2-FURALDEHYDE

(Furfural)

CAS No: 98-01-1

EINECS No: 202-627-7

SUMMARY RISK ASSESSMENT REPORT

Final report, February 2008

The Netherlands

FINAL APPROVED VERSION

Rapporteur for the risk assessment of furfural is the Ministry of Housing, Spatial Planning and the Environment (VROM) and the Ministry of Social Affairs and Employment (SZW), in consultation with the Ministry of Public Health, Welfare and Sport (VWS). Responsible for the risk evaluation and subsequently for the contents of this report is the rapporteur.

The scientific work on this report has been prepared by the Netherlands Organization for Applied Scientific Research (TNO) and the National Institute of Public Health and Environment (RIVM), by order of the rapporteur.

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 2-furaldehyde that has been prepared by The Netherlands 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 comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau[1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

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

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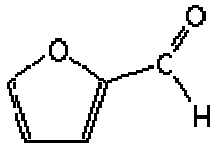
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 98-01-1
EINECS Number: 202-627-7
IUPAC Name: furfural
Molecular formula: $C_5H_4O_2$
Structural formula:



Molecular weight: 96.08
Synonyms: 2-formylfuran, fural, furan-2-aldehyd, furfuraldehyd, furfurol, 2-furaldehyde, artificial ant oil, furale, 2-furancarboxaldehyde, furaldehyde, 2-furyl-methanal, 2-furfural, furfurole, pyromucic aldehyde, furale, 2-furanaldehyde, 2-furancarbonal, "-furole, furole, furfurane carboxylic aldehyde, 2-furylaldehyde, artificial oil of ants, furan-2-carbaldehyde, 2-formylfuran

1.2 PURITY/IMPURITIES, ADDITIVES

Purity: > 98% w/w
Impurity: < 0.6% 5-methylfurfural (CAS-No. 620-02-0; EINECS-No. 210-622-6)
Additives: none

1.3 PHYSICAL-CHEMICAL PROPERTIES

A list of the physical-chemical properties of furfural is provided in **Table 1.1**.

Table 1.1 Overview of physical-chemical properties of furfural

Property	Result	Comments
Physical state	liquid	
Melting point	-36.5 - -39ºC	*
Boiling point	162ºC at 1013 hPa	*
Relative density	1.154-1.156 g/cm^3 at 25ºC 1.1594-1.16 g/cm^3 at 20ºC	*
Vapour pressure	1.33-1.73 hPa at 18.5ºC	*
Surface tension	43.5 mN/m at 20ºC 40.7 - 41.1 mN/m at 29.9ºC	*
Water solubility	83 g/l at 20ºC	*
Partition-coefficient **- n-octanol/water (log)**	0.41	*
Granulometry	not applicable	
Flammability	non-flammable	**
Flash point	61.7ºC (closed cup)	*
Auto flammability temperature	315-393ºC	*
Explosive properties	not explosive	**/***
Oxidizing properties	not oxidizing	***
Conversion factors	1 ppm = 3.93 mg/m^3 1 mg/m^3 = 0.254 ppm	Calculated
Odour threshold	0.25 - 1.0 mg/m^3	*

* No test report was available. At least one independent source. No methods are specified.
** At elevated temperatures, a risk for fire exist. However, according to EG-guidelines, no classification as flammable is applicable. Depending on the temperature, the risk for fire may change into a risk for explosion at more elevated temperatures.
*** Property is based on theoretical and structural considerations.

In conclusion, all relevant physical-chemical data were provided. They were not substantiated with test reports. However, all data are considered sufficiently reliable to fulfil the Annex VIIA requirements.

1.4 CLASSIFICATION AND LABELLING ACCORDING TO ANNEX I

Classification (30th ATP) :Carc. Cat. 3; R40
T; R23/25
Xn; R21
Xi; R36/37/38

R-phrases: 21-23/25-36/37/38-40
S-phrases: (1/2-)-26-36/37-45

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

Furfural is produced industrially from pentosan polysaccharides (xylan, arabinan), that are natural substances in non-food residues and food crops such as corncobs (primary source), cottonseed hulls, rice hulls, oat hulls, bagasse and bark of wood. The pentosans are hydrolysed to pentoses in digestors and subsequently cyclodehydrated to furfural. In all processes, raw material is charged to the digestor and treated with strong inorganic acid. High pressure steam is introduced through the mass and furfural is steam distilled after the operating temperature has been attained.

As an unintentional source, furfural is a major contamination of the sulfite pulping processes used in pulp and paper industry, where it originates from pentoses in the wood and is formed during the waste treatment in the evaporator. Furfural may also be released to the environment via the smoke from burning wood. Furfural as a natural volatile compound is identified in foods such as fruits and fruit juices, vegetables, beverages (wine), bread and bread products and in several essential oils of plants. As a thermal/chemical degradation by-product, it is also formed in the treatment of hemicelluloses feed stocks and in the refuse of chemical and fuel production.

The world production of furfural is estimated to be greater than 240,000 tonnes per year. In Europe, Spain and Austria are assumed to produce and export furfural. Furfural is also imported by several other EU countries from producers in North-America, South-Africa and several Asian countries. For the EU the furfural production and import are estimated to be about 41,350 tons/year and export is estimated to be 1000 tons/year.

2.2 USES

Furfural has many use patterns. In the EU, it is primarily used in the production of furan derivatives such as furan and furfuryl alcohol (75% of total volume) and another major application of furfural is its use as extraction solvent in refineries (13.5% of total volume), see further **Table 2.1.**

Table 2.1 The industrial use of furfural in the EU.

Use	Use volume (t/y)	Percentage of total use
Production furan derivates	32,500	75%
Use as an extraction solvent (refineries)	5850	13.5%
Manufacturing refractories	2200	5%
Manufacturing pesticides	1500	3.5%
Use as an chemical tracer in gas-oil (refineries)	1000	2%
Use unknown (Netherlands)	375	1%

Other applications of furfural (worldwide) include among others its uses as a component of gas oil marker (e.g. GOM X), as a reactive solvent and wetting agent in the manufacture of abrasive wheels and break linings, as a solvent for e.g. resins, nitrated cotton and cellulose acetate, as a chemical intermediate in pesticide manufacture, as a flavour component in a range of foods, and as a fragrance in perfume, soap and creams.

Table 2.2 below shows the industrial and use categories of furfural for the European market.

Table 2.2 The industrial and use categories of furfural

Industrial Category	**IC no.**	**Use category**	**UC no.**
Chemical industry: basic chemicals	2	Solvents	48
Chemical industry: chemicals used in synthesis	3	Binders	2
		Intermediates	33
		Activators (chemical processes); Adhesion promotors; Polymerization additives	43
		Solvents	48
Mineral oil and fuel industry	9	Fuel additives	28
		Solvents	48
		Viscosity adjusters	52
Engineering Industry	16	Surface active agent - wetting agents	50
		Others (refractories)	55/0

3 ENVIRONMENT

3.1 EXPOSURE

3.1.1 General discussion

Furfural may be released to the environment during its manufacture, formulation, or use in commercial products. Other releases may occur from natural or unintentional sources.

Degradation of furfural occurs in the atmosphere where its stability is limited by the rapid vapour-phase reactions with hydroxyl radicals. The half-life for this reaction is estimated to be 0.44 days. Night-time destruction of furfural by nitrate radicals may be an important process in urban areas. Direct photochemical degradation is expected to occur but no data exist for this process. Furfural is also readily biodegradable under both aerobic and anaerobic conditions. Acclimatization increases the capacity of the cultures to degrade furfural. This ready biodegradability is supported by a QSAR (BIODEG) result. Furfural is not expected to hydrolyse under environmental conditions.

Volatilization of furfural from surface waters may occur but is not expected to be a rapid process because calculated Henry's law constants for furfural are 0.2 $Pa.m^3/mol$, or 0.375 $Pa.m^3/mol$ if based on a water solubility of 86 g/l and a vapour pressure of 2.5 mm Hg at 25° C. Furfural is expected to be highly mobile in soil; a $logK_{ow}$ of 0.41 has been reported and a K_{oc} of 17.1 was calculated using the QSAR for non-hydrophobics. Other reported K_{oc}'s range between 1 and 40 l/kg. Because of these low values, furfural may leach into groundwater although volatilization to the atmosphere and degradation processes may decrease the movement through soil towards groundwater. Using a K_{oc} of 17.1, the K_p for soil is calculated to be 0.34 l/kg, that for sediment is 0.86 l/kg and that for suspended matter is 1.7 l/kg. Furfural may volatilize from soil to the atmosphere but this process is not expected to be rapid. Besides photochemically induced degradation, vapour-phase furfural in the atmosphere is expected to be removed by wet deposition. An overview of the environmental distribution in an STP is shown in **Table 3.1**.

Table 3.1 Theoretical distribution of furfural in an STP (SimpleTreat).

Compartment	Distribution (fraction)
Air	<0.01
Water	0.13
Sludge	<0.01
Degradated	0.87

On the basis of the high water solubility (83 g/l) of furfural and its low Log K_{ow} (0.41), no bioaccumulation is expected. No experimental data are reported to confirm this. The EUSES model (version 1.0; based on the EU TGD, 1996) calculates a bioconcentration factor for fish (BCF_{fish}) of 1.41 l/kg and a bioconcentration factor for earthworms ($BCF_{earthworm}$) of 0.95 l/kg.

3.1.2 Environmental releases

Environmental release of furfural may occur during these life cycle stages: I) production, II) processing of furan derivatives, III) processing as extraction solvent, IV) formulation and use as chemical tracer in the mineral oil and fuel industry, V) formulation for manufacturing refractories, and VI) use as chemical intermediate in pesticide manufacture. An additional life cycle stage VII) is furfural release into the environment from unintentional sources during pulping processes used in the pulp and paper industry.

3.1.3 Local exposure assessment

Whenever available, site specific values for production, processing, formulation and use were used in the EUSES calculations of PEC values for the life cycle stages considered in this report. Generic scenarios were used where no site specific data existed. A summary of local concentrations for each scenario is given in **Table 3.2**.

Measured local data in the environment

Measured local atmospheric concentrations or local soil concentrations of furfural are not available. Only a few measured local aquatic concentrations are available for furfural. One EU furfural production site mentioned that the concentrations in untreated waste water and in WWTP effluent water are below the detection limit of 100 μg/l. Furfural has been identified in the drinking water supplies of the United States and Europe.

Levels of furfural in sulphite evaporator condensate, which represents about 15% of the wastewater flow from pulp mills in the pulp, paper and board industry, have been reported to range between 10 and 1280 mg/l and between 179 and 471 mg/l (avg. 247 mg/l). Using the average value of 247 mg/l, a waste water furfural concentration can be calculated of 37 mg/l using the contribution of 15% of the waste water flow. The fraction in waste water directed to effluent water in the STP is 0.13 for furfural. With that fraction the calculated average PEC in effluent water is 4.7 mg/l, resulting in an average PEC in surface water near pulp, paper and board industry of 455 μg/l. Likewise, a maximum PEC in STP effluent water of 24.2 mg/l and a maximum PEC in surface water of 2.36 mg/l can be calculated for the measured maximum concentration of 1280 mg/l in the evaporator condensate.

Table 3.2 Summary of the local concentrations for each scenario for the different environmental compartments.

Scenario	**PEC air** µg/m3	**PEC STP** µg/l	**PEC surface water** µg/l	**PEC sediment** mg/kg_{wwt}	**PEC agricultural soil** mg/kg_{dwt}	**PEC in fish** mg/kg_{wwt}	**PEC in worm** mg/kg_{wwt}
Ia production site 1 (Austria)	$2.1.10^{-3}$	100	10.1	0.012	$3.70.10^{-3}$	$5.96.10^{-3}$	$4.70.10^{-4}$
Ib production site 2 (Spain)	2.67	0	0.11	$1.27.10^{-4}$	$4.72.10^{-4}$	$1.55.10^{-4}$	$2.05.10^{-3}$
II processing furan derivates chemical industry	0.240	0	0.11	$1.27.10^{-4}$	$5.26.10^{-5}$	$1.55.10^{-4}$	$2.45.10^{-5}$
IIIa processing extr. solvent min. oil & fuel ind: site specific 1 (air)	86.1	-	-	-	-	-	-
IIIb processing extr. solvent min. oil & fuel ind: site specific 2 (air)	1.03	-	-	-	-	-	-
IIIc processing extr. solvent min. oil & fuel ind: generic (largest site)	3.81	90	9.11	0.0105	$4.01.10^{-3}$	$6.26.10^{-3}$	$7.07.10^{-4}$
IVa production chem. Tracer min. oil & fuel ind: site specific air	0.0550	-	-	-	-	-	-
IVb production chem. tracer: generic EU tonnage	0.764	420	42.1	0.0487	$1.57.10^{-2}$	0.0246	$2.0.10^{-3}$
IVc use chem. tracer min. oil & fuel ind: site specific waste w.	0.0493	2.73	0.383	$4.43.10^{-4}$	$1.20.10^{-4}$	$3.14.10^{-4}$	$2.29.10^{-5}$
IVd use chem. tracer min. oil & fuel ind: generic (largest site)	0.0817	44.1	4.52	$5.22.10^{-3}$	$1.65.10^{-3}$	$2.72.10^{-3}$	$2.17.10^{-4}$
IVe use chem. tracer: generic EU tonnage	0.296	162	16.3	0.0189	$6.06.10^{-3}$	$9.92.10^{-3}$	$8.05.10^{-4}$
Va formulation for manufacturing refractories, site 1	1.53	841	84.2	0.0972	0.0313	0.0489	$4.0.10^{-4}$
Vb formulation for manufacturing refractories, site 2	15.2	1260	126	0.146	0.0493	0.0733	$6.97.10^{-3}$
VI use as intermediate in pesticide manufacture	11.4	2210	221	0.255	0.0835	0.128	$1.1.10^{-2}$
VII processing pulp, paper and board industry: Mean	n.a.	4,700	455	0.526	n.a.	0.53	-
Max.	n.a.	24,200	2,360	2.73	n.a.	2.74	-

n.a. not available

1) Measured concentration (detection limit)

3.1.4 Regional exposure assessment

The regional exposure PEC values were calculated and are shown in **Table 3.3**. Unintentional emissions (e.g. pulp/paper industry) are not taken into account for the regional exposure assessment.

Table 3.3 Regional PEC values.

PEC air (μg/m^3)	0.0018
PEC surface water (μg/l)	0.127
PEC sediment (mg/kg_{wwt})	$1.14.10^{-4}$
PEC agricultural soil (mg/kg_{dwt})	$5.5.10^{-6}$
PEC natural soil (mg/kg_{dwt})	$1.07.10^{-5}$

There are no measured regional aquatic, atmospheric or soil concentrations of furfural submitted or available.

3.2 EFFECTS

In a number of ecotoxicity studies no measures were taken to prevent volatilization from test vessels/tubes. In these cases, the actual concentrations may have been lower than the nominal ones in view of the volatility of furfural.

3.2.1 Aquatic compartment

Acute toxicity of furfural was tested in fish and invertebrates. All tests were performed using freshwater species. The acute LC50 values in 5 freshwater fish species (*Gambusia affinis, Lepomis macrochirus, Leuciscus idus melanotus, Pimephales promelas, and Poecilia reticulata*) ranged from 10.5 to 32 mg/l. The lowest value (10.5 mg/l) is based on a 14-d semi-static (daily renewal) test with *Poecilia reticulata;* the LC50-value from this test is corrected for furfural losses during the test and therefore considered to have the highest reliability. The other LC50 values for fish are based on tests with a duration of 48 to 96 hours. For the invertebrate *Daphnia* magna two short-term LC50 values are available from two different studies, being a 24-h LC50 of 29 mg/l and a 72-h LC50 of 13 mg/l.

Long-term toxicity of furfural was tested in fish, invertebrates and algae. Only freshwater species were used. A 12-day early-life stage toxicity test (semi-static with daily renewal of test solutions) with embryo and sac-fry stages of zebrafish *Brachydanio rerio* (OECD 212) resulted in statistically significant effects on larval behaviour and morphology, the most sensitive endpoints, at nominal concentrations of 0.94 mg/l and higher. No effects were observed at the nominal concentration of 0.47 mg/l, corresponding with a geometric mean actual exposure concentration of 0.33 mg/l; this latter value was established as the NOEC. For invertebrate *Daphnia magna*, a NOEC of 1.9 mg/l (actual concentration) was determined in a 21-day flow-through life-cycle toxicity test (OECD 211). Significant treatment-related reductions in survival, reproduction and growth were seen at 3.7 mg/l (actual concentration) only. Algal tests resulted in NOEC-values of 2.7 and 31 mg/l for blue-green alga *Microcystis aeroginosa* and green alga *Scenedesmus quadricaudata*, respectively. The algae test results

are based on 8-day tests which may not be fully equivalent to algae growth inhibition data from standard tests measuring the impact on exponentially growing algae.

Long-term test results are available for organisms representing three trophic levels (freshwater plants, invertebrates and fish, see above). The lowest long-term NOEC was found in the fish toxicity test with embryo and sac-fry stages of *Brachydanio rerio* (OECD 212); the NOEC for the most sensitive endpoints (behaviour and morphology of fish larvae) was calculated as 0.33 mg/l (actual concentration). According to the TGD, the OECD 212 study may be used as an alternative to the fish early life stage toxicity test (OECD 210) for substances with an LogKow of less than 4.
Furthermore, in addition to mortality several relevant sub-lethal endpoints were included in this test with furfural (hatching time of eggs, and behaviour and morphology of larvae) and this 12-d test with *B. rerio* covers two early life stages (embryonal stage and sac-fry stage).
Hence, the NOEC determined in this 12-day study may be used as a long-term toxicity parameter. The application of an assessment factor 10 (based on long-term tests for fish, Daphnia and algae) results in a **PNEC for aquatic organisms of 33 µg/l** (from PNEC = NOEC/10).

3.2.1.1 Effects on microorganisms

An activated sludge respiration inhibition test (OECD 209) resulted in a 30-minutes EC50 value of 760 mg/l. Tests with bacterium *Pseudomonas putida* (8-d exposure) and protozoans *Chilomonas paramaecium* (48-h exposure), *Entosiphon sulcatum* (72-h exposure) and *Uronema parduczi* (20-h exposure) resulted in NOEC values ranging from 0.59 to 16 mg/l.

According to the recent TGD (2003), toxicity data for both bacteria and protozoa should be taken into account for the derivation of the PNEC micro-organisms. However, this is restricted to ciliated protozoa, constituting the most important class of protozoa in sewage treatment plants (STPs) . The protozoa tested with furaldehyde are all flagellates and thus the PNEC derivation will only based on the bacteria data. There are two options then: 1) the *Pseudomonas putida* test result (NOEC: 16 mg/l) is used and as it is a NOEC-value, the PNEC would be equal to this NOEC, or 2) the result of the activated sludge respiration inhibition test (EC50: 760 mg/l) is used which would lead to a PNEC of 760/100 = 7.6 mg/l. Preference is given to the lowest value. This results in a **PNEC micro-organisms of 7.6 mg/l**.

3.2.1.2 Effects assessment for the sediment

There are no data for sediment-dwelling organisms. A PNEC for sediment could be calculated using the equilibrium partitioning method. However, because measured data for the concentration of furfural in sediment are lacking, a quantitative risk characterization of furfural for sediment can not be performed. In addition, the low absorption potential of furfural suggests that sediment is probably not a relevant compartment for the environmental risk assessment of furfural.

3.2.2 Atmosphere

No data are available for the atmosphere.

3.2.3 Terrestrial environment

No toxicity data are available for soil-dwelling organisms, terrestrial plants, or soil microorganisms to derive a PNEC for the terrestrial compartment. The equilibrium partitioning method leads to a **PNEC soil of 0.014 mg/kg wet weight**.

3.2.4 Non-compartment-specific effects relevant to the food chain

There are no specific data available for top-predators. Therefore the $PNEC_{oral}$ is derived from toxicity data for laboratory mammals. Starting from a lowest oral NOAEL for repeated-dose effects of 53 mg/kg bw/d derived in a semi-chronic (90-days) study with dietary dosing of furfural in microencapsulated form and using both a conversion factor (NOAEL to NOEC) of 20 (rat > 6wks) and an assessment factor of 30, a **$PNEC_{oral}$ of 35.3 mg/kg food** is derived (from $PNEC_{oral}$ = {(53 x 20)/30}).

3.3 RISK CHARACTERISATION

3.3.1 Local risk characterization

A summary of calculated PEC/PNEC ratios is shown in **Table 3.4**. A PEC/PNEC ratio below 1 suggests no risk whereas a ratio above 1 indicates hazard and that more information, testing or risk reduction measures are required.

3.3.1.1 Aquatic compartment (including sediment)

STP effluent: All PEC/PNEC ratios for microorganisms are below 1 (**conclusion ii**).
Unintentional sources: The calculated PEC/PNEC ratio for a local STP at the pulp and paper industry is 0.62 (using the mean PEC value of 4.7 mg/l) and 3.2 (using the maximum PEC value of 24.2 mg/l). For this scenario, site-specific measured effluent concentrations and measured data from other pulp and paper industries in the EU are needed to refine this conclusion. Since this considers an unintentional source beyond the scope of this EU risk assessment, there will be no follow-up of this scenario in the context of Regulation 793/93/EC.

Surface water: For some scenarios (IVb, Va, Vb and VI), the PEC/PNEC ratios are above 1. As no further refinement of either PECs or PNECs is possible, a need for further limiting the risks is indicated for these scenarios **(conclusion iii)**. For the remaining scenarios (Ia, Ib, II, IIIa,b,c, IVa,c,d,e) the PEC/PNEC values are below 1 (**conclusion ii**).
Unintentional sources: PEC/PNEC ratios for surface water for a particular pulp and paper industrial site are 13.8 if the mean surface water concentration of 455 μg/l is used or 72 if the highest surface water concentration of 2,360 μg/l is used. For this particular site, the PEC can be refined by submitting site-specific information on the dilution factor. However, more data from the pulp and paper industry in the EU are needed to refine this scenario for the pulp and paper industry. Since this considers an unintentional source beyond the scope of this EU risk assessment, there will be no follow-up of this scenario in the context of Regulation 793/93/EC.

Sediment: A quantitative risk characterisation of furfural for sediment is not performed. Neither toxicity data for sediment-dwelling organisms nor measured concentrations in sediment are available. The low absorption potential of furfural suggests that sediment is probably not a relevant compartment for the environmental risk assessment of furfural.

3.3.1.2 Atmosphere

Atmosphere: A quantitative risk characterisation for the exposure of organisms to furfural in air is not possible, because a PNEC for air could not be derived.

3.3.1.3 Terrestrial compartment

Terrestrial compartment: From **Table 3.4** it can be seen that for the scenarios Va, Vb and VI, the PEC/PNEC ratios are above 1 and hence a risk is indicated and **conclusion (i)** applies. The terrestrial PNEC is derived through the equilibrium partitioning method and there is therefore scope to refine this PNEC through testing. However, no testing is proposed for the terrestrial compartment since for these scenarios also conclusion iii is drawn for the local aquatic compartment (surface water). The development of risk reduction measures for the aquatic compartment should take account of the conclusions for the terrestrial compartment. The PEC/PNEC ratios for the remaining sites (scenarios Ia, Ib, II, IIIc, IVa,b,c,d,e) are all lower than 1 (**conclusion ii**).

3.3.1.4 Non-compartment-specific effects relevant to the food chain

The PEC values for fish-eating and worm-eating predators are calculated as the average of the local PEC values and regional PEC values in fish and worm. **Table 3.4** shows that the PEC/PNEC values are lower than 1 for all exposure scenarios (**conclusion ii**).

Table 3.4 Local risk characterisation ratios (PEC/PNEC values).

Scenario	**PEC/PNEC STP**	**PEC/PNEC water**	**PEC/PNEC Soil**	**PEC/PNEC fish-eating predators**	**PEC/PNEC worm-eating predators**
Ia production site 1 (Austria)	0.013	0.307	0.236	$8.2.10^{-4}$	$6.44.10^{-5}$
Ib production site 2 (Spain)	0	$3.84.10^{-3}$	0.031	$2.45.10^{-5}$	$2.81.10^{-5}$
II processing furan derivates chemical industry	0	$3.84.10^{-3}$	$3.36.10^{-3}$	$2.45.10^{-5}$	$3.36.10^{-6}$
IIIa processing extr. solvent min. oil & fuel ind: site specific 1 (air)	n.a.	n.a.	n.a.	n.a.	n.a.
IIIb processing extr. solvent min. oil & fuel ind: site specific 2 (air)	n.a.	n.a.	n.a.	n.a.	n.a.
IIIc processing extr. solvent min. oil & fuel ind: generic (largest site)	0.0119	0.277	0.256	$8.6.10^{-4}$	$9.68.10^{-5}$
IVa production chem. tracer min. oil & fuel ind: site specific air	n.a.	n.a.	n.a.	n.a.	n.a.
IVb production chem. tracer: generic EU tonnage	0.055	**1.28**	0.99	0.0034	$2.75.10^{-4}$
IVc use chem.. tracer min. oil & fuel ind: site specific waste w.	$3.60.10^{-4}$	0.0121	$7.66.10^{-3}$	$4.63.10^{-5}$	$3.15.10^{-6}$
IVd use chem.. tracer min. oil & fuel ind: generic (largest site)	$5.81.10^{-3}$	0.138	0.105	$3.75.10^{-4}$	$2.97.10^{-5}$
IVe use chem.. tracer: generic EU tonnage	0.0221	0.513	0.4	0.00136	$1.10.10^{-4}$
Va formulation for manufacturing refractories, site 1	0.111	**2.55**	**2.0**	0.0067	$5.48.10^{-5}$
Vb formulation for manufacturing refractories, site 2	0.166	**3.83**	**3.14**	0.0101	$9.54.10^{-4}$
VI use as intermediate for pesticide manufacture	0.29	**6.69**	**5.32**	0.0176	$1.51.10^{-}$
VII processing pulp, paper and board industry: Mean	0.62	**13.8**	n.a.	0.0	n.a.
Max.	**3.18**	**71.5**	n.a.	0.	n.a.

n.a. not available

3.3.2 Regional risk characterization

The regional PEC/PNEC ratios, presented in **Table 3.5**, shows that all regional PEC/PNEC values are lower than 1 (**conclusion ii**).

Table 3.5 Regional risk characterisation ratios (PEC/PNEC).

	PEC/PNEC Water	**PEC/PNEC Soil**
Regional scenario	$3.84.10^{-3}$	$3.53.10^{-4}$

3.4 PBT ASSESSMENT

In order to protect the marine environment against unpredictable or irreversible long-term effects, substances must be submitted to a so-called PBT-assessment. Available data must be tested to the PBT-criteria in the TGD (EC 2003). For substances that do not fulfil all three PBT criteria, but are known to be persistent and bioaccumulating, vPvB (very persistent and very bioaccumulating) criteria are set.

Persistence: For furfural several aerobic as well as anaerobic biodegradation test results are available; the total data set is considered sufficient for drawing conclusions on the degradation potential of furfural and persistence within the scope of the PBT assessment. From the overall results of the studies it is concluded that furfural is readily biodegradable. Furfural also proved rapidly biodegradable under anaerobic conditions. It is concluded that furfural does not meet the persistence criterion.

Bioaccumulation: No experimental data on bioaccumulation are available. On the basis of the high water solubility (83 g/l) and the low Log Kow (0.41), furfural is not expected to bioaccumulate. The calculated BCF_{fish} of 1.41 l/kg and $BCF_{earthworm}$ of 0.95 l/kg (from section 3.1.1.) confirm a low bioaccumulation potential. It is concluded that furfural does not meet the bioaccumulation criterion.

Toxicity: The criterion for environmental toxicity for PBT substances is NOEC (long term) < 0.01 mg/l. The lowest measured NOEC (long-term) is 0.33 mg/l. With respect to human health hazards, furfural is classified as a Category 3 carcinogen (R40; limited evidence of a carcinogenic effect). A decision whether or not this evidence is sufficient to consider furfural as (T)oxic within the framework of the PBT assessment has not been taken. Such a decision is not needed since the scientific evidence on P and B is of enough weight for a final conclusion of the PBT assessment.

Conclusion of the PBT assessment: It is concluded that furfural does not meet the criteria for PBT or vPvB substances.

4 HUMAN HEALTH

4.1 EXPOSURE

4.1.1 Occupational exposure

Occupational exposure to furfural can occur during the production of furfural and the production of its derivatives (as precursor for various compounds), during its use for the production of products or materials (resins, refractory materials) and use as a selective solvent or extractant.

The production of the substance is performed in a closed system. Breaching of the system probably occurs during autoclave and rectifier discharging, quality control sampling, drumming and cleaning and maintenance operations. During the closed production process an inhalation exposure of 0.4 mg/m^3 (0.1 ppm) is estimated. Dermal exposure during the general production process is assumed to be negligible.
For the different activities where breaching occurs during production a reasonable worst case respiratory exposure level is estimated to be 40 mg/m^3. The typical exposure is estimated to be 10 mg/m^3, based on the exposure measurements and expert judgement.
Based on a pragmatic approach, exposure levels twice that of long-term exposure levels are considered possible for short-term exposure (15 minutes). For tasks during production related to opening of the installations, the estimated short-term exposure level is therefore 80 mg/m^3.
A calculated reasonable worst case full shift exposure level for a worker involved in several processes with breaching of the closed system is 30 mg/m^3. Exposure during cleaning and maintenance at production facilities is assumed to be higher. The reasonable worst case exposure is estimated to be 70 mg/m^3. Approximately the middle of the exposure assessment by EASE will be used for the short-term exposure (120 mg/m^3).
No specific information on dermal exposure is available. Therefore the estimates made using EASE is used for risk characterisation. Dermal exposure during drumming and quality control sampling is estimated to be 42 mg/day, while dermal exposure during cleaning and maintenance is estimated to be 650 mg/day.

During the production of furfural derivatives, the highest exposure will probably occur the moment the substance is added to the reaction vessel. Since no exposure data are available, the estimates made by EASE will be used for the risk characterisation. As it probably concerns the addition of large amounts of furfural into a reactor, it is assumed that this is performed via a transfer line. A typical value for inhalation exposure during adding of furfural is estimated as 2 mg/m^3, while the reasonable worst case exposure is estimated to be 12 mg/m^3 (upper limit of the exposure assessment). The typical exposure during the conversion process is estimated to be negligible, while the reasonable worst case exposure during this process is estimated as 0.4 mg/m^3 (both based on EASE). Exposure during adding is estimated to occur up to 4 hours per day (reasonable worst case estimate). During the remainder of the working day, exposure will occur due to the conversion process. This results in a calculated reasonable worst case full shift exposure level for a worker involved in several processes with breaching of the closed system of 6 mg/m^3.
Dermal exposure during adding of furfural is estimated to be 42 mg/day. The dermal exposure during the conversion process is estimated to be negligible. For the use of furfural during moulding, vulcanisation and mixing activities, it is assumed that these activities could occur

together in one full shift. The typical value is estimated at 12 mg/m^3 (estimate made by EASE for mixing operation). The reasonable worst case exposure is estimated as 40 mg/m^3 (based on measured values). Based on the highest measured exposure levels and the estimate by EASE it is concluded that a reasonable worst case estimate for short term exposure levels (up to 15 minutes) is 100 mg/m^3.
The dermal exposure is estimated as 63 mg/day, the sum of the exposure during mixing and moulding.

For the use of furfural as a selective solvent or extractant (during refining) an exposure level of 25 mg/m^3 is chosen as a reasonable worst case full shift exposure level. This level is representative of measured levels found for different sources. The typical value during the several activities is estimated from measured data to be 2 mg/m^3. Based on the limited information on short-term exposure levels and on the estimate by EASE a short term exposure level (15 minutes) of 100 mg/m^3 is proposed.
Dermal exposure is estimated as 42 mg/day during the distillation step, and as 21 mg/day due to cleaning and maintenance activities.

A summary of occupational exposure levels is presented in **Table 4.1**.

Table 4.1. Summary of occupational exposure

Scenario	Activity	Frequency	Duration	Inhalation – RWC		Inhalation - Typical concentration		Dermal	
			(hr)	(mg/m^3)	Method	(mg/m^3)	method	$mg/cm^2/day$	dose (mg/day)
Production	general (closed system)	225	2-6	0.4	EASE	negligible	EASE	negligible	negligible
	production activities	225	4-6	40	Lit. exp.	10	EASE, lit.	0.1	42
	short term	225	0.25	80	Exp.				
	full shift	225	8	30#	Calculated	7.5#	calculated		
	cleaning and maintenance	50-100	6-8	70##	Lit. exp.	40	EASE	0.5	650
	cleaning and maintenance short term	50-100	0.25	120	Lit. exp.				
Product derivatives	general	100-200	2-6	0.4	EASE	negligible	EASE	negligible	negligible
	adding	100-200	2-4	12	EASE, exp.	2	EASE, exp.	0.1	42
	full shift	100-200	8	6#	Calculated	1#	calculated		
Production refractories etc.	mix, mould etc.	100-200	6-8	40	Lit., exp.	12	EASE	0.1	63
	short term	100-200	0.25	100	Lit., EASE				
Use of furfural	refining etc.	225	6-8	25	Lit.	2	lit.	0.1	42
	short term*	225	0.25	100	Lit., EASE				
	cleaning and maintenance	50-100						0.05	21

\# Full shift exposure is calculated by the following formula:
$E_{a1}*d_{a1} + E_{a2}*d_{a2} / d_t$ in which: $E_{a1,2}$ = estimated exposure during activity 1 or 2; $d_{a1,2}$ = duration of exposure for activity 1 or 2 (to obtain a reasonable worst case estimate, the longest duration for the highest exposure activity is taken; the total exposure duration in these cases is assumed to be 8 hours); d_t = total duration of the exposure (full shift; normally 8 hours)

short-term exposure level is 120 mg/m^3 (15 minutes)

RWC reasonable worst case exposure

Exp. expert judgement

lit. literature

• including cleaning and maintenance

4.1.2 Consumer exposure

The two most important sources for consumer exposure to furfural are its use as fragrance material in cosmetic products (e.g. perfume/eau de toilette, body lotion, creams, shampoo, deodorant) and its use as flavouring substance in several food categories (including baked goods, frozen dairy, meat products, soft candy, gelatin puddings, non-alcoholic beverages, alcoholic beverages, gravies, hard candy and chewing gum). Both uses are regulated via other EU legislation than EU Regulation 793/93/EC. Nevertheless, the consumer exposure has been estimated.

For the use of furfural as fragrance material, the main exposure route is dermal. Furfural concentrations in cosmetic products vary, but are reported to be at maximum 0.1%. Assuming conservatively that consumers will consistently use a number of cosmetic products that are all perfumed with the upper 97.5^{th} percentile level of the fragrance ingredient, the maximum total dermal exposure to furfural is estimated at 1 µg/kg bw/day.

When used as flavouring substance in food, exposure to furfural is by ingestion. The average maximum use level of furfural in the various food categories ranges from 4.2 to 63 mg/kg. The oral exposure is estimated at 9 µg/kg bw/day, using the daily 'per capita' method. This method calculates the intake of 'eaters only' on the basis of the most recent reported annual volume of furfural used as flavouring substance in Europe. A more worst case estimate of the oral exposure is 136 µg/kg bw/day, using the TAMDI (theoretical added maximum daily intake) method. This TAMDI estimate is calculated from intake estimates of flavourable beverages, foods and "particular food", under the assumption that all such foods eaten by consumers contain furfural at all times and that these foods are flavoured at maximum permitted furfural concentrations.

4.1.3 Man exposed indirectly via the environment

Environmental release of furfural may occur during production, during processing of furan derivatives, during processing as extraction solvent and formulation as chemical tracer in the mineral oil and fuel industry, during use as chemical intermediate in pesticide manufacture, and during formulation for manufacturing refractories. The latter scenario resulted in the highest total daily intake for humans from environmental sources (11 µg/kg bw/day). In this scenario intake is mainly via air, drinking water and leaf crops.
For regional exposure, the total daily intake is estimated at 4 ng/kg bw/day, mainly via drinking water.
Aside from the intentional use of furfural, humans can also be exposed to furfural unintentionally, because furfural is virtually ubiquitous in nature. The total potential intake for furfural and precursors of furfural due their natural occurrence in food, although considered outside the scope of EU Regulation 793/93/EC, has been estimated at approximately 300 µg/kg bw/day. Compared to this intake, the local and regional intakes can be considered negligible.

4.1.4 Combined exposure

Humans can be exposed to furfural during work, via consumer products (use as fragrance/flavouring substance), indirectly via the environment (intentional and unintentional sources), and via combinations thereof. However, since the consumer uses of furfural are regulated via other EU legislation and the unintentional source is outside the scope of the Existing Substances regulation, only the combination of worker exposure and exposure via the environment due to intentional sources needs to be dealt with under EU Regulation 793/93/EC. Given that the latter is very low compared to exposure to furfural at the workplace, furfural exposure via the environment will not lead to an increased exposure for workers.

4.2 EFFECTS ASSESSEMENT

In the toxicology data set of furfural animal as well as human studies were available for review. Most of the studies were not performed according to current standards, and were, in some cases, not suitable for the overall assessment.

After oral exposure of rats to ^{14}C-furfural, at least 90% is absorbed in the gastro-intestinal tract. After inhalatory exposure to furfural, pulmonary retention in humans was 78%. When humans are exposed to furfural vapours (30 mg/m^3), the dermally absorbed quantity of furfural is about 30% of the amount absorbed through inhalation. After dermal exposure to liquid furfural, about 3 µg furfural per cm^2 skin per minute is absorbed in humans.
Based on these data it is concluded that 90% oral and 100% dermal and inhalation absorption are used in the risk characterisation.
Limited data are available on the distribution of furfural after oral administration in animals. At 72 hrs post dosing, in total about 0.6% (or less) of a radioactive dose was found in the tissues examined. The concentrations of ^{14}C found in liver and kidney were proportional to the dose. Highest concentrations were found in liver and kidney with the lowest concentration in the brain. Data are too limited to speculate about placental transfer or secretion into milk.
It is proposed that biotransformation of furfural in rats and mice may take place in two ways. The major part is oxidized to furoic acid, which is excreted either free or conjugated with glycine (i.e., as furoylglycine). The smaller part condenses with acetic acid giving rise to furanacrylic acid which is excreted in conjugated form (i.e., as furanacryluric acid). An unidentified metabolite was found in urine of rats and mice. Minor differences in metabolic profile in animals as a function of dose size, sex, and species are found. The main metabolite in humans found in urine after inhalation exposure is furoylglycine. Besides furoylglycine, furanacryluric acid was found. Furoic acid was found in negligible amounts in human urine after inhalation. Differences between the metabolites observed in humans and animals may be explained by differences in exposure route and duration, and the dose levels administered (e.g., free furoic acid may be formed due a saturation of the glycine conjugation pathway) and is not necessarily due to species differences.
In animals after oral exposure, 76-100% of the radioactivity was found in urine, faecal elimination was 2-7%, 5-7% was exhaled as CO_2, and less than 1% is found in the carcasses. Biological half-life of furfural after inhalation in humans is about 2-2.5 hours.

The oral LD_{50} values for rats varied between 50 and 149 mg/kg bw. The oral LD_{50} values for mice, dogs, and guinea pigs were higher. They varied between 400-500 mg/kg bw for mice and between 650-950 mg/kg bw for dogs. The LD_{50} for guinea-pigs was 541 mg/kg bw.
The inhalation LC_{50}-value after 1 hour exposure was found to be 4075 mg/m^3 (rats), after 4 hour exposure 600-924 mg/m^3 (rats) and after 6 hour exposure 688 mg/m^3 (rats) and 490 mg/m^3 (mice).
A dermal LD_{50} of >310 mg/kg bw in rabbits, and <10000 mg/kg bw in guinea-pigs were found. A dermal dose of 620 mg/kg bw is reported to be lethal to rabbits.
Furfural has been classified as toxic after oral and inhalation exposure and as harmful in contact with skin.

Furfural liquid causes mild skin irritation after prolonged contact (i.e., 48 hours) and also after repeated exposure. After repeated dermal dosing, less extensive signs of irritation were observed with diluted furfural. Notwithstanding the limited character of the studies, the relatively high concentrations used, the exposure conditions applied (48 hours, under occlusion or repeated exposure) and the mild nature of the effect, furfural has been classified as irritating to the skin. Based on human and animal studies furfural has also been classified as irritating to eyes and respiratory tract. In a human study, eye and respiratory tract irritation were detected at furfural vapour concentrations ranging from 20 to 63 mg/m^3.

