Screening Assessment for the Challenge

Nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]-

Chemical Abstracts Service Registry Number
42739-61-7

Environment Canada
Health Canada

January 2011

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 on nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]- (herein referred to as nickel BHMB), Chemical Abstracts Service Registry Number 42739-61-7; this substance will be referred to by its derived acronym, nickel BHMB, in this assessment. Nickel BHMB was identified as a high priority for screening assessment and included in the Ministerial Challenge initiative under the Chemicals Management Plan because it had been found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and is believed to be in commerce in Canada.

The substance, nickel BHMB, was not initially considered to be a high priority for assessment of potential risks to human health, based upon application of the simple exposure and hazard tools developed for categorization of substances on the Domestic Substances List.

Nickel BHMB is an organometallic substance that is currently used in Canada primarily as a nickel alloy component for welding. In the past it was reported to be used in Canada as a colourant, which is consistent with the known use of a chemically similar substance, nickel, bis[2,3-bis(hydroxyimino)-N-phenylbutanamidato-N,N (herein referred to as (nickel BBHP) Chemical Abstracts Service Registry Number 29204-84-0, as a pigment. The substance is not naturally produced in the environment. It is not reported to be manufactured in Canada or imported into the country, and while it was reported to be used in Canada in 2006, it was at a volume below 1000 kg.

Based on certain assumptions and reported use patterns in Canada, most of the substance is chemically destroyed (chemically transformed) in the welding process. Some unused portion of the reported total mass in commerce (less than 1000 kg) may end up in waste disposal sites and a negligible amount may be conservatively estimated to be released to water. Nickel BHMB has a very low modelled solubility, consistent with the low modelled and experimental solubility of its analogue, nickel BBHP in water. Like many substances used as pigments, nickel BHMB is expected to be present in the environment primarily as chemically stable micro-particulate matter that is not volatile, and has a tendency to partition by gravity to sediments if released to surface waters, and to soils if released to air.

Based on its physical and chemical properties, nickel BHMB is expected to be persistent in the environment. No experimental, bioconcentration or bioaccumulation data were available for this organometallic substance. While quantitative structure-activity relationship models for bioconcentration and bioaccumulation were deemed to have high degrees of uncertainty, as nickel BHMB was outside of the model domains of applicability, they were used as a lower weighted line of evidence. The metabolism corrected models showed a low potential for bioaccumulation and bioconcentration

(<5000 L/kg). Qualitative lines of evidences that were relied upon included the physical and chemical properties of nickel BHMB as well as knowledge of the general qualities of pigment-like substances. Since nickel BHMB, with a high molecular weight, has a very high cross-sectional diameter, it is expected to have limited bioavailability. In addition, the high thermal decomposition and boiling point of nickel BHMB suggest that the substance is relatively inert and is not likely to be highly bioavailable. The weight of evidence (both modelled and qualitative) therefore suggests that this substance does not have significant potential to bioconcentrate or bioacccumulate.

The substance therefore meets the persistence criteria but does not meet the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations of the Canadian Environmental Protection Act*.

For this screening assessment, a very conservative generic exposure scenario was used in which an industrial operation (user of the substance) discharges nickel BHMB into the aquatic environment. A risk quotient analysis, integrating a conservative predicted environmental concentration with a predicted no-effect concentration, indicated that current concentrations of nickel BHMB in water are unlikely to cause ecological harm in Canada. The predicted environmental concentration in water was nearly two orders of magnitude below predicted no-effect concentrations calculated for sensitive aquatic organisms.

Based on the information presented in this final screening assessment, it is concluded that nickel BHMB 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.

No empirical health effects data were identified for nickel BHMB or its analogue, nickel BBHP. The outputs of qualitative structure-activity relationship predictions for nickel BHMB and information on other nickel compounds, suggests potential hazardous properties (i.e., mutagenicity, carcinogenicity and skin and respiratory sensitization) of nickel BHMB.

Exposures of the general population to nickel BHMB through environmental media (air, drinking water and soil), including food and beverages, are expected to be negligible. General population exposure to nickel BHMB from use of consumer products is not expected. As exposure of the general population through environmental media in Canada is expected to be negligible, the risk to human health is considered to be low. It is therefore concluded that nickel BHMB is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information available, it is concluded that nickel BHMB does not meet the criteria set out in section 64 of CEPA 1999.

As nickel BHMB is listed on the Domestic Substances List, its import and manufacture in Canada are not subject to notification under subsection 81(1). Given the potential health hazards of this substance, there is concern that new activities that have not been identified or assessed could lead to this substance meeting the criteria set out in section 64 of the Act. Therefore, it is recommended to amend the Domestic Substances List, under subsection 87(3) of the Act, to indicate that subsection 81(3) of the Act applies with respect to this substance, so that new manufacture, import or use of this substance is notified and undergoes ecological and human health risk assessments.

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 in Canada; 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), that 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 Nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]- was identified as a high priority for assessment of ecological risk as it was found to be persistent, bioaccumulative and inherently toxic to aquatic organisms and is believed to be in commerce in Canada. The Challenge for this substance was published in the *Canada Gazette* on June 20, 2009 (Canada 2009). 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 pertaining to the uses of the substance were received.

Although Nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]- was determined to be a high priority for assessment with respect to the environment, it did not meet the criteria for GPE or IPE and high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution. [1]

This final 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, stakeholder research reports and from recent literature searches, up to February-March 2010 for the ecological and human health sections of the document. Key studies were critically evaluated; modelling results may have been used to reach conclusions.

When available and relevant, information presented in hazard assessments from other jurisdictions was considered. The final screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the conclusion.

This final 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. The ecological portion of this assessment has undergone external written peer review/consultation.

Additionally, the draft of this screening assessment was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment Canada. Approaches used in the screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel.

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

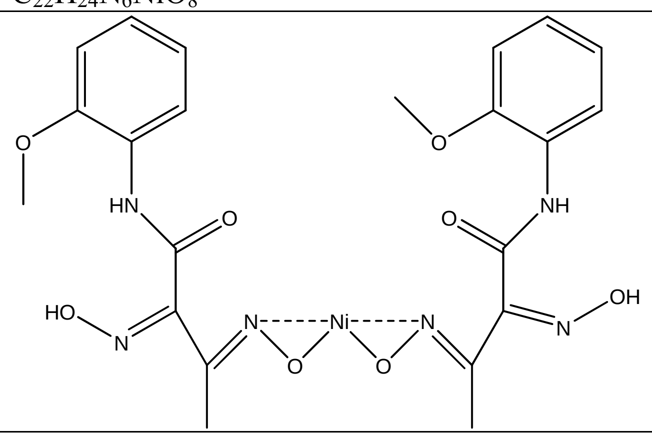
[1] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the Controlled Products Regulations, which is part of regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA 1999 does not preclude actions being taken under other sections of CEPA or other Acts.

Substance Identity

Substance name

For the purposes of this document, this substance will be referred to as nickel BHMB, derived from the Domestic Substances List (DSL) name.

Table 1. Substance identity for nickel BHMB

Chemical Abstracts Service Registry Number (CAS RN)	**42739-61-7**
DSL name	**Nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]-**
National Chemical Inventories (NCI) names[1]	*Nickel, bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butanamidato]-* (AICS, ASIA-PAC); *Bis[2,3-bis(hydroxyimino)-N-(2-methoxyphenyl)butyramidato]nickel* (EINECS)
Other names	none
Chemical group (DSL Stream)	Discrete organometallics
Major chemical class or use	Nickel containing compounds; Amides
Chemical formula	$C_{22}H_{24}N_6NiO_8$
Chemical structure	
SMILES[2]	[Ni](ON=C(C)C(=NO)C(=O)Nc2c(OC)cccc2)ON=C(C)C(=NO) C(=O)Nc1c(OC)cccc1
Molecular mass	559.17 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); EINECS (European Inventory of Existing Commercial Chemical Substances).

[2] Simplified Molecular Input Line Entry System

Physical and Chemical Properties

Table 2a contains modelled physical and chemical properties of nickel BHMB that are relevant to its environmental fate. Experimental and modelled data for a similar chemical, a pigment with a CAS registry number 29204-84-0 and a chemical name of nickel, bis[2,3-bis(hydroxyimino)-N-phenylbutanamidato-N,N]-, referred to in this document as nickel BBHP, are also presented. Nickel BHMB and nickel BBHP are both nickel organometallics with amide functional groups and have similar overall chemical structures as shown in Table 2b. Therefore, nickel BBHP is used as an analogue substance that is expected to have similar physical-chemical properties, and to exhibit similar behaviour in the environment. Since no experimental data are available for nickel BHMB, where there are experimental data for nickel BBHP, these have been used directly (read-across) as an indicator of the values for nickel BHMB.

