FORM FOR NOTIFICATION
OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

Country: CANADA

SECTION 1 IDENTITY OF CHEMICAL SUBJECT TO THE FINAL REGULATORY ACTION

1.1	**Common name**	NCC ether
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	(E,Z)-4-chlorophenyl(cyclopropyl)ketone O-(4-nitrophenylmethyl)oxime (IUPAC)
1.3	**Trade names and names of preparations**	(4-Chlorophenyl) cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime; 4-Chlorophenyl cyclopropyl ketone O-(4-nitrobenzyl)oxime; NCC ETHER; Methanone, (4-chlorophenyl)-cyclopropyl-, O-[(4-nitrophenyl)methyl]oxime

1.4	**Code numbers**	
1.4.1	CAS number	94097-88-8
1.4.2	Harmonized System customs code	Not Available
1.4.3	Other numbers (specify the numbering system)	ELINCS: EC #:406-100-4

1.5 Indication regarding previous notification on this chemical, if any

1.5.1 ☐ This is a first time notification of final regulatory action on this chemical.

1.5.2 ☒ This notification replaces all previously submitted notifications on this chemical.
Date of issue of the previous notification: 2000/5/17

SECTION 2 FINAL REGULATORY ACTION

2.1 The chemical is: ☐ **banned** **OR** ☒ **severely restricted**

2.2 Information specific to the final regulatory action

2.2.1 Summary of the final regulatory action

The *Prohibition of Certain Toxic Substances Regulations, 2005* prohibit the manufacture, use, sale, offer for sale and import of toxic substances listed in Schedules 1 and 2 to the Regulations. NCC ether is found in Schedule 1, which lists prohibited toxic substances subject to total prohibition, with the exception of incidental presence.

2.2.2 Reference to the regulatory document, e.g. where decision is recorded or published

Prohibition of Certain Toxic Substances Regulations, 2005 (SOR/2005-41) under the *Canadian Environmental Protection Act, 1999.*

2.2.3 Date of entry into force of the final regulatory action

May 15, 2005

2.3 Category or categories where the final regulatory action has been taken

2.3.1 All use or uses of the chemical in your country prior to the final regulatory action

In December, 1995, the substance "(4-Chlorophenyl)cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime" (NCC ether) was notified to the Minister of Environment pursuant to subsection 26(1) of the *Canadian Environmental Protection Act* (CEPA). The person submitting the notification proposed to import

this substance into Canada for use as a chemical intermediate in the manufacture of a substance (pesticide) intended solely for export markets.

2.3.2 Final regulatory action has been taken for the category ☒ Industrial

Use or uses prohibited by the final regulatory action

The Regulations prohibit the manufacture, use, sale, offer for sale or import of NCC ether, with the exceptions listed below.

Use or uses that remain allowed (only in case of a severe restriction)

The Regulations do not apply to the incidental presence of NCC ether or for use in a laboratory for scientific research purposes or as a laboratory analytical standard.

2.3.3 Final regulatory action has been taken for the category ☐ Pesticide

Formulation(s) and use or uses prohibited by the final regulatory action

Formulation(s) and use or uses that remain allowed (only in case of a severe restriction)

2.4 Was the final regulatory action based on a risk or hazard evaluation?

☒ **Yes**

☐ **No** (If no, you may also complete section 2.5.3.3)

2.4.1 If yes, reference to the relevant documentation, which describes the hazard or risk evaluation

New Substances Notification NSN#5509. Assessment Report of (4-Chlorophenyl) cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime, Environment Canada and Health Canada, April 1998.

2.4.2 Summary description of the risk or hazard evaluation upon which the ban or severe restriction was based.

2.4.2.1 Is the reason for the final regulatory action relevant to human health? ☒ Yes ☐ No

If yes, give summary of the hazard or risk evaluation related to human health, including the health of consumers and workers

Note: NCC ether was assessed under the original *Canadian Environmental Protection Act* (CEPA). While the Act was updated in 1999, the conclusions of the assessment remain the same. This notification is based on the assessment and therefore references the original Act.

Background

The *Canadian Environmental Protection Act* (CEPA), authorizes the Ministers of the Environment and of Health to investigate Substances New to Canada that may contaminate the environment and cause adverse effects on the environment or on human health.

