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Concise International Chemical Assessment Document 42

BROMOETHANE

First draft prepared by

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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 Organization (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 Organization (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.

International Chemical Safety Cards on the relevant chemical(s) are attached at the end of the CICAD, to provide the reader with concise information on the protection of human health and on emergency action. They are produced in a separate peer-reviewed procedure at IPCS.

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 170.¹

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 on page 2 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 IPCS Risk Assessment Steering Group advises the Coordinator, IPCS, on the selection of chemicals for an IPCS risk assessment based on the following criteria:

- there is the probability of exposure; and/or
- there is significant toxicity/ecotoxicity.

Thus, a priority chemical typically

- is of transboundary concern;
- is of concern to a range of countries (developed, developing, and those with economies in transition) for possible risk management;
- is significantly traded internationally;
- has high production volume;
- has dispersive use.

The Steering Group will also advise IPCS on the appropriate form of the document (i.e., EHC or CICAD) and which institution bears the responsibility of the document production, as well as on the type and extent of the international peer review.

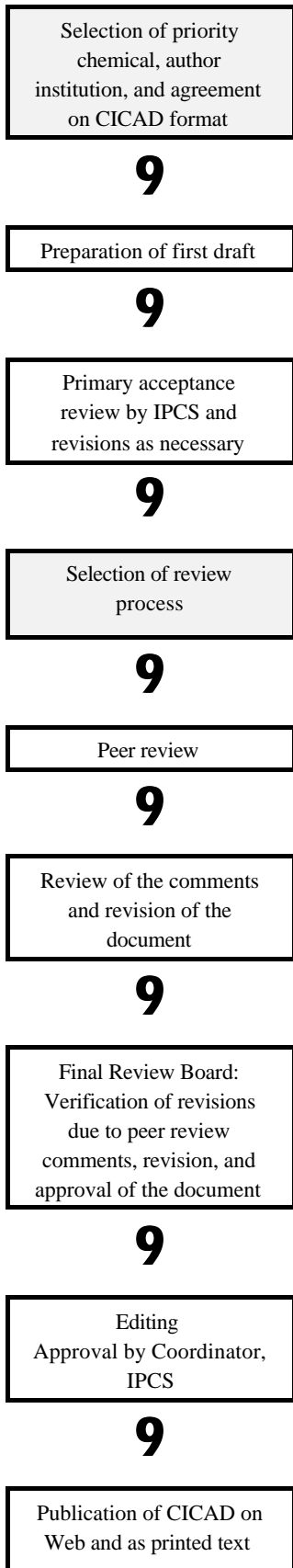
The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes 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

¹ International Programme on Chemical Safety (1994) *Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits*.

Geneva, World Health Organization (Environmental Health Criteria 170) (also available at <http://www.who.int/pics/>).

CICAD PREPARATION FLOW CHART



Advice from Risk Assessment Steering Group

Criteria of priority:

- there is the probability of exposure; and/or
- there is significant toxicity/ecotoxicity.

Thus, it is typical of a priority chemical that

- it is of transboundary concern;
- it is of concern to a range of countries (developed, developing, and those with economies in transition) for possible risk management;
- there is significant international trade;
- the production volume is high;
- the use is dispersive.

Special emphasis is placed on avoiding duplication of effort by WHO and other international organizations.

A prerequisite of the production of a CICAD is the availability of a recent high-quality national/regional risk assessment document = source document. The source document and the CICAD may be produced in parallel. If the source document does not contain an environmental section, this may be produced *de novo*, provided it is not controversial. If no source document is available, IPCS may produce a *de novo* risk assessment document if the cost is justified.

Depending on the complexity and extent of controversy of the issues involved, the steering group may advise on different levels of peer review:

- standard IPCS Contact Points
- above + specialized experts
- above + consultative group

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. At any stage in the international review process, a consultative group may be necessary to address specific areas of the science.

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 industry. 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 bromoethane was based on a review of human health concerns (primarily occupational) prepared by the Health and Safety Executive of the United Kingdom (Ryan et al., 1997). Hence, this document focuses on exposures via routes relevant to occupational settings. Data identified as of September 1995 were covered. A further literature search was performed up to September 2000 to identify any extra information published since this review was completed. 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 Ottawa, Canada, on 29 October – 1 November 2001. Participants at the Final Review Board meeting are listed in Appendix 3. The International Chemical Safety Card on bromoethane (ICSC 1378), produced by the International Programme on Chemical Safety (IPCS, 2002), has also been reproduced in this document.

Bromoethane (CAS No. 74-96-4) is a colourless liquid with a vapour heavier than air. Explosive reactions can occur with air and various metals. Bromoethane reacts vigorously with oxidizing agents and strong alkalis.

The main use of bromoethane is as an ethylating agent in chemical synthesis.

Airborne measurement techniques using charcoal sorbent tubes and solvent desorption are adequate down to 45 mg/m³ (10 ppm). At lower concentrations, measurement may be valid provided users carry out additional recovery tests as described in the published solvent desorption methods. Thermal desorption methods and polymeric sorbents have been validated for measuring concentrations in the range 0.045–45 mg/m³ (0.01–10 ppm). No validated biological monitoring methods have been found for monitoring exposure to bromoethane.

The United Kingdom has no data on levels of occupational exposure to airborne bromoethane. Therefore, estimations were made using computer-modelled exposure data from the Estimation and Assessment of Substance Exposure (EASE) model, version 1. EASE predicted that containment of bromoethane during its use in chemical synthesis is such that worker exposure is unlikely to be higher than 23 mg/m³ (5 ppm) 8-h time-weighted average, and that dermal exposure would be between 0 and 0.1 mg/cm² per day.

The main health concerns relating to exposure to bromoethane are the potential for neurotoxicity, haematological and hepatic toxicity, irritation of the respiratory tract, damage to genetic material, and carcinogenicity. The characterization of the risk of developing these effects is somewhat complicated by the lack of dose–response information. Descriptions of neurotoxicity in humans are essentially qualitative in nature, but studies in animals have indicated that such effects are seen only following exposure to high concentrations. Similarly, haematological and liver damage in animals has been observed only at high exposure concentrations.

Studies in rats have indicated inflammatory lesions in the respiratory tract following inhalation exposure to concentrations of 450 mg/m³ (100 ppm) and above, with a significant positive trend at all doses, reaching statistical significance in rats exposed to 1800 mg/m³ (400 ppm) compared with controls. Therefore, the no-effect level was uncertain.

Since bromoethane is an ethylating agent, it would, like other alkylating agents, be predicted to possess genotoxic activity, particularly at sites of initial contact. Such direct-acting genotoxicity is observed in bacteria and in Chinese hamster ovary cells *in vitro*, but there are no other relevant studies. Thus, it is not possible to assess whether or not such activity would be expressed *in vivo*.

In a 2-year carcinogenicity study by inhalation, a dose-related increase in uterine tumours was observed in female B6C3F1 mice, which indicates clear carcinogenic activity in females of this strain. The situation in rats and male mice is much less clear. A small but probably biologically important increase in brain tumours (gliomas) was seen in female rats receiving the top dose. The evidence for increased adrenal tumours (phaeochromocytomas) in rats is equivocal, while lung tumours in male mice were not significant. A no-effect level cannot be unequivocally identified from this rodent study. There are no data available on the ability of bromoethane to cause cancer in potentially exposed human populations. Furthermore, the mechanism of tumour formation remains unclear.

Overall, there is concern for carcinogenicity and genotoxicity, but it is not currently possible to reliably quantify the level of risk to human health. Therefore, exposure levels should be reduced to as low as reasonably practicable.

Bromoethane is expected to exist entirely in the vapour phase in the ambient atmosphere based upon a vapour pressure of 51 kPa at 20 °C. It is expected to degrade relatively slowly in an average ambient

atmosphere (estimated half-life of about 48 days) by reaction with photochemically produced hydroxyl radicals. Bromoethane has an atmospheric lifetime of 1.2 years based on its reaction with chlorine.

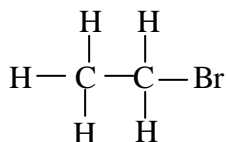
If released to water, bromoethane will be removed through hydrolysis and volatilization. Aqueous hydrolysis half-lives range from 5 days at 35 °C to 21–30 days at 25 °C. The volatilization half-lives from a model river and pond have been estimated to be 3.2 h and 38.2 h, respectively. If released to soil, bromoethane will be susceptible to hydrolysis under wet soil conditions. Its detection in landfill leachate demonstrates that environmental leaching can occur. Evaporation from moist and dry soils may occur based on its Henry's law constant and a relatively high vapour pressure. Biodegradation of bromoethane is expected to be an important fate process in both water and soil.

Bromoethane was found to be a minor component of bromomethanes and bromochloromethanes released from brown algae. It was qualitatively detected in ambient air samples collected in the vicinity of chemical manufacturing areas and has been detected in municipal landfill leachate at 170 mg/litre.

Information on the effects of bromoethane on aquatic and terrestrial organisms was not identified.

2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Bromoethane (C₂H₅Br; molecular mass 109.0; CAS No. 74-96-4) is a colourless liquid with a sweet "ethereal" smell (Ryan et al., 1997). Its structural formula is given below. A common synonym is ethyl bromide; others include monobromoethane, 1-bromoethane, hydrobromic ether, and bromic ether.



