

# 2014- 2015

## Live Attenuated Influenza Vaccine Questions and Answers for Health Care Providers

(Reviewed and Updated October 15 2014)



**BC Centre for Disease Control**  
An agency of the Provincial Health Services Authority



**ImmunizeBC**

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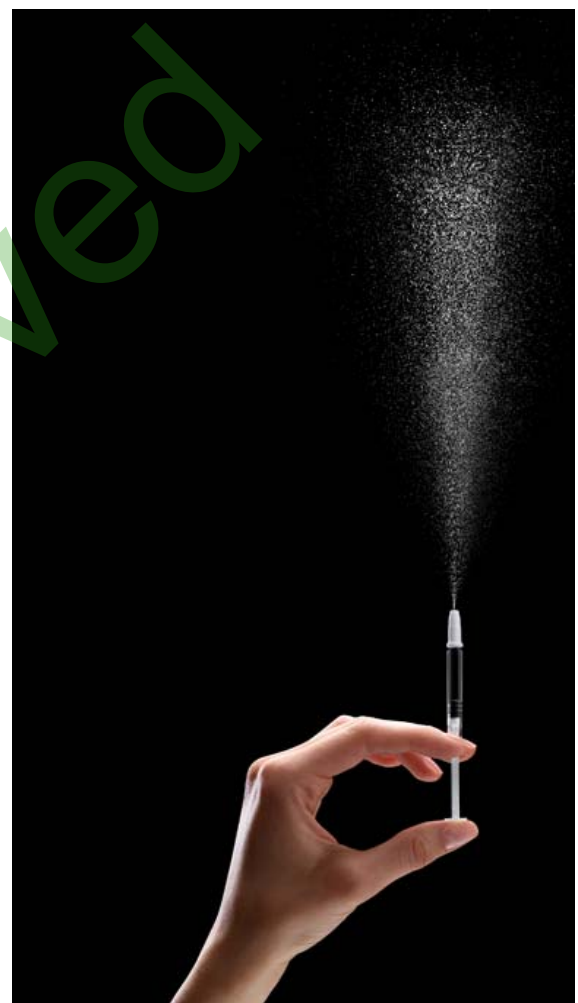
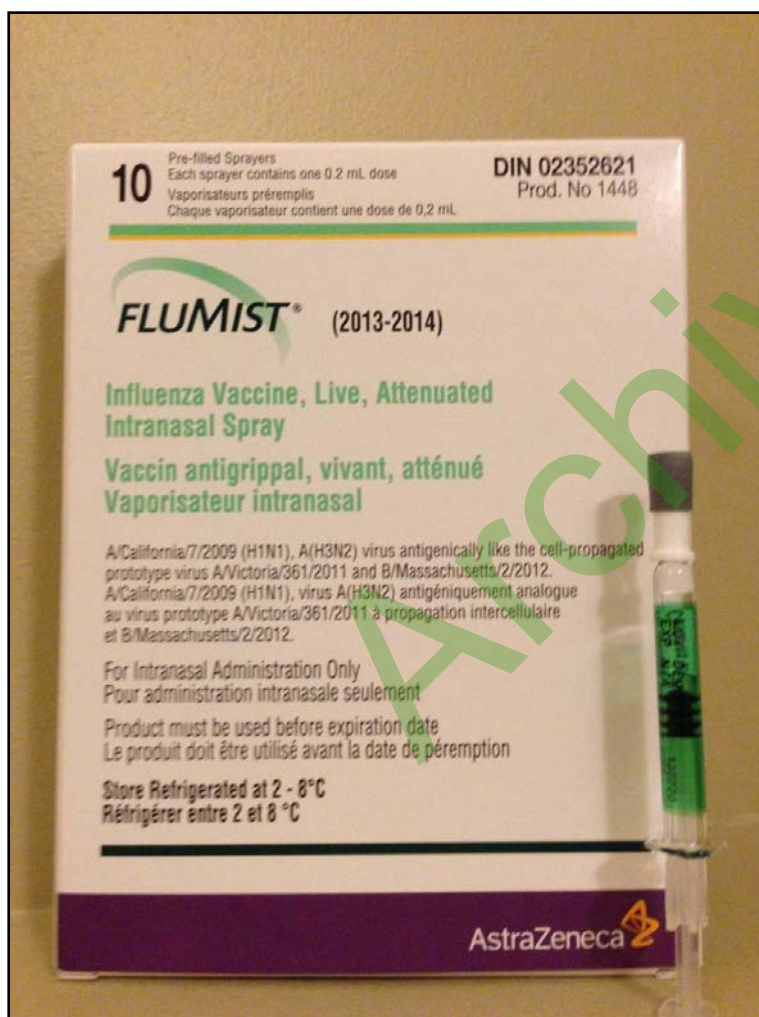
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## BACKGROUND

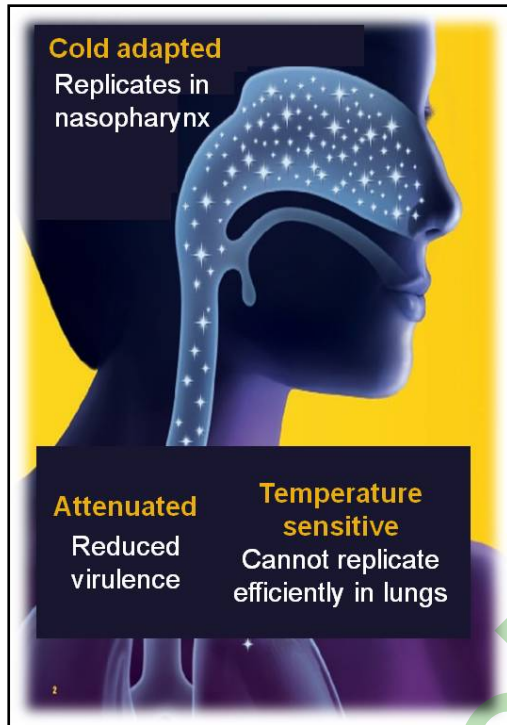
### 1. WHAT IS LIVE ATTENUATED INFLUENZA VACCINE (LAIV)?

