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4-**NONYLPHENOL (Branched)**
AND
NONYLPHENOL

CAS Nos: 84852-15-3 and 25154-52-3

EINECS Nos: 284-325-5 and 246-672-0

Summary Risk Assessment Report

2002 **Special Publication I.02.69**

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SUMMARY RISK ASSESSMENT REPORT

2002

United Kingdom

This document has been prepared by the UK rapporteur on behalf of the European Union. The scientific work on the environmental part was prepared by the Building Research Establishment (BRE) Ltd, under contract to the rapporteur.

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(The last full literature survey was carried out in 1996. Use data were added up to 1997, with some specific information more recent than this. Toxicity data have been added up until 1999.)

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 4-nonylphenol and nonylphenol (branched) that has been prepared by the United Kingdom in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the original risk assessment report that can be obtained from European Chemicals Bureau[1]. The present summary report should preferably not be used for citation purposes.

[1] European Chemicals Bureau – Existing Chemicals - http://ecb.jrc.it

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TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Nos : 84852-15-3 and 25154-52-3

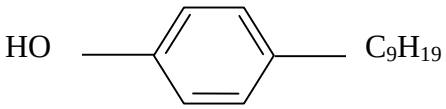
EINECS Nos: 284-325-5 and 246-672-0

IUPAC Name: 4-Nonylphenol (branched) and Nonylphenol

Molecular Formula: $C_{15}H_{24}O$

Molecular weight: 220.34 g/mole

Structural formula:



Synonyms: Isononylphenol (CAS Number 11066-49-2); Phenol, nonyl-, branched (CAS Number 90481-04-2); NP; para-Nonylphenol; Monoalkyl (C3-9) phenol

It is understood that ‘nonylphenol (CAS no. 25154-52-3)’ as originally defined by the Chemical Abstract Service covered all nonylphenols. However, subsequent revisions redefined it to cover only straight chain nonylphenol, other isomers having different CAS numbers. This assessment covers the two substances identified above, and deals with the commercially produced material (predominantly 4-nonylphenol with a varied and undefined degree of branching in the alkyl group). This material will also contain smaller amounts of other isomers and impurities, including straight chain nonylphenol.

Data from any of the isomers are assumed to be representative for nonylphenol unless specified, and nonylphenol (NP) is used as the generic name referring to these substances. In particular it should be noted that the varied degree of branching in the nonyl group might be a factor in the variability of the reported physical-chemical properties.

1.2 PURITY, IMPURITIES AND ADDITIVES

The purity of 4-nonylphenol as produced has been reported as 90% w/w. The main impurities are 2-nonylphenol (5% w/w) and 2,4-dinonylphenol (5% w/w).

1.3 PHYSICO-CHEMICAL PROPERTIES

Physical state (at ntp): clear to pale yellow viscous liquid with a slight phenolic odour.

Melting point: circa -8°C (may vary according to production process)

Relative density: 0.95 at 20°C

Vapour pressure: circa 0.3 Pa at 25°C

Water solubility: circa 6 mg/l at 20ºC and pH 7 (may be pH dependant)

n-Octanol-water partition coefficient (Log Kow): 4.48

Flash point 141-155°C

Flammability circa 370°C

Oxidising properties: not applicable

Viscosity 2,500 mPa.s at 20°C

1.4 CLASSIFICATION

The classification and labelling of nonylphenol is listed in Annex I to Directive 67/548/EEC (28th Adaptation to Technical Progress; January 2001), as follows:

Classification:	Xn; R22	Labelling:	C; N
	C; R34		R: 22-34-50/53
	N; R50-53		S: (1/2-)26-36/37/39-45-60-61

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

Four companies within the EU produced nonylphenol with a total production volume of 73,500 tonnes in 1997. In the same year exports from the EU were 3,500 and imports into the EU were 8,500 tonnes, giving the total tonnage used in the EU as 78,500 tonnes.

2.2 USE

The main uses of nonylphenol are the production of nonylphenol ethoxylates and the production of resins plastics and stabilisers. Minor uses include the production of phenolic oximes.

The breakdown of nonylphenol ethoxylates in the environment may give rise to significant quantities of nonylphenol, therefore their use is considered in the risk assessment. The main use of nonylphenol ethoxylates is in products for industrial and institutional cleaning (30% total use). This is followed by use in emulsion polymerisation, as a textile auxiliary, captive use by the chemical industry, as a leather auxiliary, agricultural use, use in paints and other niche market uses.

2.3 CONTROLS

In Europe, all the major manufacturers of detergents have agreed a voluntary ban on the use of nonylphenol ethoxylates in domestic detergents. PARCOM Recommendation 92/8 requires Member States to achieve the phase out of nonylphenol ethoxylates in domestic detergents by 1995 and in all detergent applications by 2000.

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3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Discussion on environmental fate and behaviour

Nonylphenol released to the atmosphere is likely to be degraded by reaction with hydroxyl radicals, with a half-life of around 0.3 days. It is not thought to contribute to low-level ozone formation or act as a greenhouse gas.

Abiotic degradation of nonylphenol in water is expected to be negligible. Nonylphenol undergoes biodegradation in water, sediment and soil systems. The results from standard tests indicate that nonylphenol is best classed as inherently biodegradable for these systems.
Experimental data and calculated partition coefficients suggest that nonylphenol will be strongly absorbed to soils, sludges and sediments. Evidence from measured levels indicates that adsorption to soil may be governed by factors other than organic carbon content.

The air-water partitioning coefficient is low suggesting that volatilisation is unlikely to be a significant removal mechanism for nonylphenol from water systems.

Experimental data indicate that nonylphenol bioconcentrates to a significant extent in aquatic species.

Based upon the physical and chemical properties and its environmental behaviour the fractions of nonylphenol released to surface water and adsorbed to sludge after wastewater treatment are 0.35 and 0.34 respectively.

3.1.2 Discussion of environmental exposure

Environmental exposure of nonylphenol occurs during its production and subsequent use. It may also occur due to the breakdown of some products containing a nonylphenol group, particular nonylphenol ethoxylates. The life cycle stages of nonylphenol ethoxylates considered are production, formulation and processing. Predicated environmental concentrations (PECs) have been calculated using site-specific data supplemented by defaults as specified by the EU Technical Guidance Document or emission scenario documents where no other data were available. The values are given in **Table 3.1-3** in section 3.3.

3.2 ENVIRONMENTAL EFFECTS

A wide range of acute and chronic studies is available for aquatic species. In acute studies, the lowest values are as follows: for fish a 96-hour LC_{50} of 0.128 mg/l (*Pimephales promelas*); for invertebrates a 96-hour EC_{50} of 0.0207 mg/l (*Hyalella azteca*); and for algae a 72-hour EC_{50} (biomass) of 0.0563 mg/l (*Scenedesmus subspicatus*). Comparable toxicity is observed with saltwater species (the alga *Skeletonema costatum* is slightly more sensitive than the freshwater species with a 96-hour EC_{50} (cell growth) of 0.027 mg/l, compared to a 72-hour EC_{50} (growth rate) of 0.323 mg/l for *Scenedesmus subspicatus*).

