

FOCUS ON

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COVID-19 Vaccines: Viral Vector-based Vaccines

Introduction

The novel coronavirus disease (COVID-19) pandemic has stimulated unprecedented efforts to develop vaccines that provide protection against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹

This Focus On is intended for health care providers and public health partners. It provides an overview of viral vector-based vaccines, including products authorized for use in Canada. This document will be updated as new information becomes available.

The basics: Viral vector-based vaccines

Viral vector-based vaccines have emerged as a promising alternative to conventional vaccine platforms.²⁻⁴ Viral vector-based technology has been widely used for gene therapy, cancer therapeutics and animal vaccines for several decades, and most recently for two human Ebola vaccines.³⁻⁷

What is a viral vector?

A viral vector is a harmless, attenuated (weakened) virus that has been modified to act as a delivery system for transferring genetic instructions to our cells.³⁻⁷

Vaccines work by training our immune system to recognize and respond to infectious agents. For most vaccines, this is accomplished by delivering a weakened or inactivated virus or a component of the virus (such as a specific protein) to the body, which triggers an immune response.^{2,3} In contrast, viral vector-based vaccines work by using a harmless, unrelated attenuated virus (a viral vector), to deliver genetic instructions (DNA) to human cells to produce a viral protein for the pathogen of interest, which is then recognized by the body as foreign.²⁻⁸ These proteins, known as antigens, use the body's normal processes to safely produce an immune response.²⁻⁸ There are two main types of viral vector-based vaccines:

- **Non-replicating (or replication-incompetent or replication-deficient) viral vector-based vaccines** are genetically modified so that they are unable to produce new viral particles. The viral vector enters our cells where our cell machinery is used to produce viral antigen; once this is accomplished, the viral vector is cleared.^{2,4,9} COVID-19 viral vector-based vaccines authorized for use in Canada are non-replicating vaccines.⁹⁻¹²
- **Self-replicating (or replication-competent) viral vector-based vaccines** are able to produce new viral particles in the cells they infect. These vectors use our host cell machinery to produce new viral particles, which go on to infect additional host cells and produce more viral antigen.^{2,4,9}

None of the COVID-19 viral vector-based vaccines authorized for use in Canada or other jurisdictions are replicating vaccines.¹

Mechanism of action and immune response

COVID-19 viral vector-based vaccines use our normal cell processes to safely produce the SARS-CoV-2 spike (S) glycoprotein antigen, which activates both **antibody** and **cell-mediated** immune responses.^{2,3,8,9}

- Viral vector-based vaccines use a harmless, attenuated adenovirus as a vector to deliver genetic instructions (DNA) to our cells to make the SARS-CoV-2 spike glycoprotein. Adenoviruses are a group of DNA viruses that commonly cause colds.²⁻⁷
- During manufacturing, DNA coding for the SARS-CoV-2 spike glycoprotein is inserted into the adenoviral vector, which acts as a delivery system to bring the SARS-CoV-2 spike glycoprotein code to our cells. The adenoviral vector is genetically modified so that it cannot replicate or cause infection.^{2-7,9}
- Once inside our cells, DNA encoding the SARS-CoV-2 spike glycoprotein is released from the viral vector in the cell's nucleus where the body's cellular machinery makes a transcript called messenger RNA (mRNA). This transcript is then released into the cytoplasm of our cells where it is used to make the SARS-CoV-2 spike glycoprotein antigens. The viral vector, DNA fragment and mRNA transcript are then rapidly broken down and disposed of by our cells.²⁻⁹
- Next, the SARS-CoV-2 spike glycoprotein antigen is temporarily displayed on the surface of our cells, where it is recognized as foreign and activates B (antibody-mediated) and T (cell-mediated) cells of the immune system.^{2,3,8,9}
- **Antibody-mediated** responses directed against the SARS-CoV-2 spike glycoprotein are believed to be important for blocking the virus from entering our cells.⁸ Activation of **cell-mediated** immune responses are expected to play a central role in providing us long-term protection.⁸

Key messages: COVID-19 viral vector-based vaccines

1. You cannot get COVID-19 or other infections from a viral vector-based vaccine

Viral vector-based COVID-19 vaccines are non-infectious (they do not contain whole or live virus) and are modified so that the viral vector cannot replicate inside our cells.²⁻⁷ Therefore, there is no risk of a viral vector-based vaccine causing COVID-19 or any other viral infection.⁵⁻⁷