FLUMIST® is a live, attenuated influenza vaccine (LAIV) and is administered by the intranasal route by a healthcare provider. Each pre-filled glass sprayer contains 0.2 mL dose (given as 0.1 mL in each nostril) of live, attenuated influenza virus reassortants of three strains of virus.<sup>(1)</sup> The spray is colorless to pale yellow, clear to opalescent liquid; small, white particles may be present.



### 2. WHY IS LAIV AN INTRANASAL SPRAY?

LAIV (FLUMIST®) is made from attenuated viruses that are able to replicate efficiently only at temperatures present in the nasal mucosa. LAIV is manufactured using the 3 influenza virus strains recommended by the World Health Organization (WHO) for the northern hemisphere. Through manufacturing processes the 3 influenza virus strains become:



**cold-adapted** so they are only able to replicate at cooler temperatures of the nasopharyngeal mucosa

**temperature sensitive** so they are unable to replicate at warmer temperatures of the lower airways and lungs

**attenuated** so they are unable to cause clinical influenza disease

The cumulative effect of these properties is such that the viral strains induce protective immunity without causing disease.<sup>(1)</sup>

### 3. HAS LAIV BEEN WELL STUDIED?

LAIV (FLUMIST®) has been well studied in clinical trials.<sup>(2)</sup> A number of studies (LAIV versus placebo and LAIV versus trivalent inactivated influenza vaccine (TIIV)) have been conducted in children and adults.<sup>(3)(4)</sup> The results of efficacy and safety studies have demonstrated that FLUMIST® is effective, safe and well tolerated.<sup>(3)(4)</sup>

### 4. WHY IS LAIV NOT APPROVED FOR USE IN CHILDREN < 24 MONTHS OF AGE?

LAIV (FLUMIST®) is contraindicated in this age group due to increased risk of wheezing.<sup>(4)</sup> A multi-centre efficacy trial found that rates of wheezing were statistically significantly higher among children 6 – 23 months of age (5.9% LAIV vs. 3.8% trivalent inactivated influenza vaccine (TIIV)) in the weeks following immunization.<sup>(3)</sup>

## **5. WHY DOES NACI RECOMMEND LAIV OVER TIIV FOR IMMUNIZATION OF HEALTHY CHILDREN?**

Based on efficacy data, the National Advisory Committee on Immunization (NACI) recommends LAIV as the preferred product for use in healthy children 2 to under 6 years of age, and continues to recommend LAIV use in those aged 6 to 17 years. Previously NACI recommended preferential use in those aged 2 to 17 years old. The change was made based on a closer review of available data from clinical trials. However, NACI points out that LAIV may be superior to TIIV in children older than 6, but the exact age at which these vaccines are equivalent or at which TIIV becomes the more efficacious product is not known. TIIV is recommended preferentially in adults because efficacy has been higher than for LAIV. For any given individual the age at which TIIV is the better choice may vary depending on prior influenza infection and/or vaccination history, as prior immunity may interfere with replication of the attenuated virus which is needed to generate immunity.

BC guidelines preferentially recommend LAIV for those aged 2 to 8 years. This age range is in line with ACIP's recommendations for the 2014/15 flu season, and it is also compatible with the recommended schedule of two doses for children younger than 9 in the first season they receive influenza vaccine. If LAIV is not available, TIIV should be used as it is safe and effective.

## **6. CAN YOU TELL ME MORE ABOUT THE STUDIES THAT SUPPORT THE PREFERENTIAL USE OF LAIV IN YOUNGER HEALTHY CHILDREN?**

Several clinical trials have been conducted in young children, and this literature has been systematically reviewed in two papers<sup>(5)(6)</sup> and also reviewed by NACI. In five randomized controlled clinical trials, the absolute vaccine efficacy of LAIV against laboratory confirmed influenza in children aged 6 years and under was 85% (95% CI 77 to 100%). Similar findings of vaccine efficacy were made in one trial of children up to age 7 years.<sup>(7)</sup> In contrast 2 studies of TIIV in this age group found absolute vaccine efficacy of 39% (95% CI -8 to 66%) against the same outcome of laboratory confirmed influenza. An additional benefit to use of LAIV is demonstrated cross-protection against mismatched strains, including greater cross-protection versus TIIV.<sup>(3)</sup> This is to be expected because the attenuated virus is a more complete antigenic stimulus than the antigenic components used in inactivated vaccines.

## **7. CAN YOU TELL ME MORE ABOUT THE STUDIES THAT SUPPORT THE USE OF LAIV IN OLDER CHILDREN?**

Randomized clinical controlled trials of LAIV vaccine efficacy have not been conducted in healthy children and youth older than 7 years. Several observational studies have been done, however, in children up to 18 years old with the outcomes being medically attended acute respiratory illness. Findings have generally been consistent with those described above (see question [6](#)) with some suggestion of declining effectiveness at older ages, but confidence intervals have been wide and findings are inconclusive. Therefore the data to support preferential use over TIV in this age group are not as strong, but the vaccine has demonstrated effectiveness and offers the additional advantage of needle free administration and potentially improved cross-protection to other strains, as outlined above (see question [6](#)).

One randomized open label study has been conducted in asthmatic children<sup>(8)</sup> aged 6 to 17 years, using either LAIV or TIV. During the 2002-3 influenza season, the study demonstrated a significantly greater relative efficacy of LAIV compared to TIV of 34.7% (95% CI 3.9%–56.0%). Asthma exacerbations were similar in the two groups. Those who received LAIV had higher incidence of runny nose or nasal congestion (66.2% compared to TIV at 52.5%) and about 70% of TIV recipients reported injection site reactions.

