Follow-up Report on a PSL1 Substance for Which Data Were Insufficient to Conclude Whether the Substance Was “Toxic” to Human Health

Di-n-Octyl Phthalate

May 2003
# LIST OF ACRONYMS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS</td>
<td>Chemical Abstracts Service</td>
</tr>
<tr>
<td>CEPA 1988</td>
<td><em>Canadian Environmental Protection Act</em></td>
</tr>
<tr>
<td>CEPA 1999</td>
<td><em>Canadian Environmental Protection Act, 1999</em></td>
</tr>
<tr>
<td>DnOP</td>
<td>di-n-octyl phthalate</td>
</tr>
<tr>
<td>kg-bw</td>
<td>kilogram body weight</td>
</tr>
<tr>
<td>LOAEEL</td>
<td>Lowest-Observed-Adverse-Effect Level</td>
</tr>
<tr>
<td>LOEL</td>
<td>Lowest-Observed-Effect Level</td>
</tr>
<tr>
<td>NOEL</td>
<td>No-Observed-Effect Level</td>
</tr>
<tr>
<td>PSL1</td>
<td>first Priority Substances List</td>
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<tr>
<td>PVC</td>
<td>polyvinyl chloride</td>
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</tbody>
</table>
SYNOPSIS

Di-n-octyl phthalate is used as a plasticizer to impart flexibility to polymers, particularly polyvinyl chloride used to make products such as gloves, flooring and flexible sheets. There are no Canadian producers of this substance. It is estimated that approximately 1 tonne of di-n-octyl phthalate is used annually in Canada.

Di-n-octyl phthalate was included on the first Priority Substances List (PSL1) under the 1988 Canadian Environmental Protection Act (CEPA 1988) for assessment of potential risks to the environment and human health. As outlined in the Assessment Report released in 1993, relevant data identified before August 1992 were considered insufficient to conclude whether di-n-octyl phthalate was “toxic” to human health as defined in Paragraph 11(c) under CEPA 1988.

Critical data relevant to both estimation of exposure of the general population in Canada and assessment of effects were identified following release of the PSL1 assessment and prior to December 2000. Based on this information, the margin of exposure between bounding estimates of intake for the general public and the Lowest-Observed-Effect Level in an adequate study is considered sufficient to protect human health.

Based on available data, it is concluded, therefore, that di-n-octyl phthalate is not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health. Therefore, di-n-octyl phthalate is not considered “toxic” to human health as defined in Paragraph 64(c) of the Canadian Environmental Protection Act, 1999.

Based upon current use patterns, investigation of options to reduce exposure is not considered to be a priority at this time. Uses and emissions of this compound should continue to be monitored to ensure that exposure does not increase to any significant extent, and additional data should be considered upon development of more sensitive testing strategies for assessing endocrine disrupting effects, for which phthalates are likely early candidates.
1.0 INTRODUCTION

A common Introduction, which describes the process for the preparation of the updates for the seven substances (including di-n-octyl phthalate) on the first Priority Substances List (PSL1) for which data were considered insufficient to conclude whether the substances were “toxic” to human health under the 1988 Canadian Environmental Protection Act (CEPA 1988), is posted on all web sites where the Assessment Reports appear.¹

The strategy for the literature search to identify critical new data (including commercial activity in Canada, human exposure and effects) on di-n-octyl phthalate is presented in Appendix A of this Assessment Report. Only relevant data acquired prior to December 2000 were considered in the determination of whether di-n-octyl phthalate is “toxic” to human health under Paragraph 64(c) of the Canadian Environmental Protection Act, 1999 (CEPA 1999).

A draft follow-up report was made available for a 60-day public comment period (between September 28, 2002 and November 27, 2002). No comments were received.