Bromoethane is miscible with most organic solvents and is soluble in water (9.1 g/litre). Its log octanol/water partition coefficient (log K_{ow}) is 1.61, its vapour pressure is 51 kPa at 20 °C, and its Henry's law constant is estimated to be 0.76 kPa@m³/mol at 25 °C; the dimensionless Henry's law constant (air/water partition coefficient) is 0.31 (HSDB, 2000). The vapour is heavier than air and readily forms explosive mixtures in air at normal temperatures. Bromoethane is a good ethylating

agent. In the presence of humidity, bromoethane will undergo slight hydrolysis to produce hydrobromic acid and ethyl alcohol. It becomes yellowish on exposure to air and light. Bromoethane reacts vigorously with oxidizing agents and strong alkalis. Explosive reactions can occur with alkali metals, aluminium, magnesium, zinc, calcium, and powdered metals.

Additional physical/chemical properties are presented on the International Chemical Safety Card (ICSC 1378) for bromoethane, reproduced in this document.

The conversion factors for bromoethane in air at 20 °C and 101.3 kPa are as follows (to three significant figures):

$$\begin{aligned} 1 \text{ ppm} &= 4.53 \text{ mg/m}^3 \\ 1 \text{ mg/m}^3 &= 0.221 \text{ ppm} \end{aligned}$$

3. ANALYTICAL METHODS

3.1 Workplace air monitoring

Indicating colorimetric tubes for short-term measurements in air are commercially available from several sources. Dräger and Sensidyne/Kitagawa manufacture tubes calibrated for methyl bromide (bromomethane) over the range 2–1600 mg/m³ (0.5–400 ppm). Sensitivity to bromoethane varies according to reagent chemistry and may be lower or higher than the methyl bromide calibration. MSA/Auer manufacture a trichloroethane tube also calibrated for bromoethane in the range 68–1800 mg/m³ (15–400 ppm).

Real-time selective monitoring is feasible with instruments based on infrared, infrared photoacoustic, photoionization, or semiconductor sensors. These instruments are subject to interferences from environmental conditions, such as water and carbon dioxide for infrared detectors. Typically, infrared and photoacoustic detectors can measure bromoethane down to 4.5 mg/m³ (1 ppm) at 8.0 μm.

Specific monitoring for bromoethane in air may be carried out using sorbent traps and gas chromatography with flame ionization or mass spectrometric detection. Methods include pumped sampling on charcoal tubes according to solvent desorption procedures NIOSH 1011 (NIOSH, 1994) or OSHA 07 (OSHA, 1989). Alternatively, at low concentrations, thermal desorption may be used, based on compendium methods such as EPA TO-17 (EPA, 1998) or MDHS 72 (HSE, 1993a).

Data from validation report S106 of the National Institute for Occupational Safety and Health (Taylor et al., 1977) suggest that when desorbing charcoal with isopropanol as recommended, the 75% desorption efficiency criterion may not be achieved at concentrations less than 45 mg/m³ (10 ppm). A variety of high-resolution capillary gas chromatography columns are now available, and Occupational Safety and Health Administration Chemical Sampling Information indicates that a 99:1 mixture of carbon disulfide/dimethylformamide is preferred (OSHA, 2000). No further details on desorption efficiency tests with carbon disulfide are available. In report S106, the validation range for a 4-litre air sample is equivalent to 450–2300 mg/m³ (100–500 ppm). Since the original validation did not include storage tests, it is recommended that carbon tubes be stored below 5 °C after sampling and that analysis take place within 2 weeks.

A pumped sampling thermal desorption method based on MDHS 72 and EPA TO-17 has been validated for bromoethane on Chromosorb 106. Its performance has been assessed with respect to sample breakthrough, sensitivity, desorption efficiency, and storage over 1–4 weeks (Wassell & Wright, 2001). It is suitable for sampling at or below levels of 0.045 mg/m³ (0.01 ppm). Concentrations greater than 45 mg/m³ (10 ppm) may be sampled, subject to an upper limit of about 0.2 mg bromoethane sorbed on the sample tube. Consequently, the method is well matched to the levels typically found in workplace and ambient air, but there are limitations if challenged with the relatively high concentrations of 450–2300 mg/m³ (100–500 ppm) used in the validation of NIOSH 1011. The safe sampling volume on 300 mg Chromosorb 106 in 89 mm × 6 mm sample tubes was 3 litres. Desorption efficiency was greater than 95%. Recovery after storage for 1–4 weeks at 20 °C was greater than 95%.

Alternative sorbents are feasible in thermal desorption, such as graphitized carbon and carbon molecular sieves; however, the recovery of bromoethane has not been assessed. The analogous methyl bromide has given poor results on carbon-based tubes in two independent studies (Pankow et al., 1998; Wright et al., 1998), and bromoethane may be similarly susceptible to degradation.

Diffusive badge-type devices intended for solvent desorption and potentially suitable for long-term monitoring of bromoethane are commercially available from 3M, SKC, and Dräger and are described in MDHS 88 (HSE, 1993b). The same limitations regarding desorption efficiency may apply. The effective sampling rates are fixed by the geometry of the device; therefore, there are limitations in sampling low concentrations for exposure

times less than 8 h. 3M quotes an experimental sampling rate of 36.4 ml/min for its 3500 badge.

3.2 Biological monitoring

No validated biological monitoring methods have been found for monitoring exposure to bromoethane.

It is possible that measurement of bromoethane in breath or of inorganic bromide in serum and blood (by analogy with methyl bromide) may be of use for biological monitoring. It is reported from a secondary source (IARC, 1991) that approximately 70% of an oral dose of bromoethane in rats was eliminated unchanged in expired air.

A breath sampler is now commercially available, making breath sampling a viable biological monitoring option. By analogy with other small halogenated alkanes (e.g., chloroform), analysis of bromoethane would be possible (Akrill et al., 2001). No information is available on levels of bromoethane in human breath after exposure to bromoethane.

Methods are available for the measurement of inorganic bromide in serum, blood, and urine. These include photometric methods (Muller et al., 1999), ion chromatography (Koga et al., 1991), and inductively coupled plasma mass spectrometry (Divjak et al., 1999; Elwaer et al., 2000). The mean serum bromide content in unexposed human subjects has been reported as 4–7 mg/litre (Koga et al., 1991; Tanaka et al., 1991; Muller et al., 1999), with Tanaka et al. (1991) putting a 95% confidence limit on 10 mg/litre. Dietary intake and medicines can cause increased levels of circulating inorganic bromide. No information is available on levels of serum or blood bromide following exposure to bromoethane.

4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

4.1 Natural sources

Class et al. (1986) found bromoethane to be a minor component (unquantified) of bromomethanes and bromochloromethanes released from brown algae collected from the North and South Atlantic to the surrounding air.

4.2 Production

Bromoethane is normally transported and stored in steel drums lined with polyethylene and in glass bottles when supplied for laboratory use. Up-to-date world production figures are not available, but the estimated production volume for Japan in 1999 was 100 tonnes (Chemical Daily Co. Ltd., 2001).

4.3 Use

The main use of bromoethane in the United Kingdom is as an ethylating agent in chemical synthesis, primarily in the pharmaceutical industry, but also in the manufacture of pesticides. It is estimated that about 2% of the total imported bromoethane is used in research and development laboratories, including educational establishments. The number of people occupationally exposed to bromoethane in the United Kingdom is not known but is estimated to be less than 200.

Bromoethane is normally used in sealed vessels, and the charging is carried out using vacuum transfer or by means of an air pump. The main potential for exposures to airborne bromoethane occurs while charging reaction vessels and during cleaning and disposal of used drums.

5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

Bromoethane is expected to exist entirely in the vapour phase in the ambient atmosphere based on a vapour pressure of 51 kPa at 20 °C (HSDB, 2000).

The Henry's law constant for bromoethane can be estimated to be 0.76 kPa@m³/mol based on a water solubility of 9.1 g/litre and a vapour pressure of 62 kPa at 25 °C. This value for the Henry's law constant indicates that volatilization from environmental waters is very important. The volatilization half-life from a model river (1 m deep flowing 1 m/s with a wind velocity of 3 m/s) can be estimated to be 3.2 h, and from a model pond, around 38.2 h (HSDB, 2000).

The organic carbon partition coefficient (K_{oc}) for bromoethane can be estimated to be 29 based on a water solubility of 9.1 g/litre and a regression-derived equation. Similarly, a K_{oc} of 179 can be estimated based on a measured $\log K_{ow}$ of 1.61. These values suggest that bromoethane has a moderate to high soil mobility (HSDB, 2000).

A $\log K_{ow}$ of 1.61 suggests that bromoethane will not bioaccumulate in organisms (HSDB, 2000).

The rate constant for the vapour-phase reaction of bromoethane with photochemically produced hydroxyl radicals has been estimated to be 0.334×10^{-12} cm³/molecule per second at 25 °C, corresponding to a half-life of about 48 days at an atmospheric concentration of 5×10^5 hydroxyl radicals/cm³ (Atkinson, 1987; HSDB, 2000). The atmospheric lifetimes for bromoethane based on reactions with hydroxyl radicals and chlorine were experimentally determined to be 51–73 days and 1.2 years, respectively (Donaghy et al., 1993). While methyl bromide (bromomethane) has been shown to deplete stratospheric ozone, bromoethane has a substantially greater rate constant for reaction with hydroxyl radicals and a substantially lower atmospheric half-life. Ozone depletion is not expected for bromoethane.

