Screening Assessment for the Challenge

2-Butanone, oxime
(Butanone oxime)

Chemical Abstracts Service Registry Number
96-29-7

Environment Canada
Health Canada

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of 2-butanone, oxime (butanone oxime), Chemical Abstracts Service Registry Number 96-29-7. This substance was identified in the categorization of the Domestic Substances List as a high priority for action under the Ministerial Challenge. Butanone oxime was identified as a high priority as it was considered to pose greatest potential for exposure of individuals in Canada and had been classified by the European Commission on the basis of carcinogenicity. Although butanone oxime met the ecological categorization criteria for persistence, it did not meet the criteria for bioaccumulation potential or inherent toxicity to aquatic organisms. Therefore, the focus of this assessment of 2-butanone, oxime relates primarily to human health risks.

Butanone oxime is widely used as an anti-skinning agent in the formulation of alkyd paints, varnishes, stains and coatings for both industrial and consumer use. In Canada, the substance has also been reported in a number of pesticide products, namely wood preservatives and antifouling marine paints, as well as in some adhesives, silicone sealants and printing inks. Furthermore, butanone oxime is used as a corrosion inhibitor in industrial boilers and water treatment systems and serves as a blocking agent in the manufacturing process of urethane polymers.

According to the information submitted under section 71 of CEPA 1999, butanone oxime was not manufactured by any company in Canada in the 2006 calendar year. However, approximately 500 000 kg of the substance was imported in 2006, and nearly 120 000 kg was used in the same reporting year. There are few data on the release and fate of butanone oxime in environmental media in Canada or elsewhere. Butanone oxime is not a naturally occurring substance; thus, releases of the substance to the environment are expected to result directly from anthropogenic activities. Considering the quantity of butanone oxime in commerce in Canada and its use in a variety of consumer products, exposure of the general population to the substance is expected to be moderate.

As butanone oxime was classified on the basis of carcinogenicity by the European Commission, carcinogenicity was a key focus for this screening assessment. Increased incidences of liver tumours were observed in rat and mouse lifetime studies, and there was also an increased incidence of mammary gland tumours in female rats; however, this was seen only at moderate and/or high concentrations of butanone oxime. Consideration of the available information regarding genotoxicity indicates that butanone oxime is not likely to be genotoxic. Accordingly, although the mode of induction of tumours is not fully elucidated, the tumours observed are not considered to have resulted from direct interaction with genetic material. Therefore, a threshold approach is used to assess risk to human health.

Non-neoplastic effects were observed in the nasal cavity of rats and/or mice in inhalation studies of short-term through to chronic exposure duration. Also, repeated-dose studies based on oral exposure showed effects in the spleen, liver and kidney of rats as well as

hematological effects in both rats and rabbits. Based on comparison of estimated exposures to butanone oxime in Canada with the critical effect levels, and taking into account the uncertainties in the databases on exposure and effects, it is considered that the resulting margins of exposure, particularly for consumer exposure from products containing the substance, may not be adequately protective of human health for non-cancer effects.

On the basis of the potential inadequacy of the margins between estimated exposures to butanone oxime and critical effect levels, it is concluded that butanone oxime is a substance that may be 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.

On the basis of ecological hazard and estimated releases of butanone oxime, it is concluded that the substance is not entering 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 or that constitute or may constitute a danger to the environment on which life depends. Butanone oxime does meet the criteria for persistence but does not meet the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations*.

Based on the information available, it is concluded that butanone oxime meets one or more of the criteria set out in section 64 of CEPA 1999.

This substance will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), which challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

The substance 2-butanone, oxime (butanone oxime) was identified as a high priority for assessment of human health risk because it was considered to present GPE and had been classified by another agency on the basis of carcinogenicity.

The Challenge for butanone oxime was published in the *Canada Gazette* on August 30, 2008 (Canada 2008). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information were received.

Although butanone oxime was determined to be a high priority for assessment with respect to human health and met the ecological categorization criteria for persistence, it did not meet the criteria for bioaccumulation or inherent toxicity to aquatic organisms. Therefore, this assessment focuses principally on information relevant to the evaluation of risks to human health.

Screening assessments examine scientific information and develop conclusions by incorporating a weight of evidence approach and precaution.

This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents and stakeholder research reports and from recent literature searches, up to November 2008 for the human health sections and May 2009 for the ecological sections. Key studies were critically evaluated; modelling results may have been used to reach conclusions. Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritizing the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

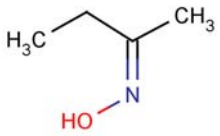
This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. Both the human health and ecological portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment (TERA), including Ms. Joan Strawson (TERA), Dr. Michael Jayjock (The LifeLine Group) and Dr. Glenn Talaska (University of Cincinnati). Additionally, the draft of this screening assessment was subject to a 60-day comment period. While external comments were taken into consideration, the final content and outcome of the screening risk assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the assessment is based are summarized below.

Substance Identity

2-Butanone, oxime is also commonly known as methyl ethyl ketoxime (MEKO). However, for the purposes of this document, this substance will be referred to as butanone oxime, based on the European Inventory of Existing Commercial Chemical Substances (EINECS) name. Information on the identity of butanone oxime is summarized in Table 1.

Table 1. Substance identity for butanone oxime

CAS RN	96-29-7
DSL name	2-Butanone, oxime
NCI names	Butanone oxime (EINECS, PICCS) 2-Butanone, oxime (AICS, ASIA-PAC, PICCS, SWISS, TSCA) Butan-2-one oxime (ENCS, PICCS) 2-Butanonoxime (PICCS) Methyl ethyl ketone oxime (PICCS) Methyl ethyl ketoxime (PICCS) Oxime 2-butanone (ECL)
Other names	Aron M 1, 2-Butoxime, Ethyl methyl ketone oxime, Ethyl methyl ketoxime, Exkin 2, Exkin II, Hiaron M 1, MEK-oxime, MEKO, Mekor 70, NSC 442, NSC 65465, Troykyd AntiSkin B
Chemical group (DSL stream)	Discrete organics
Major chemical class or use	Oximes
Major chemical subclass	Ketoximes (short-chain)
Chemical formula	C_4H_9NO
Chemical structure	
SMILES	N(O)=C(CC)C
Molecular mass	87.12 g/mol

Abbreviations: AICS, Australian Inventory of Chemical Substances; ASIA-PAC, Asia-Pacific Substances Lists; CAS RN, Chemical Abstracts Service Registry Number; DSL, Domestic Substances List; ECL, Korean Existing Chemicals List; EINECS, European Inventory of Existing Commercial Chemical Substances; ENCS, Japanese Existing and New Chemical Substances; NCI, National Chemical Inventories; NZIoC, New Zealand Inventory of Chemicals; PICCS, Philippine Inventory of Chemicals and Chemical Substances; SMILES, simplified molecular input line entry specification; SWISS, Swiss Giftliste 1 and Inventory of Notified New Substances; TSCA, *Toxic Substances Control Act* Chemical Substance Inventory.
Source: NCI 2006

Physical and Chemical Properties

Table 2 contains experimental and modelled physical and chemical properties of butanone oxime that are relevant to its environmental fate. When experimental data were not available, the property was estimated using models, as indicated in Table 2. Although butanone oxime is a weak acid and will dissociate, it does so only at very high pH (>12). Therefore, it is in the neutral form at environmentally relevant pH values (6–9), and the neutral form of butanone oxime was used for model estimation.

Table 2. Physical and chemical properties for butanone oxime

Property	Type	Value[1]	Temperature (°C)	Reference
Melting point (ºC)	Experimental	−29.5[2]		Lide 2005
Boiling point (ºC)	Experimental	152.5[2,3]		Lide 2005
Density (kg/m^3)	Experimental	923.2	20	Lide 2005
	Experimental	915		ECB 2000
	Experimental	~920	20	
Vapour pressure (Pa)	Experimental	~350[2] (~3.5 hPa)	20	ECB 2000
	Experimental	440 (4.4 hPa)	20	
	Experimental	141 (1.06 mmHg)	20	Kurita 1967
Henry's Law constant (Pa·m^3/mol)	Calculated	0.30[2]	20	
Log K_{ow} (dimensionless)	Experimental	0.63		MITI 1992
	Experimental	0.65[2]	25	ECB 2000
	Experimental	0.59	20	
Log K_{oc} (dimensionless)	Modelled	0.56		KOCWIN 2008
	Modelled	0.26[2]		EQC 2003
Log K_{oa} (dimensionless)	Modelled	4.3	25	KOAWIN 2008
Water solubility (mg/L)	Experimental	100 000		Verschueren 1977
pK_a (dimensionless)	Experimental	12.45	25	King and Marion 1944

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

[1] Values in parentheses represent the original values reported by the authors.

[2] Values used in modelling.

[3] Decomposition occurs at temperatures above 100°C (ECB 2000).

Although two geometrical isomers are possible for butanone oxime, the *trans* isomer predominates (>99%) (OECD 2003).

Sources

Butanone oxime is an anthropogenic substance and is considered to be a high production volume chemical by the Organisation for Economic Co-operation and Development (OECD 2004), the US Environmental Protection Agency (US EPA 2006) and the European Commission (ESIS 2006). Worldwide production of butanone oxime is estimated at between 10 000 and 20 000 tonnes per year (OECD 2003). According to the information submitted under section 71 of CEPA 1999, butanone oxime was not manufactured by any company in Canada in the 2006 calendar year. However, imports of the substance into Canada above the reporting threshold of 100 kg were approximately 500 000 kg in the same year (Environment Canada 2009a).

Uses

The most prevalent use of butanone oxime is as an anti-skinning agent in the formulation of alkyd paints, primers, varnishes and stains, to prevent oxidative drying and the formation of hard, gelatinous films on the surface of the paint product in the container. According to the information submitted under section 71 of CEPA 1999, nearly 120 000 kg of butanone oxime was used in Canada in 2006 (Environment Canada 2009a). The majority of these uses were in the manufacture of alkyd paint products for both industrial and consumer applications. Based on available information, the concentration of butanone oxime in alkyd paint products in Canada is ≤1% by weight (w/w), while a typical concentration ranges from 0.02 to 0.5% w/w (2009 personal communication from Canadian Paints and Coatings Assocation Working Group to Environment Canada; unreferenced). According to the section 71 responses, butanone oxime is also present in colorants or pigments used in alkyd paints or printing inks at concentrations of 0.1% and 0.2% w/w, respectively (Environment Canada 2009a).

The substance is also present as a formulant in several pesticide products, namely wood preservatives and antifouling marine paints, in use in Canada (2009 personal communication from Pest Management Regulatory Agency, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). In addition, it is a minor component of some sealants and adhesives manufactured in Canada and, to a lesser degree, of some fillers and artists' paint and printing materials (Environment Canada 2009a).

Butanone oxime is also used as a corrosion inhibitor in industrial boilers (Rumpf 1993) and water treatment systems (Newton et al. 2001; Derelanko et al. 2003) and as a blocking agent in the manufacturing process of urethane polymers (Subramani et al. 2004). According to the information submitted under section 71 of CEPA 1999, butanone oxime is used as a corrosion inhibitor and as a blocking agent in the manufacture of urethane polymers in Canada (Environment Canada 2009a).

