

New substances: risk assessment, New Substances Notifications 20433 and 20434

Schedule 1 of the *New Substances Notification Regulations (Organisms)*

Notified organisms	<i>Saccharomyces</i> species MeJi797 and <i>Saccharomyces</i> species yMHCT484	
Schedule of the NSNR(O)	Schedule 1 - Information Required in Respect of Micro-organisms	
First day of assessment period	2021/01/30	
Last day of assessment period	2021/05/29	
Organism type	Yeast	
Use	Manufacture of the notified organisms for use in bioethanol production	
Anticipated quantity	Confidential and not for disclosure	
Assessment level of concern	Human Health Hazard	Medium
	Human Exposure	Low
	Environmental Hazard	Medium
	Environmental Exposure	Low
Assessment conclusion (under section 64 of CEPA 1999)	Low risk, not suspected to be toxic	
Category	Added to the Domestic Substances List on January 5, 2022.	
Recommended Action	None	
Waiver	A waiver to submit the data from a test conducted to determine the pathogenicity or toxicity of the notified organisms under paragraph 5(a)(i) of Schedule 1 of the <i>New Substances Notification Regulations (Organisms)</i> was granted for aquatic vertebrates under paragraph 106(8)(a) of the <i>Canadian Environmental Protection Act, 1999</i> (CEPA) given the long history of safe use of the species to which the notified organisms belong to.	

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Synopsis

Saccharomyces species MeJi797 and *Saccharomyces* species yMHCT484 (hereafter referred to as the notified organisms) are genetically modified yeast strains derived from commercial strains used in the baking and wine industries. They have been genetically modified to contain several copies of fungal sourced genes required for more efficient degradation of different types of saccharides. The addition of these genes results in an increase in fermentation efficiency compared to the unmodified parental strains.

There is no evidence to suggest a potential a risk of adverse environmental and human health effects at the exposure levels predicted for the environment and general population in Canada from production of the notified organisms.

It is determined that the notified organisms are not toxic or capable of becoming toxic according to the criteria under section 64 of the Act as there is no evidence to suggest that they may 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.

No risk management is recommended.

Background information

The notified organisms are derived from commercial *Saccharomyces* strains, yeasts used in the baking and wine industries. They have been genetically modified to contain several copies of genes sourced from fungi that are required for more efficient degradation of different types of saccharides. As a result, the notified organisms will have an increase in fermentation efficiency compared to the unmodified parental strains.

The risk assessment is based on the evaluation of information submitted by the notifier and publicly available literature. The following sections give more details on the hazard and exposure.

Hazard

The environmental and human health hazard potential of the notified organisms are determined to be medium because:

- 1) The genetic modifications in the notified organisms are well-defined and stable. Antimicrobial resistance gene markers used in the construction of the notified organisms were removed and are not present in them.
- 2) Enzymes produced by the inserted genes could be potential allergens. Consequently, the notified organisms have the potential to lead to allergic reactions in some sensitized individuals.
- 3) The potential for the transfer of inserted genes from the notified organisms to other *Saccharomyces* species is very low since horizontal gene transfer has rarely been reported in yeast.
- 4) The notified organisms were not found to have any adverse effects on terrestrial plants, terrestrial invertebrates, and aquatic invertebrates.
- 5) A search of the scientific literature reported some infections in humans related to certain *Saccharomyces* species; the majority of these were reported in immunocompromised individuals or those with underlying diseases or medical conditions.
- 6) Data from animal studies conducted in mice, using the notified organisms showed no evidence of pathogenicity or other adverse effects.
- 7) Growth at high temperatures such as 42°C is a known virulence trait in food and clinical strains of *Saccharomyces*. The optimal growth temperature for the notified organisms is between 28°C and 30°C, with no growth observed at 42°C.
- 8) In the unlikely event of an infection with the notified organisms, clinically relevant antifungal agents are available for treatment purpose.
- 9) *Saccharomyces* species generally have a wide distribution in nature and a long history of use, especially in baking and alcohol production. The notified organisms have been previously notified and manufactured in Canada in containment.

Exposure

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

- 1) The notified organisms will be initially manufactured within a single contained facility where a closed system will be maintained throughout the initial manufacturing of the notified organisms. All manufacturing plant personnel should have adequate training and standard operating procedures should be in place to deal with any accidental spills or loss of culture.
- 2) Intentional releases of the notified organisms are expected to be negligible since the majority of live organisms will be harvested and they will not be present in the ultimate bioethanol product. Releases of the notified organisms into the environment may occur from the washing down of the drains when fermentation tanks and other equipment are cleaned, from spills when handling containers, or from the wastewater effluents released from the facility. As an additional security measure, aqueous waste from the facilities will be heat-treated at 65°C for at least 10 minutes before disposal or release into the environment.

- 3) If any untreated organisms were released to the municipal sewer or an anaerobic digestion facility, the level of dilution will result in a concentration of organisms that is not expected to negatively affect the environment.
- 4) Experimental studies in aquatic environments and soil using different concentrations of various strains of *Saccharomyces* have shown a wide range of survival times, from 20 to more than 120 days. Should there be a release to the environment, the notified organisms may persist for an unknown but limited time in the environment. However, they are not expected to grow and increase in number in those environments. Furthermore, given the specific conditions required for growth requirements, the notified organisms are not expected to disperse widely in the environment, therefore the likelihood of human exposure is still expected to be low.
- 5) Should the containment level of the production facility be designated as [Good Large Scale Practice \(GLSP\)](#), release of the notified organisms to the environment is expected to be minimal as the provincial and municipal oversight would minimize the releases of hazardous wastes into the environment and limit liquid discharges to sewers and sewage works.
- 6) Given the proposed use of the organisms and the containment measures to be adopted during the bioethanol production, including measures taken to ensure the notified organisms are only used in sterile fermentation equipment, the potential for dissemination of the introduced genetic material from the notified organisms to other *Saccharomyces* species is low.
- 7) Bioethanol production facilities, including the notified facility, are designed to control air emissions and the levels predicted falling on soil or water from air emissions do not present high levels of exposure to the environment or humans.

Risk characterization

Owing to the medium potential hazard and the low potential exposure, the environmental and human health risks associated with the manufacture and use of the notified organisms in bioethanol production are assessed to be low.

Risk assessment conclusion

There is no evidence to suggest a potential a risk of adverse environmental and human health effects at the exposure levels predicted for the environment and the general population from the manufacture and use of the notified organisms. The risk to the environment and human health associated with the notified organisms are not suspected to meet the criteria in paragraphs 64(a), (b), or (c) of the *Canadian Environmental Protection Act, 1999*. No further action is recommended.

References

Ando, A., Suzuki, C. and Shima, J. (2005). Survival of genetically modified and self-cloned strains of commercial baker's yeast in simulated natural environments: Environmental risk assessment. *Appl. and Env. Microbiol.* 71:7075-7082.

NIH Guidelines (2024). NIH guideline for research involving recombinant or synthetic nucleic acids molecules. https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf