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Concise International Chemical Assessment Document 21

2-FURALDEHYDE

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The International Programme on Chemical Safety (IPCS), established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organisation (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, the United Nations Institute for Training and Research, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

Concise International Chemical Assessment Documents (CICADs) are the latest in a family of publications from the International Programme on Chemical Safety (IPCS) — a cooperative programme of the World Health Organization (WHO), the International Labour Organisation (ILO), and the United Nations Environment Programme (UNEP). CICADs join the Environmental Health Criteria documents (EHCs) as authoritative documents on the risk assessment of chemicals.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents undergo extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are provided as guidance only. The reader is referred to EHC 1701 for advice on the derivation of health-based guidance values.

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact IPCS to inform it of the new information.

Procedures

The flow chart shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world — expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment.

The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes primary review by IPCS to ensure that it meets the specified criteria for CICADs.

The second stage involves international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers’ comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers’ comments.

The CICAD Final Review Board has several important functions:

– to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
– to verify that the peer reviewers’ comments have been addressed appropriately;
– to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
– to approve CICADs as international assessments.

Board members serve in their personal capacity, not as representatives of any organization, government, or

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1 Taking into account the comments from reviewers.
2 The second draft of documents is submitted to the Final Review Board together with the reviewers’ comments.
3 Includes any revisions requested by the Final Review Board.
industrial. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.
1. EXECUTIVE SUMMARY

This CICAD on 2-furaldehyde was based on a review of human health concerns (primarily occupational) prepared by the United Kingdom’s Health and Safety Executive (Gregg et al., 1997), but it also contains environmental information. Hence, this document focuses on exposures via routes relevant to occupational settings but also includes an environmental assessment. Data identified up to January 1997 were covered in the review. A further literature search was performed up to December 1997 to identify any new information published since the review was completed, but no relevant studies were identified. Information on the nature of the peer review and availability of the source document is presented in Appendix 1. Information on the peer review of this CICAD is presented in Appendix 2. This CICAD was approved as an international assessment at a meeting of the Final Review Board, held in Washington, DC, USA, on 8–11 December 1998. Participants at the Final Review Board meeting are listed in Appendix 3. The International Chemical Safety Card (ISCS 0276) produced by the International Programme on Chemical Safety (IPCS, 1993) has also been reproduced in this document.

2-Furaldehyde (C₄H₄O₂) (CAS No. 98-01-1) is a liquid with a pungent “almond-like” odour. It is found in trace amounts in a number of dietary sources and is produced commercially in batch or continuous digesters where pentosans from agricultural residues are hydrolysed to pentoses and the pentoses are subsequently cyclodehydrated to 2-furaldehyde. Industrial uses include the production of resins, abrasive wheels, and refractories, refining of lubrication oils, and solvent recovery. 2-Furaldehyde is also used, in very small quantities, as a flavouring agent.

2-Furaldehyde is present in many food items as a natural product or as a contaminant. Its presence in drinking-water and mothers’ milk has been reported, but levels were not sufficient for quantification.

Measured occupational inhalation exposures are available, and estimations have also been made using a knowledge-based computer system, Estimation and Assessment of Substance Exposure (EASE). Generally, airborne exposure in all industries is below 8 mg/m³ (2 ppm), 8-h time-weighted average (TWA). There is insufficient information to predict 15-min TWA exposures for most industries; however, a 15-min TWA exposure between 1.2 and 6.8 mg/m³ (0.3 and 1.7 ppm) has been estimated in the flavouring industry. No measured data are available for dermal exposure. EASE-predicted dermal exposures between 0.1 and 1 mg/cm² per day have been calculated for most industries, with higher exposures of between 1 and 5 mg/cm² per day calculated for the industries manufacturing refractories and abrasive wheels.

Toxicokinetic data are limited, but there are indications that 2-furaldehyde is readily absorbed via the inhalation and dermal exposure routes. Animal studies demonstrate that, following oral administration in rats, 2-furaldehyde is readily absorbed and rapidly excreted mainly via the urine, although some elimination via exhaled carbon dioxide also occurs. Metabolism is characterized by oxidation or acetylation of the aldehyde group, followed by glycerine conjugation. 2-Furoylglycine is the major urinary metabolite; other minor metabolites include furoic acid, furanacrylic acid, and furanacryluric acid.

In humans, absorption of the vapour via both the lungs and skin has been demonstrated. Metabolism in humans appears similar to that in rats, with the majority of the retained dose being excreted as urinary 2-furoylglycine. Furoic acid and furanacrylic acid are also detected as minor metabolites. Dermal absorption from liquid 2-furaldehyde has also been observed.

Acute toxicity data from animals are variable; overall, however, 2-furaldehyde is toxic by the inhalation and oral routes (4-h LC₅₀, 940 mg/m³ [235 ppm]; oral LD₅₀, about 120 mg/kg body weight), with no clear information in relation to the dermal route. Respiratory tract irritation and lung damage are consistently observed following single and repeated inhalation exposure. Skin and eye irritation are also reported. Apparently no throat or eye irritation was noted in humans exposed to 40 mg/m³ (10 ppm) for 8 h or 80 mg/m³ (20 ppm) for 4 h. In animals, no-observed-adverse-effect levels (NOAELs) of 80 mg/m³ (20 ppm) and 208 mg/m³ (52 ppm) in studies of up to 13 weeks’ duration have been identified in hamsters and rabbits, respectively, for non-neoplastic effects. Malignant and benign tumours have been observed in rats and mice following oral exposure to 60 and 30 mg/kg body weight, respectively, for 103 weeks. 2-Furaldehyde is clearly genotoxic in vitro in mammalian cells; although no firm conclusions can be drawn on the genotoxic potential of 2-furaldehyde in vivo, the possibility that genotoxicity could contribute to the carcinogenic process cannot be discounted. These factors prevent the reliable determination of a NOAEL for 2-furaldehyde.

The lack of available data to serve as a basis for estimation of indirect exposure of individuals to 2-furaldehyde from the general environment precludes the characterization of potential cancer risks for the general population.
In the occupational environment, there is a potential risk of carcinogenic and genotoxic effects. The level of risk is uncertain; as a result, there is a continuing requirement to reduce exposure levels as much as is reasonably practicable with the technology that is currently available.

There are no adequate data available regarding reproductive or developmental effects; hence, it is not possible to evaluate the risk to human health for these end-points.

The highest reported emissions of 2-furaldehyde to the environment are from the wood pulp industry. 2-Furaldehyde will be released to the atmosphere from natural and anthropogenic wood burning.

No atmospheric effects are expected, as 2-furaldehyde is destroyed by reaction with hydroxyl radicals at a calculated atmospheric half-life of 0.44 days. In urban air, reaction with nitrate radicals may be an additional degradation process. Direct photo-oxidation may also occur. Low vapour pressure and low Henry’s law constant suggest only slow volatilization of 2-furaldehyde from water and soil surfaces.

In water, hydrolysis is not expected to occur at environmental pH. The low octanol/water partition coefficient (log \(K_{ow} 0.41\)) suggests low capacity for bioaccumulation. Sorption coefficients (\(K_{oc}\)) suggest little sorption to particulates and high mobility in soils.

2-Furaldehyde is readily biodegraded in aerobic systems using sewage sludge and in surface waters. Degradation also takes place under anaerobic conditions, with a range of bacteria and other microorganisms capable of degrading the compound as sole carbon source. At high concentrations (>1000 mg/litre), 2-furaldehyde inhibits growth and metabolic activity of unadapted anaerobic cultures. However, acclimation increases the capacity of anaerobic sludges to degrade the compound.

The highest reported concentrations of 2-furaldehyde in industrial wastewaters are from sulfite evaporator condensate (about 15% of the waste stream from wood pulp mills), at an average of 274 mg/litre. A single study quantified 2-furaldehyde in indoor and outdoor air at around 1 : g/m³; other studies have detected but not quantified the compound.

Toxic thresholds for a variety of microorganisms have been reported to range from 0.6 to 31 mg/litre. Acute LC₅₀ for fish range from 16 to 32 mg/litre.

Based on estimated predicted environmental concentrations from wood pulp waste (expected to be the worst case) and the application of an uncertainty factor of 1000 to the limited acute toxicity test data, 2-furaldehyde emissions are expected to pose a low risk to aquatic organisms. There are no data on which to base a terrestrial risk assessment, but emissions to land are expected to be low.

2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

2-Furaldehyde (\(C_5H_4O_2\); molecular weight 96.09; CAS No. 98-01-1) is a liquid with a pungent “almond-like” odour. Its structural formula is given below. A common synonym is furfural. Others include furfuryl, 2-furanaldehyde, fural, furfuraldehyde, and 2-furan-carboxaldehyde. 2-Furaldehyde is colourless when freshly distilled, but it darkens in contact with air. It is completely miscible with most organic solvents, except saturated aliphatic hydrocarbons, and is soluble in water (one source quotes 83 g/litre). Its log \(K_{ow}\) is 0.41, its vapour pressure is 0.144 kPa at 20 °C, and its dimensionless Henry’s law constant (air/water partition coefficient) is \(1.5 \times 10^{-4}\) (HSDB, 1998). Additional physical/chemical properties are presented on the enclosed International Chemical Safety Card (ISCS 0276).