No current use of butanone oxime in cosmetics has been notified in Canada. Internationally, the use of butanone oxime in cosmetics is prohibited in Denmark (Danish Ministry of the Environment 2004) and in the United Kingdom (U.K. Secretary of State

2008) in accordance with an amendment to Directive 76/768/EEC of the European Commission (European Commission 2004). Butanone oxime is found in some printing inks used in the manufacture of food packaging materials, but there is no direct contact of butanone oxime with food.

Releases to the Environment

According to the information submitted under section 71 of CEPA 1999, butanone oxime was not manufactured by any company in Canada in 2006. In addition, there were no reports of any significant industrial releases of butanone oxime in the same calendar year in the section 71 responses (Environment Canada 2009a). The Canadian Chemical Producers' Association (CCPA 2009) reported the release of 356 kg of butanone oxime to the environment in 2007. The reporting of industrial releases of butanone oxime to the National Pollutant Release Inventory (NPRI 2007) is not required. The total industrial releases of butanone oxime are expected to be low, and the most significant releases of butanone oxime are expected to take place at the consumer use stage.

Environmental Fate

Based on its physical and chemical properties (Table 2), butanone oxime is characterized by high water solubility (100 000 mg/L), moderate vapour pressure (350 Pa), low log Kow (0.65), and low Henry's Law constant (0.30 $Pa \cdot m^3/mol$). Half-lives in air (modelled as 7.21 days, see Table 4b) and in water (measured as 18 days based on the hydrolysis rate, see Table 4a) are used in Level III fugacity modelling. The results are summarized in Table 3 and suggest that butanone oxime will reside largely or predominantly in the compartment to which it is released. There is somewhat moderate partitioning in water and soil, when the substance is released to air; and moderate partitioning in water if released to soil.

Table 3. Results of Level III fugacity modelling (EQC 2003) for butanone oxime

Substance released (100%) to:	Fraction of substance partitioning to each medium (%)			
	Air	Water	Soil	Sediment
Air	61.1	18.9	20.0	<0.1
Water	0.2	99.6	0.1	0.2
Soil	0.7	21.6	77.6	<0.2

Butanone oxime is considered to be a non-ionizing compound due to its high acid dissociation constant (pK_a >12); thus, it will be in the neutral form at environmentally relevant pHs (6–9).

Persistence and Bioaccumulation Potential

Environmental Persistence

Table 4a presents the empirical biodegradation and hydrolysis data for butanone oxime in water. This substance may hydrolyse, depending on the pH. At 20°C, butanone oxime is hydrolytically unstable at pH 4, whereas no hydrolysis occurs at pH 9. At pH 7, 14% of the substance was hydrolysed after 4 days (Environment Canada 2009b), which translates to a half-life of 18 days based on hydrolysis in the aquatic environment. Therefore, at neutral to acidic environmental conditions, hydrolysis may be an important degradation pathway for this substance. Hydrolysis products are 2-butanone (CAS RN 78-93-3) and hydroxylamine (CAS RN 7803-49-8) (ECB 2000a and 2000b).

The inherent biodegradation study (MITI 1992) suggests that this substance undergoes primary biodegradation, but that ultimate biodegradation is, at best, slow (Table 4a).

Table 4a. Empirical data for degradation of butanone oxime

Medium	Fate process	Degradation value (%)	Degradation endpoint	Reference
Water	Aerobic biodegradation[1]	24.7	28-day inherent biodegradation	MITI 1992
Water	Hydrolysis	14	Hydrolysis(4-day, pH 7, 20°C)	Environment Canada 2009b

[1] OECD Test Guideline 302C, Inherent biodegradability: Modified MITI Test (II).

The European Chemicals Bureau (ECB) published a datasheet on butanone oxime, reporting degradation studies with alternative OECD approved tests with conclusions of inherent, primary and ultimate biodegradability (2000a). Studies report 70% degradation related to dissolved organic carbon (DOC) in 14 days, while only ~25% degradation related to biological oxygen demand (BOD).

In addition to experimental data on the degradation of butanone oxime as above, a quantitative structure–activity relationship (QSAR)-based weight of evidence approach (Environment Canada 2007) was applied using the degradation models shown in Table 4b.

Table 4b. Modelled data for degradation of butanone oxime

Fate process	**Model and model basis**	**Model result and prediction**	**Extrapolated half-life (days)**
Air			
Atmospheric oxidation	AOPWIN 2008	$t_{½}$ = 7.21 days[1]	>2
Ozone reaction	AOPWIN 2008	n/a[2]	n/a
Water			
Hydrolysis	HYDROWIN 2008	n/a[2]	n/a
Biodegradation (aerobic)	BIOWIN 2008 Submodel 3: Expert Survey (ultimate biodegradation)	3.01[3] "biodegrades fast"	<182
Biodegradation (aerobic)	BIOWIN 2008 Submodel 4: Expert Survey (primary biodegradation)	3.72[3] "biodegrades fast"	<182
Biodegradation (aerobic)	BIOWIN 2008 Submodel 5: MITI linear probability (ultimate biodegradation)	0.50[4] "biodegrades fast"	<182
Biodegradation (aerobic)	BIOWIN 2008 Submodel 6: MITI non-linear probability (ultimate biodegradation)	0.62[4] "biodegrades fast"	<182
Biodegradation (aerobic)	TOPKAT 2004 Probability	0.0[3] "biodegrades very slowly"	>182
Biodegradation (aerobic)	CATABOL ©2004–2008 % BOD	% BOD = 20.1 "biodegrades slowly"	>182

Abbreviations: BOD, biological oxygen demand; MITI, Ministry of International Trade & Industry, Japan; n/a, not applicable; $t_{½}$, half-life.

[1] Assuming 12-h day; 1.5×10^6 hydroxyl radicals/cm^3.

[2] Model does not provide an estimate for this type of structure.

[3] Output is a numerical score.

[4] Output is a probability score.

The BIOWIN (2008) aerobic biodegradation models (BIOWIN submodels 3, 4, 5 and 6) suggest that butanone oxime biodegrades rapidly. The BIOWIN submodels 5 and 6 probability results are both greater than 0.3, the cut-off suggested by Aronson et al. (2006) to identify substances as having a half-life <60 days (based on the MITI probability models). However TOPKAT predicts that the substance may not biodegrade rapidly in water, while CATABOL suggests that the substance is just between the cut-offs for 'biodegrades slowly' (BOD < 20%) and 'may biodegrade fast' (BOD > 21%). Given the existence of experimental data, more weight is given to the empirical measures, the results of which are also supported by aerobic BIOWIN submodels 3, 4, 5 and 6. There is sufficient confidence, based on the experimental data, when taken together with the BIOWIN model predictions, to expect that there is significant biodegradation with a half-life that is likely well below 182 days.

Although little butanone oxime is expected to partition to sediment, it may remain in soil if released to this environmental compartment (see Table 3). Since BIOWIN (2008)

biodegradation prediction is expected to be fast, along with a moderate potential for hydrolysis, these data suggest that the degradation half-life in water is likely ≤ 90 days, thus the degradation half-lives for soil and sediments extrapolated using Boethling et al.'s (1995) factors ($t_{½\ water}$: $t_{½\ soil}$: $t_{½\ sediment}$ = 1:1:4), are ≤ 180 days and ≤ 365 days, respectively.

Based on the empirical and modelled data (see Tables 4a and 4b above), it is concluded that butanone oxime meets the persistence criterion in air (half-life in air ≥2 days), but does not meet the criteria for water, soil or sediment (half-lives in soil and water ≥182 days and half-life in sediment ≥ 365 days), as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

The long-range transport potential (LRTP) of this substance was predicted using two models: the Transport and Persistence Level III Model (TaPL3 v.3.00) and the OECD Pov and LRTP Screening Tool. Results are presented in Table 4c.

Table 4c. Model predictions and level of concern of the long-range transport potential of butanone oxime

Prediction Models	P_{ov}[1] (day)	CTD[2] (km)	TE[3] (%)	Level of Concern		
				Low	Moderate	High
TaPL3 v.3.00	n/a	1376	n/a	CTD<700 km	CTD=700-2000 km	CTD>2000 km
OECD Tool	23.5	3581	2.1×10^{-2}	1) P_{ov} <195 days and 2) CTD <5098 km and TE <6.5×10^{-4}%	any combination of P_{ov}, CTD, and TE other than low or high	1) P_{ov} >195 days and 2) CTD >5098 km or TE >6.5×10^{-4}%

[1] P_{ov} – Overall environmental persistence
[2] CTD – Characteristic travel distance
[3] TE – Transfer efficiency

The TaPL3 model provides an estimate of the characteristic travel distance (CTD) only for the substance, defined as the maximum distance travelled by 63% of the substance, of 1376 km. Beyer et al. (2000) proposed characteristic travel distances of > 2000 km as representing high long-range transport potential, 700–2000 km as moderate and < 700 km as low. Based on the modelled result from TaPL3, this substance is expected to have a moderate long-range transport potential.

The LRTP of butanone oxime was also assessed using the OECD tool, based on a combination of overall environmental persistence (P_{ov}) and CTD or transfer efficiency (TE). P_{ov} has been introduced as a concept to weigh half-lives according to partitioning behaviour and is a kind of average of all the half-lives in air, water, sediment and soil (Mackay 2006). This parameter is found to closely link to the potential for long-range transport, but is not currently used for decision making in hazard assessment as most regulatory authorities rely on the single-media half-life approach. TE is a measure, expressed as percentage, for the extent of the deposition of a substance onto the surface media of a target area after being transported away from the region of release (Klasmeier

et al. 2006). Based on the level of concern rating system (Scheringer et al. 2006), the long-range transport potential of butanone oxime is expected to be moderate as well.

Potential for Bioaccumulation

Experimental log K_{ow} values (0.59-0.65) for butanone oxime (see Table 2 above) suggest that this chemical has low potential to bioaccumulate in biota. Experimentally derived bioconcentration factors (BCF) of 0.5–5.8 for carp (*Cyprinus carpio*) and Japanese medaka (*Oryzias latipes*) (MITI 1992; ECB 2000a) indicate that butanone oxime is not bioaccumulative. This conclusion is also supported by modelled BCF and bioaccumulation factor (BAF) values (Table 5) using the default of no metabolism, which were used in a weight of evidence approach (Environment Canada 2007) for evaluating the bioaccumulation potential of this substance.

Table 5. Fish BAF and BCF predictions for butanone oxime with default of no metabolism

Test organism	Endpoint	Value (L/kg wet weight)	Reference
Fish	BAF	1.2	BCFBAF 2008 (Gobas BAF middle trophic level)
Fish	BCF	1.2	BCFBAF 2008 (Gobas BCF middle trophic level)
Fish	BCF	3.2[1]	BCFBAF 2008
Fish	BCF[2]	27.5	CPOPs 2008

[1] The very low BCF value of 3.16 is a default value recommended by the BCFBAF model for substances with a log K_{ow} <1; therefore, this result is not a model-generated BCF calculated specifically for butanone oxime.
[2] Maximum estimate.

Furthermore, log K_{ow} values for the hydrolysis products 2-butanone and hydroxylamine are very low (ECB 2000; OECD 2008), indicating that the hydrolytic products of butanone oxime also have low potentials to bioaccumulate.

Based on the available empirical and kinetic-based modelled values, it is concluded that butanone oxime does not meet the bioaccumulation criteria (BAF or BCF ≥5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

The approach taken in this assessment was to examine the available scientific information and develop conclusions based on a weight of evidence approach and using precaution as required under CEPA 1999. Lines of evidence considered include results from site-specific aquatic risk quotient calculations as well as information on the persistence, bioaccumulation, inherent toxicity, sources and fate of the substance.