In long-term studies, the lowest values are as follows: for fish a 33-day $NOEC_{survival}$ of 0.0074 mg/l (*Pimephales promelas*); for invertebrates a 21-day $NOEC_{surviving\ offspring}$ of 0.024 mg/l (*Daphnia magna*); and for algae a 72-hour EC_{10} (biomass) of 0.0033 mg/l (*Scenedesmus subspicatus*). A 28-day $NOEC_{length}$ of 0.0039 mg/l was also obtained for the saltwater invertebrate *Mysidopsis bahia*.

As long-term NOECs from at least three species representing three trophic levels are available, an assessment factor of 10 may be applied to the long-term NOEC for algae to give an aquatic PNEC of 0.33 μg/l. A mesocosm study has been performed, giving a 20-day NOEC of 0.005 mg/l. Due to possible issues with the test design, this study is taken as supportive of the PNEC, but cannot be used as the sole basis for deriving a PNEC to protect the aquatic compartment. Concentrations of nonylphenol at which oestrogenic effects are observed appear to be higher than those producing other effects. The calculated PNEC should therefore be protective for oestrogenic effects in fish as well. A PNEC for the sediment compartment of 0.039 mg/kg can be derived from the aquatic PNEC assuming equilibrium partitioning.

For the terrestrial compartment long-term data are available for microorganisms, plants and invertebrates. The most sensitive species group appears to be the terrestrial invertebrates with a 21-day EC_{50} (Reproduction) of 13.7 mg/kg and a 21-day EC_{10} (Reproduction) of 3.44 mg/kg reported for earthworms (*Apporec-todea calignosa*). As long-term tests are available for species from three trophic levels an assessment factor of 10 can be used on the NOEC for the species showing the most sensitive end point (in accordance with EU technical guidance), giving a $PNEC_{soil}$ of 0.3 mg/kg.

A $PNEC_{oral}$ of 10 mg/kg food for secondary poisoning can also be derived from the mammalian NOAEL of 15 mg/kg body weight for reproductive effects. A $PNEC_{microorganisms}$ 9.5 mg/l has also been derived for sewage treatment plant.

3.3 RISK CHARACTERISATION

Aquatic compartment (including sediment and STP)

Nonylphenol enters the aquatic compartment directly as nonylphenol or as the breakdown product of nonylphenol ethoxylates. While there can be a reasonable level of confidence in the total amounts of nonylphenol and nonylphenol ethoxylates used in each application, there is less information readily available as to the use and release of nonylphenol and nonylphenol ethoxylates at the local scale. The measured data suggest that local concentrations may be higher where waters are receiving inputs from industries that use either nonylphenol or nonylphenol ethoxylates. Some of the current measured levels data reflect areas where some uses have already been restricted or banned. The measured data are not comprehensive enough to allow all the possible uses of nonylphenol to be accounted for, and therefore the calculated PECs are used to indicate the levels arising from different industries.

The regional concentration of nonylphenol in surface water is 0.60 μg/l which gives a PEC/PNEC ratio greater than 1. Therefore the PEC/PNEC ratio for the local PECs will also be greater than 1. This is because the regional concentration is added to the local concentrations to take account of background levels. **Table 3.1** gives details of local concentrations before the regional concentration is added and compares these values to the PNEC for aquatic organisms. This enables those uses that are only a problem due to the addition of the regional concentration to be identified.

The concentration of nonylphenol in the influent and effluent of wastewater treatment plants has been calculated for the uses detailed above. The local effluent concentration is taken as the PEC_{stp} for risk assessment purposes. A PEC/PNEC ratio <1 is obtained for the all life cycle stages of nonylphenol and nonylphenol ethoxylate use (See **Table 3.1**).

The $PNEC_{sediment}$ is 0.039 mg/kg. This has been calculated from the $PNEC_{water}$ using an equilibrium partition method. The predicted levels in sediments from local sources are shown in **Table 3.1**, along with the resulting PEC/PNEC ratios. These suggest that nonylphenol may have adverse effects on sediment dwelling species although the assessment could be refined with test data.

There are a number of uncertainties in the risk characterisation section for the aquatic environment (including sediment). Firstly, a number of emission scenarios are based upon default estimations. This may result in significant variations between predicted concentrations and actual environmental concentrations. Secondly, the results of biodegradation studies show a wide variation in test results. The reasons for this include possible toxicity of nonylphenol to microorganisms in the test system, the level of adaptation of the microorganisms to nonylphenol and varying isomer composition of the nonylphenol. Therefore the actual half-life for nonylphenol in the environment could be different (longer or shorter) than the estimated values depending on the prevailing conditions. Thirdly, in the PEC calculations some of the calculated levels are higher than the water solubility limit of nonylphenol. This could mean that actual concentrations are over-estimated for these scenarios, but no correction for this has been applied in the calculations.

Terrestrial compartment

Direct releases of nonylphenol to the terrestrial compartment are unlikely to occur given its production method and use pattern. The exception is the use of nonylphenol ethoxylates in pesticide formulations.

Nonylphenol is strongly adsorbed to sludge in the wastewater treatment process, which may then be applied to agricultural land. Nonylphenol released to soil either directly or indirectly will be strongly bound to the soil. It is therefore unlikely to enter groundwater or be transported a considerable distance. Nonylphenol in sewage treatment plants can arise from direct discharges of nonylphenol or from the breakdown of products containing nonylphenol, such as nonylphenol ethoxylates, in the WWTP. High concentrations of nonylphenol may therefore occur in soils where sewage sludge is applied. This is reflected in the high calculated PEC values. The calculated PEC/PNEC ratios indicate that for most uses there is a concern for the terrestrial environment (**Table 3.2**). Measured levels in soil (arising from sludge application) range from 0.3-4.7 mg/kg following application. This gives PEC/PNEC ratios of 1 to 15.6. The background concentration, measured in soil with no sludge application, was <0.02 mg/kg; this is lower than the $PNEC_{soil}$.

There are a number of uncertainties in the risk characterisation section for the terrestrial environment. Firstly, a number of emission scenarios are based upon default estimations. They also assume that sludge from wastewater treatment plants treating nonylphenol ethoxylate is applied to agricultural soil, which will not always be the case. Secondly, the results of biodegradation studies show a wide variation in results. Therefore the actual half-life for nonylphenol in the environment could be different (longer or shorter) than the estimated values depending on the prevailing conditions. Thirdly, measured and calculated values for adsorption coefficient are different. Evidence from measured levels indicates that adsorption to soil may be governed by factors other than organic carbon content and the calculated levels used in the PEC calculations do not take this into account. Finally, in the PEC calculations it is assumed that

nonylphenol ethoxylates are converted instantly into nonylphenol in sludge whereas in the environment this will be a gradual process.