The conversion factors for 2-furaldehyde in air at 20 °C and 101.3 kPa are as follows:

- 1 ppm = 4.0 mg/m³
- 1 mg/m³ = 0.25 ppm

3. ANALYTICAL METHODS

Long- and short-term personal monitoring can be undertaken by pumped sampling through XAD-2 resin impregnated with 2-(hydroxymethyl) piperazine, desorbing with solvent (toluene), and analysing with gas chromatography (NIOSH, 1987). The working range is 1.2–22 mg/m³ (0.3–5.5 ppm) for a 12-litre sample. Alternatively, a thermal desorption tube may be used, in
either the pumped or diffusive mode (Patel et al., 1988). The working range for both is 4–40 mg/m³ (1–10 ppm) for a 10-litre sample. Screening measurements can be made with colorimetric detector tubes, but these are unselective and not very sensitive.

Biological monitoring of workers exposed to 2-furaldehyde is possible by the analysis of 2-furoic acid (after alkaline hydrolysis of the metabolite furoylglycine) in urine (Sedivec & Flek, 1978). Although people not occupationally exposed to 2-furaldehyde have background levels of 2-furoic acid in hydrolysed urine samples (from dietary sources), these are low compared with those resulting from occupational exposure (Nutley, 1989). The biological exposure index of the American Conference of Government Industrial Hygienists is 200 mg 2-furoic acid/g creatinine (200 mg/mol/mmol creatinine), and a study in the United Kingdom found that a 2-furoic acid concentration of over 160 mg/g creatinine (160 mg/mol/mmol creatinine) was likely to be due to exposure to 2-furaldehyde at over 8 mg/m³ (2 ppm) (Nutley, 1989).

More sensitive analytical methods are required for monitoring in food. Determination of the 2,4-dinitrophenylhydrazone derivative of 2-furaldehyde by high-performance liquid chromatography gives high specificity, with a detection limit of 10 nmol/litre in spirits (Lo Coco et al., 1992). A fast, semi-automatic, stopped-flow injection analysis in which pretreatment of diversely coloured and turbid food samples is not necessary has been developed (Espinosa-Mansilla et al., 1993).

### 4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

2-Furaldehyde is produced commercially in batch or continuous digesters where pentosans from agricultural residues, including corn cobs, oat hulls, rice hulls, and bagasse, are hydrolysed to pentoses and the pentoses are subsequently cyclodehydrated to 2-furaldehyde. 2-Furaldehyde is shipped in steel tank cars, aluminium tank trucks, and steel cans. When stored in bulk, the storage tanks normally have a nitrogen blanket to prevent ingress of oxygen, which can cause chemical degradation of the material.

Estimates of worldwide production are not available. US production in 1983 was about 52 000 t (HSDB, 1998). The estimated range of US production was 14 000–60 000 t in 1986, 2000–7000 t in 1990, and 11 000–45 000 t in 1994 (US EPA, 1998). Although 2-furaldehyde is not manufactured in the United Kingdom, it is estimated that industry in the United Kingdom used approximately 3000 t in 1992. The official statistics indicate that imports into the United Kingdom for the previous four years were 2800 t (1988), 3500 t (1989), 3000 t (1990), and 3500 t (1991) (Gregg et al., 1997).

Industrial uses of 2-furaldehyde are summarized in Table 1. About 40% of 2-furaldehyde imported into the United Kingdom is used in the production of resins, abrasive wheels, and refractories. The rest is used in the refining of lubrication oils. Contacts with United Kingdom industry in 1992 indicated that there was unlikely to be any significant change in the pattern of use of 2-furaldehyde in the foreseeable future.

<table>
<thead>
<tr>
<th>Industry</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrochemicals</td>
<td>As a selective solvent in the production of lubricating oils</td>
</tr>
<tr>
<td>Refractories</td>
<td>As a reactive wetting agent in the production of refractory components</td>
</tr>
<tr>
<td>Resin manufacture</td>
<td>(a) Production of phenolic resins</td>
</tr>
<tr>
<td></td>
<td>(b) Production of cashew nutshell polymers</td>
</tr>
<tr>
<td>Abrasive materials</td>
<td>As a reactive wetting agent for the resin binder system in the production of abrasive wheels</td>
</tr>
<tr>
<td>Solvent recovery</td>
<td>Steam distillation of spent 2-furaldehyde for reuse by industry sectors 1, 2, and 4</td>
</tr>
<tr>
<td>Flavouring</td>
<td>Used in very small quantities in synthetic/natural oil blends</td>
</tr>
</tbody>
</table>

2-Furaldehyde is found in a number of dietary sources. Because of its formation during the thermal decomposition of carbohydrates, 2-furaldehyde is found in numerous processed foods and beverages, including cocoa, coffee, tea, beer, wine, milk products, and bread (Maga, 1979). It is also found in some fruits and vegetables, and it is added as a flavouring agent to some foods. Industry in the United Kingdom is voluntarily withdrawing 2-furaldehyde from addition to food, although the chemical will still be present in food as a result of its production during the thermal processing of anything containing sugars. 2-Furaldehyde has also been found in the essential oils of camphor, citronella, sassafras, lavender, and lime (Dunlop & Peters, 1953).
5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

The highest reported emissions of 2-furaldehyde to the environment are from the wood pulp industry, with release to the hydrosphere (section 6); release to water from other uses appears to be substantially lower. The compound would be released to the atmosphere from wood fires, a natural as well as anthropogenic source.

In the atmosphere, 2-furaldehyde will exist predominantly in the vapour phase; the half-life for destruction by interaction with hydroxyl radicals has been calculated at 0.44 days (HSDB, 1998). Night-time destruction in the urban atmosphere may involve reaction with nitrate radicals (Carter et al., 1981). Direct photo-oxidation may occur in the atmosphere, based on experimental demonstration that concentrations of 2-furaldehyde in wood smoke were reduced by irradiation at sunlight and ultraviolet frequencies. Addition of nitrogen oxides to wood smoke increased the rate of disappearance of the compound (Kleindienst et al., 1986).

Virtually no degradation occurred in a solution of 2-furaldehyde in distilled water over 30 days, suggesting that hydrolysis is not an important process at environmental pH (Ettenger et al., 1954).

A Henry’s law constant of 0.37 Pa m³/mol at 25 °C has been calculated (HSDB, 1998), corresponding to a dimensionless Henry’s law constant (air/water partition coefficient) of 1.5 × 10⁻³. These values indicate slow volatilization from water and damp soil surfaces; an estimated half-life for volatilization from a model river of 9.9 days has been reported (HSDB, 1998).

2-Furaldehyde has a reported log $K_{ow}$ of 0.41, indicating low capacity for bioaccumulation; calculated bioconcentration factors were less than 1.2 (HSDB, 1998). The sorption coefficient ($K_{oc}$) can be calculated as between 1.05 (Organisation for Economic Co-operation and Development (OECD) Technical Guidance Manual) and 1.62 (Karickhoff et al., 1979), indicating little sorption to particulates and a high capacity for mobility in soil.

2-Furaldehyde was readily biodegraded in an aerobic batch culture at 200 mg chemical oxygen demand (COD)/litre, with non-adapted sewage sludge showing 96.3% degradation within 120 h and a degradation rate of 37 mg COD/g per hour (Pitter, 1976). In a flow-through aerobic laboratory bioreactor at an initial concentration of 300 mg/litre, 98% degradation of 2-furaldehyde was reported using acclimated sewage sludge. Degradation also occurred at a concentration of 1000 mg/litre (Rowe & Tullos, 1980). 2-Furaldehyde was readily biodegradable in the Japanese Ministry of International Trade and Industry (MITI) test (Kawasaki, 1980). Wang et al. (1994) screened a range of microorganisms for their ability to degrade 2-furaldehyde and reviewed the earlier literature; some strains of the aerobic bacteria Escherichia coli, Pseudomonas putida, and Rhodococcus erythropolis and the yeast Hyphozyma rosenheimer were able to degrade the compound to a greater or lesser degree. Inhibitory effects of 2-furaldehyde on Pseudomonas putida were seen at concentrations of 0.1% and above, with complete inhibition at 1% with exposure for 30 min (Kim et al., 1983).

2-Furaldehyde at 1 mg/litre was degraded completely in water from the Great Miami, Little Miami, and Ohio rivers (USA) within 3 days under aerobic conditions (Ettenger et al., 1954).

Under anaerobic conditions, 2-furaldehyde was completely degraded to methane by unacclimated sewage sludge within 30 days at an initial concentration of 580 mg/litre. The rate of methane production was initially slower than in controls, indicating some interference of the compound in the metabolism of the methanogenic bacteria. At an initial concentration of 1160 mg/litre, gas production ceased after 5 days, and none of the gas produced was methane; gas production did not resume within the 28 days of the test, indicating that this concentration was toxic to unacclimated microorganisms. Using acclimated sludge (which had received 2-furaldehyde at 310 mg/litre continuously for 8 months), full degradation occurred at 1160 mg/litre. At 2320 mg/litre, 2-furaldehyde was initially degraded rapidly, but then gas production slowed for the remainder of the test (Benjamin et al., 1984). A strictly anaerobic bacterium isolated from a fermentor degrading sulfite evaporator condensate from wood pulp production was able to use 2-furaldehyde as sole carbon source; the organism was tentatively identified as Desulfovibrio sp. (Brune et al., 1983). Methanococcus delae was found to be able to use 2-furaldehyde as sole carbon source, degrading the compound to furfuryl alcohol at initial concentrations of 5 and 10 mmol/litre (480 and 960 mg/litre); however, growth of the bacterium was inhibited at concentrations of 20 and 25 mmol/litre (1920 and 2400 mg/litre). Other methanogenic bacteria (Methanobacterium thermoautotrophicum, Methanosarcina barkeri, and Methanococcus thermolithotrophicus) were unable to degrade the compound (Belay et al., 1997).
6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

2-Furaldehyde was detected in 1 out of 204 surface water samples from heavily industrialized areas in the USA at 2 ‰ g/litre (detection limit 1 ‰ g/litre) and in 1 out of 13 samples from the Lake Michigan basin, USA, at 2 ‰ g/litre in the late 1970s (HSDB, 1998).

