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BG RCI
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TOXICOLOGICAL EVALUATIONS

BG RCI

Kurfürsten-Anlage 62 · D-69115 Heidelberg, Germany
Telefon: +49 6221 5108-28451
E-Mail: toxikologischebewertungen@bgrci.de
Internet: www.bgrci.de/toxicologicalevaluations

TOXICOLOGICAL EVALUATION

last updated: 02/2005

Isopropenyl acetate

No. 262

CAS No. 108-22-5

BG Chemie
Berufsgenossenschaft der chemischen Industrie

BG Chemie
P.O.B. 10 14 80, 69004 Heidelberg, Germany
Telephone: +49 (0) 6221 523 400
E-Mail: ToxikologischeBewertungen@bgchemie.de
Internet: www.bgchemie.de/toxicologicalevaluations

Isopropenyl acetate

1 Summary and assessment

The acute toxicity of isopropenyl acetate is low. Following oral administration and dermal application, the LD_{50} values for the rat are 3000 and > 2000 mg/kg body weight, respectively. A single 30-minute inhalation of atmosphere enriched with isopropenyl acetate at room temperature is survived by rats. In an acute inhalation study, male and female rats survived 4-hour whole-body inhalation exposure to 22000 mg/m³ (5300 ppm) isopropenyl acetate vapour for 14 days. Thus the LC_{50} for male and female rats is > 22000 mg/m³ (> 5300 ppm). In a 5-day whole-body inhalation study in which rats received daily 6-hour exposures to isopropenyl acetate vapour at concentration levels of 830, 4150 or 8300 mg/m³ (200, 1000 or 2000 ppm), the high and intermediate levels caused concentration-dependent irritation of the respiratory tract reaching down into the bronchial system, but no deaths. In a 28-day whole-body inhalation study, in which rats received five 6-hour exposures per week to isopropenyl acetate vapour at concentration levels of 207.5, 830 or 2075 mg/m³ (50, 200 or 500 ppm), the chemical caused irritation of the respiratory tract, which was marked at 2075 mg/m³ (500 ppm) and slight at 830 and 207.5 mg/m³ (200 and 50 ppm), but did not result in any systemic toxic effects. The *no observed adverse effect concentration* (NOAEC) for hyperplasia of nasal transitional epithelium and degeneration of olfactory epithelium is 830 mg/m³ (200 ppm). The NOAEC for slight irritancy of the anterior nasal mucosa is < 207.5 mg/m³ (50 ppm).

Isopropenyl acetate causes no skin or eye irritation in rabbits.

In the Magnusson and Kligman maximisation test in the guinea pig, isopropenyl acetate shows no skin-sensitising potential.

Isopropenyl acetate exhibits no mutagenic potential in the Salmonella/microsome assay, either with or without metabolic activation. In an in-vivo mouse micronucleus assay, isopropenyl acetate was non-mutagenic in bone marrow cells after single oral administration.

In the Federal Republic of Germany, the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (“MAK-Kommission”) of the Deutsche Forschungsgemeinschaft has established a MAK

value (maximum workplace concentration) for isopropenyl acetate on the suggestion of BG Chemie. It was set in the List of MAK and BAT Values 2004 at 10 ml/m³ (ppm, equivalent to 46 mg/m³).

2 Name of substance

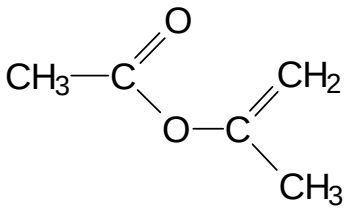
2.1	Usual name	Isopropenyl acetate
2.2	IUPAC name	1-Propen-2-ol, acetate
2.3	CAS No.	108-22-5
2.4	EINECS No.	203-562-7

3 Synonyms, common and trade names

Acetic acid isopropenyl ester
1-Acetoxy-1-methylethylene
2-Acetoxypropen
2-Acetoxypropene
2-Acetoxy-1-propene
2-Acetoxypropylene
Essigsäureisopropenylester
Isopropenylacetat
Isopropenyl acetate
Methylvinyl acetate
Methylvinylacetat
1-Propen-2-ol-acetat
1-Propen-2-yl acetate
UN 2403

4 Structural and molecular formulae

4.1 Structural formula



4.2 Molecular formula $C_5H_8O_2$

5 Physical and chemical properties

5.1	Molecular mass, g/mol	110.11	
5.2	Melting point, °C	–92.9	(Sax, 1999)
		–93	(Wacker-Chemie, 1993; Falbe and Regitz, 1997)
5.3	Boiling point, °C	96.6 (at ca. 994 hPa)	(Sax, 1999)
		97 (at 1000 hPa)	(Wacker-Chemie, 1993)
		97	(Falbe and Regitz, 1997)
5.4	Vapour pressure, hPa	23 (at 20 °C)	
		62 (at 38 °C)	
		115 (at 50 °C)	(Wacker-Chemie, 1993)
5.5	Density, g/cm³	0.918–0.92 (at 20 °C)	(Wacker-Chemie, 1993)
		0.919 (at 20 °C)	(Wacker-Chemie, 1989)
		0.9226 (at 20 °C)	(Sax, 1999)
		0.93	(Medcon, 1995 a)
5.6	Solubility in water	34 g/l (at 20 °C)	(Wacker-Chemie, 1993)
5.7	Solubility in organic solvents	No information available	
5.8	Solubility in fat	Partition coefficient n-octanol/water, log P_{ow}: 5.64	(Wacker-Chemie, 1993)
5.9	pH value	3 (at 34 g/l water)	(Wacker-Chemie, 1993)

5.10	Hydrolysis	In aqueous solutions of pH 4 and 7, there is no detectable hydrolysis of isopropenyl acetate; at a pH value of 9, 30% of the starting amount is hydrolysed to acetone and acetate within 72 hours (Wacker-Chemie, 1996)
5.11	Conversion factor	1 ml/m³ (ppm) ≙ 4.17 mg/m³ 1 mg/m³ ≙ 0.24 ml/m³ (ppm) (at 1013 hPa and 25 °C)

6 Uses

Used as a starting material for the production of acetylacetone, a comonomer for plastics and an acetylation agent in the pharmaceutical industry (Wacker-Chemie, 1989; Falbe and Regitz, 1997; Miller et al., 2002).

7 Experimental results

7.1 Toxicokinetics and metabolism

No information available.

7.2 Acute and subacute toxicity

The acute oral toxicity of isopropenyl acetate was ascertained in groups of 5 male Wistar rats (weighing 90 to 120 g) which were treated by oral gavage with single doses of the chemical given as aqueous formulations in the dose range from 1000 to 8000 mg/kg body weight. The observation period was 14 days. The LD_{50} was found to be 3000 mg/kg body weight (Smyth and Carpenter, 1944; Smyth et al., 1949).

An acute dermal toxicity study of isopropenyl acetate (99.5% pure) which was conducted in the Wistar Hsd/Cpb:WU rat in accordance with OECD guideline No. 402 and Directive 92/69/EEC yielded a dermal LD_{50} > 2000 mg/kg body weight. Single 24-hour semi-occlusive application of 2000 mg isopropenyl acetate/kg body weight to the depilated dorsal skin of 5 males and 5 females was tolerated without remarkable findings. During the sub-

sequent 14-day observation period, no animal died, no skin changes or clinical signs were observed and body weight gain was normal. Terminal necropsy was without abnormal findings (Medcon, 1995 a).

The hazard from acute inhalation of isopropenyl acetate was assessed in the inhalation hazard test conducted in groups of 6 male albino rats. To this end, air was passed through the test material in a fritted disc blubber at room temperature. The exposure time was determined after which all animals survived to the end of a 14-day observation period. It was found to be 30 minutes (Smyth and Carpenter, 1944; Smyth et al., 1949).

Isopropenyl acetate (99.45% pure) was investigated in accordance with OECD guideline No. 403, Directive 92/69/EEC and EPA guideline OPPTS 870.1130 in an acute inhalation toxicity study which was conducted as a limit test. A test group of 5 male and 5 female Wistar rats (Rj:WI(SPF Han) strain) with respective mean initial weights of 309.9 and 207.0 g underwent 4-hour whole-body exposure to isopropenyl acetate in a dynamic system and were subsequently placed under observation for 14 days. During the exposure period, the vapour concentration of isopropenyl acetate in the whole-body inhalation chamber was 22 mg/l, equivalent to approx. 5300 ppm, as determined by gas chromatography. While under exposure and during the first week of the post-exposure observation period, the rats exhibited clinical signs, some lasting for hours or even days, including accelerated respiration, eyelid closure, nasal discharge and crust formation, apathy, squatting posture, smeared fur and piloerection. During the second week of observation, the rats showed no clinical signs. During the first week, males exhibited slight weight loss, but recovered in the second week. The female rats did not gain weight throughout the 14-day post-exposure observation period. No deaths occurred, and none of the 10 rats necropsied at the end of the 14-day observation period were found to have any macroscopic organ changes or tissue changes. The LC_{50} for male and female rats was > 22000 mg/m³ (> 5300 ppm; BASF, 2000 a).

