



## **Screening Assessment**

# **Phenol, 2-(1-methylpropyl)-4,6-dinitro- (Dinoseb)**

**Chemical Abstracts Service Registry Number  
88-85-7**

**Environment and Climate Change Canada  
Health Canada**

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## Synopsis

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of phenol, 2-(1-methylpropyl)-4,6-dinitro-, commonly known as dinoseb. The Chemical Abstracts Service Registry Number (CAS RN<sup>1</sup>) for dinoseb is 88-85-7. This substance was identified as a priority for assessment on the basis of human health concerns.

Dinoseb was used in Canada as an herbicide until 2001, when all herbicidal uses were discontinued. The largest current use in Canada is as a polymerization retarder in the production of styrene monomer. Information obtained under the export notification provisions of the Rotterdam Convention and from follow-up discussions with industry indicates that between 100 000 and 1 000 000 kg of dinoseb was imported into Canada in 2015. Data obtained from the Canadian Border Services Agency indicates that smaller quantities of a related substance, dinoseb acetate, were imported into Canada between 2011 and 2015 by several companies for other unknown uses. Dinoseb acetate will dissociate to dinoseb in the environment and therefore could be contributing to total dinoseb exposure levels.

Releases of dinoseb to surface water are possible and, according to information on use patterns, these releases could be continuous. In water, dinoseb will hydrolyze slowly, and it is not readily biodegradable. Degradation by photolysis can occur at a moderate rate, but will vary depending on factors such as water depth and turbidity. Overall, it is expected to persist in water. Dinoseb is slightly persistent in air, although significant releases to that medium are not expected. Dinoseb is not expected to bioaccumulate in aquatic organisms.

Dinoseb is a reactive chemical whose principal mode of action is the uncoupling of oxidative phosphorylation, which results in the interference of energy synthesis. Dinoseb is hazardous to various forms of aquatic organisms, as well as to birds and mammals. Dinoseb has effects on reproduction (embryotoxicity), survival and growth (changes in metabolism and abnormal development), and binds to protein and DNA. Empirical studies, in vitro assays, and quantitative structure-activity relationship (QSAR) modelling all indicate potential for adverse effects in aquatic organisms at low concentrations.

There are historical environmental monitoring data for dinoseb from the time it was used as an herbicide, as well as from shortly after it was discontinued for that use. However,

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there are limited current environmental monitoring data for dinoseb in surface water, and no current data for dinoseb in air, sediment or soil in Canada. An exposure analysis was conducted to estimate the predicted environmental concentration of dinoseb in surface water due to industrial releases. A risk quotient analysis for this scenario indicates that there is possible risk of harm to aquatic organisms from dinoseb. The potential for harm is supported by other lines of evidence, including persistence and long-range transport in water. Given the high hazard of dinoseb to aquatic organisms, even very low levels of exposure may pose a risk to the environment.

Dinoseb has previously been assessed through the Organisation for Economic Co-operation and Development (OECD) Cooperative Chemicals Programme, and the OECD Screening and Information Dataset Initial Assessment Report (SIAR) was used to inform the health effects section of this screening assessment. The main endpoints of concern for dinoseb are reproductive and developmental toxicity, based on effects on sperm parameters in male rats and the subsequent decrease in gestation index in an oral study, and maternal and fetal toxicity, as determined from an oral study in rats and a dermal study in rabbits. Dinoseb is no longer used as a pesticide, nor is it used in products available to consumers. Recent drinking water monitoring data from various municipalities across Canada show no detection of dinoseb. Exposure of the general population in Canada to dinoseb through environmental media, food, or the use of products is not expected. Any population exposures resulting from potential releases to surface waters from industrial uses would still be several orders of magnitude less than levels associated with health effects. Given these considerations, the potential risk to human health is deemed to be low.

Considering all available lines of evidence presented in this screening assessment, there is risk of harm to the environment from dinoseb. It is concluded that dinoseb meets the criteria under paragraph 64(a) of CEPA as it is entering or may 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. However, it is concluded that dinoseb does not meet the criteria under paragraph 64(b) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends. It is also concluded that dinoseb does not meet the criteria under paragraph 64(c) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute a danger in Canada to human life or health.

Therefore, it is concluded that dinoseb meets one or more of the criteria set out in section 64 of CEPA.

It has also been determined that dinoseb meets the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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# 1. Introduction

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have conducted a screening assessment of phenol, 2-(1-methylpropyl)-4,6-dinitro-, commonly known as dinoseb, to determine whether this substance presents or may present a risk to the environment or to human health. This substance was identified as a priority for assessment on the basis of human health concerns (ECCC, HC [modified 2007]).

Dinoseb was reviewed internationally through the Organisation for Economic Co-operation and Development (OECD) Cooperative Chemicals Assessment Programme, and an OECD Screening Information Dataset Initial Assessment Report (SIAR) is available (OECD 2007). These assessments undergo rigorous review (including peer review) and endorsement by international governmental authorities. Environment and Climate Change Canada and Health Canada are active participants in this process and consider these assessments reliable. The health assessment section of the OECD SIAR was used to inform the health effects section of this screening assessment. Additionally, the ecological assessment section of the OECD SIAR was reviewed, and relevant information from it was considered in the ecological section of this assessment along with other sources of ecological hazard information.

This screening assessment includes consideration of information on chemical properties, uses, environmental fate, hazards, and exposures, including additional information submitted by stakeholders. Relevant data were identified up to December 2016. Empirical data from key studies, as well as some results from models, were used to reach the conclusion.

This screening assessment was prepared by staff in the CEPA Risk Assessment Program at Environment and Climate Change Canada and Health Canada (including the Pest Management Regulatory Agency) and incorporates input from other programs within these departments. The ecological portion of this screening assessment has undergone external review. Comments on the technical portions relevant to the environment were received from officials at the European Chemicals Agency (ECHA), and the United States Environmental Protection Agency (US EPA). Additionally, the draft of this screening assessment (published June 2, 2018) was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remains the responsibility of Environment and Climate Change Canada and Health Canada.

This screening assessment focuses on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA, by examining scientific

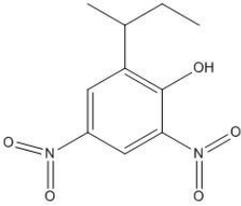
information and incorporating a weight of evidence approach and precaution.<sup>2</sup> This screening assessment presents the critical information and considerations on which the conclusion is based.

## 2. Identity of substance

Substance identity information, including the CAS RN<sup>3</sup>, Domestic Substances List (DSL) name, and common name, is presented in Table 2-1. In this assessment, the substance will be identified by its common name, dinoseb.

A list of additional chemical names (e.g., trade names) for dinoseb is available from the National Chemical Inventories (NCI 2017). One of the most common abbreviations, which is used in commerce and experimental studies, is DNBP.

**Table 2-1. Substance identity**

CAS RN	DSL name (common names and abbreviation)	Chemical structure and molecular formula	Molecular weight (g/mol)
88-85-7	Phenol, 2-(1-methylpropyl)-4,6-dinitro-  (Dinoseb, DNBP)	  C <sub>10</sub> H <sub>12</sub> N <sub>2</sub> O <sub>5</sub>	240.24

Dinoseb forms salts and esters, some of which are water soluble, with inorganic and organic bases (Worthing and Walker (eds.) 1983; Kearney and Kaufman 1976). This

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<sup>2</sup> A determination of whether one or more of the criteria of section 64 of CEPA are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and products used by consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other acts.