Organometallic chemicals such as nickel BHMB and pigments such as nickel BBHP are known to be difficult to model using quantitative structure-activity relationships (QSARs) (Macdonald et al. 2002, Zachary et al. 2009). Guidance stemming in part from a workshop organized by Environment Canada in 1999 on QSARs identified several properties of organometallics and pigments including indicators of persistence, bioaccumulation and aquatic toxicity that were deemed at that time to not be amenable to model prediction because they were considered "out of the model domain of applicability" (e.g., structural and/or property parameter domains) (Environment Canada 2007). Therefore, to determine the domain of applicability, the use of QSAR models to organometallics and pigments is reviewed on a case-by-case basis. For instance, if whole structure analogues are not present in the training data-set but substructures common to the organometallics or pigments exist, and if important factors such as molecular size are taken into account by the models then the predicted information may still be considered. Also, if the data predicted using a particular model correlates well with available experimental data, this gives more credence for the use of similarly formulated models for which no experimental data is available.

The models based on QSARs that were used to generate data for the physical and chemical properties of nickel BHMB are mainly based on fragment addition methods i.e. they rely on the structure of a chemical. The exception to this is WSKOWWIN (2008) which does not directly use a fragment addition method but is based on KOWWIN predicitions which are developed through fragment addition. Since these models only accept the neutral form of a chemical as input (in SMILES form), the modelled values shown in Table 2a are for the neutral form of nickel BHMB. Input parameters for the models used are presented in Appendix 1.

Table 2a. Physical and chemical properties for the neutral form of nickel BHMB as well as an analogue substance, nickel BBHP.

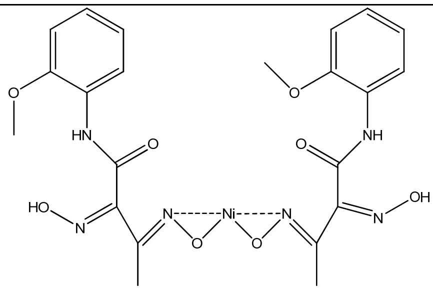
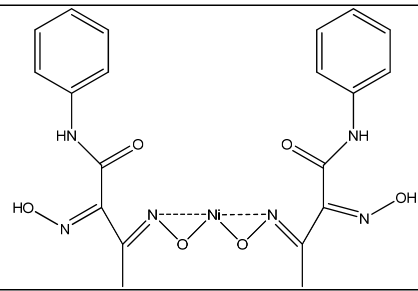
Chemicals	Type	Value[1]	Temperature (°C)	Reference
Physical State				
Nickel BBHP	Metal complex pigment (yellow in colour)	Experimental		BASF 2007[2]
Melting point[3] (ºC)				
Nickel BHMB	Modelled	349.84	-	MPBPWIN 2008
Nickel BBHP	Modelled	349.84		MPBPWIN 2008
	Experimental	> 285		BASF 2007
Thermal decomposition (ºC)				
Nickel BBHP	Experimental	>300		BASF 2007[2]
Boiling point (ºC)				
Nickel BHMB	Modelled	891.25	-	MPBPWIN 2008
Nickel BBHP	Modelled	843.84		MPBPWIN 2008
Density (kg/m^3)				
Nickel BHMB	-	Not available	-	-
Nickel BBHP	Experimental	Approx. 1600 kg/m^3 (Approx. 1.60 g/cm^3)	20	BASF 2007[2]
Vapour pressure (Pa)				
Nickel BHMB	Modelled	1.23×10^{-25} (9.23×10^{-28} mm Hg)	25	MPBPWIN 2008

Chemicals	Type	Value[1]	Temperature (°C)	Reference
Nickel BBHP	Modelled	5.44×10^{-24} (4.08e-26 mm Hg)	25	MPBPWIN 2008
Henry's Law constant ($Pa{\cdot}m^3/mol$)				
Nickel BHMB	Modelled	9.55×10^{-20} (9.43×10^{-25} $atm{\cdot}m^3/mol$)	25	HENRYWIN 2008[4]
Nickel BBHP	Modelled	1.030×10^{-17} (1.016×10^{-22} $atm{\cdot}m^3/mol$)	25	HENRYWIN 2008[4]
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)				
Nickel BHMB	Modelled	6.58[5]	25	KOWWIN 2008
Nickel BBHP	Modelled	7.54	25	KOWWIN 2008
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)				
Nickel BHMB	Modelled (estimated from log K_{ow})	4.63	25	PCKOCWIN 2008
Nickel BHMB	Modelled (estimated from MCI[5])	5.45	25	PCKOCWIN 2008
Nickel BBHP	Modelled (estimated from log K_{ow})	5.04	25	PCKOCWIN 2008
Nickel BBHP	Modelled (estimated from MCI[6])	5.82	25	PCKOCWIN 2008
Water solubility (mg/L)				

Chemicals	Type	Value[1]	Temperature (°C)	Reference
Nickel BHMB	Modelled	7.20×10^{-4}	25	WSKOWWIN 2008
Nickel BBHP	Experimental	Insoluble	unknown	BASF 2007[2]
Nickel BBHP	Modelled	2.636×10^{-4}	25	WSKOWWIN 2008
pK_a (Acid dissociation constant) (dimensionless)				
Nickel BHMB	Modelled	7.95 (result unreliable[7])		ACD/pK_a DB 2005

Abbreviations: K_{oc}, organic carbon-water partition coefficient; K_{ow}, octanol–water partition coefficient.
[1] Values in parentheses represent the original ones as reported by the authors or as estimated by the models
[2] This information was derived from a material safety data sheet for the product (Paliotol Yellow L 1772) of which nickel BBHP (CAS RN 29204-84-0) is the principal listed component. However, it is difficult to determine whether the value strictly applies to nickel BBHP or the product itself which may contain a proportion of sulphuric acid, barium salt (CAS RN 7727-43-7)
[3]While melting point and thermal decomposition point are both listed, it is likely that the substance thermally decomposes before melting can occur. Therefore, the melting point values should be interpreted as indicators of thermal decomposition.
[4]HENRYWIN resulted in incomplete results for Bond and Group approaches, Henry's Law Constant was calculated by HENRYWIN via vapour pressure divided by water solubility
[5] Used for bioaccumulation and bioconcentration modelling.
[6]First order molecular connectivity index
[7] Model output indicates that the "structure contains atoms that are not supported in this version".

Table 2b. Chemical structure, percentage similarity, molecular mass, cross-sectional diameter and a list of available empirical data for nickel BHMB and an analogue organometallic nickel compound (nickel BBHP).

CAS RN (Common Name)	Structure of analogue	Percentage Structural similarity with nickel BHMB[1]	Molecular mass (g/mol)	Minimum-maximum D_{max} (nm) [2]	Available empirical data
42739-61-7 (Nickel BHMB)		100	559.2	1.45-2.52	None
29204-84-0 (Nickel BBHP)		88.7	499.1	1.47-2.67	Physical state, melting point, thermal decomposition, density, water solubility

[1] From ChemID Plus 2010
[2] Based on range of maximum diameters (D_{max}) for 30 conformers calculated using CPOPs (2008).

Nickel BHMB and nickel BBHP closely resemble each other in chemical structure and only differ in that nickel BHMB has a methoxy group attached to each of its two benzene rings while nickel BBHP does not. Nickel BBHP is known to be an azomethine series pigment called Pigment Yellow 153 (CII 2002). Both nickel BHMB and nickel BBHP have molecular structures which are also similar to other known yellow, orange and red organometallic pigment complexes such as Pigment Yellow 179, Pigment Orange 65 and 68 as well as Pigment Red 257 and 271 (Herbst and Hunger 2004). This is significant, as much is known about the general physical and chemical properties of pigments.

Azomethine series metallic pigments are relatively free of solubilizing groups and are expected to have intermolecular interactions between the nitrogen and Ni molecules which induce planar conformational properties (Herbst and Hunger 2004). These planar structures allow molecules to stack into crystal lattices (Lincke 2003).

The pigment industry synthesizes organic pigments that typically have low to very low solubilities (i.e., < 1 mg/L and < 0.01 mg/L, respectively) in nearly all solvents (Herbst and Hunger 2004; Lincke 2003). This arises from the desire to produce colorants that will retain their colour for a long time and in various types of substrates. The majority of organic pigments generally do not exist as individual molecules in the environment, but are principally particles in the submicron range.

In developing a category approach for assessing nickel compounds in the European Union, nickel BHMB and nickel BBHP were both excluded from the main group of soluble nickel compounds that were expected to release bioavailable nickel ions (Hart 2008).

