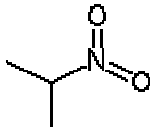
INITIAL TARGETED ASSESSMENT PROFILE

CAS No.	**79-46-9**
Chemical Name	**Propane, 2-nitro-** (2-Nitropropane)
Structural Formula	

SUMMARY CONCLUSIONS OF THE TARGETED ASSESSMENT

NOTE: The present assessment is targeted to address the following human health endpoints: carcinogenicity and genotoxicity. It cannot be considered as a full SIDS Initial Assessment. Summary information on exposure is also reported here. Other endpoints for human health and the environment are included in the Canadian screening assessment but have not been agreed upon by OECD member countries, and thus are not included in this profile.

The final screening assessment has been published under the responsibility of the Government of Canada.
[http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=3FDF4576-1]

Rationale for Targeting the Assessment

The Government of Canada "categorized" or prioritized all 23,000 chemical substances on its Domestic Substances List (DSL) from 1999 to September 2006, as required by its *Canadian Environmental Protection Act, 1999* (CEPA 1999). Using information from Canadian industry, academic research and other countries, Government of Canada scientists applied a set of rigorous tools to the 23,000 chemical substances on the DSL. They were categorized to identify those that were: **inherently toxic** to humans or to the environment and that might be **persistent** and/or **bioaccumulative**; and substances to which people might have **greatest potential for exposure**. During this priority-setting exercise, distinct approaches were taken for identifying substances of likely concern for human health and the environment, and subsequent assessment activities may have focused on either human health or ecological endpoints. Through categorization, the Government of Canada has identified approximately 4,000 of the 23,000 chemical substances on the DSL as priorities for further assessment, research and/or measures to control their use or release.

The substance, 2-nitropropane was identified as a high priority for assessment of human health risk because it was considered to present intermediate potential for exposure and had been classified by other agencies on the basis of carcinogenicity.

Physical-chemical properties

The substance, 2-nitropropane, is a liquid at room temperature with a melting point of -93°C, boiling point of 120°C and vapour pressure of 2290 Pa at 25°C (all measured values). The measured octanol-water partition coefficient (log K_{ow}) is 0.93, and the measured water solubility is 17 000 mg/L at 25°C.

Human Health Targeted Endpoints

A sufficient genotoxicity database was available. The chemical tested positive in bacterial mutation assays with and without metabolic activation. It induced gene mutations in Chinese hamster cells and rat hepatoma cells. In cultured human peripheral lymphocytes with metabolic activation, it showed clear evidence of chromosomal aberration and induction of sister chromatid exchanges (SCEs) although negative results were found in Chinese hamster ovary cells in SCEs (with and without metabolic activation). 2-Nitropropane induced unscheduled DNA synthesis in

human, rat and mouse hepatocytes. It also induced micronuclei in three rat hepatoma cell lines but not in Chinese hamster lung V79 cells (all without metabolic activation).

The genotoxic effects of 2-nitropropane were corroborated in a series of *in vivo* studies. In mice exposed by intraperitoneal injection, an increased frequency of mutations in the LacI gene and an increased expression of the tumour suppressor gene, p53, were observed in the liver. 2-Nitropropane induced micronuclei in the hepatocytes and bone marrow of rats treated orally, but not in the peripheral blood of mice treated via intraperitoneal injection. Unscheduled DNA synthesis occurred in the hepatocytes of orally treated rats. Furthermore, DNA strand breaks were reported in the bone marrow of rats, and in the stomach, colon and liver of mice after administration of 2-nitropropane via intraperitoneal injection; however, no effect on the kidney, urinary bladder, lung, brain and bone marrow of mice were observed. It also induced DNA base modifications in the liver of rats treated orally and intraperitoneally. Significant increases in 8-hydroxydeoxy-guanosine levels, an indication of oxidative stress induced DNA damage, were observed in the liver of rats and mice treated with 2-nitropropane orally or intraperitoneally, but no effect was observed on the kidney of rats. In summary, 2-NP was mutagenic *in vitro* and *in vivo* and clearly genotoxic.