Furfural is not a skin sensitiser based on the results of a Buehler test and a Maximisation test with guinea pigs. No data were available on respiratory sensitisation.

Most repeated dose toxicity studies were performed for the oral route of exposure and use gavage as the method of application. NOAELs derived via this methodology varied from 20 down to < 11 mg/kg bw/d. The various studies differed in quality of design and reporting; some were (nearly) according to OECD guidelines, whereas others were clearly not. The lowest NOAEL, i.e. <11 mg/kg bw/d, comes from a subchronic range finding study with rats: at all dose levels, cytoplasmic vacuolization of hepatocytes in the centrilobular region in male rats was found. This effect is considered treatment-related, given the occurrence of mild centrilobular necrosis in male rats in an oral carcinogenicity study with gavage administration. In more recent studies with rats, furfural was applied via the diet in a microencapsulated form (to prevent loss of the compound due to its volatility). In a 13-week dietary study, effects included minor hepatocellular alterations which were observed in males, but not in females, at doses of 82 and 160 mg/kg bw/d. The NOAEL in this study, therefore, was established at the one lower dose-level of 53 mg/kg bw/d (with corresponding nominal exposure value of 60 mg/kg bw/d), a value clearly higher than the one achieved with gavage application.
Having taken note of the fact that a complementary study showed that furfural was rapidly and completely released from this microencapsulation in an aqueous environment the NOAEL from the 13-week dietary study is selected as the starting point for the risk characterisation for repeated oral exposure for the following reasons: (i) dietary administration of a test compound is the preferred method of exposure via this route as compared to gavage application; (ii) microencapsulation adequately circumvents loss of furfural due to volatisation and results in an instantaneous release of this substance in the aqueous environment of the GI-tract; (iii) dietary exposure avoids the use of (for this substance) corn oil exposure, that is known to be associated with morphological liver changes upon prolonged exposure; (iv) the alternative key-study NOAEL of <11 mg/kg bw/d has a limited design, being a range-finding study only.

The available inhalation studies show a lowest NOAEC of <20 mg/m^3 for local effects. At this concentration metaplasia and hyperplasia of transitional respiratory epithelium were

observed at the anterior part of the nose in rats. This study is considered suitable for the risk characterisation for local effects after repeated inhalation exposure.
The lowest NOAEC for systemic effects was reported to be 320 mg/m^3. This concentration corresponds to 92 mg/kg bw/d (assuming 100% absorption, ventilation rate of 0.8 l/kg bw, and an oral absorption of 100%). This concentration of 320 mg/m^3 will be taken as starting point for the risk characterisation for systemic effects after repeated inhalation exposure.

No dermal repeated dose toxicity data are available that can be used for the risk characterisation. From the two available no observed effect levels from repeated dose toxicity studies, i.e. for oral and inhalation exposure, the oral NOAEL of the 13-week diet study with rats will be used to evaluate the systemic toxicity after dermal exposure in the risk characterisation.

It is concluded that furfural causes chromosomal aberrations and gene mutations *in vitro*. Furfural was negative in *in vitro* UDS tests with human liver slices. Furfural did not induce chromosome aberrations and SCEs in bone marrow cells of mice after i.p. treatment. One abstract reported furfural as positive in a cytogenicity study in mouse bone marrow. However, since this paper was not published in a peer reviewed journal, it could not be fully evaluated. Furfural was negative in *in vivo* UDS tests with rat and mouse hepatocytes.
The study in the λlacZ transgenic mice (strain 40.6) indicated that orally applied furfural was unable to induce gene mutations in vivo in mouse liver, a tissue in which carcinogenicity was observed. Overall, the available data indicate that furfural is not an in vivo genotoxic substance.

It appeared that furfural is carcinogenic in a 103 weeks oral gavage studies with rats and mice. In male rats, a low incidence of uncommon cholangiocarcinomas and bile duct dysplasia with fibrosis, considered to be an early stage in the development of cholangiocarcinomas, were observed by dosing (gavage) 60 mg/kg bw/d. No evidence for carcinogenicity was found in female rats. An increased incidence of hepatocellular adenomas was found in mice receiving furfural by gavage at the highest dose of 175 mg/kg bw/d. Male mice at that dose also showed an increased incidence of hepatocellular carcinomas.
Some remarks should be made here to these gavage studies. In both species dose-levels that induced tumours also led to target-organ toxicity. This toxicity induction also paralleled tumour-induction. Centrilobular necrosis was found in male rats only, and chronic inflammation occurred in the livers of both genders of mice, though it was more extensive in males.
It is well known that B6C3F1 mice are exceptionally sensitive for developing liver tumours, particularly under conditions of induced (chronic) liver injury. However, there is no clear understanding of the genesis of cholangiocarcinomas in rat liver, though it is known that the site where these tumours originate in rat liver is also often associated with a regenerative response to necrosis of hepatocytes (also in case of centrilobular necrosis) near bile ducts, noticeable by the generation of so-called ‘oval cells’.

No adequate studies are available to evaluate the carcinogenic potential of furfural after inhalation and dermal exposure. After inhalation exposure, no evidence for carcinogenic effects was found in Syrian golden hamsters. However, the exposure duration of the available study (only 12 months treatment, followed by 29 weeks of non-treatment) was too limited for a proper evaluation of carcinogenicity after inhalation. A cocarcinogenic effect of furfural on the respiratory tract of hamsters was suggested based on a study with treatment of hamsters with furfural alone or in combination with benzo(a)pyrene.

It should be noted that local toxicity is expected to occur after inhalation exposure given the effects found after repeated inhalation exposure. It is not clear from the available data whether tumours will develop by local toxicity.

Furfural has been classified as a category 3 carcinogen. Although the mode of action underlying the carcinogenic activity of furfural after oral exposure has not been fully elucidated, a genotoxic component apparently is not involved, as evidenced by the negative in vivo test using transgenic animals. The data are interpreted as indicating that the observed liver tumours were induced via some mechanism involving liver toxicity and, consequently, that at levels at which no liver toxicity is induced, tumours will not arise. Hence, as starting point for the risk characterisation for carcinogenicity the oral NOAEL for liver toxicity (i.e. 53 mg/kg bw/d, from the dietary study as established under 'repeated dose toxicity') is selected. Since the precise mechanistic background for tumour formation is not clear, an additional safety margin is required when repeated dose exposure estimates are evaluated for the carcinogenicity end-point.

No effects were observed in the male and female reproductive organs of experimental animals after oral and inhalation (sub) chronic exposures. Thus, no LOAEL/NOAEL for fertility could be established.
In a developmental toxicity study according to OECD 414, the NOAEL for developmental effects was 100 mg/kg bw/day in Sprague-Dawley rats administered furfural by gavage (highest dose-level that could be evaluated, due to low survival in 150 mg/kg bw/day group (16/25 females died at this dose level)). In the 150 mg/kg bw/day dose group a not statistically significant reduction in mean foetal body weight was observed in one litter; it cannot be excluded that this effect is caused by maternal toxicity. The NOAEL for maternal toxicity was less than 50 mg/kg bw/day.
No data on reproduction toxicity in humans are available.

4.3 RISK CHARACTERISATION

4.3.1 Workplace

An overview of the occupational risk characterisation for furfural is given in **Table 4.2a** and **Table 4.2b**.

Assuming that oral exposure is prevented by personal hygienic measures, the risk characterisation for workers is limited to the dermal and inhalation routes of exposure.
If applicable, quantitative risk assessment is performed by calculation of the MOS (the ratio between NOAEL/LOAEL and exposure levels) and comparison of this value with the minimal MOS. This minimal MOS is established via assessment factors, taking into account inter- and intraspecies differences, differences between experimental conditions and the exposure pattern of the worker, type of critical effects, dose-response relationship, confidence in the database, and correction for route-to-route extrapolation. A risk is indicated when the MOS is lower than the minimal MOS. In case of combined exposure the calculations are based on internal NOAELs and systemic exposure levels.

Acute toxicity

Furfural is classified as toxic after inhalation exposure and as harmful in contact with skin. For occupational risk assessment the short-term exposure levels are compared with the LD_{50} or LC_{50} values.

Inhalation exposure
The short-term inhalation exposure values are compared with LC_{50} values taking into account the most appropriate exposure duration. Exposure durations of 0.25 hour are evaluated using the 1 hour LC_{50} value of 4075 mg/m^3 in rats and the exposure duration of 2-4 hours is evaluated using the range of the 4 hour LC_{50} values in rats (600-924 mg/m^3).
The minimal MOS required for acute occupational exposure using these LC_{50}-values is 125[2]. Based upon the available data it can be concluded that acute toxic effects due to acute inhalation exposure cannot be excluded for all scenarios (see **Table 4.2a** and **Table 4.2b**). It is noted that the data available for evaluation of acute inhalation exposure are limited. Given the irritating properties of furfural in humans at concentrations of 20-63 mg/m^3, it is unlikely that workers will tolerate a prolonged single exposure to the reported higher exposure concentrations (see **Table 4.1**). Furthermore, it is assumed that existing controls to prevent acute respiratory irritation are applied. Based on these considerations, it is concluded that furfural is of no concern for workers with regard to acute respiratory toxicity (**conclusion ii**).

Dermal exposure
Starting-point for the risk assessment of acute dermal toxicity is a dose level of 620 mg/kg bw which was reported to be lethal in rabbits (LD_{low}). The minimal MOS required for acute occupational exposure using this value is 300[3]. Comparing the MOS values with the minimal MOS (see **Table 4.2a** and **Table 4.2b**), it can be concluded that acute toxic effects due to acute dermal exposure cannot be excluded for scenario 1 'production – cleaning and maintenance'. It is noted, however, that the given MOS-values are calculated based on exposure estimates for the unprotected worker. As a consequence of the labelling of this substance with R38 it is expected that workers will use effective personal protection products. On this basis, it is concluded that furfural is of no concern for workers with regard to acute dermal toxicity (**conclusion ii**) for all scenarios.