#### **8. CAN LAIV BE ADMINISTERED TO CHILDREN WITH CHRONIC HEALTH CONDITIONS?**

NACI recommends that LAIV can be used in children 24 months and older with stable, non-severe asthma and in children with chronic health conditions (excluding those with immunocompromising conditions and severe asthma). Based on expert review, it is expected that LAIV should be as safe, immunogenic and efficacious in immune competent children with chronic health conditions as it is in healthy children. However, at this time there is insufficient evidence available to prefer LAIV over TIV in children with chronic health conditions.<sup>(4)</sup>

#### **9. WHEN WAS LAIV APPROVED AND WHERE ELSE IS IT PROVIDED IN CANADA?**



LAIV (FLUMIST®) was approved in Canada in June 2010 for active immunization of persons 2 – 59 years of age. Since the launch of the FLUMIST® program, approximately 982,665 doses have been distributed in Canada.

<b>FLUMIST® introduction into publicly funded programs in Canada:</b> <sup>(2)</sup>
<b>2013-14</b> - Alberta, British Columbia, North West Territories, Nunavut, Prince Edward Island, Quebec, Yukon
<b>2012-13</b> - Alberta, British Columbia (pilot project in Vancouver Coastal), Nunavut, Prince Edward Island, Quebec
<b>2011-12</b> - Private market only

## 10. HAS LAIV BEEN APPROVED FOR USE IN OTHER COUNTRIES?

LAIV (FLUMIST®) has been available in the United States since 2003.<sup>(3)</sup> Since 2004, more than 79 million doses of FLUMIST® have been distributed globally. Outside of North America, countries with approval for FLUMIST® (called FLUENZ® in Europe) are: the United Kingdom, Germany, France, Sweden, Israel, Malaysia and Hong Kong.

## RESOURCES

To learn more about LAIV (FLUMIST®), please refer to the following websites:

ImmunizeBC - Health care professionals - Influenza  
<http://immunizebc.ca/node/551>

BC Centre for Disease Control (BCCDC) - Health care professionals  
<http://www.bccdc.ca/imm-vac/ForHealthProfessionals/default.htm>

HealthlinkBC files on influenza and influenza vaccines  
<http://www.healthlinkbc.ca/servicesresources/healthlinkbcfiles/>

Public Health Agency of Canada (PHAC) - Canadian Immunization Guide  
<http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-eng.php>

Recommendations on the use of live, attenuated influenza vaccine (FluMist®):  
Supplemental Statement on Seasonal Influenza Vaccine for 2015-2015

<http://www.phac-aspc.gc.ca/naci-ccni/>

National Advisory Committee on Immunization (NACI) Statement on Seasonal Influenza Vaccine for 2014-2015. Available from: <http://www.phac-aspc.gc.ca/naci-ccni/>

Astra Zeneca Canada Inc. FLUMIST® Product Monograph  
<http://www.astrazeneca.ca/en/Our-Medicines/en-Products-AZ>

Astra Zeneca Canada Inc. – Healthcare Professionals  
<http://www.astrazeneca.ca/en/Healthcare-Professionals>

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## BRITISH COLUMBIA'S LAIV PROGRAM

The following questions and answers are supplementary information to the BCCDC Communicable Disease Control Manual, Chapter II-Immunization Program, Section VII-Biological Products, Influenza Vaccine (Live attenuated influenza vaccine (LAIV)), July 2014, Pages 33 a-c. Available from: <http://www.bccdc.ca/dis-cond/comm-manual/CDManualChap2.htm>

### 11. WHICH 3 INFLUENZA VIRUS STRAINS MAKE UP THIS YEAR'S SEASONAL TRIVALENT INFLUENZA VACCINES?

For the northern hemisphere the World Health Organization (WHO)<sup>(5)</sup> recommends that the 2014/2015 Seasonal Trivalent Influenza Vaccine (Inactivated and Live Attenuated) contain:

- **A/California/7/2009 (H1N1)pdm09-like virus**
- **A/Texas/50/2012 (H3N2)-like virus**
- **B/Massachusetts/2/2012-like virus**

All three strains are unchanged from the 2013/14 season.

### 12. IN THE 2014/15 INFLUENZA SEASON, FOR WHOM IS LAIV PUBLICLY FUNDED?

LAIV (FLUMIST®) is publicly funded for eligible children aged 2 to 17 years old inclusive; those eligible are listed in the:

BCCDC Communicable Disease Control Manual, Chapter II-Immunization Program, Section VII-Biological Products, July 2014, Page 31. Available from: <http://www.bccdc.ca/dis-cond/comm-manual/CDManualChap2.htm>

### 13. WHAT ARE THE DOSING AND SCHEDULES FOR ADMINISTRATION OF LAIV?

**2 - 8 years of age:** 1 or 2 doses given as 0.2 mL (0.1 mL in each nostril) intranasal spray.

- This product should be **preferentially** offered to children in this age group. A 2<sup>nd</sup> dose of influenza vaccine is recommended 4 weeks later for children receiving influenza vaccine for the first time that season. See question [15](#).

**9 - 17 years of age:** 1 dose given as 0.2 mL (0.1 mL in each nostril) intranasal spray.

- This product is recommended for use in this age group and offers the advantage of needle-free administration.

**18 - 59 years of age:** 1 dose: 0.2 mL (0.1 mL in each nostril) intranasal spray.

- This product is approved for use in this age group but TIIV provides better protection against influenza; it is not provided free in the BC program for this age group.