2.0 SUMMARY OF THE HUMAN HEALTH RISK ASSESSMENT FOR DI-N-OCTYL PHTHALATE CONDUCTED UNDER CEPA 1988 (BASED UPON INFORMATION IDENTIFIED UP TO AUGUST 1992) (GOVERNMENT OF CANADA, 1993)²

Di-n-octyl phthalate (DnOP; Chemical Abstracts Service (CAS) registry number 117-84-0) is a phthalate ester with the molecular formula C$_{24}$H$_{38}$O$_{4}$ and a molecular weight of 390.6. It is used as a plasticizer to impart flexibility to polymers, particularly polyvinyl chloride (PVC) used to make products such as gloves, flooring and flexible sheets. At the time of release of the PSL1 Assessment Report, there were no identified Canadian producers of DnOP, and it was estimated that approximately 1 tonne of DnOP was used annually in Canada.

Relevant data were insufficient to derive quantitative estimates of exposure for the general population in Canada. Identified information was limited principally to the lack of detection of DnOP (detection limit not specified) in small numbers of fish in the Great Lakes (DeVault, 1985) and lack of detection in a majority of drinking water samples in a survey in Alberta (Halina, 1993).

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¹ See “Introduction to Assessment Reports for Reconsideration of PSL1 Substances for Which Data Were Insufficient to Conclude Whether the Substances Were ‘Toxic’ to Human Health (Paragraph 11(c), CEPA 1988; Paragraph 64(c), CEPA 1999)” at the following web site: www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm.

² The PSL1 Assessment Report for DnOP is available on the following website: www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm
At the time of completion of the Assessment Report for DnOP under CEPA 1988, identified data on toxicological effects in humans or animals following long-term exposure were inadequate as a basis for assessment of carcinogenicity or development of a Tolerable Daily Intake (i.e., the level of intake to which it is believed a person may be exposed daily over a lifetime without deleterious effect).

Data on the genotoxicity of DnOP identified in the PSL1 assessment were limited. DnOP was not mutagenic in bacterial cell assays with *Salmonella typhimurium* (including the Ames test) or *Escherichia coli* in the presence or absence of a hepatic metabolic activation system (Kuarata, 1975; Florin *et al*., 1980; Goodyear, 1981a; Seed, 1982; Yoshikawa *et al*., 1983; Zeiger *et al*., 1985). There was no evidence of DNA damage in repair-deficient strains of *E. coli* or *Bacillus subtilis* with or without metabolic activation (Kuarata, 1975; Sato *et al*., 1975; Goodyear, 1981b). In an unpublished study, a mixture of dialkyl phthalates (n-hexyl, n-octyl, n-decyl) increased the mutation frequency in cultured mouse lymphoma cells in the presence or absence of metabolic activation. However, since the observed increase was not dose-related, the investigators considered the results to be equivocal (Hazleton Biotech Co., 1986). Available data were inadequate to assess the carcinogenicity of DnOP in experimental animals owing to incomplete documentation and examination of a limited range of endpoints in identified studies (Piekacz, 1971; DeAngelo *et al*., 1986; Carter *et al*., 1989; De Angelo, 1992). Identified information on the long-term toxicity of DnOP was restricted to an incomplete report of a study in rats (DeAngelo *et al*., 1988) for which additional documentation was not available (DeAngelo, 1992), an inadequately documented study in mice (Lawrence *et al*., 1975) and investigations of a limited range of effects in rats following intraperitoneal injection (Khanna *et al*., 1990). In other identified investigations, effects examined were restricted to those on reproductive indices (Heindel *et al*., 1989; Morrissey *et al*., 1989) and immunological effects following intraperitoneal injection (Oishi, 1990).

Therefore, data were considered insufficient to conclude whether di-n-octyl phthalate was “toxic” as defined in Paragraph 11(c) of CEPA 1988.

### 3.0 POST-PSL1 ANALYSIS (BASED UPON INFORMATION IDENTIFIED BETWEEN AUGUST 1992 AND DECEMBER 2000)

#### 3.1 Production, importation, use and release

There are no domestic producers of DnOP in Canada, and volumes of import are considered negligibly small (CIS, 2001).

The estimated emission of DnOP in eight Great Lakes states and the province of Ontario in 1993 was 550 kg (Great Lakes Commission, 1998). Based on data from the National Pollutant Release Inventory, for six facilities reporting in 1997, of the total of approximately 58 tonnes emitted, 0.05 tonnes (<0.1% of total) were released to air. The remainder was either incinerated or recycled (Environment Canada, 1997). For the seven facilities reporting in 1998, of the total
of approximately 50 tonnes emitted, 0.10 tonnes (0.2% of total) were released to the air, 43 
tonnes were incinerated and 4.5 tonnes were recycled (Environment Canada, 1998).

3.2 Population exposure

The following presentation is limited to identified recent data considered critical to quantitative 
estimation of exposure of the general population in Canada to DnOP and, hence, to assessment 
of “toxic” under Paragraph 64(c) of CEPA 1999. Other sources of data that were also identified 
but were not directly relevant to estimation of exposure in Canada include Aceves and Grimalt 
(1996a,b), Webber et al. (1996), Leach et al. (1999), Blount et al. (2000) and Colon et al. 
(2000).

Reports of concentrations of DnOP in ambient air in Canada were not identified. In the 
United States, a field monitoring study was carried out at 125 homes in Riverside, California, in 
1990 (California Environmental Protection Agency, 1992). Outdoor air was collected at the sites 
of a subset of 65 of those homes. For both daytime and nighttime sampling, concentrations in 
only 1.8% of samples were above the method quantifiable limit (3.2 ng/m$^3$) for DnOP. For 
daytime and nighttime sampling, both the median and 90th percentile concentrations were below 
the method quantifiable limit.

Otson et al. (1994) did not detect DnOP in a composite sample of indoor air from 757 
single family dwellings in Canada. In the field monitoring study of indoor air at 125 homes in 
Riverside, California, levels in 30.5% of the nighttime samples were above the method 
quantifiable limit (3.2 ng/m$^3$); concentrations in 36.1% of daytime samples were above the 
method quantifiable limit (California Environmental Protection Agency, 1992). However, the 
daytime median level was below the method quantifiable limit (90th percentile, 9.7 ng/m$^3$). 
Similarly, the nighttime median value was below the method quantifiable limit (90th percentile, 
4.6 ng/m$^3$).

Health Canada has conducted several surveys of the phthalate ester content of foods. 
These include determinations in a few samples of butter and margarine, as well as the 
corresponding wrappers (Page and Lacroix, 1992), and an initial survey of a larger number of 
Subsequently, the phthalate content of 112 categories of foods purchased in 1986 was 
determined (Page and Lacroix, 1995). DnOP was not detected in samples of meat, fish, poultry, 
soft drinks, fruit juices, fruits, vegetables, butter or margarine.

DnOP was not detected in a survey of 42 children’s teethers and rattles conducted in 
Canada in 1998 (Health Canada, 1998). In a separate investigation of a limited number of 
pacifiers, trace levels of DnOP were detected in only one product (a soft PVC pacifier), which 
was subsequently voluntarily removed from the marketplace (Lalonde, 2001). In another survey, 
DnOP was not detected in samples from six PVC toys purchased in Canada (Stringer et al.2000).
Although limited, the identified concentrations of DnOP are sufficient to calculate upper bounding estimates of exposure for the general population (Table 1). The assumptions on which these estimates are based are delineated in footnotes to the table.

Owing to the limitations of the data on which they are based, these bounding estimates of intake should be considered to be semi-quantitative only. For example, estimated intake in the principal medium of exposure is based on limits of detection, since DnOP was not detected in any foodstuffs surveyed in Canada. The age group for which estimated intake is lowest is formula-fed infants (0.01 µg/kg-bw per day), with no single source predominating. The age group for which estimated intake is highest is infants not breast-fed nor formula-fed (51 µg/kg-bw per day). (No data were identified for breast milk.) Of the remaining age groups, virtually all the estimated intake is from food, although again it should be emphasized that DnOP was not detected in any foodstuff analysed.

### 3.3 Hazard characterization

Few recent studies relevant to assessment of the toxicity of DnOP were identified. These include several genotoxicity assays in which DnOP was one component of a mixture of test substances, one assay for estrogenic activity, short-term studies of effects on the liver in rats and mice and a subchronic assay in rats.