As described previously, butanone oxime is persistent in air, but not in water, soil or sediment compartments. It is also expected to have a low bioaccumulation potential. The

most sensitive experimental ecological effects data for a range of species, as well as modelled data, are summarized in Table 6. Robust study summaries were not prepared for the empirical studies, as the studies were not available. However, the lowest value of all ecotoxicity data (6.1 mg/L) collected was used as a conservative estimate of the critical toxicity value (CTV) to characterize the potential for effects on sensitive species. The modelled data generally support the empirical results.

Table 6. Empirical and modelled data for aquatic toxicity of butanone oxime

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Empirical data				
Fish (*Pimephales promelas*)	Acute	96-h LC_{50}	843	Brooke et al. 1984
Fish (*Oryzias latipes*)	Subchronic	14-day LC_{50} 14-day NOEC	>100 50	CHRIP ©2002
Invertebrate (*Daphnia magna*)	Acute	48-h EC_{50}	200	CHRIP ©2002
Invertebrate (*Daphnia magna*)	Chronic	21-day EC_{50} (reproduction)	>100	CHRIP ©2002
Alga (*Pseudokirchneriella subcapitata*)[1]	Chronic	72-h EC_{50} (growth)	6.1[2]	CHRIP ©2002
Microbial[3]	Acute	5-min EC_{50}	950	Curtis et al. 1982
Modelled data				
Fish	Acute	96-h LC_{50}	932	ECOSAR 2008[4]
Fish	Chronic	Chronic value	91	ECOSAR 2008
Fish (*Pimephales promelas*)	Acute	96-h LC_{50}	1482	AIEPS 2003–2007
Invertebrate (*Daphnia*)	Acute	48-h EC_{50}	457	ECOSAR 2008
Invertebrate (*Daphnia*)	Chronic	Chronic value	33	ECOSAR 2008
Invertebrate (*Daphnia*)		EC_{50}	1600	TOPKAT 2004
Invertebrate (*Daphnia*)	Acute	48-h EC_{50}	290	AIEPS 2003–2007
Green alga	Chronic	96-h EC_{50}	113	ECOSAR 2008
Green alga	Chronic	Chronic value	32	ECOSAR 2008
Alga (*Pseudokirchneriella subcapitata*)[1]	Chronic	72-h EC_{50}	31	AIEPS 2003–2007

Abbreviations: EC_{50}, concentration of a substance that is estimated to cause some toxic sublethal effect on 50% of the test organisms; LC_{50}, concentration of a substance that is estimated to be lethal to 50% of the test organisms; NOEC, no-observed-effect concentration.

[1] Formerly *Selenastrum capricornutum.*

[2] Critical toxicity value (CTV).

[3] *Photobacterium phosphoreum* toxicity bioassay.

[4] Based on QSAR for baseline toxicity.

The toxicity data indicate that butanone oxime has a moderate potential to be toxic to algae and a low potential for most other aquatic organisms. Furthermore, considering the toxicity of the hydrolysis products (2-butanone and hydroxylamine) to sensitive aquatic species, as well as the comparatively low rate of hydrolysis (14% in 4 days) under

environmental conditions, the risk due to the hydrolysis products of butanone oxime is not expected to be significantly higher than that of the compound itself (ECB 2000b; OECD 2008).

Toxicity data were not found for the organisms in the soil or sediment compartments.

The high importation volume of butanone oxime into Canada, together with information on its uses, indicates potential for widespread release of this substance into the Canadian environment. If released to water, butanone oxime is expected to remain in water (>99%; see Table 3). In this screening assessment, site-specific aquatic exposure scenarios were developed to estimate releases into the aquatic environment from industrial operations and resulting aquatic concentrations.

Two sewage treatment plants (STPs) were identified as having the highest releases of butanone oxime, as determined from information obtained through the section 71 survey (Environment Canada 2009a). Each site includes discharges from a certain number of industrial users of butanone oxime. One site releases to a relatively large receiving water body, whereas the other site releases to a considerably smaller one. The predicted environmental concentrations (PECs) for both sites were estimated based on the quantity of butanone oxime used by all facilities served by each STP, the fraction estimated to be discharged to the STP, the STP removal rate, the STP effluent flow and the dilution capacity of the receiving water. The key value in the PEC estimate is the fraction of the substance discharged to the STP. This fraction is 0.3%, resulting from the cleaning of semi-bulk containers or totes that are used for the transportation of the substance, and is assumed by default (Great Western Containers 2005). The higher calculated PEC for the two sites was 0.010 mg/L.

A predicted no-effect concentration (PNEC) was derived from the chronic algal toxicity value of 6.1 mg/L for *Pseudokirchneriella subcapitata* (see Table 6). An assessment factor of 100 was applied to account for uncertainties related to interspecies and intraspecies variability in sensitivity and extrapolation from a laboratory EC_{50} to a no-effect value in the field. This yielded a PNEC of 0.06 mg/L. The highest resulting risk quotient, calculated as the ratio of the PEC to PNEC, was 0.17, indicating that the substance is not anticipated to harm aquatic organisms.

Butanone oxime is thus considered unlikely to be causing ecological harm in Canada. Considering the comparatively low hydrolysis rate of butanone oxime, the hydrolysis products are not expected to pose a threat either.

It should be noted that this conclusion was reached despite the conservative assumptions that were made in response to uncertainties encountered in the assessment. A key uncertainty relates to the lack of empirical data on environmental concentrations in Canada, which was addressed by predicting realistic worst-case concentrations in water using an industrial exposure model. There is also uncertainty associated with the PNEC used in the risk quotient calculation, because details of the study were not available. However, the CTV used is considered to be conservative, as it is the lowest empirical value observed and is at least one order of magnitude lower than the next lowest toxicity

value. In addition, an assessment factor of 100 was applied to the CTV to derive the PNEC.

Also, regarding ecotoxicity, based on the predicted partitioning behaviour of this chemical, the significance of soil and sediments as important media of exposure is not well addressed by the effects data available. However, exposures near industrial point sources are expected to be highest in the aquatic compartment.

Uncertainties also exist with the conclusion for persistence. Very limited empirical data were available, and some model results were contradictory. These data were nevertheless used to estimate approximate half-lives for water, soil and sediment. However, the weight of evidence, considering both the empirical and modelled data, indicates that this substance does not meet the persistence criteria for water, soil or sediment.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Food

No measured concentrations of butanone oxime in environmental media in Canada or elsewhere were identified. Based on its high vapour pressure and half-life in air, butanone oxime is expected to exist primarily as a vapour and to persist in ambient air. However, as no significant industrial releases of butanone oxime to the air were reported in 2006, the concentration of butanone oxime in ambient air is expected to be low. Modelled estimates based on current information also predict that the concentration of butanone oxime in air is low, at approximately 1.79 ng/m^3 (ChemCAN 2003). Similarly, the predicted concentrations for water and soil are very low (0.550 ng/L and 7.08×10^{-4} ng/g, respectively).

No measured concentrations of butanone oxime in food in Canada or elsewhere were identified. Based on the uses of butanone oxime in Canada, food is unlikely to be a source of exposure. Given that the experimental log K_{ow} values for butanone oxime are low, the substance is not expected to bioaccumulate in biota, and accumulation of butanone oxime in the food chain is not considered likely.

Due to the lack of empirical data on concentrations in environmental media and food, upper-bounding daily intake estimates for the general population were not derived.

Consumer Products

With regard to consumer products, butanone oxime is most prevalent in alkyd paints, stains, varnishes and coatings, according to information submitted under section 71 of CEPA 1999. Butanone oxime is also present in a few sealants, adhesives and fillers that are used mainly by industry, but which may also be available to the general population

for home maintenance and do-it-yourself applications. Accordingly, use of alkyd paint containing butanone oxime was the primary scenario used to characterize exposure from products.

A limited number of studies report concentrations of butanone oxime during manufacture and use of products such as alkyd paints. A US study of consumer exposure to butanone oxime (Chang 1998) predicted a maximum concentration of butanone oxime in indoor air of 18 mg/m^3 based on the use of alkyd paint containing 0.293% w/w butanone oxime, the highest level of butanone oxime that was present in the products tested. A limited unpublished study measured butanone oxime concentrations of up to 9.9 ppm (30 mg/m^3) during a simulation using an indoor painting scenario with an alkyd paint containing approximately 0.2% butanome oxime (unpublished study submitted to Environment Canada, 2009b; unreferenced).

However, as butanone oxime content of alkyd paints used in Canada can be higher (up to 1% (2009 personal communication from Canadian Paints and Coatings Association to Environment Canada; unreferenced)) potential exposure at this level was modelled.

Exposure estimates were therefore derived using ConsExpo v. 4.1 software (ConsExpo 2007). Resulting estimated air concentrations and dermal exposure (external) are summarized in Table 7. The inputs and assumptions used in ConsExpo v. 4.1 modelling of each of the consumer product scenarios are provided in Appendix 1, where both external and internal exposure estimates during use of these products are presented. There were no identified data on absorption of butanone oxime following inhalation exposure. While dermal absorption have been reported to range between 13% and 29% in a study conducted in rats (Burka et al. 1998), the estimates of internal exposure were derived using 100% uptake for inhalation and dermal absorption.

Table 7. Summary of estimated air concentrations and dermal external applied dose of butanone oxime during use of consumer products

Consumer product	Maximum concentration of butanone oxime (%)	Inhalation mean event concentration (mg/m^3)	Dermal: External applied dose (mg/kg-bw)
Alkyd coating	1	223	0.0353
Alkyd paint (high solid)	1	113	0.508
Alkyd paint (solvent rich)	1	72.7	0.508
Alkyd paint (aerosol)	1	3.75	0.212
Silicone sealant (joint)	5	150	1.06
Adhesive (gasketing)	2	3.39	0.0226

Abbreviation: kg-bw, kilogram body weight.

The US EPA's Wall Paint Exposure Assessment Model v. 3.2 (WPEM 2001) predicted a maximum indoor air concentration of butanone oxime of 227 mg/m^3 for the alkyd paints and an 8-hour average concentration of 195 mg/m^3.

Based on the available information, the most likely route of exposure to butanone oxime for the general population is likely from inhalation during use of alkyd paints and coatings, based on the maximum mean event concentration. However, in light of the limited data available on concentrations in environmental media, confidence in this estimate is very low.

Health Effects Assessment

Appendix 2 contains a summary of the available health effects information for butanone oxime.

The European Commission has classified butanone oxime as Category 3 for carcinogenicity (*causes concern for humans owing to possible carcinogenic effects*) (European Commission 2000, 2001). In chronic lifetime studies in both rats and mice exposed by inhalation to butanone oxime, there was an increased incidence of liver tumours (adenomas and carcinomas) in both species at all tested exposure concentrations. However, statistically significant increases in incidence were observed only at 267 and 1333 mg/m^3 for liver adenomas in male rats and at 1333 mg/m^3 for liver carcinomas in male rats and mice. A statistically significant increased incidence of mammary gland fibroadenomas was also observed in female rats at 1333 mg/m^3. Non-neoplastic effects observed in rats included histopathological effects in the spleen (congestion, increased pigmentation in the reticuloendothelial cells and extramedullary hematopoiesis) and in the nasal turbinates (degeneration of the olfactory epithelium) at all exposure concentrations, in the liver (increased incidences of basophilic foci and hepatocyte vacuoles) at 267 and 1333 mg/m^3, changes in blood parameters at 1333 mg/m^3 and enlarged testes in males at 267 and 1333 mg/m^3. Non-neoplastic effects observed in mice included dose-related increases in liver hypertrophy and necrosis as well as in olfactory epithelium degeneration in the nasal turbinates at all exposure concentrations, changes in blood parameters at 267 and 1333 mg/m^3 and changes in serum chemistry parameters at 1333 mg/m^3. The lowest-observed-adverse-effect concentration (LOAEC) for non-neoplastic effects was 53 mg/m^3 (15 ppm), based on effects in the spleen and nasal turbinates of rats and effects in the liver and nasal turbinates of mice (Newton et al. 2001). Long-term oral or dermal studies using butanone oxime were not identified.