Atmospheric compartment

Nonylphenol is not released in any significant quantities to the atmosphere. In the atmosphere nonylphenol is relatively short lived, based upon its reaction with hydroxyl radicals. It is therefore unlikely to be transported very far from its point of emission. It is unlikely to move from the troposphere to the stratosphere and contribute to ozone depletion. Nonylphenol is not thought to contribute to low-level ozone formation nor act as a greenhouse gas.

Secondary poisoning of predators

Nonylphenol shows a high bioconcentration potential in aquatic organisms. The concentration of nonylphenol in fish and earthworms for predators has been estimated using the EUSES program. The resultant PEC/PNEC ratios are detailed in **Table 3.3**. In addition to these scenarios, a calculation was performed for indirect exposure through consumption of plants sprayed with pesticide containing ethoxylates. This gave a PEC in food of 6 mg/kg. Compared to the PNEC, the PEC/PNEC ratio is 0.6. As this calculation included several additive worst-case assumptions, this indicates there should not be any concern for this route.

There are a number of uncertainties in the risk characterisation section for secondary poisoning. Firstly, as already discussed, a number of emission scenarios are based upon default estimations. This may result in significant variations between predicted concentrations and actual environmental concentrations. Secondly, the aquatic and terrestrial PECs are subject to a number of uncertainties that will similarly affect the PECs for secondary poisoning.

The conclusions of the risk characterisation for each part of the life cycle are summarised in **Table 5.1** in Section 5.

Table 3.1 Comparison of calculated concentrations for water and sediment and PNECs for water, sediment and microorganisms

Life Cycle Stage	PEC_{stp} ($Clocal_{eff}$)	PECstp/ PNECmicro organisms	$Clocal_{water}$	$Clocal_{water}$/ $PNEC_{water}$	$PEClocal_{water}$	$PEClocal_{water}$/ $PNEC_{water}$	$PEClocal_{sediment}$ (wet weight)	$PEC_{sediment}$/ $PNEC_{sediment}$
Direct releases of nonylphenol								
Nonylphenol Production Sites								
A	n/a	n/a	n/a	n/a	<0.2 μg/l (m)	<0.6	<23.5 μg/kg	0.6
B	n/a	n/a	<0.0208 μg/l (m)	<0.006	<60 μg/l	<1.8	<70.4 μg/kg	1.8
C	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
D	<1 μg/l (m)	0.0001	<0.019 μg/l	<0.06	<0.60 μg/l	<1.8	<70.4 μg/kg	1.8
Nonylphenol ethoxylate production sites								
B	n/a	n/a	n/a	n/a	3.02 μg/l (m)	9.15	355 μg/kg	9.1
C 1+2	2.55, 7.29 mg/l	0.27, 0.77	0.26 mg/l	787	0.26 mg/l	787	30.5 mg/kg	782
C 3	2.98 mg/l	0.31	0.30 mg/l	909	0.30 mg/l	909	35.2 mg/kg	903
D 1	30 μg/l	0.003	1.49 μg/l	4.52	2.09 μg/l	6.33	245 μg/kg	6.28
D 2	15 μg/l	0.0015	1.36 μg/l	4.09	1.95 μg/l	5.91	230 μg/kg	5.87
E	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
F	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
G	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Production of nonylphenol/ Formaldehyde resin	15.75-26.25 μg/l	0.002-0.003	1.6-2.6 μg/l	3.09-7.9	2.2-3.2 μg/l	4.9-9.7	258-376 μg/kg	3.05-9.6
Production of TNPP	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Table 3.1 continued overleaf

Table 3.1 continued

Life Cycle Stage	**PEC_{stp} ($Clocal_{eff}$)**	**PECstp/ PNECmicro organisms**	**$Clocal_{water}$**	**$Clocal_{water}$/ $PNEC_{water}$**	**$PEClocal_{water}$**	**$PEClocal_{water}$/ $PNEC_{water}$**	**$PEClocal_{sediment}$ (wet weight)**	**$PEC_{sediment}$/ $PNEC_{sediment}$**
Production of epoxy resin	0.46 μg/l	0.00005	0.05 μg/l	0.15	0.65 μg/l	1.97	76 μg/kg	1.94
Production of other plastic stabilisers	28 μg/l	0.003	2.78 μg/l	8.42	3.38 μg/l	11.3	397 μg/l	11.2
Phenolic oxime production	0.318 mg/l (m)	0.033	0.004 μg/l	0.01	0.60 μg/l	1.79	70.4 μg/kg	1.78
Indirect releases of nonylphenol due to the breakdown of nonylphenol ethoxylates								
Formulation	12.5, 31, 125 μg/l	0.001, 0.003, 0.013	1.24, 3.08, 12.4 μg/l	3.76, 9.33, 37.6	1.84, 3.68, 13.0 μg/l	5.79, 11.12, 39.4	216, 433, 1,526 μg/kg	5.7, 13.1, 39.1
Life Cycle Stage	PEC_{stp} ($Clocal_{eff}$)	PECstp/ PNECmicro organisms	$Clocal_{water}$	$Clocal_{water}$/ $PNEC_{water}$	$PEClocal_{water}$	$PEClocal_{water}$/ $PNEC_{water}$	$PEClocal_{sediment}$ (wet weight)	$PEC_{sediment}$/ $PNEC_{sediment}$
Agriculture (pesticide application)	n/a	n/a	0.08-0.33 μg/l	0.24-1	0.68-0.93 μg/l	2-2.8	79.8-109 μg/kg	2.02-2.77
Captive use by chemical industry	51 μg/l	0.005	0.02 μg/l	0.06	0.62 μg/l	1.88	73 μg/kg	1.87
Electrical engineering industry	30.8 μg/l	0.003	3.05 μg/l	9.24	3.65 μg/l	11.0	428 μg/kg	10.9
Industrial and institutional cleaning	259 μg/l	0.027	25.7 μg/l	77.9	26.3 μg/l	79.7	3.09 mg/kg	79.2
Leather processing	169-845 μg/l	0.018-0.089	16.7-83.8 μg/l	50.6-254	17.3-84.4 μg/l	52.4-255.8	2.03-9.91 mg/kg	52.1