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assessment focuses on dinoseb (CAS RN 88-85-7) which is on the DSL and is known to be in commerce in Canada. However, it is recognized that dinoseb salts, in particular dinoseb acetate, once released to the environment, will dissociate to produce dinoseb itself, and therefore could be contributing to total dinoseb exposure levels. Therefore, potential dinoseb exposure resulting from dinoseb acetate has also been considered.

### 3. Physical and chemical properties

A summary of relevant experimental and modelled physical and chemical property values or ranges of values for dinoseb are presented in Table 3-1.

**Table 3-1. Experimental and modelled values for physical and chemical properties of dinoseb**

Property	Value	Reference
Physical state	Yellow crystals or orange solid, with a pungent odour	Hartley and Kidd 1983; Worthing and Walker (eds.) 1983; WSSA 1979
Melting point (°C)	39.74–41.94	ECHA c2007-2015a
Boiling point (°C)	>230 <sup>a</sup>	ECHA c2007-2015a
Vapour pressure (Pa)	0.007 (@ 20 °C )	IPCS 2011
Water solubility (mg/L)	52 (average)	Barbash and Resek 1996
Water solubility (mg/L)	25.8	MITI 1992
Other solubilities (mg/L): ethanol; <i>n</i> -heptane	480 000; 270 000	WSSA 1979
Henry's law constant (Pa·m <sup>3</sup> /mol)	4.5 x 10 <sup>-1</sup>	Tremp et al. 1993
log K <sub>ow</sub> (dimensionless)	3.00 (avg. value, at pH 7) * – 3.69	Bromilow et al. 1991; MITI 1992; de Bruijn et al. 1989; IPCS 2011
log K <sub>oc</sub>	3.82 (at pH 3) <sup>b</sup> , 1.9 (at pH 7)*	Hodson and Williams 1988; calculated <sup>c</sup>
log K <sub>oa</sub>	8.29 (modelled)	EPI Suite c2000-2012
log K <sub>aw</sub>	2 x 10 <sup>-5</sup> (modelled)	EPI Suite c2000-2012
pK <sub>a</sub> (dimensionless)	4.47 * –4.65	Schwarzenbach et al. 1988; Worthing and Walker (eds.) 1983; ECHA c2007-2015a

Abbreviations:  $K_{ow}$ , octanol–water partition coefficient;  $K_{oc}$ , organic carbon–water partition coefficient;  $pK_a$ , acid dissociation constant.

\* Indicates that this value was chosen for use in modelling.

<sup>a</sup> The boiling point could not be determined because the sample started to decompose before reaching the boiling point (onset temperature approximately 230°C; ECHA c2007-2015a). When dinoseb decomposes on heating, it produces harmful fumes of nitrogen oxides (IPCS 2011).

<sup>b</sup> Reported as  $K_{oc}$  of 6607.

<sup>c</sup>  $K_{oc}$  at pH 7 calculated from the  $pK_a$  using an equation from Franco and Trapp (2008) for ionizing substances.

## 4. Sources, uses, and releases

Dinoseb is not known to occur naturally in the environment.

Dinoseb and its salts and esters are listed under the Rotterdam Convention as chemicals that require prior informed consent (PIC) before they can be exported from one Party to another (UNEP 2010). Chemicals and pesticides can be listed under the Rotterdam Convention when two or more Parties, located in different geographical regions of the world, have taken regulatory action to prohibit or severely restrict the substance as a consequence of a risk to health and/or the environment. Canada is a Party to the Rotterdam Convention and does not consent to the import of dinoseb and its salts and esters for pesticidal use (Environment Canada 2015). Although the Convention and its PIC procedure do not explicitly apply to exports of these substances for other uses, such as industrial uses, Environment and Climate Change Canada (ECCC) receives export notifications from some Parties who choose to notify importing countries when companies intend to export dinoseb for industrial uses. Since 2013, ECCC has received notifications about intended exports to Canada of dinoseb under the PIC classification of dinoseb and its salts and esters.

According to the export notification information described above and to follow-up discussions with industry, dinoseb was imported into Canada in the range of 100 000 to 1 000 000 kg in 2015 for use as a polymerization retarder in the production of styrene monomer. Although this use involves a closed industrial process, waste effluents from this process are sent off-site to a wastewater treatment system (WWTS)<sup>4</sup> and, after treatment, discharged to surface water. Therefore, there is a potential for release of dinoseb to surface water; however, there are limited monitoring data available to confirm what quantities, if any, are being released.

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<sup>4</sup> In this assessment, the term “wastewater treatment system” refers to a system that collects domestic, commercial and/or institutional household sewage and possibly industrial wastewater (following discharge to the sewer), typically for treatment and eventual discharge to the environment. Unless otherwise stated, the term wastewater treatment system makes no distinction of ownership or operator type (municipal, provincial, federal, indigenous, private, partnerships). Systems located at industrial operations and specifically designed to treat industrial effluents will be identified by the terms “on-site wastewater treatment systems” and/or “industrial wastewater treatment systems.”

Information on the import of dinoseb was also obtained from the Canadian Border Services Agency (CBSA). Data were received for imports between the years 2011 and 2015 under the Harmonized System (HS) code for “Dinoseb (ISO) acetate”. These data indicated that eight different companies imported dinoseb acetate over the five-year period at low quantities, typically less than 100 kg per company per year (CBSA 2016). It is not known how these smaller imported quantities are being used.

Historically, dinoseb was imported into Canada for use as an herbicide, specifically as a pre-emergent or contact spray and as a desiccant. It was available commercially for these purposes as an aqueous solution and also as an emulsifiable concentrate (NCBI [accessed 2020]). The registration of all non-essential pesticidal (in this case, herbicidal) uses of dinoseb was suspended by Agriculture Canada in 1990 when health concerns about dinoseb were raised. No further uses were registered after December 31, 2000. The use of dinoseb as an herbicide has been discontinued as of December 31, 2001 (PMRA 2000). Historical releases of dinoseb in Canada were due to its use as an herbicide.

No other uses of dinoseb were identified (Table 4-1).

**Table 4-1. Additional uses in Canada for dinoseb**

Database	Dinoseb
Food additive <sup>a</sup>	No
Food packaging materials <sup>b</sup>	No
Drug Product Database <sup>c</sup>	No
Natural Health Products Ingredients Database <sup>d</sup>	No
Licensed Natural Health Products Database being present as a medicinal or non-medicinal ingredient in natural health products in Canada <sup>e</sup>	No
List of Prohibited and Restricted Cosmetic Ingredients <sup>f</sup>	No
Notified to be present in cosmetics, on the basis of notifications submitted under the <i>Cosmetic Regulations</i> Health Canada <sup>g</sup>	No
Formulant in pest control products registered in Canada <sup>h</sup>	No

<sup>a</sup> Personal communications, emails from Food Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; dated November 2016; unreferenced.

<sup>b</sup> Personal communications, emails from Food Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; dated November 2016; unreferenced.

<sup>c</sup> DPD (modified 2015).

<sup>d</sup> NHPID (modified 2016).

<sup>e</sup> LNHPD (modified 2016).

<sup>f</sup> Health Canada (modified 2015).

<sup>g</sup> Personal communications, emails from Consumer Product Safety Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; dated December 2014; unreferenced.

<sup>h</sup> Health Canada 2010.

## 5. Environmental fate and behaviour

### 5.1 Environmental distribution

Table 5-1 presents the results of the Level III fugacity modelling for the neutral form of dinoseb, showing percent partitioning into each environmental medium for three release scenarios. The neutral form of dinoseb was used as the model (EQC) cannot make predictions for charged substances. Therefore, these results should be interpreted with caution as the dissociated (charged) form of dinoseb may behave differently in some media.

