THE ARET

SUBSTANCE SELECTION PROCESS

and

GUIDELINES

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1. Introduction

This report describes the process and guidelines that were followed in developing a prioritized list of toxic substances slated for action under the Accelerated Reduction/Elimination of Toxics (ARET) project. The substances were selected from the Chemical Evaluation Search and Retrieval System (CESARS) database, a database of substances found in the Great Lakes basin.

The ARET Committee, which guides this project, is made up of representatives from industry associations, health and professional groups, and federal and provincial governments. It has been supported by multistakeholder technical sub-committees, which have developed the process and recommendations for a prioritized list of candidate substances. This list is the basis for ARET's challenge to facilities that emit these substances to voluntarily reduce or eliminate emissions, and to draw up action plans for this purpose by September 1994.

The ARET Committee wishes to acknowledge the extensive groundwork on substance selection done by the Ontario Ministry of Environment and Energy (MOEE) in its document, "Candidate Substances List for Bans and Phase-outs, April 1992" and its most recent update in October 1993 (ref. ISBN 0-7729-9764-0 and ISBN 0-7778-0774-2 respectively).

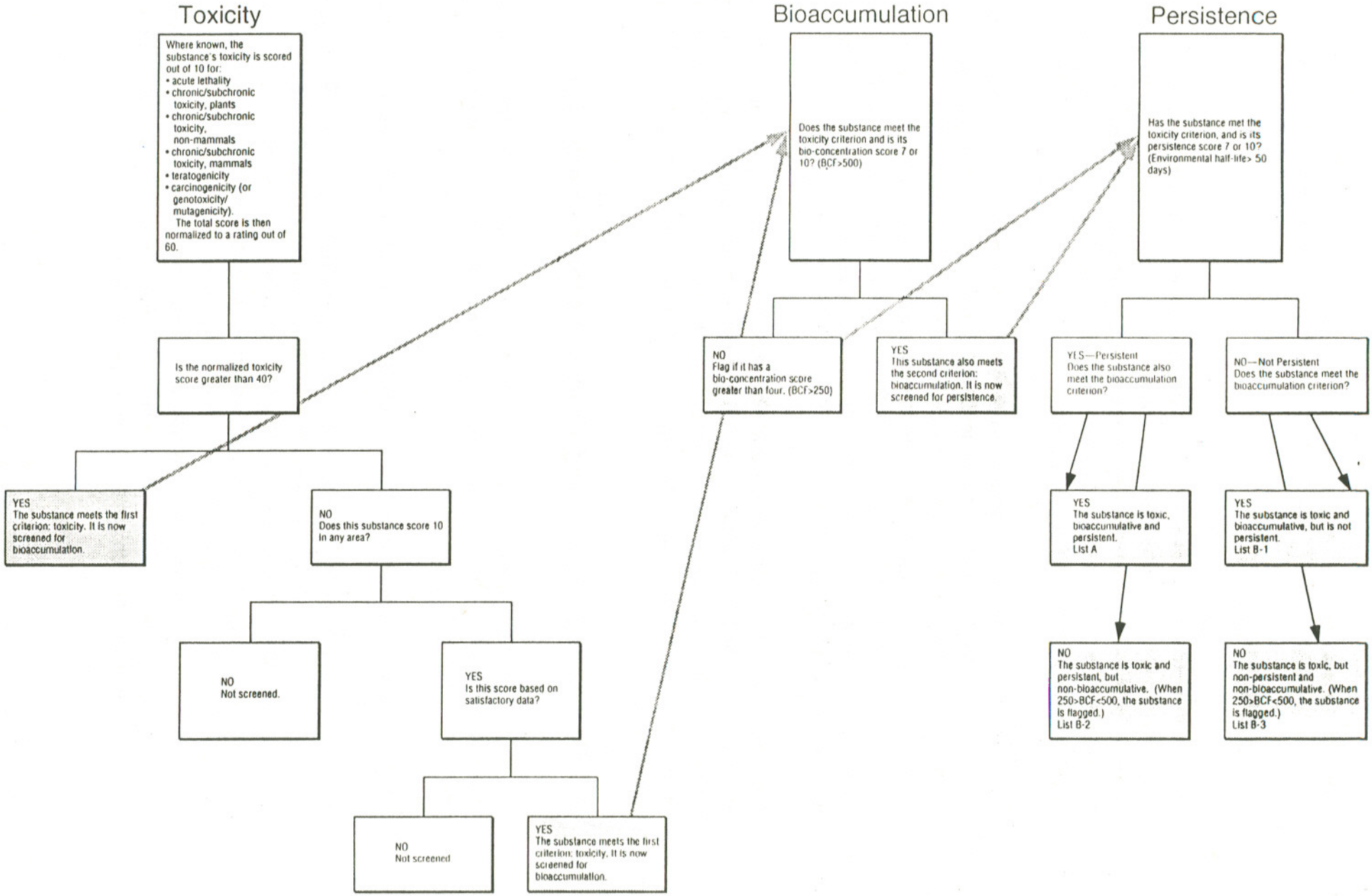
2. The process for candidate substance selection

The ARET Committee placed highest priority on action for substances that are toxic, bioaccumulative and persistent. Accordingly, these were the three criteria used for the selection process.

