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

New Substances Notification 19832: *Escherichia coli* CBS

Regulatory decisions

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 living organism *Escherichia coli* CBS, and have determined that it is is 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 in Canada to human life or health.

Organism identity

Escherichia coli CBS is a genetically modified bacterium.

Notified and potential uses

Escherichia coli CBS was notified according to the requirements for Schedule 2 of the *New Substances Notification Regulations (Organisms)* [NSNR(O)], which applies to micro-organisms that are not intended for introduction outside a contained facility or for export only. It is proposed to be manufactured in Canada for the production of cystathionine β–synthase enzyme to be used in a diagnostic medical assay. The micro-organism is not eligible for addition to the *Domestic Substances List* on the basis of this assessment, and a new notification would be required before the micro-organism is imported or manufactured for any use outside of a contained facility.

Environmental fate and behaviour

E. coli CBS was developed under conditions that are unlikely to be present in the environment and possesses inherent characteristics that limit its survival and persistence in the environment.

Environmental assessment

Hazard Considerations

The environmental hazard potential of *E. coli* CBS is considered to be low for the following reasons:

- The parental strain of *E. coli* CBS is a non-pathogenic, common laboratory strain that has a well-documented history of safe use and is unable to cause any harm to aquatic and terrestrial plants, vertebrates and invertebrates.

- The plasmid used for modification of the parental strain does not contain any genetic elements conferring a selective advantage that may result in any adverse environmental effects.

- The inserted gene and the enzyme it encodes are not known to have any negative impacts in aquatic or terrestrial environments.

Exposure Considerations

The environmental exposure potential of *E. coli* CBS is considered to be low for the following reasons:

- *E. coli* CBS will be manufactured in Canada for the notified use, with no sale or distribution of living culture from the notified micro-organism.

- With the manufacturing process adhering to the Large Scale requirements of the Canadian Biosafety Standards and Guidelines – Containment Level 1: Physical Design and Operational Practices, potential for environmental releases will be limited.

- Additionally, it is expected that all manufacturing plant personnel will be adequately trained on relevant containment practices, and detailed standard operating procedures for decontamination and disposal of wastes will be followed. There are also emergency procedures in place to deal with any accidental spills or loss of culture.

Human health assessment

Hazard Considerations

The human health hazard potential of *E. coli* CBS is considered to be low for the following reasons:

- The parental strain of *E. coli* CBS is a non-pathogenic, common laboratory strain that has a well-documented history of safe use and is unable to cause infections in humans.

- The plasmid used for modification of the parental strain does not contain any genetic elements conferring a selective advantage or human disease-causing properties to the bacterial host.

- There are no reported cases of human infection with *E. coli* CBS even though it grows at human physiological temperature.

- No pathogenicity and toxicity testing has been conducted on the notified strain; however, whole genome sequencing of the micro-organism did not indicate any genes of concern.

- In-house analysis of the enzyme produced by the notified strain using publically available databases did not predict any allergy inducing properties for that compound.

- *E. coli* CBS is susceptible to a number of antimicrobial drugs so in the unlikely event of human infection with the notified strain, clinically relevant antibiotics are available for treatment.

Exposure Considerations

The human exposure potential of *E. coli* CBS is considered to be low for the following reasons:

- *E. coli* CBS will be manufactured in Canada for the notified use with no anticipated external sale or distribution of living culture from the notified micro-organism.

- With the manufacturing process adhering to the Large Scale requirements of the Canadian Biosafety Standards and Guidelines – Containment Level 1: Physical Design and Operational Practices, potential for human exposure and environmental releases will be limited.

Risk assessment conclusion

Risk is typically described as the probability of an adverse effect occurring based on the known hazards and a particular scenario of exposure (Environment Canada and Health Canada, 2011). In the present case, *E. coli* CBS will be manufactured for use in the production of an enzyme to be used in a diagnostic medical assay. Due to the specialized nature of modifications to the notified micro-organism, no other uses are envisaged.

Given the low environmental hazard potential and the low environmental exposure potential, the environmental risk associated with the use of *E. coli* CBS for the production of an enzyme to be used in a diagnostic medical assay is assessed to be low.

Given the low human health hazard potential and the low human exposure potential, the human health risk associated with the use of *E. coli* CBS for the production of an enzyme to be used in a diagnostic medical assay is assessed to be low.

Therefore, *E. coli* CBS is not anticipated to enter the environment in a quantity 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 in Canada to human life or health.

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 June 2020).

Public Health Agency of Canada (2017) Canadian Biosafety Guideline - Containment Level 1: Physical Design and Operational Practices. https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/guidance/containment-level-1-physical-design-operational-practices.html#a33 (viewed June 2020).