

## FOCUS ON

# Influenza Vaccines for the 2021-2022 Influenza Season



September 2021

## Purpose

This document is intended to provide an overview of the publicly-funded influenza vaccines that are available in Ontario as part of the [Universal Influenza Immunization Program](#)<sup>1</sup> (UIIP) for the 2021-2022 influenza season. It focuses on:

- The egg-based standard-dose quadrivalent vaccine (QIV) for individuals five years of age and older: **Afluria® Tetra**.
- The cell-based standard-dose quadrivalent vaccine for individuals two years of age and older: **Flucelvax® Quad**.
- The vaccines available for adults 65 years of age and older only:
  - A high-dose quadrivalent vaccine (QIV-HD): **Fluzone® High-Dose Quadrivalent**; and
  - A standard-dose adjuvanted trivalent vaccine (TIV-adj): **Fluad®**.

## Available Influenza Vaccines

Most vaccine products provided through the UIIP this season are quadrivalent (QIV), meaning that they contain hemagglutinin antigen (HA) for each of the four influenza strains recommended by the World Health Organization (WHO) for the 2021-2022 northern hemisphere influenza season (i.e., an influenza A(H3N2) and A(H1N1) strain and two influenza B strains, one from each B virus lineage [B/Yamagata and B/Victoria]). The four standard-dose QIVs contain 15 mcg of HA for each strain, whereas the high-dose quadrivalent (QIV-HD) – available only for adults 65 years of age and older – contains 60 mcg of HA for each strain.

In addition to the QIV products, adjuvanted trivalent vaccine (TIV-adj) is also provided through the UIIP this season for adults 65 years of age and over, which contains 15 mcg of HA for three influenza strains (i.e., an influenza A(H3N2) and A(H1N1) strain but only one influenza B strain from the B/Victoria lineage).

Note that the live attenuated influenza vaccine will not be available as part of the UIIP for the 2021-2022 influenza season. The vaccines available through the UIIP for people 6 months of age and over are outlined in Table 1.

**Table 1. Vaccines available through the UIIP for the 2021-2022 influenza season**

Ages	Type of influenza vaccines	Influenza vaccine products
6 months to 1 year	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent
2 years to 4 years	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent Flucelvax® Quad ( <b>new for 2-8 year olds for 2021-2022</b> )
5 years to 64 years	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent Flucelvax® Quad Afluria® Tetra ( <b>new for 2021-2022</b> )
65 years and older	High-dose quadrivalent (QIV-HD) Adjuvanted trivalent (TIV-adj) Standard-dose quadrivalent (QIV)	Fluzone® High-Dose Quadrivalent ( <b>new for 2021-2022*</b> ) Fluad® ( <b>new for 2021-2022</b> ) FluLaval Tetra Fluzone® Quadrivalent Flucelvax® Quad Afluria® Tetra ( <b>new for 2021-2022</b> )

\*In previous seasons, Fluzone® High-Dose was available only as a trivalent vaccine.

# New Influenza Vaccines Available in Ontario

## Afluria® Tetra

[Afluria® Tetra](#)<sup>2</sup> (Seqirus Inc., Kirkland, Quebec) is an egg-based, split virion, quadrivalent inactivated influenza vaccine. Afluria® Tetra contains a standard dose of hemagglutinin antigen (15 mcg).

### Key Points Regarding the Use of Afluria® Tetra

- In Canada, Afluria® Tetra is authorized for use in children and adults aged five years or older.
- Afluria® Tetra is considered equivalent to other standard dose quadrivalent influenza vaccines available through the UIIP.
- As with other inactivated vaccines, Afluria® Tetra can be given to pregnant women.<sup>3</sup>
- The Canadian Immunization Guide states that egg allergy is not a contraindication to influenza vaccination, and individuals with egg protein allergies can receive any age-appropriate influenza product (egg-based or cell-culture based).<sup>4</sup>

## Flucelvax® Quad

[Flucelvax® Quad](#)<sup>5</sup> (Seqirus Inc., Kirkland, Quebec) is a mammalian cell-culture based, quadrivalent, inactivated influenza vaccine. Flucelvax® Quad was part of the Ontario UIIP in the 2020-2021 season, but only for children and adults nine years of age and older. As of March 8, 2021, it is authorized for use in children and adults two years of age and older.