2. Viral vector-based vaccines are a newer vaccine platform, but not new technology

Viral vector therapeutics (e.g., gene therapy, animal and human vaccines) have been studied for over four decades, with a well-established manufacturing and safety profile. Most recently, this technology has been used to develop vaccines to respond to recent Ebola outbreaks.⁴⁻⁷

3. Viral vector-based vaccines do not affect or interact with our DNA

Genetic material delivered by a viral vector is genetically stable and does not integrate or interact with our DNA.³⁻⁷ Human cells break down and get rid of the viral vector and DNA as soon as they finish using its instructions.⁵⁻⁷

Advantages and limitations of viral vector-based vaccines

Recent advances in viral vector-based vaccine technology offer several advantages over classical vaccine platforms. Adenoviral vector-based vaccines are highly immunogenic and trigger strong antibody and cell-mediated immune system responses that are anticipated to provide longer-term protection.^{2,3,8} In the context of limited vaccine supply, viral vector-based vaccines offer several operational benefits including a single dose product series (i.e. Janssen) and less stringent storage and handling conditions (i.e. refrigerated temperatures, due to greater product stability) relative to other vaccine platforms.^{4,10-18}

Limitations of viral vector-based vaccines include diminished immune responses and vaccine effectiveness in individuals with pre-existing immunity to the viral vector.^{3,4,6,7} Since adenoviruses are a common cause of colds, individuals with pre-existing adenoviral immunity achieved through natural infection may neutralize the viral vector and mount a limited immune response, however this limitation is overcome for COVID-19 vaccines by using adenovirus serotypes that rarely cause infections or using a non-human adenovirus.^{3,4,6,7}

COVID-19 viral vector-based vaccines

In Canada, two COVID-19 viral vector-based vaccines have been authorized for use under Health Canada's [Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19](#).⁵ Detailed characteristics of each vaccine are outlined in **Table 1**.

Table 1: Characteristics of COVID-19 viral vector-based vaccines authorized for use in Canada

	AstraZeneca/Oxford University (UK)¹	Janssen Inc. (Johnson & Johnson) (USA)
Vaccine Name	COVID-19 vaccine, ChAdOx1-S (recombinant) ^{10,11}	SARS-CoV-2 vaccine Ad26.COVS.2 (recombinant) ¹²
Vaccine Platform	Recombinant, replication-deficient (non-replicating) chimpanzee adenovirus (ChAdOx1) vector-based vaccine ^{10,11,13,14}	Recombinant, replication-incompetent (non-replicating) adenovirus serotype 26 (Ad26) vector-based vaccine ^{12,15,16}
Antigenic Target	SARS-CoV-2 spike (S) glycoprotein ^{10,11}	Pre-fusion SARS-CoV-2 spike (S) glycoprotein ^{12, 15,16}
No. of Doses Administered	2 doses ^{10,11}	1 dose ¹²
Dosage	5 x 10 ¹⁰ viral particles per 0.5 mL dose ^{10,11}	5 x 10 ¹⁰ viral particles per 0.5 mL dose ¹²
Adjuvant	No ^{10,11}	No ¹²
Diluent	No ^{10,11}	No ¹²
Schedule	Authorized Interval: 4 to 12 weeks ^{10,11,17} Extended Interval: 16 weeks ^{10,11,17,18} Minimum Interval: 28 days ^{10,11,17}	N/A
Route of Administration	Intramuscular (IM) ^{10,11}	Intramuscular (IM) ¹²
Storage Conditions	2 °C to 8°C ^{10,11} Do not freeze ^{10,11} Keep vials in original packaging to protect from light ^{10,11}	2 °C to 8°C ¹² Do not freeze ¹² Keep vials in original packaging to protect from light ¹²

¹ Health Canada has authorized two manufacturers to produce the COVID-19 vaccine ChAdOx1-S: AstraZeneca (brand name AstraZeneca COVID-19 vaccine) and Verity Pharmaceuticals and the Serum Institute of India (SSI) (brand name COVISHIELD vaccine).

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