#### **14. WHAT IF A CHILD < 24 MONTHS OF AGE RECEIVES LAIV?**

LAIV (FLUMIST®) is not approved for this age group due to an increased risk of wheezing found in clinical trials in this age group.<sup>(4)</sup> If FLUMIST® is inadvertently administered to a child < 24 months of age there is no need to offer TIIV subsequently as LAIV provides protection in this age group.<sup>(10)</sup> However, inform the parent/guardian of risk of increased wheezing and recommend that they contact the child's primary care provider as well as report to public health if wheezing occurs. Complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

Children under 9 years of age who have not previously received seasonal influenza vaccine require 2 doses given 4 weeks apart. When a child < 24 months inadvertently given LAIV for the 1<sup>st</sup> dose presents for a 2<sup>nd</sup> dose, give TIIV.

#### **15. WHAT IF A CHILD PRESENTS FOR LAIV AND THE PRODUCT IS NO LONGER AVAILABLE?**

If a child presents for a 1<sup>st</sup> or 2<sup>nd</sup> dose of LAIV and the product is no longer available, offer TIIV. LAIV is the preferred product; however, TIIV may be given interchangeably if LAIV is not available.<sup>(12)</sup>

Children under 9 years of age who have not previously received seasonal influenza vaccine require 2 doses given 4 weeks apart. If the child has received 1 or more doses in any previous season, only a single dose is required.

### 16. IS THE EXPIRY DATE OF LAIV DIFFERENT FROM TIIV?

The shelf-life of LAIV is considerably shorter than that of trivalent inactivated influenza vaccines (TIIV). The default expiry date of this product is **NOT** the last day of the month. Be sure to check the expiry date as vaccine lots received in BC will expire during the period of January through May 2015. All immunization service providers are asked to optimize planning of use to ensure that the product quantities allocated to your branch office are used up prior to expiry.

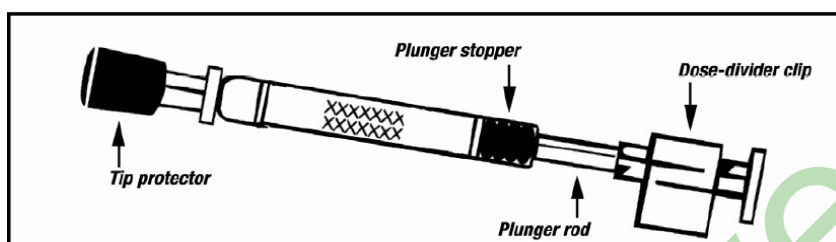


### 17. WHAT IF A CHILD RECEIVES AN EXPIRED DOSE OF LAIV?

If an expired product is given inadvertently, the dose must be repeated. To ensure that a child is protected against the 3 seasonal influenza strains contained in the vaccine, offer a valid dose of LAIV on the same day the expired vaccine was given or as soon as the error is discovered. There is no minimum interval between an expired and a valid dose of LAIV as it is the same product being administered and protection against influenza should not be delayed.

If the child or parent/guardian refuses to repeat LAIV administration, offer TIIV as an alternative. To document the administration of an expired dose, complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

## 18. WHAT ARE THE STEPS FOR INTRANASAL ADMINISTRATION OF LAIV?

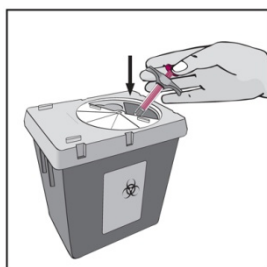


### FLUMIST IS AN INTRANASAL SPRAY AND IS NOT FOR INJECTION.

The product is provided in a 'sprayer' in a firm device that looks like a syringe with a tip protector at one end and a plunger with a dose divider clip at the other end. Details and accompanying diagram on how to administer the product are contained in the product monograph on page 11 and 12 and the accompanying text is reproduced below:

1. Remove the rubber tip protector. Do not remove the dose-divider clip at the other end of the sprayer.
2. With the recipient sitting upright, place tip of the sprayer just inside a nostril to ensure vaccine is delivered into the nose.
3. In one motion depress the plunger as rapidly as possible until the dose-divider clip prevents you from going further.
4. Pinch and remove the dose divider clip from the plunger.
5. Place the tip of the sprayer just inside the other nostril and with a single motion depress the plunger as rapidly as possible to deliver the rest of the vaccine.

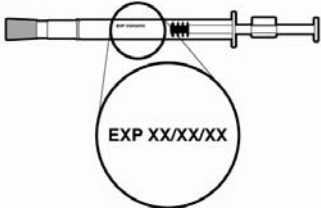
## 19. HOW SHOULD THE SPRAYER BE DISPOSED AFTER USE?




The sprayer should be disposed of according to the standard procedures for medical waste (e.g.,) sharps container or biohazard container.<sup>(1)</sup>

## 20. CAN YOU PROVIDE AN ILLUSTRATION OF THE STEPS OF LAIV INTRANASAL ADMINISTRATION?


### Administering FluMist<sup>®3</sup>

- 


**1**

**Check expiration date.** Product must be used before the date on sprayer label.
- 


**2**

Remove rubber tip protector. Do not remove dose-divider clip at the other end of the sprayer.
- 


**3**

With the patient in an upright position, place the tip just inside the nostril to ensure FluMist<sup>®</sup> is delivered into the nose.
- 

**4**

With a single motion, depress plunger **as rapidly as possible** until the dose-divider clip prevents you from going further.
- 

**5**

Pinch and remove the dose-divider clip from plunger.
- 

**6**

Place the tip just inside the other nostril and with a single motion, depress plunger **as rapidly as possible** to deliver remaining vaccine.

