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

New Substances Notification 21280: 1-Propanaminium, *N*-(3-aminopropyl)-2-hydroxy-*N*,*N*-dimethyl-3-sulfo-, *N*-(C_{12-18} and C_{18}-unsatd. acyl) derivs., inner salts (Chemical Abstracts Service Registry Number 691400-36-9)

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. 21280 published in the *Canada Gazette* Part I, Vol. 157, No. 10, March 11th, 2023.

Substance identity

The notified chemical is 1-propanaminium, *N*-(3-aminopropyl)-2-hydroxy-*N*,*N*-dimethyl-3-sulfo-, *N*-(C_{12-18} and C_{18}-unsatd. acyl) derivs., inner salts (Chemical Abstracts Service Registry Number[1] 691400-36-9), and is considered a substance of Unknown or Variable composition, Complex reaction products or Biological materials (UVCB).

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 as a surfactant in commercial and consumer rinse-off cosmetic products. Potential uses may include use in the full spectrum of cosmetics, personal and home care products as well as pesticide and fertilizer formulants, fire-fighting agents, oil drilling, electroplating solution, fracking and petroleum manufacture.

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 water. As a surfactant, some of the substance will also be present at the surface of the water or suspended organic matter. The substance is not expected to be persistent in water based on ready biodegradation (60-85% over 28 days). The substance is not expected to bioaccumulate based on its low octanol-water partition coefficient (log K_{ow} 0-3) and low predicted bioconcentration factor (< 250 L/kg).

1 The Chemical Abstracts Service Registry Number is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society.

Environmental risk assessment

Based on the available hazard information, the substance is expected to have moderate acute toxicity to fish (median lethal concentration (LC_{50}) 1-100 mg/L), moderate acute toxicity to aquatic invertebrates (LC_{50} 1-100 mg/L and median effective concentration (EC_{50}) 1-10 mg/L), and moderate toxicity to algae (EC_{50} 1-100 mg/L and no-observed-effect-concentration (NOEC) 0.1-10 mg/L). Using the LC_{50} from the most sensitive organism (fish) and by applying an assessment factor of 40 to account for acute to chronic extrapolation, lethal to sub-lethal extrapolation, median to low effect level extrapolation, species sensitivity variation, and mode of action, the predicted no-effect concentration (PNEC) was calculated to be in the range of 0.01-0.1 mg/L, which was used to estimate the risk to the environment.

The notified and other 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 expected to be mainly from consumer use and industrial formulation and blending by release of the substance to water. Environmental exposure from potential activities is expected to be mainly from consumer use of additional products and increase in industrial formulation and blending by release of substance to water. The notified and potential activities both result in a predicted environmental concentration (PEC) in the range of 0.001-0.01 mg/L, with the exact value being below the PNEC value.

Comparing the PEC with the PNEC, the ratio is less than 1 for both notified and potential activities. This, along with other lines of evidence including environmental fate, hazard, and exposure, indicates that the substance is unlikely to cause harm to the environment in Canada.

Human health risk assessment

Based on the available hazard information, the substance is expected to have 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 (28-day no-observed-adverse-effect level (NOAEL) 30-300 mg/kg-bw/day). The substance is expected to have a low reproductive/developmental toxicity following repeated oral doses in mammalian test animals (NOAEL > 300 mg/kg-bw/day). It is not expected to be a skin sensitizer (0% response in a guinea pig maximization test), although impurities in the substance (fatty acid amidopropyl dimethylamines (amidoamines) and 1,3-propanediamine, *N,N*-dimethyl- (DMAPA))[2] are expected to have moderate to high potential for dermal sensitization (weight of evidence no expected sensitization induction levels (WoE NESIL) based on human and local lymph node assay datasets: 100-500 µg/cm^2). The notified substance is not expected to be mutagenic *in vitro* or clastogenic *in vitro* or *in vivo*. Therefore, the substance is unlikely to cause genetic damage.