### Key Points Regarding the Use of Flucelvax® Quad

- In Canada, Flucelvax® Quad is licensed for use in children and adults two years of age and older.
- Flucelvax® Quad is considered equivalent to other standard dose quadrivalent influenza vaccines available through the UIIP.
- Although Flucelvax® Quad is grown in cells of canine origin, allergy to dogs is not a contraindication to its use.
- As with other inactivated influenza vaccines, Flucelvax® Quad can be given to pregnant women.<sup>3</sup>
- The Canadian Immunization Guide states that egg allergy is not a contraindication to influenza vaccination, and individuals with egg protein allergies can receive any age-appropriate influenza product (egg-based or cell-culture based).<sup>4</sup>
- For additional information, see the National Advisory Committee on Immunization (NACI) [Supplemental Statement – Mammalian Cell Culture-Based Influenza Vaccines](#).<sup>6</sup>

## Fluad®

[Fluad](#)<sup>7</sup> (Seqirus Inc., Kirkland, Quebec) is an egg-based, surface antigen, trivalent inactivated influenza vaccine that is adjuvanted with MF59C.1 (an oil-in-water emulsion composed of squalene as the oil phase, stabilised with the surfactants polysorbate 80 and sorbitan trioleate, in citrate buffer). Fluad® contains a standard dose of hemagglutinin antigen (15 mcg) for each of three influenza strains recommended by the WHO. Fluad® was not available in the UIIP in the 2020-2021 season, but has been part of the UIIP in previous seasons for adults 65 years of age and older.

## Fluzone® High-Dose Quadrivalent

[Fluzone® High-Dose Quadrivalent](#)<sup>8</sup> (Sanofi Pasteur Limited, Toronto, Ontario) is an egg-based, split virion, quadrivalent inactivated influenza vaccine. Fluzone® High-Dose Quadrivalent contains a high dose of hemagglutinin antigen (60 mcg) for each of the four influenza strains recommended by the WHO for the northern hemisphere's 2021-2022 influenza season.

### Key Points Regarding the Use of Fluzone® High-Dose Quadrivalent

- In Canada, Fluzone® High-Dose Quadrivalent is authorized for use only in adults 65 years of age or older.
- The recommended dose of Fluzone® High-Dose Quadrivalent is **0.7mL** (compared to only 0.5mL for the standard-dose QIVs).

## Influenza Vaccines for Adults 65 Years of Age and Over

For the 2021-2022 influenza season, one high-dose quadrivalent vaccine (QIV-HD), one adjuvanted trivalent vaccine (TIV-adj), and four standard-dose quadrivalent vaccines (QIV) are available in Ontario through the UIIP for adults 65 years of age and older.

## High-Dose Quadrivalent Influenza Vaccine

### Canadian Recommendations Regarding High-Dose QIV

The [NACI Statement on Seasonal Influenza Vaccine for 2021-2022](#)<sup>3</sup> has provided the following recommendation for adults 65 years of age and older regarding high-dose QIV:

At the individual-level decision-making, “IIV-HD (*high-dose QIV*) should be used over IIV-SD (*standard-dose QIV*), given the burden of influenza A(H3N2) disease and the good evidence of IIV3-HD (*high-dose TIV*) providing better protection compared to IIV3-SD (*standard-dose TIV*) in adults 65 years of age and older.”

