

Chapter 5.1

Acrylonitrile

General Description

Acrylonitrile ($\text{CH}_2 = \text{CH} - \text{C} \equiv \text{N}$) is a volatile, flammable, colourless liquid with a characteristic odour. It is somewhat soluble in water and miscible with most organic solvents. Technical-grade acrylonitrile is more than 99% pure, with minor quantities of impurities and stabilizers (1,2).

Sources

Acrylonitrile does not occur as a natural product. It is used in the production of acrylic and modacrylic fibres, resins and rubbers, and as a chemical intermediate. It may enter the environment during production, processing (manufacture), handling and storage, transportation and disposal of wastes. As well as emissions during manufacture, there are also losses to the atmosphere due to accidents and inadequate maintenance. Acrylonitrile emissions from plants in the USA in 1974 were estimated to be 14 100 tonnes, 2.2% of the total production. More recent estimates, following the introduction of stricter emission controls in the USA, indicate an overall reduction in emissions and a change in pattern: in 1981, 800 tonnes for acrylonitrile production and 3000 tonnes for end-product manufacture (1). Total emissions from 41 factories in 10 western European countries in 1981 were estimated to be 4970 tonnes, the proposed emission factor for Europe being 0.05% for acrylonitrile production and 0.2-0.5% for acrylonitrile processing (2).

Occurrence in air

The dispersion of acrylonitrile is closely related to wind patterns; the highest levels in the ambient air were found close to plants, especially downwind (3), and they rapidly declined with distance. Dry deposition and wet deposition (by rainfall) are believed to play a negligible role (2).

The degradation processes of acrylonitrile in the air are primarily chemical; they result in the formation of hydrocyanic acid in 50% of the mass and (based upon measurement of reaction rates between acrylonitrile and hydroxyl radicals at concentrations present in the air) are believed to be mainly responsible for the half-time (9-32 hours) of acrylonitrile in ambient air (1,2). In the soil, acrylonitrile is degraded by microorganisms (1). Its half-time in water was found to be 5-7 days (1). However, an accidental spillage of 91 000 litres of acrylonitrile from a tanker resulted in contamination of the soil and groundwater for more than a year, despite a cleaning process lasting 108 days after the accident (1).

In the Netherlands, national emissions are estimated to be about 230 tonnes/year and, with a similar contribution from foreign sources, make up an average acrylonitrile concentration in the ambient air of unpolluted areas of $0.01 \mu\text{g}/\text{m}^3$. This exposure was estimated to concern 12.91 million of the country's 14 million population. Apart from these large-scale calculations, small-scale calculations relevant to the largest Dutch sources were also made (2). Neither of the two types of calculation was confirmed by measurements. Of the total population of the Netherlands, an estimated 2100 are exposed to an annual average concentration of $3 \mu\text{g}/\text{m}^3$, 42 100 to $1 \mu\text{g}/\text{m}^3$ or more, and 1.1 million to $0.1 \mu\text{g}/\text{m}^3$ or more.

In the vicinity of two acrylonitrile-producing plants in Japan, acrylonitrile concentrations in the range of 390-608 mg/m^3 were found near the exhausts of both ships and storage tanks (1). In a study of acrylonitrile concentrations in different media near 11 industrial sites in the

United States, the highest air concentrations were found close to the plants and downwind, with levels decreasing from, for instance, 249.4 mg/m³ at 0.5 km to 0.3 mg/m³ at 1.3 km from the plant (3). From a comparison of measured and calculated concentrations, estimates based on models have been validated (1).

Workplace levels are mostly far higher than concentrations in the ambient air. Concentrations vary considerably in different countries, factories, and even types of occupation/operation. The ranges of concentration at some workplaces may be extremely wide but, with a short duration of peak levels, the average concentrations may be markedly less than the maxima. The highest occupational concentrations reported have been up to 600 mg/m³. In Polish factories, concentrations of up to 20 mg/m³ were measured, while maxima of 11 mg/m³ were described for the USSR. Workplace concentrations in the fabrication of articles from polymers containing acrylonitrile and in the handling of polyacrylic fibres were found to be very low and well below 2.2 mg/m³ (1 ppm) (1). The mean workplace concentration in the Dutch industries was reported to be less than 4.4 mg/m³ in 90-95% of the cases (2).