Irritation and corrosivity

Dermal irritation after single and repeated exposure
Given the effects observed in the skin irritation studies with rabbits and in view of the dermal occupational exposure in the different scenarios (<0.5 mg/m^2), it is concluded that furfural is of concern for workers with regard to acute skin irritation. However, it is assumed that existing controls (i.e., engineering controls and personal protective equipment based on classification and labelling with R38) are applied. Therefore, it is concluded that furfural is of no concern for workers with regard to skin irritation (**conclusion ii**).
Given the results from the skin irritation studies, it is concluded that furfural is of no concern for workers with regard to corrosivity (**conclusion ii**).

No repeated dose toxicity study with regard to dermal irritation of furfural is available and thus it is not possible to make a quantitative risk assessment for local effects after repeated dermal exposure.

[2] Minimal MOS acute inhalation toxicity 125 = 2.5 (interspecies) x 5 (intraspecies) x 10 (Dose response / Type of critical effect)
[3] Minimal MOS acute dermal toxicity 300 = 2.4*2.5 (interspecies) x 5 (intraspecies) x 10 (Dose response / Type of critical effect)

Eye irritation
Based on the available human and animal data furfural is considered irritating to the eyes. However, it is assumed that existing controls (i.e., engineering controls and personal protective equipment based on classification and labelling with R36) are applied. Therefore, it is concluded that furfural is of no concern for workers with regard to eye irritation (conclusion ii).

Respiratory irritation after single and repeated exposure
Given the effects observed after single exposure to furfural vapour in animals and humans, and the short-term exposure level (reasonable worst-case ranging from 12 to 120 mg/m^3), it is concluded that furfural is of concern for workers with regard to acute respiratory tract irritation. However, it is assumed that existing controls (i.e., engineering controls and personal protective equipment based on classification and labelling with R37) are applied. Therefore, it is concluded that furfural is of no concern for workers with regard to acute respiratory irritation (**conclusion ii**). It is noted that the studies available did not allow a quantitative comparison of (no) effect concentrations with estimated exposure levels.

Repeated inhalation exposure may induce respiratory tract irritation. The human data available cannot be used quantitatively. As starting point, the animal LOAEL of 20 mg/m^3 is used. The minimal MOS is 112.5[4]. Comparing the MOS values with the minimal MOS (see **Table 4.2a** and **Table 4.2b**), it is concluded that local effects due to repeated inhalation exposure cannot be excluded for any scenario (**conclusion iii**).

Sensitisation

Dermal sensitisation
Given the results from the dermal sensitisation studies with guinea pigs, it is concluded that furfural is of no concern for workers with regard to skin sensitisation (**conclusion ii**).

Respiratory sensitisation
There are neither data from animal studies nor indications from the human case study for respiratory sensitisation.

Repeated dose toxicity
In the section on 'carcinogenicity', risk characterisation for carcinogenic effects is described.

Inhalation exposure
Starting-point for the risk characterisation for workers exposed by inhalation for systemic effects is the NOAEL of 320 mg/m^3 from the 28-day inhalation study with rats. The minimal MOS is calculated to be 112.5[5]. Given the MOS values for inhalation exposure (see **Table 4.2a** and **Table 4.2b**), it is concluded that systemic effects due to repeated inhalation exposure cannot be excluded for all scenarios (**conclusion iii**).

[4] Minimal MOS local effects after repeated inhalation exposure 112.5 = 2.5 (interspecies) x 5 (intraspecies) x 3 (differences between experimental conditions and exposure pattern of the worker) x 3 (Dose response / Type of critical effect)
[5] Minimal MOS systemic effects after repeated inhalation exposure 112.5 = 2.5 (interspecies) x 5 (intraspecies) x 3 (differences between experimental conditions and exposure pattern of the worker) x 3 (Dose response / Type of critical effect)

Dermal exposure
Starting point for the risk characterisation for workers exposed by skin contact for systemic effects is the NOAEL of 53 mg/kg bw/day from the 13-week oral toxicity study with rats. The minimal MOS is calculated to be 55[6]. Given the MOS values for dermal exposure (see **Table 4.2a** and **Table 4.2b**), it is concluded that systemic effects due to repeated dermal exposure cannot be excluded for the scenario: 'production - cleaning and maintenance' (**conclusion iii**).

Combined exposure
Given the conclusions for scenario's 1-4 for the inhalation route, it is clear that uptake via both the dermal and inhalation route in these scenarios will give rise to adverse systemic health effects (**conclusion iii**). It should be noted, though, that exposure to furfural vapour is not taken into account in the dermal exposure assessment.

Mutagenicity
From the results of the mutagenicity studies it is concluded that furfural is not genotoxic *in vivo*. Hence, this endpoint is not of concern: **conclusion ii**.

Carcinogenicity
Furfural induced tumours in the livers of male rats (cholangiosarcomas) and hepatocellular adenomas and carcinomas in female and male mice, respectively, after oral (gavage) administration. The mechanism by which these tumours are induced does not involve genotoxicity, as furfural is not genotoxic *in vivo*. Furfural is for that reason considered a threshold carcinogen.
As the liver tumours were observed at exposure levels that also induced liver toxicity, it is assumed that at levels at which no liver toxicity is induced, no tumours will arise. A similar rationale as for the role of systemic toxicity in tumour-induction is proposed with respect to local toxicity at the site of entrance i.e. as long as no cytotoxicity occurs, it is not expected that locally tumours will be induced.
However, as the true mechanism underlying these liver tumours is unclear so far, this uncertainty should be reflected in the final evaluation of the comparison between the MOS and minimal MOS. Therefore, the scenario-specific MOS should be clearly in excess of the minimal MOS value for a conclusion of no concern.
From **Table 4.2a** and **Table 4.2b** it can then be concluded that all scenarios are of concern, i.e. lead to conclusion iii. This applies to all inhalation exposure scenarios (local and systemic effects) as well as (for systemic effects) to the dermal exposure scenarios 1 ('production - cleaning and maintenance'), and, additionally, scenario 3 ('Production of refractories, etc.- mix, mould, etc.'). The latter scenario is included because of the low (MOS/minMOS) ratio, as well as the fact that exposure to furfural vapour is not taken into account in the dermal exposure assessments. Thus, for this latter scenario the (MOS/minMOS) ratio is considered insufficient for deriving a conclusion ii for this endpoint (while a conclusion ii was derived for this scenario for repeated dose toxicity).
For combined exposure, clearly there is concern for carcinogenic effects for all exposure scenarios: **conclusion iii**.

Toxicity for reproduction

Inhalation exposure

[6] Minimal MOS systemic effects after repeated dermal exposure 55 = 4 * 2.5 (interspecies) x 5 (intraspecies) x 1.1 (route-to-route extrapolation; 90% oral absorption, 100% dermal absorption)

- Effects on fertility
There are no indications for effects on fertility (**conclusion ii**).

- Developmental toxicity
Developmental studies by inhalation exposure are lacking. The NOAEL for developmental effects is 100 mg/kg bw/day (highest dose level that could be evaluated, because of low survival of parent female animals in the 150 mg/kg bw/day group (16/25 females died at this dose level)). In the 150 mg/kg bw/day dose group a not statistically significant reduction in mean foetal body weight was observed in one litter; it cannot be excluded that this effect is caused by maternal toxicity. The NOAEL for maternal toxicity was less than 50 mg/kg bw/day.
The minimal MOS value is 55[7]. Based on the finding that a developmental toxicity effects only occurred at maternally toxic dose levels, MOS values which are slightly lower (i.e. a factor 1-3) than the minimal MOS are not considered of toxicological relevance. Therefore, it is concluded that with regard to inhalation exposure in the occupational scenario 1 'production – full shift', scenario 3 'Production of refractories, etc. - mix, mould, etc.' and scenario 4 'Use of furfural- refining, etc.', there is no concern for workers with respect to developmental toxicity (**conclusion ii**). It is concluded that effects cannot be excluded for scenario 1 'production - cleaning and maintenance', given the low associated MOS value (see **Table 4.2a** and **Table 4.2b**) i.e. a **conclusion iii** is derived for this scenario.

Dermal exposure
- Effects on fertility
There are no indications for effects on fertility (**conclusion ii**).

- Developmental toxicity
Developmental studies by dermal exposure are lacking. The NOAEL for developmental effects is 100 mg/kg bw/day (highest dose level that could be evaluated, because of low survival of parent female animals in the 150 mg/kg bw/day group (16/25 females died at this dose level)). In the 150 mg/kg bw/day dose group a not statistically significant reduction in mean foetal body weight was observed in one litter; it cannot be excluded that this effect is caused by maternal toxicity. The NOAEL for maternal toxicity was less than 50 mg/kg bw/day.
The minimal MOS value is 55[8]. It is concluded that these effects cannot be excluded for scenario 1 'production - cleaning and maintenance', given the low associated MOS values (see **Table 4.2a** and **Table 4.2b**) i.e. a **conclusion iii** is derived for this scenario.

Combined exposure
The available data indicate a concern for effects developmental toxicity (**conclusion iii)**.

[7] Minimal MOS developmental toxicity after inhalation exposure 55 = 4 * 2.5 (interspecies) x 5 (intraspecies) x 1.1 (route-to-route extrapolation; 90% oral absorption, 100% inhalation absorption)
[8] Minimal MOS developmental toxicity after dermal exposure 55 = 4 * 2.5 (interspecies) x 5 (intraspecies) x 1.1 (route-to-route extrapolation; 90% oral absorption, 100% dermal absorption)

Table 4.2a. Overview of the conclusions with respect to occupational risk characterisation[1] (scenario 1 and 2).

Scenario's	Scenario 1 – Production										Scenario 2 – Product derivatives					
Subscenario's	general (closed system)		production activities (full shift)		production activities (short term)		clearing and maintenance (full shift)		clearing and maintenance (short term)		general		adding		full shift	
	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.
Acute toxicity																
- inhalation	n.a.	-	n.a.	-	n.a.	-	n.a.	-	34	ii	n.a.	-	50-77	ii	n.a.	-
- dermal	n.a.	-	n.a.	-	1033	ii	n.a.	-	67	ii	n.a.	-	1033	ii	n.a.	-
Repeated dose toxicity																
- inhalation (local)	n.a.	-	0.7	iii	n.a.	-	n.a.	-	n.a.	-	n.a.	-	n.a.	-	3	iii
- inhalation (systemic)	n.a.	-	11	iii	n.a.	-	5	iii	n.a.	-	n.a.	-	n.a.	-	53	iii
- dermal (systemic)	n.a.	-	88	ii	n.a.	-	5.7	iii	n.a.	-	n.a.	-	n.a.	-	88	ii
-combined (systemic)	n.a.	-		iii	n.a.	-		iii	n.a.	-	n.a.	-	n.a.	-		iii
Carcinogenicity	n.a.	-	iii, see text		n.a.	-	iii, see text		n.a.	-	n.a.	-	n.a.	-	iii, see text	
Developmental toxicity																
- inhalation	n.a.	-	23	ii	n.a.	-	10	iii	n.a.	-	n.a.	-	n.a.	-	117	ii
- dermal	n.a.	-	167	ii	n.a.	-	11	iii	n.a.	-	n.a.	-	n.a.	-	167	ii

n.a. = not applicable.