Also, pursuant to section 29 of the Act, where Ministers have assessed any information, and suspect that a substance is "toxic", the Minister may prohibit any person from manufacturing or importing the substance, before the period for assessing the information is expired. Under Section 11 of CEPA, a substance is considered "toxic" if:

"... it is entering or may enter the environment in a quantity or concentration or under conditions

a. having or that may have an immediate or long-term harmful effect on the environment;

b. constituting or that may constitute a danger to the environment on which human life depends; or

c. constituting or that may constitute a danger in Canada to human life or health."

In December, 1995, NCC ether "(4-Chlorophenyl)cyclopropylmethanone, O-[(4-nitrophenyl)-methyl]oxime" was notified to the Minister of Environment pursuant to subsection 26(1) of CEPA and was subsequently assessed pursuant to subsection 28(1). The assessment led to a suspicion that the substance was toxic and, consequently, its manufacture and importation was prohibited on December 20, 1995.

In view of the demonstrated contact sensitization, adverse health effects in the subchronic study, clear evidence of *in vitro* genotoxicity in the Ames test and

equivocal and/or inconclusive evidence of genotoxicity in one *in vitro* and in one *in vivo* test, NCC ether was considered capable of posing at least a moderate degree of health hazard.

There was reason to suspect NCC ether is toxic under paragraph 11(c) of CEPA. It may enter the environment in quantity or concentration or under conditions constituting or that may constitute a danger in Canada to human life or health.

Expected effect of the final regulatory action

NCC ether was originally prohibited under the Prohibition Regulations. At that time NCC ether was not used, sold, produced, imported or exported in Canada. The only way to ensure that it was not introduced into the Canadian market was through a ban. The amended Regulations continue to prohibit the manufacture, use, sale, offer for sale, or import of NCC ether towards the objective of virtual elimination.

2.4.2.2 Is the reason for the final regulatory action relevant to the environment? ☒ Yes ☐ No

If yes, give summary of the hazard or risk evaluation related to the environment

Note: NCC ether was assessed under the original *Canadian Environmental Protection Act* (CEPA). While the Act was updated in 1999, the conclusions of the assessment remain the same. This notification is based on the assessment and therefore references the original Act.

Background

The *Canadian Environmental Protection Act* (CEPA), authorizes the Ministers of the Environment and of Health to investigate Substances New to Canada that may contaminate the environment and cause adverse effects on the environment or on human health.

Also, pursuant to section 29 of the Act, where Ministers have assessed any information, and suspect that a substance is "toxic", the Minister may prohibit any person from manufacturing or importing the substance, before the period for assessing the information is expired. Under Section 11 of CEPA, a substance is considered "toxic" if:

"... it is entering or may enter the environment in a quantity or concentration or under conditions

a) having or that may have an immediate or long-term harmful effect on the environment;

b) constituting or that may constitute a danger to the environment on which human life

depends; or

c) constituting or that may constitute a danger in Canada to human life or health."

In December, 1995, NCC ether "(4-Chlorophenyl)cyclopropylmethanone, O-[(4-nitrophenyl)-methyl]oxime" was notified to the Minister of Environment pursuant to subsection 26(1) of CEPA and was subsequently assessed pursuant to subsection 28(1). The assessment led to a suspicion that the substance was toxic and, consequently, its manufacture and importation was prohibited on December 20, 1995.

Based on the ecotoxicological data, *Daphnia magna* was the most sensitive aquatic species tested. The 48 hour EC_{50} was reported to be 18 µg/L and the "no observed effect concentration" was reported to be 4.7 µg/L. These data were used to establish freshwater organism "concentrations of concern" for chronic and acute effects of 18 and 470 ng/L, respectively. Manufacture, processing and use information submitted indicated that the substance's release into the environment would have been primarily into receiving waters via plant effluent. The predicted environmental concentration was estimated to be 800 ng/L in receiving waters under potential production conditions.

The predicted environmental concentration in the receiving water exceeded the concern concentration for chronic and acute effects by factors of 40 and 2 respectively.

NCC ether is expected to persist in the environment as degradation was not observed in "ready biodegradation" tests and significant hydrolysis did not occur under environmentally relevant conditions. In addition, the log of the octanol/water partition coefficient (log K_{ow}) for NCC ether is 6.3, indicating the substance has the potential to bioaccumulate in organisms.