Numerous nonfatal and fatal cases of poisoning occurred in Florida in homes that had been fumigated with mixtures of acrylonitrile and carbon tetrachloride or dichloromethane and considered safe for occupancy by subjective evaluation (1). Similar fatalities were reported in the Federal Republic of Germany (1). Indoor acrylonitrile concentrations, with outdoor acrylonitrile in ambient air being the source of acrylonitrile contamination, may follow a pattern known with sulfur dioxide; due to its reactivity, acrylonitrile may be present indoors at lower concentrations. Acrylonitrile in cigarettes might contribute to acrylonitrile concentrations in the indoor air, but no measurements are available. Nevertheless, according to one study, cigarettes contain 1-2 mg acrylonitrile per 100 cigarettes (1). It is not known if acrylonitrile results from the combustion process itself or from the fumigation of tobacco. Acrylonitrile has been used as a fumigant for stored tobacco (4).

Conversion factors

$$\begin{aligned} 1 \text{ ppm in air} &= 2.205 \text{ mg/m}^3 \\ 1 \text{ mg/m}^3 &= 0.4535 \text{ ppm (20}^\circ\text{C, 101.3 kPa)} \end{aligned}$$

Routes of Exposure

Air

Using calculated concentration isopleths of yearly averages near the largest Dutch sources of acrylonitrile, regional maps and population density data, together with an estimate of foreign contribution to ambient air concentrations of acrylonitrile, the average daily intake for the Dutch population (14 million) was estimated to be 0.2 µg for 12.91 million, 2 µg for 0.9 million, 20 µg for 30 000 and 60 µg for 2100 persons. If respiratory ventilation at rest (6-7 litres/minute) and 46% pulmonary retention of acrylonitrile (1) were considered, a 24-hour exposure to an acrylonitrile concentration of 1 µg/m³ would result in an average daily uptake of 4.0-4.6 µg (2). The actual exposure at this concentration may be lower because of exposure to lower indoor air concentrations. Furthermore, the calculation of a relative emission per km² in 10 European countries indicated that, as far as domestic sources are concerned, 8 out of 10 countries should have ambient concentrations of acrylonitrile lower or markedly lower than those in the Netherlands.

Occupational exposure

If one applies a pulmonary retention of 46% acrylonitrile observed in three human volunteers exposed to 20 mg/m³ (1) to people occupationally exposed to 10 mg/m³ and assumes a

ventilation of 20 litres/minute, there would be an intake of 44 mg acrylonitrile during an 8-hour working shift. People occupationally exposed to 1 mg/m^3 would have an intake of 4.4 mg during a working shift.

People exposed at work may be expected to live near the factory, and such areas would have higher acrylonitrile concentrations in ambient air than the national average, but such additional exposure would only be a fraction of the occupational exposure.

Smoking

Cigarette smoking can be a significant source of acrylonitrile indoor air pollution. If only 10% of the 1-2 mg acrylonitrile per 100 cigarettes (1) were absorbed, smoking 20 cigarettes per day would result in a daily intake of 20-40 μg . Therefore, cigarettes may be the most important source of nonoccupational acrylonitrile exposure.

Drinking-water

No data are available on acrylonitrile concentrations in drinking-water. Two studies in the USA determined acrylonitrile concentrations in effluents from a chemical plant at 100 mg/litre and 3.5-4.3 mg/litre near an acrylic-modacrylic fibre plant (1). Acrylonitrile was not detected in the soil or sediments near industrial sites (3).

