periods with acetylsalicylic acid, because of the potential increase of Reye's syndrome associated with influenza
- Pregnant individuals
- People of any age who are residents of nursing homes and other chronic care facilities
- Adults 65 years of age and older; and
- Indigenous peoples

People capable of transmitting influenza to those at high risk

- Health care and other care providers in facilities and community settings who, through their activities, are capable of transmitting influenza to those at high risk
- Household contacts, both adults and children, of individuals at high risk, whether or not the individual at high risk has been vaccinated:
  - household contacts of individuals at high risk
  - household contacts of infants less than 6 months of age, as these infants are at high risk but cannot receive influenza vaccine
  - members of a household expecting a newborn during the influenza season
- Those providing regular child care to children 0-59 months of age, whether in or out of the home
- Those providing services within closed or relatively closed settings to people at high risk (e.g., crew on a ship)

Additional populations:

- People providing essential community services
- People who are in direct contact with poultry infected with avian influenza during culling operations

Who should not receive the influenza vaccine?

Influenza vaccination should usually be postponed in:

- People with serious acute illnesses until their symptoms have abated
  - Note: Vaccination should not be delayed because of minor or moderate acute illness, with or without fever. Immunizers should refer to NACI's **Guidance on the use of influenza vaccine in the presence of COVID-19** document for amended advice during the COVID-19 pandemic.

All influenza vaccines* should not be administered to:

- People who have had an anaphylactic reaction to a previous dose of influenza vaccine;
- People who have had an anaphylactic reaction to any of the vaccine components of a specific influenza vaccine, with the exception of egg
  - Note: Consideration may be given to offering a patient another influenza vaccine that does not contain the implicated component, in consultation with an allergy expert.
- People who have developed Guillain-Barré Syndrome (GBS) within 6 weeks of a previous influenza vaccination, unless another cause was found for GBS.

* *Influenza vaccines include: IIV (inactivated influenza vaccine), RIV4 (recombinant quadrivalent influenza vaccine) and LAIV (live attenuated influenza vaccine)*

LAIV4 (quadrivalent live attenuated influenza vaccine) should not be administered to:

- People with immune-compromising conditions, due to underlying disease, therapy, or both
  - Note: This excludes children with stable HIV infection on antiretroviral therapy (ART) and with adequate immune function.
- People with severe asthma (defined as currently on oral or high-dose inhaled glucocorticosteroids or active wheezing) or medically attended wheezing in the 7 days prior to the proposed date of vaccination.
  - Note: LAIV is not contraindicated for people with a history of stable asthma or recurrent wheezing which is not active.
- Children less than 24 months of age, due to increased risk of wheezing
- Children 2 to 17 years of age currently receiving aspirin or aspirin-containing therapy, because of the association of Reye's syndrome with aspirin and wild-type influenza infection
- Pregnant individuals
  - Note: LAIV is not contraindicated in breastfeeding (lactating) individuals.

Additional precautions for LAIV4

- LAIV4 should not be administered until 48 hours after antiviral agents active against influenza (e.g., oseltamivir, zanamivir) are stopped.
- Antiviral agents, unless medically indicated, should not be administered until 2 weeks after receipt of LAIV4 so that the antiviral agents do not kill the replicating vaccine virus.
- Significant nasal congestion might impede delivery of LAIV4 to the nasopharyngeal mucosa.
  - Therefore, IIV can be administered or LAIV4 can be deferred until congestion is resolved.
- LAIV4 recipients should avoid close association with people with severe immune-compromising conditions (e.g., bone marrow transplant recipients requiring isolation) for at least 2 weeks following vaccination, because of the theoretical risk for transmitting a vaccine virus and causing infection.
- LAIV4 recipients who are less than 18 years of age should avoid the use of aspirin containing products for at least 4 weeks after receipt of LAIV4.

Co-administration of influenza vaccine with other vaccines

As of September 2021, all seasonal influenza vaccines, including LAIV4, may be administered **at the same time as, or any time before or after, administration of other vaccines** (either live or inactivated). This includes COVID-19 vaccines for people 5 years of age or older.

Based on expert opinion, NACI recommends that LAIV4 can be given together with or at any time before or after the administration of any other live attenuated or inactivated vaccine. However, NACI recognizes that some vaccine providers may continue to choose to give LAIV4 and other live vaccines separated by at least 4 weeks as a professional preference.

For more information regarding vaccine co-administration, please refer to **Timing of Vaccine Administration** of the Canadian Immunization Guide.

How to co-administer more than one injection

When administering more than one injection at a single clinic visit, it is preferred to vaccinate in different limbs. If this is not possible, injections given in one limb should be separated by a distance of at least 2.5cm (1 inch).
A separate needle and syringe should be used for each injection.