Table 3.1 continued overleaf

Table 3.1 continued

Life Cycle Stage	PEC_{stp} ($Clocal_{eff}$)	PECstp/ PNECmicro organisms	$Clocal_{water}$	$Clocal_{water}$/ $PNEC_{water}$	$PEClocal_{water}$	$PEClocal_{water}$/ $PNEC_{water}$	$PEClocal_{sediment}$ (wet weight)	$PEC_{sediment}$/ $PNEC_{sediment}$
Metal extraction and processing	1.43 mg/l	0.15	141 μg/l	427	141 μg/l	427	1.66 mg/kg	42.6
Mineral fuel and oil industry	n/a	n/a	1-35 μg/l (m)	3-106	1.6-35.6 μg/l	4.8-108	0.19-4.18 mg/kg	4.87-10.7
Photographic industry	0.1-15.5 μg/l	0.00001-0.0016	0.009-1.54 μg/l	0.03-4.67	0.61-2.14 μg/l	2.06-6.45	71.6-251 μg/kg	2.05-6.41
Polymer industry	12.5 μg/l	0.0013	1.24 μg/l	3.76	1.84 μg/l	5.55	216 μg/kg	5.51
Pulp, paper and board industry	160 μg/l	0.017	15.9 μg/l	48	16.5 μg/l	50	1.94 mg/kg	49.7
Textile industry	3.5 mg/l	0.37	350 μg/l	1,060	350 μg/l	1,060	41.1 mg/kg	1,053
Paint Production Domestic use Industrial use	 0.05 mg/l 0.1 μg/l 0.125 μg/l	 0.005 0.00001 0.00001	 4.96 μg/l 0.01 μg/l 0.012 μg/l	 15 0.03 0.04	 5.5 μg/l 0.60 μg/l 0.60 μg/l	 16.7 1.8 1.8	 653 μg/kg 70.4 μg/kg 70.4 μg/kg	 16.6 1.811.81
Civil engineering	0.31 mg/l	0.033	30.75 μg/l	93	31.3 μg/l	94.8	3.67 mg/kg	94.1
Regional and Continental PECs due to direct emissions of nonylphenol and the breakdown of nonylphenol ethoxylates								
Regional					0.60 μg/l	1.78	103 μg/kg	2.64
Continental					0.072 μg/l		13.1 μg/kg	

Table 3.2 PEC/PNEC ratios for the terrestrial compartment

Source	**PEClocal $_{agri,soil}$ (mg/kg wet wt) (Averaged over 30 days)**	**PEC/PNEC**
Direct release of nonylphenol		
Nonylphenol production sites A B C D	 n/a 0.0242 n/a n/a	 n/a 0.08 n/a n/a
Nonylphenol ethoxylates production sites B C D E F G	 n/a 15.5, 15.2 1.27, 1.17 n/a n/a n/a	 n/a 51.7, 50.7 4.23, 3.9 n/a n/a n/a
Production of nonylphenol/formaldehyde resin	0.159	0.53
Production of TNPP	n/a	n/a
Production of epoxy resins	0.0028	0.009
Production of other plastic stabilisers	0.17	0.57
Phenolic oximes production	n/a	n/a
Indirect releases of nonylphenol due to the breakdown of nonylphenol ethoxylates		
Formulation	1.07 (Small scale) 2.67 (Medium scale) 10.6 (Large scale)	3.57 (Small scale) 8.9 (Medium scale) 35.3 (Large scale)
Use in agriculture Pesticide application Veterinary medicine use	 0.0386 0.46, 0.30, 0.82	 0.13* 1.5, 1, 2.7
Captive use by the chemical industry	4.33	14.4
Electrical engineering industry	2.61	8.7
Industrial and institutional cleaning	21.9	73
Leather processing	14.3 (Average user), 71.6 (Large user)	42.7 (Average user) 239 (Large user)
Metal extraction and processing	121	403
Mineral fuel and oil industry	4.33	14.4
Photographic industry	0.009 (Small processor) 1.31 (Large processor)	0.03 (Small processor) 4.37 (Large processor)
Polymer industry	1.06	3.53
Pulp, paper and board industry	13.3	44.3
Textile industry	297	990
Paint Production Domestic use Industrial use	 4.24 0.0085 0.0106	 14.1 0.028 0.035
Civil engineering	26.3	87.7
Regional	0.265	0.88

*The calculation of the PEC for this scenario is based on a single application of pesticide, from which all of the NPEO breaks down to NP. It is possible that multiple applications will occur. However it is calculated that up to 7 simultaneous applications would not give a PEC/PNEC ratio >1, so it is considered that there is no concern based on a worst-case assessment.

Table 3.3 PEC/PNEC ratio for predators of fish and earthworms

Life Cycle Stage	Concentration in fish (mg/kg wet weight)	$PEC_{fish}/PNEC_{oral}$	Concentration in earthworms (mg/kg wet weight)	$PEC_{earthworms}$ / $PNEC_{oral}$
Direct release of nonylphenol				
Nonylphenol production Site A Site B Site C Site D	 0.795 0.775 n/a 0.764	 0.08 0.08 0.08	 n/a 1.82 n/a n/a	0.18
Nonylphenol ethoxylate production Company B Company C Company D Company E Company F Company G	 2.34 134, 156 1.55, 1.48 n/a n/a n/a	 0.23 1.34, 1.56 0.16, 0.15	 n/a 84.7, 98.5 8.52, 7.95 n/a n/a n/a	8.47, 9.85 0.85, 0.80
Phenol/formaldehyde resin production	2.14	0.21	2.55	0.25
TNPP production	n/a		n/a	
Epoxy resin production	0.787	0.08	1.71	0.17
Production of other plastic stabilisers	2.23	0.22	2.6	0.26
Phenolic oximes	0.766	0.08	n/a	
Indirect releases of nonylphenol from the use of nonylphenol ethoxylates				
Formulation of nonylphenol ethoxylates	1.42, 2.4, 7.3	0.14, 0.24, 0.73	7.51, 16, 58.7	0.75, 1.6, 5.87
Agriculture Pesticide application Veterinary medicine use	0.79	0.08	1.9 6.1	0.19 0.61
Captive use by the chemical industry	0.774	0.08	24.9	2.49
Electrical engineering industry	2.37	0.23	15.7	1.57
Industrial and institutional cleaning	14.3	0.98	120	12.0
Leather processing	9.59, 44..9	0.96, 4.5	78.6, 386	7.86, 38.6
Metal extraction and processing	75.3	7.53	651	65.1
Mineral fuel and oil industry	2.38	0.24	24.9	2.49
Photographic industry	0.769, 1.57	0.08, 0.16	1.74, 8.75	0.17, 0.87
Polymer industry	1.42	0.14	7.38	0.74
Pulp, paper and board industry	8.93	0.89	72.9	7.29
Textile industry	184	18.4	1,600	160
Paint production and use	3.38 (Man) 0.769 (Dom) 0.77 (Ind)	0.21 0.08 0.08	24.5 (Man) 1.74 (Dom) 1.75 (Ind)	2.45 0.17 0.17
Civil engineering	17	1.7	143	14.3
Regional	0.764	0.08	1.69	0.17

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

Nonylphenol is understood to be used as a chemical intermediate, and in the manufacture and use of speciality paints. Apart from during the use of speciality paints, nonylphenol is always likely to be processed in closed plant. Since production is also in closed plant, occupational exposure to nonylphenol is likely to only occur when the plant is breached. This may include charging vessels, taking process samples, product filling and maintenance. It also has low volatility and is heated to above 50 °C to allow the viscous material to be handled. Companies generally do not measure exposure to nonylphenol due to the nature of its use and the low concern for occupational exposure. Control is, in some cases, demonstrated by measuring exposure to other more hazardous substances, for example, ethylene oxide and phenol.