The industry is mostly situated in densely populated areas where tapwater is available. Rain washout of acrylonitrile from ambient air is believed to play a minor role in removing acrylonitrile from the atmosphere (2). The accidental spillage of transported acrylonitrile caused contamination of wells lasting more than a year, but the affected area was small and the probability of such accidents occurring is low (in the USA it was calculated that, with transport by rail, one accident would occur approximately every 6 years). Acrylonitrile intake from drinking-water thus appears doubtful.

Food

The use of acrylonitrile copolymers for making beverage bottles was banned in the USA in 1977 (1) owing to the risk that remaining monomers might enter the contents. Such copolymers are still used in other products: analysis of acrylonitrile in soft margarines, concentrated butter and shortening showed contamination in the range of 0.01-0.04 mg/kg (1). The acrylonitrile content of beverages in nitrile resin bottles was usually 2-3 $\mu\text{g/kg}$, but levels of up to 9 $\mu\text{g/kg}$ were found (1). Acrylonitrile concentrations of 0-19 mg/kg were found in dry food experimentally fumigated with acrylonitrile at a concentration of 10 g/m^3 (1); the level decreased by 30-70% over a period of 2 months. Shelled walnuts contained 0-8.5 mg/kg (1). Some goods (e.g. walnuts) have been fumigated with mixtures containing acrylonitrile, a practice now discontinued in some countries (4).

The reported contamination with acrylonitrile of soft margarine and butter (up to 40 $\mu\text{g/kg}$) by containers made of acrylonitrile copolymers would, on the basis of a consumption of 100 g/day, result in a daily acrylonitrile intake of 4 μg (probably less due to lower acrylonitrile level and consumption). A government survey of the acrylonitrile content in food suggested that the average daily intake of acrylonitrile in the United Kingdom was likely to be less than 0.3 $\mu\text{g/person}$ (1). On the basis of the reported acrylonitrile content of beverages in Sweden (1), a 0.33-litre bottle would give an intake of 1-3 μg .

Other routes of exposure

Free acrylonitrile monomers have been found in commercial acrylonitrile polymers at levels of less than 1 mg/kg (acrylic and modacrylic fibres), 15 mg/kg (ABC resin) and 0-750 mg/kg (nitrile rubbers and latex materials) (1). There is no record or estimate of human intake from these sources.

Relative significance of different routes of exposure

Uptake by nonoccupationally exposed persons living in the vicinity of plants, especially downwind, may be close to 20 µg acrylonitrile per day, and 20-40 µg acrylonitrile per day by people smoking acrylonitrile-fumigated cigarettes. Consumption of average amounts of butter or soft margarine in acrylonitrile copolymer containers could result in an acrylonitrile intake of 1-4 µg/day, while the drinking of beverages distributed in such containers could represent an acrylonitrile intake of 1-10 µg/day. As data on both these sources are as yet uncertain, due to the introduction of new regulations in some countries, it cannot be estimated conclusively which of these routes is the more important in a particular country. However, if cigarettes or tobacco are fumigated with acrylonitrile, smoking may be an important source of nonoccupational exposure.

Kinetics and Metabolism

Absorption

The retention of acrylonitrile in the respiratory tract of three volunteers exposed for up to 4 hours to a concentration of 20 mg/m³ was 46 ± 1.6% and did not change throughout the inhalation period (1). Dermal absorption of acrylonitrile vapours in rabbits was estimated to be 100 times less efficient than respiratory absorption (1). Absorption from the gastrointestinal tract of rats was complete but much slower, especially from the stomach, than from other routes (5).

Distribution

Acrylonitrile is apparently uniformly distributed in the organism. It is rapidly eliminated from the blood of rats (5), the elimination half-time being 15-19 minutes.