The selection process was carried out as illustrated in the flow chart following this page:

a) ARET's Substance Selection Sub-Committee used MOEE scores that were based on available toxicity, persistence and bioaccumulation data. Scores on the substances were available in the CESARS database which was developed by the Michigan Department of Natural Resources (MDNR), and is maintained and updated by MOEE and MDNR. The scores were often based on the most sensitive species and in other ways represented "worst case" assumptions. Out of approximately 2000 substances in the CESARS database, about one quarter had sufficient data on toxicity, persistence and bioaccumulation to be screened for selection.

How substances were selected and categorized



b) Normalized Toxicity Scores (NTS) were calculated for the substances, based on six elements of toxicity, each with a maximum score of 10 (refer to Table 1a):
Acute lethality
Chronic/subchronic toxicity, plants
Chronic/subchronic toxicity, non-mammals
Chronic/subchronic toxicity, mammals
Teratogenicity
Carcinogenicity or genotoxicity/mutagenicity (the latter are used only in the absence of carcinogenicity data)

Data on at least three elements were required to calculate a normalized toxicity score. Where possible, professional judgement was used to fill data gaps to meet this requirement.

A substance with:
an Acute lethality score of 8,
a Carcinogenicity score of 10, and
a Chronic toxicity (plants) score of 6, would score 24/30, for an NTS of 48/60.

c) The substances were ranked by NTS, and the Substance Selection Sub-Committee chose a cut-off score above which substances would be further screened. The sub-committee agreed that all substances with an NTS greater than 40 met the first selection criterion (toxicity).

d) As well, substances that scored 10 on any one of the six toxicity elements also met the first selection criterion, toxicity. Substances with a single score of 10 based on limited, qualified, or unsatisfactory data were not included in the screening, unless professional judgement decided otherwise.

e) Substances with bioconcentration scores of 7 or 10 (i.e., Bioconcentration Factor [BCF] greater than 500) met the second selection criterion, bioaccumulation (refer to Table 1b). For substances with a BCF score of 4, the sub-committee obtained additional information and flagged the substances with a BCF between 250 and 500.

f) Substances with persistence scores of 7 or 10 (i.e., environmental half-lives of greater than 50 days) met the third selection criterion, persistence (refer to Table 1b).

g) This screening process resulted in four lists:
List A: Toxic, bioaccumulative and persistent
List B-1: Toxic and bioaccumulative, but not persistent
List B-2: Toxic and persistent, but not bioaccumulative
List B-3: Toxic, but neither persistent nor bioaccumulative

h) The sub-committee reviewed the scores used for these listings to ensure consensus on the findings.

3. The selection guidelines

In applying the screening steps noted above, the Substance Selection Sub-Committee **used** the following ground rules:

a) Decisions on listing compounds were made on the basis of consensus.

b) Where there were inconsistencies in the scoring, professional judgement would apply.

c) Persistence

- Field data were preferred over laboratory data, which, in turn, were preferred over estimates generated from models.

- Data for persistence in groundwater were not used because the CESARS data does not differentiate well between soil and groundwater. Furthermore, virtually all substances in groundwater have half-lives greater than 50 days, and would, if the data were used, all meet the persistence criterion.

- Data for persistence in sediment were accepted.

- Because of the elemental nature of their metallic component, metal compounds were all assigned a persistence score of 10. Organometallic substances were scored on the basis of available data.

d) Bioaccumulation

- Measured bioconcentration factor (BCF) or bioaccumulation factor (BAF) were preferred over octanol-water coefficient data, K_{ow}.

- Data generated for freshwater fish in flow-through systems were preferred over data from other vertebrate species.

- Professional judgement was exercised concerning accumulation in specific organs or tissues.

- Bioaccumulation in invertebrates and other "non fish" organisms were considered, but with discretion. For example, BCF data for invertebrates are particularly relevant for polycyclic aromatic hydrocarbons (PAHs). The discretionary use of "non fish" BCFs would also apply to food items such as shellfish.

e) Mammalian Chronic/subchronic toxicity data

- Data from 90-day studies were preferred. For studies lasting less than 90 days, a five-fold safety factor was applied to the no-effect level (NOEL) to produce the score (i.e., the end-point concentration from the study was divided by five).