The rate constant for the aqueous hydrolysis of bromoethane at 25 °C and pH 7 has been reported to be 2.64×10^{-7} /s, which corresponds to a half-life of 30 days (Mabey & Mill, 1978). Jeffers & Wolfe (1997) report half-lives of 21 and 5 days for bromoethane at 25 °C and 35 °C, respectively.

In groundwater under reducing conditions in the presence of hydrogen sulfide, bromoethane may react with naturally occurring nucleophiles (such as the sulfhydryl ion found near sulfur and sulfide deposits) to form aliphatic sulfur-containing products (Schwarzenbach et al., 1985).

The bacteria *Xantobacter autotrophicus* and *Acinetobacter* sp. grew using bromoethane as the sole carbon and energy source (Janssen et al., 1985, 1987). In a 4-week closed bottle ready biodegradation test (OECD 301C) with 100 mg bromoethane/litre and 30 mg sludge/litre, bromoethane had a theoretical biochemical oxygen demand of 13–45% (MITI, 1992).

Suspensions of the ammonia-oxidizing bacterium *Nitrosomonas europaea* were able to degrade 75% of 1 mg bromoethane/litre within 24 h when ammonia was also added and to degrade 50% of the same amount without added ammonia (Vannelli et al., 1990).

Freitas dos Santos & Livingston (1997) observed complete aerobic degradation (mineralization) of bromoethane (50 mg/litre) within 2 days of incubation with mixed cultures from existing bioreactors degrading 1,2-dibromoethane.

6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

Bromoethane was qualitatively detected in ambient air samples collected in the vicinity of the organic bromine chemical manufacturing areas in El Dorado and Magnolia, Arkansas, USA (DeCarlo, 1979). No further details were available.

Class et al. (1986) found bromoethane to be a minor component (unquantified) of bromomethanes and bromochloromethanes released from brown algae collected from the North and South Atlantic to the surrounding air.

Gould et al. (1983) detected bromoethane in municipal landfill leachate that had been treated with chlorine. A bromoethane concentration of 170 mg/litre has been reported for municipal landfill leachate (Brown & Donnelly, 1988).

6.2 Human exposure

No data on occupational levels of exposure to airborne bromoethane were available. Therefore, the sections below describe the use of computer-modelled exposure data from the Estimation and Assessment of Substance Exposure (EASE) model, version 1. This is a knowledge-based computer system for predicting workplace exposures in the absence of measured occupational exposure data.¹

The boiling point of bromoethane is 38.4 °C. Given that the temperature inside the process vessels may be higher than the boiling point, a temperature of 40 °C was chosen for the EASE modelling.

6.2.1 Inhalation exposure

EASE predicts exposures at 40 °C ranging from 0–0.45 mg/m³ (0–0.1 ppm) for closed systems to 450–900 mg/m³ (100–200 ppm) for control by local exhaust ventilation. However, due to the control regimes known to be in place in this industry, it is estimated that exposures would range from 0 mg/m³ (0 ppm) to about 23 mg/m³ (5 ppm), with 23 mg/m³ (5 ppm) being experienced only for drum cleaning and some forms of drum

discharge. Neither of these tasks occupies the whole shift, and 8-h time-weighted averages would be correspondingly lower.

6.2.2 Dermal exposure

For direct handling and non-dispersive use with a contact level assumed to be incidental from the process descriptions, EASE predicts dermal exposures to be from 0 to 0.1 mg/cm² per day.

7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Very little information is available on the toxicokinetics of bromoethane. It is rapidly absorbed through the lungs of mice, rabbits, and guinea-pigs; details of the extent and time course were poorly reported. Absorption also occurs across the gastrointestinal tract and possibly the skin; however, the extent to which bromoethane was absorbed is difficult to quantify, because the available data are poor (Schwander, 1936; Miller & Haggard, 1943). Once absorbed, bromoethane is distributed in the body, at least to the brain and liver via the blood in rabbits and to the liver in mice, although again the data are limited (Leuze, 1922; Abreu & Emerson, 1940). Much (70–75%) of the absorbed bromoethane may be eliminated unchanged via exhaled air, urine, and faeces within hours of a single oral dose to rats, although no relationship between elimination time and exposure could be established (Miller & Haggard, 1943).

Early studies indicated that debromination and glutathione conjugation may occur (Heppel & Porterfield, 1948; Thomson et al., 1958; Barnsley et al., 1964; Johnson, 1965; Jones, 1973). Recent work has supported these earlier findings by showing that bromoethane can be conjugated by glutathione transferase theta hGSTT1-1 present in lysate from isolated human erythrocytes (Thier et al., 1999). One study indicated potential for haloalkanes to degrade cytochrome P450 (Ivanetich et al., 1978).

In humans, after acute exposure by inhalation, it may take several days for the garlicky odour associated with bromoethane to leave the breath (von Oettingen, 1937). It has been stated that raised blood bromide is observed following exposure, although there are no details of the relationship between airborne concentrations and blood bromide levels (Reznikov, 1945). The same review states that in individuals displaying signs of severe bromoethane toxicity, both blood and spinal

¹ Technical Guidance Document in support of the risk assessment directive (93/67/EEC) for substances notified in accordance with the requirements of Council Directive 67/548/EEC; published May 1994.

fluid bromide levels are raised. Again, though, no details are given of any quantitative relationships between exposure levels and the level of bromide in the body fluids.

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

8.1 Single exposure

8.1.1 Inhalation

In a single exposure study, groups of five mice and five rats of each sex were exposed to bromoethane at concentrations of 0, 2800, 5700, 11 000, 23 000, or 45 000 mg/m³ (0, 625, 1250, 2500, 5000, or 10 000 ppm) for 4 h (Roycroft, 1989). Mortalities were observed at 5700 mg/m³ (1250 ppm) or more in mice and only at 45 000 mg/m³ (10 000 ppm) in rats. At 45 000 mg/m³ (10 000 ppm), clinical signs of toxicity prior to death included dyspnoea, hyperactivity, and incoordination. No further information was available. LC₅₀ values determined from these data were 21 200 mg/m³ (4681 ppm) for rats and 12 300 mg/m³ (2723 ppm) for mice.

As a comparison, 1-h LC₅₀ values were calculated as 122 000 mg/m³ (26 986 ppm) for rats and 73 500 mg/m³ (16 230 ppm) for mice (MacEwen & Vernot, 1972). The primary response seen in both rats and mice was central nervous system (CNS) depression, although no further details were given. The authors reported seeing diarrhoea in rats exposed to the highest concentration, 180 000 mg/m³ (40 000 ppm), and in mice exposed to concentrations ranging from the highest of 90 000 mg/m³ (20 000 ppm) down to 57 000 mg/m³ (12 600 ppm). (The lowest concentrations used were 90 000 mg/m³ [20 000 ppm] for rats and 45 000 mg/m³ [10 000 ppm] for mice.)

Other LC₅₀ values quoted are 53 000 mg/m³ (11 700 ppm) for rats and 36 000 mg/m³ (7950 ppm) for mice following 2-h exposures, with "general damage to the nervous system" occurring (Izmerov et al., 1977).

Early, generally poorly reported, studies in mice, guinea-pigs, and cats confirm the toxicity of bromoethane by inhalation (Müller, 1925; Bachem, 1927; Glaser & Frisch, 1929; Sayers & Yant, 1929). In guinea-pigs, for example, toxic signs were observed within 1 min of exposure to 45 000 mg/m³ (10 000 ppm) (Leuze, 1922; Sayers & Yant, 1929; Abreu & Emerson, 1940).

8.1.2 Oral

An oral LD₅₀ of 1350 mg/kg body weight in rats has been listed with no further details (Izmerov et al., 1977), although in another study, Miller & Haggard (1943) observed "no serious ill effects" in rats from an oral dose of 1200 mg/kg body weight in olive oil.

8.1.3 Dermal

Schwander (1936) reported no signs of toxicity following a study in which an unspecified quantity of liquid bromoethane was placed in direct contact with the skin of one rabbit for 6 h.

8.2 Short-term exposure

Fourteen-day inhalation range-finding studies have been carried out in F344/N rats and B6C3F1 mice (Roycroft, 1989). The studies used groups of five animals of each sex, which were exposed to 0, 1100, 2300, 4500, 9000, or 18 000 mg/m³ (0, 250, 500, 1000, 2000, or 4000 ppm) of the vapour for 6 h/day, 5 days/week. All animals died after exposure to 9000 and 18 000 mg/m³ (2000 and 4000 ppm). Males of both species showed difficulty standing and dyspnoea, with male rats only lachrymating prior to death. There were no adverse effects on body weight in survivors. Histopathological examination of the upper and lower respiratory tract only was performed on the 4500 and 9000 mg/m³ (1000 and 2000 ppm) groups and revealed largely dose-related signs of acute inflammation and minimal to mild pulmonary congestion.

Guinea-pigs exposed to 8000–25 500 mg bromoethane/m³ (1760–5630 ppm) for 15 min daily for 6 days showed dyspnoea during exposure and developed hind limb paresis after the sixth exposure, but recovered within 2 weeks (Glaser & Frisch, 1929). Details of dose-response were not reported.