Biotransformation

Acrylonitrile is metabolized essentially along three pathways. First, an oxidative pathway, catalysed by microsomal monooxygenases, forms glycidonitrile, with subsequent reactions leading to several final products: thiocyanate via cyanide, cyanoacetic and acetic acid, and 2-cyanoethanol. Second, acrylonitrile and glycidonitrile are metabolized to glucuronide(s). Third, acrylonitrile and glycidonitrile react with glutathione (catalysed by GSH S-transferases) to form mercapturic acids, the final metabolites excreted in urine. A cyclic metabolite has also been reported (1). Glycidonitrile is suspected to be the reactive intermediate responsible for the mutagenic properties of acrylonitrile (1), and the cyanide formed may significantly contribute to acute acrylonitrile toxicity by inhibiting cytochrome oxidase (1).

Elimination

Acrylonitrile mercapturic acids represent the most promising metabolites for biological monitoring. Methods for determining them have been elaborated (1), and these metabolites have been identified in the urine of humans occupationally or experimentally exposed to acrylonitrile. In animals, the chemobiokinetics and metabolism of acrylonitrile were significantly modified by the simultaneous administration of organic solvents, and low doses of these chemicals also significantly increased the acute toxicity of acrylonitrile (5). Fatalities observed after home fumigation with acrylonitrile mixed with carbon tetrachloride or dichloromethane may have been due to such metabolic interference (1).

Health Effects

Effects on experimental animals and *in vitro* test systems

Toxicological effects

The range of LD₅₀ values for acrylonitrile given by various routes to different animal species is between 25 and 186 mg/kg (1). The range of LC₅₀ for 4-hour inhalation of acrylonitrile is between 300 and 990 mg/m³ in several species (1). Acute toxicity studies showed effects on respiration, circulation, adrenals and brain, but only at high concentrations or with lethal doses. Irritation of mucous membranes and the skin was also reported (1).

Ninety-day inhalation studies in dogs, mice and rats at 58 mg/m³ showed no lethal effects. At 117 mg/m³ some dogs died and at 234 mg/m³ mice and rats died. Pulmonary inflammation was reported in rats exposed to 240 mg/m³ for 6 months. Studies in which acrylonitrile was administered in drinking-water at concentrations up to 300 mg/litre failed to show specific changes other than those mentioned above. Histological lesions were minimal or absent in the liver of rats that had drunk water with acrylonitrile concentrations of 100-300 mg/litre for 12 months (1). Daily exposure of rats to 22 mg/m³ for 7 weeks resulted in enlargement of the liver, kidneys, heart and spleen. In a conditioned food reflex test, rats given acrylonitrile intraperitoneally at 20 mg/kg per day for 6 weeks were affected (1).

Histological liver changes were observed in cats, but not in rats, guinea pigs, rabbits, dogs and rhesus monkeys exposed for 8 weeks to 220-230 mg/m³, while kidney and lung changes were found in all the species. The weights of the liver, kidneys, spleen, pituitary gland, lungs, gonads, thyroid gland, adrenals, heart and brain of rats, mice and dogs exposed to 234 mg/m³ for 13 weeks were within normal limits, while in another study the exposure of rats to 22-100 mg/m³ for 13 weeks caused enlargement of the liver, kidneys, heart and spleen (1).

Animal experiments have shown that the mechanism(s) of acute acrylonitrile toxicity may be related to the liberated cyanide and reaction with sulfhydryls and sulfhydryl-dependent processes; interactions with microsomal monooxygenases and induction of lipid peroxidation may also play a role in acrylonitrile toxicity (1). The relevance of these studies to human toxicity has yet to be established.

Exposure to low doses of toluene or styrene markedly increases the lethal effects of acrylonitrile in animals and markedly influences the metabolism of acrylonitrile.

Teratogenic effects were observed in rats exposed to 174 mg/m³ for 6 hours per day or receiving 25 mg acrylonitrile per kg body weight orally during days 6-15 of gestation, whereas embryotoxic effects were absent at a dose of 10 mg/kg (1).

