

## **Screening Assessment for the Challenge**

**Ethanamine,*N*-ethyl-*N*-hydroxy-, reaction products with  
hexamethylcyclotrisiloxane, silica and 1,1,1-trimethyl-*N*-(trimethylsilyl)silanamine**

**Pyridine, 2-[3-(3-chlorophenyl)propyl]-**

**1*H*-Indene, 2,3-dihydro-1,1,3,3,5-pentamethyl-4,6-dinitro-  
(musk moskene)**

**Chemical Abstracts Service Registry Number**

**68583-58-4**

**101200-53-7**

**116-66-5**

**Environment Canada  
Health Canada**

**June 2013**

## 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 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 these substances identified as high priorities.

The substances listed below were identified as high priorities for screening assessment and were included in the Challenge because they were found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and were believed to be in commerce in Canada. These substances were not 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* (DSL).

CAS RN*	DSL Name
68583-58-4	Ethanamine, <i>N</i> -ethyl- <i>N</i> -hydroxy-, reaction products with hexamethylcyclotrisiloxane, silica and 1,1,1-trimethyl- <i>N</i> -(trimethylsilyl)silanamine
101200-53-7	Pyridine, 2-[3-(3-chlorophenyl)propyl]-
116-66-5	1 <i>H</i> -Indene, 2,3-dihydro-1,1,3,3,5-pentamethyl-4,6-dinitro-

\*CAS RN = Chemical Abstracts Service Registry Number, The Chemical Abstracts Service (CAS) Registry Number is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the government when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society

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.

The Notice for the Challenge for the above substances was published in the *Canada Gazette* on December 26, 2009 (Canada 2009). The Substance Profiles were released at the same time. The Substance Profiles presented the technical information available prior to December 2005 that formed the basis for categorization of these substances. Based on the outcome of the Challenge, the Ministers of the Environment and of Health have conducted a screening assessment for these substances. The critical information and considerations upon which the assessment is based are summarized below.

### **Summary of Information Used as Basis for this Screening Assessment**

Based on categorization results, the substances listed in this report have been found to meet the ecological criteria for persistence, bioaccumulation and inherent toxicity to non-human organisms (PBiT). These substances were not found to meet the human health categorization criteria (Environment Canada, 2006).

To establish whether certain high priority substances, including PBiT substances, were currently being manufactured in or imported into Canada, a survey was conducted by issuing a *Notice with Respect to Selected Substances Identified as Priority for Action* pursuant to paragraphs 71(1)(a) and (b) of CEPA 1999. The Notice was published in Part I of the *Canada Gazette* on March 4, 2006 (Canada, 2006a).

In response to this notice, there were no reports of industrial activity (import or manufacture) with respect to these substances in Canada, above the reporting threshold of 100 kg, for the specified reporting year of 2005. However, some companies did identify themselves as having a stakeholder interest in these substances. Therefore, these substances were believed to be potentially in commerce in Canada and were included in the Challenge.

Results from a similar notice issued under paragraph 71(1)(b) of CEPA 1999 on December 26, 2009, as part of the Challenge (Canada 2009) also revealed no reports of industrial activity (import or manufacture) with respect to these substances in Canada, above the reporting threshold of 100 kg, for the specified reporting year of 2006. These results indicate that currently these substances are not in use above the specified reporting threshold, and therefore the likelihood of exposure to these substances in Canada resulting from commercial activity is low. Other sources of entry into the environment have not been identified at this time.

Responses to the above notices and the accompanying questionnaire of December 26, 2009 (Canada, 2006a; Canada 2009) also revealed no new information relevant to the PBiT properties of these substances. Given the lack of any significant commercial activity for these substances, no further collection or analysis relevant to the persistence, bioaccumulation and ecological effects of these substances, beyond what was done for categorization, has been completed for CAS RN 68583-58-4 and CAS RN 101200-53-7. However, new information on ecotoxicity and environmental fate for CAS RN 116-66-5 (musk moskene) has been identified and considered since categorization. The results of an experimental study on biodegradation in water (Givaudan Roure 1993) indicate that CAS RN 116-66-5 is not inherently biodegradable and, therefore, is also not readily biodegradable. This result is in agreement with the estimates from three models indicating that CAS RN 116-66-5 is not readily biodegradable (BIOWIN 2008; TOPKAT 2004; CPOPs 2008). Low experimental water solubility and high experimental log Kow values suggest that CAS RN 116-66-5 is a lipophilic substance which is

expected to be bioaccumulative in aquatic organisms. Using experimental water solubility and log  $K_{ow}$  values as inputs in bioconcentration/ bioaccumulation models, the modelled data indicate that the bioconcentration potential of this substance is very high (BCFBAF 2008; CPOPs 2008). Two additional ecotoxicological studies for CAS RN 116-66-5 studies have been identified. The results from these studies were considered as inconclusive and contradictory. The study by Schramm et al. (1996) contains an inconclusive result (no effects at saturation, i.e., a median effects concentration (EC50) > 0.046 mg/L). In the other study (Chou and Dietrich 1999), a statistically significant reduction of viability of frog larvae (62 to 94%) was observed. However, because of large fluctuations of measured concentrations and use of an inappropriate test system for lipophilic substances (semi-static instead of flow-through), this was not considered to be a high-quality study; nonetheless, a significant – almost 40% – biological effect (i.e., reduced viability of frog larvae) indicates that CAS RN 116-66-5 can be toxic to aquatic organisms. This was supported by modelled data. The estimates from three different ecotoxicological models (ECOSAR 2008; AIEPS 2003-2007; CPOPs 2008) indicate that CAS RN 116-66-5 is expected to cause harm to aquatic organisms at low concentrations (acute median lethal concentrations (LC<sub>50s</sub>) below 1 mg/L). Therefore, the new information supports that CAS RN 116-66-5 is highly persistent and bioaccumulative as defined in the *Persistence and Bioaccumulation Regulations* of CEPA 1999 (Canada 2000), and has inherent toxicity to aquatic organisms.