Occupational exposure data are available for two companies. The first company reported short-term measurements ranging from 0.001 to 0.005 ppm, with one further result of 21 ppm. The second company reported results for 4-hour, 8-hour and 12-hour TWAs, and short-term measurements. It was not reported why the results were reported as these three different TWAs. The results, however, were all less than the LOQ for the method, <0.05 ppm to <0.16 ppm for the long-term measurements; 0.08 ppm to 0.28 ppm for the short-term measurements. The SVC was calculated to provide an indication of the maximum likely concentration in air that can be generated at a given temperature. The SVC for nonylphenol is 2.96 ppm (calculated) at 25°C. This concentration cannot be achieved in the open workplace due to air movement and dilution effects, thus exposures will be significantly below 2.96 ppm. Nonylphenol is used at elevated temperatures, however, this is in closed systems therefore any releases of nonylphenol at higher temperatures are likely to be minimal. Releases of hot vapour are likely to immediately cool and condense on to external plant surfaces. Therefore any increase in processing temperature is unlikely to result in a significant increase in airborne concentration in the work place. The reported measurement of 21 ppm therefore seems unlikely given the SVC of 2.96 ppm.

Considering the SVC and the industry exposure data, it was concluded that exposures are likely to be less than 1 ppm 8-hour TWA, and in most cases significantly less for manufacturers and chemical intermediate users. It seems reasonable to further assume that most exposures will be less than 0.1 ppm 8-hour TWA since only one actual result exceeded this value; therefore this value represents the reasonable worse-case scenario. The only other figures above this were up to 0.16 ppm 8-hour TWA, which is the limit of quantification. It is also likely that exposures during the manufacture of speciality paints containing nonylphenol are similarly low.

Occupational exposure to residual nonylphenol may also occur during the use of its derivatives. It is unlikely that this exposure will be significant. Chemical intermediate manufacturers appear not to monitor residual levels of nonylphenol. The reactivity of nonylphenol in ethoxylate manufacture is such that residual levels sufficient to generate significant occupational exposure for users is unlikely.

Exposure to nonylphenol during speciality paint manufacture is estimated to be controlled below 0.01 ppm 8-hour TWA. During charging of the mixing vessel with nonylphenol, exposure may reach 0.1 ppm for up to 30 minutes. These exposure estimates do not take into account the effects of respiratory protective equipment (RPE), which is reported to be worn.

Exposure to nonylphenol during on-site paint mixing is also estimated to be low (below 0.01 ppm). Exposure during spray application is estimated to be 25 to 50 ppm 8-hour TWA using the EASE model. However, these exposures are significant overestimates by the EASE model since it is not particularly suited to predicting exposures to low volatility substances that are sprayed. The model will give a value that represents the vapour more than the aerosol. Since there is likely to be minimal vapour during the application of these paints the above predictions are clearly wrong. Based on an alternative model, an exposure of 1.7 mg/m^3 8-hour TWA is predicted for the spray application of speciality paints containing nonylphenol. Although there are a number of uncertainties surrounding the estimate of exposure for this scenario, it is likely that the figure of 1.7 mg/m^3 (0.2 ppm) 8-hour TWA is a more realistic value to use than that of 50 ppm (approx. 450 mg/m^3) predicted using EASE. However, in view of the uncertainties a value of 1 ppm (9.1 mg/m^3) was taken forward for the risk characterisation.

Dermal exposure was predicted using EASE to be in the range of 0 to 0.1 mg/cm^2/day, for almost all activities, although exposure is predicted to be towards the bottom of this range. The higher end of the range is likely to represent exposure during activities such as maintenance.

The potential for dermal exposure during paint spraying was estimated to be higher than that for other activities, at up to 0.25 mg/cm^2/day. This figure does not take into account the effects of any gloves worn. This value is consistent with measured data for exposure during a similar activity, although not with nonylphenol, based paint.

4.1.1.2 Consumer exposure

There are limited data on the potential exposure to nonylphenol from consumer products but estimates are available for the most likely sources of exposure. The potential systemic exposure arising from consumer use of pesticide products is calculated to be 21 µg via inhalation and 3.2 µg via dermal contact which, if used daily by a 70 kg adult, would be equivalent to 0.35 µg/kg/day. That for use of hair dyes is 3 µg/kg per event (equivalent to 0.1 µg/kg/day). Exposure from food contact materials is estimated to be 2 µg/kg/day. Systemic bioavailability by the oral route is 10%, thus systemic exposure from food contact materials is estimated to be 0.2 µg/kg/day. These values will be used in the risk characterisation. Other sources are considered to be minimal and most are being phased out in the near future.

For total daily exposure to nonylphenols it is assumed that a consumer uses pesticide products daily, uses hair dyes regularly and is exposed via food contact materials. The systemic exposure estimate is about 0.6 µg/kg/day.

4.1.1.3 Indirect exposure via the environment

Nonylphenol has several uses that can result in release into surface water. Nonylphenol has been shown to bioconcentrate to some extent in aquatic organisms and so may enter the food chain, although biomagnification is not expected to occur. Low levels of nonylphenol are predicted to occur in air. The main source of exposure to humans via the environment is therefore likely to be via food and, to a lesser extent, drinking water.

The EUSES model has been used to estimate various concentrations in food, air and drinking water and from these a daily human intake figure is derived. The local figures were derived from the default estimates of releases from production and use of nonylphenol, and are not based on measured data. These release estimates are used in the absence of reliable exposure information and may grossly overestimate the actual situation.

The highest daily human intake figure of 4.42 mg/kg/day is derived for the textile industry. Intake figures for other local sources were 4.32, 2.28 and 0.245 mg/kg/day for nonylphenol ethoxylate production sites, $8.31 \cdot 10^{-3}$ mg/kg/day for use of nonylphenol as a monomer in polymer production, 0.015 mg/kg/day for use of nonylphenol as a stabiliser in polymer production and 1.66 mg/kg/day for use in metal extraction. At a regional level the estimated human intake is $5.31 \cdot 10^{-3}$ mg/kg/day. The largest contributor to the figures is through the intake of fish. This accounts for around 70-80% of the daily dose. The other significant contributor to the figures is through intake of roots (1-29%).

There is considerable uncertainty in the estimated human daily intake figures, consequently the accuracy of the predictions is difficult to determine. The first cause of uncertainty results from the lack of reliable data on the quantities of nonylphenol released into the environment from the various uses. Releases and hence concentrations from actual use sites are likely to be much lower than the figures used here. The second cause of uncertainty concerns the assumptions made in the local calculations that all of the water, air and food comes from close to a point source of release. Concentrating on the most important contributors (fish and root crops), while it can reasonably be argued that it is extremely unlikely that all fish and roots would be supplied from local sources, it is equally reasonable to argue that (i) local sources may be significant for a small number of individuals and (ii) that the models demonstrate that these sources are a potential cause for concern.