## **21. WHAT IF A CHILD SNEEZES RIGHT AFTER BEING IMMUNIZED WITH LAIV?**

Both NACI<sup>(3)</sup> and Advisory Committee on Immunization Practices (ACIP)<sup>(13)</sup> support that if the vaccine recipient sneezes immediately after administration the dose should not be repeated. The binding of the virus to epithelial cells occurs very rapidly and there are more virus particles in the vaccine than are needed to establish immunity. Therefore sneezing or blowing your nose immediately after immunization with LAIV will not affect immunity.<sup>(11)</sup>

## **22. WHAT IF A CHILD RECEIVES BOTH HALF DOSES OF LAIV IN THE SAME NOSTRIL?**

It is recommended that LAIV be administered as 2 divided sprays (0.1 mL into each nostril) to maximize the vaccine's contact surface area of epithelial cells within the nasopharynx. No clinical trials have been conducted using a single-nostril administration. However, there is no need to repeat immunization as each half dose (0.1 mL) contains enough viral particles to induce an immune response.<sup>(14)</sup> Complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

## **23. WHAT IF DURING LAIV ADMINISTRATION A CHILD IS SPRAYED IN THE EYE INSTEAD OF THE NOSTRIL?**

Immediately flush the area with water or saline; if irritation persists refer to physician to assess for possible conjunctivitis. If at least half of the LAIV dose (0.1 mL) was administered into the nostril the client does not need further vaccine at that time.<sup>(15)</sup> However, if the 1<sup>st</sup> half of the vaccine dose went into the eye, the 2<sup>nd</sup> half of the dose (0.1 mL) should be offered. If at that time the child or the parent/guardian does not want to attempt further administration of LAIV offer TIIV. Complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

## **24. WHAT IF DURING LAIV ADMINISTRATION A CHILD REFUSES THE 2<sup>ND</sup> HALF OF THE DOSE?**



If a child refuses the 2<sup>nd</sup> half of the LAIV dose, attempt to give the 2<sup>nd</sup> half (0.1 mL) of the LAIV dose in the other nostril. If you are unsuccessful there is no need to repeat immunization as each half dose (0.1 mL) of LAIV contains enough viral particles to induce an immune response.<sup>(14)</sup> Complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

## 25. DO I HAVE TO USE PERSONAL PROTECTIVE EQUIPMENT TO ADMINISTER LAIV?

The use of personal protective equipment such as gloves and masks are not needed to administer FLUMIST®. Using routine practices, as when administering any immunization, is adequate in settings where FLUMIST® is being given.<sup>(16)</sup>

## 26. WHAT ARE THE CONTRAINDICATIONS TO RECEIPT OF LAIV?

- History of anaphylactic reaction to a previous dose of any type of influenza vaccine or to any component of FLUMIST®.
- Egg allergy. Such individuals should receive inactivated influenza vaccine.
- Severe asthma or active wheezing (on high dose inhaled or oral steroids or medically attended wheezing in the 7 days prior to vaccination). (see questions [28](#), [29](#))
- Adults and children with immune compromising conditions. (see question [27](#))
- HCWs working with immunocompromised individuals. (see questions [27](#), [33](#), [34](#))
- Individuals less than 2 years of age or ≥ 60 years of age. (see questions [4](#), [14](#))
- Pregnancy. (see question [30](#))
- Individuals 2-17 years of age receiving aspirin-containing therapy because of the association of Reye syndrome with aspirin and wild-type influenza infection. It is recommended that aspirin-containing products in children < 18 years of age be delayed for 4 weeks after receipt of FLUMIST®.
- History of Guillain-Barré syndrome (GBS) within 8 weeks of receipt of a previous dose of influenza vaccine without another cause being identified.

## 27. CAN YOU PROVIDE SOME EXAMPLES OF IMMUNOCOMPROMISING CONDITIONS?

Examples of immunocompromising conditions <sup>(17)</sup> include (but are not limited to):

- cancer
- immunodeficiency (including human immunodeficiency virus [HIV] infection)
- immunosuppression due to underlying disease or therapy (e.g., severe rheumatoid arthritis requiring immunosuppressive therapies)

## 28. CAN YOU DEFINE SEVERE ASTHMA?

According to NACI severe asthma is "...defined as currently on oral or high dose inhaled glucocorticosteroids or active wheezing or those with medically-attended wheezing in the 7 days prior to vaccination." <sup>(3)</sup>

High dose systemic steroids interfere with vaccine induced immune responses (i.e., consider persons receiving  $\geq 2$  mg/kg per day or  $\geq 20$  mg daily of prednisone for more than 14 days duration to be immune-suppressed). Topical and locally injected steroids do not have an impact on vaccines unless there is clinical or laboratory evidence of immunosuppression from such therapy. <sup>(17)</sup>

According to the British Columbia Medical Association, high dose inhaled corticosteroids in pediatric patients are those treated with  $\geq 200$  ug/day fluticasone (or equivalent) because this high dosage may be associated with systemic side effects. <sup>(18)</sup>

In children with asthma, if a parent or guardian of a child cannot identify a child's current dosage of oral or inhaled steroid, TIIV should be offered.

## 29. CAN A CHILD RECEIVING DAILY INTRANASAL STEROIDS FOR CONDITIONS OTHER THAN ASTHMA RECEIVE LAIV?

Yes. Intranasal steroids typically used for treatment of allergic rhinitis are not a contraindication because the effects are local and not systemic. These products do not cause immunosuppression so they are not a contraindication to LAIV. Topical and locally injected steroids do not have an impact on vaccines unless there is clinical or laboratory evidence of immunosuppression from such therapy. <sup>(17)</sup>

### 30. WHAT ABOUT THE USE OF LAIV IN PREGNANT AND BREASTFEEDING WOMEN?

LAIV should not be administered to pregnant women because of the lack of safety data.<sup>(3)</sup> Although LAIV has not been studied in pregnant women, no unexpected patterns of pregnancy complications or fetal outcomes have been identified after the inadvertent administration of LAIV to pregnant women. In the event of an inadvertent administration of LAIV to a pregnant woman complete the required patient safety/vaccine error (e.g. Patient Safety Learning System) documentation within your organization.