Zacharewski et al. (1998) reported the results of an assay for estrogenic activity, in which 10 Sprague-Dawley rats per group were exposed by gavage to 20, 200 or 2000 mg/kg-bw per day for 4 days. There was no significant increase in uterine weight in immature ovariectomized rats and no effect upon degree of vaginal epithelial cell cornification in mature ovariectomized rats.

Smith et al. (2000) exposed five rats per group for either 2 or 4 weeks to 0, 1000 or 10 000 ppm (0, 50 or 500 mg/kg-bw per day; Health Canada, 1994) in the diet. At the end of the exposure period, livers were examined for gap junctional intercellular communication, replicative DNA synthesis and peroxisomal beta-oxidation activity. There were no effects at 50 mg/kg-bw per day after either 2 or 4 weeks (No-Observed-Effect Level, or NOEL). At 500 mg/kg-bw per day (Lowest-Observed-Effect Level, or LOEL), effects at 2 weeks included significant increases in relative liver weight, peroxisomal beta-oxidation activity and hepatic DNA synthesis. Only the latter was significantly increased at 4 weeks.

In a similar assay, Smith et al. (2000) exposed mice for either 2 or 4 weeks to 0, 500 or 10 000 ppm (0, 65 or 1300 mg/kg-bw per day; Health Canada, 1994) in the diet. At 65 mg/kg-bw per day (LOEL), there was a significant increase in peroxisomal beta-oxidation activity at 4 weeks (significant at both 2 and 4 weeks at the highest dose).
The only subchronic study identified in which a wide range of endpoints was examined was the dietary study in rats conducted by Health Canada (Poon et al., 1997). Groups of 10 male and female Sprague-Dawley rats were administered four dose levels for 13 weeks (males: 0, 0.4, 3.5, 37 or 350 mg/kg-bw per day; females: 0, 0.4, 4.1, 41 or 403 mg/kg-bw per day). In both sexes, effects were observed at the highest dose only. These included a significant increase in hepatic ethoxyresorufin-O-deethylase activity (12-fold in males, 3-fold in females). Moderate accentuation of zonation was observed in the hepatic lobes of all animals, and mild to moderate perivenous cytoplasmic vacuolation, accompanied by increased perivenous cytoplasmic volume, was observed in most males and half of the females. In the liver interstitium, mild nuclear endothelial prominence was observed in most animals. A reduction in size of follicles and a mild decrease in colloid density were observed in the thyroid. The dose level of 37 mg/kg-bw per day is considered a NOEL.

Results were reported to be negative in an Ames test and the Chinese hamster ovary cell/HRPT locus assay with a mixture of DnOP and di-n-decyl phthalate, although additional relevant information on protocol was not identified (CMA, 1999).

3.4 Human health risk characterization and conclusions

There has been no convincing evidence of the mutagenicity of DnOP based on the results of a small number of investigations in *in vitro* bacterial assays including *S. typhimurium* and *E. coli*. Moreover, the weight of evidence for the genotoxicity of phthalates for which the database for this endpoint is more extensive is convincingly negative.

In the only study of sufficient duration in which a wide range of endpoints was examined, histopathological effects upon the liver and thyroid were observed in male rats at 350 mg/kg-bw per day (Lowest-Observed-Adverse-Effect Level, or LOAEL). No effects were observed at 37 mg/kg-bw per day (NOEL). The LOAEL is 6900 times greater than the highest bounding estimate of intake (51 µg/kg-bw per day in infants). The NOEL is 700 times greater than this estimate. (Alternatively, the LOAEL and NOEL are 4 and 3 orders of magnitude greater, respectively, than the highest bounding estimate of exposure.)

For each age group considered, intake from food was estimated to be virtually the only source of exposure to DnOP. Moreover, since they are based not on measured concentrations but on limits of detection in various foodstuffs for the expected principal medium of exposure, these bounding estimates exceed actual intake by an unquantified and, perhaps, considerable amount. Therefore, the margin of exposure between the observed effects in the subchronic study in rats and bounding estimates of intake is considered adequate to address elements of uncertainty dealing with inter- and intraspecies variation and a less than chronic study.