2-Furaldehyde was not detected (detection limit 0.4 ng/litre) in 33 samples of surface waters in the 1996 monitoring of the general environment in Japan (Japan Environment Agency, 1998). However, the compound was detected in 6 out of 15 air samples (detection limit 40 ng/m³) in two cities (range 42–120 ng/m³). The analytical method was not stated in the publication.

Levels of 2-furaldehyde in sulfite evaporator condensate, which represents about 15% of the waste-water flow from pulp mills, have been reported to range between 10 and 1280 mg/litre (Ruu, 1964) and between 179 and 471 mg/litre (average 274 mg/litre) (Benjamin et al., 1984). The 2-furaldehyde derives from pentoses in the wood pulp and is formed during the waste treatment in the evaporator. 2-Furaldehyde was detected in the wastewater of a synthetic rubber plant at 1.7 ‰ g/litre (Keith, 1974).

2-Furaldehyde was detected but not quantified in the air above the Black Forest, Germany, in 1984–85 (Juttner, 1986). Although 2-furaldehyde has been identified in vehicle exhaust, it was not detectable in air sampled from a road tunnel in the USA (Hampton et al., 1982). The compound has been identified in smoke from burning wood (Lipari et al., 1984; Kleindienst et al., 1986). Mean concentrations of 2-furaldehyde measured in indoor and outdoor air in suburban New Jersey, USA, in summer 1992 were 1.06 g/m³ (0.27 ppb) and 0.67 g/m³ (0.17 ppb), respectively. The presence of the compound in indoor air was presumed to be from emissions during cooking (Zhang et al., 1994).

6.2 Human exposure

6.2.1 Oral exposure

2-Furaldehyde has been identified but not quantified as a major flavour component in a range of food items, including beef, soy sauce, roasted nuts, fried bacon, nectarines, baked potatoes, clove oil, preserved mangoes, rum, roasted coffee, and blue cheese (HSDB, 1998). Levels reported in food are as follows: non-alcoholic beverages, 4 mg/litre; alcoholic beverages, 10 mg/litre; ice creams, ices, etc., 13 mg/kg; candy, 12 mg/kg; baked goods (unspecified), 17 mg/kg; gelatins and puddings, 0.8 mg/kg; chewing gum, 45 mg/kg; and syrups, 30 mg/litre (HSDB, 1998). 2-Furaldehyde was qualitatively identified in two out of eight samples of mothers’ milk from urban sites in the USA (Pellizzari et al., 1982). Qualitative identification of 2-furaldehyde in drinking-water has been reported from both the USA and Europe; no quantification was reported (Kool et al., 1982).

6.2.2 Inhalation exposure

The remainder of the human exposure data available to the authors of this CICAD are restricted to the occupational environment.

Measured inhalation exposure information was provided to the United Kingdom’s Health and Safety Executive by the petrochemical industry. The Health and Safety Executive’s National Exposure Data Base contains information on exposure for the use of 2-furaldehyde in the refractory industry and for a number of miscellaneous processes. In all the exposure groupings below, when routine and breakdown maintenance takes place and significant exposure to airborne 2-furaldehyde is anticipated, it is expected that appropriate respiratory protective equipment would be used to minimize inhalation exposure.

Exposures in the petrochemicals, resin and polymer manufacture, and distillation industries are likely to be very similar. EASE (Version 2) predictions seem to be in accord with the limited amount of measured exposure information provided by the petrochemicals industry (Gregg et al., 1997). The EASE predictions indicate that 8-h TWA exposures will be somewhat below 8 mg/m³ (2 ppm). There is insufficient information to predict 15-min TWA exposures for these industries.

Exposures in the refractories and abrasive wheels manufacturing industries are likely to be very similar. The high exposures measured by the Health and Safety Executive in the refractories industry (20% of 8-h TWA exposures are greater than 40 mg/m³ [10 ppm]) are likely to be reduced following advice given about the application of efficient local exhaust ventilation and the enclosure of the process where possible (Gregg et al., 1997). The EASE-predicted 8-h TWA exposures likely to result from these improvements will be between 2 and 12 mg/m³ (0.5 and 3 ppm) (Gregg et al., 1997). There is every likelihood that exposures will actually be at the lower end of the range — i.e., less than 8 mg/m³ (2 ppm). There is insufficient information to predict 15-min TWA exposures for these industries.
2-Furaldehyde

In the flavouring industry, very little 2-furaldehyde appears to be used. The EASE model predicts exposures to be low: the 15-min TWA exposure is between 1.2 and 6.8 mg/m$^3$ (0.3 and 1.7 ppm), and the 8-h TWA is between 0.04 and 0.2 mg/m$^3$ (0.01 and 0.05 ppm) (Gregg et al., 1997).

For oilseed residue application, no personal exposure was detected. The extent of this industry is not known, but it seems that 8-h exposures to 2-furaldehyde are likely to be well below 8 mg/m$^3$ (2 ppm) (Gregg et al., 1997). No comment can be made upon likely short-term exposures.

Little is known about the extent of the use of 2-furaldehyde in the glass reinforced plastics industry. It is very likely that the application of appropriate controls would result in 8-h TWA exposures to 2-furaldehyde being reduced to below 8 mg/m$^3$ (2 ppm) (Gregg et al., 1997). No comment can be made upon possible short-term exposures.

### 6.2.3 Dermal exposure

The industrial processes can be grouped in a similar manner to that adopted for the general discussion of inhalation exposure above (section 6.2.2). These predictions do not take account of personal protective equipment that may be worn. Such equipment may significantly reduce dermal exposure.

The EASE-predicted dermal exposures for the petrochemicals, resin and polymer manufacture, and distillation industries are similar — namely, between 0.1 and 1 mg/cm$^2$ per day (Gregg et al., 1997).

For the refractories and abrasive wheels manufacturing industries, the EASE-predicted dermal exposures are between 1 and 5 mg/cm$^2$ per day (Gregg et al., 1997). If improvements are made to the process containment, opportunities for dermal contact will be reduced, and predicted exposures will be reduced to between 0.1 and 1 mg/cm$^2$ per day.

For the use of 2-furaldehyde in the flavourings industry, the EASE prediction for dermal exposure is between 0 and 0.1 mg/cm$^2$ per day (Gregg et al., 1997). Insufficient information is provided for the other minor uses to make predictions of dermal exposure.

### 7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

No animal studies are available examining the toxicokinetics of 2-furaldehyde by the inhalation or dermal routes; however, signs of systemic toxicity observed in animal studies (see section 8) indicate that 2-furaldehyde is readily absorbed via both these routes of exposure.

Animal studies demonstrate that, following oral administration in rats, 2-furaldehyde is readily absorbed and rapidly excreted, with up to 85% of the administered dose being detected in the urine within 24 h (Nomier et al., 1992). Some elimination via exhaled carbon dioxide (7% of dose) also occurs. Metabolism is characterized by oxidation or acetylation of the aldehyde group, followed by glycine conjugation. 2-Furoylglycine is the major urinary metabolite, accounting for approximately 80% of the administered dose (Laham & Potvin, 1989; Nomier et al., 1992; Parkash & Caldwell, 1994). Other minor metabolites include furoic acid, furanacrylic acid, and furanacryluric acid.

In humans, absorption of the vapour via both the lungs and skin has been demonstrated (Flek & Sedivec, 1978a,b). Metabolism appears similar to that in rats, with the majority of the retained dose being excreted as urinary 2-furoylglycine. Furoic acid and furanacryluric acid are also detected as minor metabolites. Dermal absorption from liquid 2-furaldehyde has also been observed.

### 8. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS

#### 8.1 Single exposure

Unpublished or briefly reported papers indicate 1-, 4-, and 6-h inhalation LC$_{50}$ values in rats of 4148, 940, and 700 mg/m$^3$ (1037, 235, and 175 ppm), respectively (Woods & Seevers, 1956; Terrill et al., 1989). In contrast, an apparently well-conducted published study indicated a 1-h LC$_{50}$ value in rats of 756 mg/m$^3$ (189 ppm) (Gupta et al., 1991; Mishra et al., 1991). In the rat and other species, respiratory tract irritation and lung damage were consistently observed following inhalation exposure, with lung oedema and congestion being reported in one study in rats immediately after exposure to 380 mg/m$^3$ (95 ppm) for 1 h. Oral LD$_{50}$ values in rats were in close agreement, ranging from 122 to 158 mg/kg body weight (Woods & Seevers, 1955; SRI International, 1982). Toxic
signs observed indicated central nervous system depressant effects, with convulsions also observed. The lungs also appeared to be a target organ via oral dosing. No reliable information was available for the dermal route of exposure.

8.2 Irritation and sensitization

No signs of skin irritation were noted in rabbits following a single application of liquid 2-furaldehyde for 12 h, although mild irritation was observed following a 48-h application (Woods & Seevers, 1955). Intense but reversible skin irritation was reported in guinea-pigs after repeated application of undiluted liquid 2-furaldehyde (Agakishiyev, 1989, 1990).

A single instillation of liquid 2-furaldehyde produced gross corneal opacities in rabbits (Woods & Seevers, 1955). 2-Furaldehyde vapour produced eye irritation in several studies following repeated exposure in different species (Gardner, 1925; Feron et al., 1979; Gupta et al., 1991).

No information is available on the ability of 2-furaldehyde to act as a skin or respiratory sensitizer.