**Table 5-1. Level III fugacity modelling (New EQC 2011) for the neutral form of dinoseb**

Dinoseb released to	Air (%)	Water (%)	Soil (%)	Sediment (%)
Air (100%)	29.22	16.96	53.70	0.12
Water (100%)	0.20	98.74	0.36	0.69
Soil (100%)	0.12	7.01	92.82	0.05

Fugacity modelling indicates that, when released into water, the neutral form of dinoseb is predicted to largely remain in that medium. However, the pKa for dinoseb (4.47) indicates that it will be present in water largely in the dissociated form at environmentally relevant pH values (6 to 9). Therefore, partitioning to sediment could vary from that predicted by fugacity modelling because natural sediments have a net negative charge (Blaskó 2008). On the basis of the modelled air-water partition coefficient ( $K_{aw}$ ) of  $2 \times 10^{-5}$  (EPI Suite c2000-2012), partitioning from water to air is expected to be negligible.

The Transport and Persistence Level III Model (TaPL3 2003) can be used to predict long-range transport (LRT) in water, a concept developed by Beyer et al. (2000). Using TaPL3, the characteristic travel distance (CTD) of dinoseb in water was calculated. The CTD is defined as the maximum distance travelled by 63% of the substance after being released into the environment. Zarfl et al. (2011) have proposed a threshold CTD of 5200 km for classifying organic substances as having long-range transport potential in water. The predicted CTD for dinoseb is approximately 17 000 kilometres, assuming a river with a current of 3.6 km/h and depth of 20 metres. This means that releases of dinoseb to a river would likely result in its transport along the full length of the river, and dilution, rather than degradation, will be the main factor affecting exposure concentrations. Chronic exposures could therefore be expected in the far-field.

The TaPL3 model can also be used to predict the CTD of dinoseb in air. The estimated CTD in air from this model, and the estimated CTD from the OECD  $P_{ov}$  and LRTP Screening Tool (OECD 2009), are 900 km and 1065 km, respectively. These values indicate that dinoseb, if released to air, is expected to be transported through the atmosphere moderate distances from its emission sources.

The fate of dinoseb in soil depends on many factors, including the form of dinoseb (neutral or dissociated), the type of soil, the form and concentration of ionic species in the soil (e.g.,  $\text{Ca}^{2+}$ ), and especially, the pH of the soil (Aharonson 1987; Saltzman and Yariv 1974; Tulp et al. 2009; US EPA 1987; Cornell University 1987; Agriculture Canada 1991).

In terms of loss from plant surfaces, Menzie (1978) reported that 72% of dinoseb was lost 28 days after topical application to apples. Although the author indicates that the loss was likely due to volatilization, it was more likely due to photolysis or water run-off, given that the vapour pressure for dinoseb is relatively low. Translocation of dinoseb in plants does not appear to occur because no residues have been traced to foliar or root uptake (WSSA 1983; Kearney and Kaufman 1976).

## 5.2 Environmental persistence

The key experimental and modelled data for the abiotic degradation of dinoseb are summarized in Table 5-2.

**Table 5-2. Summary of key experimental and modelled data for the abiotic degradation of dinoseb**

Medium and fate process	Degradation end-point or prediction	Value	Reference
Air; photo-oxidation	Half-life	2.65 days	AOPWIN 2010
Water; photolysis	Half-life	12 days	ECHA c2007-2015a
Water; hydrolysis (pH = 4, 7, and 9)	Half-life	Uncertain (but stable for 5 days @ 50°C)*	CERI 2003a
Water; hydrolysis (pH = 5-9)	Half-life	Uncertain (but stable for 5 days @ 50°C)*	US EPA 1987
Soil surfaces; photolysis in soil	Half-life (predicted)	6–102 days	ECHA c2007-2015a; Stevens et al. 1989
Plant surfaces; photolysis	Half-life	<1 hour to 6 days	Matsuo and Casida 1970; Hawkins and Sagers 1974

\* The dinoseb molecule does not have any hydrolysable groups.

In air, dinoseb reacts with photochemically produced hydroxyl radicals. Dinoseb is not expected to react with other photo-oxidative species in the atmosphere, such as ozone, but it could react with nitrate radicals (AOPWIN 2010). However, it is expected that reactions with hydroxyl radicals will be the most important fate process in the

atmosphere for dinoseb. With a half-life of 2.65 days via reactions with hydroxyl radicals, dinoseb is considered to be persistent in air. When present in air, dinoseb is expected to largely (> 80%) remain in the gaseous phase and to not partition significantly to airborne particulates (AEROWIN 2010).

Photolysis of dinoseb on plant surfaces could be a significant fate process for the degradation of dinoseb. Photolysis of dinoseb on soil surfaces could also be significant, but there is a great deal of uncertainty given the wide range of modelled half-lives that have been predicted (see Table 5-2).

In water, hydrolysis does not appear to be a significant fate process. Under certain conditions, photolysis in water can result in moderate degradation rates. However, photolysis is expected to vary considerably with water depth and turbidity and thus was not factored into the consideration of the residence time of dinoseb in water.

Table 5-3 summarizes the key experimental and modelled data for the biodegradation of dinoseb. The results of tests using OECD Guidelines 301B and 301C indicate that dinoseb is not readily biodegradable (ECHA c2007-2015a; CERI 2003b). Therefore, given these results, dinoseb is unlikely to undergo significant biodegradation in most natural waters (NCBI [accessed 2020]; OECD 2007). The experimental data are supported by modelled results for the neutral form of dinoseb (EPI Suite c2000-2012).

**Table 5-3. Summary of key experimental and modelled data for the biodegradation of dinoseb in water**

Fate process	Test conditions	Degradation endpoint or prediction	Reference
Aerobic biodegradation	OECD 301B (activated sludge)	CO <sub>2</sub> evolution 24% (after 28 days)	ECHA c2007-2015a
Aerobic biodegradation	OECD 301C (activated sludge, non-adapted)	BOD 0% (after 28 days)	CERI 2003b
Aerobic biodegradation	NA	Ready biodegradability prediction: No	EPI Suite c2000-2012

Abbreviations: BOD, biological oxygen demand; NA, Not Available

Test results for the biodegradation of dinoseb in soil are variable. Factors affecting biodegradation include the concentration of dinoseb, previous exposure to dinoseb, soil conditions (e.g., type of soil, pH), and the sorption of dinoseb to soil surfaces (Stevens et al. 1990; Stojanovic et al. 1972; Kearney and Kaufman 1976). Organisms that have been found to degrade dinoseb under aerobic conditions include *Pseudomonas aeruginosa* and *Pseudomonas putida* (Doubos and Reid 1956; Stevens et al. 1990), as well as *Azotobacter* (Wallnöfer et al. 1978) and *Clostridium bifermentans* (KMR-1) (Hammill and Crawford 1996). A number of studies report that dinoseb can also be

degraded anaerobically (Hammill and Crawford 1996; Stevens et al. 1991; Kaake et al. 1992).

Dinoseb has been classified as unlikely to be degraded by even extended exposure to conventional biological sewage treatment processes (Verschuren 1983). This assertion is supported by modelling results for the neutral form, which show an overall WWTS removal rate of 15.4% (SimpleTreat 2003), and by the results of treatability studies by Monnig and Zweidinger (1980). However, Monnig and Zweidinger also discovered that a treatment system involving activated carbon filtration removed dinoseb. Specifically, after passage through a carbon-filled column, no dinoseb was detected in the water collected from the column, even though water samples had an initial dinoseb concentration of 750 mg/L.