On this basis, di-n-octyl phthalate is not considered “toxic” as defined in Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999*. 
3.5 **Uncertainties and degree of confidence in human health risk characterization**

In extensive sampling by Health Canada, DnOP was not reported in any foodstuffs. Therefore, there is high confidence that, for the likely principal medium of exposure, intake by the general population in Canada is less than that estimated here, but there is low confidence in the actual quantitative values for intake.

3.6 **Considerations for follow-up**

Based upon current use patterns, investigation of options to reduce exposure is not considered to be a priority at this time. Uses and emissions of this compound should continue to be monitored to ensure that exposure does not increase to any significant extent. Consideration of relevant data is also desirable upon development of more sensitive testing strategies for assessing endocrine disrupting effects, for which phthalates are likely early candidates.
4.0 REFERENCES


Environment Canada. 2000. Personal communication from Y. Bovet, Use Patterns and Controls Implementation Section, Commercial Chemicals Evaluation Branch.


Table 1: Estimated average daily intake of DnOP by the population of Canada

<table>
<thead>
<tr>
<th>Route of exposure</th>
<th>Estimated intake (µg/kg-bw per day) of DnOP by various age groups</th>
<th>0–6 months¹</th>
<th>0.5–4 years³</th>
<th>5–11 years⁴</th>
<th>12–19 years⁵</th>
<th>20–59 years⁶</th>
<th>60+ years⁷</th>
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<tr>
<td></td>
<td>formula fed²</td>
<td>not formula fed</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Ambient air³</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>Indoor air⁹</td>
<td>0.002</td>
<td>0.002</td>
<td>0.005</td>
<td>0.004</td>
<td>0.002</td>
<td>0.002</td>
<td>0.002</td>
</tr>
<tr>
<td>Drinking water¹⁰</td>
<td>0.001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td>Food¹¹</td>
<td>51</td>
<td>28</td>
<td>16</td>
<td>8.6</td>
<td>5.7</td>
<td>4.7</td>
<td></td>
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<tr>
<td>Soil¹²</td>
<td>0.004</td>
<td>0.004</td>
<td>0.0065</td>
<td>0.0021</td>
<td>0.0005</td>
<td>0.0004</td>
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<tr>
<td>Total intake¹³</td>
<td>0.01</td>
<td>51</td>
<td>28</td>
<td>16</td>
<td>8.6</td>
<td>5.7</td>
<td>4.7</td>
</tr>
</tbody>
</table>

¹ Assumed to weigh 7.5 kg, to breathe 2.1 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 30 mg soil per day and to drink 0.2 L of water per day. Consumption of food groups reported in EHD (1998).
² For formula-fed infants, intake from water is synonymous with intake from food. Infants are assumed to consume 0.8 L of reconstituted formula daily. No data on concentrations of DnOP in formula were identified for Canada.
³ Assumed to weigh 15.5 kg, to breathe 9.3 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 100 mg soil per day and to drink 0.2 L of water per day. Consumption of food groups reported in EHD (1998).
⁴ Assumed to weigh 31.0 kg, to breathe 14.5 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 65 mg soil per day and to drink 0.4 L of water per day. Consumption of food groups reported in EHD (1998).
⁵ Assumed to weigh 59.4 kg, to breathe 15.8 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 30 mg soil per day and to drink 0.4 L of water per day. Consumption of food groups reported in EHD (1998).
⁶ Assumed to weigh 70.9 kg, to breathe 16.2 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 30 mg soil per day and to drink 0.4 L of water per day. Consumption of food groups reported in EHD (1998).
⁷ Assumed to weigh 72.0 kg, to breathe 14.3 m³ per day (21 hours indoors, 3 hours outdoors), to ingest 30 mg soil per day and to drink 0.4 L of water per day. Consumption of food groups reported in EHD (1998).
⁸ In autumn of 1990, a field monitoring study was carried out in the vicinity of 65 homes at Riverside, California (California Environmental Protection Agency, 1992). For daytime and nighttime sampling, both the median and 90th percentile were below the method quantifiable limit (3.2 ng/m³).
⁹ In autumn of 1990, a field monitoring study was carried out at Riverside, California, in 125 homes (California Environmental Protection Agency, 1992). The daytime median was below the method quantifiable limit; the daytime 90th percentile was 9.7 ng/m³.
¹⁰ Concentrations of DnOP in Canadian drinking water were not identified. The highest concentration of DnOP reported in surface water in Canada was 5.197 ng/L, in the study with the most sensitive limit of detection (Niagara River Data Interpretation Group, 1990).
¹¹ DnOP was an analyte in surveys for plasticizers in foods and food packaging carried out by Health Canada (Page and Lacroix, 1992, 1995). Detection limits for DnOP were as follows: meat/fish/poultry, 0.1 µg/g; soft
drinks/fruit juices, 0.05 µg/g; fruits and vegetables, 0.2 µg/g; butter, 0.5 µg/g; margarine, 0.5 µg/g; maple syrup, 0.01 µg/g.