8.3 Short-term exposure

The principal effects of repeated inhalation exposure were similar to those seen in single-exposure experiments. Groups of rats were exposed to 0 or 160 mg 2-furaldehyde/m³ (0 or 40 ppm) 1 h/day for 5, 15, or 30 days (Gupta et al., 1991; Mishra et al., 1991), and groups of rabbits were exposed to 208, 520, or 1040 mg/m³ (52, 130, or 260 ppm) 4 h/day, 5 days/week, for at least 60 exposures (Castellino et al., 1963). Respiratory irritation, hyperplasia and degeneration of the olfactory epithelium, and lung congestion, oedema, and inflammation were observed in rats following exposure to 160 mg/m³ (40 ppm) (Gupta et al., 1991; Mishra et al., 1991) and in rabbits following exposure to 1040 mg/m³ (260 ppm) (Castellino et al., 1963). There was also evidence of kidney damage seen histopathologically and anaemia in rabbits following exposure to 520 mg 2-furaldehyde/m³ (130 ppm). A NOAEL of 208 mg/m³ (52 ppm) was identified in rabbits; a NOAEL was not identified for rats.

8.4 Long-term exposure

8.4.1 Subchronic exposure

Groups of hamsters were exposed to 0, 80, 460, or 2208 mg/m³ (0, 20, 115, or 552 ppm) 6 h/day, 5 days/week, for 13 weeks (Feron et al., 1979). Respiratory irritation, hyperplasia and degeneration of the olfactory epithelium, and lung congestion, oedema, and inflammation were observed in hamsters following exposure to 2208 mg/m³ (552 ppm) (Feron et al., 1979). Slight atrophy and hyperplasia of the olfactory epithelium were also seen following exposure to 460 mg/m³ (115 ppm). A NOAEL of 80 mg/m³ (20 ppm) was identified.

Groups of 20 male and female rats received 0, 11, 22, 45, 90, or 180 mg 2-furaldehyde/kg body weight per day by oral gavage, 5 days/week for 13 weeks (NTP, 1990). Mild to moderate centrilobular vacuolation of hepatocytes was observed among all treated groups, although there was no clear relationship between dose and incidence or severity of the observed effect.

Groups of 20 male and 20 female mice received 0, 75, 150, 300, 600, or 1200 mg 2-furaldehyde/kg body weight per day by oral gavage, 5 days/week for 13 weeks (NTP, 1990). Relative liver weights were increased in a dose-related manner in all treated groups. Centrilobular coagulative necrosis of hepatocytes was seen at 150 mg/kg body weight per day or more, and mild mononuclear inflammatory cell infiltrate was seen in all treated groups.

8.4.2 Chronic exposure and carcinogenicity

No inhalation carcinogenicity studies in rats or mice were available. An inhalation study in hamsters showed no evidence that 2-furaldehyde vapour had carcinogenic potential following 52 weeks' exposure to 1000–1600 mg/m³ (250–400 ppm), 7 h/day, 5 days/week, by this route (Feron & Kruysse, 1978). Nor was there any indication that 2-furaldehyde was carcinogenic to hamsters after 36 weekly intratracheal instillations (Feron, 1972). However, both these studies are not satisfactory negative studies, owing to their limited duration.

In a gavage study, groups of 50 male and 50 female F344/N rats were treated with 0, 30, or 60 mg 2-furaldehyde/kg body weight per day, 5 days/week for 103 weeks (NTP, 1990). Animals were observed twice daily, weighed monthly, and subjected to a thorough gross and microscopic examination either at death or at the end of the study. Mortality in males was not significantly affected by 2-furaldehyde treatment throughout the study. Corresponding survival rates among females were 18/50, 32/50, and 28/50. However, 19 of the 22 top-dose deaths in females were attributed to accidental gavage errors. There were no differences in body weight between test and control animals throughout the study, and there were no treatment-related clinical signs of toxicity. The main non-neoplastic changes observed in test animals were minimal to mild centrilobular necrosis of the liver in male rats (3/50, 9/50, 12/50) and biliary dysplasia with fibrosis in two top-dose males.
Two cases of cholangiocarcinoma were seen in two other top-dose males. The historical incidence of bile duct neoplasms in corn oil vehicle control male F344/N rats in this laboratory was reported to be 3/2145 (0.1%). No other findings of biological significance were observed. Hence, in this study, treatment by gavage with 2-furaldehyde produced an increase in bile duct carcinoma in male rats only, although a valid assessment of the carcinogenicity of 2-furaldehyde in female rats cannot be made because of the low numbers of animals surviving to the end of the study. Also, the high incidence of accidental deaths casts doubt over the quality of the experimental conditions.

Groups of 50 male and 50 female B6C3F₁ mice were also dosed with 0, 50, 100, or 175 mg 2-furaldehyde/kg body weight per day by gavage, 5 days/week for 103 weeks, in the NTP study (NTP, 1990). Animals were observed twice daily, weighed monthly, and subjected to a thorough gross and microscopic examination either at death or at the end of the study. No significant differences in survival were observed between 2-furaldehyde-treated and untreated animals throughout the study. There were no differences in body weight gain between test and control animals throughout the study, and there were no clinical signs of treatment-related toxicity.

Non-neoplastic changes included chronic inflammation and multifocal green-brown, granular pigmentation of the subserosa of the liver in mid- and top-dose mice of each sex and forestomach hyperplasia in 2-furaldehyde-treated female mice only. The principal neoplastic changes observed were increases in hepatocellular adenomas and hepatocellular carcinomas in males (adenoma: 9/50 [18%], 13/50 [26%], 11/49 [22%], 19/50 [38%]; carcinoma: 7/50 [14%], 12/50 [24%], 6/49 [12%], 21/50 [42%]; in control, low-, mid-, and top-dose animals, respectively). Only adenomas were observed in females, the incidences being dose-related: 1/50 (2%), 3/50 (6%), 5/50 (10%), 8/50 (16%). Increases in adenomas and/or carcinomas were statistically significant only in the top-dose animals of both sexes. An increase in squamous cell papillomas of the forestomach was also seen in top-dose female mice, although this increase was not statistically significant (1/50 [2%], 0/50 [0%], 1/50 [2%], 6/50 [12%] in control, low-, mid-, and top-dose animals). No other findings of biological significance were observed.

In an initiation/promotion study in mice using the dermal route, an increased incidence of skin tumours was seen when 2-furaldehyde was applied in combination with the promoting agent 5/20 compared with 1/20 in controls that received the promoting agent in combination with dimethyl sulfoxide) (Miyakama et al., 1991).

When 2-furaldehyde was applied in combination with acetone, no skin tumours were seen.

Following the administration of an unstated amount of 2-furaldehyde to rats for 5 months, evidence of pre-neoplastic changes (the formation of glutathione S-transferase placental form, GST-P, foci) was seen in livers (Shimizu et al., 1989). Liver cirrhosis was observed in treated rats; overall, however, it is impossible to reach any conclusions about the possible mechanisms underlying cancer induction from this study (e.g., to what extent cell proliferation or direct mutagenicity may be involved in liver tumour formation).

### 8.5 Genotoxicity and related end-points

Experiments in cell-free systems have demonstrated that 2-furaldehyde causes DNA damage (Hadi & Rehman, 1989). Although bacterial mutation studies with 2-furaldehyde have been largely negative, they have in general been inadequately reported (Zdzienicka & Tudek, 1978; McMahon et al., 1979; Loquet et al., 1981; Joska et al., 1981; Marnett et al., 1985; Mortelmans et al., 1986; Shinohara & Omura, 1986; Kim et al., 1987, 1988; Nakamura et al., 1987; Shane et al., 1988; Kato et al., 1989). However, 2-furaldehyde is clearly genotoxic in vitro in mammalian cell test systems, producing chromosomal aberrations, gene mutations, and sister chromatid exchanges (Stich et al., 1981; Gomez-Arroyo & Souza, 1985; McGregor et al., 1988; Nishi et al., 1989; NTP, 1990). In addition, one positive result and one negative result were obtained in Drosophila tests (Woodruff et al., 1985; Rodriguez-Arnaiz et al., 1992).

The genotoxic potential of 2-furaldehyde in vivo is less certain, with positive results being claimed in a briefly reported cytogenetics study and negative results being reported in another cytogenetics study and a sister chromatid exchange study (Subramanyam et al., 1989; NTP, 1990). Further details of these studies are provided in the source document to this CICAD (Gregg et al., 1997). Overall, no firm conclusions can be drawn from these reports.

Point mutations in K-ras and H-ras genes were seen in the 2-furaldehyde-treated mouse livers taken from the NTP carcinogenicity assay, demonstrating genotoxicity (possibly direct) at the tumour site (Reynolds et al., 1987).

### 8.6 Reproductive and developmental toxicity

No studies specifically addressing these endpoints are available.
8.7 Immunological and neurological effects

No studies specifically addressing these end-points are available.

9. EFFECTS ON HUMANS

The only effects reported following single exposure in humans relate to irritation. Throat and eye irritation was apparently experienced by a small group of workers exposed to 200 mg/m$^3$ (50 ppm) for at least 12 min.$^1$ Apparently no irritation was noted with 40 mg/m$^3$ (10 ppm) for 8 h or 80 mg/m$^3$ (20 ppm) for 4 h.

An unknown volume of 50% liquid 2-furaldehyde did not produce skin irritation in workers (Nazyrov & Yampol’skaya, 1969). Insufficient information is available on the ability of 2-furaldehyde to act as a skin or respiratory sensitizer in humans.

A limited number of studies have investigated the effects of repeated occupational exposure to 2-furaldehyde. One study suggested that 2-furaldehyde led to eye, nose, and throat irritation in situations where 10-min average 2-furaldehyde concentrations of 12–64 mg/m$^3$ (3–16 ppm) were measured (Apol & Lucas, 1975). However, other substances, including creosote and liquid resins, may have contributed to the effects, and no firm conclusions with respect to the role of 2-furaldehyde can be drawn. In another study, no evidence of respiratory effects in 2-furaldehyde-exposed workers was noted when the highest average concentration was given as around 8 mg/m$^3$ (2 ppm) (Pawlowicz et al., 1984). However, no duration for this level of exposure and no indication of peak concentrations were presented. No conclusions can be drawn from other studies because of poor reporting of exposure to 2-furaldehyde or because of the potential for confounding factors to influence the findings.

No information was available on carcinogenicity in humans. The only genotoxicity information available in humans comes from an inadequate study that did not demonstrate any significant increase in the incidence of sister chromatid exchanges in a group of only six employees potentially exposed to unknown concentrations of 2-furaldehyde (Gomez-Arroyo & Souza, 1985).

No information is available on reproductive toxicity in humans.

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

10.1 Aquatic organisms

Results of acute toxicity tests on aquatic organisms are summarized in Table 2. All concentrations are nominal.

10.2 Terrestrial organisms

An estimated oral LD$_{50}$ value of >98 mg/kg body weight has been reported for the red-winged blackbird (Agelaius phoeniceus) (Schafer et al., 1983).

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 Hazard identification and dose–response assessment

Acute toxicity data from animals are variable; overall, however, 2-furaldehyde is toxic by the inhalation and oral routes (4-h LC$_{50}$ 940 mg/m$^3$ [235 ppm]; oral LD$_{50}$ about 120 mg/kg body weight), with no clear information in relation to the dermal route.

Human data on effects of 2-furaldehyde are extremely limited and of poor quality, although mucous membrane irritation has been identified as the principal effect following exposure to concentrations apparently as low as 12 mg/m$^3$ (3 ppm) (10-min average). However, peak exposure concentrations were not given, and co-exposure with other substances was possible. In another study, exposure to 40 mg/m$^3$ (10 ppm) for 8 h or 80 mg/m$^3$ (20 ppm) for 4 h apparently did not cause throat or eye irritancy.

From repeated-inhalation exposure studies in animals, the main non-neoplastic effects are toxicity to the lung and respiratory tract. NOAELs of 80 and 208 mg/m$^3$ (20 and 52 ppm) have been identified in hamsters and rabbits, respectively, from studies of up to

---

Table 2: Acute toxicity of 2-furaldehyde to aquatic organisms.

<table>
<thead>
<tr>
<th>Organism</th>
<th>End-point</th>
<th>Concentration (mg/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria and cyanobacteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas putida</em></td>
<td>Toxic threshold (16-h EC₃₀ growth)</td>
<td>16</td>
<td>Bringmann &amp; Kuhn (1976)</td>
</tr>
<tr>
<td><em>Microcystis aeruginosa</em></td>
<td>Toxic threshold (8-day EC₅₀ growth)</td>
<td>2.7</td>
<td>Bringmann &amp; Kuhn (1976)</td>
</tr>
<tr>
<td><strong>Yeast</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Saccharomyces cerevisiae</em></td>
<td>EC₁₄, growth</td>
<td>1</td>
<td>Banerjee et al. (1981)</td>
</tr>
<tr>
<td><strong>Algae</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Scenedesmus quadricaudata</em></td>
<td>Toxic threshold (7-day EC₃₀ growth)</td>
<td>31</td>
<td>Bringmann &amp; Kuhn (1980a)</td>
</tr>
<tr>
<td><strong>Protozoa</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Entosiphon sulcatum</em></td>
<td>Toxic threshold (72-h EC₃₀ growth)</td>
<td>0.6</td>
<td>Bringmann &amp; Kuhn (1980a)</td>
</tr>
<tr>
<td><em>Uronema parduici</em></td>
<td>Toxic threshold (growth)</td>
<td>11</td>
<td>Bringmann &amp; Kuhn (1980b)</td>
</tr>
<tr>
<td><em>Chilomonas paraamaecium</em></td>
<td>Toxic threshold (48-h EC₅₀ growth)</td>
<td>3.9</td>
<td>Bringmann &amp; Kuhn (1980c)</td>
</tr>
<tr>
<td><strong>Fish</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mosquito fish <em>Gambusia affinis</em></td>
<td>96-h LC₅₀ NOEC</td>
<td>2410</td>
<td>Wallen et al. (1957)</td>
</tr>
<tr>
<td>Bluegill sunfish <em>Lepomis macrochirus</em></td>
<td>96-h LC₅₀</td>
<td>16</td>
<td>Turnbull et al. (1954)</td>
</tr>
<tr>
<td>Fathead minnow <em>Pimephales promelas</em></td>
<td>96-h LC₅₀</td>
<td>32</td>
<td>Mattson et al. (1976)</td>
</tr>
</tbody>
</table>

*ECₙ is the effective concentration inhibiting the stated end-point (growth) by n%.

4–6 h/day, 5 days/week, for 13 weeks. Chronic oral exposure to 2-furaldehyde produced increased incidences of bile duct carcinomas in male rats, malignant and benign tumours in the liver in male mice, and benign tumours in the liver and forestomach in female mice. The development of the liver and forestomach tumours may be related to the chronic inflammatory effects noted at the same organ sites.

The results of mutagenicity tests with bacteria were largely negative, although 2-furaldehyde is clearly genotoxic in vitro in mammalian cells, producing chromosomal aberrations, gene mutations, and sister chromatid exchanges. In vivo genotoxicity has not been adequately studied, and no firm conclusions can be drawn.

There are no adequate data available regarding reproductive or developmental effects; hence, it is not possible to evaluate the risk to human health for these end-points.

11.1.2 Criteria for setting guidance values for 2-furaldehyde

2-Furaldehyde vapour and liquid are readily absorbed through the skin, and experiments suggest that skin absorption of vapour may account for a significant proportion of the total body burden. In view of the potential for skin absorption, biological monitoring is an important aspect of occupational exposure assessment. This is achieved by measuring 2-furoic acid (after alkaline hydrolysis of the metabolite furoylglycine) in urine.

The relative importance of genotoxicity and chronic inflammation in tumorigenesis is uncertain; because of this uncertainty, it is not possible to reliably identify a threshold below which exposure to 2-furaldehyde would not result in some risk to human health.

The lack of available data to serve as a basis for estimation of indirect exposure of individuals to 2-furaldehyde from the general environment precludes the characterization of potential cancer risks for the general population.

11.1.3 Sample risk characterization

It is recognized that there are a number of different approaches to assessing the risks to human health posed by genotoxic and carcinogetic substances. In some jurisdictions, there are a number of models for
characterizing potency, which may be of some benefit in priority-setting schemes.

The scenario chosen here as an example is occupational exposure in the United Kingdom. With respect to the irritant effects, in general, in the industries where 2-furaldehyde is used, the measured and predicted (using EASE modelling) exposure concentrations indicate that there is little risk that irritation to the respiratory tract or eyes will occur. However, in the manufacture of refractories and abrasive wheels, current exposures in some parts of these industries give rise to concern that there would be the risk of developing irritation. Given the eye irritation potential of 2-furaldehyde, there is a risk of developing eye irritation if appropriate personal protective equipment is not employed to prevent eye contact with the liquid.

With respect to the risk of genotoxicity and carcinogenicity, the picture is unclear. Although the measured and predicted levels of exposure to 2-furaldehyde generally are relatively low in these industries, the risk of developing genetic damage at sites of initial contact cannot be discounted, and thus there is cause for concern that this may occur. The relative importance of genotoxicity and chronic inflammation in tumorigenesis is uncertain, and a NOAEL cannot be reliably identified because of this uncertainty. Consequently, it is concluded that because of this toxicological picture, it is not possible to reliably quantify this.

In view of the irritative effects reported in workers occupationally exposed to low exposure concentrations of 2-furaldehyde, a short-term limit is likely to be appropriate in addition to the 8-h TWA.

11.2 Evaluation of environmental effects

Although some emission to the atmosphere is expected from wood burning, no atmospheric effects are expected given the short half-life for reaction with hydroxyl and other radicals and possible photodegradation of 2-furaldehyde. The low volatility of the compound from water and soil would not be expected to add significantly to atmospheric levels.

The majority of 2-furaldehyde released to the environment will be released to surface waters. Release from the wood pulp industry seems to be the major source.

2-Furaldehyde has a low capacity for bioaccumulation. Binding to particulates in soil and aquatic sedi-

ment is expected to be very low, making 2-furaldehyde mobile in the environment.

2-Furaldehyde is readily biodegraded in aerobic sewage sludge and has also been shown to degrade in anaerobic systems. Acclimation of the sludge improves degradation. The compound is toxic to anaerobic degrading bacteria at concentrations above 1000 mg/litre in unacclimated sludges (these concentrations have been reported in wood pulp waste), although acclimation allows full degradation at these concentrations.

LC\textsubscript{50}s in fish range from 16 to 32 mg/litre, with a reported NOEC in an acute test of 10 mg/litre. There are no test results for aquatic invertebrates. Toxic thresholds (EC\textsubscript{1} to EC\textsubscript{5} for cell multiplication) for bacteria, cyanobacteria, algae, and protozoa range from 0.6 to 31 mg/litre.

Only one estimated toxicity value is available for terrestrial organisms, and little emission to land is expected; on this basis, no quantitative risk assessment can be attempted for the terrestrial environment.