Butanone oxime was not mutagenic in the majority of bacterial mutation assays using *Salmonella typhimurium*, but it was positive in a mouse lymphoma cell mutation assay with and without activation (Allied Corporation 1983b; Rogers-Back et al. 1988; JETOC 1999; NTP 1999). *In vitro* assays for chromosomal aberration in Chinese hamster ovary and lung cells, for sister chromatid exchange in Chinese hamster ovary cells and for unscheduled deoxyribonucleic acid (DNA) synthesis in rat hepatocytes all showed negative responses (Allied Corporation 1983a; IHF Inc. 1995; JETOC 1999; NTP 1999). *In vivo* assays for micronuclei were both negative for bone marrow cells in rats and for peripheral blood cells in mice; rats and mice were dosed orally (Microbiological Associates Inc. 1990; NTP 1999). In an *in vivo* assay in rats exposed by inhalation, butanone oxime was negative for DNA adducts but positive for ribonucleic acid (RNA) adducts in rat liver cells (Honeywell International Inc. 2000).

Fully elucidated modes of action analysis for induction of the observed tumours have not been identified. The European Commission (2000) considered that a possible mechanism for the increased incidences of liver tumours in male rats and mice was the metabolism of butanone oxime to a carcinogenic agent, mediated by sulfotransferase. The sex and organ specificity of tumour formation correlated with the typically higher activity of this enzyme in male rodents. Völkel et al. (1999) showed that the incubation of liver microsomes from mice, rats and humans with butanone oxime resulted in the formation of nitronates, but that the rates of formation did not correlate with sex and species differences in liver tumour response; they concluded that "other mechanisms of tumourigenicity not related to nitronate mutagenicity and DNA-damage may thus be operative." The European Commission (2000) did not comment on whether the mode of action for liver tumours in rats was due to threshold mechanisms. However, the *in vitro* and *in vivo* genotoxicity results for butanone oxime were mostly negative, including an *in vivo* study that utilized inhalation exposure and was found to be negative for DNA adducts in rat liver cells. Therefore, based on the available data, butanone oxime appears to lack mutagenic potential. This lack of mutagenic potential may also explain why the European Commission (2000) did not comment on whether the mode of action for mammary gland tumours in rats was due to threshold mechanisms.

In a mouse inhalation study with exposures to butanone oxime for 1, 2 or 4 weeks, degeneration of the olfactory epithelium in the nasal cavity was observed in males at concentrations of 107 and 356 mg/m^3 (incidence and severity increased with increasing exposure concentration) (Newton et al. 2002). In 13-week inhalation studies, degeneration of the olfactory epithelium in the nasal cavity was observed in male mice at concentrations of 36–356 mg/m^3 (incidence and severity increased with increasing exposure concentration), whereas increased relative liver weights were observed in male rats at 267 and 1333 mg/m^3 (Newton et al. 2001, 2002). The LOAEC for subchronic exposure was 36 mg/m^3, based on degeneration of the olfactory epithelium in the nasal cavity of mice.

In a 4-week oral rat study, changes in hematological parameters (increase in reticulocytes, platelets and red blood cells) and increased relative spleen weight with accompanying histopathological abnormalities (increases in congestion, extramedullary hematopoiesis and hemosiderin granules) were observed in both sexes at 20 and 100 mg/kg body weight (kg-bw) per day, whereas hemosiderin granules in the liver were observed in females at the same doses (Japan MHW 1996; JETOC 1999). Butanone oxime was administered via drinking water in a 13-week rat study. Relative liver weights were increased in males at doses of 25–280 mg/kg-bw per day (NTP 1999). In another 13-week rat study, in which butanone oxime was administered via gavage, changes in liver and spleen weights, hemosiderosis of spleen and hematological effects were observed in both sexes at doses of 25–225 mg/kg-bw per day (Allied Signal Inc. 1977). The lowest-observed-adverse-effect level (LOAEL) for short-term and subchronic oral exposure was 20 mg/kg-bw per day, based on changes in hematological parameters, increased relative spleen weight with accompanying histopathological abnormalities, and hemosiderin granules in the liver observed in the 4-week rat study.

In a one-generation oral rat study, the LOAEL for reproductive toxicity was 100 mg/kg-bw per day, the highest dose, based on a statistically significant decrease in female delivery index (%)[1] (Japan MHW 1998), whereas no treatment-related effects on reproductive parameters were observed in a two-generation study in which rats were dosed by gavage at 0–200 mg/kg-bw per day (Tyl et al. 1996). In both the one-generation and two-generation rat studies, a parental LOAEL of 10 mg/kg-bw per day, the lowest dose tested, was established, based on histopathological effects in the spleen and liver (and in the kidney in the one-generation study).

Teratogenicity was not observed in pregnant rats and rabbits dosed orally with butanone oxime during gestation (Springborn Laboratories 1990a, b; Mercieca et al. 1991; Derelanko et al. 2003). The lowest oral LOAEL for developmental toxicity was 40 mg/kg-bw per day, the highest dose, based on abortions in 3 of 10 adult females in pregnant rabbits dosed by gavage during gestation (Springborn Laboratories 1990b; Derelanko et al. 2003). The lowest oral LOAEL for maternal toxicity was 10 mg/kg-bw per day, based on signs of anemia (increased reticulocytes and methemoglobin) in rabbits dosed at 0–80 mg/kg-bw per day in a range-finding developmental study (Springborn Laboratories 1990b; Derelanko et al. 2003).

Studies designed to determine median lethal dose or concentration (LD_{50} or LC_{50}) values were also able to determine lowest effect levels based on acute exposure. The lowest LOAEC for inhalation exposure was 190 mg/m^3, based on decreased body weight gain in the observation period (7 or 14 days) after 4 hours of inhalation exposure in rats (Allied Corporation 1984b). The lowest LOAEL for dermal exposure was 180 mg/kg-bw, based on methemoglobin production and splenic erythrophagocytosis in a 24-hour dermal rabbit study (Allied Corporation 1984a; US EPA 1986).

Toxicokinetic studies on butanone oxime in mice and rats show that it is rapidly absorbed from the gastrointestinal tract, undergoes widespread uptake, distributes over the entire body, is extensively metabolized and does not accumulate in tissues. Excretion of butanone oxime and its metabolites occurs in the urine and bile or as volatiles in expired air (ICCA MEKO 2003). In single-dose studies in rats, significantly greater amounts of volatiles were excreted following dermal administration than after gavage or intravenous administration (NTP 1999). However, no toxicokinetic data based on repeated dosing via the oral, inhalation, nor dermal pathways were identified. The toxicokinetic studies of butanone oxime demonstrated the existence of two metabolic pathways and the possibility of a third one (based on acute oral, dermal and intravenous doses only). The major pathway is the hydrolysis of butanone oxime to 2-butanone (methyl ethyl ketone), and the second pathway is the oxidation of butanone oxime to butane 2-nitronate by microsomal monooxygenases, but this occurs at very low rates (ICCA MEKO 2003). ICCA MEKO (2003) reported that "With respect to the three [metabolic] pathways, there were no quantitative differences in the extent of MEKO [butanone oxime] metabolism between male and female rats."

[1] (No. of pups born/no. of implantations) × 100.

The confidence in the toxicity database for butanone oxime is considered to be low to moderate, as adequate information is available to address effects that may be of concern and identify critical endpoints based on inhalation exposures of acute to long-term duration. However, there was a lack of reproductive and developmental toxicity studies based on inhalation exposure; and limited studies via the dermal route.

Characterization of Risk to Human Health

Carcinogenicity was considered in the health effects assessment for butanone oxime, as the substance had been classified as carcinogenic by the European Commission (2000, 2001). As shown under the "Health Effects Assessment" section, increased incidences of liver tumours were observed in rat and mouse lifetime studies, and there was also an increased incidence of mammary gland tumours in female rats. However, these were seen only at mid- and/or high concentrations of butanone oxime. Consideration of the available information on genotoxicity indicates that butanone oxime is not likely to be genotoxic. Accordingly, although the mode of induction of tumours is not fully elucidated, the tumours observed are not considered to have resulted from direct interaction with genetic material. Therefore, a threshold approach is used to assess risk to human health.

With respect to non-cancer effects, the lowest inhalation LOAEC for chronic exposures was 53 mg/m^3, based on degeneration of the olfactory epithelium in the nasal cavities of both mice and rats, liver cell hypertrophy and necrosis in mice, and histopathological effects in the spleen of rats observed in lifetime studies with these species. For subchronic exposures, the lowest inhalation LOAEC was 36 mg/m^3, based on degeneration of the olfactory epithelium in the nasal cavity of mice observed in a 13-week inhalation study. Likewise, for short-term exposures, the lowest inhalation LOAEC was 107 mg/m^3, based on degeneration of the olfactory epithelium of the nasal cavity of mice exposed to a butanone oxime exposure regime of 6 hours/day, 5 days/week, for 1, 2 or 4 weeks. The occurrence of toxicological sequelae following five exposures (30 total hours of exposure) is relevant for the acute exposure risk assessment. For acute exposures, an inhalation LOAEC of 190 mg/m^3 was determined based on decreased body weight gain in rats in a 4-hour inhalation study. The changes in body weight gain were not noted at critical effect levels in short-term inhalation studies. However, an analysis of the change in the dose–response curve over time (190 mg/m^3 acutely, 107 mg/m^3 after 5 days and 36 mg/m^3 after subchronic exposure) suggests that the body weight gain deficits occur in the appropriate dose range following acute exposure.

The lowest oral LOAEL for short-term and subchronic exposures was 10 mg butanone oxime/kg-bw per day, based on histopathological effects in the spleen and liver of adult rats observed in both a one-generation and a two-generation reproduction study (and in the kidney in the one-generation study) (Tyl et al. 1996; Japan MHW 1998) and based on signs of anemia in adult female rabbits observed in a range-finding developmental study (Springborn Laboratories 1990b; Derelanko et al. 2003). For acute exposures, an oral lowest-observed-effect level (LOEL) of 300 mg/kg-bw was determined based on transient neurotoxic effects in rats (Schulze and Derelanko 1993), and a dermal LOAEL

of 180 mg/kg-bw was determined based on methemoglobin production and splenic erythrophagocytosis in a 24-hour rabbit study (Allied Corporation 1984b; US EPA 1986).

As stated under "Exposure Assessment", due to the lack of empirical data on concentrations in several media, estimates of daily intake for the general population were not derived. Thus, margins of exposure could not be derived for comparisons between critical effect levels based on repeated daily exposures to butanone oxime and upper-bounding estimates of daily intake.