The evidence for persistence, presented above, indicates that dinoseb is a relatively persistent chemical under many conditions. It has a predicted overall persistence ( $P_{ov}$ ) in the environment of 195 days (OECD 2009). It is persistent in air, according to modelled results, with a predicted half-life of 2.56 days. It is not readily biodegradable and does not hydrolyze rapidly in water. While photolysis in water could occur relatively quickly under the appropriate conditions, it is expected to vary considerably with water depth and turbidity and was therefore not factored into the consideration of the residence time of dinoseb in water. Similarly, degradation in soil could occur relatively quickly, but will vary considerably depending on conditions such as soil type and pH.

### **5.3 Potential for bioaccumulation**

Table 5-4 summarizes the key experimental data for the bioconcentration of dinoseb in aquatic organisms. On the basis of these experimental results, dinoseb is considered to have a low potential for bioaccumulation. However, it should be noted that dinoseb will bind predominantly to plasma and protein (Luk'yanchuk et al. 1983; Rutherford et al. 1984), not lipids, and will therefore distribute throughout an organism differently than a lipophilic substance. This phenomenon, and the resulting body burden in non-fatty tissue, might not be accounted for by some tests for bioaccumulation potential.

Care must also be taken for chemicals classified as polar non-volatiles, such as dinoseb, with  $\log K_{ow} > 2$  and  $\log K_{oa} > 5$ . This group of substances has a low bioaccumulation potential in aquatic organisms, but a high bioaccumulation potential in air-breathing organisms, unless they are rapidly metabolized (Kelly 2006). Phenolic pesticides appear to be readily assimilated by animals, but excreted slowly over a period of many weeks (Kearney and Kaufman 1976).

**Table 5-4. Summary of experimental bioconcentration factors (BCFs) for dinoseb**

Test organism	Experimental concentration (duration)	BCF (L/kg)	Reference
Common carp ( <i>Cyprinus carpio</i> )	10 mg/L (6 weeks)	< 0.3–1.0	CERI 1985 <sup>a</sup>
Common carp ( <i>Cyprinus carpio</i> )	1 mg/L (6 weeks)	< 2.5	CERI 1985 <sup>a</sup>
Fathead minnow ( <i>Pimephales promelas</i> )	0.62 µg/L (24 days)	61.5	Call et al. 1983 <sup>b</sup>
Fathead minnow ( <i>Pimephales promelas</i> )	7.22 µg/L (24 days)	64.1	Call et al. 1983 <sup>b</sup>
Fathead minnow ( <i>Pimephales promelas</i> )	7.76 µg/L (28 days)	56.2	Call et al. 1983 <sup>b</sup>

<sup>a</sup> Test conditions not specified.

<sup>b</sup> Tests were whole body.

## 6. Potential to cause ecological harm

### 6.1 Ecological effects assessment

#### 6.1.1 Mode/mechanism of action

Dinoseb is known to be a reactive, non-narcotic chemical. It interferes with energy synthesis through the process of uncoupling oxidative phosphorylation (Escher et al. 2010). This mechanism of action is consistent with what is generally expected for polynitroaromatic compounds (US EPA 2010). Uncoupling occurs when the transport of electrons (derived from carbohydrate or fat metabolism) into mitochondria is delinked from the production of adenosine triphosphate (ATP), which is an energy carrying molecule in the cell. This mechanism of action can occur in plants, animals, and fungi because they have similar biochemical pathways for creating energy (Felsot 1998).

Uncoupling can also stimulate metabolism, leading to the production of reactive oxygen species and enhancement of oxidative damage. Oxidative damage is a possible factor that contributes to embryotoxicity, potentially due to rapid cellular growth and incomplete metabolic development during embryogenesis (Paskova et al. 2011). In medaka (*Oryzias latipes*) embryos, significant changes in metabolism and increased abnormal development and post-exposure mortality were observed at low concentrations of dinoseb (Viant et al. 2006b). In mammals, an increase in oxidative metabolism can lead to various adverse effects, including the depletion of carbohydrate and fat stores (Morgan 1982; WSSA 1983; NRC 1983; Toxipedia 2014).

Supporting evidence for the mechanism of action of dinoseb was obtained from the ToxCast and Tox21 high-throughput in vitro assays (US EPA [updated 2016]). This included one assay addressing mitochondrial membrane depolarization, which underlies

uncoupling (Sakamuru et al. 2012), and zebrafish assays addressing developmental effects (Padilla et al. 2012; Truong et al. 2014).

Protein and DNA binding, which are molecular mechanisms associated with high hazard in aquatic organisms, have also been noted for dinoseb (Call et al. 1983; ACD/Percepta c1997-2012; NCBI [accessed 2020]).

While some effects of dinoseb on the endocrine system have been found, including abnormal sperm and decreased thyroid weight (Linder et al. 1992; Van den Berg et al. 1991), dinoseb is not expected to be a binder of estrogen or androgen steroid receptors given its structure-activity relationships (ACD/Percepta c1997-2012, CATALOGIC 2014). Dinoseb appears in the European Union's updated ranked endocrine disruptor priority list and is currently designated a Category 3b substance, meaning a substance with no or insufficient information gathered (EC-Environment 2016).

### **6.1.2 Effects on aquatic organisms**

The acute and chronic toxicity of dinoseb to aquatic organisms is well characterized. The key experimental aquatic toxicity studies are summarized in Appendix A. Results show that dinoseb is harmful to fish, aquatic invertebrates, and algae.

On the basis of the available data set, freshwater invertebrates appear to be less sensitive to dinoseb than fish. The toxicity of dinoseb to fish is dependent on species and life stage, and as dinoseb is an ionizing substance, its toxicity is also influenced by pH, water hardness, and temperature (Johnson and Finley 1980; Woodward 1976; Lipschuetz and Cooper 1961; McCorkle et al. 1977; Skelley 1989).

In fish, acute median lethal concentration (LC<sub>50</sub>) values range from 0.032 to 0.96 mg/L. Chronic toxicity values, mostly no observed effect concentrations (NOECs) and lowest observed effect concentrations (LOECs), range from 0.0005 to 0.059 mg/L (Call et al. 1983, 1984; Call 1987; Woodward 1976; see Appendix A). The range of the observed chronic toxicity values is supported by other toxicity metrics. For example, these values, when converted to body residues (at 0.00012 to 0.01 mmol/kg), correspond to the range of critical body residues (CBR) for respiratory uncouplers (0.00015 to 0.094 mmol/kg) identified in McCarty and Mackay (1993). Similarly, ToxCast high-throughput zebrafish assays show embryonic toxicity between 0.0001 and 0.0004 mmol/L (reported as 0.137 to 0.430 µmol/L) from lethal and sublethal observations (Padilla et al. 2012; Truong et al. 2014). Assuming that extracellular and intracellular concentrations are comparable in the zebrafish assays, the observed embryonic toxicity follows the range for the chronic CBR.

The critical toxicity value selected for effects to aquatic organisms is the 60-day (post-hatch) LOEC of 0.5 µg/L ( $5 \times 10^{-4}$  mg/L) for effects on the length and weight of lake trout fry (Woodward 1976). An assessment factor (AF) of 3 was selected to account for extrapolation from a 35% reduction in weight and length of fish fry, to a

no-effect concentration. No extrapolation to account for interspecies variation was required because there are effects data available for a large number of species (i.e., greater than 10). After application of the AF, the predicted no-effect concentration (PNEC) for effects of dinoseb on aquatic organisms is 0.17 µg/L ( $1.7 \times 10^{-4}$  mg/L).

### **6.1.3 Effects on birds and mammals**

The effects of dinoseb on birds are summarized in OECD (2007). Studies pertain to toxicity by dietary exposure only. For example, the 5-day LC<sub>50</sub> for Mallard duck (*Anas platyrhynchos*) is 410 ppm (Hill et al. 1975).

Studies from the 1980s that found reproductive and developmental effects in laboratory mammals were the initial reason why regulatory actions were undertaken in many countries, including Canada, to control the use of dinoseb as an herbicide. Studies reporting such effects on laboratory animals are summarized in the human health section of this assessment. Recently, the adverse reproductive and developmental effects of dinoseb have been acknowledged by a number of international jurisdictions. For example, dinoseb has been identified as a substance of very high concern (SVHC) because of its reprotoxic properties and has been added to the Candidate List (for eventual inclusion in Annex IV to the Registration, Evaluation, Authorisation and Restriction of Chemicals [REACH] regulation) under article 57(c) of REACH (ECHA c2007-2015b).

The Canadian Water Quality Guidelines for the Protection of Agricultural Water Uses (CCME 1999) summarizes other effects of dinoseb on laboratory and domestic mammals. PNECs for effects on birds and mammals were not derived because exposure in air and soil in Canada are not likely to be significant given the current use of dinoseb. Additionally, it is expected that food web transfers to birds will be low given its low bioaccumulation potential.

### **6.1.4 Effects on plants**

Most studies of the effects of dinoseb on higher plants are efficacy field trials conducted when dinoseb was used as an herbicide. The results of these studies, which pertain mainly to effects on seed emergence and growth, are summarized in OECD (2007). No additional information for effects on plants was found.

### **6.1.5 Effects on soil-dwelling organisms**

In a 2006 study (Staempfli et al.), the authors found that, after 6 days of exposure at 15 to 30 mg of dinoseb/g dry soil, the weight, lipid, and protein content of the exposed springtails (*Folsomia candida*) were higher than the controls. This suggests that growth increased in order to improve reproduction, which was confirmed by the greater number of eggs laid in exposed organisms. However, after 21 days, all measured parameters decreased and lethality increased.

As a protein and DNA binder, dinoseb could also be potentially quite toxic to skin-breathing organisms such as earthworms or frogs, potentially acting as a skin sensitizer (Princz et al. 2014). However, there are currently no studies available on exposure of dinoseb to these types of organisms.

## 6.2 Ecological exposure assessment

Current monitoring data for environmental concentrations of dinoseb in Canada are limited. There are historical environmental monitoring data for dinoseb in Canada from the time it was used as an herbicide (Environment Canada 2011; Frank et al. 1979; Wan 1989; O'Neill et al. 1989; Milburn et al. 1991), as well as from 2003–2005, shortly after it was banned for that use (Environment Canada 2011). The results for dinoseb from the monitoring of surface water in Quebec from 2003 to 2005 were all non-detects, at a method detection limit (MDL) of 0.04 µg/L (Environment Canada 2011). More recently, analysis of water samples collected from three locations in the St. Clair River in 2018 showed no detection of dinoseb at a detection limit of  $4.0 \times 10^{-4}$  µg/L (personal communication, presentation from the Water Quality Monitoring and Surveillance Division, Environment and Climate Change Canada (ECCC), October 24, 2018; unreferenced).

Industry data on dinoseb concentrations measured daily for a number of years in untreated wastewater from a facility that uses dinoseb were provided to Environment and Climate Change Canada. All results show that dinoseb is not present at or above the MDL of 50 µg/L. This MDL, for the method used by the facility, is high; analytical methods with much lower detection limits are available. If it is assumed that dinoseb is present at half the MDL, then the concentration of dinoseb in untreated wastewater would be 25 µg/L. Process information provided by the user indicates that dilution will occur in the wastewater treatment system; therefore, a dilution factor of 10 was applied. Assuming a 15.4% removal in the treatment systems (as estimated with SimpleTreat 2003), the resulting concentration of dinoseb in the treated wastewater discharged to the environment is estimated to be 2.1 µg/L. A further dilution factor of 10 was applied to account for dilution once the treated wastewater is released to surface water. Therefore, a concentration of dinoseb in surface water of 0.21 µg/L is estimated as an upper bound of potential environmental concentrations resulting from use in a large facility.

More recently, industry data on dinoseb concentrations measured using a more sensitive analytical method in several samples of untreated wastewater from a facility that uses large volumes of dinoseb were provided to Environment and Climate Change Canada. Out of ten samples, dinoseb was not present at levels above the method detection limit of 0.05 µg/L in nine of them. There was one sample where a concentration of 0.117 µg/L was measured (personal communication, confidential data provided by email to Environment and Climate Change Canada, dated October 24, 2018; unreferenced). Given that these more recent data were collected over a short time period and comprise a small number of samples, it is not known how

representative they might be. Therefore, the older and more extensive dataset is still considered relevant, despite the higher detection limit.

For other low-volume uses that may be occurring (as indicated by CBSA data; CBSA 2016), a generic analysis was conducted to determine the predicted environmental concentrations (PECs) in surface water resulting from releases from small industrial facilities. Multiple PECs were calculated by varying the inputs for certain parameters to capture a range of potential situations. Calculations were based on a total quantity of 85 kg of dinoseb used per year (the mass of dinoseb that would be present in 100 kg of dinoseb acetate), representing a small-sized operation. The number of days of release was varied between 50, 100 and 350 days per year. An emission factor of 0.3% was used, which is a default industrial release emission factor for generic operations (EC 2003). Releases from industrial facilities were assumed to occur via wastewater treatment systems (WWTS). A wastewater treatment removal estimation model (SimpleTreat 2003) was used to estimate the removal of dinoseb at a WWTS via sorption, volatilization and degradation. Using the water solubility, Henry's law constant, organic-carbon partitioning coefficient and biodegradation rate constant for dinoseb as inputs to SimpleTreat, a 15.4% removal rate was estimated; this percent removal was used in all of the PEC calculations. The daily dilution volume of the receiving water (calculated as the WWTS effluent flow multiplied by the dilution factor of the receiving water body) was based on either the 10<sup>th</sup> or 50<sup>th</sup> percentile of the distribution of daily dilution volume for selected WWTS receiving industrial effluents, in Canada. Based on these inputs, 6 different generic PECs were calculated, representing a range of potential conditions. The PECs ranged from 0.01 to 0.82 µg/L, with a median of 0.09 µg/L.

There are no monitoring data for dinoseb concentrations in air in Canada. Significant releases to air would not be expected from the current use given that dinoseb is used in what is considered to be a closed process (OECD 2007).<sup>5</sup> However, minor releases could be possible. For example, small releases of dinoseb to air at chemical manufacturing facilities have been reported under the US EPA's Toxics Release Inventory (TRI) program (US EPA 2016) as recently as 2015.

There are also no current monitoring data for dinoseb concentrations in soil and sediment in Canada.

### **6.3 Characterization of ecological risk**

The approach taken in this ecological screening assessment was to examine assessment information and develop conclusions based on a weight-of-evidence approach and precaution. Evidence was gathered to determine the potential for dinoseb to cause harm to the Canadian environment. Lines of evidence considered include

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<sup>5</sup> "Closed" is not defined by the OECD.

those evaluated in this assessment that support the characterization of ecological risk in the Canadian environment. Secondary or indirect lines of evidence are considered when available, including regulatory decisions and classification of hazard or fate characteristics made by other regulatory agencies.

### **6.3.1 Risk quotient analysis**

Risk quotient analyses were performed by comparing the various realistic worst-case estimates of exposure (PECs; see the Ecological Exposure Assessment section) with ecotoxicity information (PNECs; see the Ecological Effects Assessment section) to determine whether there is potential for ecological harm in Canada. Risk quotients (RQs) were calculated by dividing the PEC by the PNEC for relevant environmental compartments and associated exposure scenarios.

Given its current main use in the chemical sector, any releases of dinoseb are expected to occur to surface water. Once released to surface water, dinoseb is expected to primarily remain in that medium because of its water solubility and low partitioning to sediments. Therefore, the RQ analysis for dinoseb focussed on the aquatic ecosystem. Potential releases of dinoseb acetate to surface water were also considered, as this substance will dissociate in the environment to produce dinoseb.

For the exposure scenario that considered releases via wastewater from large facilities using dinoseb, a PEC of 0.21 µg/L was estimated. Comparing this PEC with the PNEC for effects on aquatic organisms of 0.17 µg/L, the resulting RQ is 1.2. This indicates that facilities using high volumes of dinoseb could potentially pose a risk to the environment, depending on the handling practices used at the facility.

On the basis of potential releases of wastewater containing dinoseb to surface water, from the use of dinoseb acetate in small industrial facilities, PECs for dinoseb in surface water were calculated to range from 0.01 to 0.82 µg/L. Dividing these PECs by the PNEC of 0.17 µg/L, the resulting RQs for harm to aquatic organisms (PEC/PNEC) range from 0.06 to 4.8, with a median of 0.54. Of the 6 PECs estimated, 2 resulted in risk quotients greater than one. These results indicate the potential for exposure concentrations resulting from industrial activities to exceed chronic no-effect thresholds in the receiving environment, even when dinoseb is used in very low quantities.

### **6.3.2 Consideration of the lines of evidence**

To characterize the ecological risk of dinoseb, technical information for various lines of evidence was considered (as discussed in the relevant sections of this report) and qualitatively weighted. The key lines of evidence supporting the assessment conclusion are presented in Table 6-1, with an overall discussion of the weight of evidence provided in section 6.3.3. The level of confidence refers to the combined influence of

data quality and variability, data gaps, causality, plausibility, and any extrapolation required within the line of evidence. The relevance refers to the impact the line of evidence has when determining the potential to cause harm to the Canadian environment. Qualifiers used in the analysis ranged from low to high, with the assigned weight having five possible outcomes.

Direct lines of evidence presented in Table 6-1 relate to environmental fate and distribution, ecotoxicity, environmental release and concentrations, and the result from the risk quotient analysis. Indirect lines of evidence, such as regulatory decisions in other jurisdictions (e.g., SVHC candidate listing under REACH, multi-national pesticide restrictions, Rotterdam Convention listing) were also considered, but they were not given a qualitative weight because of the regulatory context of these decisions in other jurisdictions.

**Table 6-1. Weighted lines of key evidence considered to determine the potential for dinoseb to cause harm to the Canadian environment**

Line of evidence	Level of confidence <sup>a</sup>	Relevance in assessment <sup>b</sup>	Weight assigned <sup>c</sup>
Persistence in the environment	moderate	high	moderate to high
Long-range transport	moderate	moderate	moderate
Bioaccumulation in aquatic organisms	moderate	moderate	moderate
Mode of action and other non-apical data	high	high	high
PNEC for aquatic organisms	high	high	high
PEC in water (releases from large facilities using dinoseb)	low	high	moderate
PECs in water (releases from small facilities using dinoseb acetate)	low	high	moderate
Risk quotient for water	low	high	moderate

<sup>a</sup> Level of confidence is determined according to data quality, data variability, data gaps and if the data are fit for purpose.

<sup>b</sup> Relevance refers to the impact of the evidence in the assessment.

<sup>c</sup> Weight is assigned to each line of evidence according to the combined level of confidence and relevance in the assessment.

### 6.3.3 Weight of evidence for determining potential to cause harm to the Canadian environment

Evidence presented in this assessment indicates that dinoseb is water soluble and relatively persistent in the environment. Structural and empirical evidence, as well as modelled results based on consistent high-quality measured physicochemical

properties, mutually support the assertion that dinoseb has an overall persistence (Pov) in the environment in the order of months. When released to water (i.e., its primary potential mode of entry to the environment), dinoseb is likely to reside in the water column and undergo long-range transport in water where it will become distributed throughout a river system. Therefore, dilution by surface water bodies becomes the governing factor controlling environmental concentrations relevant to organism exposure. There is some uncertainty with half-life estimates as well as model estimates, which are mostly limited to the neutral form of dinoseb. A primary degradation pathway involves photolysis in surface water, which is expected to vary considerably with water depth and turbidity and thus was not factored into the consideration of residence time. Dinoseb is not expected to partition significantly to air from surface water; release to air at industrial facilities is uncertain. Furthermore, the evidence for CTD in air is modelled on the neutral form, and its accuracy is uncertain. Consequently, fate and transport of dinoseb in air is of low relevance in this assessment. Given its multimedia fate, dinoseb is not expected to be highly removed in waste treatment systems. Therefore, a low rate of removal from waste effluents (estimated at 15.4% by SimpleTreat for secondary treatment) is expected, while transfer of dinoseb to the terrestrial environment from biosolids application is not expected to be significant.

There is relatively consistent evidence indicating that dinoseb has low bioaccumulation potential in aquatic species. Dinoseb is not expected to biomagnify significantly in aquatic organisms. There is uncertainty about bioaccumulation in terrestrial organisms because dinoseb is internally distributed in blood plasma and structural proteins and is not rapidly metabolized and excreted.

Several lines of evidence of high weight mutually support the assertion that dinoseb is a highly reactive toxicant, with acute and chronic effects observed in all organisms tested. There are many reliable and mutually supportive empirical studies showing acute and chronic effects in aquatic organisms in the  $\mu\text{g/L}$  range, which is consistent with the mode of action. Mutually supportive evidence from *in silico*, *in vitro* and *in vivo* studies, shows that dinoseb interacts with biological tissues (e.g., proteins and DNA) at very low internal or external exposure concentrations resulting in embryo toxicity and chronic reproductive effects ultimately affecting organisms at the population level. The evidence indicates that exposure to dinoseb can result in more than one adverse outcome (death, growth reduction, embryo toxicity, reproductive effects). Dinoseb was identified as a substance of very high concern (SVHC) in the European Union and appears on the Candidate List (ECHA c2007-2015b) as a CMR (carcinogenic, mutagenic or toxic for reproduction) substance, specifically for reproductive effects. Little ecotoxicity data exist for dinoseb in soil organisms, and no sediment toxicity data were found for this assessment. Given the reactivity of dinoseb, it is likely that it would also be hazardous to soil and sediment organisms. However, given the lack of exposure in these media, soil and sediment scenarios were not considered in this assessment.

The PNEC calculated for dinoseb reflects a high level of confidence from several mutually supportive and highly weighted lines of evidence. There is some uncertainty in

the PEC that was derived for large facilities using dinoseb, due to the high detection limit that was used for effluent monitoring data. More recent effluent monitoring data using a lower detection limit did not find dinoseb at concentrations above the PNEC for a small number of samples. Therefore, a low weight was given to this PEC.

There is also some uncertainty in the PECs that were determined for small facilities using dinoseb acetate given that they were derived using generic industrial release assumptions. The lower weight given to the aquatic PECs reflects these uncertainties. Nonetheless, a low annual usage rate was assumed in all calculations, and still indicated risk in two cases. The RQ values would be sensitive to any errors associated with the PECs. The moderate weight assigned to the RQs reflects these potential weaknesses.

On the basis of the above lines of evidence, dinoseb is considered to have potential to cause ecological harm in Canada. It has also been determined that dinoseb meets the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

#### **6.3.4 Sensitivity of conclusion to key uncertainties**

Multiple lines of evidence mutually support the understanding of the fate and effects of dinoseb in the aquatic environment, which is the primary media of concern in this assessment. Thus, the conclusion is not sensitive to refinement of fate or ecotoxicity determination in water or other media and would not change with additional information on these aspects.

There is some uncertainty in the estimates of exposure concentrations. However, even assuming very low use quantities, two estimated PECs indicated a potential for risk. Given the very high hazard of this substance, any releases of dinoseb to the environment could pose a concern. The limited sampling of surface waters and industrial effluents indicate that dinoseb concentrations are very low at these locations. More extensive wastewater effluent monitoring or monitoring for dinoseb in receiving waters could help reduce exposure uncertainty. However, monitoring for dinoseb at distances from source emissions (e.g., >1 km) may not result in its detection where the receiving water body has a high dilution capacity.

## **7. Potential to cause harm to human health**

### **7.1 Exposure assessment**

Dinoseb was used in the past as an herbicide, but that use has been discontinued in Canada since 2001 (PMRA 2000). There have been no identified consumer uses for dinoseb, and the main industrial use of this substance in a closed industrial system is

not expected to result in exposure of the general population. Dinoseb (including any dinoseb formed as a result of the dissociation of dinoseb acetate) is routinely tested for in drinking water and has not been found above the limit of detection (0.1 to 1.0 µg/L) in recent surveys (Exova 2010; AGAT Laboratories 2013; WSH Labs 2015; City of Markham 2015; City of Barrie 2016; City of Guelph 2016; Regional Municipality of Wood Buffalo 2015). Dinoseb was included in the Guidelines for Canadian Drinking Water established by the Federal-Provincial-Territorial Committee on Drinking Water in 1996, but this guideline has since been withdrawn because dinoseb is no longer registered for use as a pesticide in Canada and it is no longer found in Canadian drinking water supplies “at levels that could pose a risk to human health” (Health Canada 2019). Dinoseb is not expected in air, drinking water or food and is not used in products; therefore, exposure of the general population is not expected.

## **7.2 Health effects assessment**

Dinoseb was previously assessed by the US EPA Integrated Risk Information System (IRIS 1997-) and the OECD (2007). The OECD SIAR was used to inform the health effects characterization in this screening assessment. Dinoseb is classified by the European Commission as a category 1B reproductive toxicant (may damage the unborn child; suspected of damaging fertility) (EU 2008). A literature search was conducted from the year prior to the OECD SIDS initial assessment meeting (SIAM) (i.e., April 2006) to September 2016. No health effects studies that could impact the risk characterization (i.e., result in different critical endpoints or lower points of departure than those stated in OECD 2007) were identified. This section provides critical endpoints and corresponding effect levels for dinoseb, as cited directly from OECD 2007.

In a combined repeated dose toxicity study and reproduction/developmental toxicity screening test (OECD TG 422), rats were administered dinoseb by gavage at doses of 0, 0.78, 2.33 or 7 mg/kg bw/day (MHLW, Japan, 2005, as cited in OECD 2007). Males were dosed for a total of 42 days from 14 days before mating, and females were dosed from 14 days before mating throughout the mating and pregnancy period to day 6 of lactation. Males in the 7.0 mg/kg bw/day dose group had significantly decreased motile sperm rate, progressive sperm rate, path velocity and viability rate. In addition, the amplitude of lateral head displacement, abnormal sperm rate and abnormal tail rate were significantly increased in the males of this dose group. Females in the 7.0 mg/kg bw/day dose group had a significantly lower gestation index compared with controls. On the basis of the above findings, the NOEL for reproductive and developmental toxicity was determined to be 2.33 mg/kg bw/day. At doses of 0.78 mg/kg bw/day and higher, a significant increase in hematocrit count was observed in males. At doses of 2.33 mg/kg bw/day and higher, a significant decrease in extramedullary hematopoiesis in the spleen was observed in females. Mortalities occurred in females administered the 7.0 mg/kg bw/day dose. On the basis of these observations, the LOAEL for males and the NOAEL for females were considered to be 0.78 mg/kg bw/day (MHLW, Japan, 2005, as cited in OECD 2007).

In another reproductive toxicity study, dinoseb was administered in the diet of male rats, equivalent to 0, 3.8, 9.1, 15.6 or 22.2 mg/kg bw/day, for up to 77 days (Linder et al. 1982, as cited in OECD 2007). At doses of 9.1 mg/kg bw/day and higher, animals displayed a significant decrease in sperm counts and a significant increase in atypical spermatozoa. The NOAEL was determined to be 3.8 mg/kg bw/day.

In a developmental toxicity study, dinoseb was applied dermally to pregnant rabbits for 6 hours per day on gestation days 7 through 19 at doses of 0, 1, 3, 9 or 18 mg/kg bw/day (Johnson et al. 1988, as cited in OECD 2007). There was an increased incidence of hydrocephaly and anophthalmia in fetuses from dams exposed to 3 mg/kg bw/day and higher. In dams exposed to 9 mg/kg bw/day, there were a decreased number of live fetuses in addition to an increased incidence of fetuses with cleft palate, microcephaly and microphthalmia. Maternal mortality and hyperthermia were observed at doses of 3 mg/kg bw/day and higher. On the basis of the above findings, the NOEL for maternal toxicity and reproductive and developmental toxicity is considered to be 1 mg/kg bw/day.

In another developmental toxicity study, dinoseb was administered to pregnant rats either by gavage at doses of 0, 2.5, 5, 10 or 15 mg/kg bw/day, or in the diet at approximately 15 mg/kg bw/day, between gestation days 6 and 15 (Giavini et al. 1986, as cited in OECD 2007). At gavage doses of 10 mg/kg bw/day and higher, there was an increased incidence of fetuses with skeletal variations, and at gavage doses of 15 mg/kg bw/day, offspring displayed delayed ossification, significantly decreased body weight and an increased incidence of fetuses with skeletal variations. In addition, offspring from dams administered 15 mg/kg bw/day through diet (the only tested dose) displayed microphthalmia and significantly decreased body weight. Maternal body weight gain was reduced at gavage doses of 10 mg/kg bw/day and higher. The NOAEL for maternal and developmental toxicity was considered to be 5 mg/kg bw/day.

In vitro studies showed that dinoseb was not mutagenic in bacteria. In addition, dinoseb did not induce chromosomal aberrations in cultured mammalian cells (MHLW Japan 2005, as cited in OECD 2007). The limited carcinogenicity studies in rats and mice available gave no indication of carcinogenic effect (US EPA 1987, unpublished, as cited by OECD 2007).

### **7.3 Characterization of risk to human health**

Exposure of the general population in Canada to dinoseb through environmental media, food, or the use of products is not expected. Any population exposures resulting from potential releases of dinoseb or dinoseb acetate to surface waters from industrial uses would still be several orders of magnitude less than levels associated with health effects. Given these considerations, the potential risk to human health is considered to be low.

While exposure of the general population to dinoseb is not of concern at current levels, this substance is considered to have a health effect of concern because of its potential reproductive and developmental toxicity. Therefore, there may be a concern for human health if exposure were to increase.

