TSCA Section 5(a)(3) Determination for Microbial Commercial Activity Notice (MCAN) J-18-0001

Number: J-18-0001
TSCA Section 5(a)(3) Determination: Microorganism not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Modified *Corynebacterium glutamicum*

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended use(s) (specific): Production of L-alanine
Known and reasonably foreseen use(s): None

Summary: The microorganism is not likely to present an unreasonable risk based on low human health hazard and low environmental hazard associated with the recipient microorganism and introduced genetic material. *C. glutamicum* is not pathogenic to humans or animals and has been used for over 50 years for the production of amino acids for food, feed, and other uses, including the production of industrially-important biochemicals. The introduced genetic modifications pose low concern for health and environmental hazard.

Human Health Hazard[2]: Human health hazard is relevant to whether a new microorganism is likely to present an unreasonable risk because the significance of the risk is dependent upon both the hazard (pathogenicity/toxicity) of the microorganism and the extent of exposure to the microorganism. EPA estimated the human health hazard of this microorganism based on data for the recipient parental strain as well as the genetic modifications. There is low concern for human health hazard for the microorganisms based on the recipient strain not being a human pathogen and the introduced genetic material only including genes encoding

[1] Under TSCA § 3(4), the term "conditions of use" means "the circumstances, as determined by the Administrator, under which a chemical substance (including an intergeneric microorganism) is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." In general, EPA considers the intended conditions of use of a new chemical substance to be those identified in the section 5(a) notification. Known conditions of use include activities within the United States that result from manufacture that is exempt from MCAN submission requirements. Reasonably foreseen conditions of use are future circumstances, distinct from known or intended conditions of use, under which the Administrator expects the MCAN microorganism to be manufactured, processed, distributed, used, or disposed of. The identification of "reasonably foreseen" conditions of use will necessarily be a case-by-case determination and will be highly fact-specific. Reasonably foreseen conditions of use will not be based on hypotheticals or conjecture. Accordingly, EPA will apply its professional judgment, experience, and discretion when considering such factors as evidence of current use of the new microorganism outside the United States, evidence that the MCAN microorganism is sufficiently likely to be used for the same purposes as existing microorganisms that are similar, and conditions of use identified in an initial MCAN submission that the submitter omits in a revised MCAN. The sources EPA uses to identify reasonably foreseen conditions of use include searches of internal confidential EPA MCAN databases (containing use information on analogous microorganisms), other U.S. government public sources, and Internet searches.

[2] A microorganism is considered to have low human health hazard if it is not known to be a frank human pathogen that causes disease in healthy adults, and/or animal studies have demonstrated a lack of pathogenicity or toxicity; a microorganism is considered to have high human health hazard if there is evidence of adverse effects in humans or conclusive evidence of severe effects in animal studies. In the absence of animal data on a microorganism, EPA may use other data or information obtained through literature searches.

enzymes involved in amino acid synthesis and an antibiotic resistance gene.

Environmental Hazard[3]: Environmental hazard is relevant to whether a new microorganism is likely to present unreasonable risks because the significance of the risk is dependent upon both the hazard (pathogenicity/toxicity) of the microorganism and the extent of exposure to the microorganism. EPA estimated the environmental hazard of this microorganism based on data for the recipient parental strain as well as information on the genetic modifications. There is low concern for environmental hazard for the microorganism based on the recipient not being an animal or plant pathogen, and the introduced genetic material consists of genes that encode basic metabolic enzymes and two selection marker genes, none of which are expected to be hazardous to plants or animals.

Exposure and Risk Characterization: The exposure to a new microorganism is potentially relevant to whether a new microorganism is likely to present unreasonable risks because the significance of the risk is dependent upon both the hazard (e.g., pathogenicity/toxicity) of the microorganism and the nature and extent of exposure to the substance. EPA estimated environmental releases to water, air, and landfill as well as worker exposures, and the only potential concern noted was for introduced genetic material encoding resistance to an antibiotic in the new microorganism. The antibiotic is not commonly used in the treatment of human bacterial infections in the U.S., and resistance to the antibiotic is already so widespread such that any potential additional contribution from the use described in the MCAN is expected to be inconsequential. Therefore, EPA concludes that the new microorganism is not likely to present unreasonable risk under the conditions of use.

Potentially Exposed or Susceptible Subpopulation(s): Workers are potentially exposed. Given the low hazard of this microorganism, EPA finds that the microorganism is not likely to present unreasonable risk to workers.

8/2/18
Date:

/s/
Jeffery T. Morris, Director
Office of Pollution Prevention and Toxics

[3] A microorganism is considered to be of low ecological hazard if it is not known to be an animal or plant pathogen, and the genetic modifications do not impart pathogenic or toxigenic traits, and the introduced genetic material does not provide a selective growth advantage in outcompeting indigenous microbial communities in the environment.