COVID-19 Vaccine Testing & Administration Guidance for Allergists/Immunologists from the CSACI

Current as of January 15, 2023, and based on available evidence to date

Reports of possible anaphylaxis following immunization with the Pfizer-BioNTech mRNA COVID-19 vaccine in the UK on December 9, 2020, on the first day that public immunizations began worldwide, immediately raised concerns about their safety for use in individuals with allergies.[1,2] Though early warnings raised in the UK were echoed around the world, the CSACI was among the first globally to issue guidance to temper these early broad restrictions[3,4]. In contrast to most initial guidance at the time, the CSACI stated that "those with a history of serious allergic reactions or anaphylaxis to substances that are not an ingredient in this vaccine, and those with food allergy, eczema, allergic rhinitis (hayfever), asthma, or stinging insect allergy" should safely be able to be vaccinated for COVID-19[4]. Since then, evidence has reassuringly confirmed the safety of the COVID-19 vaccines currently available, including in those individuals with unrelated allergies.[5–7]

This document is an update of a living document originally posted on the CSACI website and published in its journal to address vaccine safety concerns and provide guidance for CSACI members[8,9].

Vaccine Name	Manufacturer	Vaccine Type	Excipients of Note
Comirnaty	Pfizer-BioNTech	mRNA vaccine	polyethylene glycol [PEG], tromethamine [trometamol or Tris]
Comirnaty Bivalent	Pfizer-BioNTech	mRNA vaccine	polyethylene glycol [PEG], tromethamine [trometamol or Tris]
Spikevax	Moderna	mRNA vaccine	polyethylene glycol [PEG], tromethamine [trometamol or Tris]
Spikevax Bivalent	Moderna	mRNA vaccine	polyethylene glycol [PEG], tromethamine [trometamol or Tris]
Nuvaxovid	Novavax	Protein subunit vaccine	polysorbate 80
Covifenz	Medicago Inc.	Virus-like particle (VLP) vaccine	polysorbate 80, may contain trace amounts of PEG, kanamycin and carbenicillin[10]
Vaxzevria	AstraZeneca	Viral vector (non-replicating adenovirus) vaccine	polysorbate 80
Jcovden	Janssen	Viral vector (non-replicating adenovirus) vaccine	polysorbate 80
Sources[5,10]			

Following the initial emergency approval of the Pfizer-BioNTech mRNA vaccine in Canada in December 2020, multiple vaccine preparations are currently authorized for use in Canada, including four mRNA vaccines, two utilizing SARS-CoV-2 recombinant spike proteins, and two adenovirus vector vaccines (see Table).[5]

Suggested approach to vaccination in individuals with confirmed or suspected allergic conditions:

- **Assessment by an allergist is NOT WARRANTED prior to receiving COVID-19 vaccination for individuals with a history of unrelated allergic conditions or adverse reactions, INCLUDING ANAPHYLAXIS, such as:**
    - **Other vaccines**
    - **Foods**
    - **Insect venom**
    - **Environmental allergies**
    - **Unrelated oral/injected medication**
    - **Radiocontrast media (RCM), and**
    - **Asthma, allergic rhinitis, or atopic dermatitis**

  In these individuals, the available COVID-19 vaccines can be administered without any special precautions or investigations. The COVID-19 vaccines available do not contain any food products (e.g. egg protein) or latex.[5,11] As with the routine administration of all vaccines, the COVID-19 vaccine should be administered in a healthcare setting capable of managing anaphylaxis, and individuals should be observed for a minimum of 15 minutes following vaccination.[5]

- **Assessment by an allergist is NOT WARRANTED for any individual who has a history of a localized reaction to a prior dose of the COVID-19 vaccine or to any of its components.** The risk of anaphylaxis is low and these individuals can be safely receive a subsequent dose of the same vaccine[7].

- **Assessment by an allergist is WARRANTED for any individual with anaphylaxis following the COVID-19 vaccine or to any of its components.** This is strongly preferred over not being vaccinated or withholding vaccination, and includes anyone who has experienced a suspected severe immediate allergic reaction after administration of a COVID-19 vaccine, or someone with a confirmed allergy to a component of the vaccine.[5,7] Significant evidence now exists that these individuals can safely receive a subsequent dose of the same vaccine with low risk of a systemic reaction under the supervision of an allergist or other healthcare individual with expertise in anaphylaxis and vaccine allergy.[5,7,12,13] The National Advisory Committee on Immunization (NACI) and Public Health Agency of Canada currently recommends that revaccination with the same vaccine or same mRNA platform may be offered in consultation with an allergist or other appropriate physician.[5]

- While the studies to date have been predominantly in adults, there have been no specific safety signals identified in pediatric patients and this guidance applies to individuals of all ages.

- These recommendations will be updated as evidence evolves to reflect ongoing best practice.

Summary:

1. *There is a low risk for allergic reactions associated with vaccines. Non-allergic reactions to vaccines are much more frequent than allergic reactions.*
2. *The nature and cause of the reported allergic reactions to COVID-19 vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.*
3. *The role of allergy testing for COVID-19 vaccines and their excipients is not currently recommended.*
4. *In someone with anaphylaxis following the COVID-19 vaccine or to one of its components for whom an additional dose is required, revaccination with the same platform vaccine has been demonstrated to be safe under the supervision of an allergist or other healthcare provider with management expertise of anaphylaxis and vaccine allergy. A prolonged observation period of at least 30 minutes is recommended.*

1. <u>There is a low risk for allergic reactions associated with vaccines. Non-allergic reactions to vaccines are much more frequent than allergic reactions.</u>

Vaccines activate the immune system, which commonly result in minor local and systemic side effects, including fever and local inflammatory reactions (redness, swelling, pain and warmth) at the site of the injection.[11,14] As with other vaccines, local cutaneous reactions after vaccination with COVID-19 vaccines are common.[11] These reactions may include acute localized urticaria and/or angioedema and tend to be mild and self-limiting[15,16]. These reactions are not a contraindication to receiving the same vaccine in the future, as they do not pose a risk for future severe allergic reactions.[11,15,16]

Non-allergic reactions to vaccines also include immunization stress-related responses that can mimic allergic reactions, and may include breath-holding, hyperventilation, and vasovagal syncope (fainting).[11,14]

To date, there have been approximately 670 million reported cases of COVID-19 worldwide and over 6.7 million deaths[17]*. In Canada, there have been over 4.5 million confirmed cases and almost 50,000 deaths from COVID-19*[17]*, over 96.6 million vaccine doses have been administered*[17]*, and anaphylaxis has been reported 897 times (~1 per 100,000 doses administered).*[6] *By comparison, while approximately 12.9 billion COVID-19 vaccine doses have been administered worldwide, there have been neither reported fatalities nor long-term morbidity associated with anaphylaxis following COVID-19 vaccine administration*[6,17]*.*

2. **The nature and cause of the reported allergic reactions to COVID-19 vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.**

The worldwide incidence of anaphylaxis following COVID-19 vaccination is estimated at about 7.91 cases per million doses administered.[7] There have been no fatalities or long-term morbidity described with these events. The nature and cause of the reported allergic reactions to these vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.

Allergic reactions to vaccines can be elicited by the active vaccine component, or more commonly, by one of the excipients in the vaccine.[18] Polyethylene glycol (PEG), polysorbate 80, tromethamine (trometamol or Tris), kanamycin and carbenicillin are identified as possible excipients that may trigger allergic reactions in various COVID-19 vaccines available in Canada (see Table).[5] However, there is increasing evidence that either these are not the culprit excipients and/or the reactions are not IgE-mediated.[7,12,13,19] This remains under investigation.

3. **Allergy testing for COVID-19 vaccines and their excipients is not currently recommended.**

Epicutaneous and intradermal testing protocols to COVID-19 vaccines and their excipients (PEG, polysorbate) have been published. However, evidence has now convincingly illustrated that skin test results do not affect tolerance of a second COVID-19 dose even in individuals with an immediate reaction to the first dose.[7,20] As a result, testing is not currently recommended.

4. **In someone with anaphylaxis following the COVID-19 vaccine or to one of its components for whom an additional dose is required, revaccination with the same platform vaccine has been demonstrated to be safe under the supervision of an allergist or other healthcare provider with management expertise of anaphylaxis and vaccine allergy. A prolonged observation period of at least 30 minutes is recommended.**

For a patient with a history of a severe allergic reaction (anaphylaxis) to a COVID-19 vaccine or any of its components for whom an additional dose is required, allergy testing to the vaccine and its components is not recommended.[7,12,13,20] Evidence reveals that the risk of severe repeat reactions to the same vaccine is low,[7] such that a safe option for consideration as part of shared decision-making includes re-administration of the same vaccine with prolonged observation. This recommendation is also in keeping with NACI recommendations that in those with anaphylaxis following the COVID-19 vaccine, revaccination with the same vaccine platform or same vaccine may be offered in consultation with an allergist and with at least 30 minutes observation.[5] Several studies have demonstrated safe revaccination of individuals with an immediate reaction to the first dose of a COVID-19 vaccine, and it is increasingly recognized that these reactions may not be allergen-driven or IgE-mediated.[7,19]

With the goal of safe reimmunization and reducing vaccine hesitancy, shared decision-making is necessary. For higher-risk patients who are hesitant to proceed with vaccine administration, allergy testing remains an option after education that the predictive value of such testing is unknown. Allergy testing for lower-risk patients is NOT recommended and may unnecessarily

delay administration of COVID-19 vaccines. As discussed above, though evidence increasingly reveals the safety of revaccination among those with anaphylaxis using a single full dose protocol[7], graded vaccine administration or a split-dose protocol may be considered as part of shared decision-making. In addition, if an assessment deems a specific vaccine platform is contraindicated, selection of an alternative vaccine with a different platform and excipients remains a reasonable and safe option.

Addendum: Previous CSACI guidance included a section on vaccination of individuals with immunocompromise as this was prior to the COVID-19 vaccines being recommended in these individuals. The Public Health Agency of Canada and NACI now recommend a complete COVID-19 vaccine series in immunocompromised individuals. For information on vaccination of individuals with immunocompromise please refer to the Canadian Immunization Guide for COVID-19 vaccine[5].

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