#### **7.4 Uncertainties in evaluation of risk to human health**

Overall, given that the uses and properties of dinoseb have been well characterized, a qualitative approach to risk characterization is considered appropriate for this assessment.

### **8. Conclusion**

Considering all available lines of evidence presented in this screening assessment, there is risk of harm to the environment from dinoseb. It is concluded that dinoseb meets the criteria under paragraph 64(a) of CEPA as it is entering or may 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. However, it is concluded that dinoseb does not meet the criteria under paragraph 64(b) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends. It is also concluded that dinoseb does not meet the criteria under paragraph 64(c) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Therefore, it is concluded that dinoseb meets one or more of the criteria set out in section 64 of CEPA.

It has also been determined that dinoseb meets the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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## Appendices

### Appendix A. Aquatic toxicity data

**Table A-1. Key experimental aquatic toxicity studies for dinoseb**

Test organism	Endpoint	Value (mg/L) <sup>a</sup>	Reference
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.088	Skelly 1989
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.13	Gersich and Mayes 1986
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.17	Gersich and Mayes 1986
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.41	Geiger et al. 1984
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.54	Call 1987
Fathead minnow ( <i>Pimephales promelas</i> )	96 h LC <sub>50</sub>	0.7	Call et al. 1983
Mosquitofish ( <i>Gambusia affinis</i> ) (insecticide-resistant)	96 h LC <sub>50</sub>	0.96	Fabacher and Chambers 1974
Cutthroat trout ( <i>Salmo clarki</i> )	96 h LC <sub>50</sub>	0.071	Mayer and Ellersieck 1986
Cutthroat trout ( <i>Salmo clarki</i> )	96 h LC <sub>50</sub>	0.041	Woodward 1976
Lake trout ( <i>Salvelinus namaycush</i> )	96 h LC <sub>50</sub>	0.032	Woodward 1976
Cutthroat trout ( <i>Salmo clarki</i> )	96 h LC <sub>50</sub>	0.067	Johnson and Finley 1980
Lake trout ( <i>Salvelinus namaycush</i> )	96 h LC <sub>50</sub>	0.044	Johnson and Finley 1980
Coho salmon ( <i>Oncorhynchus kisutch</i> )	144 h LC <sub>50</sub>	0.088	Lorz et al. 1979
Chinook salmon ( <i>Oncorhynchus tshawytscha</i> )	96 h LC <sub>50</sub>	0.071	Viant et al. 2006a
Channel catfish ( <i>Ictalurus punctatus</i> )	96 h LC <sub>50</sub>	0.058	Skelley 1989
Channel catfish ( <i>Ictalurus punctatus</i> )	96 h LC <sub>50</sub>	0.118	McCorkle et al. 1977
Medaka ( <i>Oryzias latipes</i> )	96 h LC <sub>50</sub>	0.28	MOE (Japan) 2015
Guppy ( <i>Poecilia reticulata</i> )	96 h LC <sub>50</sub>	0.35	Saarikoski and Viluksela 1981

Test organism	Endpoint	Value (mg/L) <sup>a</sup>	Reference
Fathead minnow ( <i>Pimephales promelas</i> )	60 d NOEC (mortality, fry weight)	0.0145 – 0.0485	Call et al. 1983; Call et al. 1984
Fathead minnow ( <i>Pimephales promelas</i> )	32 d NOEC (growth)	0.059	Call 1987
Lake trout ( <i>Salvelinus namaycush</i> )	60 d LOEC (fry weight and length)	0.0005	Woodward 1976
Daphnid ( <i>Daphnia magna</i> Strauss)	96 h LC <sub>50</sub>	0.24	Gersich and Mayes 1986
Daphnid ( <i>Daphnia magna</i> )	48 h EC <sub>50</sub> (reproduction)	0.18	Chèvre et al. 2005
Daphnid ( <i>Daphnia magna</i> )	48 h EC <sub>50</sub>	0.40	MOE (Japan) 2015
Daphnid ( <i>Daphnia magna</i> )	48 h EC <sub>50</sub> (immobilization)	0.24	MITI 1992
Scud ( <i>Gammarus fasciatus</i> )	96 h EC <sub>50</sub>	1.8	Sanders 1970
Shrimp ( <i>Crangon septemspinosa</i> )	96 h LC <sub>50</sub>	5.1	McLeese et al. 1979
Soft-shelled clam ( <i>Mya arenaria</i> )	84 h LC <sub>50</sub>	2.6	McLeese et al. 1979
American lobster larvae ( <i>Homarus americanus</i> )	96 h LC <sub>50</sub>	0.0075	Zitko et al. 1976
Daphnid ( <i>Daphnia magna</i> )	21 d EC <sub>50</sub>	0.17	MOE (Japan) 2015
Green algae ( <i>Chlamydomonas reinhardtii</i> )	EC <sub>5</sub> (toxicity threshold)	0.34	Brack and Frank 1998
Green algae ( <i>Chlorella pyrenoidosa</i> )	EC <sub>50</sub> (growth rate inhibition)	1.03	Hawxby et al. 1977
Blue-green algae ( <i>Lyngbya</i> sp.)	EC <sub>50</sub> (growth rate inhibition)	1.42	Hawxby et al. 1977
Green algae ( <i>Chlorella pyrenoidosa</i> )	EC <sub>50</sub> (inhibition of photosynthesis)	0.43	Hawxby et al. 1977
Blue-green algae ( <i>Lyngbya</i> sp.)	EC <sub>50</sub> (inhibition of photosynthesis)	0.74	Hawxby et al. 1977

Test organism	Endpoint	Value (mg/L) <sup>a</sup>	Reference
Green algae ( <i>Pseudokirchneriella subcapitata</i> )	72 h EbC <sub>50</sub>	0.81	MOE (Japan) 2015
Green algae ( <i>Pseudokirchneriella subcapitata</i> )	72 h ErC <sub>50</sub>	1.4	MOE (Japan) 2015
Green algae ( <i>Pseudokirchneriella subcapitata</i> )	72 h ErC <sub>50</sub>	0.49	Chèvre <i>et al.</i> 2005
Green algae ( <i>Chlorella pyrenoidosa</i> )	18-36 h IC <sub>50</sub> (inhibition of chlorophyll production)	0.15	Kratky and Warren 1971
Green algae ( <i>Chlorella pyrenoidosa</i> )	60–120 minute IC <sub>50</sub> (inhibition of O <sub>2</sub> evolution)	8.0	Kratky and Warren 1971
Natural plankton (Jack's Lake, Ontario)	2 d IC <sub>50</sub> (depression of proportional carbon, assimilation rates)	1	Brown and Lean 1995
Natural plankton (Jack's Lake, Ontario)	2 d IC <sub>50</sub> (depression of proportional phosphate, assimilation rates)	12	Brown and Lean 1995
Natural plankton (Jack's Lake, Ontario)	2 d EC <sub>50</sub> (50% depression of proportional ammonium assimilation rates)	5	Brown and Lean 1995

Abbreviations: LC<sub>50</sub>, the lethal concentration required to kill 50% of the population; d, day; EC, effect concentration; EC<sub>50</sub>, the concentration which induces a response halfway between the baseline and maximum; EbC<sub>50</sub>, the concentration at which 50% reduction of algal biomass is observed; ErC<sub>50</sub>, the concentration at which a 50% inhibition of algal growth rate is observed; h, hour; IC, inhibition concentration; LOEC, lowest observed effect concentration; NOEC; no effect concentration.

<sup>a</sup> In some studies, endpoint values are expressed in ppm, ppb, or µM/L. For consistency in the table, all such values were converted to mg/L.