AstraZeneca does not maintain a registry for inadvertent administration of FLUMIST® to pregnant women. However, they do have an Adverse Event Reporting phone line (1-800-668-6000) and e-mail ([medinfo.canada@astrazeneca.com](mailto:medinfo.canada@astrazeneca.com)).

It is not known whether LAIV is excreted in human milk; however LAIV is not contraindicated in breastfeeding women.<sup>(3)</sup>

### 31. WHAT ARE THE POTENTIAL ALLERGENS AND PRODUCT COMPONENTS OF LAIV?

**FLUMIST® potential allergens:** ovalbumin, gelatin hydrolysate (porcine Type A), gentamicin, arginine hydrochloride.

**FLUMIST® other components:** sucrose, dibasic potassium phosphate, monobasic potassium phosphate, monosodium glutamate.

### 32. SHOULD FAITH-BASED CLIENTS BE CONCERNED ABOUT THE GELATIN CONTENT IN LAIV?

LAIV (FLUMIST®) contains porcine-type gelatin. Scholars from the Muslim and Jewish faiths have determined that receipt of gelatin in vaccines is permissible and does not constitute a violation of religious practice. Religious leaders' statements on the use of vaccines containing porcine gelatin are available from:

<http://www.vaccinesafety.edu/Porcine-vaccineapproval.htm>

### **33. ARE THERE PRECAUTIONS TO THE RECEIPT OF LAIV?**

Severe oculo-respiratory syndrome (ORS) after previous receipt of an influenza vaccine is a precaution to the administration of LAIV.

Also, vaccine recipients should be informed that FLUMIST® is a vaccine that contains a weakened strain of influenza virus and could potentially be transmitted to another person through contact with respiratory secretions. An infection with this weakened virus could cause a serious infection in a small category of patients who are severely immunocompromised and receiving care in hospital in a protected environment (e.g., post bone marrow transplant). Both health care workers and close contacts of such patients should avoid contact with these patients for 2 weeks after getting FLUMIST®. If such contact cannot be avoided, offer TIIV instead of FLUMIST®.

### **34. CAN YOU PROVIDE ME WITH MORE INFORMATION ON LAIV AND VIRAL SHEDDING?**

Both children and adults can shed vaccine viruses after LAIV administration and studies have shown that younger children are more likely to shed and shed higher titers than older children and adults. Children may shed for a mean duration of 7.6 days and shedding is rare after day 11.<sup>(3)</sup>

Viral shedding is not synonymous with transmission of vaccine virus. Shedding is generally below levels needed to transmit infection, although in rare instances shed vaccine viruses can be transmitted from vaccine recipients to unvaccinated persons. Serious illness has not been reported among unvaccinated persons inadvertently infected with vaccine virus and no transmission of vaccine virus has ever been reported in a health care setting.<sup>(3)</sup>

It is important to note that wild type influenza virus is a community acquired infection readily transmitted person to person through fomites and droplet contact during influenza season, with attack rates ranging from 5 to 25% depending on the severity of the season. The attenuated virus contained in the vaccine is a much weakened strain of influenza compared to wild influenza viruses.

### **35. ARE THERE ANY SPECIAL CONSIDERATIONS FOR CO-ADMINISTRATION OF LAIV AND OTHER LIVE VACCINES?**

As for other live vaccines, LAIV can be given concurrently with MMR and varicella vaccines to young children without reducing the immunogenicity or safety of any of the vaccines. If not given at the same visit, administration of LAIV and other live vaccines should be separated by at least 4 weeks to reduce or eliminate interference from the vaccine given 1<sup>st</sup> on the vaccine given later.

### **36. ARE THERE ANY SPECIAL CONSIDERATIONS FOR A CHILD TAKING ANTIVIRAL MEDICATIONS?**

LAIV should not be administered when taking antiviral agents because these drugs interfere with the immune response to FLUMIST®. FLUMIST® should not be administered to individuals while taking antiviral agents active against influenza (oseltamivir and zanamivir). Such individuals should receive inactivated influenza vaccine. If antiviral agents are administered from 48 hours before to 2 weeks after receipt of FLUMIST®, revaccinate when antiviral agents have been discontinued for at least 48 hours.

### **37. ARE THERE ANY SPECIAL CONSIDERATIONS FOR ADMINISTRATION OF LAIV AND A TUBERCULOSIS (TB) SKIN TEST?**

No information on the effect of FLUMIST® on a tuberculosis (TB) skin test is available. It is prudent to do TB skin testing on the same day as FLUMIST® immunization, or delay TB skin testing  $\geq 4$  weeks, to avoid having a false negative TB skin test result. This advice is extrapolated from the experience with measles vaccine.<sup>(19)</sup>

### **38. WHAT ARE THE COMMON SIDE EFFECTS OF LAIV?**

Most people have no reaction to the vaccine. Reactions that do occur are typically mild and last for 1 – 3 days. For children requiring 2 doses of vaccine, symptoms tend to be less frequent following the 2<sup>nd</sup> dose.<sup>(3)</sup> As with any immunization, unexpected or unusual side effects can occur, including anaphylaxis.

#### **Common Local Side Effects:**

Adults and Children - runny nose or nasal congestion.

**Common Systemic Side Effects:**

Children - decreased appetite, weakness, headache, fever.

Adults - headache, sore throat, cough, weakness.

**Oculo-respiratory syndrome (ORS).** Fewer than 1 in 20 people may develop ORS and symptoms include: red eyes, a cough, and/or sore throat and/or hoarseness.

**39. IS THERE A LIST OF SCREENING QUESTIONS FOR THE CONTRAINDICATIONS, PRECAUTIONS AND SPECIAL CONSIDERATIONS FOR LAIV?**

Yes, a list of LAIV (FLUMIST®) screening questions is available for your use (see [APPENDIX B](#)).

