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

New Substances Notification No. 19289: D-Glucitol, 1,5-anhydro-1-C-[3-[[5-(4-fluorophenyl)-2-thienyl]methyl]-4-methylphenyl]-, (1*S*)- (Chemical Abstracts Service No. 842133-18-0)

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 have determined that it 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.

Substance identity

The notified chemical is D-glucitol, 1,5-anhydro-1-C-[3-[[5-(4-fluorophenyl)-2-thienyl]methyl]-4-methylphenyl]-, (1*S*)- (Chemical Abstracts Service Registry Number[1] 842133-18-0).

Notified and potential activities

The substance is proposed to be imported into Canada in quantities greater than 10 000 kg/yr for the notified use as an ingredient in pharmaceuticals. Potential activities may include manufacturing.

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, soil and sediment. The substance is not expected to be persistent in these compartments based on its susceptibility to degradation over time. The substance is not expected to bioaccumulate based on its low to moderate octanol-water partition coefficient (log K_{ow} <5) and expected low bioconcentration factor (<250 L/kg).

Ecological assessment

Based on the available hazard information on structurally related chemicals, the substance is expected to have low acute toxicity in fish, aquatic invertebrates and algae (no adverse effects observed in saturated solutions), moderate chronic toxicity in fish and aquatic invertebrates (no-observed-effect-concentration (NOEC) and lowest-observed-effect-concentration in the range of 0.1-10 mg/L), and low chronic toxicity in sediment invertebrates (NOEC >10 mg/kg). Using the NOEC from the most sensitive organism (aquatic invertebrates) and by applying an assessment factor of 10 to account for species sensitivity variation, 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 ecological risk.

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 activity is expected to be mainly from consumer use by release of the substance to water resulting in a predicted environmental concentration (PEC) in the range of 0.001-0.01 mg/L. For potential activities such as manufacturing, environmental exposure is expected to be mainly from use by release of the substance to water resulting in a PEC in the range of 0.01-0.1 mg/L.

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

Human health assessment

Based on the available hazard information on structurally related chemicals, the substance is expected to have a low acute toxicity by the oral route (oral median lethal dose >2000 mg/kg body weight) and high subchronic toxicity following repeat oral doses in mammalian test animals (6-12- month lowest-observed-adverse-effect level (LOAEL) <10 mg/kg-bw/day). No reproductive/developmental toxicity was observed in studies with mammalian test animals. It is not a skin sensitizer (>10% effective concentration to induce stimulation index of 3 (local lymph node assay)). It is not expected to be mutagenic *in vitro* and or clastogenic *in vitro* or *in vivo*. Also, carcinogenicity studies with mammalian test animals indicate that the substance is not expected to be a carcinogenic hazard. Therefore, the substance is unlikely to cause genetic damage. The point of departure (POD) is in the range of 1000-10 000 µg/kg-bw/day based on the LOAEL of the oral subchronic toxicity study in mammalian test animals.

When the notified substance is used as an active ingredient in pharmaceuticals, direct exposure of the general population is assessed by the Therapeutics Products Directorate of Health Canada. Exposure will be limited to targeted patient groups. Indirect exposure of the general population from environmental media such as drinking water is expected to be at levels in the range of 0.01-0.1 µg/kg-bw/day for children and adults. No potential uses which could significantly increase human health risks compared to the notified uses were identified.

Based on a comparison of the POD to the estimated indirect human exposure, the substance is not likely to pose a significant health risk to the general population from indirect exposure and is therefore unlikely to be harmful to human health.

Assessment conclusion

When the substance is used as notified or for other identified potential activities, it is not expected to be harmful to human health or the environment according to the criteria under section 64 of the Act.

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 *Hazardous Products Regulations* for products intended for the workplace.