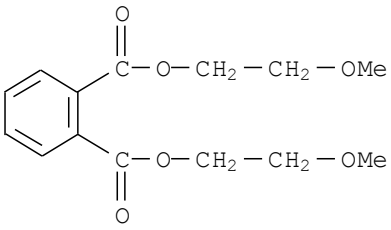
INITIAL TARGETED ASSESSMENT PROFILE

CAS No.	117-82-8
Chemical Name	1,2-Benzenedicarboxylic acid, bis(2-methoxyethyl) ester (Di(methoxyethyl)phthalate)
Structural Formula	

SUMMARY CONCLUSIONS OF THE TARGETED ASSESSMENT

NOTE: The present assessment is targeted to address the following human health endpoints: reproductive and developmental toxicity. 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.chemicalsubstanceschimiques.gc.ca/challenge-defi/batch-lot-6/index-eng.php#final]

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 1,2-benzenedicarboxylic acid, bis(2-methoxyethyl) ester or di(methoxyethyl)phthalate, abbreviated as DMEP, 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 the European Commission on the basis of reproductive and developmental toxicity (Category 2 for developmental toxicity with risk phrase R61 (“May cause harm to the unborn child”) and as a Category 3 for reproductive toxicity with risk phrase R62 (“Possible risk of impaired fertility”)).

Physical-chemical properties

The substance DMEP is a liquid at room temperature with a measured melting point of -45°C, measured boiling points of 313 and 340°C and modelled vapour pressures of 0.03 and 0.07 Pa at 25°C. The measured octanol-water partition coefficient (log K_{ow}) is 0.04, and the measured water solubility is 8500 mg/L at 15-25°C.

Human Health Targeted Endpoints

There is a limited dataset on DMEP, but it is supported by the fact that DMEP is metabolized quickly to a well-characterized reproductive and developmental toxicant, 2-methoxyethanol (2-ME). A health risk assessment on

2-ME was completed by the Government of Canada earlier.

Few adequate studies were identified in which DMEP was administered to laboratory animals by routes that are relevant to human exposure (i.e., oral, dermal or inhalation). A five-generation oral study with very limited data reported did not reveal any signs of reproductive toxicity induced by DMEP in rats given up to 900 mg/kg diet per day (45 mg/kg-bw per day: original report did not state clearly what the actual dosage was. This dose was estimated based on the assumption that DMEP was applied to rats in diet). DMEP-induced testicular effects were observed in rats following acute or 2-week gavage administration. Significant reductions in absolute and relative testis weights with seminiferous tubule atrophy and sperm degeneration and the appearance of giant spermatids were observed at 1000 mg/kg-bw per day in the 2-week study; a no-observed-adverse-effect level (NOAEL) of 100 mg/kg-bw per day for testicular effects was identified. In addition, haematological effects as well as thymic effects, exhibiting a limited dose–response relationship, were observed in the 2-week oral study at 100 mg/kg-bw per day and above in male rats. The purity of the test material in this study was 78%, which may have introduced some confounding factors. Significantly reduced testis weights and increased abnormal sperm levels were also observed in the single gavage dosing study at a higher dose level (1500 mg/kg-bw) following single dosing.

Significantly reduced relative testis weights were observed in mice administered DMEP by intraperitoneal (i.p.) injection for 6 weeks at a dose level of 250 mg/kg-bw per day, the only dose tested and determined to be the lowest-observed-adverse-effect level (LOAEL). Thus, based on a weight of evidence approach in which oral and i.p. exposures resulted in similar testicular effects, a hazard to fertility cannot be excluded.

Developmental effects of DMEP were observed in rats following oral (gavage) administration on gestation days 6 to 16. Significantly reduced pup body weight gain and slightly reduced pup survival from day 1 to 5 postpartum were observed at the lowest dose tested (60 mg/kg-bw per day, LOAEL). At a higher dose level (180 mg/kg-bw per day), significantly reduced pup survival and pup body weight gain as well as pup abnormalities including a shortened lumbosacral region, acauda (i.e. no tail) and filamentous tails were observed. At the highest dose tested (600 mg/kg-bw per day), a complete resorption of the litters was observed accompanied by maternal toxicity such as significantly reduced body weight gain and mean body weights as well as food consumption. A NOAEL for maternal toxicity was identified at 180 mg/kg-bw per day. Similar teratogenic and fetotoxic effects were also observed in a number of i.p. developmental toxicity studies in rats and mice.

DMEP possesses properties indicating a hazard for the human health endpoints, developmental and reproductive toxicity (teratogenic and embryotoxic effects, testicular atrophy, reduced testes weights and sperm abnormalities).

Exposure Summary Information

No information regarding any current uses of DMEP in the Canadian marketplace has been identified. Based on the global decline of manufacture of DMEP and the information reported under a survey conducted in Canada, use of DMEP in Canada is not expected to be significant.

The general applications of DMEP have included its use as a plasticizer in the production of nitrocellulose, acetyl cellulose, polyvinyl acetate, polyvinyl chloride and polyvinylidene chloride intended for contact with food or drink, giving these polymeric materials good light resistance, and as a solvent. DMEP can improve the durability and toughness of cellulose acetate and can be used in enamelled wire, film, high-strength varnish and adhesive. It can also be used in pesticide products.

There was no manufacture or import of DMEP in a quantity greater than or equal to the 100 kg reporting threshold or use of DMEP in a quantity greater than or equal to the 1000 kg reporting threshold in Canada in 2006; therefore, industrial releases are not expected to be significant. DMEP is not a reportable substance under the National Pollutant Release Inventory in Canada, the US Toxics Release Inventory, the Australian National Pollutant Inventory or the Japanese Chemical Survey.

The historical uses of DMEP as a plasticizer and as a solvent suggest that DMEP may be released to the environment through various waste streams.