Summary Report of Risk Assessment Conducted Pursuant to subsection 108(1) of the *Canadian Environmental Protection Act, 1999*

New Substances Notification 20657: Recombinant replication-defective chimpanzee adenovirus Ox1 expressing Spike protein (S protein) of SARS-CoV-2 (ChAdOx1-S)

Regulatory decision

Under the provisions for Animate Products of Biotechnology in Part 6 of the *Canadian Environmental Protection Act, 1999* (CEPA), and pursuant to section 108 of the Act, the Minister of the Environment and the Minister of Health have assessed information in respect of the substance, ChAdOx1-S, that is a living organism. It was determined that ChAdOx1-S is not suspected to be toxic and not anticipated to enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity, constitute or may constitute a danger to the environment on which life depends, or constitute or may constitute a danger to human life or health in Canada. Therefore, no further action is recommended as a result of this assessment.

Identity

The notified organism ChAdOx1-S is a genetically modified chimpanzee adenovirus. The modifications render the virus incapable of replication and allow the expression of a gene encoding the Spike (S) protein of SARS-CoV-2. Upon administration as a vaccine to humans, the notified organism expresses the S protein of SARS-CoV-2 leading to the production of the S-protein specific antigens in the human body. These antigens are expected to trigger immune response and offer protection against SARS-CoV-2 infection and COVID-19 disease.

Notified and potential uses

ChAdOx1-S was notified for import into Canada as a commercial vaccine in adults for the prevention of COVID-19. Other than the manufacture of the vaccine in Canada, no other potential uses were identified.

Hazard assessment

The environmental and human health hazard potential of ChAdOx1-S is assessed to be low because:

1. The wild-type adenovirus, ChAdY25, is known to cause mild infections in chimpanzees, which is its natural host. There is no evidence to suggest that wild-type ChAdY25 can infect aquatic plants, invertebrates or vertebrates, or terrestrial plants or invertebrates. The genetic changes made in ChAdOx1-S are not expected to alter its behaviour in hosts.
2. Adenoviruses are ubiquitous and rarely cause disease in humans. There is no evidence of ChAdY25 circulating in the human population and there are no reports of adverse effects in humans (O'Hara et al., 2012).

3. The genetic modifications in ChAdOx1-S are well-defined and stably integrated. ChAdOx1-S can only replicate in cells expressing adenoviral E1 genes. The probability of E1 complementation resulting in a replication-competent virus in natural environments or during human infection is low, and if it occurred, the transgene would be lost as it occupies the locus of the E1 genes.
4. The deletion of the E1 region in ChAdOx1-S impairs replication, and thereby attenuates virulence.
5. Data from animal studies conducted by the notifier in non-human primates and other mammalian models indicated no observable adverse effects in treated animals.
6. Preliminary results from human clinical trials with ChAdOx1-S conducted outside of Canada indicated that treatment is well-tolerated without serious adverse effects. Only clinically manageable adverse events were reported.[1]

Hazards related to micro-organisms used in the workplace should be classified accordingly under the Workplace Hazardous Materials Information System (WHMIS)[2].

Exposure assessment

The environmental exposure and indirect human exposure potential of ChAdOx1-S is assessed to be low because:

1. Only planned target doses of ChAdOx1-S will be imported into Canada and transported to multiple healthcare centres in secured containers for the purpose of immunization of the Canadian population. ChAdOx1-S may be administered to up to 10 million subjects under controlled conditions and by properly trained healthcare professionals.
2. General biosafety measures in healthcare settings and contingency plans for accidental spills are expected to be in place to minimize the spread of the virus.
3. ChAdOx1-S is replication-deficient and therefore not expected to remain viable, persist or proliferate in the environment.
4. Minimal shedding of ChAdOx1S is anticipated following administration of the vaccine to humans, based on the biodistribution and shedding studies conducted in mice.
5. The notifier does not intend to manufacture ChAdOx1-S in Canada. Should it be manufactured in Canada, exposure to the environment or general population is not expected to significantly increase, as ChAdOx1-S cannot survive in the environment outside the body of vaccinated patients.

Risk characterization

[1] In Canada, biologic drugs are assessed for safety, quality and efficacy under the *Food and Drugs Act* and Regulations, administered by the Biologic and Radiopharmaceutical Drugs Directorate of Health Canada.

[2] A determination of whether one or more of the criteria of section 64 of CEPA are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposure in the general environment. For humans, this includes, but is not limited to, exposure from air, water and the use of products containing the substances. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the criteria in the *Hazardous Products Regulations,* which is part of the regulatory framework for the Workplace Hazardous Materials Information System (WHMIS) for products intended for workplace use.

Risk is typically described as the probability of an adverse effect occurring based on hazards and a particular scenario of exposure. Different exposure scenarios can be described based on the intended and/or potential uses (if any) involved. In the present case, the organism will be imported and used as a commercial vaccine in adults for the prevention of COVID-19 in Canada.

Owing to the low potential for environmental hazard and the low potential for environmental exposure, the environmental risk associated with the use of ChAdOx1-S as a commercial vaccine drug product for the prevention of COVID-19 in adults in Canada is assessed to be low.

Owing to the low potential for human health hazard and the low potential for human exposure, the indirect human health risk associated with the use of ChAdOx1-S as a commercial vaccine drug product for the prevention of COVID-19 in adults in Canada is assessed to be low.

The assumptions made in the assessment are adequately protective for the general population as well as for subpopulations who may be more susceptible or highly exposed.

Risk assessment conclusion

There is no evidence to suggest a potential risk of adverse environmental effects at the exposure levels predicted for the Canadian environment from the use of ChAdOx1-S as a commercial vaccine drug product for the prevention of COVID-19 in adults in Canada. The risk to the environment associated with ChAdOx1-S is not suspected to meet the criteria in paragraphs 64(a) or (b) of CEPA. No further action is recommended.

Similarly, there is no evidence to suggest a potential risk of adverse human health effects at the exposure levels predicted for the general Canadian population from the use of ChAdOx1-S as a commercial vaccine drug product for the prevention of COVID-19 in adults in Canada. The risk to human health associated with ChAdOx1-S is not suspected to meet the criteria in paragraph 64(c) of CEPA. No further action is recommended.

References:

Canada (1999). *Canadian Environmental Protection Act*, 1999. S.C. 1999, c.33. Part 6: Animate Products of Biotechnology. https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/publications/canadian-environmental-protection-act-1999/part-6.html (viewed 2023-04-14).

O'Hara, G.A., Duncan, C.J., Ewer, K.J., Collins, K.A., Elias, S.C., Halstead, F.D., Goodman, A.L., Edwards, N.J., Reyes-Sandoval, A., Bird, P., *et al*. (2012). Clinical assessment of a recombinant simian adenovirus ChAd63: a potent new vaccine vector. *J Infect Dis*, 205**:**772-781.