Exposure to butanone oxime is most likely to occur through use of consumer products. Based on product scenario modelling using ConsExpo, the highest air concentrations resulted from inhalation during use of alkyd paints and coatings, resulting in a range of 73–223 mg/m^3. Using the Wall Paint Exposure Assessment Model, an 8-hour average air concentration of 195 mg/m^3 was derived for alkyd paints. Comparison of these conservative air concentrations with the acute to short-term critical effect levels for inhalation exposure (107–190 mg/m^3) results in margins of exposure of 0.5–2.6. A limited number of studies measured air concentrations ranging from 6.0 to 18 mg/m^3 under various simulated paint scenarios using products with lower concentrations of butanone oxime (0.2 – 0.6%). Resulting margins of exposures from these scenarios range from 6 to 30.

Acute dermal exposures during use of alkyd paints and coatings were estimated to be 0.0226–1.06 mg/kg-bw. These estimates were compared to a dermal critical effect level of 180 mg/kg-bw, which leads to margins of exposure ranging from 170 to 8000.

In light of the uncertainties in the databases on exposure and effects, it is considered that the derived margins of exposure for these consumer product scenarios (all estimated margins of exposure based on inhalation exposure, and the lower margins of exposure based on dermal exposure) may not be adequately protective of human health for non-cancer effects.

Uncertainties in Evaluation of Risk to Human Health

This screening assessment does not include a full analysis of the mode of induction of effects, including cancer, of butanone oxime. In addition, only limited information is available concerning the potential toxicity of butanone oxime following oral and dermal exposure and for reproductive toxicity, developmental toxicity and genotoxicity studies based on inhalation exposures. Thus, critical effect levels determined in this screening assessment are limited by the toxicity database and by uncertainties in the interpretation of the biological significance of effects, including uncertainties in the interpretation of intraspecies and interspecies variation.

Uncertainty in exposure to butanone oxime from the environmental media and food in Canada is high, as no empirical data were available with which to derive exposure estimates. While empirical data is absent, food is not expected to be a source of exposure to butanone oxime. While the most likely source of exposure of the general population to

butanone oxime is expected to be alkyd paint products, uncertainty is associated with the use of default assumptions. However, the concentrations of butanone oxime in the selected products used for modelling consumer product exposure scenarios are based on Canadian-specific information.

Conclusion

Based on the information presented in this screening assessment, it is concluded that butanone oxime is not entering 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 or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the potential inadequacy of the margins between estimated exposures to butanone oxime and critical effect levels, it is concluded that butanone oxime is a substance that may be 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.

It is therefore concluded that butanone oxime meets one or more of the criteria set out in section 64 of CEPA 1999. Additionally, butanone oxime meets the criteria for persistence but does not meet the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

This substance will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment and, where appropriate, the performance of potential control measures identified during the risk management phase.

References

[AIEPS] Artificial Intelligence Expert Predictive System. 2003–2007. Version 2.05. Ottawa (ON): Environment Canada, Existing Substances Division, New Substances Division. Model developed by Stephen Niculescu. Available from: Environment Canada, Existing Substances Division, New Substances Division.

Allied Corporation. 1983a. Evaluation of methyl ethyl ketoxime (MEKO) in the sister chromatid exchange (SCE) test: *in vitro* results in Chinese hamster ovary (CHO) cells. Report No.: MA-224-82-6. [cited in ICCA MEKO 2003].

Allied Corporation. 1983b. Evaluation of methyl ethyl ketoxime for enzyme mediated mutagenicity in *Salmonella typhimurium*. Report No.: MA-224-82-3. [cited in ICCA MEKO 2003].

Allied Corporation. 1984a. Acute dermal toxicity study of methylethylketoxime (MEKO). Report No. MA-224-82-9 [cited in ICCA MEKO, 2003].

Allied Corporation. 1984b. Acute inhalation toxicity study of MEKO. Report No.: MA-224-82-7. [cited in ICCA MEKO 2003].

Allied Signal Inc. 1977. Final report: 13-week toxicity study in rats. Hazleton Laboratories America, Inc. Project No. 165-161. [cited in ICCA MEKO 2003].

Allied Signal Inc. 1995. A 4-week peroxisome proliferation study of MEKO in the rat via oral gavage administration. Pharmaco-LSR Study No. 94-2368. [cited in ICCA MEKO 2003].

[AOPWIN] Atmospheric Oxidation Program for Windows [Estimation Model]. 2008. Version 1.92a. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Aronson D, Boethling B, Howard P, Stiteler W. 2006. Estimating biodegradation half-lives for use in chemical screening. Chemosphere 63: 1953–1960.

[BCFBAF] BioConcentration Factor Program for Windows [Estimation Model]. 2008. Version 3.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Beyer A, Mackay D, Matthies M, Wania F, Webster E. 2000. Assessing long-range transport potential of persistent organic pollutants. Environ Sci Technol 34(4): 699–703.

Bio/Dynamics Inc. 1990. A four week inhalation study of MEKO in the rat and mouse. USA Project 90-8249. Committed by MEKO producers and importers in the USA, in regard of EPA final test rule under TSCA. [cited in ICCA MEKO 2003].

Biosearch Inc. 1982. Summary of results of acute toxicity study on 2-butanone oxime; study report 81-2870A, conducted for Mooney Chemicals, Inc.; TSCA OTS0513319, Document ID: 86870000134. [cited in ICCA MEKO 2003].

[BIOWIN] Biodegradation Probability Program for Windows [Estimation Model]. 2008. Version 4.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Boethling RS, Howard PH, Beauman JA, Larosche ME. 1995. Factors for intermedia extrapolations in biodegradability assessment. Chemosphere 30(4): 741–752.

Brooke LT, Call DJ, Geiger DL, Northcott CE, editors. 1984. Acute toxicities of organic chemicals to fathead minnows (*Pimephales promelas*). Vol. 1. Superior (WI): University of Wisconsin-Superior, Center for Lake Superior Environmental Studies. p. 105–106.

Burka LT, Black SR, Mathews JM. 1998. Disposition of methyl ethyl ketoxime in the rat after oral, intravenous and dermal administration. Xenobiotica 28(10): 1005–1015.

Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C., 1999, c. 33. Available from: http://www.gazette.gc.ca/archives/p3/1999/g3-02203.pdf

Canada. 2000. *Canadian Environmental Protection Act, 1999: Persistence and Bioaccumulation Regulations*, P.C. 2000-348, 23 March 2000, SOR/2000-107. Available from: http://www.gazette.gc.ca/archives/p2/2000/2000-03-29/pdf/g2-13407.pdf

Canada, Dept. of the Environment, Dept. of Health. 2006. *Canadian Environmental Protection Act, 1999*: *Notice of intent to develop and implement measures to assess and manage the risks posed by certain substances to the health of Canadians and their environment*. Canada Gazette, Part I, vol. 140, no. 49, p. 4109–4117. Available from: http://www.gazette.gc.ca/archives/p1/2006/2006-12-09/pdf/g1-14049.pdf

Canada, Dept. of the Environment, Dept. of Health. 2008. *Canadian Environmental Protection Act, 1999: Notice with respect to Batch 7 Challenge substances.* Canada Gazette, Part I, vol. 142, no. 35. Available from: http://www.gazette.gc.ca/rp-pr/p1/2008/2008-08-30/pdf/g1-14235.pdf

CATABOL [Computer Model]. ©2004–2008. Version 5.10.2. Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. [cited 2009 Mar 3]. Available from: http://oasis-lmc.org/?section=software&swid=1

[CCPA] Canadian Chemical Producers' Association. 2009. Reducing emissions 16: 2007 emissions inventory and five-year projections. Ottawa (ON): CCPA. Available from: http://www.ccpa.ca/files/Library/Documents/Environment/Reducing_Emissions_16_FINAL.pdf

Chang JCS. 1998. Exposure and emission evaluations of methyl ethyl ketoxime (MEKO) in alkyd paints. Indoor Air 8(4): 295–300.

ChemCAN [Level III fugacity model of 24 regions of Canada]. 2003. Version 6.00. Peterborough (ON): Trent University, Canadian Centre for Environmental Modelling and Chemistry. [cited 2009 May 11]. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/CC600.html

[CHRIP] Chemical Risk Information Platform, Total Search System for Chemical Substances [database on the Internet]. ©2002. Butanone oxime, CAS RN 96-29-7. Tokyo (JP): National Institute of Technology and Evaluation. [updated 2009 Apr 27; cited 2009 May 1]. Available from: http://www.safe.nite.go.jp/english/Haz_start.html

[ConsExpo] Consumer Exposure Model [Internet]. 2007. Version 4.1. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment). Available from: http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp#tcm:13-42840

[CPOPs] Canadian POPs Model. 2008. Gatineau (QC): Environment Canada, Existing Substances Division; Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. [Model developed based on Mekenyan et al. 2005]. Available upon request.

Curtis C, Lima A, Lozano SJ, Veith GD. 1982. Evaluation of a bacterial luminescent bioassay as a method for predicting acute toxicity of organic chemicals to fish. In: Pearson JG, Foster RB, Bishop WE, editors.

Aquatic toxicology and hazard assessment: fifth conference. Philadelphia (PA): American Society for Testing and Materials. ASTM Special Technical Publication 766. p. 170–178. [cited in Kaiser and Ribo 1988].

Danish Ministry of the Environment. 2004. List of undesirable substances 2004. Copenhagen (DK): Danish Ministry of the Environment, Environmental Protection Agency. Environmental Review Report No. 15. p. 24.

Derelanko MJ, Rinehart WE, Rodwell DE. 2003. Developmental toxicity studies of methyl ethyl ketoxime (MEKO) in rats and rabbits. Drug Chem Toxicol 26(3): 147–168.

Dow Corning Corporation. 1983. A 28-day vapor inhalation toxicity study of methyl ethyl ketoxime (MEKO) with the rat. Reference No.: TX-82-4160-01. [cited in ICCA MEKO 2003].

[ECB] European Chemicals Bureau. 2000a. IUCLID dataset: Butanone oxime, CAS No. 96-29-7 [Internet]. Year 2000 CD-ROM edition. [created 2000 Feb 19; cited 2009 Jan 14]. Available from: http://ecb.jrc.ec.europa.eu/iuclid-datasheet/96297.pdf

[ECB] European Chemicals Bureau. 2000b. IUCLID dataset: Butanone, CAS No. 78-93-3 [Internet]. Year 2000 CD-ROM edition. [created 2000 Feb 19; cited 2009 Jan 14]. Available from: http://ecb.jrc.ec.europa.eu/iuclid-datasheet/78933.pdf

[ECOSAR] Ecological Structure Activity Relationships [Internet]. 2008. Version 1.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Environment Canada. 2007. Guidance for conducting ecological assessments under CEPA, 1999: science resource technical series: draft module on QSARs. Reviewed draft working document. Gatineau (QC): Environment Canada, Existing Substances Division.