The calculations may be overestimates but the degree of over estimation is uncertain. Whatever the degree of sourcing of food from the local area, the concern needs to be addressed. Further information is needed on emissions into the local environment from production and use plant.

4.1.1.4 Combined exposure

The highest exposure an individual is likely to experience would occur if they apply speciality paints (2 mg/kg/day), use a pesticide product (0.35 µg/kg/day), cosmetics (0.1 µg/kg/day) and are exposed via food packaging materials (0.2 µg/kg/day) while living in the locality of a textile factory (4.42 mg/kg/day). The total exposure would be approximately 6.4 mg/kg/day.

4.1.2 Effects assessment: hazard identification and dose (concentration) – response (effect) assessment

Few significant human data are available so this assessment of the hazardous properties of nonylphenol is based mainly on animal data.

Most of the information on the toxicokinetics of nonylphenol concerns oral exposure and is based on a small number of limited rat and human studies, supported by a read across from data relating to octylphenol, an alkyl phenol with a close structural relationship to nonylphenol. The available data, though sparse, do provide the basis for a general understanding of the main features of the toxicokinetic profile. Absorption from the gastrointestinal tract is initially rapid, and probably extensive. The major metabolic pathways are likely to involve glucuronide and sulphate conjugation, and there is evidence of extensive first pass metabolism of nonylphenol absorbed through the gastrointestinal tract. Because of first pass metabolism, the bioavailability of unconjugated nonylphenol is probably limited following oral exposure, at no more than 10-20% of the administered dose. Nonylphenol is distributed widely throughout the body, with the highest concentration in fat. The major routes of excretion are via the faeces and urine. Regarding bioaccumulation, there are insufficient data to allow a conclusion to be drawn on whether or not nonylphenol has this potential. There are no data on the toxicokinetics of nonylphenol following inhalation exposure, but on the basis of the oral absorption data and high partition coefficient, it would be prudent to assume that significant absorption via this route can occur. Furthermore, because first pass metabolism will not take place following exposure by the inhalation route, the systemic bioavailability is likely to be substantially greater than is associated with the oral route. Concerning the dermal route, *in vitro* data indicate that nonylphenol is poorly absorbed across skin, although some limited skin penetration, especially to the stratum corneum, can occur. For the risk characterisation, it is assumed that absorption by the oral and inhalation routes is 100%, but for the oral route systemic bioavailability is 10%. For the dermal route, it is assumed that 10% of a dose will be absorbed and be systemically bioavailable. Using these values the risk assessment will err on the side of caution.

Nonylphenol is moderately toxic by the oral route, with LD_{50} values for the rat in the range of about 1200 to 2400 mg/kg. The dose-response curve for lethality appears to be steep. Erosion of the stomach mucosa is sometimes seen following the administration of a lethal dose. The acute toxicity of nonylphenol by the dermal route is similar, with an LD_{50} of about 2000 mg/kg in rabbits. No data are available on the acute inhalation toxicity, although the corrosive nature of nonylphenol suggests that acute toxicity could be elicited following exposure by this route. Liquid nonylphenol can be corrosive to the skin, although its potency might vary according to source and exact composition. The liquid is also a severe eye irritant. Exposure to the saturated vapour (400 ppm) elicited mild sensory irritation of the respiratory tract in mice, but no reaction was elicited at 30 ppm. The results of several guinea pig maximisation tests suggest that nonylphenol does not have significant skin sensitising potential. No information on respiratory tract sensitisation is available, although it can be predicted from its low chemical reactivity that nonylphenol is unlikely to be a respiratory allergen.

In a multigeneration study in the rat involving oral exposure for up to 20 weeks, a LOAEL for repeated dose of 15 mg/kg/day was identified, based on histopathological changes in the kidneys (tubular degeneration or dilatation), although such changes were not apparent at this dose level in a 90-day rat study. At higher dose levels the liver may also be a target organ; minor histopathological changes in the liver (vacuolation in the periportal hepatocytes or occasional individual cell necrosis) were seen at doses of 140 mg/kg/day and above in some studies. No repeated-dose studies involving dermal or inhalation exposure have been conducted.

Concerning mutagenicity, nonylphenol tested negative in two bacterial assays and an *in vitro* mammalian cell gene mutation assay. An *in vivo* micronucleus test, conducted using the intraperitoneal route, was negative. A second *in vivo* micronucleus test, which used the oral route, was also negative, although there were methodological weaknesses in this study. These results show that nonylphenol is not mutagenic.

Carcinogenicity has not been directly studied. However, some information on the carcinogenic potential can be derived from other data. On the basis of the information currently available it is unlikely that nonylphenol is mutagenic, so concerns for cancer caused by a genotoxic mechanism are low. Considering the potential for carcinogenicity by a non-genotoxic mechanism, no evidence of sustained cell proliferation or hyperplasia was seen in the standard repeated exposure toxicity studies. Nonylphenol has been reported to induce cell proliferation in the mammary gland of the Nobel rat following subcutaneous exposure at levels down to 0.05 mg/kg/day, but this finding could not be reproduced in a duplicated study; furthermore there are doubts about the relevance of this model to humans because of the route of exposure and sensitivity of the strain selected. Overall, there are low concerns for carcinogenicity by a non-genotoxic mechanism.

Nonylphenol has been shown to have oestrogenic activity in a number of *in vitro* and *in vivo* assays. The potency of this oestrogenic activity in these assays ranged from 3 to 6 orders of magnitude less than that of oestradiol. The effects of nonylphenol on fertility and reproductive performance have been investigated in a good quality oral multigeneration study in the rat. This study provided evidence that nonylphenol exposure over several generations can cause minor perturbations in the reproductive system of offspring, namely slight changes in the oestrous cycle length, the timing of vaginal opening and possibly also in ovarian weight and sperm/spermatid count, although functional changes in reproduction were not induced at the dose levels tested. The NOAEL for these changes was 15 mg/kg/day. The observed perturbations in offspring are compatible with the predictable or hypothesised effects of exogenous oestrogenic activity. Evidence of testicular toxicity, seen as seminiferous tubule vacuolation, cell necrosis and a reduction in tubule diameter, was reported at exposure levels which also cause mortality in a repeated dose gavage study in rats. The LOAEL for testicular toxicity was 100 mg/kg/day. The toxicity of nonylphenol appears to be enhanced by gavage administration in comparison to dietary administration, presumably because higher peak blood concentrations of nonylphenol are achieved by gavage. No evidence that nonylphenol is a developmental toxicant was seen in a standard oral developmental toxicity study in the rat. In contrast, in a gavage study involving *in utero*, lactational and direct post-weaning exposure, there was evidence of a reduction in sperm count at 250 mg/kg/day, although it is not possible to state whether this is a developmental effect or as a result of direct exposure after weaning. In an intraperitoneal study designed to investigate the effects of nonylphenol on male reproductive tract development of neonatal rats, evidence of impaired development was observed. However, this study was difficult to interpret, such that these results carry little weight in the overall assessment of the available data. Overall, the observations of oestrogenic activity in the *in vitro* and *in vivo* assays, minor perturbations in the reproductive system of offspring in the multigeneration study, and testicular changes in gavage studies collectively raise concerns for reproductive toxicity, possibly mediated through action on the oestrogen receptor. These concerns are addressed in the risk characterisation, although there are uncertainties.