8.3 Medium-term exposure

In a 14-week inhalation study, groups of F344/N rats and B6C3F1 mice were exposed to bromoethane for 6 h/day, 1–5 days/week, totalling 65 exposures (Roycroft, 1989). Exposure levels were 0, 450, 900, 1800, 3600, and 7200 mg/m³ (0, 100, 200, 400, 800, and 1600 ppm); necropsy was carried out on all animals, but histopathology was performed only at 3600 and 7200 mg/m³ (800 and 1600 ppm). Deaths occurred at 7200 mg/m³ (1600 ppm) in rats and at 1800 mg/m³ (400 ppm) and above in mice. Atmospheric concentrations of 7200 mg/m³ (1600 ppm) produced clinical signs of neurotoxicity in rats and mice, histopathological evidence of CNS lesions in rats, and, secondary to the neurotoxicity, atrophy of the skeletal muscle of the thigh

in both species. At the same dose, atrophy of testis and uterus (in male rats and in female rats and mice, respectively) was noted, with a decrease in size of the ovary and number of corpora lutea in female mice at both 3600 and 7200 mg/m³ (800 and 1600 ppm).

Haemosiderosis of the spleen and depletion of the haematopoietic cells of the bone marrow were confined to rats of both sexes receiving 7200 mg/m³ (1600 ppm). The no-observed-adverse-effect level (NOAEL) from this study was 3600 mg/m³ (800 ppm) in rats and 900 mg/m³ (200 ppm) in mice.

Two studies in rats and rabbits, for which full reports are unavailable, indicated some disruption of hepatic function and histopathological changes of pituitary and adrenal glands after exposure for 4 h/day to 2400 mg bromoethane/m³ (538 ppm) for 6 months (Anon, 1990).

No information relating to repeated oral or dermal exposure was available.

8.4 Long-term exposure and carcinogenicity

A 2-year carcinogenicity study of bromoethane was conducted using F344/N rats and B6C3F1 mice (Roycroft, 1989). In this study, groups of 49 or 50 animals of each sex were exposed to atmospheric concentrations of 0, 450, 900, or 1800 mg/m³ (0, 100, 200, or 400 ppm) for 6 h/day, 5 days/week, for 103 or 104 weeks.

There were no significant effects on survival rates in rats (41–66%). Mice exposed to 1800 mg/m³ (400 ppm) showed both reduced survival (48% compared with approximately 72% for the other groups) and a slight decrease in body weight gain. Female rats exposed to 1800 mg/m³ (400 ppm) had an increased incidence of conjunctivitis, although this was not considered significant.

Hyperplasia and/or metaplasia were seen in the nose and lungs of exposed rats as a result of bromoethane-induced chronic inflammation. The incidence of alveolar epithelial hyperplasia in male rats was increased with a significant positive trend at all doses, reaching statistical significance in rats exposed to 1800 mg/m³ (400 ppm) compared with controls. Thus, in male rats, the incidence rose from 6% in controls to 14, 15, and 38% in the 450, 900, and 1800 mg/m³ (100, 200, and 400 ppm) groups, respectively. The numbers were somewhat lower in female rats, rising from 10, 8, and 11% in the control, 450 mg/m³ (100 ppm), and 900 mg/m³ (200 ppm) groups, respectively, to 20% in the 1800 mg/m³ (400 ppm) group. The incidences of both nasal hyperplasia and metaplasia were also increased at 1800 mg/m³ (400 ppm) in both

sexes. Increased lung inflammation was also seen in female mice exposed to 900 and 1800 mg/m³ (200 and 400 ppm). The significant positive trend in male rats across all three dose levels indicates that exposure to concentrations as low as 450 mg/m³ (100 ppm) induced effects of biological significance, and therefore a no-effect level cannot be set.

Dilatation of the hepatic sinusoid and unspecified focal hepatocellular changes were observed at increased incidences in female mice exposed to 900 and 1800 mg/m³ (200 and 400 ppm). Percentage incidences were 4% in controls and the 450 mg/m³ (100 ppm) group, 16% in the 900 mg/m³ (200 ppm) group, and 14% in the 1800 mg/m³ (400 ppm) group.

Pathological examinations of rats showed an increase in the incidence of adrenal pheochromocytomas occurring predominantly in males. The percentage combined benign or malignant pheochromocytoma incidences were, in order of ascending atmospheric concentration starting with controls, 17, 49, 36, and 43% (statistically significant for all treated groups separately and for trend). Results for females were, in the same sequence, 4, 4, 9, and 10% (statistically not significant), respectively. Background rates for this tumour type in untreated control males in the six studies performed in this laboratory ranged from 6% to 45%, with a mean and standard deviation of 19.3% and 16.1%, respectively (Roycroft, 1989). Single malignant pheochromocytomas were seen in females at 900 and 1800 mg/m³ (200 and 400 ppm) and in males at 900 mg/m³ (200 ppm). Despite the high and variable historical background incidence, these results indicate a treatment-related increase in pheochromocytomas.

Brain tumours arising from both “granular” and glial cells were also seen in rats. A dose-related increase in the incidence of glioma was seen in female rats; no gliomas were seen in control animals, a 2% incidence was observed in the 450 and 900 mg/m³ (100 and 200 ppm) groups, and a 6% incidence was found in the 1800 mg/m³ (400 ppm) group. Historically, one glioma has been observed in the 297 female control rats investigated in the six studies performed in this laboratory for the US National Toxicology Program (NTP) (Roycroft, 1989), and therefore the 6% incidence after exposure to bromoethane is probably biologically important. A 12% incidence of all brain tumours was seen in males exposed to 450 mg/m³ (100 ppm), but there were no such increases at higher doses (6% had “granular cell” tumours, 2% had a glioma, 2% had an astrocytoma, and 2% had an oligodendroglioma). No brain tumours were found in mice.

In mice, but not rats, a dose-related increase in uterine tumours was seen at all exposure levels, reaching statistical significance at the top two doses: 4% in control animals and 8, 20, and 61% in animals exposed to 450, 900, and 1800 mg/m³ (100, 200, and 400 ppm), respectively. Of these, most were adenocarcinomas, the percentage incidence being 0, 4, 6, and 40% in the control, 450, 900, and 1800 mg/m³ (control, 100, 200, and 400 ppm) groups, respectively.

In male mice, dose-related increases in both alveolar/bronchiolar adenoma and carcinoma were seen. Percentage incidences in the control, 450, 900, and 1800 mg/m³ (control, 100, 200, and 400 ppm) groups, respectively, were, for adenoma, 10, 12, 16, and 18%, and for carcinoma, 4, 0, 10, and 12%. Few tumours were seen in the respiratory systems of rats, with no difference in incidence between controls and treated animals.

In an investigation of the effects of bromoethane on hormone status with respect to the mechanism of the formation of uterine tumours (Bucher et al., 1995), groups of 30 female 3-month-old virgin B6C3F1 mice were sham exposed for 6 h/day for 21 days. One group was then exposed to 1800 mg bromoethane/m³ (400 ppm) and a control group sham exposed to filtered air for 6 h/day for 21 days (an extra group was exposed to ethyl chloride, a substance also found to induce uterine tumours). Vaginal cytology was performed daily during both the pre-exposure period and the experimental exposure period, in order to assess the estrous cycle. Immediately after the end of the last exposure to bromoethane, final vaginal cytology was performed, a blood sample was taken, and serum was prepared. All animals underwent necropsy, and the liver, uterus, pituitary, adrenal glands, and ovaries were examined by histopathology. Also, the liver and uterus were weighed. Determinations were also made of serum estradiol and progesterone by radio-immunoassay.

Further to these experiments, a review was made of the histopathology of archived microscope slides of ovaries of 12–15 mice from the control and high-dose (i.e., 1800 mg/m³ [400 ppm]) groups of the original NTP carcinogenicity study. Each ovary was evaluated for evidence of continued function based on the presence of secondary or tertiary follicles or corpora lutea. All ovaries examined from bromoethane-treated animals were taken from mice with uterine carcinoma; none of the control mice had neoplasia. All the re-examined mice were of equivalent ages to avoid any variations due to normal aging processes.

Bromoethane had no effect on either the overall or stage-specific durations of the estrous cycle. Similarly, no consistent differences or trends either overall or

between cycle stages were observed for the serum levels of estradiol and progesterone. There were no differences in organ weights or histopathological findings between the control and bromoethane-treated groups. The review of archived slides did not reveal any difference in ovarian morphology between the control and bromoethane-treated tumour-bearing mice.

Overall, the results of this study do not provide any evidence that treatment with bromoethane, at least over a short time period, has any effect on the reproductive hormone status of female mice. Furthermore, the review of archived material from the original carcinogenicity bioassay did not provide any evidence for altered ovarian activity in bromoethane-treated animals.

No data were available on the carcinogenic activity of bromoethane when given by oral or dermal routes.

Dipple et al. (1981) gave single injections of 12.5, 4.2, or 1.25 mmol (1362, 457, or 136 mg) bromoethane/kg body weight to female CB hooded rats and looked for the appearance of tumours at the injection site over 90 weeks. No injection site tumours were observed.

In a 24-week screening assay based on the frequency of pulmonary tumours in strain A mice, Poirier et al. (1975) injected groups of 10 males and 10 females with 11, 27.5, or 55 mmol (1200, 3000, or 6000 mg) bromoethane/kg body weight 3 times a week for 8 weeks. The apparently large doses given lead one to question whether there had been a typographical error overlooked by the editors. The proportion of mice (males and females combined) with lung tumours was 34/154, 4/19, 4/16, and 6/20 in the control, low-, intermediate-, and high-dose groups (incidence 22%, 21%, 25%, and 30%, respectively). This relatively short repeated-dose study failed to show carcinogenic activity.