Since pigments tend to form stacked crystalline structures and tend to be relatively inert, these characteristics are important factors in determining their environmental fate, and in some cases are even more influential than their underlying specific chemical formulas. Nickel BHMB and its analogue nickel BBHP are thus expected to share many qualities with pigments in general, which tend to have high molecular weights (i.e., generally > 300 g/mol), are solid particles at room temperature, decompose at temperatures greater than 220^{o}C and have extremely low solubility in water (Danish EPA 1999). In addition, these substances generally have limited solubility in *n*-octanol, have a negligible vapour pressure and are stable under environmental conditions.

Sources

Nickel BHMB is not reported to occur naturally. According to the data submitted under the Challenge, in response to the section 71 survey for the year 2006, no manufacture or import of nickel BHMB was reported in Canada (Environment Canada 2009a). Fewer than four companies reported using the substance in Canada under the 1000 kg reporting threshold in 2006 (Environment Canada 2009a).

No manufacture or import of nickel BHMB was reported in a separate survey for the year 2005 (Environment Canada 2006).

Elsewhere, nickel BHMB is included in the list of low production volume nickel compounds in Europe and one German company is identified as an importer/producer of the substance (ESIS 2009).

Uses

Nickel BHMB has been reported to be used in Canada in dual shield low alloy flux cored welding electrodes and in stainless steel and nickel alloy covered electrodes.

Nickel BHMB has also been previously identified by Canadian DSL use codes as a colourant and for a potential use in plastics. Nickel BHMB is not currently listed on the Colour Index (CII 2002) which is a repository for a large amount of information on pigments, dyes and other colourants, nor does it appear in any known material safety data sheets (MSDS) as a colourant. Nickel BHMB is, as previously noted, chemically similar to nickel BBHP (CAS RN 29204-84-0) which is a known essential colourant in several pigments (e.g. C.I. Pigment Yellow 153 and Paliotol Yellow L 1772) and is listed on the Colour Index (CII 2002) as well as many other nickel based azomethine series pigments.

Nickel BHMB was not notified as an ingredient in cosmetic products in Canada (CNS 2010) and does not appear on the Cosmetic Ingredient Hotlist, Health Canada's administrative list of ingredients that are intended to be prohibited or restricted for use in cosmetics in Canada (Health Canada 2009). Nickel BHMB is not currently present in Canada as a formulant in pesticide products (PMRA 2007; March 2010 email from Pest Management Regulatory Agency, Health Canada to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced). Nickel BHMB is not listed as an approved food additive under Division 16 of the *Food and Drug Regulations* (Canada 1978). Nickel BHMB was not identified in food packaging applications or in incidental additives (January 2010 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). Nickel BHMB is not listed in the Drug Product Database (DPD), the Therapeutic Products Directorate's Non-Medicinal Ingredient Database, the Natural Health Products Ingredients Database or the Licensed

Natural Health Products Database as a medicinal or a non-medicinal ingredient present in final pharmaceutical products, natural health products or veterinary drugs (November 2009 to January 2010 emails from Therapeutic Products Directorate, Natural Health Products Directorate and Veterinary Drugs Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

Releases to the Environment

Based on the quantity of nickel BHMB in commerce in Canada (Environment Canada 2009a), releases of this substance are expected to be low. However, there is little specific information available regarding its industrial use and potential releases to the environment. In the absence of this information it is not possible to generate a quantitative life cycle analysis of losses/releases for this substance. Instead, a qualitative release scenario is presented based on its reported uses.

The sole use considered in this scenario is that of nickel BHMB as a component of nickel alloy covered electrodes which are considered to be used in the process of welding.

Exposure Scenario

Welding can result in a significant level of waste but welding waste can be easily recovered and either re-used in situ, or sent for recovery at a specialist organization. Welding waste that is not sent for recovery is disposed of as scrap metal waste or sent to landfill. The presence of dust is possible and it may be swept out to water. Therefore, releases from handling welding rods is possible but could be considered as a conservative assumption. To capture this potential loss due to handling, a default value of 0.01% is used in Emission Scenario Documents from the Organisation for Economic Co-operation and Development (OECD) where emissions are expected but considered as negligible and no available measurements can confirm it (OECD 2004).

In the process of welding, the temperatures are assumed to reach over 2000 ^{o}C which is well above the thermal decomposition and boiling points of nickel BHMB (Table 2a). This is because nickel alloys are commonly used when corrosion resistance is required. Nickel and nickel alloys are also widely used as filler metals for joining dissimilar materials and cast iron. The nickel alloys will acquire a surface oxide coating which melts at a temperature approximately 538^{o}C above the melting point of the base metal (Key to metals 2010). If iron (melting point of 1538^{o}C; Swartzendruber 1984) is assumed as the base metal, the temperature of welding with nickel should be over 2000 ^{o}C. For this reason it is highly probable that nickel BHMB will be destroyed during this operation and there would be no release of nickel BHMB. If nickel BHMB is destroyed during welding, release of the substance during the service life of the weld would also not be possible.

Elemental nickel from the nickel BHMB would not be consumed but the majority is expected to be incorporated into the welded material or into the welding waste product.

Conclusion

Release of nickel BHMB to water is expected from dust during handling operations but is considered as negligible (0.01%). Due to the high temperatures of the welding process, nickel BHMB is considered destroyed (chemically transformed) and therefore cannot be released.

Environmental Fate

As indicated by the results of the release scenario, only a conservative estimate (0.01%) of nickel BHMB may be released to water in Canada during its lifecycle.

The expected particulate character of nickel BHMB should have a key influence on its fate in the environment. Its high expected density (higher than water since the density of analogue nickel BBHP is approximately 1600 kg/m^3 vs. approximately 1000 kg/m^3 for water), together with its chemical stability (high thermal decomposition points of >300° C and boiling point of 894° C) and low aqueous solubility (Table 2a), indicate that it will tend to partition by gravity to sediments if released to surface waters, and will tend to remain in soils if released to terrestrial environments.

The pKa model output indicated that the "structure contains atoms that are not supported in this version", suggesting that the model results are unreliable. Because of this, and other evidence indicating that this compound is generally stable, has a high thermal decomposition point and very low solubility, and (like many pigments) exists mainly in a solid particulate form in nature, it is considered unlikely to ionize as suggested by the modelled pKa.

The relatively high estimated log K_{ow} values for nickel BHMB and nickel BBHP (6.58 and 7.54 respectively; see Table 2) indicate that these substances may have affinity for organic solids. Also, the MSDS for Paliotol Yellow L 1772, which is primarily comprised of nickel BBHP (BASF 2007), states that the pigment is likely to be eliminated from water by adsorption on activated sludge. However, both log K_{ow} values are predicted and the adsorption potential of organometallics and pigments are generally not well understood, therefore the degree of adsorption of nickel BHMB is uncertain.

According to aerobic biodegradation models, nickel BHMB is not expected to biodegrade quickly (see Table 3 below).

Persistence and Bioaccumulation Potential

Environmental Persistence

As nickel BHMB may have been used as a pigment itself and has an analogue (nickel BPHP) which is a pigment, when evaluating the persistence of nickel BHMB the lines of evidence considered include consideration of the general qualities of pigments, as well as QSAR predictions for degradation, the chemical's structure and its physical and chemical properties.

No experimental degradation data for nickel BHMB have been identified. Thus, a QSAR-based weight-of-evidence approach (Environment Canada 2007) was applied using the models shown in Table 3. Due to the ecological importance of the water compartment, the fact that most of the available models apply to water and the fact that nickel BHMB may be released to this compartment, persistence in water was primarily examined using predictive QSAR models for biodegradation. Nickel BHMB does not contain functional groups expected to undergo hydrolysis.

Some of the modeled values in Table 3 however have a lower level of reliability as few or no chemicals of structural comparability to nickel BHMB are contained in the training sets of the models. No predictions were produced for nickel BHMB using the TOPKAT QSAR model (TOPKAT 2004) because the program does not have nickel in its training sets for organic compounds. Also, while the CATABOL QSAR program (CATABOL 2008), part of the Canadian POPS Model (CPOPs 2008), produced a biological oxygen demand value, the output stated that the prediction was outside of the model's domain due to lack of structural coverage in the training set (approximately 10.8% coverage). Consequently, the reliability of the CATABOL QSAR value produced for nickel BHMB is low. Therefore, the standard weight-of-evidence approach had to be adapted for application to this substance.