### Vaccine Effectiveness of High-Dose QIV

A [phase 3 randomized clinical trial](#)<sup>9</sup> involving 2,670 adults 65 years of age and older compared the safety and immunogenicity of the high-dose QIV (QIV-HD) to that of two high-dose trivalent vaccines, each containing a different influenza B strain (TIV-HD1 and TIV-HD-2) over one influenza season. The results demonstrated that the hemagglutination inhibition antibody responses of the QIV-HD were non-inferior to those induced by the TIV-HD1 and TIV-HD2 for the three shared strains, and superior for the

additional B-lineage strain. The authors concluded that the addition of a second B-lineage strain did not inhibit the immunogenicity induced by the other three strains or compromise the vaccine’s tolerability.

## Standard-Dose Adjuvanted Trivalent Vaccine

### Canadian Recommendations Regarding Standard-Dose Tiv-Adj

The [NACI Statement on Seasonal Influenza Vaccine for 2021-2022](#) does not include specific recommendations for the individual-level use of the TIV-adj.<sup>3</sup>

### Vaccine Effectiveness of Standard-Dose Tiv-Adj

There are currently no studies that have directly compared the effectiveness of TIV-adj to standard-or high-dose QIVs. A [literature review](#)<sup>10</sup> published by NACI in May 2018 concluded that:

“There is fair evidence that the MF59-adjuvanted Fludax<sup>®</sup> may be effective at reducing the risk of hospitalization for influenza and influenza complications in the elderly compared to unvaccinated individuals (Grade B Evidence);

There is insufficient evidence that Fludax<sup>®</sup> is effective at reducing the risk of hospitalization for influenza and influenza complications in the elderly compared to those who received unadjuvanted trivalent inactivated subunit vaccine (Grade I Evidence); and

There is no identified evidence on how the high-dose vaccine (*TIV-HD*) directly compares to the MF59-adjuvanted Fludax<sup>®</sup> (Grade I Evidence).”

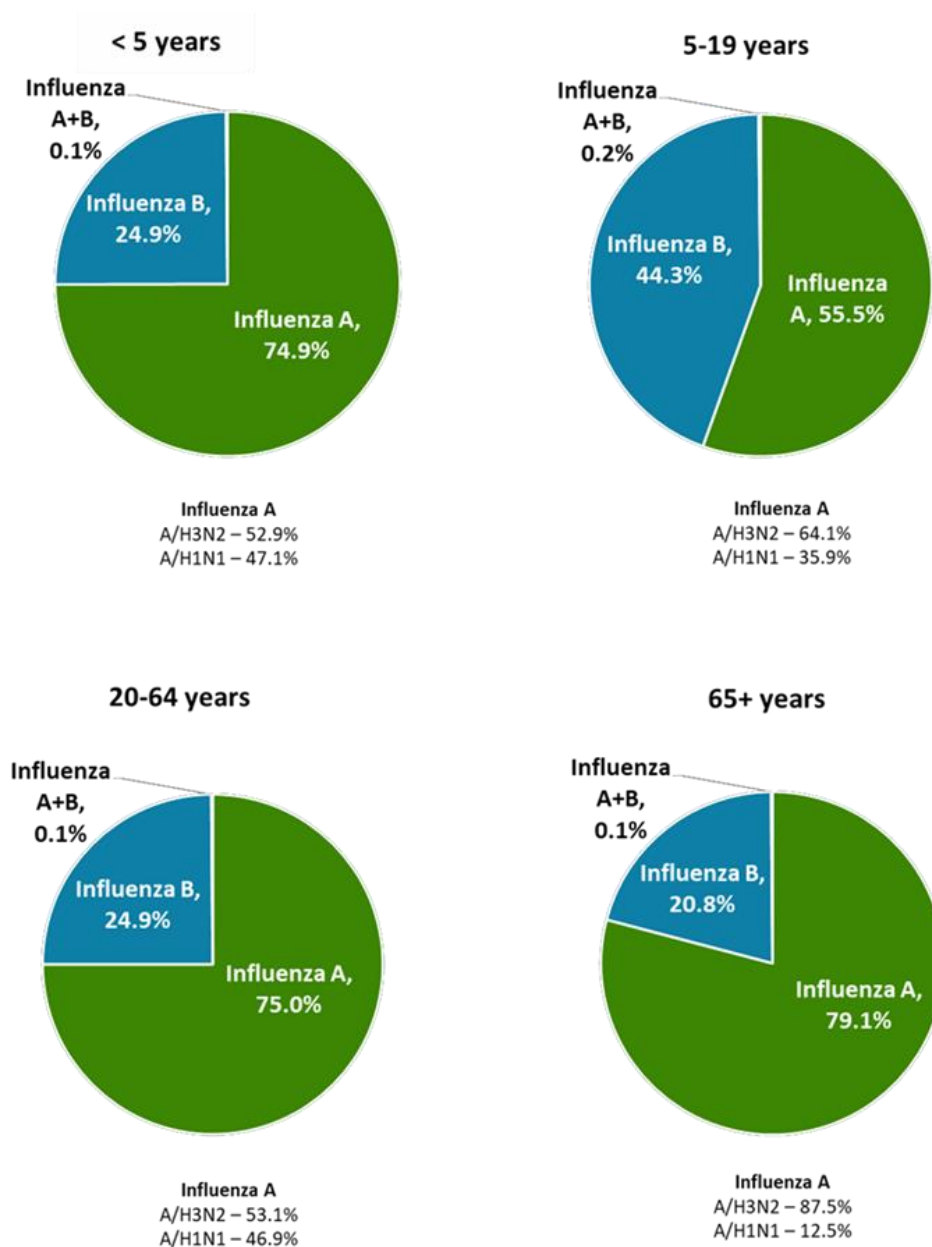
### Burden of Influenza A (H3N2) Compared To Influenza B