[1] Regarding the toxicological endpoints, skin irritation and corrosivity, local effects after repeated dermal exposure, eye irritation, skin and respiratory sensibilisation, mutagenicity and effects on fertility no quantitative risk assessment was performed. For these endpoints conclusion ii was drawn.

Table 4.2b. Overview of the conclusions with respect to occupational risk characterisation[1] (scenario 3 and 4).

Scenario's	Scenario 3 – Production refractories etc.				Scenario 4 – Use of furfural					
Subscenario's	mix, mould etc.		short-term		refining etc,.		short-term		clearing and maintenance	
	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.	MOS	concl.
Acute toxicity										
- inhalation	n.a.	-	40	ii	n.a.	-	40	ii	n.a.	-
- dermal	n.a.	-	689	ii	1033	ii	n.a.	-	2067	ii
Repeated dose toxicity										
- inhalation (local)	0.5	iii	n.a.	-	0.8	iii	n.a.	-	n.a.	-
- inhalation (systemic)	8	iii	n.a.	-	13	iii	n.a.	-	n.a.	-
- dermal (systemic)	59	ii	n.a.	-	88	ii	n.a.	-	177	ii
-combined (systemic)		iii	n.a.	-		iii	n.a.	-		ii
Carcinogenicity	iii, see text		n.a.	-	iii, see text		n.a.	-	ii, see text	
Developmental toxicity										
- inhalation	18	ii	n.a.	-	28	ii	n.a.	-	n.a.	-
- dermal	111	ii	n.a.	-	167	ii	n.a.	-	333	ii

n.a. = not applicable.

[1] Regarding the toxicological endpoints, skin irritation and corrosivity, local effects after repeated dermal exposure, eye irritation, skin and respiratory sensibilisation, mutagenicity and effects on fertility no quantitative risk assessment was performed. For these endpoints conclusion ii was drawn.

4.3.2 Consumers

Although the uses of furfural as fragrance material in cosmetic products (scenario I) and as flavouring substance in food (scenario II) are regulated via other EU legislation than EU Regulation 793/93/EC, a risk characterisation is performed using as starting points the dermal (external) exposure of 1 µg/kg bw/day for scenario I, the oral (external) exposure estimates of 9 and (worst case) 136 µg/kg bw/day for scenario II, and absorption percentages of 100% and 90% for the dermal and oral route, respectively. For both scenarios it is considered that exposure occurs frequently.

Irritation (scenario I)
Depending on the concentration, furfural liquid can be irritating to the skin, and for this property the substance has been classified. For concentrations as low as 0.1 % (the reported maximum concentration in cosmetic products) no skin irritation was observed. Hence, for consumers there is no concern for skin irritation (**conclusion ii**). Furfural is considered to be an eye irritant and is classified/labelled accordingly (**conclusion ii**).

Sensitisation (scenario I)
Furfural is not a skin sensitiser. Consumers are therefore not at risk after repeated dermal exposure (**conclusion ii**).

Repeated dose toxicity (scenario I and II)
Starting points for the risk assessment for consumers are the dermal and oral exposure estimates and the oral NOAEL of 53 mg/kg bw/day from the dietary 13-week oral toxicity study with rats. Studies to assess the systemic toxicity after repeated dermal exposure are lacking. Route-to-route extrapolation is applied for scenario I, taking into account the oral and dermal absorption percentages of 90 and 100%, respectively. The (external) NOAEL of 53 mg/kg bw/day, observed in the 13 week oral study, corresponds to an internal NOAEL for systemic effects of 47.7 mg/kg bw/day.

For scenario I: The external dermal dose of 1 µg/kg bw/day corresponds to a systemic dose of 1 µg/kg bw/day. Comparing the internal NOAEL with this systemic dose, the MOS is 47700.

For scenario II: Comparing the oral NOAEL with the oral exposure estimate of 9 µg/kg bw/day, the MOS is 5889. When taking into account the worst case estimate of 136 µg/kg bw/day, the MOS is 390. Using assessment factors of 10 for both intra- and interspecies differences, the minimal MOS is 100. There is no need for a factor for duration extrapolation because furfural has been studied in a chronic bioassay and no effect of exposure duration was found in relation to the NOAEL, or the nature of the observed effects.
The MOSs for scenarios I and II do not indicate a concern for consumers for repeated dermal and oral exposure (**conclusion ii**).

Mutagenicity (Scenario I and II)
Furfural is not genotoxic in vivo. Hence, this endpoint is not of concern (**conclusion ii**).

Carcinogenicity (Scenario I and II)
Furfural induced tumours in the livers of male rats (cholangiosarcomas) and hepatocellular adenomas and carcinomas in female and male mice, respectively, after oral (gavage) administration. The mechanism by which these tumours are induced does not involve

genotoxicity, as furfural is not genotoxic in vivo. As the liver tumours were observed at exposure levels that also induced liver toxicity, it is assumed that at levels at which no liver toxicity is induced, no tumours will arise. Hence, as starting point for the risk characterisation for carcinogenicity the oral NOAEL for liver toxicity (i.e. 53 mg/kg bw/day, as established under 'repeated dose toxicity') is taken. Route-to-route extrapolation is applied for scenario I, taking into account the oral and dermal absorption percentages of 90 and 100%, respectively. The (external) NOAEL of 53 mg/kg bw/day corresponds to an internal NOAEL of 47.7 mg/kg bw/day.

For scenario I: The external dermal dose of 1 µg/kg bw/day corresponds to a systemic dose of 1 µg/kg bw/day. Comparing the internal NOAEL with this systemic dose, the MOS is 47700.

For scenario II: Comparing the oral NOAEL with the oral exposure estimate of 9 µg/kg bw/day, the MOS is 5889. When taking into account the worst case estimate of 136 µg/kg bw/day, the MOS is 390. Using assessment factors of 10 for both intra- and interspecies differences, the minimal MOS is 100. There is no need for a factor for duration extrapolation because furfural has been studied in a chronic bioassay and no effect of exposure duration was found in relation to the NOAEL, or the nature of the observed effects.
Even in the light of the need for a slightly higher MOS than the required minimal MOS of 100, because of the unknown exact mechanism for carcinogenicity, the current MOSs of 47700 and 390-5889 for scenarios I and II do not indicate a concern for consumers with regard to carcinogenicity (**conclusion ii**).

Reproductive toxicity (Scenario I and II)
There are no indications for effects on fertility. Developmental studies by inhalation or dermal exposure are lacking. An oral developmental toxicity study with rats is available. Developmental toxicity occurred only at maternally toxic dose levels. Furfural is not teratogenic. The NOAEL for developmental effects is 100 mg/kg bw/day and the NOAEL for maternal toxicity was <50 mg/kg bw/day. This latter value is used to characterise the risk for the pregnant population. Route-to-route extrapolation is applied for scenario I, taking into account the oral and dermal absorption percentages of 90 and 100%, respectively. This results in internal NOAELs of 90 mg/kg bw/day for developmental effects and <45 mg/kg bw/day for maternal toxicity, respectively.

For scenario I: The external dermal dose of 1 µg/kg bw/day corresponds to a systemic dose of 1 µg/kg bw/day. Comparing the internal NOAELs of 90 and <45 mg/kg bw/day with this systemic dose, MOSs of 90000 and <45000, respectively, can be calculated.

For scenario II: Comparing the oral NOAELs of 100 and <50 mg/kg bw/day with the oral exposure estimate of 9 µg/kg bw/d, MOSs of 11100 and <5555, respectively, can be calculated. When taking into account the worst case estimate of 136 µg/kg bw/day, MOSs of 735 and <368, respectively, can be calculated. Using assessment factors of 10 for both intra- and interspecies differences and 3 for the LOAEL for maternal toxicity, the minimal MOS is 100 for developmental effects and 300 for maternal effects.
Taking into account the magnitude of these MOSs and the worst case character of the highest exposure estimate, for both scenario I and II there is no concern for consumers for reproductive toxicity after repeated dermal and oral exposure (**conclusion ii**).

4.3.3 Man indirectly exposed via the environment

Local exposure

Risk characterisation is performed for the scenario with the highest total daily intake, i.e. formulation for manufacturing refractories, for which the (internal) exposure estimate was 11 µg/kg bw/day.

Repeated dose toxicity

Starting points for the risk assessment for human exposed indirectly via the environment are the above mentioned (internal) exposure estimate, the oral NOAEL of 53 mg/kg bw/day from the dietary 13-week oral toxicity study with rats, and an absorption percentage of 90% for the oral route. Based on the latter, the oral NOAEL of 53 mg/kg bw/day corresponds to an internal NOAEL for systemic effects of 47.7 mg/kg bw/day.
Comparing the internal NOAEL to the exposure estimate of 11 µg/kg bw/day, the MOS is 4336. Using assessment factors of 10 for both intra- and interspecies differences, the minimal MOS is 100. There is no need for a factor for duration extrapolation because furfural has been studied in a chronic bioassay and no effect of exposure duration was found in relation to the NOAEL, or the nature of the observed effects.
The MOS does not indicate a concern for human exposed indirectly via the environment (local) for repeated exposure (**conclusion ii**).

Mutagenicity

Furfural is not genotoxic in vivo. Hence, this endpoint is not of concern (**conclusion ii**).