Table 3. Modelled data for degradation of nickel BHMB

Fate Process	Model and model basis	Model Result and Prediction	Extrapolated Half-life (days)
AIR			
Atmospheric oxidation	AOPWIN 2008[1]	$t_{1/2}$ = 0.437 days	< 2
Ozone reaction	AOPWIN 2008[1]	n/a[2]	n/a
WATER			
Hydrolysis	HYDROWIN 2008[1]	n/a[2]	n/a
Primary biodegradation			
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 4: Expert Survey (qualitative results)	3.61[3] "biodegrades relatively fast"	< 182
Ultimate biodegradation			
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 3: Expert Survey (qualitative results)	1.74[3] "biodegrades slowly"	> 182
Biodegradation	BIOWIN 2008[1]	-0.24[4]	> 182

(aerobic)	Sub-model 5: MITI linear probability	"biodegrades very slowly"	
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 6: MITI non-linear probability	0.0003[4] "biodegrades very slowly"	> 182
Biodegradation (aerobic)	TOPKAT 2004 Probability	No predictions produced	
Biodegradation (aerobic)	Canadian POPs Model 2008 (CPOPs) % BOD (biological oxygen demand)	% BOD = 27.07 biodegradation rate uncertain	> or < 182

[1] EPIsuite (2008)
[2] Model does not provide an estimate for this type of structure.
[3] Output is a numerical score from 0 to 5.
[4] Output is a probability score.

In air, a predicted atmospheric oxidation half-life value of 0.437 days (see Table 3 above) demonstrates that this substance is likely to be rapidly oxidized in air. The compound is not expected to react (or react appreciably) with other photo-oxidative species in the atmosphere, such as ozone. Photolysis, may be possible since the absorption maximum of pigments tends to lie within the range of visible and ultraviolet light (Danish EPA 1999). However, azomethine metal complex pigments of similar structures to nickel BHMB are known to have a lightfastness that ranges from relatively good to excellent (Herbst and Hunger 2004) which is an indication of reduced likelihood of rapid photolysis. Therefore, it is expected that reactions with hydroxyl radicals will be the most important fate process in the atmosphere for nickel BHMB. With a half-life of 0.437 days via reactions with hydroxyl radicals, nickel BHMB is considered not persistent in air.

Three of the four ultimate biodegradation model results (for BIOWIN submodels 3, 5 and 6) are below the threshold for "biodegrades slowly" by a wide margin and suggest that biodegradation is very slow and that the half-life in water would be >182 days. It should be noted that these EPIWIN based predictions may also be outside of the model domain of applicability as there were no nickel organometallics found in the training sets for BIOWIN, HYDROWIN, or AOPWIN. Unfortunately, EPIWIN (2004) primary and ultimate biodegradation output do not show warnings when the predictions for a substance outside of the training set is made. In addition, as discussed above, TOPKAT (2004) did not yield a prediction. The CATABOL Model from CPOPs (2008) produced a borderline prediction of 27.07% biological oxygen demand, which is below the 40% threshold indicating "may biodegrade fast" and above the 20% threshold indicating "biodegrades slowly" (i.e., indicating half-lives of < 182 days or >182 days, respectively). However, this prediction is highly uncertain because nickel BHMB was outside the structural domain of the model's training set and is therefore attributed less weight.

The result for primary biodegradation from BIOWIN Sub-model 4 suggests the substance has a primary half-life of <182 days. However, because the identities of the degradation products are not known, this result is given less weight.

Because of its very low solubility in water, this pigment-like organometallic may be considered not to be available for aerobic biodegradation. Industries manufacturing pigments recognize that their substances are persistent. For example, the Color Pigments Manufacturers Association, Inc. (CPMA 2003) has indicated that pigments are designed to be durable or persistent in the environment in order to provide lasting color to finished coatings, inks and paints. Also, azomethine metal complex pigments with chemical structures similar to nickel BHMB are known to have “very good to excellent weatherfastness” which is also indicative of persistence (Herbst and Hunger 2004).

While the model results have some degree of uncertainty, they nonetheless provide a relatively good indication of the persistence of the organic part of the molecule. In addition, the metallic aspect of the molecule is known to be infinitely persistent. Therefore, considering all model results, even with the inherent model uncertainties, in combination with the similarity of this compound to other pigments which are typically recognized as substances with a high degree of persistence, there is more reliable evidence to suggest the biodegradation half-life of nickel BHMB is > 182 days in water.

Using an extrapolation ratio of 1:1:4 for a water: soil: sediment biodegradation half-life (Boethling et al. 1995), the half-life in soil is also > 182 days and the half-life in sediments is > 365 days. This indicates that nickel BHMB is persistent in soil and sediment.

In addition, the long-range transport potential of nickel BHMB from its point of release to air is estimated to be negligible based on its very low partitioning to air and low persistence in this medium.

Based on the information available, nickel BHMB meets the persistence criteria in water, soil and sediment (half-lives in soil and water ≥ 182 days and half-life in sediment ≥ 365 days), but does not meet the criteria for air (half-life in air ≥ 2 days) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

No experimental logK_{ow}, bioaccumulation or bioconcentration data are available for this substance. Nickel BHMB was categorized as bioaccumulative as it had QSAR modelled bioaccumulation and bioconcentration factors (BAFs) above the threshold of 5000 L/kg without accounting for any potential biotransformation. These BAF and BCF values were based on a high predicted log K_{ow} of 6.58. However, as previously mentioned, QSAR based log K_{ow}, bioconcentration and bioaccumulation models do not generally have training set data for organometallics nor pigments. In this case, no appropriate analogue substances could be found in the training set for KOWWIN (2008), which is used to predict log K_{ow}, or in BCFWIN (2008) which is used to predict bioaccumulation and bioconcentration. However, as part of a weight of evidence approach, and for transparency, modelled bioaccumulation and log K_{ow} data are presented here with the caveat that they are associated with a high level of uncertainty.

BCF and BAF estimates, corrected for potential biotransformation, were generated using the BCFBAF model (EPIsuite 2008). Metabolic rate constants were derived using structure activity relationships described further in Arnot et al. (2008a, 2008b, 2009). Since metabolic potential can be related to body weight and temperature (Hu and Layton 2001, Nichols et al. 2007), the BCFBAF model (2008) further normalizes the k_M (the concentration of substrate that leads to half-maximal enzyme velocity) of 0.73 day^{-1} for a 10g fish at 15°C to the body weight of the middle-trophic-level fish in the Arnot-Gobas model (184 g) (Arnot et al. 2008b).

Table 7: Modelled data for bioaccumulation for nickel BHMB

Test organism	Model and model basis	Trophic Level	Endpoint	Value wet weight (L/kg)	Reference
Fish	BCFBAF: Steady state mass balance	Middle trophic	BCF	305.5	BCFBAF 2008
Fish	BCFBAF: Steady state mass balance	Middle trophic	BAF	970.9	BCFBAF 2008
Fish	Baseline model with mitigating factors	A combination of fish from different trophic levels	BCF	1000	CPOPS 2008

Steady state mass balance models from BCFBAF (2008) based on middle trophic level fish resulted in predicted values corrected for metabolism of 305.5 and 970.9 L/kg for BCF and BAF respectively.

The Baseline model with mitigating factors which is included in CPOPs (2008) showed that nickel BHMB is likely to break-down through the n-glucuronidation pathway which is a Phase II reaction that results in elimination of the metabolite through fish. When this pathway is taken into account, the predicted BCF value is 1000 L/kg. The k_M used for this prediction is 0.022. It should be noted that, as with the BCFBAF predictions, the CPOPs models were outside of the domain of applicability and hence this is an important uncertainty. These predictions may be considered a worst case scenario as they assume that the modelled logK_{ow} (which is high) is correct and that the substance may be more bioavailable than is indicated by other supporting qualitative data.

Considering modelled bioaccumulation and bioconcentration data adjusted for metabolism using two different models, nickel BHMB does not meet the bioaccumulation criterion (BAF $\geq$ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

While the modelled data are considered as a line of evidence (with significant uncertainty), a qualitative evaluation of other relevant physical and chemical properties was also applied and will be given greater weight.

Strict cut-offs for molecular size should not be used as the sole indicator of bioaccumulation potential as large substances may show even slower elimination rates, which could lead to bioaccumulation despite slow uptake rates. However, information regarding molecular size and cross-sectional diameter are useful to consider and are commonly used by international jurisdictions such as the European Union (ECHA 2008) in conclusions on bioaccumulation potential. Recent investigations relating fish BCF data and molecular size parameters (Dimitrov et al. 2002, 2005) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with increasing maximum diameter (D_{max}). The probability of passive diffusion decreases appreciably when the maximum diameter is greater than ~1.5 nm and much more so for molecules having a maximum diameter of greater than 1.7 nm. Sakuratani et al. (2008) have also investigated the effect of cross-sectional diameter on passive diffusion in a BCF test set of about 1200 new and existing chemicals. They observed that substances that do not have a very high bioconcentration potential (BCF < 5000) often have a D_{max} of > 2.0 nm and an effective diameter (D_{eff}) > 1.1 nm.