11.2.1 Predicted environmental concentration

Very limited monitoring studies are available for surface waters, with only two isolated measurements at 2 \textsuperscript{g}/litre reported. The sample risk assessment will be based on emissions from the wood pulp industry, the expected worst case. Reported concentrations in sulfite evaporator condensate range up to 1280 mg/litre, with average concentrations at 274 mg/litre in a more recent study. Since the evaporator condensate represents 15\% of the total wastewater flow, the concentration in wastewater would be 41.1 mg/litre average.

Based on the average concentration and mainly default values from the OECD Technical Guidance Manual, the initial concentration in rivers receiving treated wastewater would be as follows:

\[
\text{PEC}_{\text{local (water)}} = \frac{C_{\text{effluent}}[(1 + K_{\text{p(susp)}} \times C_{\text{(susp)}}) \times D]}{1 + K_{\text{p(susp)}} \times C_{\text{(susp)}}}
\]

where:

\begin{itemize}
  \item \text{PEC}_{\text{local (water)}} is the predicted environmental concentration (\text{g/litre})
  \item \text{C}_{\text{effluent}} is the concentration of the chemical in the wastewater treatment plant effluent (\text{g/litre}),
\end{itemize}
calculated as $C_{\text{effluent}} = I \times (100 - P)/100$, where:

- $I$ = input concentration to the wastewater treatment plant (0.041 g/litre)
- $P$ = percent removal in the wastewater treatment plant (91%, based on the “ready biodegradability” of the compound)

- $K_{p(susp)}$ is the suspended matter/water adsorption coefficient, calculated as $K_{p(susp)} = f_{oc(susp)} \times K_{oc}$, where:
  - $f_{oc(susp)}$ = the fraction of organic carbon in suspended matter (default 0.1)
  - $K_{oc}$ = the organic carbon/water partition coefficient (1.05; see section 5)

- $C_{(susp)}$ is the concentration of suspended matter in the river water in kg/litre (default concentration 15 mg/litre)

- $D$ is the dilution factor for river flow (taken as 1000 minimum, as the wood pulp process requires large water input and as plants will normally be sited on moderate to large rivers)

Under these conservative conditions, $P_{EC_{local(water)}} = 3.7$ g/litre.

### 11.2.2 Predicted no-effect concentration

As no test results are available for aquatic invertebrates and no long-term test results are available, an uncertainty factor of 1000 will be applied to the lowest reported acute LC$_{50}$ of 16 mg/litre for the bluegill sunfish (*Lepomis macrochirus*) to give a predicted no-effect concentration (PNEC) of 16 g/litre. It is not considered justifiable to base the PNEC on toxic threshold values.

### 11.2.3 Environmental risk factors

The risk factor (PEC/PNEC ratio) for aquatic organisms is, therefore, 0.23, indicating low risk. The distribution of reported toxicity test results against the worst-case PEC is plotted in Figure 1, illustrating the safety margin.

### 12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

The International Agency for Research on Cancer concluded that “There is inadequate evidence in humans for the carcinogenicity of 2-furaldehyde” and that “There is limited evidence in experimental animals for the carcinogenicity of 2-furaldehyde.” Its overall evaluation is that “2-Furaldehyde is not classifiable as to its carcinogenicity to humans” (IARC, 1995).
2-Furaldehyde has previously been evaluated by the Joint Expert Committee on Food Additives (JECFA, 1999), whose conclusions are summarized as follows:

Because of concern about the tumours observed in male mice given furfural and the fact that no NOEL [no-observed-effect level] was identified for hepatotoxicity in rats, the Committee was unable to allocate an ADI [acceptable daily intake]. Before reviewing the substance again, the Committee would wish to review the results of studies of DNA binding in mice and of a 90-day study of toxicity in rats to identify a NOEL for hepatotoxicity.

13. HUMAN HEALTH PROTECTION AND EMERGENCY ACTION

Human health hazards, together with preventive and protective measures and first aid recommendations, are presented in the International Chemical Safety Card (ICSC 0276) reproduced in this document.

13.1 Health surveillance advice

An exposure surveillance program could include monitoring of 2-furoic acid in urine after alkaline hydrolysis of the main metabolite of 2-furaldehyde, furoylglycine, immediately following exposure.

13.2 Advice to physicians

In case of poisoning, treatment is supportive.

13.3 Spillage

In the event of spillage, measures should be undertaken to prevent this chemical from mixing with acids, bases, or oxidants because of the risk of fire or explosion.

14. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Information on national regulations, guidelines, and standards is available from the International Register of Potentially Toxic Chemicals (IRPTC) legal file.

The reader should be aware that regulatory decisions about chemicals, taken in a certain country, can be fully understood only in the framework of the legislation of that country. The regulations and guidelines of all countries are subject to change and should always be verified with appropriate regulatory authorities before application.
**FURFURAL**

<table>
<thead>
<tr>
<th>CAS No: 98-01-1</th>
<th>RTECS No: LT7000000</th>
<th>UN No: 1199</th>
<th>EC No: 605-010-00-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Furancarboxyaldehyde</td>
<td>2-Furaldehyde</td>
<td>2-Furylmethanal</td>
<td>C₅H₄O₂ / C₄H₃OCHO</td>
</tr>
<tr>
<td>Molecular mass: 96.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### TYPES OF HAZARD/EXPOSURE

<table>
<thead>
<tr>
<th>FIRE</th>
<th>COMBUSTIBLE.</th>
<th>NO open flames.</th>
<th>Powder, alcohol-resistant foam, water spray, carbon dioxide.</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXPLOSION</td>
<td>ABOVE 60°C EXPLOSIVE VAPOUR/AIR MIXTURES MAY BE FORMED.</td>
<td>ABOVE 60°C USE A CLOSED SYSTEM, VENTILATION, AND EXPLOSION-PROOF ELECTRICAL EQUIPMENT.</td>
<td></td>
</tr>
</tbody>
</table>

### EXHIBITION

<table>
<thead>
<tr>
<th>INHALATION</th>
<th>COUGH. HEADACHE. LABoured BREATHING. SHORTNESS OF BREATH. SORE THROAT.</th>
<th>VENTILATION, LOCAL EXHAUST, OR BREATHING PROTECTION.</th>
<th>FRESH AIR, REST. REFER FOR MEDICAL ATTENTION.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKIN</td>
<td>MAY BE ABSORBED! DRY SKIN. REDNESS. PAIN.</td>
<td>PROTECTIVE CLOTHING.</td>
<td>REMOVE CONTAMINATED CLOTHES. RINSE SKIN WITH PLENTY OF WATER OR SHOWER. REFER FOR MEDICAL ATTENTION.</td>
</tr>
<tr>
<td>EYES</td>
<td>REDNESS. PAIN.</td>
<td>FACE SHIELD.</td>
<td>FIRST RINSE WITH PLENTY OF WATER FOR SEVERAL MINUTES (REMOVE CONTACT LENSES IF EASILY POSSIBLE), THEN TAKE TO A DOCTOR.</td>
</tr>
<tr>
<td>INGESTION</td>
<td>ABDOMINAL PAIN. DIARRHOEA. HEADACHE. SORE THROAT. VOMITING.</td>
<td>DO NOT EAT, DRINK, OR SMOKE DURING WORK.</td>
<td>RINSE MOUTH. GIVE PLENTY OF WATER TO DRINK. REFER FOR MEDICAL ATTENTION.</td>
</tr>
</tbody>
</table>

### SPILLAGE DISPOSAL

Collect leaking liquid in sealable containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT let this chemical enter the environment (extra personal protection: self-contained breathing apparatus).

### PACKAGING & LABELLING

UN Hazard Class: 6.1
UN Subsidiary Risks: 3
UN Pack Group: II

Do not transport with food and feedstuffs.

### EMERGENCY RESPONSE

Transport Emergency Card: TEC (R)-84
NFPA Code: H2; F2; R0;

Separated from strong bases, strong acids, strong oxidants, food and feedstuffs. Keep in the dark. Well closed. Ventilation along the floor.

### STORAGE

Separated from strong bases, strong acids, strong oxidants, food and feedstuffs. Keep in the dark. Well closed. Ventilation along the floor.

---

Prepared in the context of cooperation between the International Programme on Chemical Safety and the European Commission © IPCS 1999

SEE IMPORTANT INFORMATION ON THE BACK.
### IMPORTANT DATA

**Physical State:** Appearance  
COLOURLESS TO YELLOW LIQUID, WITH CHARACTERISTIC ODOUR. TURNS RED-BROWN ON EXPOSURE TO AIR AND LIGHT.

**Physical Dangers**  
The vapour is heavier than air.

**Chemical Dangers**  
The substance polymerizes under the influence of acid(s) or base(s) with fire or explosion hazard. Reacts violently with oxidants. Attacks many plastics.

**Occupational Exposure Limits**  
TLV (as TWA): 2 ppm; 7.9 mg/m³ (skin) (ACGIH 1998).

**Routes of Exposure**  
The substance can be absorbed into the body by inhalation, through the skin and by ingestion.

**Effects of Short-term Exposure**  
The substance irritates the eyes, the skin and the respiratory tract.

**Effects of Long-term or Repeated Exposure**  
The liquid defats the skin. The substance may have effects on the liver.

### PHYSICAL PROPERTIES

- Boiling point: 162°C
- Melting point: -36.5°C
- Relative density (water = 1): 1.16
- Solubility in water, g/100 ml at 20°C: 8.3
- Vapour pressure, kPa at 20°C: 0.144
- Relative vapour density (air = 1): 3.31
- Flash point: 60°C (c.c.)
- Auto-ignition temperature: 315°C
- Explosive limits, vol% in air: 2.1-19.3
- Octanol/water partition coefficient as log Pow: 0.41

### ENVIRONMENTAL DATA

This substance may be hazardous to the environment; special attention should be given to water organisms.

