

ADDENDUM – LAIV Use in Egg Allergic Individuals Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI) †

Canadian Immunization Guide Chapter on
Influenza and Statement on Seasonal Influenza
Vaccine for 2016-2017

PROTECTING CANADIANS FROM ILLNESS



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PREAMBLE

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (PHAC) with ongoing and timely medical, scientific, and public health advice relating to immunization. The Agency acknowledges that the advice and recommendations set out in this statement are based upon the best current available scientific knowledge and is disseminating this document for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph(s). Recommendations for use and other information set out herein may differ from that set out in the product monograph(s) of the Canadian manufacturer(s) of the vaccine(s). Manufacturer(s) have sought approval of the vaccine(s) and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of the Agency's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

This addendum to the Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2016-2017 has been issued to address updated recommendations regarding the administration of live attenuated influenza vaccine to egg allergic individuals.

NACI recommendation: Administration of live attenuated influenza vaccine (LAIV) to egg allergic individuals

After careful review of recently published studies, NACI concludes that egg allergic individuals may be vaccinated against influenza using the low ovalbumin-containing live attenuated influenza vaccine (LAIV) licensed for use in Canada. The full dose of LAIV may be used without prior vaccine skin test and in any settings where vaccines are routinely administered. LAIV also appears to be well tolerated in individuals with a history of stable asthma or recurrent wheeze; however, it remains contraindicated for individuals with severe asthma (defined as currently on oral or high dose inhaled glucocorticosteroids or active wheezing) or for those with medically attended wheezing in the 7 days prior to immunization. The waiting period post immunization is as recommended in the Canadian Immunization Guide. As with all vaccine administration, immunizers should be prepared with the necessary equipment, knowledge and skills to respond to a vaccine emergency at all times.

The use of LAIV in egg allergic individuals is a change from previous NACI statements.

Live Attenuated Influenza Vaccine (LAIV)

FluMist® Quadrivalent is a live attenuated influenza vaccine manufactured by MedImmune (a subsidiary of AstraZeneca) for administration by intranasal spray, and authorized for use for persons 2-59 years of age in Canada. The influenza strains in FluMist® Quadrivalent are attenuated so that they do not cause influenza and are cold-adapted and temperature sensitive, so that they replicate in the nasal mucosa, rather than in the lower respiratory tract.

All influenza vaccine products authorized for use in Canada are manufactured from influenza virus grown in chicken eggs, which may result in the vaccines containing trace amounts of residual egg protein. The formulation of LAIV licensed for use in Canada contains a low amount of residual ovalbumin (<0.24 µg/dose) (Written communication from AstraZeneca), which is comparable to the amounts in inactivated influenza vaccines available for use in Canada.

Egg Allergic Individuals

The safety of LAIV in egg-allergic individuals has now been studied in more than 1100 children and adolescents, 2–18 years of age, in the United Kingdom (UK) and Canada. Two prospective cohort studies conducted by Turner et al. in the UK recruited individuals with egg allergy, including those with a history of anaphylaxis to egg or a history of severe but stable asthma, from multiple hospital-based allergy centres.^{1,2} In both studies, a previous history of requiring invasive ventilation for an anaphylactic reaction to egg was an exclusion criterion; however, no children were excluded based on this criterion. A history of severe, unstable asthma was also an exclusion criterion. One study (n=779) used quadrivalent LAIV with a detectable level of residual ovalbumin (>0.3 ng/mL), and the other (n=282) used a trivalent LAIV with an undetectable level of residual ovalbumin (<0.3 ng/mL). In both studies, no systemic reactions were reported within one hour or within 72 hours post-immunization. Fewer than 10 participants in each study experienced AEFI of possible allergic cause during the one hour post-immunization observation period; the reactions were mild and self-limiting, and occurred within 30 minutes of immunization. When looking at delayed symptoms, 221 participants who received quadrivalent LAIV reported events potentially related to the vaccine. Sixty-two of these individuals reported lower respiratory tract symptoms, of which 29 reported wheeze. Of those who received trivalent LAIV, 91 children reported a delayed event; 26 experienced lower

respiratory tract symptoms, of which 13 reported wheeze. No serious adverse events attributable to LAIV were reported.

In the Canadian study by Des Roches et al.,³ individuals with and without egg allergy (n=68 and n=55, respectively) were recruited to receive trivalent LAIV (<0.24 µg of ovalbumin/dose) to evaluate the incidence of anaphylaxis at one hour and 24 hours after immunization. Of the 68 participants with egg allergy, 40 had mild asthma, and 52 had previously received TIV. No allergic reactions were reported after one hour, and seven patients reported non-specific AEFI after 24 hours, but none were suggestive of an allergic reaction.

Post-licensure safety data are available in Canada from two sources: reports by manufacturers and others to Health Canada, and spontaneous reporting through local, provincial and territorial public health authorities to the Public Health Agency of Canada (<http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php>). Reports received by the Public Health Agency of Canada are recorded in the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS). These reports describe adverse events occurring following vaccination, and while the system is not designed to determine whether immunization caused the event, it may identify signals or trends that require further investigation.

A total of 131 reports of adverse events in influenza vaccine recipients who describe a history of allergy to eggs have been reported in CAEFISS between January 1997 and January 2016. Analysis of the CAEFISS data shows that overall, case series of individuals with and without a medical history of confirmed or possible egg allergy demonstrated similar proportions (approximately 30%) of spontaneous reports of anaphylaxis, allergic or allergic type reactions (including ORS) after receipt of any influenza vaccine. Thus a reported medical history of egg allergy does not appear to be associated with a greater proportion of spontaneous reports of anaphylaxis, allergic, or allergic-type adverse events following influenza vaccination. There has been no significant change in the number of these reports since the change in NACI's recommendation for immunization with inactivated influenza vaccine in egg allergic individuals in 2011.

After careful review of these recently published studies, and the fact that the quantity of ovalbumin in LAIV is comparable to that in inactivated influenza vaccines, NACI concludes that egg allergic individuals may also be vaccinated against influenza using the full dose of LAIV without prior vaccine skin test and in any settings where vaccines are routinely administered. LAIV also appears to be well tolerated in individuals with a history of stable asthma or recurrent wheeze; however, it remains contraindicated for individuals with severe asthma (defined as currently on oral or high dose inhaled glucocorticosteroids or active wheezing) or for those with medically attended wheezing in the 7 days prior to immunization. There are also additional contraindications for LAIV (see *Contraindications and Precautions* Section II of the *Statement on Seasonal Influenza Vaccine for 2016–2017* for details).

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References

¹ Turner, PJ; Southern, J; Andrews, NJ; et al. Safety of live attenuated influenza vaccine in atopic children with egg allergy. *Journal of Allergy and Clinical Immunology* 2015; 136: 376–381.

² Turner, PJ; Southern, J; Andrews, NJ; et al. Safety of live attenuated influenza vaccine in young people with egg allergy: multicenter prospective cohort study. *British Medical Journal* 2015; 351:h6291.

³ Des Roches, A; Samaan, K; Graham, F; et al. Safe vaccination of patients with egg allergy by using live attenuated influenza vaccine. *Journal of Allergy and Clinical Immunology Practice* 2015; 3(1): 138–139.