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RECOMMENDED DOSAGE

The dose and route of administration vary by influenza vaccine product.

Age group	Number of doses required	IIV3-SD[a] or IIV4-SD[b] (IM)	IIV4-cc (Flucelvax® Quad) (IM)	IIV3-Adj (Fluad Pediatric® (6–23 months) or Fluad®) (IM)	IIV4-HD (Fluzone® High-Dose Quadrivalent) (IM)	RIV4 (Supemtek™) (IM)	LAIV4 (FluMist® Quadrivalent) (intranasal)
6-23 months	1 or 2 *	0.5 mL **	0.5 mL	0.25 mL	-	-	-
2-8 years	1 or 2 *	0.5 mL	0.5 mL	-	-	-	0.2 mL (0.1 mL per nostril)
9-17 years	1	0.5 mL	0.5 mL	-	-	-	0.2 mL (0.1 mL per nostril)
18-59 years	1	0.5 mL	0.5 mL	-	-	0.5 mL	0.2 mL (0.1 mL per nostril)
60-64 years	1	0.5 mL	0.5 mL	-	-	0.5 mL	-
65+ years	1	0.5 mL	0.5 mL	0.5 mL	0.7 mL	0.5 mL	-

Abbreviations:

IIV3-Adj: adjuvanted trivalent inactivated influenza vaccine;

IIV4-cc: quadrivalent mammalian cell-culture based inactivated influenza vaccine;

IIV4-HD: high-dose quadrivalent inactivated influenza vaccine;

IIV3-SD: standard-dose trivalent inactivated influenza vaccine;

IIV4-SD: standard-dose quadrivalent inactivated influenza vaccine;

RIV4: quadrivalent recombinant influenza vaccine;

IM: intramuscular;

LAIV4: quadrivalent live attenuated influenza vaccine.

(a) IIV3-SD formulations (Agriflu® and Influvac®) are authorized, but will not be available for use in Canada during the 2022-2023 influenza season.

(b) Afluria® Tetra (5 years and older), Flulaval® Tetra (6 months and older), Fluzone® Quadrivalent (6 months and older), Influvac® Tetra (3 years and older).

*Children 6 months to less than 9 years of age receiving a seasonal influenza vaccine for the first time in their life should be given 2 doses of influenza vaccine, with a minimum interval of 4 weeks between doses. Children 6 months to less than 9 years of age who have been properly vaccinated with one or more doses of seasonal influenza vaccine in the past should receive 1 dose of influenza vaccine per season thereafter.

**Evidence suggests moderate improvement in antibody response in infants, without an increase in reactogenicity, with the use of full vaccine doses (0.5 mL) for unadjuvanted inactivated influenza vaccines. This moderate improvement in antibody response without an increase in reactogenicity is the basis for the full dose recommendation for unadjuvanted, inactivated vaccine for all ages.

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CHOICE OF VACCINE PRODUCT

Population	Type(s) of influenza vaccine
Children 6-23 months	• **IIV4-SD** or **IIV4-cc** is recommended for this age group • If **IIV4-SD** is not available, any **IIV3-SD** or **IIV3-Adj** is recommended
Children **without** immune compromising or chronic health conditions, 2-17 years	• **IIV4-SD**, **IIV4-cc**, or **LAIV4** can be used • Any of the above quadrivalent vaccine formulations are recommended. If a quadrivalent formulation is unavailable, **IIV3-SD** should be used
Children **with** immune compromising conditions, with the exception of stable HIV infection*	• **IIV4-SD** or **IIV4-SD** is recommended • If **IIV4-SD** or **IIV4-cc** are not available, **IIV3-SD** is recommended
Children with severe asthma, medically attended wheezing in the previous seven days, or who are on aspirin or aspirin-containing therapy	• **IIV4-SD** or **IIV4-SD** is recommended • If **IIV4-SD** or **IIV4-cc** are not available, **IIV3-SD** is recommended
Children with other chronic health conditions	• **IIV4-SD, IIV4-cc, LAIV4,** and **IIV3-SD** can all be used without contraindications
Adults 18-59 years **without** chronic health conditions	• **IIV3-SD, IIV4-SD, IIV4-cc, RIV4, LAIV4**** can all be used unless contraindicated
Adults 18-59 years **with** chronic health conditions	• **IIV3-SD, IIV4-SD, IIV4-cc,** and **RIV4** are recommended • Please see the list on page one under the heading **People at high risk of severe disease, influenza-related complications, or hospitalization** for a list of chronic health conditions
Adults 60-64 years	• **IIV3-SD, IIV4-SD, IIV4-cc, RIV4** can all be used without contraindications
Adults 65+	• If available, **IIV4-HD** should be used for persons 65+ • If **IIV4-HD** is not available, **IIV3-SD, IIV3-Adj, IIV4-SD, IIV4-cc,** or **RIV4** can be used
Pregnant persons	• An age-appropriate **quadrivalent** or **trivalent IIV** should be used • **LAIV** should not be used
Healthcare workers	• Age-appropriate **trivalent** and **quadrivalent IIV** or **RIV** vaccines are recommended unless contraindicated • **LAIV** should not be used