However, as Arnot et al. (2010) have noted, there are uncertainties associated with the thresholds proposed by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008) since the BCF studies used to derive them were not critically evaluated. Arnot et al. (2010) point out that molecular size influences solubility and diffusivity in water and organic phases (membranes), and larger molecules may have slower uptake rates. However, these same kinetic constraints apply to diffusive routes of chemical elimination (i.e., slow in = slow out). Thus, significant bioaccumulation potential may remain for substances that are subject to slow absorption processes, if they are slowly biotransformed or slowly eliminated by other processes. Consequently, when evaluating bioaccumulation potential, molecular size information should be considered with care and used together with other relevant lines of evidence in a weight-of-evidence approach.

Nickel BHMB and its analogue nickel BBHP have large molecular weights (> ~ 500 g/mol) and very high cross-sectional diameters (up to 2.5 and 2.7 nm respectively), which are properties likely to limit bioavailability. In addition, the high modelled thermal decomposition and boiling point data (350 and 891 degrees C, respectively) for nickel BHMB and high experimental thermal decomposition point data for its analogue BBHP (> 300°C and 285°C) indicate that the substance is relatively chemically stable and also is indicative of low potential bioavailability. For example, Chu and Yalkowsky (2009) found that in general, high melting compounds are less likely to be well absorbed than lower melting compounds for any given dose. Also, Kim et al (2007) stated that high melting point and limited solubility in either water or oil-based solvents often results in poor *in vivo* availability.

Combined with the experimental result that nickel BBHP is insoluble in water (Table 2a), that both nickel BHMB and nickel BBHP have very low modelled water solubilities, and that pigments tend to also have low solubility in octanol, the available evidence indicates that nickel BHMB is expected to have a low bioaccumulation potential due to its physical and chemical properties which result in a very low uptake rate either from the gills or gut of biota (i.e., low dietary assimilation efficiency). Any portion of the substance transmitted across membranes is likely then transformed by in vivo metabolism or eliminated via growth dilution.

Based on the available physical and chemical properties, nickel BHMB does not meet the bioaccumulation criteria (BAF or BCF $\geq$ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

A - In the Aquatic Compartment

The Government of Canada has previously assessed nickel compounds in a Priority Substances List report (Canada 1994, 1999). It was concluded that dissolved and soluble forms of inorganic nickel are entering or may enter the environment in a quantity or concentration or under conditions that are having or that may have a harmful effect on the environment. However, since the Priority Substances List assessment focused on dissolved and soluble inorganic forms of nickel, while organometallic substances such as nickel BHMB were beyond the scope of the report, the same conclusions do not apply.

Since there are no experimental data available on the aquatic toxicity of this substance, modelled data were used to estimate the potential for aquatic toxicity (Table 8). The modelled data originate from the ECOSAR (2008) program which uses log K_{ow} in order to predict aquatic toxicity. As discussed in the section on bioaccumulation, due to nickel BHMB and its analogue being outside of the training set for the calculation of log K_{ow}, the reliability of this value has some uncertainty. However, in the absence of experimental data these predicted values are used in a QSAR weight-of-evidence approach for aquatic toxicity (Environment Canada 2007).

The toxicity of nickel BHMB is modelled using results for the neutral organic structure-activity relationship (SAR) in ECOSAR (2008) and does not account for any potential toxicity from free nickel ions released into solution as this substance is predicted to be stable under environmentally relevant conditions.

Predicted ecotoxicity values obtained for nickel BHMB are shown in Table 8.

Table 8. Modelled data for aquatic toxicity of nickel BHMB based upon a neutral organic SAR

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 hours)	LC_{50}[1]	0.058[3]	ECOSAR 2008
Fish	Chronic	EC_{50}[2]	0.005[3]	ECOSAR 2008
Daphnia	Acute (96 hours)	EC_{50}[2]	0.058[3]	ECOSAR 2008
Daphnia	Chronic	EC_{50}[2]	0.012[3]	ECOSAR 2008
Algae	Acute (96 hours)	EC_{50}[2]	0.164[3]	ECOSAR 2008
Algae	Chronic	EC_{50}[2]	0.137[3]	ECOSAR 2008

[1] EC_{50} – The concentration of a substance that is estimated to cause some effect on 50% of the test organisms.
[2] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[3] In excess of modelled water solubility

The most sensitive organisms were fish with a chronic toxicity value of 0.005 mg/L for an EC50 endpoint and an acute toxicity value of 0.058 for a 96 hour LC50 test.

The modelled toxicity values presented here are likely very conservative in light of the physical and chemical properties of the substance including high molecular weight, high estimated and analogue thermal decomposition points and cross-sectional diameter as well as low solubility, which tend to make the substance relatively inert and not highly bioavailable. The toxicity predictions have an additional source of uncertainty as all are in excess of the modelled solubility for nickel BHMB (7.20×10^{-4} mg/L). However, generally, due to the uncertainty of modelled results, a disparity between water solubility and toxicity values of approximately a factor of 10, is considered acceptable. In this case, the lowest chronic toxicity value (0.005 mg/L) is within a factor of 10 of the predicted water solubility.

These results suggest that the substance may potentially be highly hazardous to aquatic organisms (acute $LC/EC_{50} \leq 1.0$ mg/L and chronic no-observed-effect concentration [NOEC] ≤ 0.1 mg/L).

B - In Other Environmental Compartments

No ecological effects studies were found for this compound or its analogue in media other than water.

When nickel BHMB is released into a water body, it is likely to partition into suspended particulate matter and to bottom sediments, where sediment-dwelling organisms would be exposed to the substance. While no toxicity data specific to sediment-dwelling organisms are available for this substance,,given the low expected bioavailability, the toxicity of nickel BHMB in soil and sediment is also expected to be low. In addition, the low bioaccumulation potential of nickel BHMB may also limit exposure in soil and sediment..

Ecological Exposure Assessment

No data concerning concentrations of this substance in water in Canada have been identified. Therefore, environmental concentrations are estimated from available information, including substance quantities and estimated release rates, and assumptions about the size of receiving water bodies.

A – Industrial Release

As nickel BHMB is used industrially and may be released to water, a worst-case industrial release scenario is used to estimate the aquatic concentration of the substance with the help of Environment Canada's (2009b) Industrial Generic Exposure Tool – Aquatic (IGETA). The scenario is made conservative by assuming that the total quantity of the substance used by Canadian industry is within one facility at a small, hypothetical industrial site. The scenario also assumes that the release occurs 250 days per year, typical for small and medium-sized facilities, and is sent to a local sewage treatment plant (STP) with a zero removal rate for the substance. Upon combining with the STP effluent, the receiving water at a small site such as this normally has an actual or equivalent flow of approximately 34 560 m^3 per day. For this scenario, the loss to sewer water is conservatively set at 0.01% (OECD 2004) of the total quantity used for welding operations due to loss during handling. These assumptions, and an upper limit total quantity in use of 1 000 kg/yr, results in an aquatic concentration of 1.16×10^{-5} mg/L (Environment Canada 2010).

Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine various supporting 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 a conservative risk quotient calculation, as well as information on persistence, bioaccumulation, toxicity, sources and fate of the substance.

Nickel BHMB is expected to be persistent in water, soil and sediment; and is also expected to have a low bioaccumulation potential. Nickel BHMB is not expected to have potential for widespread release into the Canadian environment. Once released into the environment, it is expected to be found mainly in water and sediment, and potentially in soil. It also may have a high potential for toxicity to aquatic organisms.

A risk quotient analysis, integrating conservative estimates of exposure with toxicity information, was performed for the aquatic medium to determine whether there is potential for ecological harm in Canada. The generic industrial scenario for a hypothetical small industrial site presented above yielded a predicted environmental concentration (PEC) of 1.16 x 10^{-5} mg/L (Environment Canada 2010). A predicted no-effect concentration (PNEC) was derived from the chronic toxicity value of 5 x 10^{-3} mg/L for fish, by dividing this value by an assessment factor of 10 (to extrapolate to a no effect level and to account for interspecies and intraspecies variability in sensitivity) to give a value of 5 x 10^{-4} mg/L. The resulting risk quotient (PEC/PNEC) = 0.023. Therefore harm to aquatic organisms is unlikely.

For this substance, a risk quotient based on exposure in sediment pore water may also be calculated based on the aquatic compartment PEC and PNEC values presented above and used for sediment risk characterization. In the calculation, bottom sediment and its pore water are assumed to be in equilibrium with the overlying water and benthic and pelagic organisms are assumed to have similar sensitivities to the substance. Therefore the PEC and PNEC for pore water is considered to be the same as for the aquatic compartment. This equilibrium approach would result in a risk quotient (PEC/PNEC) for the sediment compartment that is the same as for the aquatic compartment.

Based on the above analysis, nickel BHMB is unlikely to be causing harm to populations of aquatic organisms in Canada.