### NOTES

The odour warning when the exposure limit value is exceeded is insufficient.

### ADDITIONAL INFORMATION

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**LEGAL NOTICE**  
Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible

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REFERENCES


Ettinger M et al. (1954) In: Proceedings of the 8th Industrial Waste Conference, Purdue University, West Lafayette, IN [cited in HSDB, 1998].


Gardner H (1925) Physiological effects of vapours from a few solvents used in paints, varnishes and lacquers. Scientific Section, Educational Bureau, Paint Manufacturers’ Association of the U.S. (Circulation No. 250).


2-Furaldehyde


Gregg et al. (1997): 2-Furaldehyde (Risk Assessment Document EH72/6)

The authors' draft version of this Health and Safety Executive report was initially reviewed internally by a group of approximately 10 Health and Safety Executive experts (mainly toxicologists, but also scientists from other relevant disciplines, such as epidemiology and occupational hygiene). The toxicology section of the amended draft was then reviewed by toxicologists from the United Kingdom Department of Health. Subsequently, the entire risk assessment document was reviewed by a tripartite advisory committee to the United Kingdom Health and Safety Commission, the Working Group for the Assessment of Toxic Chemicals (WATCH). This committee is composed of experts in toxicology and occupational health and hygiene from industry, trade unions, and academia.

The members of the WATCH committee at the time of the peer review were Mr Steve Bailey, Confederation of British Industries; Professor Jim Bridges, University of Surrey; Dr Ian Guest, Confederation of British Industries; Dr Alastair Hay, Trade Unions Congress; Dr Jenny Leeser, Confederation of British Industries; Dr Len Levy, Institute of Occupational Hygiene, Birmingham; Dr Mike Molyneux, Confederation of British Industries; Mr Alan Moses, Confederation of British Industries; Dr Ron Owen, Trade Unions Congress; Mr Jim Sanderson, Independent Consultant; and Dr Mike Sharratt, University of Surrey.

The draft CICAD on 2-furaldehyde was sent for review to institutions and organizations identified by IPCS after contact with IPCS national Contact Points and Participating Institutions, as well as to identified experts. Comments were received from:

- Chinese Academy of Preventive Medicine, Ministry of Health, Beijing, People’s Republic of China
- Federal Institute for Health Protection of Consumers & Veterinary Medicine, Berlin, Germany
- National Institute of Health Sciences, Tokyo, Japan
- National Institute of Public Health and Environmental Protection (RIVM), Bilthoven, The Netherlands
- Senatskommission der Deutschen Forschungsgemeinschaft, Bonn, Germany
- United States Department of Health and Human Services (National Institute for Occupational Safety and Health, Cincinnati; National Institute of Environmental Health Sciences, Research Triangle Park), USA
- United States Environmental Protection Agency (Region VIII; National Center for Environmental Assessment, Washington, DC), USA
- World Health Organization/International Programme on Chemical Safety, Montreal, Canada
APPENDIX 3 — CICAD FINAL REVIEW BOARD

Washington, DC, USA, 8–11 December 1998

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Mr A. Strawson, Health and Safety Executive, London, United Kingdom
Dr P. Toft, Programme for the Promotion of Chemical Safety, World Health Organization, Geneva, Switzerland
RÉSUMÉ D’ORIENTATION


Le 2-furaldéhyde (C₉H₆O₂) (No CAS 98-01-1) se présente sous la forme d’un liquide à l’odeur piquante, rappelant celle des amandes. On le trouve à l’état de traces dans diverses denrées alimentaires et il est produit industriellement par digestion en continu ou en discontinu des pentosanes contenus dans les déchets agricoles. Ces pentosanes sont hydrolysés en pentoses qui subissent ensuite une cyclodéshydratation en 2-furaldéhyde. On utilise ce composé dans l’industrie pour la production de résines, de meules et de substances réfractaires, pour le raffinage des huiles lubrifiantes et la récupération des solvants. On l’emploie également en très petites quantités comme aromatisant.

Le 2-furaldéhyde est présent dans de nombreuses denrées alimentaires, soit naturellement soit comme contaminant. On en a signalé la présence dans l’eau destinée à la boisson et le lait maternel, mais en quantités non mesurables.

On dispose de mesures portant sur l’exposition professionnelle par inhalation et des estimations ont été obtenues au moyen d’un système expert appelé Estimation and Assessment of Substance Exposure (EASE). En règle générale, dans l’ensemble des industries, l’exposition au 2-furaldéhyde présent dans l’air est inférieure à 8 mg/m³ (2 ppm) en moyenne pondérée par rapport au temps calculée sur 8 h (TWA). Pour la plupart des industries, cette donnée ne permet pas de prévoir l’exposition moyenne pondérée sur 15 minutes. Toutefois, on a calculé que dans l’industrie des aromatisants, l’exposition moyenne pondérée sur 15 min devait se situer entre 1,2 et 6,8 mg/m³ (c’est-à-dire entre 0,3 et 1,7 ppm). On ne dispose d’aucune mesure de l’exposition par voie cutanée. Le système EASE donne une exposition cutanée comprise entre 0,1 et 1 mg/cm² j⁻¹ pour la plupart des industries, avec des valeurs plus élevées (entre 1 et 5 mg/cm² j⁻¹) dans la fabrication de matériaux abrasifs et de meules.

Les données toxicocinétiques sont limitées, mais on est fondé à penser que le 2-furaldéhyde est facilement résorbé par la voie respiratoire et la voie percutanée. L’expérimentation animale montre qu’après administration par voie orale à des rats, le composé est facilement absorbé et rapidement excreté, principalement dans les urines, mais une petite partie passe également dans l’air expiré sous la forme de dioxyde de carbone. Le métabolisme du 2-furaldéhyde se caractérise par l’oxydation ou l’acétylation du groupement aldéhyde, suivie par une conjugaison avec la glycine. La 2-furoylglycine est le principal métabolite urinaire à côté de l’acide furoïque, de l’acide furanacrylique et de l’acide furanacrylurique, dont l’importance est moindre.

Chez l’Homme, on a mis en évidence une résorption du 2-furaldéhyde gazeux au niveau des poumons et de la peau. L’organisme humain métabolise ce composé de manière analogique à celui du rat, la majeure partie de la dose absorbée se retrouvant dans les urines sous la forme de 2-furoylglycine. L’acide furoïque et l’acide furanacrylurique sont également présents en moindre quantité. On observé une résorption du 2-furanaldehyde par la voie percutanée.

Chez l’animal, la toxicité aiguë du composé est variable : globalement, le 2-furaldéhyde est toxique par la voie respiratoire et la voie orale (CL₅₀ à 4 h, 940 mg/m³, [235 ppm]; DL₅₀ par voie orale, environ 120 mg/kg de poids corporel) et l’on ne possède pas de données claire au sujet de la voie percutanée. Après exposition unique ou répétée au produit par inhalation, on observe systématiquement une irritation des voies respiratoires et des lésions pulmonaires. On a également fait état d’irritation de la peau et des yeux. Il semble en revanche qu’on n’ait pas noté d’irritation de la gorge ou des yeux chez des sujets humains exposés à une concentration de 40 mg/m³ (10 ppm) pendant 8 h ou de 80 mg/m³ pendant 4 h. Chez l’animal, on a obtenu, pour la dose sans effet nocif observable (NOAEL) relative aux effets cancérogènes, une valeur de 80 mg/m³ (20 ppm) dans le cas du hamster et de 208 mg/m³ (52 ppm) dans le cas du hamster, lors d’études qui se sont prolongées jusqu’à 13 semaines. Après avoir fait ingérer le composé à rats et des souris pendant 103 semaines, à des doses respectivement égales à 60 et 50 mg/kg de poids corporel, on a observé des tumeurs malignes et bénignes. Le 2-furaldéhyde est indéniably
2-furaldehyde génotoxique in vitro sur des cultures de mammifères; on ne peut tirer de conclusions définitives quant à la génotoxicité de ce composé in vivo, mais on ne peut pas exclure non plus que cette génotoxicité soit réelle et qu’elle puisse contribuer au processus de cancerisation. Dans ces conditions, il n’est pas possible de déterminer avec certitude la valeur de la NOAEL.

Faute de données utilisables pour l’estimation de l’exposition individuelle indirecte au 2-furaldéhyde présent dans l’environnement général, il est impossible de préciser le risque cancérogène que ce composé représente pour la population dans son ensemble.

En milieu professionnel, il existe un risque d’effets cancérogènes et génotoxiques. Il y cependant incertitude quant au degré de risque; il est donc nécessaire de continuer à réduire l’exposition autant qu’il est techniquement possible de le faire.

On ne dispose pas de données suffisantes concernant les effets du composé sur la reproduction et le développement; il n’est donc pas possible de déterminer s’il existe des risques de cette nature pour l’Homme.

C’est l’industrie de la pâte à papier qui rejette le plus de 2-furaldéhyde dans l’environnement. La combustion du bois, qu’elle soit naturelle ou d’origine humaine, entraîne également la libération de ce composé dans l’atmosphère.

On ne prévoit pas d’effets atmosphériques étant donné que le 2-furaldéhyde est détruit par réaction sur les radicaux hydroxyle, sa demi-vie calculée dans l’atmosphère étant égale à 0,44 jours. Dans l’air des villes, il peut également être décomposé par réaction avec des radicaux nitrate. Une photo-oxidation directe n’est pas non plus à exclure. Étant donné la faible valeur de la tension de vapeur et de la constante de Henry, sa volatilisation à partir de l’eau et du sol devrait être lente.