8.5 Genotoxicity and related end-points

Based on the known behaviour of other alkylating agents, it may be expected that bromoethane could ethylate intracellular macromolecules *in vivo*.

8.5.1 Studies *in vitro*

Bromoethane has been studied in a variety of mutagenicity tests employing various strains of *Salmonella typhimurium*, for which a dose–response and at least a doubling of scores formed the basis of a positive response. In two well conducted closed system assays, positive responses were recorded in strains TA1535 and TA100 with and without metabolic activation (Barber et al., 1981; Roycroft, 1989). A negative result was obtained with TA98 in both studies. Simmon (1981),

using only TA100 in a closed system assay, also reported a positive response with bromoethane.

Plate incorporation and preincubation studies produce results that are fairly consistent with those obtained from closed system assays. One plate incorporation study of bromoethane produced positive results with strains TA98, TA100, and TA104 in the presence of Aroclor 1254-induced rat liver S9 and with strain TA97 both with and without metabolic activation (Strobel & Grummt, 1987).

An abstract reports positive results for TA100 and TA102 in a preincubation (60 min) study (Simmons et al., 1986). A second abstract also records a positive response in these two strains following a 10-min preincubation (Hughes et al., 1987). Haworth et al. (1983) obtained negative results following a 20-min preincubation of bromoethane with strains TA98, TA100, TA1535, and TA1537. The preincubation method they describe suggests that open vessels were used. This would allow bromoethane to escape and so reduce the actual exposure concentration, resulting in possibly false-negative results.

The above data indicate that bromoethane is directly mutagenic to *Salmonella* strains.

Only one *in vitro* mammalian cell genotoxicity study of bromoethane was available (Loveday et al., 1989). In this study, Chinese hamster ovary cells were used to study the clastogenicity and sister chromatid exchange (SCE)-inducing potential of bromoethane at concentrations of up to 1 mg/ml, the limit of solubility in dimethyl sulfoxide in this test system. No evidence of cell death was seen at this concentration.

In the clastogenicity experiment, cells were exposed to bromoethane in the absence of an exogenous metabolic activation system for 8 h and harvested 2 h later. It is possible that the exposure times did not cover a complete cell cycle. In the presence of rat liver S9, cells were exposed for 2 h and harvested 10 h later. At concentrations of up to 1 mg/ml, bromoethane did not induce any increase in the incidence of chromosome aberrations in the cells under either of these test conditions.

SCE-inducing potential was investigated by treating cells for 26 h in the absence of, or for 2 h in the presence of, Aroclor 1254-induced rat liver S9. Cells treated with S9 were then incubated for a further 24 h so that both sets of cells were sampled 26 h after the experiment began. Dose-dependent increases were seen in both the number of SCEs per chromosome and the number of SCEs per cell in the absence or presence of S9. In the

absence of metabolic activation, 1.75- to 3.7-fold increases in the number of SCEs per cell were seen when compared with solvent controls, whereas the increases seen with metabolic activation were not sufficiently large to be considered positive.

Negative results were reported in a sex-linked recessive lethal test on *Drosophila* using Berlin K males for solutions containing bromoethane at concentrations up to 8.2 mmol/litre (0.9 mg/ml) (Vogel & Chandler 1974).

8.5.2 Studies in vivo

No *in vivo* genotoxicity data in either animals or humans were available.

8.6 Reproductive toxicity

No formal reproductive toxicity studies using bromoethane have been carried out in animals; however, the occurrence of severe testicular atrophy in all male rats exposed to 7200 mg/m³ (1600 ppm) for 14 weeks may indicate a potential for effects on male fertility (Roycroft, 1989). Short-term treatment of mice with 1800 mg bromoethane/m³ (400 ppm) did not have any effect on the estrous cycle or sex hormones (Bucher et al., 1995) (see section 8.4 for further details).

No data on developmental toxicity are available.

8.7 Irritation and sensitization

An unsubstantiated secondary source suggests that bromoethane is an eye and skin irritant in rabbits, but no further details are available (Torkelson & Rowe, 1981). In contrast, no irritation was apparently seen in a study in which the skin of one rabbit was continuously exposed to bromoethane liquid contained within a sealed chamber for 6 h (Schwander, 1936). Evidence from long-term animal studies suggests that the vapours of bromoethane may be irritating to the eyes (Roycroft, 1989). No information is available from animal studies on the ability of bromoethane to induce skin or respiratory allergy.

9. EFFECTS ON HUMANS

The only information available in humans relates to acute toxicity at high but generally unquantified exposure levels. Effects seen in cases of acute bromoethane poisoning are similar to effects seen in animal studies where single high exposures to bromoethane have

occurred and include narcosis leading to death (von Oettingen, 1937; Reznikov, 1945). Secondary sources suggest that neurotoxic effects have been induced in humans exposed to bromoethane (Scherbatscheff, 1902; Anon, 1990). Exposure to concentrations of at least 29 000 mg/m³ (6500 ppm) were reported to be rapidly irritating to the eyes (Sayers & Yant, 1929), but there are no other data on skin, eye, or respiratory tract irritation or skin defatting. No information is available on the ability of bromoethane to induce allergic skin disease or asthma.

No information is available on the effects of repeated exposure to bromoethane in humans or on its carcinogenicity or genotoxic activity in human populations exposed to bromoethane.

No information is available on whether human populations exposed to bromoethane suffer adverse reproductive effects.

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

Relevant information on the effects of bromoethane on aquatic and terrestrial organisms was not identified.

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 *Hazard identification and dose–response assessment*

Very little information is available on the toxicokinetics of bromoethane. It is rapidly absorbed through the lungs. Absorption also occurs across the gastrointestinal tract and possibly the skin; however, the extent to which bromoethane was absorbed was difficult to quantify, because the available data were poor. Once absorbed, bromoethane is distributed widely in the body. Much of the absorbed bromoethane may be eliminated unchanged within hours, although no relationship between elimination time and exposure could be established. Once in the body, debromination and glutathione conjugation may occur.

Signs of toxicity in animals following single exposures are consistent with CNS depression. LC₅₀ values

following inhalation exposure for 4 h are reported to be 12 300 mg/m³ (2723 ppm) in mice and 21 200 mg/m³ (4681 ppm) in rats. An oral LD₅₀ value in rats of 1350 mg/kg body weight has been reported. The only information available in humans relates to acute toxicity at high but generally unquantified exposure levels. Effects seen in cases of acute bromoethane poisoning are similar to effects seen in animal studies where single high exposures to bromoethane have occurred. Secondary sources suggest that neurotoxic effects have been induced in humans exposed to bromoethane.

An unsubstantiated secondary source suggests that bromoethane is an eye and skin irritant in rabbit, although no irritation was seen in another study. Evidence from long-term animal studies and one report in humans suggests that the vapours of bromoethane may be irritating to the eyes. No information is available from either human experience or animal studies on the ability of bromoethane to induce skin or respiratory allergy.

The effects of short-term exposure were examined in a 14-day inhalation range-finding study in rats and mice using exposures of 1100–18 000 mg/m³ (250–4000 ppm). Exposures at and above 9000 mg/m³ (2000 ppm) were lethal. Histopathological examination of the upper and lower respiratory tract was performed on the 4500 and 9000 mg/m³ (1000 and 2000 ppm) groups and revealed signs of acute inflammation.

No information is available on the effects of repeated exposure to bromoethane in humans. In a 14-week inhalation study, deaths occurred at 7200 mg/m³ (1600 ppm) in rats and at 18 000 mg/m³ (400 ppm) and above in mice. Doses of 7200 mg/m³ (1600 ppm) produced clinical signs of neurotoxicity in rats and mice, histopathological evidence of CNS lesions in rats, and, secondary to the neurotoxicity, atrophy of the skeletal muscle of the thigh in both species. At the same dose, atrophy of testis and uterus (in male rats and in female rats and mice, respectively) was noted, with a decrease in size of the ovary and number of corpora lutea in female mice at both 3600 and 7200 mg/m³ (800 and 1600 ppm). Haemosiderosis of the spleen and depletion of the haematopoietic cells of the bone marrow were confined to rats of both sexes receiving 7200 mg/m³ (1600 ppm). The NOAEL from these 14-week studies was 3600 mg/m³ (800 ppm) in rats and 900 mg/m³ (200 ppm) in mice. In a 2-year study, bromoethane-induced chronic inflammation was seen in the nose and lungs of exposed rats. A significant positive trend in male rats across all dose levels used in the study indicated that exposure to bromoethane concentrations as low as 450 mg/m³ (100 ppm) induced effects of biological significance, and therefore a no-effect level cannot be set. No information

relating to repeated oral or dermal exposure was available.

In a 2-year carcinogenicity study by inhalation, a dose-related increase in uterine tumours was observed in B6C3F1 mice, which indicates clear carcinogenic activity in females of this strain. The situation in rats and male mice is much less clear. A small but probably biologically important increase in brain tumours (gliomas) was seen in female rats receiving the top dose. The evidence for increased adrenal tumours (phaeochromocytomas) in rats is equivocal, while lung tumours in male mice were not significant. There are no data available on the ability of bromoethane to cause cancer in potentially exposed human populations.

As might be expected of an alkylating agent, bromoethane is a direct-acting mutagen in bacteria. It has also induced SCE in Chinese hamster ovary cells in the absence of metabolic activation. There are no adequate data on clastogenicity *in vitro* and no *in vivo* genotoxicity data.

