Risk Assessment Summary

for

NSN-18740: *Aspergillus* species strain

(Production of an active pharmaceutical ingredient)

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA), animate products of biotechnology (i.e. “living organisms”) not listed on the Domestic Substances List (DSL) are considered “new” to Canada. Information and data prescribed by the *New Substances Notification Regulations (Organisms)* [NSNR(O)] must be submitted before they are manufactured or imported, and Environment and Climate Change Canada (ECCC) and Health Canada (HC) must assess their potential to harm human health and the environment.

Aspergillus species strain, a mold that was proposed to be manufactured for use in the production of an active pharmaceutical ingredient, was assessed according to the requirements of Schedule 2 of the NSNR(O), which applies to substances that are not intended for introduction outside a contained facility or for export only. Living organisms notified under this schedule are not eligible for addition to the DSL.

Regulatory Decision

Based on the assessment described below, *Aspergillus* species strain is not considered to be harmful to human health or the environment for the intended use in the production of an active pharmaceutical ingredient. As *Aspergillus* species strain is not entering the environment in a quantity or under conditions that pose a danger to the environment or human health, no further action is recommended as a result of this assessment.

After September 24, 2016, the contained manufacture of *Aspergillus* species strain could proceed in Canada.

Background

Aspergillus species strain is a mould that was developed through sequential steps of gene modification, culturing and strain selection. As a result of the modifications, the

micro-organism is able to produce high yields of a substance to be used as an active pharmaceutical ingredient, allowing it to be used for industrial production of that substance.

Hazard Considerations

With respect to the environment
The environmental hazard potential of *Aspergillus* species strain is considered to be low-medium for the following reasons:

- Aspergillus species does not commonly cause diseases in animals or plants and the notified strain is not expected to behave any differently. However, the substance that it produces in higher amounts, may act as a virulence factor and, in the absence of specific pathogenicity or toxicity testing on the notified strain, the risk assessment concluded with an environmental hazard level of low-medium, in order to account for these factors.

With respect to human health
The human hazard potential of *Aspergillus* species strain is considered to be low for the following reasons:

- There is no history of use of *Aspergillus* species strain in Canada; however, there is a long history of safe use of other strains of this species in enzyme production for the food industry around the world.

- As *Aspergillus* species strain is susceptible to amphotericin B, itraconazole and voriconazole, in the unlikely event of an infection with the notified organism, clinically relevant antifungals are available for treatment.

The following considerations were also taken into account in the assessment of human health and environmental hazard:

- The taxonomic identity of the notified strain was demonstrated by a recognised authority.

- The genetic modifications introduced into *Aspergillus* species strain did not involve the introduction of foreign genetic material and resulted only in increased production of an active pharmaceutical ingredient. These modifications are not expected to significantly increase the virulence or toxicity of the notified strain to humans or animals.

- The *Aspergillus* species strain does not produce fungal toxins of concern.

Exposure Considerations

With respect to the environment and humans
The environmental and human exposure potential of *Aspergillus* species strain are considered to be low for the following reasons:

- Annually, a maximum of 80,000 L of *Aspergillus* species strain will be manufactured for production of a substance as an active pharmaceutical ingredient for export.
- The manufacturing process will adhere to Containment Level 2 – Large Scale requirements, as defined in the Canadian Biosafety Standard (CBS) 2nd edition.
- All manufacturing plant personnel have adequate training and detailed SOPs, including emergency procedures, are in place to deal with any accidental spills or loss of culture.
- The fermentation runs are conducted in a closed system. All liquid, solid and gaseous wastes containing *Aspergillus* species strain will be adequately treated and inactivated prior to disposal or release of the waste into the environment. As a result, no significant releases into the environment are expected.
- *Aspergillus* species strain, like other strains of its species, could persist in the Canadian environment; however, introduced populations are unlikely to survive the winter successfully enough to be maintained in many parts of Canada.

Risk assessment conclusion

Risk is typically described as the probability of an adverse effect occurring based on hazards and a particular scenario of exposure (Environment Canada and Health Canada, 2011). Different exposure scenarios can be described based on intended and any potential uses. In the present case, *Aspergillus* species strain will be used as in production of an active pharmaceutical ingredient. Given the specialized modifications, no other uses are envisaged.

With respect to the environment (as production organism used in containment)
While Aspergillus species strain was assigned a low-medium potential environmental hazard, given the low potential environmental exposure, the environmental risk associated with the use of *Aspergillus* species strain in the production of an active pharmaceutical ingredient is assessed to be low.

With respect to human health (as a production organism used in containment)
Given the low potential hazard to the general population in Canada and the low potential human exposure, the human health risk associated with the use of *Aspergillus* species strain in the production of an active pharmaceutical ingredient is assessed to be low.

References

(excluding proprietary information or references provided by the notifier)

Environment Canada and Health Canada (2011). Framework for Science-Based Risk Assessment of Micro-Organisms Regulated under the Canadian Environmental Protection Act, 1999 (2011). http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=120842D5_1 (viewed May, 2018).

Public Health Agency of Canada (2015) Canadian Biosafety Standard (CBS) Second Edition. https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/second-edition.html (viewed June 2018).