New substances: risk assessment summary, new substances notifications 22147, 22148 and 22149

Official title: New substances: risk assessment summary, New Substances Notifications 22147, 22148 and 22149 – Schedule 2 of the *New Substances Notification Regulations (Organisms)*

Notified organisms:

- Alphainfluenzavirus influenzae A/Victoria/4897/2022 IVR-238
- Alphainfluenzavirus influenzae A/California/122/2022 SAN-022
- Betainfluenzavirus influenzae B/Michigan/01/2021

Schedule of the NSNR(O): Schedule 2 - Information Required in Respect of Micro-organisms Manufactured in or Imported to a Contained Facility That Are Not for Introduction Outside the Contained Facility or That Are for Export Only

Organism type: Virus

Use: Import and manufacture of the notified strains for vaccine manufacturing process validation activities

Anticipated quantity: confidential and not for disclosure

Assessment level of concern:

- Human health hazard: Low
- Human exposure: Low
- Environmental hazard: Low
- Environmental exposure: Low

Assessment conclusion under section 64 of the *Canadian Environmental Protection Act, 1999* (CEPA): Low risk, not suspected to be toxic

Recommended action: None.

Waiver: Requested for information element 4(b) of Schedule 2 of the NSNR(Organisms), under paragraph 106(8)(a) of CEPA.

Synopsis

Alphainfluenzavirus influenzae A/Victoria/4897/2022 IVR-238, Alphainfluenzavirus influenzae A/California/122/2022 SAN-022 and Betainfluenzavirus influenzae B/Michigan/01/2021 (hereafter**,** the notified strains) were notified for their import and manufacture in a contained facility (i.e., B200 facility in Toronto, ON) for the purpose of vaccine manufacturing process validation activities. No live organisms will be released from the facility. There is no evidence to suggest a potential risk of adverse effects to the environment and for the general population in Canada from the notified use. Owing to the low potential for hazard and the low potential for exposure to the environment and the general population in Canada, the notified strains are not suspected to meet the criteria in paragraphs 64(a), (b), or (c) of CEPA. It was recommended that a waiver of information requirements under subparagraph 4(b) of the NSNR (Organisms) under CEPA 106(8)(a) be accepted as the information is not needed in order to determine whether the living organism is toxic or capable of becoming toxic.

Background

The notified strains are live influenza vaccine strains. They will be manufactured in a contained facility in Canada. The final inactivated (killed) reassortant viruses are intended to be used as components of a vaccine drug product, Fluzone® High-Dose (aka Fluzone® HD).

Hazard

The environmental and indirect human hazard potential of the notified strains was determined to be low because:

1. Alphainfluenzavirus influenzae A/Victoria/4897/2022 IVR-238 and Alphainfluenzavirus influenzae A/California/122/2022 SAN-022 were produced by reassorting two influenza viruses. Betainfluenzavirus influenzae B/Michigan/01/2021 is a wild type influenza B virus.
2. The two reassorted strains are classified as risk group (RG) 2 human and animal pathogens and the wild type strain is classified as a RG2 human pathogen and a RG1 animal pathogen by the Public Health Agency of Canada (PHAC).
3. Reassortments leading to genetic modifications in the two reassorted strains are well-defined and stable. The introduced genetic modifications are not known to confer any pathogenic or toxic properties. Considering the complete inactivation of the virus in the vaccine drug substance and drug product, no further reassortment with wild type influenza viruses is expected. The wild type strain has not been genetically modified, attenuated or has undergone any intentional reassortments.
4. The notified strains are RNA viruses which are known to mutate resulting in potential viral variants during their propagation. However, the notifier intends to do only one passage, to manufacture drug substance, which is expected to limit its ability to mutate and create new viral strains.

5. There is no evidence to suggest that wild type influenza A and B viruses can infect aquatic or terrestrial plants or invertebrates.
6. The host range of wild type influenza A viruses is limited to humans, avian, and mammalian species and the host range of wild type influenza B viruses is primarily limited to humans although some strains of influenza B viruses have been isolated from harbor seals. Wild type influenza A and B viruses cause self-limiting infections in humans that usually resolve within a week, with outbreaks occurring seasonally in Canada.
7. Genome analyses of the notified strains did not identify any antimicrobial or antiviral resistance genes. Furthermore, antiviral agents are available for treatment in case of infection by the notified strains.

Hazards related to micro-organisms used in the workplace should be classified accordingly under the Workplace Hazardous Materials Information System (WHMIS)[1].

Exposure

The environmental and indirect human exposure potential of the notified strains is determined to be low because:

1. The notified strains will be imported into and manufactured in a contained facility in Toronto, ON (B200).
2. The notified strains will be imported into Canada from the USA, transported in secured containers, and manufactured in the B200 facility to validate process activities.
3. The notified strains will be chemically inactivated during the production of the drug substance and prior to their use in the final drug product. Validated inactivation procedures were provided by the notifier and deemed adequate by the New Substances program. The final vaccine drug product will not contain any live virus.
4. Use of this inactivated virus in vaccine products is subject to the Food and Drugs Act[2].
5. Releases of live virus into the environment are expected to be negligible since all liquid, solid, and gaseous wastes containing the notified organism will be inactivated prior to disposal or release into the environment.
6. All facility personnel have received adequate training, and standard operating procedures are in place to deal with any accidental spills.
7. In the unlikely event of an accidental release from the facility, similar to the wild-type influenza A and B viruses, the notified strains are not expected to persist for long in the

[1] 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.

[2] 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.

environment without a mammalian host, and they would be rapidly inactivated by temperature, pH, UV, light, and humidity in the environment.

Risk Characterization

Owing to the low potential hazard and the low potential exposure, the environmental and human health risks associated with the import and manufacture of the notified strains in a contained facility were assessed to be low.

Risk Assessment Conclusion

Available evidence does not indicate a potential risk of adverse environmental or human health effects from the import and manufacture of the notified strains in a contained facility. The risk to the environment and human health associated with the import and use of the notified strains in a contained facility is not suspected to meet criteria in paragraphs 64(a), (b), or (c) of CEPA. No further action is recommended.