No formal reproductive toxicity studies have been carried out using bromoethane; however, the occurrence of severe testicular atrophy in all male rats exposed to 7200 mg/m³ (1600 ppm) for 14 weeks may indicate a potential for effects on male fertility. As indicated above, short-term treatment of mice with bromoethane at 1800 mg/m³ (400 ppm) did not have any effect on the estrous cycle or sex hormones. No information is available on whether human populations exposed to bromoethane suffer reproductive effects.

11.1.2 Criteria for setting tolerable intakes/ concentrations or guidance values for bromoethane

The main health concerns relating to exposure to bromoethane in chemical synthesis are the potential for neurotoxicity, haematological and hepatic toxicity, irritation of the respiratory tract, damage to genetic material, and carcinogenicity. The characterization of the risk of developing these effects is somewhat complicated by the lack of dose–response information. Descriptions of neurotoxicity in humans are essentially qualitative in nature, but studies in animals have indicated that such effects are seen only following exposure to high concentrations. Similarly, haematological and liver damage in animals has been observed only at high exposure concentrations.

Studies in rats have indicated inflammatory lesions in the respiratory tract following exposure by inhalation to concentrations of 450 mg/m³ (100 ppm) and above, with a significant positive trend at all doses, reaching statistical significance in rats exposed to 1800 mg/m³

(400 ppm) compared with controls. Therefore, the no-effect level was uncertain.

Since bromoethane is an ethylating agent, it would, like other alkylating agents, be predicted to possess genotoxic activity, particularly at sites of initial contact. Such direct-acting genotoxicity is observed in bacteria and in Chinese hamster ovary cells *in vitro*, but there are no other relevant studies, and thus it is not possible to assess whether or not such activity would be expressed *in vivo*.

An increase in the number of gliomas in female rats receiving bromoethane by inhalation at 1800 mg/m³ (400 ppm), but not 900 mg/m³ (200 ppm), was probably biologically important. The prevalence of uterine tumours in mice was increased at the lowest dose level studied, although statistical significance was not reached until 900 mg/m³ (200 ppm). Likewise, treatment-related phaeochromocytomas occurred in male rats at all dose levels, but high background control rates made interpretation uncertain. For these reasons, a no-effect level cannot be unequivocally identified. The mechanism of tumour formation remains unclear.

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 carcinogenic and possibly genotoxic chemicals. In some jurisdictions, there are a number of models for characterizing potency, which may be of benefit in priority-setting schemes.

The scenario chosen here as an example is occupational exposure in the United Kingdom. In this scenario, containment of bromoethane during its use in chemical synthesis is such that worker exposure is estimated to be less than 23 mg/m³ (5 ppm) 8-h time-weighted average. Dermal exposure is considered not to add significantly to body burden. Overall, therefore, the best prediction based on the information available from animal studies is that the risk of developing damage to the nervous and haematological systems or liver, which was seen with repeated inhalation of about 2300 mg/m³ (500 ppm) and above, would be very small, giving no cause for concern.

The lowest effect level for respiratory tract lesions in a 2-year repeated inhalation study in rodents was 450 mg/m³ (100 ppm). Since the predicted occupational exposure level is considerably below this level, adverse effects are unlikely, and there is little cause for concern in relation to such effects.

With respect to the risk of carcinogenicity and possible genotoxicity, the picture is unclear. In the carcinogenicity study in rodents, it has not been possible

to identify a level at which tumour formation would not occur. Although exposure to bromoethane during chemical synthesis is controlled as indicated above, there may be a risk of carcinogenicity, but the overall picture is unclear.

Overall, there is concern for carcinogenicity and genotoxicity, but it is not currently possible to reliably quantify the level of risk to human health. Therefore, exposure levels should be reduced to as low as reasonably practicable.

11.1.4 Uncertainties

No occupational exposure data were available; hence, estimates of exposure are based on modelling. At present, therefore, the occupational risk assessment is limited. There are very limited data in relation to the toxicokinetics of bromoethane; little is known about absorption, metabolism, or distribution. Such data would prove useful in determining the toxicological profile.

Studies in rats have indicated that lesions in the respiratory tract occur after repeated inhalation of concentrations of 450 mg/m³ (100 ppm) and above for 2 years. However, as 450 mg/m³ (100 ppm) was the lowest dose used, it is not known whether these lesions would have been observed at lower exposure concentrations. Thus, it is difficult to assess whether or not there is a risk that humans might develop such lesions when exposed to bromoethane during its use in chemical synthesis.

With respect to genotoxic potential, there are a number of significant uncertainties that make it difficult to characterize whether or not bromoethane presents a risk of inducing genotoxic damage during use in chemical synthesis. Since bromoethane is an ethylating agent, it would, like other alkylating agents, be predicted to possess genotoxic activity, particularly at sites of initial contact. Such direct-acting genotoxicity is observed in bacteria and in Chinese hamster ovary cells *in vitro*, but there are no other relevant studies, and thus it is not possible to assess whether or not such activity would be expressed *in vivo*. Overall, because of the lack of information on genotoxicity for this substance, it is not possible to make any meaningful assessment of the risk that such activity may be expressed in workers, although such a risk cannot be dismissed. This is compounded by the lack of clear occupational exposure data.

The mechanism of tumour formation in animals is unclear. In a 2-year study of carcinogenicity by inhalation, a dose-related increase in uterine tumours was observed in B6C3F1 mice, which indicates clear carcinogenic activity in females of this strain. In addition, a small but probably biologically important increase in brain tumours (gliomas) was seen in female

rats receiving the top dose of 1800 mg/m³ (400 ppm). Bromoethane would be predicted to have genotoxic activity at the site of contact only, due to its alkylating activity, although there have been no *in vivo* studies carried out to investigate this. On the basis of this premise, the occurrence of tumours at sites distant to the area of contact indicates that a genotoxic mechanism may not be involved. Moreover, the clear increase in uterine tumours, together with a possible rise in phaeochromocytomas, is suggestive of endocrine imbalance. In the absence of further relevant information, no firm conclusions can be drawn.

Major uncertainties remain regarding the relevance of the rodent tumours to humans, since there are no data available on the ability of bromoethane to cause cancer in potentially exposed human populations.

11.2 Evaluation of environmental effects

Due to the very limited environmental exposure data and the lack of information on environmental effects, it is not possible to evaluate the environmental effects of bromoethane.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

The International Agency for Research on Cancer concluded that "There is limited evidence in experimental animals for the carcinogenicity of bromoethane." Its overall evaluation is that "Bromoethane is not classifiable as to its carcinogenicity to humans (Group 3)" (IARC, 1999).

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APPENDIX 1 — SOURCE DOCUMENT

Ryan E, Rajan B, Evans S, Widdowson E (1997)
Bromoethane risk assessment document EH 72/3.
Sudbury, Suffolk, HSE Books (ISBN 0 7176 1357
7)

The authors' draft version is initially reviewed internally by a group of approximately 10 Health and Safety Executive experts, mainly toxicologists, but also experts from other relevant disciplines, such as epidemiology and occupational hygiene. The toxicology section of the amended draft is then reviewed by toxicologists from the United Kingdom Department of Health. Subsequently, the entire criteria document is 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 comprises 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 S.R. Bailey (Independent Consultant)
 Professor J. Bridges (University of Surrey)
 Dr A. Hay (Trades Union Congress)
 Dr L. Levy (Institute of Occupational Health, Birmingham)
 Mr A. Moses (Independent Consultant)
 Mr J. Sanderson (Independent Consultant)
 Dr M. Sharrat (Health and Safety Executive nominee)
 Dr A.E. Smith (Confederation of British Industry)

APPENDIX 2 — CICAD PEER REVIEW

The draft CICAD on bromoethane 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:

M. Baril, International Programme on Chemical Safety/
 Institut de Recherche en Santé et en Sécurité du Travail
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APPENDIX 3 — CICAD FINAL REVIEW BOARD

Ottawa, Canada,
29 October – 1 November 2001

Members

Mr R. Cary, Health and Safety Executive, Merseyside, United Kingdom

Dr T. Chakrabarti, National Environmental Engineering Research Institute, Nehru Marg, India

Dr R. Chhabra, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA (*teleconference participant*)

Dr B.-H. Chen, School of Public Health, Fudan University (formerly Shanghai Medical University), Shanghai, China

Dr C. De Rosa, Agency for Toxic Substances and Disease Registry, Department of Health and Human Services, Atlanta, GA, USA (*Chairman*)

Dr S. Dobson, Centre for Ecology and Hydrology, Huntingdon, Cambridgeshire, United Kingdom (*Vice-Chairman*)

Dr O. Faroon, Agency for Toxic Substances and Disease Registry, Department of Health and Human Services, Atlanta, GA, USA

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Dr A. Hirose, National Institute of Health Sciences, Tokyo, Japan

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Dr M.H. Sweeney, Document Development Branch, Education and Information Division, National Institute for Occupational Safety and Health, Cincinnati, OH, USA

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Ms D. Willcocks, National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Sydney, Australia

Representative of the European Union

Dr K. Ziegler-Skylakakis, European Commission, DG Employment and Social Affairs, Luxembourg

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Dr R.M. David, Eastman Kodak Company, Rochester, NY, USA

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Dr A. Aitio, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Mr T. Ehara, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr P. Jenkins, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

CAS No: 74-96-4
RTECS No: KH6475000
UN No: 1891
EC No: 602-055-00-1

Ethyl bromide
CH₃CH₂Br / C₂H₅Br
Molecular mass: 109.0

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Extremely flammable.	NO open flames, NO sparks, and NO smoking.	Powder, water spray, foam, carbon dioxide.
EXPLOSION			
EXPOSURE		STRICT HYGIENE!	IN ALL CASES CONSULT A DOCTOR!
Inhalation	Drowsiness. Unconsciousness.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
Skin		Protective gloves.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
Eyes	Pain. Redness.	Safety goggles, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion		Do not eat, drink, or smoke during work.	Refer for medical attention.