However, you are not required to use this checklist as all the contraindications, precautions and special considerations for LAIV, are listed in the BCCDC Communicable Disease Control Manual.

Please refer to the BC CDC Manual, Chapter II-Immunization Program, Section VII-Biological Products, Influenza Vaccine (Live attenuated influenza vaccine (LAIV)), July 2014, pages 33a-c. Available from: <http://www.bccdc.ca/dis-cond/comm-manual/CDManualChap2.htm>

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## APPENDIX A – QUADRIVALENT LIVE ATTENUATED INFLUENZA VACCINE (LAIV-Q)

### 1. WILL QUADRIVALENT INFLUENZA VACCINES BE AVAILABLE FOR THE PUBLICLY FUNDED PROGRAM FOR 2014/15?

Yes. Due to an unexpected delay in supply of FLUMIST trivalent to the Canadian market experienced by Astra-Zeneca, the supplier of both quadrivalent and trivalent LAIV, US labeled and packaged FLUMIST® QUADRIVALENT is being supplied for the 2014/15 season to meet the requirements of public health programs. FLUMIST® QUADRIVALENT is the only quadrivalent influenza vaccine that will be publicly funded in BC for this influenza season. As of October 2014, it is expected that about 75% of LAIV used in the BC program in 2014/15 will be quadrivalent product.

### 2. IS THERE A PREFERENTIAL RECOMMENDATION FOR USE OF LAIV-Q?

Although LAIV is the preferred influenza product for children 2 to 8 years of age, at this time the National Advisory Committee on Immunization (NACI) does not preferentially recommend LAIV-Q over trivalent live attenuated influenza vaccine (LAIV-T) for this age range. Either product can be given.

### 3. HOW DOES LAIV-Q DIFFER FROM LAIV-T?

Both LAIV-Q and LAIV-T are live attenuated influenza vaccines. LAIV-T contains two A virus strains (H1N1 and H3N2) and a strain from one B virus lineage (Yamagata or Victoria). LAIV-Q contains the two A virus strains as well as strains from both B lineages. This additional B strain is what differentiates quadrivalent and trivalent influenza vaccines. Both quadrivalent and trivalent formulations are manufactured using the same process.

### 4. ARE THERE DIFFERENCES IN ADMINISTRATION CONSIDERATIONS FOR QUADRIVALENT AND TRIVALENT LAIV?

No, all administration considerations remain unchanged for LAIV-Q. For example, indications, screening questions, and method of administration are the same for both FLUMIST® Quadrivalent and FLUMIST®.

## 5. ARE THERE DIFFERENCES IN THE SAFETY AND SIDE EFFECT PROFILE BETWEEN LAIV-Q AND LAIV-T?

The safety and reactogenicity profile of both products are similar. A randomized, active-controlled study compared FLUMIST® QUADRIVALENT and FLUMIST® in children and adolescents 2 to 17 years of age. The rates of solicited adverse reactions reported were similar between subjects who received LAIV-Q and LAIV-T. The following table is an excerpt from the FLUMIST® QUADRIVALENT product monograph:

**Summary of Solicited Adverse Reactions Observed Within 14 Days after Dose 1 for FLUMIST QUADRIVALENT and FLUMIST Recipients in Study MI-CP208 in Children and Adolescents 2 through 17 Years of Age**

	FluMist Quadrivalent	FluMist <sup>a</sup>
	N = 1341-1377 <sup>b</sup>	N = 901-920 <sup>b</sup>
<b>Event</b>	%	%
Runny Nose/Nasal Congestion	32	32
Headache	13	12
Decreased Activity (Lethargy)	10	10
Sore Throat	9	10
Decreased Appetite	6	7
Muscle Aches	4	5
Fever		
≥38°C by any route	6	4
≥38.5°C by any route	3	2
≥39.0°C by any route	2	1

<sup>a</sup> Represents pooled data from the two FluMist study arms.

<sup>b</sup> Number of evaluable subjects for each event.

## 6. CAN LAIV-Q AND LAIV-T BOTH BE USED WITHIN A 2 DOSE SERIES FOR CHILDREN AGED 2 TO 8?

Yes. If a child who received LAIV-Q for the first dose presents for the 2<sup>nd</sup> dose within the season and LAIV-Q is unavailable, administer either LAIV-T or trivalent inactivated influenza vaccine (TIIV).

## 7. WHY DOES LAIV-Q CONTAIN UNITED STATES (US) LABELING AND PACKAGING?

FLUMIST® QUADRIVALENT is manufactured in the US by MedImmune and distributed in Canada by AstraZeneca. In agreement with Health Canada and because of the supply situation with trivalent LAIV this season, AstraZeneca is supplying this US-labeled quadrivalent product. AstraZeneca had not planned to market quadrivalent LAIV in Canada until the 2015/16 season, although the product is approved for use by Health Canada.

A health care provider letter will accompany each box of LAIV-Q which confirms that the product composition licensed in the US “is identical to the product composition currently authorized in Canada utilizing the same facilities, manufacturing processes and comparable quality controls for production.” This letter also contains the drug identification number (DIN).

A picture of the packing and label are included below:

### 2014–2015 FORMULA

#### Influenza Vaccine Live, Intranasal FluMist® Quadrivalent

**STORE REFRIGERATED**  
at 2°- 8°C (35°- 46°F)  
**RX ONLY**



**Influenza Vaccine Live, Intranasal**  
**FluMist® Quadrivalent**  
2014–2015 FORMULA

**FOR INTRANASAL  
ADMINISTRATION ONLY**  
Contents: 10 pre-filled sprayers  
One 0.2 mL dose each  
(0.1 mL per nostril)

For indications and directions,  
see enclosed package insert.