NCC ether was determined to be toxic under paragraph 11(a) of CEPA. It may enter the environment in a quantity or concentration or under conditions that may have an immediate or long-term effect on the environment.

Expected effect of the final regulatory action

NCC ether was originally prohibited under the Prohibition Regulations. At that time NCC ether was not used, sold, produced, imported or exported in Canada. The only way to ensure that it was not introduced into the Canadian market was through a ban. The amended Regulations continue to prohibit the manufacture, use, sale, offer for sale, or import of NCC ether towards the objective of virtual elimination.

2.5 Other relevant information regarding the final regulatory action

2.5.1 Estimated quantity of the chemical produced, imported, exported and used

	Quantity per year (MT)	Year
produced	Not Available	Not Available
imported	Not Available	Not Available
exported	Not Available	Not Available
used	Not Available	Not Available

2.5.2 Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions

The amended Regulations continue to ensure that NCC ether is not introduced into the Canadian market. The Regulations therefore represent no change in use in Canada. Any state and region in a similar situation may find these Regulations relevant.

2.5.3 Other relevant information that may cover:

2.5.3.1 Assessment of socio-economic effects of the final regulatory action

The Regulations continue to ensure that NCC ether, which is not deliberately used in Canada, does not enter widespread use, which could increase the environmental risks in Canada. Given that the substance was never used, sold, produced, imported or exported in Canada, there should have been no significant impact on industry and compliance costs were expected to be minimal. Incremental costs to government resulting from the Regulations, including administrative and enforcement costs, were expected to be minimal as well.

2.5.3.2 Information on alternatives and their relative risks, e.g. IPM, chemical and non-chemical alternatives

Not Available

2.5.3.3 Basis for the final regulatory action if other than hazard or risk evaluation

Not Applicable

2.5.3.4 Additional information related to the chemical or the final regulatory action, if any

At the time of the original notification, NCC ether was not listed on the United States Toxic Substances Control Act (US TSCA) Inventory, but was identified on the European List of Notified Chemical Substances (ELINCS) Inventory. In 1991, the UK Department of the Environment proposed that the substance be classified as "Dangerous to the Environment" with the following two risk phrases: R50 very toxic to aquatic organisms R53 may cause long term adverse effects in the aquatic environment.

SECTION 3 PROPERTIES

3.1 Information on hazard classification where the chemical is subject to classification requirements

International classification systems e.g. WHO, IARC, etc.	**Hazard class**
Not Available	Not Available
Not Available	Not Available

Other classification systems e.g. EU, USEPA	**Hazard class**
ELINCS	R50 and R53

3.2 Further information on the properties of the chemical

3.2.1 Description of physico-chemical properties of the chemical

NCC ether is a yellow crystalline solid with the following properties:

- empirical molecular formula: $C_{14}H_{15}ClN_2O_3$
- molecular weight of 331.8 g/mol
- water solubility of 195µg/L at 25°C
- Log K_{ow} of 6.3

- vapour pressure of 3.2 x 10^{-6} Pa at 25°C
- Henry's law constant of 5.36 x 10^{-8} atm m^3/mol

NCC ether does absorb UV radiation, with maximum absorbance at 263 nm. Some absorbance is observed in the 280-300 nm range which may be significant in photolysis.

Reference

New Substances Notification NSN#5509. Assessment Report of (4-Chlorophenyl) cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime, Environment Canada and Health Canada, April 1998.

3.2.2 Description of toxicological properties of the chemical

Dermal irritation was not seen in a study using rabbits. In an eye irritation study, mild conjunctival congestion and chemosis was seen one hour after instillation, completely reverting back to normal by 24 h.

The notified substance was a dermal sensitizer in guinea.

At the highest dose used in a subchronic 28 day toxicity test on rats (1000 mg/kg/day given daily by gavage), the NCC ether caused mortality and acute adverse health effects. At the next dose level, 225 mg/kg/day, a variety of health effects were seen. At the lowest dose of 50 mg/kg/day, haematopoietic changes and increased relative renal weights were seen in the females, whereas, increased liver weights were seen in the male animals. In view of the health effects seen at 50 mg/kg/day, this dose was considered to be the LOEL for this study.

NCC ether induced mutagenic changes (base-pair substitution) in the TA-100 strain of Salmonella typhimurium in the presence of metabolic activation. The increased mutagenicity was equivocal in the absence of metabolic activation in this strain. The other strains used (98, 1535, 1537) did not show evidence of mutagenic activity.