* i.e., if the child is treated with HAART (highly active antiretroviral therapy) (for at least 4 months) and has adequate immune function;

** There is some evidence that IIV may provide better efficacy than LAIV in healthy adults

References: Centers for Disease Control and Prevention. Types of Influenza Viruses. (2021.) https://www.cdc.gov/flu/about/viruses/types.htm

National Advisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022-2023. (2022.) https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023/naci-2022-2023-statement.pdf

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Influenza Vaccine Technologies Factsheet

Influenza is a respiratory disease in humans that can cause mild to severe illness, which can lead to hospitalization, complications, and death.

Influenza in humans is caused by two main types of influenza viruses: influenza A and influenza B. Luckily, we have influenza vaccines that can help protect us against seasonal influenza. This document will discuss and explain the current vaccine technologies used this 2022-2023 influenza season in Canada.

Categories of Influenza Vaccines in Canada

There are **three categories of influenza vaccines** (commonly known as flu shots) offered in Canada: inactivated influenza vaccines (IIV), recombinant influenza vaccines (RIV), and live attenuated influenza vaccines (LAIV).

- **Inactivated influenza vaccines (IIV)** use an inactivated (killed) version of the flu virus in the vaccine. They are given as an intramuscular (IM) injection.
- **Recombinant influenza vaccines (RIV)** teach your body to recognize a small protein on the surface of the influenza virus. Similar to IIV, it does not contain the live virus. They are given as an intramuscular (IM) injection.
- **Live attenuated influenza vaccines (LAIV)** use an attenuated (weakened) form of the live flu virus in the vaccine. They are given as a nasal spray.

In the chart below, we can see that there are different formulations and types of IIV, RIV and LAIV. All are proven to be safe and effective.

Influenza vaccine category	Formulation	Type	Current NACI* abbreviation
Inactivated influenza vaccine (IIV)	**Trivalent (IIV3)**	• Adjuvanted, IM administered, egg-based	**IIV3-Adj**
	Quadrivalent (IIV4)	• Standard dose, IM administered, egg-based	**IIV4-SD**
		• Standard dose, IM administered, cell culture-based	**IIV4-cc**
		• High dose, IM administered, egg-based	**IIV4-HD**
Recombinant influenza vaccine (RIV)	**Quadrivalent (RIV4)**	• Recombinant, IM administered	**RIV4**
Live attenuated influenza vaccine (LAIV)	**Trivalent (LAIV3)**	• Nasal spray, egg-based	**LAIV3**
	Quadrivalent (LAIV4)	• Nasal spray, egg-based	**LAIV4**

* National Advisory Committee on Immunization

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Formulations of Influenza Vaccines

Every year, the World Health Organization (WHO) monitors and predicts which influenza strains will be most prevalent in a given influenza season. Once the strains are decided upon, they are incorporated into the **trivalent** influenza vaccines and **quadrivalent** influenza vaccines.

Trivalent influenza vaccines protect against three different influenza virus strains. Trivalent influenza vaccines include three of the most common influenza strains predicted to be circulating in a given influenza season. These vaccines typically include two strains of influenza A and one strain of influenza B.

Quadrivalent influenza vaccines protect against four different influenza virus strains. Quadrivalent influenza vaccines include four of the most common influenza virus strains predicted to be circulating in a given influenza season. These vaccines typically include two strains of influenza A and two strains of influenza B.

Types of Influenza Vaccines

Standard-dose influenza vaccines provide protection against influenza and are offered for persons 6 months of age and older. They contain a standard amount of influenza virus antigen, the part of a vaccine that triggers your immune system to create protective proteins called **antibodies**. In the case of influenza vaccines, the antibodies created specifically target influenza viruses to protect you against future infections. For standard-dose influenza vaccines, they provide enough antigen so that individuals aged 64 and under can gain better protection against influenza.

High-dose influenza vaccines contain four times the amount of antigen than the amount contained in standard-dose influenza vaccines. High-dose influenza vaccines are specifically made and recommended for persons 65+ to improve their immune response to the vaccine. The additional antigen present in the high-dose vaccines helps persons 65+ produce a strong enough immune response to get better protection against influenza.

