Summary of Risk Assessment Conducted Pursuant to subsection 83(1) of the *Canadian Environmental Protection Act, 1999*

New Substances Notification 21471: Ethane, 1-ethoxy-2-(2-methoxyethoxy)- (Chemical Abstracts Service Registry Number 1002-67-1)

Regulatory decisions

Under the provisions for Substances and Activities New to Canada in Part 5 of the *Canadian Environmental Protection Act, 1999* (CEPA), and pursuant to section 83 of the Act, the Minister of the Environment and the Minister of Health have assessed information in respect of the substance and determined that the substance is anticipated to enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

In order to ensure that the substance does not cause harm to the Canadian environment or human health, its manufacture and import are authorized subject to conditions as described in Ministerial Condition No. 21471 published in the *Canada Gazette* Part I, Vol. 157, No. 20 on May 2, 2023.

Substance identity

The notified chemical is ethane, 1-ethoxy-2-(2-methoxyethoxy)- (Chemical Abstracts Service Registry Number[1] 1002-67-1).

Notified and potential uses

The substance is proposed to be imported into Canada in quantities greater than 10 000 kg/yr for the notified use in commercial and industrial printing and printer cleaning applications. Potential uses may include lithium battery production, plastic production, pharmaceuticals and natural health products, consumer inkjet printing inks, toner and paper colouring, chemical synthesis, paints and coatings, adhesives or sealants, cleaning products, automotive care products, air fresheners, and cosmetics.

Environmental fate and behaviour

Based on its physical and chemical properties, if the substance is released to the environment, it will tend to partition to air and water. The substance is not expected to be persistent in air and water based on the expected short air-oxidation half-life (1-7 hours) and inherent biodegradation of an analogue substance. The substance is not expected to bioaccumulate

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based on the very low octanol-water partition coefficient (log K_{ow} < 0) and the low predicted bioaccumulation and bioconcentration factors (< 250 L/kg).

Environmental risk assessment

Based on the available hazard information, the substance has low acute toxicity to fish and aquatic invertebrates (nominal median lethal concentration and median effective concentration > 100 mg/L) and low chronic toxicity to fish, aquatic invertebrates, and algae (nominal no-observed-effect-concentration and lowest-observed-effect-concentration ≥ 10 mg/L). A predicted no-effect concentration was not calculated given the low potential for risk to the environment.

The notified and potential activities in Canada were assessed to estimate the environmental exposure potential of the substance throughout its life cycle. Environmental exposure from the notified activities is not expected. For potential activities such as manufacturing and transportation in its pure form, environmental exposure is expected to be mainly by release of the substance to water resulting in a predicted environmental concentration (PEC) in the range of 10-100 µg/L. For potential activities such as formulation, environmental exposure is expected to be mainly by release of the substance to water resulting in a PEC in the range of 1-10 µg/L. For potential activities such as use in consumer cleaning products, environmental exposure is expected to be mainly from down-the-drain releases to water that would be widely dispersed throughout the country. The low levels of acute and chronic aquatic toxicity exhibited by the notified substance indicate that releases from these activities would be of low concern. Therefore, a PEC was not calculated for these scenarios.

Based on the low potential for ecotoxicity, the substance is unlikely to cause harm to the environment in Canada.

Human health risk assessment

Based on the available hazard information, the substance has a low acute toxicity by the oral and dermal routes (median lethal dose > 2000 mg/kg body weight) and moderate subchronic toxicity following repeated oral doses in mammalian test animals (42-day no-observed-adverse-effect level (NOAEL) 30-300 mg/kg-bw/day). The substance is suspected of being a reproductive and developmental toxicant following repeated oral doses in mammalian test animals (NOAEL 30-300 mg/kg-bw/day). It is not a skin sensitizer (0% response in a guinea pig maximization test). It is not mutagenic *in vitro* or clastogenic *in vivo*. Therefore, the substance is unlikely to cause genetic damage.