SPILLAGE DISPOSAL

Evacuate danger area! Consult an expert! Remove all ignition sources. Ventilation. Collect leaking liquid in sealable metal containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Chemical protection suit including self-contained breathing apparatus.

PACKAGING & LABELLING

F Symbol
Xn Symbol
R: 11-20/22-40
S: (2-)36/37
Note: E
UN Hazard Class: 6.1
UN Pack Group: II

Unbreakable packaging; put breakable packaging into closed unbreakable container.

EMERGENCY RESPONSE

Transport Emergency Card: TEC (R)-61S1891
NFPA Code: H2; F1; R0

STORAGE

Fireproof. Separated from incompatible materials. Cool. Dry. Well closed. Ventilation along the floor.

IMPORTANT DATA

Physical State; Appearance

COLOURLESS LIQUID, WITH CHARACTERISTIC ODOUR.

Physical dangers

The vapour is heavier than air and may travel along the ground; distant ignition possible.

Chemical dangers

The substance decomposes on burning producing toxic and corrosive gases. Reacts violently with oxidants, strong bases, aluminium, zinc and magnesium. Attacks plastic and rubber.

Occupational exposure limits

TLV: 5 ppm (skin) A3 (ACGIH 2001).
MAK: 2 (DFG 2000).

Routes of exposure

The substance can be absorbed into the body by inhalation and by ingestion.

Inhalation risk

A harmful contamination of the air can be reached very quickly on evaporation of this substance at 20°C.

Effects of short-term exposure

The substance is irritating to the eyes.
The substance may cause effects on the central nervous system. Exposure may result in unconsciousness.

PHYSICAL PROPERTIES

Boiling point: 38.4°C

Melting point: -119°C

Relative density (water = 1): 1.4

Solubility in water, g/100 ml at 20°C: 0.91

Vapour pressure, kPa at 20°C: 51

Relative vapour density (air = 1): 3.76

Relative density of the vapour/air-mixture at 20°C (air = 1): 2.4

Flash point: -20°C c.c.

Auto-ignition temperature: 511°C

Explosive limits, vol% in air: 6.8-11

Octanol/water partition coefficient as log Pow: 1.61

ENVIRONMENTAL DATA

NOTES

ADDITIONAL INFORMATION

LEGAL NOTICE

Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information

RÉSUMÉ D'ORIENTATION

Ce CICAD consacré au bromoéthane repose sur un bilan des problèmes sanitaires (principalement en milieu professionnel) effectué par le *Health and Safety Executive* du Royaume-Uni (Ryan et al., 1997). Ce document vise donc principalement les voies d'exposition à prendre en considération sur les lieux de travail. La bibliographie utilisée va jusqu'à septembre 1995. Un dépouillement complémentaire de la littérature a été effectué jusqu'à septembre 2000 afin de recueillir toutes données supplémentaires publiées après l'achèvement de la première étude. Des renseignements sur la nature de l'examen par des pairs et sur les sources documentaires existantes sont donnés à l'appendice 1. L'appendice 2 contient des informations sur l'examen par des pairs du présent CICAD. Ce CICAD a été approuvé en tant qu'évaluation internationale lors de la réunion du Comité d'évaluation finale qui s'est tenue à Ottawa (Canada) du 29 octobre au 1er novembre 2001. La liste des participants à cette réunion figure à l'appendice 3. La fiche internationale sur la sécurité chimique du bromoéthane (ICSC 1378) établie par le Programme international sur la sécurité chimique (IPCS, 2002) est également reproduite dans le présent CICAD.

Le bromoéthane (No CAS 74-96-4) se présente sous la forme d'un liquide incolore dont la vapeur est plus lourde que l'air. Des réactions explosives peuvent se produire en présence d'air ou de divers métaux. Le bromoéthane réagit énergiquement avec les oxydants et les bases fortes.

Le bromoéthane est principalement utilisé comme agent d'éthylation en synthèse chimique.

Les méthodes de dosage dans l'air basées sur le captage dans des tubes à charbon actif suivi d'une désorption par solvant conviennent pour les teneurs supérieures ou égales à 45 mg/m³ (10 ppm). Lorsque la concentration est inférieure à cette valeur, la méthode est encore valable à condition de pratiquer les tests de récupération complémentaires indiqués dans les méthodes de désorption par solvant qui ont été publiées. Des méthodes de désorption thermique ainsi que la sorption sur matériaux polymères ont été validées dans la gamme de concentrations 0,045-45 mg/m³ (0,01-10 ppm). La recherche bibliographique n'a pas permis de trouver de méthode validée pour la surveillance de l'exposition au bromoéthane par analyse d'échantillons biologiques.

Le Royaume-Uni ne possède pas de données sur les niveaux d'exposition professionnelle au bromoéthane dans l'air des lieux de travail. On a donc procédé à des estimations à l'aide de données obtenues par modélisation sur ordinateur (au moyen du modèle EASE - *estimation et évaluation de l'exposition à une*

substance - version No 1). Le modèle EASE indique que le confinement du bromoéthane au cours de son utilisation en synthèse est tel qu'il rend improbable toute exposition des travailleurs à des concentrations supérieures à 23 mg/m³ (5 ppm) en moyenne pondérée par rapport au temps sur 8 h et qu'en outre, l'exposition cutanée journalière devrait se situer entre 0 et 0,1 mg/cm².

Ce qui est principalement à craindre en cas d'exposition au bromoéthane, c'est le risque de neuro-, d'hémo- et d'hépatotoxicité, d'irritation des voies respiratoires, de lésions génomiques et de cancérogénicité. L'absence de données sur la relation dose-réponse ne facilite pas la caractérisation de ce risque. Les cas humains de neurotoxicité ont été décrits de façon essentiellement qualitative, mais l'expérimentation animale montre que ces effets ne s'observent qu'après exposition à des concentrations élevées. De même, des anomalies hématologiques et des lésions hépatiques n'ont été observées chez l'animal qu'en cas de forte exposition.

Des études sur le rat ont révélé la présence de lésions inflammatoires des voies respiratoires après inhalation de bromoéthane à des concentrations supérieures ou égales à 450 mg/m³ (100 ppm), avec une tendance positive à la significativité statistique à toutes les doses, celle-ci étant atteinte à la concentration de 1800 mg/m³ (400 ppm) dans une étude comportant un groupe témoin. La valeur de la concentration sans effet observable reste donc incertaine.

Étant donné que le bromoéthane est un agent d'éthylation, on peut s'attendre qu'à l'instar d'autres agents alkylants, il présente une activité génotoxique, en particulier au point de contact initial. On peut observer ce genre de génotoxicité directe sur des bactéries ainsi que sur des cellules ovariennes de hamster chinois *in vitro*, mais ce sont les seules études significatives que l'on possède. Il n'est donc pas possible de déterminer si cette activité est également susceptible de se produire *in vivo*.

Lors d'une étude de cancérogénicité de 2 ans comportant l'exposition de souris B6C3F1 par la voie respiratoire, on a observé une augmentation, liée à la dose, des tumeurs utérines chez les femelles, ce qui indique clairement que le bromoéthane a eu une activité cancérigène chez les femelles de cette souche. Chez celles qui avaient reçu la dose la plus élevée, on a également observé une faible mais sans doute biologiquement importante augmentation des tumeurs cérébrales (gliomes). Chez le rat, les preuves d'une augmentation des tumeurs surrenaliennes (phéochromocytomes) sont douteuses et les tumeurs pulmonaires observées chez des souris mâles ne peuvent être considérées comme significatives. Il n'est pas possible de déterminer avec certitude la valeur de la dose sans effet observable sur la

certitude la valeur de la dose sans effet observable sur la base de l'étude effectuée sur ces rongeurs. On ne possède pas de données indiquant un risque de cancers imputables au bromoéthane parmi les populations humaines qui pourraient être exposées à ce composé. Par ailleurs, on n'a pas éclairci par le mécanisme de son action cancérigène chez l'animal.

D'une façon générale, on peut craindre que ce composé ne soit cancérigène et génotoxique, sans qu'il soit pour l'instant possible de chiffrer le niveau de risque pour la santé humaine. Dans ces conditions, le niveau d'exposition à cette substance doit être ramené à la valeur la plus faible qu'il soit raisonnablement possible d'obtenir.

Etant donné que la tension de vapeur du bromoéthane est de 51 kPa à 20 °C, il devrait se trouver entièrement à l'état de vapeur dans l'air ambiant. On estime qu'il se décompose relativement lentement dans l'air ambiant moyen (demi-vie estimative d'environ 48 jours) par réaction avec les radicaux hydroxyles produits par voie photochimique. Sa durée de séjour atmosphérique est de 1,2 ans, compte tenu de sa réaction avec le chlore.