When the notified substance is used as a surfactant in rinse-off cosmetics or household cleaning products, direct (systemic) exposure of the general population is expected to be mainly by contact with the skin and/or by ingestion at levels in the range of 0.01-1 mg/kg-bw/day. Potential industrial uses of the substance include pesticide and fertilizer formulants, fire-fighting agents, oil drilling, electroplating solution, fracking and petroleum manufacture, where direct exposure of the general population is not expected due to the industrial nature of the use. However, if the substance is used in leave-on cosmetics, an increased level of direct (systemic) exposure may exist, compared to the rinse-off uses, by

[2]Amidoamines include many substances with various Chemical Abstracts Service Registry Numbers, DMAPA has Chemical Abstracts Service Registry Number 109-55-7

contact with the skin at levels in the range of 1-10 mg/kg-bw/day for children and adults. When the notified substance is used in cosmetics or household cleaning products, direct exposure by contact with the skin of the general population to the impurities is expected to be at levels in the range of 0.001-10 μg/cm^2/day, provided levels of these impurities are limited to 0.01% DMAPA and 1.5% amidoamines. Indirect exposure of the general population from environmental media such as drinking water is expected to be at low levels given the low potential for release to the environment.

The point of departure (POD) for the notified substance is in the range of 30-300 mg/kg-bw/day based on the oral subchronic (systemic) toxicity study in mammalian test animals. The POD is the dose above which a biological response associated with exposure to a substance is first observed. The PODs for the amidoamines and DMAPA impurities are in the range of 100-500 μg/cm^2 based on multiple studies of sensitization in humans and animals.

The target margin of exposure (MOE_T) for subchronic (systemic) toxicity was calculated to be 100 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 POD value to the available exposure doses and is compared to the MOE_T. The MOE_D for notified and potential uses in rinse-off cosmetics and household cleaning products was calculated to be in the range of 100-10 000. The MOE_D is higher than the MOE_T. As such, the substance is not likely to pose a significant health risk to the general population for the notified and potential rinse-off cosmetic and household cleaning uses, and is therefore unlikely to be harmful to human health. However, the MOE_D for potential uses in leave-on cosmetics was calculated to be in the range of 1-100. Because the MOE_D is less than the MOE_T, the notified substance is anticipated to be harmful to human health when formulated in leave-on cosmetic products.

The MOE_T for sensitization from the impurities in the substance was calculated to be 30-100 based on the available information. The MOE_D for notified and potential uses was calculated to be in the range of 100-100 000. The MOE_D is higher than the MOE_T. As such, the substance is not likely to pose a significant health risk to the general population for the notified and potential rinse-off uses, and is therefore unlikely to be harmful to human health. However, the presence of the DMAPA impurity above 0.01% or the amidoamines impurity above 1.5% could result in the substance becoming harmful to human health. These risks are associated with use of the substance in cosmetics and household cleaning products.

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

Other considerations

Similar substances are risk managed under Ministerial Condition No. 18685, Ministerial Condition No. 20381, Ministerial Condition No. 20502, Ministerial Condition No. 20551, Ministerial Condition No. 20654 and Ministerial Condition No. 21256, limiting DMAPA and amidoamine impurities to ≤ 0.01% and ≤ 1.5%, respectively, in order to address health concerns regarding dermal sensitization. Ministerial Condition No. 18427 limits DMAPA and amidoamine impurities to ≤ 0.01% and ≤ 0.3%, respectively, in order to address health concerns regarding dermal sensitization. A similar substance is also risk managed under Significant New Activity Notice 12498 based on sensitization and subchronic toxicity from potential use in consumer products including cosmetics.

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 dermal sensitization from the impurities and suspected subchronic (systemic) toxicity of the notified substance, a ministerial condition was issued to restrict the manner in which the notifier may manufacture or import the substance with conditions on its impurities concentration and conditions on its formulation (concentration limit on the notified substance in leave-on cosmetics) in order to mitigate these potential risks. Ministerial Condition No. 21280 was published in the *Canada Gazette* Part I, Vol. 157, No. 10, March 11th, 2023.

A conclusion under CEPA, on 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.