Il ne devrait pas y avoir d’hydrolyse aux valeurs du pH rencontrées dans l’environnement. La faible valeur du coefficient de partage entre l’octanol et l’eau (log $K_{ow} = 0.41$) indique que la capacité de bioaccumulation est faible. Le coefficient de sorption ($K_{oc}$) montre que la fixation aux particules n’est pas importante et que le composé est par conséquent très mobile dans le sol.

Le 2-furaldéhyde subit une biodégradation aérobie rapide dans les boues d’égout ainsi que dans les eaux superficielles. Cette décomposition se produit également en anaérobie et de nombreuses bactéries et autres microorganismes sont capables d’utiliser ce composé comme seule source de carbone. A forte concentration (>1000 mg/litre), le 2-furaldéhyde inhibe la croissance et l’activité métabolique des cultures anaérobies non adaptées. En revanche, le produit est plus facilement biodégradable par acclimatation des boues anaérobies.
RESUMEN DE ORIENTACIÓN

El presente CICAD sobre el 2-furaldehído, preparado por la Dirección de Salud y Seguridad del Reino Unido (Gregg et al., 1997), se basa en un examen de los problemas relativos a la salud humana (fundamentalmente ocupacionales), pero también contiene información ambiental. Por consiguiente, este documento se concentra sobre todo en la exposición a través de las rutas que son de interés para el entorno ocupacional, pero incluye también una evaluación ambiental. En este examen se han incorporado los datos identificados hasta enero de 1997. Se realizó una ulterior búsqueda bibliográfica hasta diciembre de 1997 para localizar la nueva información que se hubiera publicado desde la terminación del examen, pero no se encontraron estudios de interés. La información acerca del carácter del examen colegiado del documento original y su disponibilidad figura en el apéndice 1. La información sobre el examen colegiado de este CICAD aparece en el apéndice 2. Este CICAD se aprobó como evaluación internacional en una reunión de la Junta de Evaluación Final celebrada en Washington, DC, Estados Unidos, los días 8-11 de diciembre de 1998. La lista de participantes en esta reunión figura en el apéndice 3. La Ficha internacional de seguridad química (ICSC 0276) preparada por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 1993), también se reproduce en el presente documento.

El 2-furaldehído ($\text{C}_5\text{H}_4\text{O}_2$) (CAS Nº 98-01-1) es un líquido de olor acre “semejante al de la almendra”. Se encuentra en cantidades ínfimas en diversas fuentes de alimentos y se produce comercialmente en digestores de lotes o continuos en los cuales se hidrolizan pentosanos procedentes de residuos agrícolas a pentosas y éstas se ciclodeshidratan a 2-furaldehído. Entre los usos industriales cabe mencionar la producción de resinas, aceites lubricantes y recuperación de disolventes. El 2-furaldehído (CAS Nº 98-01-1) es un líquido de olor acre “semejante al de la almendra”. Se encuentra en cantidades ínfimas en diversas fuentes de alimentos y se produce comercialmente en digestores de lotes o continuos en los cuales se hidrolizan pentosanos procedentes de residuos agrícolas a pentosas y éstas se ciclodeshidratan a 2-furaldehído. Entre los usos industriales cabe mencionar la producción de resinas, aceites lubricantes y recuperación de disolventes. El 2-furaldehído se utiliza también, en cantidades muy pequeñas, como aromatizante.

El 2-furaldehído está presente en numerosos alimentos, como producto natural o como contaminante. Se ha notificado su presencia en el agua potable y en la leche materna, pero las concentraciones no fueron suficientes para su cuantificación. Se dispone de mediciones de la exposición por inhalación en el puesto de trabajo y también se han efectuado estimaciones utilizando un sistema de computadora basado en los conocimientos. Estimación y evaluación de la exposición a la sustancia (EASE) que se ha utilizado en el presente documento se basa en un examen de los problemas relativos a la salud humana (fundamentalmente ocupacionales), pero también contiene información ambiental. Por consiguiente, este documento se concentra sobre todo en la exposición a través de las rutas que son de interés para el entorno ocupacional, pero incluye también una evaluación ambiental. En este examen se han incorporado los datos identificados hasta enero de 1997. Se realizó una ulterior búsqueda bibliográfica hasta diciembre de 1997 para localizar la nueva información que se hubiera publicado desde la terminación del examen, pero no se encontraron estudios de interés. La información acerca del carácter del examen colegiado del documento original y su disponibilidad figura en el apéndice 1. La información sobre el examen colegiado de este CICAD aparece en el apéndice 2. Este CICAD se aprobó como evaluación internacional en una reunión de la Junta de Evaluación Final celebrada en Washington, DC, Estados Unidos, los días 8-11 de diciembre de 1998. La lista de participantes en esta reunión figura en el apéndice 3. La Ficha internacional de seguridad química (ICSC 0276) preparada por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 1993), también se reproduce en el presente documento.

Los datos toxicocinéticos son limitados, pero hay indicios de que el 2-furaldehído se absorbe fácilmente por las vías de exposición por inhalación y cutánea. Los estudios en animales demuestran que, tras la administración oral a ratas, el 2-furaldehído se absorbe fácilmente y excreta con rapidez sobre todo en la orina, aunque también se produce alguna eliminación a través del anhidrido carbónico exhalado. El metabolismo se caracteriza por la oxidación o la acetilación del grupo aldehído, seguida de la conjugación de la glicina. La 2-furoilglicina es el principal metabolito urinario; otros metabolitos secundarios son el ácido furanoacético y el ácido furanacrílico.

En el ser humano, se ha demostrado la absorción del vapor a través de los pulmones y la piel. El metabolismo en las personas parece ser semejante al de las ratas, excretándose la mayor parte de la dosis retenida como 2-furoilglicina urinaria. Se han detectado también como metabolitos secundarios el ácido furanoacético y el ácido furanacrílico. Se ha observado asimismo absorción cutánea a partir del 2-furaldehído líquido.

Los datos sobre la toxicidad aguda en los animales son variables; en general, sin embargo, el 2-furaldehído es tóxico por inhalación y por vía oral (CL₅₀ a los cuatro horas, 940 mg/m³ [235 ppm]; DL₅₀ por vía oral, 120 mg/kg de peso corporal), no disponiéndose de información clara en relación con la vía cutánea. Se ha observado sistemáticamente irritación del sistema respiratorio y lesiones en los pulmones tras la exposición por inhalación a una dosis única y repetida. También se ha notificado irritación cutánea y ocular. Aparentemente no se detectó irritación en la garganta o en los ojos en personas expuestas a 40 mg/m³ (10 ppm) durante ocho horas o a 80 mg/m³ (20 ppm) durante cuatro horas. En animales se han determinado concentraciones sin efectos adversos observados (NOAEL) de 80 mg/m³ (20 ppm) y 208 mg/m³ (52 ppm) en estudios de hasta 13 semanas de duración en hámsteres y conejos, respectivamente, para los efectos no neoplásicos. Se han observado tumores malignos y benignos en ratas y ratones tras la exposición oral a 60 y 50 mg/kg de peso corporal, respectivamente, durante 103 semanas. El 2-furaldehído es claramente genotóxico en células de mamíferos; aunque no se puede llegar a una conclusión definitiva sobre el potencial genotóxico del 2-furaldehído in vivo, no se puede descartar la posibilidad...
de que la genotoxicidad pueda contribuir al proceso carcinogénico. Estos factores impiden determinar de manera fidedigna una NOAEL para el 2-furaldehído.

La falta de datos disponibles que sirvan de base para la estimación de la exposición indirecta de las personas al 2-furaldehído del medio ambiente general impiden la caracterización de los posibles riesgos de cáncer para la población general.

En el entorno del puesto trabajo, existe un riesgo potencial de efectos carcinogénicos y genotóxicos. El nivel de riesgo es incierto; en consecuencia, existe el requisito permanente de reducir los niveles de exposición todo lo que sea posible razonablemente con la tecnología disponible en la actualidad.

No hay datos adecuados sobre los efectos en la reproducción o en el desarrollo; por consiguiente, no es posible evaluar el riesgo para la salud humana con respecto a estos efectos finales.

Las emisiones más altas notificadas de 2-furaldehído al medio ambiente son las de la industria de la pasta de madera. El 2-furaldehído se libera a la atmósfera en la combustión natural y antropogénica de madera.

No se prevén efectos atmosféricos, puesto que el 2-furaldehído se destruye al reaccionar con los radicales hidroxilo, con una semivida atmosférica calculada de 0,44 días. En el aire urbano, la reacción con radicales nitrato puede representar un proceso de degradación adicional. También se puede producir fotooxidación directa. Los bajos valores de la presión de vapor y de la constante de Henry parecen indicar que solamente se produce una volatilización lenta del 2-furaldehído de la superficie del agua y del suelo.

No se prevé que con el pH del medio ambiente se produzca hidrólisis en el agua. El bajo coeficiente de reparto octanol/agua (log $K_{ow}$ 0,41) deja entrever una escasa capacidad de bioacumulación. Los coeficientes de sorción ($K_{oc}$) parecen indicar una sorción escasa a partículas y una movilidad alta en el suelo.

El 2-furaldehído se biodegrada fácilmente en sistemas aeróbios utilizando fangos cloacales y en el agua superficial. También se produce degradación en condiciones anaerobias, gracias a una serie de bacterias y otros microorganismos capaces de utilizar el compuesto como única fuente de carbono. A concentraciones altas (>1000 mg/litro), el 2-furaldehído inhibe el crecimiento y la actividad metabólica de cultivos anaerobios no adaptados. Sin embargo, la aclimatación aumenta la capacidad de degradación del compuesto en los fangos anaerobios.

Las concentraciones más altas notificadas de 2-furaldehído en aguas residuales industriales corres-