- Data from studies lasting less than 28 days were not considered.

f) Carcinogenicity

- Preferred data for carcinogenicity were from human and animal studies, and caution was exercised when data were available for only one species (MOEE scores were flagged as limited).

- Where there was a MOEE carcinogenicity score of 10, an attempt was made to corroborate this score with the International Agency for Research on Cancer (IARC) classification. Discrepancies were investigated between MOEE scores and IARC classification. In the event that the IARC classification was 1, 2A, or 2B, it would normally override a lower MOEE carcinogenicity score, unless it could be demonstrated that the score in CESARS was based on more recent data.

g) Genotoxicity

- Data on genotoxicity were used only if no data were available on carcinogenicity or reproductive endpoints.

- Mammalian studies were preferred over studies on mammalian cells in vitro, insects or bacteria.

h) Metals

- The intent was to address metal speciation on a case-by-case basis, with data to be examined to determine which chemical species or form(s) of a given metal were used in tests. This was not always possible (see 5(d) below). Consideration was given to the routes of exposure, e.g., respirable forms, water soluble forms.

4. Additional considerations

a) Clustering or grouping substances

- Most candidate lists tend to lump together all "families" or groups of chemically similar compounds, e.g., polychlorinated dibenzo-p-dioxins and furans, polycyclic aromatic hydrocarbons. The sub-committee attempted to resolve whether it was scientifically acceptable and practical to "lump" or "split" each of the major potential groupings, and noted this in the detailed list of substances.

b) Listing substances that degrade to more hazardous forms in the environment

- A number of substances are altered by chemical, physical or biological processes in the environment. Mercury, for instance, is relatively benign in certain inorganic species, but frequently becomes methylated, particularly in water. Methyl mercury is a List A substance, while inorganic mercury is not.

  Where degradation or derivative substances were well known, the sub-committee made clear cross references in the lists, in order to highlight opportunities where emitters can address both primary and derivative substances.

c) Pesticides

- The sub-committee screened the CESARS database for pesticides and grouped them in the screened categories. However, the ARET Committee decided to remove pesticides from the publicly released list of candidate substances because it was not possible to have specific pesticide stakeholder participation in the substance selection process. As well, pesticides are strictly controlled under the *Pest Control Products Act*. The ARET Committee included on the list those pesticides that also have non-pesticidal uses or releases.

5. Limitations to the selection process

a) Data availability

Scoring was based on data in the CESARS database, and for a small number of substances, additional data was available through sub-committee or committee members. However, the inability to weigh all possible data for a substance during screening was noted as a limitation.

b) Evaluation of multiple studies

Where more than one study was available on the same species, or where data were available on multiple species, the "worst case" value was often chosen for scoring by the MOEE. These scores were generally accepted by ARET unless a representative challenged the score based on personal experience or knowledge about the specific substance. "Worst case" values were rejected in some cases, eg. when the species was not appropriate (not in the Canadian environment) or the study design was an inappropriate model for the Canadian environment.

c) Pragmatic use of criteria

The sub-committee was required to screen some 450 substances in a relatively short period of time. As a result, it was not possible to give each substance the detailed attention and review required to weigh the data. In most cases the MOEE scores were adopted without modification.

d) Metal speciation

The listing of metals proved to be a challenge for the sub-committee. Because of the limited time and resources available, the complex environmental chemistry of metals in general, and the question of their speciation in particular could not be addressed in a completely satisfactory manner. Therefore, to be cautious, the sub-committee decided to use qualifiers such as "respirable, soluble, inorganic, etc." to describe the metal compounds it scored. The screening process relied on composite scores for metal compounds, resulting in a worst-case score for some metals.

e) Action responses

The decision to group and list substances for prioritization was based on intrinsic properties only, and based on the data in the CESARS database. There was no consideration of risks, emission volumes, or actual damage to the environment or to health. The ARET Committee expects that emitters, in developing their action plans and setting priorities, will take into account the relative volume of emissions and the socio-economic factors involved in dealing with the substances.

For more information on the list, the selection process, or on the development of action plans, please contact the ARET Secretariat at 819-953-9086 or 953-7832.