Therefore, the decisions on PBiT properties made during categorization remain unchanged and accordingly the above three substances are considered to be inherently toxic to non-human organisms. They are also considered to meet the criteria for both persistence and bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations* (Canada, 2000).

As mentioned above, since the results from notice issued under paragraph 71(1)(b) of CEPA 1999 in December 26, 2009 suggest that these substances are not currently in use above the specified reporting threshold, the likelihood of exposure to the general population in Canada is considered to be low; hence the potential risk to human health is considered to be low. Two of these substances (CAS RN 68583 and CAS RN 101200-53-7) were not 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. Also, they are not on the European Union's Candidate List of Substances of Very High Concern for Authorisation (SVHC) (EU 2009).

Based on analogue health effects information, a potential hazard to human health may be associated with CAS RN 116-66-5 (musk moskene). Two other nitromusks, musk xylene and musk ketone were both classified by the European Union as carcinogen category 3 (causes concern for humans owing to possible carcinogenic effects) based on evidence of liver tumours in mice. Member states of the European Union have voted to add musk xylene to the European Union's Candidate List of SVHC (ENDS Europe 2010).

## Conclusion

Based on available information, and until new information is received indicating that these substances are entering, or may enter the environment, from commercial activity or from other sources, it is concluded that the above substances are currently 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 constitute a danger to the environment on which life depends or that constitute a danger in Canada to human life or health. Therefore, it is concluded that they do not meet the any of the criteria as set out in section 64 of CEPA 1999.

As substances listed on the DSL, import and manufacture of these substances in Canada are not currently subject to notification under subsection 81(1). Given their hazardous PBiT properties, as well as the potential hazard to human health associated with CAS RN 116-66-5, there is concern that new activities for the above substances which have not been identified or assessed under CEPA 1999 could lead to the substances meeting the criteria as 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 the above substances be subject to the Significant New Activity provisions specified under subsection 81(3) of the Act, to ensure that any new manufacture, import or use of this substance in quantities greater than 100 kg/year is notified and will undergo ecological and human health risk assessments as specified in section 83 of the Act, prior to the substance being considered for introduction into Canada.

## References

- [AIEPS] Artificial Intelligence Expert Predictive System. 2003–2007. Version 2.05. Ottawa (ON): Environment Canada. Model developed by Stephen Niculescu. Available from: Environment Canada, Ecological Assessment Division, New Chemicals Evaluation Section.
- [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](http://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](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)
- Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C., 1999, c. 33, Canada Gazette. Part III. vol. 22, no. 3. Available from: <http://canadagazette.gc.ca/partIII/1999/g3-02203.pdf>
- Canada. 2000. *Canadian Environmental Protection Act: 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://canadagazette.gc.ca/partI/2006/20061209/pdf/g1-14049.pdf>.
- Canada, Dept. of the Environment, Dept. of Health. 2006a. *Canadian Environmental Protection Act, 1999: Notice with respect to selected substances identified as priority for action*. Canada Gazette, Part I, vol. 140, no. 9, p. 435–459. Available from: <http://canadagazette.gc.ca/partI/2006/20060304/pdf/g1-14009.pdf>
- Canada, Dept. of Environment. 2009. *Canadian Environmental Protection Act, 1999: Notice with respect to Batch 12 substances*. Canada Gazette, Part I, vol. 143, no. 39, p2865 -2888. Available from: <http://www.gazette.gc.ca/rp-pr/p1/2009/2009-12-26/pdf/g1-14352.pdf#page=7>
- Chou Y-J, Dietrich R. 1999. Toxicity of nitromusks in early lifestages of South African clawed frog (*Xenopus laevis*) and zebrafish (*Danio rerio*). Toxicology Letters 111: 17-25.
- [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.

[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](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Environment Canada. 2006. CEPA DSL Categorization Overview and Results [CD-ROM]. Gatineau (QC): Environment Canada, Existing Substances Division. Available on request.

[EU] European Union. 2009. Candidate List of Substances of Very High Concern for Authorisation. European Chemicals Agency. Available from: [http://echa.europa.eu/chem\\_data/authorisation\\_process/candidate\\_list\\_table\\_en.asp](http://echa.europa.eu/chem_data/authorisation_process/candidate_list_table_en.asp) (accessed November 2009)

ENDS Europe. 2010. Europe's environmental news and information service. Haymarket publication [cited 2010 Sept 21]. Available from: <http://www.endseurope.com/24711?referrer=channel%2Dchemicals>

Givaudan Roure. 1993. Test Report No. 93-E14: Inherent biodegradability of musk moskene according to OECD Guideline 302C. May 1993. (cited in OSPAR 2000)

[IARC] International Agency for Research on Cancer. 1996. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 65: Printing processes and printing inks, carbon black and some nitro compounds. WHO, International Agency for Research on Cancer, Lyon, France. Musk ambrette and musk xylene, 477-495.

OSPAR Commission. 2000. OSPAR background document on musk xylene and other musks. 38 p.

Schramm KW, Kaune A, Beck B, Thumm W, Behechti A, Kettrup A, Nickolova P. 1996. Acute toxicities of five nitromusk compounds in *Daphnia*, algae and photoluminescent bacteria. *Wat. Res.* Vol. 30, No.10, pp. 2247-2250.

[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>