[Figure 1](#) illustrates the proportion of laboratory-confirmed influenza cases by type, sub-type and age reported through Ontario’s reportable disease information system (the integrated Public Health Information System (iPHIS)) averaged over nine influenza seasons (2010–2011 to 2019–2020).<sup>11</sup> The figure illustrates that the distribution of strains varies by age. In adults 65 years of age and over, 79.1% of strains were influenza A and only 20.8% were influenza B. Further subtyping of a subset (41.7%) of laboratory confirmed influenza A strains among these older adults revealed 87.5% were A(H3N2) and only 12.5% were influenza A(H1N1). Thus, in adults 65 years of age and older in Ontario, the greatest burden of influenza disease is due to influenza A (H3N2).

### Trivalent Influenza Vaccines May Provide Some Protection against the Opposite B-Lineage Strain

Some recent studies (e.g., [McLean HQ et al.](#), [Pebody R et al.](#), [Ohmit SE et al.](#), [Beyer WEP et al.](#))<sup>12-15</sup> have demonstrated protection from the influenza B lineage in the vaccine against the opposite B lineage, referred to as cross-protection; however, cross protection may not always occur and may vary by season, age and past vaccination history. Examples of cross protection can be seen in Canadian data from the Sentinel Practitioner Surveillance Network. In the 2017–2018 influenza season ([Skowronski D et al.](#)),<sup>16</sup> the B strain that circulated was predominantly B/Yamagata; the interim adjusted vaccine effectiveness against influenza B was 55% (95% CI: 38% to 68%) for both QIV and TIV together. The TIV contained B/Victoria (i.e., not the circulating strain) and TIV represented more than two-thirds of the vaccine doses distributed through the publicly-funded programs in the Canadian provinces that participated in the vaccine effectiveness study suggesting that there was some cross-protection.

**Figure 1. Proportion of influenza cases by type and subtype for influenza A, by age group: Ontario, 2010–2011 to 2019–2020 influenza seasons**



**Data source:** Ontario Ministry of Health, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario on July 31, 2020.

**Notes:** The data only represent laboratory-confirmed influenza cases reported to public health and recorded in iPHIS. Influenza A subtype information is only available for 37.2% of influenza A cases. The possibility of duplicates exists because duplicate sets were not identified and/or excluded unless they were resolved prior to data extraction either at the local or provincial level.

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