The highest reported concentration in soil in urban residential and parkland locations in Port Credit, Oakville and Burlington was 1.0 µg/g (Golder Associates, 1987).

Medium-specific and total intakes were calculated on a Microsoft Excel spreadsheet. Only significant numbers have been presented, which accounts for seemingly inaccurate totals.
APPENDIX A: SEARCH STRATEGY — NEW INFORMATION FOR THE ASSESSMENT OF “TOXIC” TO HUMAN HEALTH UNDER PARAGRAPH 64(C) OF CEPA 1999

To identify relevant information (up to December 2000) on production, importation, use and environmental release, searches of the National Pollutant Release Inventory (Environment Canada, 1997, 1998), the Toxic Release Inventory (U.S. EPA, 2000), the Pesticide Management Regulatory Agency of Health Canada (Health Canada, 2000) and the Use Patterns and Controls Implementation Section of Environment Canada (Environment Canada, 2000) have been performed and information has been compiled under contract by Camford Information Services (CIS, 2001).

A comprehensive literature search was conducted (up to August 2000) of monitoring data in Canada (or elsewhere) and toxicological studies in animals and humans to identify critical new data for the assessment of human health risk under Paragraph 64(c) of CEPA 1999. A search was conducted by name or CAS registry number in the following databases: Canadian Research Index, CCRIS (Chemical Carcinogenesis Research Information System, U.S. National Cancer Institute; 1982–2000), Chemical Abstracts (Chemical Abstracts Service, Columbus, Ohio), EMBASE (on-line version of Excerpta Medica), EMIC (Environmental Mutagen Information Center database, Oak Ridge National Laboratory), Enviroline (R.R. Bowker Publishing Co.), Environmental Bibliography (Environmental Studies Institute, International Academy at Santa Barbara), Food Science & Technology Abstracts, HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine), Pascal (Institut de l’Information Scientifique et Technique, French National Research Council), Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine) and Toxnet. Name and registry number were searched in the Toxline (U.S. National Library of Medicine; 1993–2000) and Medline (U.S. National Library of Medicine; 1993–2000) databases. A search of the following web sites was also conducted (up to December 2000): Agency for Toxic Substances and Disease Registry, International Agency for Research on Cancer, International Programme on Chemical Safety, Micromedix TOMES Plus System™ (composed of CHRIS, ERG2000, HAZARDTEXT, HSDB, INFOTEXT, IRIS, MEDITEXT, New Jersey Fact Sheets, NIOSH Pocket Guide, OHM/TADS and RTECS), National Toxicology Program, Organisation for Economic Co-operation and Development, TNO BIBRA International and U.S. Environmental Protection Agency.

A more limited search was carried out for mono-n-octyl phthalate (CAS No. 5393-10-1) in the following databases: DART (Developmental and Reproductive Toxicology, U.S. National Library of Medicine), EMIC, ETIC (Environmental Teratology Information Center database, U.S. Environmental Protection Agency and U.S. National Institute of Environmental Health Sciences), GENE-TOX (Genetic Toxicology, U.S. Environmental Protection Agency), HSDB, IRIS (Integrated Risk Information System, U.S. Environmental Protection Agency), Medline, Toxline and ToxlinePlus.