Adjuvanted influenza vaccines contain an adjuvant, an ingredient added to some vaccines to help produce a stronger immune response in vaccine recipients. Adjuvants have been safely used in vaccines for over 70 years and have a good safety record. Adjuvanted influenza vaccines are specifically made and recommended for children 6-23 months and persons 65+ to improve their immune response to the vaccine. The adjuvant in the vaccine may help children 6-23 months and persons 65+ produce a strong enough immune response to get better protection against influenza.

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Types of Vaccine Manufacturing

Egg-based influenza vaccine manufacturing has been used for the past 70 years and is the most common way influenza vaccines are made. This process uses influenza viruses that are grown in chicken eggs to create influenza vaccines. Influenza viruses are injected into a chicken egg and left for several days. This gives the viruses time to make copies of themselves. The influenza viruses are then collected from the eggs and either inactivated (killed) for use in IIVs, or weakened for use in LAIVs. Egg-based influenza vaccines are safe for use in persons with egg allergies as safety data has shown that the risk of having an adverse reaction to an egg-based influenza vaccine is low.

Cell culture-based influenza vaccine manufacturing uses influenza viruses that are grown in mammalian (animal) cells to create influenza vaccines. Influenza viruses are injected into mammalian cells that are grown in the lab, and left for several days. This gives the viruses time to make copies of themselves. The fluid that contains the influenza viruses is then collected. The viruses are then inactivated (killed) for use in IIVs.

Recombinant influenza vaccine (**RIV**) manufacturing uses the hemagglutinin (HA) protein (an antigen) located on the surface of the influenza virus to create influenza vaccines. To create the HA protein, scientists take the genetic code for the HA protein and combine it with a baculovirus (a virus that does not infect humans). The baculovirus is then introduced to a lab-grown cell, and passes on the genetic information for how to create the HA protein. The lab-grown cell uses this genetic material to create many HA proteins. These HA proteins are then collected and purified in the lab. The purified hemagglutinin proteins are used to create RIVs. Because the HA protein is not a living influenza virus, RIVs cannot give you influenza. **As well, RIVs contain three times the amount of antigens contained in standard-dose vaccines**.

Another way to think about how RIVs are made is comparing it to a car manufacturing plant. Let's say you want to create a hood for a new car model and need the blueprints to do so. An automobile engineer (the influenza virus) has the blueprints (the genetic code) for the hood (the HA protein) and gives the blueprints to the department head at a car manufacturing plant (the baculovirus). The department head would then pass the blueprints to a line supervisor (the lab-grown cell) so that the line supervisor and their unit can begin manufacturing the hood in mass quantities. By the end of this process, the hoods are taken from the manufacturing line and incorporated into a car (the RIV).

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How Influenza Vaccines are Administered

Method 1: Intramuscular (IM) Injection

IM injections are administered in a person via their muscle. This requires a needle. Children under one year of age are usually given the IM injection in their thigh, whereas IM injections are usually administered in the upper arm (deltoid) in persons over the age of one. All influenza vaccines are given as an IM injection, with the exception of LAIVs.

Method 2: Nasal Spray

Nasal spray is administered in a person via each nostril. It does not require a needle. Only LAIVs are given as a nasal spray.

References

World Health Organization. Types of seasonal influenza vaccines. (2010.)
https://www.who.int/europe/news-room/fact-sheets/item/types-of-seasonal-influenza-vaccine

Yale Health. Standard Vaccine (quadrivalent) vs. High Dose Vaccine (quadrivalent). (2021.)
https://yalehealth.yale.edu/standard-vaccine-quadrivalent-vs-high-dose-vaccine-quadrivalent

Dr. British K. Tosh for Mayo Clinic. High-dose flu vaccines: How are they different from other flu vaccines? (2022.)
https://www.mayoclinic.org/diseases-conditions/flu/expert-answers/fluzone/faq-20058032

Centers for Disease Control and Prevention. High-Dose Flu Vaccine: High-dose flu vaccine, brand name Fluzone High-Dose Quadrivalent. (2022.)
https://www.cdc.gov/flu/prevent/qa_fluzone.htm

Centers for Disease Control and Prevention. Adjuvants (2022.)
https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html

Centers for Disease Control and Prevention. Adjuvanted Flu Vaccine: Flu Vaccine with Adjuvant, brand names Fluad and Fluad Quadrivalent (2022.)
https://www.cdc.gov/flu/prevent/adjuvant.htm

Centers for Disease Control and Prevention. How Flu Vaccines are Made (2022.)
https://www.cdc.gov/flu/prevent/how-fluvaccine-made.htm#:~:text=Egg%2Dbased%20vaccine%20manufacturing%20is,nasal%20spray%20flu%20vaccine%E2%80%9D)

National Advisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022-2023. (2022.)
https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023/naci-2022-2023-statement.pdf

Vaccine Knowledge Project. Types of Vaccine (2021.)
https://vk.ovg.ox.ac.uk/vk/types-of-vaccine