Mutagenic and carcinogenic effects

Acrylonitrile was mutagenic in several strains of *Salmonella typhimurium* (1,2). Positive results were observed with 0.5-1.5 mg acrylonitrile per plate, microsomal metabolic activation was required and the effect was dose-related in the TA 1535 strain. Urine from acrylonitrile-treated animals was mutagenic. Glycidonitrile (acrylonitrile epoxide) did not require metabolic activation to exert mutagenic effects in *S. typhimurium* (1). In *Escherichia coli* and *Saccharomyces cerevisiae* the mutagenic activity of acrylonitrile did not require metabolic activation while, in the former microorganisms, 10 µg acrylonitrile per plate was not mutagenic (1).

Several *in vitro* tests have indicated effects of acrylonitrile on DNA: induced strand breakage, cell transformation and a shift in the sedimentation pattern of DNA reminiscent of that observed in treatment with carcinogens were seen in Syrian golden hamster embryo cells. Sister chromatid exchange frequency was increased in Chinese hamster ovary cells and human lymphocytes with an activation system. Chromosome aberrations in hamster lung

fibroblast cells were also observed (1,6).

Three studies in rats and mice, using doses of up to 40 mg/kg per day for 16 days, up to 21 mg/kg per day for 30 days and up to 500 ppm (mg/litre) in drinking-water for 90 days, did not reveal chromatic or chromosomal aberrations or bone marrow abnormalities, nor chromosomal aberrations in somatic or germ cells; the dominant lethal assay in mice was also negative (1,2). The only positive study on bone marrow chromosome aberrations gave no details on the exposure (2). A comparison with vinyl chloride revealed that DNA alkylation occurs to a much lesser extent with acrylonitrile (1).

In carcinogenicity studies in rats, oral administration of acrylonitrile corresponding to 10 mg/kg body weight for 20 months, or drinking-water containing 10, 30 or 100 mg/litre for 23-26 months, or water containing 0, 35, 100 or 300 mg/litre (mean dosage levels about 0, 4, 9 or 22 mg/kg body weight daily in both males and females) induced increased occurrence of tumours of the central nervous system (CNS), Zymbal gland (ear canal), nonglandular portion of the stomach, tongue, mammary glands and small intestine, while in the last study the incidence of tumours of the pituitary, thyroid, adrenals, pancreas and uterus was lower than in the controls (1,7-9). In rats, inhalation of 11, 22, 44 or 88 mg/m³ for 52 weeks (and observation for another year) resulted in an increased incidence of some tumours, e.g. mammary tumours, forestomach papillomas and acanthomas and encephalic gliomas (10). In rats, inhalation of 0, 44 or 176 mg/m³ of acrylonitrile for 2 years (11) resulted in an increased incidence of tumours of the central nervous system, Zymbal gland, tongue, stomach, small intestine, mammary glands and nasal turbinates, and an apparent decrease in tumours of the pituitary gland, adrenals, thyroid, pancreas and testes. These results, obtained only with rats, have been considered sufficient evidence that acrylonitrile is a carcinogen in rats (1,2,12,13).

Effects on humans

Toxicological effects

Workmen exposed to acrylonitrile concentrations varying from 35 to 220 mg/m³ for 20-45 minutes complained of dull headaches, fullness of the chest, and irritation of the eyes, nose and throat; some reported "intolerable" itching of the skin and nervous irritability. In some cases higher concentrations also caused vertigo, nausea, vomiting, tremors, uncoordinated movements, convulsion, diarrhoea and jaundice. The symptoms were reversible. Some of the symptoms were reported on chronic exposure to concentrations ranging from 0.6 to 11 mg/m³ (1).

Brief skin contact with liquid acrylonitrile caused dermatitis lasting up to 3 months (24 months according to other reports). Dermatitis caused by chronic exposure to acrylonitrile has frequently been observed (1). Contact with liquid acrylonitrile is the most likely source of this dermatitis.

Haematological changes have been reported in employees exposed to acrylonitrile at 2.5-5 mg/m³, but not observed in other investigations in humans, nor in animals exposed to markedly higher acrylonitrile concentrations for long periods of time (1).