Environment Canada. 2009a. Data for Batch 7 substances collected under the Canadian Environmental Protection Act, 1999, Section 71: *Notice with respect to Batch 7 Challenge substances*. Data prepared by: Environment Canada, Existing Substances Program

Environment Canada. 2009b. Unpublished confidential study submitted to Environment Canada, Existing Substances Division, under the Chemical Management Plan Challenge initiative. Available as Robust Study Summary, Identification No.: 3450Challenge001

[EQC] Equilibrium Criterion Model. 2003. Version 2.02. Peterborough (ON): Trent University, Canadian Centre for Environmental Modelling and Chemistry. [cited 2009 May 1]. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/EQC2.new.html html

[ESIS] European Chemical Substances Information System [database on the Internet]. 2006. Result for CAS No. 96-29-7. Butanone oxime. ESIS Version 4.50. Database developed by the European Chemicals Bureau. Available from: http://ecb.jrc.ec.europa.eu/esis/

European Commission. 2000. Summary Record: Meeting of the Commission Working Group on the Classification and Labelling of Dangerous Substances. ECB Ispra, 19–21 January 2000. European Commission, Directorate General JRC, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. ECBI/19/00 – Rev. 1. Available from: http://ecb.jrc.it/classlab/SummaryRecord/1900r1_sr_CMR0100.doc

European Commission. 2001. 2-Butanone oxime. Commission Directive 2001/59/EC of 6 August 2001. Annex IB. Official Journal of the European Communities. 21.08.2001. L 225/36. European Commission. 28th ATP [Adaptation to Technical Progress]. Available from: http://www.legaltext.ee/text/en/PH0711.htm

European Commission. 2004. Commission Directive 2004/93/EC of 21 September 2004 amending Council Directive 76/768/EEC for the purpose of adapting its Annexes II and III to technical progress (text with EEA relevance). Official Journal of the European Union. 25/09/2004. L 300/13–41. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32004L0093:EN:HTML

Friedewald M, Filser J, Janku S, Derelanko M, Dekant W. 2001. RNA-modifications after inhalation of methyl ethyl ketoxime in rats. Toxicologist 1: 93 [abstract].

Great Western Containers. 2005. Operations manual: Standard for return of empty IBC [Internet]. Edmonton (AB): Great Western Containers, Inc. [issued 2005 May 2; cited 2009 May 12]. Available from: http://www.gwcontainers.com/Portals/0/Return%20Standards.pdf

Haskell Laboratory. 1966. Laboratory report on methylethylketoxime with cover letter dated 021087. Study report 53-66, conducted for Du Pont Company; TSCA OTS0510675, Document ID: 86870000199.

Henkel Technologies. 2007. Material safety data sheet: Loctite Ready Gasket Silicone Rubber Sealant. Mississauga (ON): Henkel Canada, Inc. [cited 2009 May 20]. Available from http://henkelconsumerinfo.com/products/henkel.datasheets.Search.pdf?BUSAREA=0006&DOCTYPE=MSDS&LANG=EN&COUNTRY=CA&MATNR=743914&VKORG=3400

[HENRYWIN] Henry's Law Constant Program for Microsoft Windows [Estimation Model]. 2008. Version 3.20. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Honeywell International Inc. 2000. Biotransformation, toxicokinetics and DNA-binding of methyl ethyl ketoxime and its metabolites. Work conducted by W. Dekant and J.G. Filser. Report No.: MA-RR-00-2602. [cited in ICCA MEKO 2003].

[HYDROWIN] Hydrolysis Rates Program for Microsoft Windows [Estimation Model]. 2008. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

[ICCA MEKO] International Council of Chemical Associations Methyl Ethyl Ketoxime Consortium. 2003. Unpublished draft (23 July 2003) SIDS [Screening Information Data Set] initial assessment report on 2-butanoneoxime, CAS# 96-29-7. Prepared for Organisation for Economic Co-operation and Development SIAM [SIDS Initial Assessment Meeting] 17 by ICCA MEKO Consortium. Sponsored by the United States and Japan/ICCA.

[IHF Inc.] Industrial Health Foundation, Inc. 1995. Unscheduled DNA synthesis assay in rat primary hepatocytes. Rockville (MD): Microbiological Associates, Inc. Project No.: G94BA66.380. [cited in ICCA MEKO 2003].

[Japan MHW] Ministry of Health and Welfare (JP). 1996. Toxicity Testing Reports of Environmental Chemicals 4. p. 199–221. [cited in ICCA MEKO 2003].

[Japan MHW] Ministry of Health and Welfare (JP). 1998. Toxicity Testing Reports of Environmental Chemicals 6. p. 63–75. [cited in ICCA MEKO 2003].

[JETOC] Japan Chemical Industry Ecology-Toxicology and Information Center. 1999. JETOC Information Sheet 37, Special Issue No. 4.

Kaiser KLE, Ribo JM. 1988. *Photobacterium phosphoreum* toxicity bioassay. II. Toxicity data compilation. Toxic Assess 3: 195–237.

King CV, Marion AP. 1944. The ionization constants of very weak acids. Acetoxime, methyl ethyl and diethyl ketoximes. J Am Chem Soc 66(6): 977–980.

Klasmeier J., M. Matthies, M. MacLeod, K. Fenner, M. Scheringer, M. Stroebe, A. C. Le Gall, T. McKone, D. van de Meent, and F. Wania. 2006. Application of Multimedia Models for Screening Assessment of Long-Range Transport Potential and Overall Persistence. Environmental Science and Technology: 40(1), 53-60.

[KOAWIN] Octanol Air Partition Coefficient Program for Microsoft Windows [Estimation Model]. 2008. Version 1.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

[KOCWIN] Soil Adsorption Coefficient Program for Windows [Estimation Model]. 2008. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2009 May 1]. Available from: http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Kurita H. 1967. Experimental studies on methyl-ethyl-ketoxime toxicity. Nagoya J Med Sci 29: 393–418. [cited in US EPA 1986].

Lide DR, editor. 2005. CRC handbook of chemistry and physics. 86th ed. Boca Raton (FL): CRC Press/Taylor and Francis.

Mackay, D. 2006. The OECD Persistence and Long Range Transport Potential Screening Tool, Paper prepared for distribution at an OECD workshop held in Ottawa, Canada, May 31 to June 2, 2006.

Mercieca MD, Rinehart WE, Hodgson JR, Derelanko MJ. 1991. Developmental toxicity study of methyl ethyl ketoxime (MEKO) in two species. Teratology 43: 454–455.

Microbiological Associates Inc. 1990. Acute in-vivo cytogenetics assay in rats. MBA study T9293.105009. Committed by USA producers and importers of MEKO, in regard of EPA final test rule under TSCA. Bethesda (MD): Microbiological Associates Inc. [cited in ICCA MEKO 2003].

[MITI] Ministry of International Trade & Industry (JP), Basic Industries Bureau, Chemical Products Safety Division. 1992. Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan. Tokyo (JP): Japan Chemical Industry Ecology-Toxicology & Information Center.

[NCI] National Chemical Inventories [database on CD-ROM]. 2006. Columbus (OH): American Chemical Society. Available from: http://www.cas.org/products/cd/nci/index.html

Newton PE, Wooding WL, Bolte HF, Derelanko MJ, Hardisty JF, Rinehart WE. 2001. A chronic inhalation toxicity/oncogenicity study of methylethylketoxime in rats and mice. Inhal Toxicol 13: 1093–1116.

Newton PE, Bolte HF, Derelanko MJ, Hardisty JF, Rinehart WE. 2002. An evaluation of changes and recovery in the olfactory epithelium in mice after inhalation exposure to methylethylketoxime. Inhal Toxicol 14: 1249–1260.

[NRPI] National Pollutant Release Inventory [database on the Internet]. 2007. Gatineau (QC): Environment Canada. [cited 2008 Mar 18]. Available from: http://www.ec.gc.ca/inrp-npri/

[NTP] National Toxicology Program (US). 1999. NTP technical report on the toxicity studies of methyl ethyl ketoxime (CAS No. 96-29-7) administered in drinking water to F344/N rats and B6C3F1 mice. Research Triangle Park (NC): US Department of Health and Human Services, National Toxicology Program. Toxicity Report Series No. 51, NIH Publication 99-3947.

[OECD] Organisation for Economic Co-operation and Development. 2003. SIDS [Screening Information Data Set] Initial Assessment Profile for 2-Butanone oxime (MEKO) (CAS No. 96-29-7). SIAM [SIDS Initial Assessment Meeting] 17, 11-14 November 2003. Available from: http://cs3-hq.oecd.org/scripts/hpv/index.asp

[OECD] Organisation for Economic Co-operation and Development. 2004. The 2004 OECD list of high production volume chemicals. Available from: http://www.oecd.org/dataoecd/55/38/33883530.pdf

[OECD] Organisation for Economic Co-operation and Development. 2008. SIDS [Screening Information Data Set] Initial Assessment Profile for Bis(hydroxylammonium)sulphate . SIAM [SIDS Initial Assessment Meeting] 27, 14–16 October 2008. .Available from: http://cs3-hq.oecd.org/scripts/hpv/index.asp

Permatex Canada. 2009. Material safety data sheet: Ultra Black Gasket Maker. Milton (ON): Permatex Canada, Inc. [cited 2009 May 20]. Available from: http://www.permatex.com/documents/msds/03_Canada-English/82080_03.pdf

Rogers-Back AM, Lawlor TE, Cameron TP, Dunkel VC. 1988. Genotoxicity of six oxime compounds in the *Salmonella*/mammalian-microsome assay and mouse lymphoma TK +/− assay. Mutat Res 204: 149–162.

[RTECS] Registry of Toxic Effects of Chemical Substances. 2006. Record for 2-butanone, oxime (96-29-7). [updated 2006 Aug; cited 2009 Mar 16]. Cincinnati (OH): US Department of Health and Human Services, National Institute for Occupational Safety and Health.

Rumpf RR, Gonzalez W. 1993. No single answer controls corrosion. Power Eng. 97:33-35

Scheringer, M.; M. MacLeod; and F. Wegmann. 2006. The OECD P_{OV} and LRTP Screening Tool. Version 2.0

Schulze GE, Derelanko MJ. 1993. Assessing the neurotoxic potential of methyl ethyl ketoxime in rats. Fundam Appl Toxicol 21: 476–485. [cited in ICCA MEKO 2003].

Springborn Laboratories. 1990a. Teratology studies in rats with MEKO. Study SLS 3224.6. Test performed by Springborn Laboratories, Inc. (SLS) Spencerville, USA [cited in ICCA MEKO, 2003].

Springborn Laboratories. 1990b. Teratology studies in rabbits with MEKO. Study SLS 3224.5. Springborn Laboratories, Inc. [cited in ICCA MEKO 2003].

Subramani S, Cheong IW, Kim JH. 2004. Synthesis and characterizations of silylated polyurethane from methyl ethyl ketoxime-blocked polyurethane dispersion. Eur Polymer J 40: 2745–2755.

[TaPL3] Long Range Transport and Persistence Level III model [Internet]. 2000. Version 2.10. Peterborough (ON): Trent University, Canadian Centre for Environmental Modelling and Chemistry. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/TaPL3.html

[TOPKAT] TOxicity Prediction by Komputer Assisted Technology [Internet]. 2004. Version 6.2. San Diego (CA): Accelrys Software Inc. [cited 2009 Mar 3]. Available from: http://www.accelrys.com/products/topkat/index.html

Tyl RW, Gerhart JM, Marr MC, Brine DR, Gilliam AF, Seely JC, Derelanko MJ, Rinehart WE. 1996. Reproductive toxicity evaluation of methylethyl ketoxime by gavage in CD rats. Fundam Appl Toxicol 31: 149–161.