Carcinogenicity

Furfural induced tumours in the livers of male rats (cholangiosarcomas) and hepatocellular adenomas and carcinomas in female and male mice, respectively, after oral (gavage) administration. The mechanism by which these tumours are induced does not involve genotoxicity, as furfural is not genotoxic in vivo. As the liver tumours were observed at exposure levels that also induced liver toxicity, it is assumed that at levels at which no liver toxicity is induced, no tumours will arise. Hence, as starting point for the risk characterisation for carcinogenicity the oral NOAEL for liver toxicity (i.e. 53 mg/kg bw/day, as established under ‘repeated dose toxicity’) is taken. The (external) NOAEL of 53 mg/kg bw/day corresponds to an internal NOAEL of 47.7 mg/kg bw/d, taking into account an oral absorption of 90%.
Comparing the internal NOAEL to the exposure estimate of 11 µg/kg bw/day, the MOS is 4336. Using assessment factors of 10 for both intra- and interspecies differences, the minimal MOS is 100. There is no need for a factor for duration extrapolation because furfural has been studied in a chronic bioassay and no effect of exposure duration was found in relation to the NOAEL, or the nature of the observed effects.
Even in the light of the need for a slightly higher MOS than the required minimal MOS of 100, because of the unknown exact mechanism for carcinogenicity, the current MOS does not indicate a concern for human exposed indirectly via the environment (local) with regard to carcinogenicity (**conclusion ii**).

Reproductive toxicity

There are no indications for effects on fertility. Developmental studies by inhalation or dermal exposure are lacking. An oral developmental toxicity study with rats is available. Developmental toxicity occurred only at maternally toxic dose levels. Furfural is not teratogenic. The NOAEL for developmental effects is 100 mg/kg bw/day and the NOAEL for maternal toxicity was <50 mg/kg bw/day. This latter value is used to characterise the risk for

the pregnant women. The internal NOAELs are 90 mg/kg bw/day for developmental effects and <45 mg/kg bw/day for maternal toxicity, respectively.
Comparing the exposure estimate of 11 µg/kg bw/day to the internal NOAELs, MOSs of 8182 and <4091, respectively, can be calculated. Using assessment factors of 10 for both intra- and interspecies differences and 3 for the LOAEL for maternal toxicity, the minimal MOS is 100 for developmental effects and 300 for maternal effects. Taking into account the magnitude of these MOSs, there is no concern for human exposed indirectly via the environment (local) for reproductive toxicity after repeated exposure (**conclusion ii**).

Regional exposure

For regional exposure, the total daily intake was estimated at 4 ng/kg bw/day, i.e. three orders of magnitude lower than the highest local exposure for which a conclusion ii was reached for all relevant endpoints. Given this, also for the regional scenario a **conclusion ii** is reached for all relevant endpoints.

Natural occurrence

For the natural occurrence of furfural and precursors in food, a total potential intake of approximately 300 µg/kg bw/day has been estimated. No formal risk characterisation is performed for this unintentional source of exposure to furfural because it is outside the scope of EU Regulation 793/93/EC. However, to have some indication of the margins between the estimated 'natural' exposure to furfural and the N(L)OAELs for the endpoints of concern, please see the table below.

	Repeated dose toxicity	Carcinogenicity	Reproductive toxicity	
			Developmental toxicity	Maternal toxicity
Oral NOAEL (mg/kg bw/day)	53	53	100	<50
MOS	177	177	333	<167

4.3.4 Combined exposure

The only combined exposure to be dealt with under EU Regulation 793/93/EC is the combination of worker exposure and exposure via the environment due to intentional sources. The latter can be considered negligible compared to exposure to furfural at the workplace. Therefore, the risk characterisation for combined exposure is completely driven by the risk characterisation for workers, for which a **conclusion iii** was reached for the endpoints repeated dose toxicity, carcinogenicity, and developmental toxicity for some or all scenarios.

4.4 HUMAN HEALTH (PHYSICAL-CHEMICAL PROPERTIES)

Furfural does not need to be classified regarding flammability. Based on theoretical and structural considerations, furfural is not expected to have explosive properties and oxidising potential. Therefore, there is no need for further information and/or testing with regard to physical-chemical properties. Furfural is considered of no concern with regard to physical-chemical properties (**conclusion ii**).

5 OVERALL RESULTS OF THE RISK ASSESSMENT

5.1 ENVIRONMENT

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 and for risk reduction measures beyond those which are being applied already
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account

Conclusion (i) is reached because the PEC_{soil} exceeds the $PNEC_{soil}$ in the scenarios 'formulation for manufacturing refractories Va, Vb' and 'use as intermediate in pesticide manufacture VI'. The terrestrial PNEC is derived through the equilibrium partitioning method and there is therefore scope to refine this PNEC through testing. However, no testing is proposed for the terrestrial compartment since for these scenarios conclusion (iii) is also drawn for the local aquatic compartment. The development of risk reduction measures for the aquatic compartment should take account of the conclusions for the terrestrial compartment for these three scenarios.

Conclusion (iii) is reached because the PEC water exceeds the $PNEC_{surface\ water}$ in the scenarios 'formulation chemical tracer in mineral oil and fuel industry IVb', 'formulation for manufacturing refractories Va, Vb' and 'use as intermediate in pesticide manufacture VI'. As no further refinement of the PECs and PNECs is possible, there is a need for limiting the risks.

For all remaining scenarios a conclusion (ii) is drawn for the environment.

Risks of 2-furaldehyde as a result of emissions by the pulp and paper industry (unintentional source):
The PEC_{STP} and the $PEC_{surface\ water}$ exceed the corresponding PNECs in the 'pulp and paper industry, scenario VII' (unintentional source). For the refinement of this scenario site-specific measured effluent or surface water concentrations are needed. Additionally, measured data from other pulp and paper industries in the EU are needed to refine this scenario. Since this considers an unintentional source beyond the scope of this EU risk assessment, there will be no follow-up of this scenario in the context of Regulation 793/93/EC.

5.2 HUMAN HEALTH

5.2.1 Workers

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

Conclusion (iii) is reached because:

- systemic effects and local effects on respiratory tract cannot be excluded after repeated inhalation exposure in all scenarios;
- systemic effects cannot be excluded after repeated dermal exposure in scenario 1 'production – cleaning and maintenance';
- carcinogenic effects cannot be excluded after repeated dermal and inhalation exposure in all scenarios; and
- developmental effects due to repeated dermal and inhalation exposure cannot be excluded in scenario 1 'production – cleaning and maintenance'.

It might be possible that in some workplaces adequate worker protection measures are already being applied.

5.2.2 Consumers

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

5.2.3 Humans exposed via the environment

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

5.2.4 Combined exposure

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

Conclusion (iii) is reached because the risk characterisation for combined exposure is completely driven by the risk characterisation for the occupational settings.

5.2.5 Human health risks arising from physical-chemical properties

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

6 GLOSSARY

Standard term Abbreviation	Explanation/Remarks and Alternative Abbreviation(s)
Ann.	Annex
AF	assessment factor
BCF	bioconcentration factor
bw	body weight / *Bw*, *b.w.*
°C	degrees Celsius (centigrade)
CAS	Chemical Abstract System
CEC	Commission of the European Communities
CEN	European Committee for Normalisation
CEPE	European Council of the Paint, Printing Ink and Artists' Colours Industry
d	day(s)
d.wt	dry weight / dw
DG	Directorate General
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{50lab}	period required for 50 percent dissipation under laboratory conditions (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
$DT_{90field}$	period required for 90 percent dissipation under field conditions (define method of estimation)
EC	European Communities
EC	European Commission
EC_{50}	median effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
EU	European Union
EUSES	European Union System for the Evaluation of Substances
f_{oc}	Fraction of organic carbon
G	gram(s)

PNEC(s)	Predicted No Effect Concentration(s)
$PNEC_{water}$	Predicted No Effect Concentration in Water
(Q)SAR	Quantitative Structure Activity Relationship
STP	Sewage Treatment Plant
TGD	Technical Guidance Document[9]
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products or Biological material
v/v	volume per volume ratio
w/w	weight per weight ratio
w	gram weight
GLP	Good Laboratory Practice
h	hour(s)
ha	Hectares / *h*
HPLC	High Pressure Liquid Chromatography
IARC	International Agency for Research on Cancer
$+C_{50}$	median immobilisation concentration or median inhibitory concentration 1 / *explained by a footnote if necessary*
ISO	International Standards Organisation
IUPAC	International Union for Pure Applied Chemistry
kg	kilogram(s)
kPa	kilo Pascals
K_{oc}	organic carbon adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	Solids water partition coefficient
l	litre(s)
log	logarithm to the basis 10
$L(E)C_{50}$	Lethal Concentration, Median
LEV	Local Exhaust Ventilation

[9] Commission of the European Communities, 1996. Technical Guidance Documents in Support of the Commission Directive 93/67/EEC on risk assessment for new substances and the Commission Regulation (EC) No 1488/94 on risk assessment for existing substances. Commission of the European Communities, Brussels, Belgium.
ISBN 92-827-801[1234]

m	Meter
µg	microgram(s)
mg	milligram(s)
MAC	Maximum Accessibility Concentration
MOS	Margins Of Safety
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
OEL	Occupational Exposure Limit
OECD	Organisation for Economic Co-operation and Development
OJ	Official Journal
pH	potential hydrogen -*logarithm* (to the base 10) of the hydrogen ion concentration $\{H^+\}$
pKa	-*logarithm* (to the base 10) of the acid dissociation constant
pKb	-*logarithm* (to the base 10) of the base dissociation constant
Pa	Pascal unit(s)
PEC	Predicted Environmental Concentration
STP	Sewage Treatment Plant
WWTP	Waste Water Treatment Plant

The report provides summary of the comprehensive risk assessment of the substance 2-furaldehyde. It has been prepared by the Netherlands in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I - Environment
This part of the evaluation considers the emissions and the resulting exposure to the environment in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined.

The environmental risk assessment concludes that there is a need for limiting the risks for the aquatic compartment as a consequence of exposure arising from formulation of chemical tracer in mineral oil and fuel industry, formulation for manufacturing refractories and use as intermediate in pesticide manufacture. In addition there is a need for better information to adequately characterise the toxic effects of 2-furaldehyde to the terrestrial ecosystems.
At present, there is no concern for the atmosphere, for macro-organisms in the sewage treatment plant.

Part II – Human Health
This part of the evaluation considers the emissions and the resulting exposure to human populations in all life cycle steps. The scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

There is concern for workers only, but not for consumers and humans exposed via the environment.

The conclusions of this report will lead to risk reduction measures proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.