Workmen occupationally exposed to 35-220 mg/m³ for 20-45 minutes with unspecified frequency did not show signs of liver damage. Some abnormal liver function tests were reported at acrylonitrile occupational exposures of up to 44 mg/m³, but were later absent after the concentrations fell below 9 mg/m³.

Considering the results of animal and human studies, there is little probability that exposures below 9 mg/m³ cause impairment of the liver or other parenchymal organs.

In one study, blepharoconjunctivitis was seen in all employees examined; some of them had severe alterations ascribed to acrylonitrile, but the exposure concentration was not cited (1).

Carcinogenic effects

Seven of the 12 available carcinogenicity studies present no evidence of carcinogenic risk from exposure to acrylonitrile (1,2); the other five studies give some indication that such exposure is associated with cancer (14-18). All these studies, and particularly the seven that show no relationship between exposure to acrylonitrile and cancer, have some deficiencies with regard to methodology, size of population and exposure to other chemicals, including carcinogens, and they reveal insufficient consideration of smoking habits.

In a retrospective cohort study, O'Berg (14) investigated 1345 male employees of a textile fibre plant in the USA up to the end of 1976. The employees were identified as having had potential exposure to acrylonitrile between the commissioning of the plant in 1950 and 1966. Estimates for exposure were made retrospectively, assuming 44 mg/m³ (20 ppm) for high and 22 mg/m³ (10 ppm) for medium exposure (4). Twenty-five cancer cases occurred versus 20.5 expected, based on company rates; however, 25.5 would have been expected according to the data of the National Cancer Institute. In particular, an excess of lung cancer (8 cases versus 4.4 expected) was found, but 7 of these 8 employees were known to have been smokers. Among the employees who had been exposed when the plant started production, 23 cancer cases were found versus 12.9 expected. A latency of 20 years was postulated. In an occupational study (15), Thiess et al. found an excess of mortality from lung cancer, but exposure to other substances, some of them known carcinogens, makes interpretation difficult. Delzell & Monson (16) reported a higher mortality from lung cancer among 322 employees of a chemical rubber plant (9 versus 5.9 for white males and 4.7 for other rubber workers from the same city), with the greatest risk among men who had worked for 5-14 years and had started working at least 15 years before death. The lack of significant differences in "all cancer" and "lung cancer" mortality despite marked differences in the found versus expected rates is due to the low number of employees followed. Workers employed in the polymerization of acrylonitrile and the spinning of acrylic fibres were followed by Werner & Carter (17), who considered the excess of lung cancer in workers younger than 44 years to be particularly relevant; however, owing to several insufficiencies, their own interpretation was that the results were inconclusive.

There was a marked "healthy worker effect" in total mortality (found/expected deaths) in the studies of O'Berg (89/121), Thiess et al. (89/99), Werner & Carter (68/72.4) and Delzell & Monson (74/89.5) (6).

No excess of lung cancer was found in 9525 Japanese workers exposed to acrylonitrile (18). There was no increase in the total number of deaths due to cancer, nor in the numbers of deaths from colon cancer, while 7 deaths due to liver, gall bladder or cystic duct cancer were found versus 5 expected.

Evaluation of Human Health Risks

Exposure

On the basis of large-scale calculations using dispersion models, the average annual ambient air concentration of acrylonitrile in the Netherlands was estimated to be about 0.01 µg/m³ (2), which is below the present detection limit of 0.3 µg/m³ (2,3). Production figures (2) indicate that, in 8 out of 10 European countries for which data are available, ambient concentrations of acrylonitrile are lower or markedly lower than this. Near industrial sites, acrylonitrile air concentrations can exceed 100 µg/m³ over a 24-hour period, but are usually less than 10 µg/m³ at a distance of about 1 km. Acrylonitrile concentrations in the air at the workplace have exceeded 100 mg/m³, but shift averages are usually in the range of 1-10 mg/m³. Exposure from smoking is possible, if acrylonitrile is used for tobacco fumigation, and could

amount to 20-40 µg daily for an average smoker.