APPENDIX I : DEFINITIONS

1. TOXICITY ELEMENTS

a) Acute lethality describes the capacity of a substance to cause the death of an organism after short-term exposure to that substance. Acute effects that are not fatal (irritation, allergic reactions, general narcosis, etc.) are considered in other toxicity elements. Criteria for substances toxic to plants are not included here because it is difficult to assess lethality in plants.

b) Chronic/sub-chronic toxicity on non-mammalian species describes the possible effects from long-term exposure of non-mammalian species to chemicals. The data may be expressed as median effect concentration (EC50), maximum acceptable toxicant concentration (MATC), or no-observed-adverse-effect-concentration (NOAEC).

c) Chronic/sub-chronic toxicity data on plants can be highly variable depending on the toxicant. In some cases, results expressed in concentration units are appropriate, but in most instances the length of exposure time is very important. Chronic toxicity data on plants should be provided, however, when dealing with phytotoxic substances.

d) Chronic/sub-chronic toxicity on mammals describes a chemical's potential toxic effects on mammals after repeated doses. It is expressed as the dose at which toxic effects in humans are expected to be very unlikely, although the level will most often be derived from the "no-observed-effects" level (NOEL) in studies on laboratory animals. Toxic effects were restricted to those that were sub-lethal and systemic, including reproductive (non-teratogenic) and neurotoxic effects. Carcinogenic, mutagenic, or teratogenic effects are included in other parameters.

e) Teratogenicity is the capacity to cause permanent functional or structural abnormalities in an embryo. The process involves the interaction of chemical, biological and physical agents with embryonic structure during prenatal life. Scoring of this parameter considered the spectrum of effects ranging from minor variations, anomalies, and malformations against their normal background incidence, as well as the more subtle effects on the health of newborns and their future development.

f) Carcinogenicity is the potential of a chemical to induce malignant tumours. Consideration must be given to the substance's pharmacokinetics and metabolism, its mechanism of action (e.g., genetic as opposed to epigenetic mechanisms), whether the tumours are malignant or benign, whether they reduce the life span and similar factors.

g) Genotoxicity/mutagenicity is the capacity to induce genetic mutations. The process is an interaction of chemical and physical agents with the cell's hereditary apparatus. It can be manifested in either gene alterations, or changes in chromosomal structure or number -- characteristics that may be incorporated in subsequent generations of that cell (i.e. mutations). Such outcomes may indicate a chemical's potential to cause cancer or adversely affect reproduction.

2. BIOCONCENTRATION

Bioconcentration is a substance's capacity to accumulate in the tissues of organisms. A parameter often used to express bioconcentration is the bioconcentration factor (BCF). Most BCF values pertain to fish or other aquatic organisms, and are calculated as the ratio of the concentration of a substance in the organism (or some specific tissue) on a wet weight basis, to the concentration of a substance in the water at steady state. The tendency of organic substances to bioconcentrate in tissue has often been related to their hydrophobicity or lipophilicity. Various regression equations have been suggested for predicting BCF values for aquatic organisms, based on the octanol-water partition coefficient (K_{ow}) and other physico-chemical properties.

3. PERSISTENCE

Persistence is the tendency for a substance to remain in the environment. A chemical's net resistance to processes such as biodegradation, oxidation, hydrolysis and photodegradation can be expressed as its overall persistence in the environment. Persistence is usually expressed as the length of time required for one-half of the original amount of a substance to be degraded (half-life). Substances having short half-lives generally cause less concern in this context.