In another *in vitro* test system (Chinese hamster ovary cell culture), there was an equivocally-positive indication of genotoxicity at two dose levels (10 and 100 ug/ml, but not at 33 ug/ml) at the 11 hr. sampling in the presence of metabolic activation. The positive results were statistically significant when compared to the solvent control, however, the concurrent solvent control values were the lowest of all solvent control values obtained in this study (adding to the equivocality of the positive response).

An *in vivo* mouse bone marrow micronucleus test was carried out. The test results

were negative, however, only one dose (MTD; 1500 mg/kg) of NCC ether was utilized and no evidence of cytotoxicity was demonstrated. While this was interpreted by the notifier as a negative evidence of *in vivo* genotoxicity, it could also be due to inadequate delivery of the test substance to the bone marrow site. Without a suitable toxicokinetic study demonstrating adequate bioavailability of NCC ether in the bone marrow, the findings of this study were considered inconclusive.

In view of the demonstrated contact sensitization, adverse health effects in the subchronic study, clear evidence of *in vitro* genotoxicity in the Ames test and equivocal and/or inconclusive evidence of genotoxicity in one *in vitro* and in one *in vivo* test, NCC ether is considered as capable of posing at least a moderate degree of health hazard.

Reference

New Substances Notification NSN#5509. Assessment Report of (4-Chlorophenyl) cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime, Environment Canada and Health Canada, April 1998.

3.2.3 Description of ecotoxicological properties of the chemical

The effects-related information for NCC ether includes acute data for fish and invertebrate species. No information was identified on effects of NCC ether on mammalian wildlife. The log of the octanol/water partition coefficient for the substance is 6.3, suggesting that NCC ether has considerable potential to bioaccumulate in organisms.

Acute toxicity testing on *Daphnia magna* determined a 48 hour EC_{50} of 18 µg/L with a 95% confidence interval of 15-21 µg/L. This value is based on initial measured concentrations. The "no observed effect concentration" (NOEC) is 4.7 µg/L.

Testing on guppies (*Poecilia reticulata*) determined the 96 hour LC_{50} to be greater than 77 µg/L, which is the mean measured concentration of the highest nominal concentration. The two nominal concentrations tested (60 and 100 µg/L) were renewed every 24 hours. Neither mortality nor signs of toxicity were observed at either of the concentrations tested.

While a water solubility value of 195 µg/L was obtained using OECD method 105, the toxicity testing laboratory assumed 100 µg/L approached its practical solubility in water. Tests were not run at higher concentrations.

Reference

New Substances Notification NSN#5509. Assessment Report of (4-Chlorophenyl) cyclopropylmethanone, O-[(4-nitrophenyl)methyl]oxime, Environment Canada and

Health Canada, April 1998.

SECTION 4 DESIGNATED NATIONAL AUTHORITY

Institution	Environment Canada Environmental Stewardship Branch Chemical Sectors Directorate Chemicals Management Division
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PLEASE RETURN THE COMPLETED FORM TO:

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Definitions for the purposes of the Rotterdam Convention according to Article 2:

(a) 'Chemical' means a substance whether by itself or in a mixture or preparation and whether manufactured or obtained from nature, but does not include any living organism. It consists of the following categories: pesticide (including severely hazardous pesticide formulations) and industrial;

(b) 'Banned chemical' means a chemical all uses of which within one or more categories have been prohibited by final regulatory action, in order to protect human health or the environment. It includes a chemical that has been refused approval for first-time use or has been withdrawn by industry either from the domestic market or from further consideration in the domestic approval process and where there is clear evidence that such action has been taken in order to protect human health or the environment;

(c) 'Severely restricted chemical' means a chemical virtually all use of which within one or more categories has been prohibited by final regulatory action in order to protect human health or the environment, but for which certain specific uses remain allowed. It includes a chemical that has, for virtually all use, been refused for approval or been withdrawn by industry either from the domestic market or from further consideration in the domestic approval process, and where there is clear evidence that such action has been taken in order to protect human health or the environment;

(d) 'Final regulatory action' means an action taken by a Party, that does not require subsequent regulatory action by that Party, the purpose of which is to ban or severely restrict a chemical.