A more sensitive method of determination, with a detection limit below 0.1 µg/m³, is required in order to examine concentrations in the ambient air and to allow populations at possible risk to be identified.

Health risk evaluation

Acute and noncancer chronic toxicity may occur at concentrations still reported in some industries. Subjective complaints were reported in acute exposure to 35 mg/m³, and in chronic exposure to 11 mg/m³, 4.2-7.2 mg/m³ or 0.6-6 mg/m³. Teratogenic effects in animals were observed at 174 mg/m³ and carcinogenicity was shown in rats exposed for 2 years to 44 mg/m³.

Twelve epidemiological studies investigating the relationship between acrylonitrile exposure and cancer are available; only five indicate a carcinogenic risk from exposure to acrylonitrile (2). Negative studies suffered from small cohort size, insufficient characterization of exposure, short follow-up times and relatively youthful cohorts. Although four of the remaining five epidemiological studies indicate a higher risk of lung cancer and one study showed a higher mortality rate for liver, gall bladder and cystic duct cancer, all have problems with regard to methodology, definition and/or size of the population, existence of exposure to other carcinogens, and duration of the follow-up period.

In laboratory animals an increased incidence of tumours of the CNS, Zymbal gland, stomach, tongue, small intestine and mammary glands was observed at all doses tested (12). However, there is a clear difference between animal and human studies concerning the tumorigenic response to acrylonitrile: no lung tumours have been produced in animals and no brain tumours have been observed in humans.

Acrylonitrile was categorized in Group 2A by IARC (12) on the basis of the sufficient evidence of its carcinogenicity in experimental animals and the limited evidence of its carcinogenicity in humans.

The epidemiological study by O'Berg (14) presents the clearest available evidence of acrylonitrile as a human lung carcinogen. Furthermore, in this study there were no confounding exposures to other carcinogenic chemicals during exposure to acrylonitrile. It was therefore used to make an estimate of the incremental unit risk. As this study has now been updated to the end of 1983 for cancer incidence and to the end of 1981 for overall mortality, the most recent data are used here (19). Out of 1345 workers exposed to acrylonitrile, a total of 43 cases of cancer occurred versus 37.1 expected. Ten cases of lung cancer were observed versus 7.2 expected, based on the company rates. Lung cancer, which had been the focus of the previous report (14), remained in excess, but not as high as before; two new cases occurred since 1976, with 2.8 expected. This means that the relative risk (RR) would be $10/7.2 = 1.4$, significantly lower than in the previous report. On the assumption made by the US Environmental Protection Agency (4) for the first O'Berg study (14) that the 8-hour time-weighted average exposure was 33 mg/m³ (15 ppm), and with an estimated work duration of 9 years, the average lifetime daily exposure (X) is estimated to be 930 µg/m³ [$X = 33 \text{ mg/m}^3 \times 8/24 \times 240/365 \times 9/70$].

Using the average relative risk model, the lifetime unit risk (UR) for exposure to 1 µg/m³ can be calculated to be 1.7×10^{-5} [$UR = P_0 (RR - 1) / X = 0.04(1.4 - 1)/930$].

Using animal data, an upper-bound risk of cancer associated with a lifetime inhalation exposure to acrylonitrile was calculated from a rat inhalation study (11) to be 1.5×10^{-5} (4).

The calculated unit risk based on the human study is consistent with that of the animal study, although the human estimate is uncertain, particularly because of the lack of documentation on exposure.

Guidelines

Because acrylonitrile is carcinogenic in animals and there is limited evidence of its carcinogenicity in humans, it is treated as if it were a human carcinogen. Therefore, no safe level for acrylonitrile can be recommended. At an air concentration of 1 µg acrylonitrile per m³, the lifetime risk is estimated to be 2×10^{-5} .

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