Uncertainties in Evaluation of Ecological Risk

There is some uncertainty regarding the breakdown and release of small amounts of nickel ions into the environment if this substance is less stable than predicted. Also, there is uncertainty as to whether or to what degree this substance will degrade in anaerobic environments such as sediment. However, given that the releases of nickel BHMB are predicted to be very small, the quantity of nickel ions released in comparison with natural concentrations of nickel in the Canadian environment is expected to be negligible.

There is also some uncertainty related to the bioaccumulation potential of organometallic complexes in general. While the physical and chemical properties of nickel BHMB indicate that it is unlikely to bioaccumulate, there is a general lack of experimental data in the scientific literature and of models with reliable training sets for water and octanol solubility as well as bioaccumulation potential of organometallics and pigments. If more empirical bioaccumulation potential data were available, or if models of higher reliability existed for organometallics and pigments, these could be used to increase confidence in the bioaccumulation conclusion.

The predicted concentrations, associated with toxicity for aquatic organisms have an additional source of uncertainty when these concentrations exceed the predicted solubility of nickel BHMB in water. Given that concentrations for both toxicity and water solubility are uncertain, toxicity values that exceeded solubility estimates by up to a factor of 10 were considered to be acceptable.

The persistence assessment is limited by the absence of empirical biodegradation data, which necessitated generation of model predictions. There also remains some uncertainty regarding possible anaerobic degradation and photo-degradation of nickel BHMB due to the absence of data. Although all model prediction has some degree of error, the aerobic biodegradation model outputs confirmed the expected persistence of nickel BHMB given its potential uses and structural characteristics.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Food

Empirical data on concentrations of nickel BHMB in environmental media in Canada were not identified. Nickel BHMB is not expected to be found in food or beverages in Canada due to a lack of identifiable data. Environmental concentrations were estimated using a default release value of 0.01% to water from metal alloy contact (OECD 2004). The percentage was applied to the total quantity of nickel BHMB in Canadian commerce in 2006. The total quantity in commerce was conservatively assumed to be up to 1 000 kg (Environment Canada 2009a). The loss quantity is estimated as 0.1 kg per year to surface water.

The estimated loss was used in ChemCAN, a Canada-specific environmental exposure model, to estimate concentrations in various environmental media (ChemCAN 2003). This model differs from the point source models used in the ecological assessment section of the document, which provide estimates of exposure near release points, in that it is a regional far-field level III fugacity model that is used to estimate average concentrations in various media to inform human exposure estimates. The PECs are presented in Appendix 2. Conservative upper-bounding daily intakes of nickel BHMB for the general population in Canada were derived based on the estimated environmental concentrations, resulting in negligible exposure on the order of magnitude of nanograms (10^{-9} gm) per kg-bw (kilogram of body weight) per day.

Consumer Products

Nickel BHMB is used in Canada in dual shield low alloy flux cored welding electrodes and nickel alloy covered electrodes (Environment Canada 2009a). This is considered an industrial use. No consumer products were identified from literature searches or responses to a notice issued under section 71 of CEPA 1999.

Health Effects Assessment

Nickel BHMB is an organometallic compound containing nickel. No empirical health effects data for nickel BHMB or its analogue, nickel BBHP, were identified. Experimental data regarding the physical and chemical properties of nickel BHMB were not available. However, a model estimated low water solubility (see Table 2; WSKOWWIN 2008).

The Government of Canada has previously assessed nickel compounds in a Priority Substances List report (Canada 1994, 1999). Based principally on the weight of evidence of carcinogenicity in occupationally exposed human populations for the groups of compounds examined in an epidemiological analysis and limited supporting data on individual compounds in experimental animals, the groups, "oxidic" (including nickel oxide, nickel-copper oxide, nickel silicate oxides, and complex oxides), "sulphidic" (including nickel subsulphide) and "soluble" (primarily nickel sulphate and nickel chloride) nickel compounds have been classified as harmful to human health. The critical effect was carcinogenicity. The supporting dataset for this conclusion includes carcinogenicity and genotoxicity data predominantly from less water soluble nickel compounds, such as nickel subsulphide and nickel oxide (Canada 1994; ATSDR 2005).

The International Agency for Research on Cancer (IARC) has classified nickel compounds as Group 1 substances – “carcinogenic to humans” (IARC 1990). Nickel compounds are listed as “known to be human carcinogens” by the National Toxicology Program (NTP 2002, 2005).

Qualitative structure-activity relationship (SAR) – based toxicity predictions for nickel BHMB are summarized in Appendix III. These predictions provided indications of mutagenicity in mammals (based on oxime functional group); skin sensitization (based on nickel ion) and respiratory sensitization (based on nickel ion and hydroxylamine functional group) (DEREK for Windows_12.0, DEREK 2009). Quantitative (SAR) models, TOPKAT version 6.2 (TOPKAT 2004) and CASETOX version 2.1 (CASETOX 2009), as well as the qualitative models, DEREK for Windows_12.0 and Leadscope Model Applier version 1.3.2 (Leadscope Model Applier 2010), could not provide endpoint predictions for organometallic compounds. Thus, it was not possible to assess carcinogenic potential using QSAR models.

The information from one SAR model for nickel BHMB, as well as information on nickel compounds, suggests potential hazardous properties (i.e., mutagenicity, carcinogenicity and skin and respiratory sensitization) of nickel BHMB.

The confidence for nickel BHMB health effects assessment is low as neither empirical health effects data nor substance specific information were identified.

Characterization of Risk to Human Health

No empirical health effects data were identified for nickel BHMB, or its analogue, nickel BBHP. The information from a structure-activity relationship (SAR) model for nickel BHMB suggests mutagenic potential, but the compound could not be assessed for carcinogenic potential using qualitative/quantitative SAR models. However, empirical data on other nickel compounds suggest a potential for carcinogenicity.

With respect to non-cancer effects, qualitative evidence from SAR results for nickel BHMB suggest that nickel BHMB may induce skin and respiratory sensitization.

Exposures of the general population to nickel BHMB through environmental media were estimated to be on the order of magnitude of nanograms (10^{-9} gm) per kg-bw (kilogram of body weight) per day, and thus are expected to be negligible. General population exposure to nickel BHMB from use of consumer products is not expected.

As exposure of the general population through environmental media in Canada is expected to be negligible, the risk to human health is considered to be low.

Uncertainties in Evaluation of Risk to Human Health

Confidence in the environmental exposure estimate for nickel BHMB is low. Data in the literature were not identified for concentrations of this substance in environmental media. However, quantities in commerce for the 2006 calendar year are known and were combined with an estimated loss percentage from an OECD emissions scenario document to model environmental concentrations. As the maximum value of the quantity in commerce range was used in the modeling, it is likely that the modeled results are conservative estimates of environmental exposure. No consumer product data were identified from literature searches and only one industrial use (in nickel alloy electrodes) was identified in response to a notice issued under section 71 of CEPA 1999.

Due to an absence of empirical health effects data and the use of qualitative structure – activity relationship models, confidence in the determination of critical health effects is low. However, based on the physical and chemical properties of nickel BHMB, the bioavailability of this substance is likely to be low.

Conclusion

Based on the information available, it is concluded that nickel BHMB 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. Nickel BHMB meets the criteria for persistence but not the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Based on the information available, it is concluded the nickel BHMB is not a substance 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 nickel BHMB does not meet the criteria as set out in section 64 of CEPA 1999.

As nickel BHMB is listed on the Domestic Substances List, its import and manufacture in Canada are not subject to notification under subsection 81(1). Given the potential health hazards of this substance, there is concern that new activities that have not been identified or assessed could lead to this substance meeting the criteria set out in section 64 of the Act. Therefore, it is recommended to amend the Domestic Substances List, under subsection 87(3) of the Act, to indicate that subsection 81(3) of the Act applies with respect to this substance, so that new manufacture, import or use of this substance is notified and undergoes ecological and human health risk assessments.

Considerations for Follow-up

This substance belongs to a chemical group of potential concern for human health; nickel-containing compounds, where the critical effect may be carcinogenicity. However, note that in Canada, the "oxidic", "sulphidic" and "soluble" nickel compounds have been classified as harmful to human health. Nickel BHMB does not fall into these subgroups.

Given the potential hazardous properties of this class of substances, additional activity (e.g., research, assessment, monitoring and surveillance) may be undertaken to characterize the risk to human health in Canada of this broader group of substances.

References

ACD/pK_aDB [Prediction Module]. 2005. Version 9.04. Toronto (ON): Advanced Chemistry Development. Available from: http://www.acdlabs.com/products/phys_chem_lab/pka/. [restricted access]

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

Arnot JA, Mackay D, Bonnell M. 2008a. Estimating metabolic biotransformation rates in fish from laboratory data. Environ Toxicol Chem 27(2):341–351.