To conduct the risk characterisation for workers and consumers, it is necessary to compare human exposure for the inhalation/dermal route with oral N(L)OAELs from repeated-dose animal studies, because of the absence of significant inhalation/dermal toxicity data. A direct

comparison between exposure and effects is not valid because first pass liver metabolism is likely to limit systemic bioavailability by the oral route. To compensate for this limited oral bioavailability (assumed to be 10% of administered dose), the animal N(L)OAELs have been reduced by a factor of 10 for the comparison of inhalation or dermal exposure and effects. Thus, the "systemic" values used for comparison in the risk characterisation are a LOAEL of 1.5 mg/kg/day for repeated dose toxicity, and a NOAEL of 1.5 mg/kg/day for reproductive effects. It is assumed that the acute oral toxicity of nonylphenol is mainly the result of a local effect in the gastrointestinal tract, related to corrosivity. Therefore, compensation for limited systemic bioavailability is not applicable for this endpoint.

4.1.3 Risk Characterisation

The key health effects are acute toxicity, corrosivity, repeated dose toxicity and effects on the reproductive system. Sensitisation, mutagenicity and carcinogenicity are of low concern.

4.1.3.1 Workers

With respect to the industry sectors involving the manufacture of nonylphenol and its use as an intermediate, the margins between actual exposure and the N(L)OEALs for repeated dose toxicity and reproductive effects are low, giving rise to concerns for risks to human health. The corrosivity of the substance in relation to the skin and eye is unlikely to be expressed when good occupational hygiene practices are in operation. However, if there is contact with the skin or eye, which could occur accidentally, then local damage is possible. For acute toxicity the margin between exposure and the lethal dose is large and hence there are no concerns.

In the manufacture of speciality paints, the margins between exposure and the LD_{50} or N(L)OAEL values are of sufficient magnitude to provide reassurance that health effects will not occur. Regarding the spray application of speciality paint, the margin between exposure and a lethal dose is of sufficient magnitude to provide reassurance that health effects will not occur. Because of the variation in hygiene practice for the spraying of paints, conclusion iii is considered appropriate for corrosivity. The N(L)OAELs for repeat dose toxicity and reproductive effects are similar to the exposure estimate, and hence there are concerns for human health.

4.1.3.2 Consumers

Nonylphenol is not used directly in products with which the consumer comes into contact. However it is used to make other products which are sold to consumers. Consumer products may therefore contain very low levels of residual nonylphenol and in certain products the derivative compound may break down to release small amounts of nonylphenol. These are the potential sources of consumer exposure.

The consumer products considered in the assessment, from which potential consumer exposure to nonylphenol could arise, are pesticide formulations, cosmetics and food contact materials.

There may be other product types for which risk characterisations have not been provided; this has occurred where insufficient data are available. The product types for which risk characterisations are presented probably represent the worst-case exposures given that pesticide use is a spray application, the hair product involves direct application to the body and the food contact materials result in potential oral exposure. However, even considering these exposures

together on a daily basis, there is no concern for human health. There is also sufficient confidence in the MOS derived that if similar low exposures were to occur from one or two other products there would still be no cause for concern for human health.

4.1.3.3 Indirect exposure via the environment

There are concerns for human health with respect to local exposure, based on MOSs of about 3 for repeated dose toxicity and reproductive effects. In order to refine the exposure estimate, further information is needed on emissions into the local environment from production and use plant. Acute toxicity and corrosivity are of low concern where exposure is dissipated throughout the environment.

4.1.3.4 Combined exposure

The maximum combined daily exposure for an individual is approximately 6.4 mg/kg/day from the estimates provided in this report. The risk characterisation for combined exposure with respect to repeated dose toxicity and reproductive effects is influenced by both the exposure to workers and to those exposed in the locality of a textile plant. The MOS values indicate a cause for concern. However, **conclusion (i)** is proposed because the risk characterisation can be refined when risk reduction measures have been considered for workers and further information on local environmental exposure has been obtained as described in the relevant sections. Acute toxicity and corrosivity are of low concern.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

The physicochemical properties of nonylphenol (as defined in this risk assessment document) are not easily available in the literature but can be established by contacting manufacturers and via safety data sheets. There is some evidence that the physicochemical properties vary slightly depending on the particular manufacturing process. Nonylphenol is a complex mixture of isomers, so this is not unexpected.

The substance is of high viscosity, low vapour pressure and flammability and does not have any explosive potential that would be a cause for concern either from the substance directly or in solution in water. There are no specific major hazard regulations associated with this material and controls on storage and use should be addressed at a local level.

During the manufacture, storage and use of this substance the control measures that are used ensure that risks arising from the physicochemical properties are of no concern to workers. No risk from physicochemical properties is considered to arise from consumer plastics and phenolic coatings or other consumer goods; no cause for concern is identified for consumers from any of these exposures. There is also considered to be no cause for concern to humans from indirect exposure via the environment. Therefore **conclusion (ii)** is reached.

5 RESULTS

5.1 ENVIRONMENT

Table 5.1 summarises the environmental risk characterisation conclusions for each stage in nonylphenol's life cycle.

Table 5.1 Summary of risk characterisation conclusions for the environment

Life cycle stage		Risk characterisation					
		Waste water treatment plant microorganisms	Aquatic compartment (Surface water)	Aquatic compartment (Sediment)[a]	Terrestrial compartment	Atmosphere	Secondary poisoning
Nonylphenol production		(ii)	(iii)	(i)	(ii)	(ii)	(ii)
Nonylphenol ethoxylate production		(ii)	(iii)	(i)	(iii)	(ii)	(iii)
Production of phenol/formaldehyde resins		(ii)	(iii)	(i)	(ii)	(ii)	(ii)
Production of TNPP		(ii)[b]	(ii)[b]	(ii)[b]	(ii)	(ii)	(ii)
Production of epoxy resins		(ii)	(iii)	(i)	(ii)	(ii)	(ii)
Production of other plastic stabilisers		(ii)	(iii)	(i)	(ii)	(ii)	(ii)
Production of phenolic oximes		(ii)	(iii)	(i)	(ii)	(ii)	(ii)
Formulation of nonylphenol ethoxylate		(ii)	(iii)	(i)	(iii)	(ii)	(iii)
Use of nonylphenol ethoxylates							
	Agriculture (pesticides)	(ii)	(iii)	(i)	(ii)	(ii)	(ii)
	Agriculture (veterinary medicines)	(ii)[b]	(ii)[b]	(ii)[b]	(iii)	(ii)	(ii)
	Captive use by the chemical industry	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Electrical engineering industry	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Industrial and institutional cleaning	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Leather processing	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Metal extraction and processing	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Mineral fuel and oil industry	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Photographic industry	(ii)	(iii)	(i)	(iii)	(ii)	(ii)
	Polymer industry	(ii)	(iii)	(i)	(iii)	(ii)	(ii)
	Pulp, paper and board industry	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Textile industry	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Paint production	(ii)	(iii)	(i)	(iii)	(ii)	(iii)
	Domestic paint use	(ii)	(iii)	(i)	(ii)	(ii)	(iii)
	Industrial paint use	(ii)	(iii)	(i)	(ii)	(ii)	(iii)
	Civil engineering	(ii)	(iii)	(i)	(iii)	(ii)	(iii)