En cas de décharge dans l'eau, le bromoéthane est éliminé par hydrolyse et évaporation. En milieu aqueux, le temps de demi-hydrolyse va de 5 jours à 35 °C à 21-30 jours à 25 °C. En modélisant le devenir du composé dans un cours d'eau ou un étang on estime que le temps de demi-évaporation est respectivement égal à 3,2 et 38,2 h. En cas de décharge dans le sol, le bromoéthane peut subir une hydrolyse si le sol est humide. Sa présence dans le lixiviat de décharges contrôlées montre que le composé peut subir un lessivage dans l'environnement. A en juger d'après la valeur de sa constante de Henry et sa tension de vapeur relativement élevée, on peut s'attendre à une évaporation à partir de sols humides ou secs. La biodégradation est probablement un facteur important du devenir de ce composé dans l'eau comme dans le sol.

Le bromoéthane est présent en faible proportion aux côtés des bromométhanes et les bromochloréthanes dégagés par les algues brunes. On a pu le mettre en évidence et le doser dans des échantillons d'air prélevés à proximité d'une zone de production de produits chimiques et on en a trouvé à la concentration de 170 mg/litre dans les eaux de lessivage d'une décharge contrôlée municipale.

Il n'a pas été possible de trouver des données relatives aux effets du bromoéthane sur les organismes terrestres et les organismes aquatiques.

RESUMEN DE ORIENTACIÓN

Este CICAD sobre el bromoetano se basó en un examen de las preocupaciones concernientes a la salud humana (fundamentalmente profesionales) preparado por la Dirección de Salud y Seguridad del Reino Unido (Ryan et al., 1997), de ahí que se centre en las vías de exposición de interés para el entorno ocupacional. Figuran los datos identificados hasta septiembre de 1995. Posteriormente se realizó otra búsqueda bibliográfica hasta septiembre de 2000 para localizar cualquier información nueva que se hubiera publicado desde la terminación del examen. La información acerca del carácter del examen colegiado y la disponibilidad del documento original figuran 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 Ottawa (Canadá) del 29 de octubre al 1 de noviembre de 2001. La lista de participantes en esta reunión figura en el apéndice 3. La Ficha internacional de seguridad química sobre el bromoetano (ICSC 1378), preparada por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 2002), también se reproduce en el presente documento.

El bromoetano (CAS N° 74-96-4) es un líquido incoloro con un vapor más pesado que el aire. Puede dar lugar a reacciones explosivas con el aire y con diversos metales. El bromoetano reacciona enérgicamente con agentes oxidantes y álcalis fuertes.

El bromoetano se usa principalmente como agente etilante en síntesis químicas.

Las técnicas de medición del bromoetano suspendido en el aire mediante tubos de carbón absorbente y desorción con disolventes son adecuadas para concentraciones de hasta 45 mg/m³ (10 ppm). Para concentraciones más bajas, la medición puede ser válida siempre que los usuarios realicen pruebas de recuperación adicionales, como las descritas en los métodos publicados sobre desorción con disolventes. Se han validado métodos de desorción térmica y absorbentes poliméricos para medir concentraciones del orden de 0,045-45 mg/m³ (0,01-10 ppm). No se han encontrado métodos validados de vigilancia biológica para el control de la exposición al bromoetano.

En el Reino Unido no hay datos sobre los niveles de exposición ocupacional al bromoetano suspendido en el aire. Por consiguiente, se hicieron estimaciones utilizando datos de exposición elaborados por ordenador a partir del modelo de estimación y evaluación de la exposición a la sustancia (EASE), versión 1. EASE predecía que la contención del bromoetano durante su

uso en síntesis químicas es tal que hace poco probable una exposición del trabajador a concentraciones superiores a 23 mg/m³ (5 ppm) como promedio ponderado por el tiempo de ocho horas, y que la exposición cutánea sería de entre 0 y 0,1 mg/cm² al día.

Las principales preocupaciones que plantea la exposición al bromoetano con respecto a la salud guardan relación con su neurotoxicidad, la toxicidad hematológica y hepática, la irritación del tracto respiratorio, los daños al material genético y la carcinogenicidad. La caracterización del riesgo de aparición de estos efectos es algo complicada, debido a la falta de información sobre la relación dosis-respuesta. Las descripciones de la neurotoxicidad en las personas son esencialmente de carácter cualitativo, pero los estudios en animales han puesto de manifiesto que sólo se observan dichos efectos tras la exposición a concentraciones altas. De la misma manera, se han detectado daños hematológicos y hepáticos en animales sólo con una exposición a concentraciones altas.

En los estudios realizados con ratas se han detectado lesiones inflamatorias en el tracto respiratorio tras la exposición por inhalación a concentraciones de 450 mg/m³ (100 ppm) y superiores, con una tendencia positiva importante a todas las dosis, que alcanza significación estadística en comparación con los testigos en las ratas expuestas a 1800 mg/m³ (400 ppm). Por consiguiente, el nivel sin efectos sigue siendo una incógnita.

Puesto que el bromoetano es un agente etilante, es de prever que, al igual que otros agentes alquilantes, tenga actividad genotóxica, sobre todo en los lugares del contacto inicial. Esta genotoxicidad de acción directa se observa *in vitro* en bacterias y en células ováricas de hámsteres chinos, pero no hay otros estudios de interés al respecto. Así pues, no es posible evaluar si dicha actividad se expresaría *in vivo* o no.

En un estudio de carcinogenicidad por inhalación de dos años, se observó en ratones hembra B6C3F1 un aumento de los tumores uterinos relacionado con la dosis, lo cual indica una actividad carcinogénica clara en las hembras de esa estirpe. La situación en ratas y ratones macho es mucho menos clara. En ratas hembra que recibieron la dosis más alta se observó un aumento pequeño, pero probablemente importante desde el punto de vista biológico, de tumores cerebrales (gliomas). Las pruebas del aumento de tumores adrenales (feocromocitomas) en ratas son equívocas, mientras que los tumores de pulmón en ratones macho no fueron significativos. A partir de este estudio con roedores no se puede identificar de manera inequívoca un nivel sin efectos. No se dispone de estudios sobre la capacidad del bromoetano para provocar cáncer en poblaciones de

personas potencialmente expuestas. Además, sigue sin estar claro el mecanismo de formación de tumores.

En general, la carcinogenicidad y la genotoxicidad despiertan preocupación, pero no es posible cuantificar actualmente de manera fidedigna el nivel de riesgo para la salud humana. Por consiguiente, los niveles de exposición se deberían reducir hasta el nivel más bajo razonablemente practicable.

Teniendo en cuenta una presión de vapor de 51 kPa a 20 °C, el bromoetano tiene que encontrarse en la atmósfera ambiente totalmente en fase de vapor. Cabe prever una degradación relativamente lenta en una atmósfera ambiente tipo (semivida estimada de unos 48 días) por reacción con los radicales hidroxilo producidos por vía fotoquímica. El bromoetano tiene una vida atmosférica de 1,2 años por su reacción con el cloro.

Si se libera en el agua, el bromoetano se elimina mediante hidrólisis y volatilización. La semivida por hidrólisis acuosa oscila entre 5 días a 35 °C y 21-30 días a 25 °C. La semivida por volatilización a partir de un río o estanque se ha estimado en 3,2 h y 38,2 h, respectivamente. Liberado en el suelo, el bromoetano puede sufrir hidrólisis en condiciones de suelo húmedo. Su detección en los productos de lixiviación de vertederos pone de manifiesto que se puede producir lixiviación en el medio ambiente. Según la ley de la constante de Henry, y teniendo en cuenta la presión de vapor relativamente alta, es posible la evaporación a partir de suelos húmedos y secos. Cabe suponer que la biodegradación del bromoetano es un proceso de eliminación importante tanto en el agua como el suelo.

Se ha observado que el bromoetano es un componente secundario de los bromometanos y los bromoclorometanos que liberan las algas pardas. Se ha detectado cualitativamente en muestras de aire ambiente tomadas en las cercanías de zonas de fabricación de productos químicos, y se ha encontrado en productos de lixiviación de vertederos municipales a concentraciones de 170 mg/litro.

No se ha encontrado información sobre los efectos del bromoetano en los organismos acuáticos y terrestres.

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Bromoethane | CH₃CH₂Br or C₂H₅Br | CID 6332 - structure, chemical names, physical and chemical properties, classification, patents, literature, biological activities, safety/hazards/toxicity information, supplier lists, and more. Bromoethane. Molecular Formula C₂H₅Br. Average mass 108.965 Da. More details: Systematic name. Bromoethane. SMILES. CBr. Bromoethane CAS 74-96-4 WIKI information includes physical and chemical properties, USES, security data, NMR spectroscopy, computational chemical data and more. [C]CBr 1-bromethane 1-bromo ethane 1-Bromoethane 1-BROMO-ETHANE 21298-EP2314295A1 2-ethyl bromide 45281-EP2298746A1 45281-EP2298756A1 45281-EP2311806A2 45281-EP2371831A1 45378-EP2272822A1 45378-EP2280012A2 45378-EP2287165A2 45378-EP2287166A2. Bromoethane, also known as ethyl bromide, is a chemical compound of the haloalkanes group. It is abbreviated by chemists as EtBr (which is also used as an abbreviation for ethidium bromide). This volatile compound has an ether-like odour. Bromoethane is inexpensive and would rarely be prepared in the laboratory. A laboratory synthesis includes reacting ethanol with a mixture of hydrobromic and sulfuric acids.