Table 1a

ELEMENT NAME	ENDPOINT & UNITS	Scoring Criteria 0	2	4	6	8	10
Acute lethality	oral LD_{50} (mg/kg)	> 5000	> 500- 5000	> 50- 500	> 5- 50	> 0.5- 5	≤ 0.5
	dermal LD_{50} (mg/mg)	> 5000	> 500- 5000	> 50- 500	> 5- 50	> 0.5- 5	≤ 0.5
	inhal LC_{50} (mg/m^3)	> 15000	> 1500-15000	> 150-1500	> 15-150	> 1.5- 15	≤ 1.5
	aquatic LC_{50} (mg/L)	> 1000	> 100- 1000	> 10- 100	> 1- 10	> 0.1- 1	≤ 0.1
Chronic/Sub-chronic toxicity, Non-Mammals	**aquatic**						
	EC_{50} (mg/L)	≥ 20	2 - < 20	0.2 - < 2	0.02 - < 0.2	< 0.02*	< 0.02*
	MATC (mg/L)	≥ 2	0.2 - < 2	0.02 - < 0.2	0.002 - < 0.02	< 0.002*	< 0.002*
	NOAEC (mg/L)	≥ 0.2	0.02 - < 0.2	0.002-<0.02	0.0002 - <0.002	< 0.0002*	< 0.0002*
	terrestrial						
	subchronic (NOEL mg/kg/d)	≥ 1000	100 - < 1000	10 - < 100	1 - < 10	< 1*	< 1*
	chronic (NOEL mg/kg/d)	≥ 500	50 - < 500	5 - < 50	0.5 - < 5	< 0.5* *in one genus	< 0.5* *in different genera
Chronic/Sub-chronic toxicity, Plants	% growth reduction:						
	≤5 (= NOEL)						
(water, mg/L)	water	> 10	> 1 - 10	> 0.1- 1	> 0.01-0.1	0.001-0.01	< 0.001
($air, mg/m^3$)	air	> 100	> 10 - 100	> 1 - 10	> 0.1- 1	0.01- 0.1	< 0.01
(soil, mg/kg)	soil	> 100	> 10 - 100	> 1 - 10	> 0.1- 1	0.01- 0.1	< 0.01
	>5-50 (=EC_{50})						
	water	> 100	> 10 - 100	> 1 - 10	> 0.1- 1	0.01- 0.1	< 0.01
	air	> 1000	> 100 -1000	> 10 - 100	> 1- 10	0.1- 1	< 0.1
	soil	> 1000	> 100 -1000	> 10 - 100	> 1- 10	0.1- 1	< 0.1
	>50						
	water	> 1000	> 100 -1000	> 10 - 100	> 1- 10	0.1- 1	< 0.1
	air	> 10000	> 1000 -10000	> 100 -1000	> 10- 100	1- 10	< 1
	soil	> 10000	> 1000 -10000	> 100 -1000	> 10- 100	1- 10	< 1
Chronic/Sub-chronic toxicity, Mammals (These criteria are based on studies of ≥ 90 days duration. If only shorter-term subchronic studies are available, the **NOEL is divided by** 5, prior to scoring for toxicity.)	oral NOEL (mg/kg/day)	> 1000	> 100- 1000	> 10- 100	> 1- 10	> 0.1- 1	≤ 0.1
	inhal. NOEL (mg/m^3)	> 3000	> 300- 3000	> 30- 300	> 3- 30	> 0.3- 3	≤ 0.3

Table 1a, continued

ELEMENT NAME	ENDPOINT & UNITS	Scoring Criteria 0	2	4	6	8	10
Teratogenicity	mg/kg/day	no terata, or terata only at > 1000	terata or developmental anomalies at > 50-1000	terata or developmental anomalies at > 10-50	terata or developmental anomalies at > 1-10	terata > 0.1-1, without overt maternal toxicity	terata at ≤0.1 without overt maternal toxicity
Carcinogenicity	human and animal bioassay data	no tumours in adequate studies on at least two species, and does not interact with genetic material	tumours in only one animal species, negative results in others	causes benign tumours in more than one species, and does not interact with genetic material; promotor only; or causes cell transformation *in vitro* only (negative evidence *in vivo*)	tumourigenic in bioassays at doses causing metabolic enzyme saturation, or associated with lesions that predispose to tumours. No interaction with genetic material	indirect-acting carcinogen, no interaction with genetic material	direct-acting carcinogen that interacts with genetic material - or - IARC Group 1, 2A or 2B carcinogen classification - or - U.S. EPA Class A, B1 or B2 carcinogen classification
Genotoxicity/ Mutagenicity (This data element is only used if no reliable data is available on carcinogenic or reproductive endpoints.)	*in vivo* and *in vitro* cell assays	not genotoxic or mutagenic, negative results *in vivo* and *in vitro*	mutagenic in *in vitro* assays only, negative *in vivo*	mutagenic in prokaryotic cells only; negative results in eukaryotic cell assays	causes DNA induction or repair, with no direct interaction with nuclear material	causes clastogenic effects, sister chromatid exchange, crosslinks; no evidence of mutation	mutagenic *in vivo* (no negative results from *in vitro* assays)

* Adapted from Table 1.6, in the Ontario Ministry of the Environment document "Candidate Substances List for Bans or Phase-outs" (Ref. ISBN 0-7729-9764-0).

Table 1b

Scoring Criteria (cont'd)

ELEMENT NAME	ENDPOINT & UNITS	0	4	7	10
Environmental persistence in air, water or sediment	t½ (days)	≤ 10	> 10 to 50	> 50 to 100	> 100
Bio-accumulation in freshwater fish*	BCF Log K_{ow}	≤20 ≤2.0	> 20 to 500 > 2.0 to 4.0	> 500 to 15000 > 4.0 to 6.0	> 15000 > 6.0

If freshwater fish data not available, information from other vertebrate species may be used with judgement.

* Adapted from Table 1.6, in the Ontario Ministry of the Environment document "Candidate Substances List for Bans or Phase-outs."