U.K. Secretary of State. 2008. The Cosmetic Products (Safety) Regulations 2008. Statutory Instruments, 2008 No. 1284, Consumer Protection. 144 p. Available from: http://www.opsi.gov.uk/si/si2008/uksi_20081284_en_1

[US EPA] US Environmental Protection Agency. 1986. Nineteenth report of the Interagency Testing Committee to the Administrator; receipt and request for comments regarding priority list of chemicals. Fed Register 51(220): 41417–41432. Available from: http://tsca-itc.syrres.com/itcrep/docs/19.pdf

[US EPA] US Environmental Protection Agency. 2006. High production volume (HPV) challenge program: the 1990 HPV voluntary challenge chemical list. Revised January 20, 2006. Washington (DC): US EPA, Office of Pollution Prevention and Toxics. Available from: http://www.epa.gov/chemrtk/pubs/update/hpv_1990.pdf

Verschueren K. 1977. Handbook of environmental data on organic chemicals. New York (NY): Van Nostrand Reinhold Company.

Völkel W, Wolf N, Derelanko M, Dekant W. 1999. Slow oxidation of acetoxime and methylethyl ketoxime to the corresponding nitronates and hydroxy nitronates by liver microsomes from rats, mice and humans. Toxicol Sci 47: 144–150.

[WPEM] Wall Paint Exposure Assessment Model. 2001. Version 3.2 (developed by GEOMET Technologies Inc., a Division of Versar, Inc., Germantown, MD). Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; National Paint and Coatings Association. Available from http://www.epa.gov/oppt/exposure/pubs/wpem.htm

Appendix 1: Upper-bounding estimates of exposure to butanone oxime in consumer products

Type of product	Assumptions[1]	Exposure estimates[2]
Alkyd paint (high solid)	Maximum butanone oxime concentration: 1% w/w[3] **Inhalation[4]:** exposure frequency of 1/year, applied amount of 1300 g, release area of 1.0 × 10^5 cm^2, molecular weight matrix of 550 g/mol, mass transfer rate of 4000 m/min. **Dermal: direct contact with product at constant rate:** exposed area of 0.367 m^2, contact rate of 30 mg/min, release duration of 120 min, uptake fraction of 29%[5]	Inhalation mean event concentration: 113 mg/m^3 Inhalation acute (internal) dose: 2.36 mg/kg-bw Inhalation chronic (internal) dose: 0.006 46 mg/kg-bw per day Dermal load: 0.009 81 mg/cm^2 Dermal external dose: 0.508 mg/kg-bw Dermal acute (internal) dose: 0.147 mg/kg-bw Dermal chronic (internal) dose: 0.000 403 mg/kg-bw per day Integrated total external dose: 2.87 mg/kg-bw Integrated total acute dose: 2.51 mg/kg-bw Integrated total chronic dose: 0.006 87 mg/kg-bw per day
Alkyd paint (solvent rich)	Maximum butanone oxime concentration: 1% w/w[3] **Inhalation[4]:** exposure frequency of 1/year, applied amount of 1300 g, release area of 1.0 × 10^5 cm^2, molecular weight matrix of 300 g/mol, mass transfer rate of 4000 m/min **Dermal: direct contact with product at constant rate:** exposed area of 0.367 m^2, contact rate of 30 mg/min, release duration of 120 min, uptake fraction of 29%[5]	Inhalation mean event concentration: 72.7 mg/m^3 Inhalation acute (internal) dose: 1.52 mg/kg-bw Inhalation chronic (internal) dose: 0.004 17 mg/kg-bw per day Dermal load: 98.1 mg/cm^2 Dermal external dose: 0.508 mg/kg-bw Dermal acute (internal) dose: 0.147 mg/kg-bw Dermal chronic (internal) dose: 0.000 403 mg/kg-bw per day Integrated total external dose: 2.03 mg/kg-bw Integrated total acute dose: 1.67 mg/kg-bw Integrated total chronic dose: 0.004 57 mg/kg-bw per day
Alkyd paint (aerosol)	Maximum butanone oxime concentration: 1% w/w[3] **Inhalation: exposure to spray, spraying away from exposed person:** exposure frequency of 2/year, exposure duration of 20 min, room volume of 34 m^3, ventilation rate of 1.5/h, mass generation rate of 0.33 g/s, spray duration of 15 min, airborne fraction of 1, weight fraction non-volatile of 0.3, density	Inhalation mean event concentration: 3.75 mg/m^3 Inhalation acute (internal) dose: 0.0119 mg/kg-bw Inhalation chronic (internal) dose: 0.000 065 2 mg/kg-bw per day Dermal load: 40.9 mg/cm^2 Dermal external dose: 0.212 mg/kg-bw Dermal acute (internal) dose: 0.0614

Type of product	Assumptions[1]	Exposure estimates[2]
	non-volatile of 1.5 g/cm^3, room height of 2.25 m, non-respirable uptake fraction of 100%, inhalation cut-off diameter of 15 µm **Dermal: direct contact with product at constant rate:** exposed area of 0.367 m^2, contact rate of 100 mg/min, release duration of 15 min, uptake fraction of 29%[5]	mg/kg-bw Dermal chronic (internal) dose: 0.000 336 mg/kg-bw per day Oral non-respirable (external) dose: 0.0112 mg/kg-bw Oral acute (internal) dose: 0.0112 mg/kg-bw Oral chronic (internal) dose: 0.000 061 1 mg/kg-bw per day Integrated total external dose: 0.235 mg/kg-bw Integrated total acute dose: 0.0844 mg/kg-bw Integrated total chronic dose: 0.000 462 mg/kg-bw per day
Alkyd coating	Maximum butanone oxime concentration: 1% w/w[3] **Inhalation:** exposure duration of 60 min, room volume of 34 m^2, ventilation rate of 1.5/h,[4] exposure frequency of 0.33/year, applied amount of 3000 g, release area of 15 m^2, molecular weight matrix of 3000 g/mol, mass transfer rate of 4000 m/min **Dermal: instant application:** exposed area of 108 cm^2, product amount of 0.25 g, uptake fraction of 29%[5]	Inhalation mean event concentration: 223 mg/m^3 Inhalation acute (internal) dose: 2.12 mg/kg-bw Inhalation chronic (internal) dose: 0.001 92 mg/kg-bw per day Dermal load: 0.0231 mg/cm^2 Dermal external dose: 0.0353 mg/kg-bw Dermal acute (internal) dose: 0.0102 mg/kg-bw Dermal chronic (internal) dose: 0.000 009 24 mg/kg-bw per day Integrated total external dose: 2.16 mg/kg-bw Integrated total acute dose: 2.13 mg/kg-bw Integrated total chronic dose: 0.001 93 mg/kg-bw per day
Silicone sealant (joint)	Maximum butanone oxime concentration: 5% w/w[6] **Inhalation: exposure to vapour: evaporation:** exposure frequency of 3/year, applied amount of 75 g, release area of 250 cm^2, molecular weight matrix of 3000 g/mol, mass transfer rate of 4000 m/min **Dermal: direct contact with product at constant rate:** exposed area of 2 cm^2, contact rate of 50 mg/min, release duration of 30 min, uptake fraction of 29%[5]	Inhalation mean event concentration: 150 mg/m^3 Inhalation acute (internal) dose: 1.07 mg/kg-bw Inhalation chronic (internal) dose: 0.008 81 mg/kg-bw per day Dermal load: 37.5 mg/cm^2 Dermal external dose: 1.06 mg/kg-bw Dermal acute (internal) dose: 0.307 mg/kg-bw Dermal chronic (internal) dose: 0.002 52 mg/kg-bw per day Integrated total external dose: 2.13 mg/kg-bw

Type of product	Assumptions[1]	Exposure estimates[2]
		Integrated total acute dose: 1.38 mg/kg-bw Integrated total chronic dose: 0.0113 mg/kg-bw per day
Adhesive (gasketing)	Maximum butanone oxime concentration: 2% w/w[7] **Inhalation: exposure to spray, spraying away from exposed person:** exposure frequency of 52/year, applied amount of 9 g, release area of 200 cm^2, molecular weight matrix of 3000 g/mol, mass transfer rate of 4000 m/min **Dermal: instant application:** exposed area of 2 cm^2, product amount of 0.08 g, uptake fraction of 29%[5]	Inhalation mean event concentration: 3.39 mg/m^3 Inhalation acute (internal) dose: 0.129 mg/kg-bw Inhalation chronic (internal) dose: 0.0184 mg/kg-bw per day Dermal load: 0.8 mg/cm^2 Dermal external dose: 0.0226 mg/kg-bw Dermal acute (internal) dose: 0.006 54 mg/kg-bw Dermal chronic (internal) dose: 0.000 932 mg/kg-bw per day Integrated total external dose: 0.152 mg/kg-bw Integrated total acute dose: 0.136 mg/kg-bw Integrated total chronic dose: 0.0193 mg/kg-bw per day

[1] For all calculations, an adult body weight of 70.9 kg and an inhalation rate of 16.2 m^3/day are assumed.
[2] Exposure estimate was calculated "per event": acute exposure during use of product.
[3] Maximum concentrations obtained [2009 personal communication from Canadian Paints and Coatings Working Group to Environment Canada; unreferenced]
[4] The following assumptions were applied: Inhalation model was based on "exposure to vapour by evaporation" with the following default parameters: exposure duration of 132 min, room volume of 20 m^3, ventilation rate of 0.6/h, application duration of 120 min and uptake fraction of 100%.
[5] Henkel Technologies 2007.
[6] Permatex Canada 2009.
[7] Burka et al. 1998.

Appendix 2: Summary of health effects information for butanone oxime

Endpoints	Lowest effect levels[1]/Results
Acute toxicity	**Lowest oral LD_{50}** (rat) = 930 mg/kg-bw (Biosearch Inc. 1982). **Other oral LD_{50}s** = >900–2528 mg/kg-bw in three studies (ICCA MEKO 2003). **LOEL** = 300 mg/kg-bw based on transient neurotoxic effects in rats; 10 rats per sex per group dosed at 0, 100, 300 or 900 mg/kg-bw with 14-day observation period (no other effects observed) (Schulze and Derelanko 1993). **Lowest inhalation LC_{50}** (rat, 4 h) = >4800 mg/m^3. **LOAEC** = 190 mg/m^3, based on statistically significant decreased body weight gain in females in the observation period after exposure (7 or 14 days); 5 rats per sex per group were exposed to 0, 190, 1450 or 4800 mg/m^3. Other effects included methemoglobin formation at middle and high concentrations and evidence of anesthesia at high concentration (Allied Corporation 1984b). **Other inhalation LC_{50}** (rat, 2 h) = >10 500 mg/m^3 (OECD 2003). **Lowest dermal LD_{50}** (rabbit) = 184 mg/kg-bw (RTECS 2006). **Other dermal LD_{50}s** = 1000 and between 180 and 1800 mg/kg-bw in two studies (ICCA MEKO 2003). **LOAEL** = 180 mg/kg-bw based on methemoglobin production and splenic erythrophagocytosis in rabbits (LOEL = 18 mg/kg-bw based on reversible narcotic effects) (24-h exposure). Five rabbits per sex per group dosed at 0, 18, 180 or 1800 mg/kg-bw for 24 h under occlusive skin application (no other effects observed) (Allied Corporation 1984a; US EPA 1986).
Short-term repeated-dose toxicity	**Lowest inhalation LOAEC** = 107 mg/m^3 (30 ppm), based on degeneration of the olfactory epithelium of the nasal cavity (incidence and severity increased with increasing exposure concentration) in male CD-1 mice exposed whole body to 0, 3, 10, 30 or 100 ppm (0, 11, 36, 107 or 356 mg/m^3), 6 h/day, 5 days/week, for 1, 2 or 4 weeks (10 males per concentration per time point) (Newton et al. 2002). **Other inhalation LO(A)ECs** = 356–1899 mg/m^3 in rats or mice (Haskell Laboratory 1966; Dow Corning Corporation 1983; Bio/Dynamics Inc. 1990). **Lowest oral LO(A)EL** = 20 mg/kg-bw per day, based on hematological changes (increase in reticulocytes, platelets and red blood cells), increased relative spleen weight with accompanying histopathological abnormalities (increases in congestion, extramedullary hematopoiesis and hemosiderin granules) in both sexes and hemosiderin granules in livers of females in Crj:CD (SD) rats dosed by gavage (in olive oil) at 0, 4, 20 or 100 mg/kg-bw per day by gavage for 28 days (Japan MHW 1996; JETOC 1999). **Other oral LO(A)EL** = 250 mg/kg-bw per day, based on hypertrophy of the liver in male Fischer 344 rats dosed by gavage (15 males per dose) at 0, 250 or 500 mg/kg-bw per day for 28 days (Allied Signal Inc. 1995). No dermal studies were identified.