Conclusion (i):There is need for further information and/or testing:
Conclusion (ii):There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied already.
Conclusion (iii): There is a need for limiting the risks; risk reduction measures that are already being applied should be taken into account.
a No further work is recommended because the sediment risk characterisation is dependant upon the aquatic risk characterisation for which a conclusion (iii) is reached.
b A conclusion (ii) is reached because there are no emissions to the aquatic compartment from these uses.

5.2 HUMAN HEALTH

The hazardous properties of nonylphenol have been evaluated in animals to the extent that the minimum data requirements according to Article 9(2) of Regulation 793/93 have been met. The key health effects of acute toxicity, corrosivity, repeated dose toxicity and reproductive effects have been identified. For acute toxicity, the oral LD_{50} is in the range 1200 - 2400 mg/kg and the dermal LD_{50} is around 2000 mg/kg. The inhalation LC_{50} is not known but the corrosive nature of nonylphenol suggests that nonylphenol may cause acute toxicity by this route. No dose response information is available on corrosivity. Mild sensory irritation of the respiratory tract is elicited at 400 ppm, but not at 30 ppm. An oral LOAEL for repeated dose toxicity is 15 mg/kg/day. Concerns for mutagenicity and carcinogenicity are low. Regarding the effects on the reproductive system,, the observations of oestrogenic activity in *in vitro* and *in vivo* assays, minor perturbations in the reproductive system of offspring in a multigeneration study, and testicular changes in gavage studies collectively raise concerns. The oral NOAEL for reproductive effects is 15 mg/kg/day.

Thus, the result of the hazard assessment is that **conclusion (ii)** is reached because the minimum data requirements according to Article 9(2) of Regulation 793/93 have been met and no further data are required.

Conclusion (ii): There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

5.2.1 Occupational assessment

Inhalation exposures to nonylphenol during manufacture and use as an intermediate are likely to be less than 0.1 ppm (8-hour TWA). During the manufacture of speciality paints, inhalation exposures to nonylphenol are estimated to be less than 0.01 ppm (8-hour TWA). Routine dermal exposure during nonylphenol manufacture, use as an intermediate and manufacture of speciality paints is negligible and consequently this route of exposure is considered unlikely to contribute significantly to the overall systemic body burden. Infrequent accidental dermal contact with contaminated surfaces may occur, but because of the corrosive nature of the substance, the duration of contact will be brief and significant systemic exposure is unlikely. The potential inhalation exposure during speciality paint spray application is estimated to be up to 1 ppm (8-hour TWA), not taking account of the effects of RPE or the dilution afforded by working outdoors. Dermal exposure during this activity is estimated to be 0.25 mg/cm^2/day.

With respect to manufacture of nonylphenol and its use as an intermediate, the margins between actual exposure values and N(L)OAELs for repeated dose toxicity and reproductive effects are low, giving rise to concerns for risks to human health. For acute toxicity the margin between exposure and the lethal dose is large and hence there are no concerns. In the manufacture of speciality paints, the margins between exposure and the LD_{50} or N(L)OAEL values are of sufficient magnitude to provide reassurance that health effects will not occur. Regarding the spray application of paint, the margins between exposure and the N(L)OAELS for repeat dose toxicity and reproductive effects are low, hence there are concerns for human health. For acute toxicity the margin between exposure and the lethal dose is large and hence there are no concerns. Although there are risks to the skin in relation to corrosivity in all these industry sectors, it is considered that these are suitably mitigated by adherence to good occupational

hygiene practices; however there are concerns for corrosivity in the spray application of speciality paint because hygiene practice can be variable.

Thus, **conclusion (iii)** applies for workers in the industry sectors of: manufacture of nonylphenol, use of nonylphenol as an intermediate and use of speciality paints.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures that are already being applied should be taken into account.

Conclusion (ii) is reached for the remaining scenario: the manufacture of speciality paint.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

5.2.2 Consumer assessment

Consumer exposure is so low from the quantifiable estimates that there are no concerns for risks to human health from the hazardous properties of acute toxicity, corrosivity, repeated dose toxicity and reproductive effects and **conclusion** (**ii**) applies for all these endpoints. Concerns for mutagenicity and carcinogenicity are low.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

5.2.3 Indirect exposure via the environment

There is considerable uncertainty in the estimated human daily intake figures, consequently the accuracy of the predictions is difficult to determine. However, modelled data have been used to construct risk characterisations. Acute toxicity and corrosivity are of low concern and lead to a **conclusion (ii)** for both regional and local scenarios.

For regional exposure, the best estimate for exposure is $5.13 \cdot 10^{-3}$ mg/kg/day. The MOS for both repeated dose toxicity and reproductive effects are high and provide reassurance that adverse health effects will not occur. Therefore **conclusion (ii)** is reached for these endpoints. Acute toxicity is not a relevant endpoint of concern, and corrosivity is of no concern.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

For local exposure the available modelled data suggest that there are concerns for human health, based on low margins between modelled exposures and the N(L)OAELs for repeated dose and reproductive toxicity. Acknowledging that the model exposures may overestimate real exposures from local sources, **conclusion (i)** applies.

Conclusion (i) There is need for further information and/or testing.

In order to refine the estimates of exposure from local sources, further information is needed on emissions into the local environment from production and use plant.

Conclusion (ii) is reached for acute toxicity and corrosivity, which are of low concern for this scenario where exposure is dissipated throughout the environment.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied already.

5.2.4 Combined exposure

The MOS values for repeated toxicity and reproductive effects indicate a cause for concern. However, **conclusion (i)** is proposed because the risk characterisation can be refined when risk reduction measures have been considered for workers and further information on local environmental exposure has been obtained as described in the relevant sections.

Conclusion (i) There is need for further information and/or testing.

Conclusion (ii) is reached for acute toxicity and corrosivity, which are of low concern for this scenario.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

5.2.5 Risks from physicochemical properties

There are no significant risks to humans from the physicochemical properties of nonylphenol. Therefore **conclusion (ii)** is reached.

Conclusion (ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.