Carcinogenicity potential was determined on the basis of oral toxicity (subchronic exposure but assessed after a lifetime) and subchronic to long-term inhalation studies. There were no human cancer data available. Liver tumours were observed in rats treated with 2-nitropropane via different routes of exposure. In one carcinogenicity study, male rats were orally administered 2-nitropropane at 0 or 40 mg/kg-bw, 3 times a week for 16 weeks, at which time dosing was discontinued due to high mortality. Animals were observed for the following 61 weeks (total duration of the test 77 weeks). All of the animals treated with 2-nitropropane developed benign or malignant liver tumours, Metastases were also observed in the lungs of some of these rats. In another study, male rats were administered 2-nitropropane via inhalation (whole body) at 0, 98 or 755 mg/m^3 for 1 to 6 months. All of the rats exposed to 755 mg/m^3 for 6 months developed multiple hepatocellular carcinomas. Although there were no tumours seen in the rats exposed to 755 mg/m^3 for 3 months, hyperplastic changes in the liver were observed. No tumours were noted in the rats exposed to 98 mg/m^3. In addition to these cancer studies, it was reported that inhalation or intraperitoneal exposure to 2-nitropropane had been shown to have an initiating action in rats treated also with established promoters.

Exposure to 2-nitropropane has also induced non-cancer effects, mainly on the liver, in experimental animals. In rats exposed by inhalation to 78 mg/m^3 2-nitropropane for 22 months, slightly increased focal vacuolization of the cytoplasm of hepatocytes and focal areas of hepatocellular nodules were observed in males. 78 mg/m^3 was determined to be the lowest LOAEC amongst the chronic toxicity studies; a NOAEC was not determined. In a sub-chronic oral study in male rats exposed to 2-nitropropane at 89 mg/kg-bw, 3 times a week (equivalent to 38 mg/kg-bw per day), for 4 months, no consistent effect on numbers of preneoplastic or neoplastic renal lesions, or neoplasms in the liver was observed. However, in a sub-chronic inhalation study, liver cellular damage, which was considered to be preneoplastic, was observed at 755 mg/m^3 in rats exposed via inhalation for 3 to 6 month. The lung was also a target for non-cancer effects in rodents exposed to 2-nitropropane. Pulmonary lesions in male rats exposed to 2-nitropropane via inhalation for 1 to 6 months was observed at 755 mg/m^3. However, no adverse effects were observed in rabbits subjected to the same treatment conditions.

2-Nitropropane possesses properties indicating a hazard for the human health endpoints, carcinogenicity and genotoxicity (increased incidence of liver tumours and lung metastases, clear evidence of genotoxicity).

Exposure Summary Information

2-Nitropropane is used as a solvent and chemical intermediate. As a solvent, it may be used in vinyl inks, electrostatic paints, adhesives, varnishes, polymers, and synthetic materials. 2-Nitropropane may be used to dissolve a large number of resins; these solvent-resin mixtures have reportedly found use as coatings in the lining of beverage cans.

2-Nitropropane is also reportedly used as a component of explosives and propellants, and in fuels for internal combustion engines. The information available suggests that use of 2-nitropropane in paints and coatings is limited to a few specific industrial applications, thus no consumer scenarios for use of paints and coatings were generated. The exposure of the general population as a result of industrial use of 2-nitropropane within Canada is likely to be negligible. It is acknowledged that the information that has been presented in published reviews to characterize the uses of this substance may be somewhat dated, and may not reflect the current exposure

conditions for the Canadian population.

No companies in Canada reported manufacturing 2-nitropropane in a quantity greater than or equal to the 100 kg reporting threshold, but 100 to 1000 kg of the substance was reported to be imported in 2006. No domestic releases were reported to Canada's National Pollutant Release Inventory between 1997 and 2007 (most recent data available). Additionally, no releases to the environment were reported for 2006 under a survey conducted in Canada. In the United States, the Toxic Release Inventory database indicates on-site releases from 8 facilities totalling 11,725 kg (25,850 lbs) in 2007.