Endpoints	Lowest effect levels[1]/Results
Subchronic toxicity	**Lowest inhalation LOAEC** = 36 mg/m^3, based on degeneration of the olfactory epithelium in the nasal cavity (incidence and severity increased with increasing exposure concentration) in male CD-1 mice exposed by inhalation (whole body) to 0, 3, 10, 30 or 100 ppm (0, 11, 36, 107 or 356 mg/m^3), 6 h/day, 5 days/week, for 13 weeks (10 males per concentration per time point) (Newton et al. 2002). **Other inhalation LO(A)EC** = 267 mg/m^3, based on increased relative liver weight in males in F344 rats (10 per sex per concentration) exposed to 0, 15, 75 or 374 ppm (0, 53, 267 or 1333 mg/m^3), 6 h/day, 5 days/week, for 3 months (Newton et al. 2001). **Lowest oral LO(A)EL** = 25 mg/kg-bw per day, based on increased relative liver weight in males in one 13-week rat study (NTP 1999: male and female F344/N rats dosed at 0, 312, 625, 1250, 2500 or 5000 ppm in drinking water for 13 weeks, equal to 0, 25, 50, 100, 175 or 280 mg/kg-bw per day in males; 0, 30, 65, 120, 215 or 335 mg/kg-bw per day in females) and changes in liver and spleen weights, hemosiderosis of spleen and hematological effects in another 13-week rat study (Allied Signal Inc. 1977: male and female Sprague-Dawley rats dosed at 0, 25, 75 or 225 mg/kg-bw per day by gavage, 5 days/week for 13 weeks). **Other oral LOAELs** = 40 mg/kg-bw per day in a 13-week rat study (Schulze and Derelanko 1993) and 200 mg/kg-bw per day in a 13-week mouse study (NTP 1999). No dermal studies were identified.
Chronic toxicity/ carcinogenicity	**Inhalation study in rats:** Groups of 50 F-344 rats per sex were exposed to butanone oxime by inhalation (whole body) at 0, 15, 75 or 374 ppm (0, 53, 267 or 1333 mg/m^3) 6 h/day, 5 days/week, for 26 months. There was an increased incidence of liver tumours in both sexes at 75 and 374 ppm (males: liver carcinomas 0/50, 0/50, 1/50 and 12/50 at 0, 15, 75 and 374 ppm, respectively; statistically significant at 374 ppm; liver adenomas 0/50, 2/50, 5/50 and 18/50, respectively; statistically significant at 75 and 374 ppm; females: liver adenomas 0/50, 0/50, 2/50 and 4/50, respectively; not statistically significant) and in mammary gland fibroadenomas in females at the highest dose (2/50, 2/50, 4/50 and 9/50 at 0, 15, 75 and 374 ppm, respectively; statistically significant at 374 ppm). **Non-neoplastic LOAEC** = 53 mg/m^3 (15 ppm), based on effects in the spleen (congestion, increased pigmentation in the reticuloendothelial cells and extramedullary hematopoiesis) first observed at 12 months and in the nasal turbinates (degeneration of the olfactory epithelium) observed at 18 months. Other non-neoplastic effects included increased incidences of basophilic foci and hepatocyte vacuoles in the liver of males at 75 and 374 ppm and in females at 374 ppm, enlarged testes in males at 75 and 374 ppm and blood effects (decreases in hemoglobin and red blood cells, increases in methemoglobin, platelets and white blood cells) in both sexes at 374 ppm (Newton et al. 2001). **Other inhalation studies:** Groups of 50 CD-1 mice per sex were exposed to butanone oxime by inhalation (whole body) at 0, 15, 75 or 374 ppm (0, 53, 267 or 1333 mg/m^3) 6 h/day, 5 days/week, for 18 months. There was an increased incidence of liver tumours in males at all doses and in females at 75 and 374 ppm (males: liver carcinomas 2/50, 2/50, 1/50 and 10/50 in control, low-, mid- and high-dose groups, respectively, statistically significant at 374 ppm; liver adenomas 4/50, 11/50, 10/50, 11/50, respectively, but within historical control range; females: liver adenomas 0/50, 0/50, 1/50, 3/50 in control, low-, mid- and high-dose groups, respectively, none of which were statistically significant). **Non-neoplastic LOAEC** = 53 mg/m^3 (15 ppm), based on dose-related effects observed in liver (hypertrophy and necrosis) and in the nasal turbinates (degeneration of the olfactory epithelium) observed at both 12 and 18 months. Other non-neoplastic effects

Endpoints	Lowest effect levels[1]/Results
	included changes in blood (dose-related increase in methemoglobin in males, slight decrease in hemoglobin in females at 75 and 374 ppm, increased platelets in both sexes at 374 ppm) and serum chemistry parameters (decreased chloride and increased creatinine, total protein and albumin in males at 374 ppm; and increased liver enzyme levels in females at 374 ppm) observed at 12 months (Newton et al. 2001). No oral or dermal studies were identified.
Reproductive toxicity	**Lowest LOAEL for reproductive toxicity:** 100 mg/kg-bw per day, based on statistically significant decrease in female delivery index (%) ([no. of pups born/no. of implantations] × 100) in male and female Crj: CD (Sprague-Dawley) rats exposed by gavage to 0, 10, 30 or 100 mg/kg-bw per day in a one-generation study (males treated for 48 days prior to mating; females treated from 14 days prior to mating until day 3 of lactation). **LOAEL for systemic toxicity** = 10 mg/kg-bw per day, based on histopathological abnormalities of spleen, liver and kidney in both sexes (Japan MHW 1998). **Other oral study:** Male and female CD (Sprague-Dawley) rats were exposed by gavage to 0, 10, 100 or 200 mg/kg-bw per day in a two-generation study (F_0 and F_1 males and females treated daily from 10–11 weeks prior to mating, during a 3-week mating period and then throughout pregnancy and until day 21 of lactation). No treatment-related effects on reproductive parameters were observed. **LOAEL for systemic toxicity** = 10 mg/kg-bw per day based on effects in the spleen (hematopoietic cell proliferation, pigmentation and congestion) and liver (hematopoiesis and pigmentation) in both sexes of F_0 and F_1 adults (Tyl et al. 1996). No inhalation or dermal studies were identified.
Developmental toxicity	**Lowest oral LOAEL** = 40 mg/kg-bw per day, based on abortions in 3/10 adult females in pregnant New Zealand White rabbits dosed by gavage during days 6–18 of gestation to 0, 8, 14, 24 or 40 mg/kg-bw per day (the highest dose "did not appear to be teratogenic," although complete evaluation of developmental toxicity was not possible). **LOAEL for maternal toxicity** = 40 mg/kg-bw per day, based on 8/18 deaths (Springborn Laboratories 1990b; Derelanko et al. 2003). **Other oral studies:** The range-finding study in New Zealand White rabbits (dosed during gestation days 6–18) did not find evidence of developmental toxicity at doses of 0–80 mg/kg-bw per day, although the **LOAEL for maternal toxicity** = 10 mg/kg-bw per day, based on signs of anemia in the dams at all dose levels. At 10 mg/kg-bw per day, the increase in methemoglobin and reticulocytes appeared at day 13 of gestation and progressively increased with time until day 19 of gestation (3 days after the end of exposure) (Springborn Laboratories 1990b; Derelanko et al. 2003). Two studies in Sprague-Dawley rats (dosed during gestation days 6–15) resulted in **NOAELs** of 400 and 600 mg/kg-bw per day for developmental toxicity and maternal toxicity **LOAELs** of 25 mg/kg-bw per day, based on signs of anemia, and 60 mg/kg-bw per day, based on spleen enlargement (Springborn Laboratories 1990a; Mercieca et al. 1991; Derelanko et al. 2003). No inhalation or dermal studies were identified.
Genotoxicity and related endpoints: *in vivo*	**Micronuclei** **Negative:** bone marrow cells, Sprague-Dawley rats, oral (300, 600 or 1200 mg/kg-bw) (Microbiological Associates Inc. 1990). **Negative:** peripheral blood cells, B6C3F1 mice, oral (0, 625, 1250, 5000 or 10 000 mg/L in drinking water, equal to 0, 128, 270, 573, 883 or 2250 mg/kg-bw per day; assay conducted on mice from 13-week study) (NTP 1999). **DNA and RNA adducts**

Endpoints	Lowest effect levels[1]/Results
	Negative for DNA adducts; positive for RNA adducts: liver cells, rats (strain not stated), inhalation (0, 375 or 1000 ppm [0, 1336 or 3563 mg/m^3]) (Honeywell International Inc. 2000; Friedewald et al. 2001).
Genotoxicity and related endpoints: *in vitro*	**Mutagenicity in bacteria** **Negative:** *Salmonella typhimurium* strains TA97, TA98, TA100, TA1537 and TA1538 with and without S9 activation (Allied Corporation 1983b; Rogers-Back et al. 1988; JETOC 1999; NTP 1999). **Equivocal:** *S. typhimurium* TA1535 positive in presence of hamster liver S9 but not in presence of rat liver S9; negative without S9 (NTP 1999). **Negative:** *S. typhimurium* strains TA98 and TA100 with and without S9; tested as a vapour by placing plates in a desiccator (NTP 1999). **Mammalian cell mutation assay** **Positive:** Mouse lymphoma L5178Y TK+/− with and without S9 (Rogers-Back et al. 1988). **Chromosomal aberration assay** **Negative:** Chinese hamster ovary cells with and without S9 (NTP 1999). **Negative:** Chinese hamster lung cells with and without S9 (JETOC 1999). **Sister chromatid exchange assay** **Negative:** Chinese hamster ovary cells with and without S9 (Allied Corporation 1983a; NTP 1999). **Unscheduled DNA synthesis assay** **Negative:** Rat hepatocytes (IHF Inc. 1995).
Human studies	No relevant human studies were identified.

[1] LC_{50}, median lethal concentration; LD_{50}, median lethal dose; LOAEL/LOAEC, lowest-observed-adverse-effect level/concentration; LOEL/LOEC, lowest-observed-effect level/concentration; NOAEL/NOAEC, no-observed-adverse-effect level/concentration.