NDC 66019-301-01

**Influenza Vaccine Live, Intranasal**  
**FluMist® Quadrivalent 2014–2015**

For Intranasal Administration Only  
0.2 mL dose (0.1 mL per nostril)  
MedImmune, LLC Gaithersburg, MD 20878  
U.S. Govt. License No. 1799 Rx Only

EXP  
LOT

7001910  
PAL v3.1

## 8. WHERE CAN I GET MORE INFORMATION ON LAIV-Q?

The Canadian product monograph is published online and can be found on AstraZeneca's website under FLUMIST® QUADRIVALENT:

<http://www.astrazeneca.ca/en/Our-Medicines/en-Products-AZ>

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## APPENDIX B - Screening Questions

<b>LIVE ATTENUATED INFLUENZA VACCINE (FLUMIST®) SCREENING QUESTIONS:</b>
Questions to ask the parent/guardian of the child or vaccine recipient prior to administration of live attenuated influenza vaccine (LAIV)
<b>CONTRAINDICATIONS:</b>
1. Do you have a history of anaphylactic reaction to a previous dose of any type of influenza vaccine or to any component of FLUMIST®?
2. Do you have an allergy to eggs?
3. Do you have severe asthma (on high dose inhaled or oral steroids) or medically attended wheezing in the 7 days?
4. Are you immunocompromised due to disease or treatment?
5. Are you a health care worker (HCW) working with immunocompromised individuals?
6. Are you less than 2 years of age or older than 17 years of age?
7. Are you pregnant or could become pregnant in the next month?
8. Are you currently/have you received aspirin/containing therapy in the last 4 weeks?
9. Do you have a history of Guillain-Barré syndrome (GBS) within 8 weeks of receipt of a previous dose of influenza vaccine without another cause being identified?
<b>PRECAUTIONS:</b>
10. Do you have a history of severe oculo-respiratory syndrome (ORS) after previous receipt of an influenza vaccine?
11. Are you in contact with someone who is severely immunocompromised and receiving care in hospital in a protected environment? (e.g., post bone marrow transplant)
<b>SPECIAL CONSIDERATIONS:</b>
12. Have you received any live vaccines in the past 4 weeks?
13. Are you currently/have you received anti-viral medications in the past 2 weeks?
14. Have you received a tuberculosis (TB) skin test in the past 4 weeks?

<b>INFORMATION FOR HEALTH CARE PROFESSIONALS: LIVE ATTENUATED INFLUENZA VACCINE (FLUMIST®) SCREENING QUESTIONS</b>
<b>CONTRAINDICATIONS:</b>
1. LAIV is contraindicated for those with a history of anaphylactic reaction to a previous dose of any type of influenza vaccine or to any component of FLUMIST®.
2. LAIV is contraindicated for individuals with an egg allergy. <b>They should be offered trivalent inactivated influenza vaccine (TIIV).</b>
3. LAIV is contraindicated for individuals with severe asthma (on high dose inhaled or oral steroids) or medically attended wheezing in the 7 days; <b>they should be offered TIIV.</b> High dose inhaled corticosteroids in pediatric patients are those treated with $\geq 200$ ug/day fluticasone (or equivalent). High dose oral corticosteroids are those treated with $\geq 2$ mg/kg per day or $\geq 20$ mg daily of prednisone for more than 14 days.
4. LAIV is contraindicated for individuals immunocompromised due to disease or treatment. <b>They should be offered TIIV.</b>
5. LAIV is publicly funded for children aged 2 to 17 years old, inclusive and therefore it is unlikely that those eligible for this product will be Health Care Workers (HCWs). <b>They should be offered TIIV.</b>
6. In BC, LAIV is publicly funded for children aged 2 to 17 years old, inclusive and LAIV is not approved for children < 24 months of age. Individuals not eligible for LAIV <b>should be offered TIIV.</b>
7. LAIV is contraindicated for pregnant women because of the lack of safety data. <b>They should be offered TIIV.</b>
8. LAIV is contraindicated for individuals receiving aspirin-containing therapy. <b>They should be offered TIIV.</b> It is recommended that use of aspirin-containing products in children < 18 years of age be delayed for 4 weeks after receipt of LAIV.
9. LAIV is contraindicated for individuals with a history of Guillain-Barré syndrome (GBS) within 8 weeks of receipt of a previous dose of influenza vaccine without another cause being identified.
<b>PRECAUTIONS:</b>
10. A history of severe oculo-respiratory syndrome (ORS) after previous receipt of an influenza vaccine is a precaution to the receipt of LAIV.
11. LAIV is a vaccine that contains a weakened strain of influenza virus and could potentially be transmitted to another person through contact with respiratory secretions. An infection with this weakened virus could cause a serious infection in a small category of patients who are severely immunocompromised and receiving care in hospital in a protected environment. Both health care workers and close contacts of such patients should avoid contact with these patients for 2 weeks after getting LAIV. <b>If such contact cannot be avoided they should be offered TIIV.</b>
<b>SPECIAL CONSIDERATIONS:</b>
12. LAIV can be given concurrently with other live vaccines. If not given at the same visit, administration of LAIV and other live vaccines should be separated by at least 4 weeks.
13. LAIV should not be administered when taking antiviral agents because they interfere with the immune response to LAIV. <b>They should be offered TIIV.</b> LAIV should not be administered to individuals while taking antiviral agents active against influenza (oseltamivir and zanamivir). If antiviral agents are administered from 48 hours before to 2 weeks after receipt of LAIV, revaccinate when antiviral agents have been discontinued for at least 48 hours.
14. Do tuberculosis (TB) skin testing on the same day as LAIV immunization, or delay tuberculosis

(TB) skin testing  $\geq$  4 weeks, to avoid having a false negative TB skin test result.

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