When the notified substance is used in industrial and commercial printing applications, direct exposure of the general population is not expected due to the industrial nature of the use. Indirect exposure of the general population from environmental media such as air and drinking water is expected to be at low levels given the low potential for release to the environment.

Potential uses of the substance include as a solvent carrier in a variety of products available to consumers including cosmetics, air fresheners, cleaning products, paints and other do-it-yourself (DIY) products. Direct exposure to these products is expected to be mainly by contact with skin and by inhalation. For cosmetics, cumulative direct systemic exposure is expected to be in the range of 1-10 mg/kg-bw/day for children and 10-100 mg/kg-bw/day for adults. For air fresheners, direct systemic exposure is expected to be in the range of 1-10 mg/kg-bw/day for children and 0.1-10 mg/kg-bw/day for adults. For cleaning products, direct systemic exposure is expected to be in the range of 0.1-10 mg/kg-bw/day for adults. For paints and other DIY products, direct systemic exposure is expected to be in the range of 0.1-10 mg/kg-bw/day for adults. Indirect exposure of the general population from environmental media such as drinking water, as a result of potential uses of the substance in products available to consumers and other industrial activities, was estimated to be in the range of 0.0001-0.001 mg/kg-bw/day for adults and 0.001-0.01 mg/kg-bw/day for children.

The target margin of exposure (MOE_T) was calculated to be 1000 based on the available information. The MOE_T is the level of exposure at or above which there is no expected risk in the exposed population. The derived margin of exposure (MOE_D) is the ratio of the point of departure (POD) value to the available exposure doses and is compared to the MOE_T. The POD is based on the oral repeated dose reproduction-developmental toxicity study conducted in mammalian test animals using the notified substance.

Based on the low potential for exposure when the substance is used for industrial and commercial printing applications, an MOE_D was not calculated. The substance is not likely to pose a significant health risk to the general population when used as notified, and is unlikely to be harmful to human health.

However, the MOE_D for total direct exposure from potential use in cosmetics was calculated to be in the range of 1-10 for children and 1-100 for adults and the MOE_D for potential use in consumer products was calculated to be in the range of 10-1000. Because the MOE_D is less than the derived MOE_T for the majority of potential uses in cosmetics and consumer products, the substance is anticipated to be harmful to human health. These risks are associated with use of the substance in cosmetics and consumer products, and it is anticipated that there could be cumulative exposures if different products containing the substance where used at the same time.

The assumptions made in the assessment and the risk management measures applied are adequately protective for the general population as well as for subpopulations who may be more susceptible or highly exposed.

Other considerations

A similar substance, diglyme (ethane, 1,1'-oxybis[2-methoxy-; Chemical Abstracts Service Registry Number 111-96-6) was subject to a Significant New Activity Order in Canada, a Significant New Use Rule (SNUR) in the United States, and has been classified as toxic to reproduction under the European Union's REACH where it is prohibited from use in cosmetics

and is on the Restricted Chemical List: Candidate List of Substances of Very High Concern. Another similar substance, ethyldiglyme (ethane, 1,1'-oxybis[2-ethoxy-; Chemical Abstracts Service Registry Number 112-36-7) is subject to a SNUR in the United States.

Assessment conclusion

The substance is suspected to constitute a danger to human health according to the criteria under paragraph 64 (c), but is not suspected to have a harmful effect on the environment according to the criteria under paragraph 64 (a) or (b) of the Act.

Due to the identified risk to human health related to reproductive and developmental toxicity, a ministerial condition was issued to restrict the manner in which the notifier may manufacture or import the substance with conditions placed on its use in order to mitigate these potential risks. Ministerial Condition No. 21471 was published in the *Canada Gazette* Part I, Vol. 157, No. 20 on May 2, 2023.

A conclusion under CEPA for this substance is not relevant to, nor does it preclude, an assessment against the hazard criteria for Workplace Hazardous Materials Information System that are specified in the *Controlled Products Regulations* or the *Hazardous Products Regulations* for products intended for the workplace.