Arnot JA, Mackay D, Parkerton TF, Bonnell M. 2008b. A database of fish biotransformation rates for organic chemicals. Environ Toxicol Chem 27(11): 2263-2270.

Arnot JA, Meylan W, Tunkel J, Howard PH, Mackay D, Bonnell M, Boethling RS. 2009. A quantitative structure-activity relationship for predicting metabolic biotransformation rates for organic chemicals in fish. Environ Toxicol Chem 28(6): 1168-1177.

Arnot JA, Arnot MI, Mackay D, Couillard Y, MacDonald D, Bonnell M, Doyle P. 2010. Molecular size cutoff criteria for screening bioaccumulation potential: fact or fiction?. Integr Environ Assess Manag. 6(2):210–224.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2005. Toxicological profile for nickel. Washington (DC): US Department of Health and Human Services, Public Health Service. [cited 2010 April 08]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp15.html

BASF. 2007. Safety Data Sheet (Paliotol Yellow L 1772). Version 1.0.
Available from:
http://worldaccount.elastogran.com/wa/NAFTA~en_US/Catalog/Pigments/doc4/BASF/PRD/30041694/.pdf?title=&asset_type=msds/pdf&language=EN&validArea=CA&urn=urn:documentum:ProductBase_EU:09007af8800fef36.pdf

[BBM] Baseline Bioaccumulation Model. 2008. Gatineau (QC): Environment Canada, Ecological Assessment Division. [Model developed based on Dimitrov et al. 2005]. Available upon request.

[BCFBAF] Bioaccumulation 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. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[BCFWIN] BioConcentration Factor Program for Windows [Estimation Model]. 2008. Version 2.15. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[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. Available from: 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.

Canada. 1978. *Food and Drug Regulations*, C.R.C., c. 870. Available from: http://laws.justice.gc.ca/en/showdoc/cr/C.R.C.-c.870

Canada, Dept. of Environment, Dept. of Health. 1994. Canadian Environmental Protection Act, Priority Substances List Assessment Report, Nickel and its Compounds. http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/psl1-lsp1/compounds_nickel_composes/nickel-eng.pdf

Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C., 1999, c. 33, Canada Gazette. Part III, vol. 22, no. 3. 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, Canada Gazette, Part II, vol. 134, no. 7, p. 607−612. 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. 2009. *Canadian Environmental Protection Act, 1999: Notice with respect to Batch 10 Challenge substances.* Canada Gazette, Part I, vol. 143, no. 25, p. 1796–1810.. Available from: http://www.gazette.gc.ca/rp-pr/p1/2009/2009-06-20/pdf/g1-14325.pdf

CASETOX [Prediction Module]. 2009. Version 2.1. Beachwood (OH): MultiCASE. Available from: http://www.multicase.com/products/prod03.htm [restricted access].

[CATABOL] Probabilistic assessment of biodegradability and metabolic pathways [Computer Model]. 2008. Version 5.10.2. Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. Available from: http://oasis-lmc.org/?section=software&swid=1

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 2010 Feb 15]. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/CC600.html

ChemID Plus [database on the Internet]. 2010. [accessed 2010 Feb 15]. Available from: http://chem.sis.nlm.nih.gov/chemidplus

Chu KA, Yalkowsky SH, 2009. An interesting relationship between drug absorption and melting point. Int J Pharm. 373(1-2): 24-40.

[CII] Colour Index International [database on the Internet]. 2002 – . 4th Ed. Research Triangle Park (NC): American Association of Textile Chemists and Colourists. [cited 2010 Feb]. Available from: http://www.colour-index.org/

[CNS] Cosmetic Notification System [Proprietary Database]. 2010. Available from Health Canada, Cosmetics Division.

[CPMA] Color Pigments Manufacturers Association, Inc. 2003. Comments of the Color Pigments Manufacturers Association, Inc. on the Draft Guidance Manual for the Categorization of Organic and Inorganic Substances on Canada's Domestic Substances List ('DSL') and Environment Canada's Computer Generated Estimates and Empirical Data on Approximately 12,000 Discrete Organic Chemicals on the DSL. Available upon request from: Existing Substances Division, Environment Canada, Ottawa, K1A 0H3.

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

[Danish EPA] Danish Environmental Protection Agency. 1999. Survey of azo-colorants in Denmark. Consumption, use, health and environmental aspects. Miljøprojekt No. 509. Henriette, Danish Technological Institute, Environment, Ministry of Environment and Energy, Denmark, Danish Environmental Protection Agency, 1999. Report prepared by Øllgaard H, Frost L, Galster J, Hansen OC. Available from: http://www2.mst.dk/common/Udgivramme/Frame.asp?http://www2.mst.dk/Udgiv/publications/1999/87-7909-548-8/html/default_eng.htm

[DEREK] Deductive Estimation of Risk from Existing Knowledge [Prediction model]. 2009. Version 12.0.0.. Lhasa Limited, Leeds, UK. Available from: https://www.lhasalimited.org/derek/ [restricted access].

Dimitrov S, Dimitrova N,Walker J, Veith G, Mekenyan O. 2002. Predicting bioconcentration potential of highly hydrophobic chemicals. Effect of molecular size. Pure and Appl Chem. 74(10): 1823-1830.

Dimitrov S, Dimitrova N, Parkerton T, Comber M, Bonnell M, Mekenyan O. 2005. Base-line model for identifying the bioaccumulation potential of chemicals. SAR QSAR Environ Res 16(6):531–554.

[ECHA] European Chemicals Agency. 2008. Guidance on information requirements and chemical safety assessment. Chapter R.11: PBT Assessment. Available from: http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r11_en.pdf?vers=20_08_08

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

Environment Canada. 2006. Data for selected substances collected under the *Canadian Environmental Protection Act, 1999*, Section 71: *Notice with respect to selected substances identified as priority for action*. Data compiled by: Environment Canada, Program Development and Engagement Division.

Environment Canada. 2007. Guidance for Conducting Ecological Assessments under CEPA, 1999, Science Resource Technical Series, Technical Guidance Module: QSARs. Reviewed Draft Working Document. Gatineau (QC): Environment Canada, Ecological Assessment Division.

Environment Canada. 2009a. Data for Batch 10 substances collected under the *Canadian Environmental Protection Act, 1999*, Section 71: *Notice with respect to certain Batch 10 Challenge substances.* Data compiled by: Environment Canada, Program Development and Engagement Division.

Environment Canada. 2009b. Guidance for Conducting Ecological Assessments under CEPA, 1999, Science Resource Technical Series, Technical Guidance Module: The Industrial Generic Exposure Tool – Aquatic (IGETA). Working document. Gatineau (QC): Environment Canada, Ecological Assessment Division.

Environment Canada. 2010. IGETA report: CAS RN 42739-61-7, 2010-02-16. Unpublished report. Gatineau (QC): Environment Canada, Ecological Assessment Division.

[EPIWIN] Estimation Programs Interface for Microsoft Windows [Estimation Model]. 2004. Version 3.12. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[EPIsuite] Estimation Programs Interface Suite for Microsoft Windows [Estimation Model]. 2008. Version 4.0. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuitedl.htm

[ESIS] European Chemical Substances Information System [database on the Internet]. 2009. Version 5. Ispra [IT]: European Commission, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. Available from: http://ecb.jrc.ec.europa.eu/esis/

[ETAD] Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers Canadian Affiliates, Dayan J, Trebitz H, consultants. 1995. Health and environmental information on dyes used in Canada. Unpublished report submitted to Environment Canada, New Substances Division.

Hart J. 2008. Nickel compounds – a category approach for metals in EU legislation (a report for the Danish Environmental Protection Agency). 52 p.

Health Canada. 2009. The Cosmetic Ingredient Hotlist – September 2009 [Internet]. Ottawa (ON): Health Canada, Consumer Product Safety. [cited 2010 Mar 1]. Available from: http://www.hc-sc.gc.ca/cps-spc/person/cosmet/info-ind-prof/_hot-list-critique/hotlist-liste-eng.php

[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. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Herbst W, Hunger K. 2004. Industrial organic pigments, 3rd edition. Weinheim (Germany): Wiley-VCH, Verlag GmbH & Co. KGaA. 660 p.

Hu TM, Layton WL. 2001. Allometric scaling of xenobiotic clearance: uncertainty versus universality. AAPS PharmSci [Internet]. Vol. 3(4): Article 29. Available from: http://www.aapsj.org/view.asp?art=ps030429

[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. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[IARC] International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans. 1990. IARC Monographs on the evaluation of carcinogenic risks to humans chromium, nickel and welding Vol. 49. Available from: http://monographs.iarc.fr/ENG/Monographs/vol49/volume49.pdf

Key to metals. 2010 Cast Nonferrous: Welding the Nonferrous Metals: General Overview, Key to metal; the world's most comprehensive metal database. [Cited 2010 March]. Available from: http://www.keytometals.com/Article52.htm

Kim I-H, Nishi K, Tsai H-J, Bradford T, Koda Y, Watanabe T, Morisseau C. 2007. Design of bioavailable derivatives of 12-(3-adamantan-1-yl-ureido)dodecanoic acid, a potent inhibitor of the soluble epoxide hydrolase. Bioorganic & Medicinal Chemistry. 15(1): 312-323.

