Influenza Vaccines for the 2020–2021 Influenza Season

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 (UIIP) for the 2020–2021 influenza season. It focuses on:

- the cell-culture based influenza vaccine (Flucelvax® Quad) being used this influenza season for the first time in Ontario; and
- the vaccines available for adults 65 years of age and over.

Available Vaccines

Most vaccine products provided through the UIIP this season are quadrivalent, meaning they contain an A(H3N2) and A(H1N1) strain and two influenza B strains, one from each B virus lineage (B/Victoria and B/Yamagata). The exception is the high-dose influenza vaccine for adults 65 years of age and over, which is trivalent and contains an A(H3N2), A(H1N1) and only one B strain (from the B/Victoria lineage). The high-dose product has a higher hemagglutinin antigen content for each of the three strains it contains (60 µg per strain in the high-dose trivalent product versus 15 µg per strain in the standard-dose quadrivalent products). 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 2020-2021 influenza season

<table>
<thead>
<tr>
<th>Ages</th>
<th>Type of influenza Vaccines</th>
<th>Influenza Vaccine Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months up to and including 8 years</td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>FluLaval Tetra</td>
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<tr>
<td></td>
<td></td>
<td>Fluzone® Quadrivalent</td>
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<tr>
<td>9 years up to and including 64 years</td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>FluLaval Tetra</td>
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<td></td>
<td></td>
<td>Fluzone® Quadrivalent</td>
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<tr>
<td></td>
<td></td>
<td>Flucelvax® Quad</td>
</tr>
<tr>
<td>65 years and over</td>
<td>High-dose trivalent (TIV)</td>
<td>Fluzone® High-Dose</td>
</tr>
<tr>
<td></td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>FluLaval Tetra</td>
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<td>Fluzone® Quadrivalent</td>
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<td></td>
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<td>Flucelvax® Quad</td>
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</table>
Note that the live attenuated influenza vaccine will not be available as part of the UIIP.

Additional information about vaccines available through the UIIP can be found on the Ministry of Health website.¹

**Mammalian Cell-Culture Based Influenza Vaccine - Flucelvax® Quad**

*Flucelvax® Quad* (Seqirus Inc., Kirkland, Quebec) is a mammalian cell-culture based, quadrivalent, inactivated influenza vaccine available for the first time in Ontario.² In comparison to most influenza vaccines that are manufactured using eggs, Flucelvax® Quad is manufactured using cultured cells of mammalian origin (Madin-Darby Canine Kidney [MDCK] cells). While Flucelvax® Quad is the first cell-culture based influenza vaccine approved by Health Canada, cell-culture based influenza vaccines have been available in Europe since 2007 and the United States since 2012.

Flucelvax® Quad contains a standard dose of hemagglutinin antigen (15 µg) per strain. It has been found to have similar safety and effectiveness profiles to egg-based influenza vaccines.

**Key Points Regarding the Use of Flucelvax® Quad:**

- In Canada, Flucelvax® Quad is licensed for use in adults and children 9 years of age and older. Although Flucelvax® Quad is licensed in other countries for children 4 years of age and over, in Canada it should not be used for children younger than 9 years of age.

- 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.

- 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).³

For additional information, see the National Advisory Committee on Immunization (NACI) Supplemental Statement – Mammalian Cell Culture-Based Influenza Vaccines.⁴

**Vaccines for Adults 65 Years of Age and Over**

**High Dose Trivalent versus Standard Dose Quadrivalent Vaccines**

High-dose trivalent vaccine (TIV) and standard dose quadrivalent vaccines (QIV) are both available for adults 65 years of age and over. Table 2 provides an overview of the considerations when assessing the high-dose TIV compared to standard-dose QIV.
<table>
<thead>
<tr>
<th>Factors</th>
<th>Considerations</th>
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</table>
| **Influenza A** | • High-dose TIV provides better protection than standard-dose TIV against the A(H3N2) strain as demonstrated in a [large randomized-controlled trial](#). The A(H3N2) strain is the same in the standard-dose TIV and standard-dose QIV vaccines.  
• In adults 65 years of age and over, the burden of influenza A(H3N2) is higher compared to influenza A(H1N1) and influenza B. Seasons with circulation of influenza A(H3N2) result in more outbreaks, hospitalizations and deaths, most commonly among older adults. |
| **Influenza B** | • Although high-dose TIV contains one less influenza B strain than QIV, influenza B occurs less frequently than influenza A in adults 65 years of age and older.  
• There may be some cross protection against B lineages, such that a TIV vaccine that contains B/Victoria may offer some protection against B/Yamagata and vice versa. Therefore, high-dose TIV may afford some protection against the B lineage not included in that vaccine. |
| **Safety**   | • QIV and high-dose TIV are expected to have a generally similar safety profile. Local reactions and systemic adverse events occur somewhat more frequently with high-dose TIV than standard-dose TIV. The systemic reactions are described as generally mild and resolved within three days. |

**Canadian Recommendations Regarding High-Dose TIV**

The [National Advisory Committee on Immunization (NACI) Statement on Seasonal Influenza Vaccine for 2020-2021](#) has provided the following recommendation for adults 65 years of age and older regarding high-dose TIV:

> At the individual level and when available, “IIV3-HD (high-dose TIV) should be used over IIV3-SD (standard-dose TIV), given the burden of influenza A (H3N2) disease and the good evidence of better protection compared to IIV3-SD in adults 65 years of age and older. There is insufficient evidence to recommend the use of IIV3-HD over IIV4-SD (standard-dose QIV). However, given the increased burden of disease associated with influenza A(H3N2) in older adults, better protection against influenza A(H3N2) may be more important than better protection against influenza B.” [6](#)  

**Vaccine Effectiveness of High-Dose TIV**

A [large randomized, double-blinded controlled clinical trial](#) involving almost 32,000 individuals 65 years of age and over compared high-dose TIV to standard-dose TIV over two influenza seasons. The trial showed high-dose TIV to be 24.2% (95% confidence interval (CI): 9.7% to 36.5%) more efficacious compared to standard-dose TIV in preventing laboratory-confirmed influenza. The improved efficacy for high-dose TIV was particularly notable for A(H3N2), with high-dose TIV being 23.3% (95% CI: 6.0% to 37.5%) more efficacious. Two NACI literature reviews, one published in [May 2018](#) and the other published in [2016](#),
identified a number of other studies that support NACI’s recommendation to offer high-dose TIV over standard-dose TIV at the individual level. There are currently no studies that have directly compared high-dose TIV to standard-dose QIV.

**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). 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**

Some recent studies (e.g., McLean HQ et al., Pebody R et al., Ohmit SE et al., Beyer WEP et al.) 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.), 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. Additional information on influenza vaccines, including for adults 65 years of age and over, is available on the Ministry of Health’s website.
Figure 1. Proportion of influenza cases by type and subtype for influenza A, by age group: Ontario, 2010–11 to 2019–2020 influenza season

Data Caveats and Technical Notes for Figure 1

- Data source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario on July 31st, 2020.
- The data only represent laboratory-confirmed cases of influenza reported to public health and recorded in iPHIS.
- Influenza A subtype information is only available for 37.2% of influenza A.
- The possibility of duplicates exists because duplicate sets were not identified and excluded unless they were resolved prior to data extraction either at the local or provincial level.
References


8. Public Health Agency of Canada. A review of the literature of high dose seasonal influenza vaccine for adults 65 years and older. Ottawa, ON: Her Majesty the Queen in Right of Canada, as