[KOWWIN] Octanol-Water Partition Coefficient Program for Microsoft Windows [Estimation Model]. 2008. Version 1.67. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Leadscope Model Applier [Prediction module]. 2010. Version 1.3.2. Leadscope, Inc., Columbus, OH, USA. Available from: http://www.leadscope.com/all_products.php [restricted access].

Lincke G. 2003. Molecular stacks as a common characteristic in the crystal lattice of organic pigment dyes A contribution to the "soluble–insoluble" dichotomy of dyes and pigments from the technological point of view. Dyes Pigm. 59(1): 1-24.

Macdonald D, Breton R, Sutcliffe R, Walker J. 2002. Uses and limitations of quantitative structure-activity relationships (QSARS) to categorize substances on the Canadian Domestic Substance List as persistent and/or bioaccumulative, and inherently toxic to non-human organisms. SAR QSAR Environ Res. 13(1): 43-55.

Mekenyan G, Dimitrov SD, Pavlov TS, Veith GD. 2005. POPs: A QSAR system for creating PBT profiles of chemicals and their metabolites. SAR QSAR Environ Res 16(1-2):103−133.

[MPBPWIN] Melting Point Boiling Point Program for Microsoft Windows [Estimation Model]. 2008. Version 1.43. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[NCI] National Chemical Inventories [database on CD-ROM]. 2007. Issue 1. Columbus (OH): American Chemical Society. [cited 2007 Dec 11]. Available from: http://www.cas.org/products/cd/nci/index.html

Nichols JW, Fitzsimmons PN, Burkhard LP. 2007. In vitro – in vivo extrapolation of quantitative hepatic biotransformation data for fish. II. Modeled effects on chemical bioaccumulation. Environ Toxicol Chem 26:1304−1319.

[NTP] National Toxicology Program. 2002. 10th Report on carcinogens. Substance profile: nickel compounds and metallic nickel. Research Triangle Park (NC): National Toxicology Program.

[NTP] National Toxicology Program. 2005. 11th Report on carcinogens. Substance profile: nickel compounds and metallic nickel. Research Triangle Park (NC): National Toxicology Program.

[OECD] Organisation for Economic Co-operation and Development. 2004. Emission scenario document on plastics additives [Internet]. Paris (FR): OECD, Environment Directorate. Series on Emission Scenario Documents No. 3. Report No. ENV/JM/MONO(2004)8, JT00166678. [2010 Feb]. Available from: http://www.olis.oecd.org/olis/2004doc.nsf/LinkTo/env-jm-mono(2004)8

[PCKOCWIN] Organic Carbon Partition 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. [2010 02]. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[PMRA] Pest Management Regulatory Agency. 2007. Regulatory Note REG 2007-04: PMRA list of formulants [Internet]. Ottawa (ON): Health Canada, Pest Management Regulatory Agency. [cited 2010 Mar 1]. Available from: http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_decisions/reg2007-04/index-eng.php

Sakuratani Y, Noguchi Y, Kobayashi K, Yamada J, Nishihara T. 2008. Molecular size as a limiting characteristic for bioconcentration in fish. J Environ Biol. 29(1):89-92.

Swartzendruber LJ. Melting point of iron (Erratum). Journal of Phase Equilibria. 5(4): 339.

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

UK Environment Agency 2008, Emission Scenario Document for chemical used in the Electronics Industry. Draft document. Published by UK Environment Agency, presented to the 16th task Force Meeting in October 2008 at Desseau, Germany. Available upon request to Environment Canada

[WSKOWWIN] Water Solubility for Organic Compounds Program for Microsoft Windows [Estimation Model]. 2008. Version 1.41. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Zachary M, Greenway GM. 2009. Comparative PBT screening using (Q)SAR tools within REACH legislation. SAR QSAR Environ Res. 20(1–2): 145–157.

Appendix I – PBT Model Inputs Summary Table

	Phys-Chem/Fate	**Fate**	**Fate**	**PBT Profiling**	**Ecotoxicity**
Model Input Parameters	EPIWIN Suite (all models, including: AOPWIN, KOCWIN, BCFWIN BIOWIN and ECOSAR)	OECD POPs Tool	Arnot-Gobas BCF/BAF Model	Canadian-POPs (including: Catabol, BCF Mitigating Factors Model, OASIS Toxicity Model)	Artificial Intelligence Expert System (AIES)/ TOPKAT/ ASTER
SMILES Code[1]	x	x	x	x	x

[1] The SMILES Code for nickel BHMB was used to generate the model results.

Appendix II: Estimated concentrations of nickel BHMB in environmental media using ChemCAN version 6.00 (ChemCAN 2003).[1]

Medium[2]	**Estimated concentration**
Ambient air[3]	0.602 ng/m^3
Surface water	9.53 ng/L
Soil	377 ng/g solids
Sediment	652 ng/g solids

[1]The concentrations were estimated for the area of southern Ontario.
[2]Default inflow concentrations of 2 ng/m^3 in air and 3 ng/L in water were specified by ChemCAN v6.00.
[3]The oxidative degradation half-life in air was assumed to be 0.437 days (AOPWIN 2008).

Appendix III: Summary of QSAR Results for the Health Assessment on nickel BHMB

QSAR PREDICTIONS ON CARCINOGENICITY

Model/ Species	Mice		Rat		Rat	Mice	Rodent	Mammal
	Male	Female	Male	Female				
Model Applier	NA	NA	NA	NA	NA	NA	NA	-
Multicase Casetox	NA	NA	NA	NA	-	-	-	-
Topkat	NA	NA	NA	NA	-	-	-	-
Derek	-	-	-	-	-	-	-	NR

NA – not applicable
'-' no model available in QSAR suite
NR – no result
P – Positive

QSAR PREDICTIONS ON GENOTOXICITY

Model/endpoints	chrom. ab.	chrom. ab. other rodent	chrom. ab. rat	micronucleus mice	micronucleus rodent	drosophila	drosophila HT	drosophila SLRL	mam. mutation	mam. mutation DL	UDS	UDS human lymphocytes	UDS rat hepatocytes	mouse lymphoma mut	s. cerevisiae	yeast	hgprt	e. coli	e. coli w	Microbial/bacteria	salmonella
MA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
CT	NA	-	-	NA	-	NA	-	-	-	-	NA	-	-	NA	-	-	-	-	-	-	NA
TK	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	NA
Derek	NR	NR	NR	-	-	-	-	-	P	-	-	-	-	-	-	-	-	IC	IC	IC	IC

MA – model applier
CT - Multicase Casetox
TK – Topkat
NA – not applicable
'-' no model available in QSAR suite
NR – no result
P – Positive
IC - Inconclusive

QSAR PREDICTIONS ON DEVELOPMENTAL TOXICITY

Model Applier

Endpoint/ Species	Mice	Rabbit	Rat	Rodent
Retardation	NA	NA	NA	NA
Weight decrease	NA	NA	NA	NA
Fetal death	NA	NA	NA	NA
Post impl. loss	NA	NA	NA	NA
Pre impl. loss	NA	NA	NA	NA
Structural	NA	NA	NA	NA
Visceral	NA	-	NA	NA

NA – not applicable
'-' no model available in QSAR suite

Multicase Casetox

Endpoint/Species	Hamster	Mammal	Miscellaneous
Teratogenicity	-	NA	NA
Developmental	NA	-	-

NA – not applicable
'-' no model available in QSAR suite

QSAR PREDICTIONS ON REPRODUCTIVE TOXICITY

Model Applier

Model/ endpoint	Female			Male		
Species	mice	rat	rodent	mice	rat	rodent
repro	NA	NA	NA	NA	NA	NA
sperm	-	-	-	NA	NA	NA

NA – not applicable
'-' no model available in QSAR suite

Multicase Casetox

mice	rat	rabbit	human
NA	NA	NA	NA

NA – not applicable

QSAR PREDICTIONS ON SENSITIZATION

Model/endpoints	RS - dog	RS – guinea pig	RS - hamster	RS - human	RS - mammal	RS - monkey	RS - mouse	RS - primate	RS - rabbit	RS - rat	RS - rodent	SS - dog	SS – guinea pig	SS - hamster	SS - human	SS - mammal	SS - monkey	SS - mouse	SS - primate	SS - rabbit	SS - rat	SS - rodent
Derek	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

P – Positive
RS – respiratory sensitization
SS – skin sensitization