In order to select concentrations for a 28-day inhalation study, a 5-day whole-body inhalation study of isopropenyl acetate (99.45%) was carried out in accordance with OECD guideline No. 412 and Directive 92/69/EEC. Groups of 5 male and 5 female Wistar rats (Crl:WI (Glx/BRL/HAN)BR) strain) with respective mean weights of 221.8 and 161.0 g at the beginning of exposure underwent whole-body exposure to dynamic isopropenyl ace-

tate atmospheres in inhalation chambers for 6 hours on 5 consecutive days. The rats were kept singly in compartmentalised wire cages in the chambers. The intended target concentrations were 830, 4150 and 8300 mg/m³, equivalent to 200, 1000 and 2000 ppm. The concurrent control rats were exposed to air in the same manner. In order to accustom the rats to the exposure conditions, they were kept in the chambers as of day 5 before the beginning of exposure (study day –5). On study day –4 and study day 3, clinical observations were conducted in an open field, and ophthalmology was similarly carried out on study day –3 and study day 4. During the exposure period, the concentration levels of isopropenyl acetate were determined daily by gas chromatography in all 4 groups and used in order to calculate mean concentrations for the entire study period.

Table 1. Concentrations of isopropenyl acetate as used in a 5-day range-finding study (BASF, 2000 b)

Target concentration		Measured concentration (mean ± standard deviation)	
mg/m³	ppm	mg/m³	ppm
0	0	0	0
830	200	858 ± 41.7	207
4150	1000	4277 ± 102	1031
8300	2000	8534 ± 173	2056

In the preflow period, clinical examinations of the animals were carried out twice a day on working days and once a day on weekends or public holidays. During the exposure period, examinations were performed before, during and after exposure. In addition, body weight changes and food and water consumption were determined regularly. At the end of the study, all rats underwent necropsy. Absolute and relative weights of the main organs were determined and the nasal cavity, larynx, trachea and lungs examined by light microscopy. The 200 ppm animals showed no substance-related lesions. Rats in the 1000 ppm group exhibited slight apathy and eyelid closure, and the males showed sight reductions in body weight gain and food consumption compared with the concurrent control. Histopathologically, some rats were found to have muco-purulent rhinitis of the nasal cavity and atrophy of the olfactory epithelium, epithelial metaplasia or hyperplasia of the trachea and chronic bronchitis of the lungs. All males and females in the 2000 ppm group displayed signs of respiratory tract irritation (wiping of

snouts, eyelid closure, nasal crusts and respiratory sounds), apathy, piloerection and, as compared with the concurrent control, decreased body weight development and sporadically decreased water and food consumption. Histopathologically, all rats from the top concentration group were found to have muco-purulent rhinitis of the nasal cavity and atrophy of the olfactory epithelium, epithelial metaplasia of the trachea and chronic bronchitis of the lungs. One female rat additionally exhibited focal epithelial metaplasia of the larynx. Absolute and relative liver weights were significantly reduced in animals from the intermediate and top dose groups. The top and intermediate concentrations of isopropenyl acetate caused significant concentration-dependent irritation of the respiratory tract down to the bronchial system, leading to the clinical effects and the macroscopic and histopathological lesions discussed above. Based on the results of the study, the highest isopropenyl acetate concentration for a 28-day inhalation study was not to exceed 2000 mg/m³ (approx. 500 ppm; BASF, 2000 b).

Groups of 5 male and 5 female Wistar rats (Crl:WI (GLX/BRL/HAN)IGS BR) strain) with respective mean weights of 184.3 and 154.2 g at the beginning of exposure underwent whole-body exposure to dynamic isopropenyl acetate atmospheres in inhalation chambers for 6 hours on 5 consecutive working days over a period of 28 days (20 exposures in total). The experiments were carried out in accordance with OECD guideline No. 412, Directive 92/69/EEC and EPA guideline OPPTS 870.3465. The purity of the isopropenyl acetate used was ascertained by gas chromatography prior to and after the inhalation study and found to be 99.45% and 98.9%, respectively. Rats were kept singly in wire cages during exposures in the whole-body inhalation chambers as well as during exposure-free periods. The intended target concentrations were 50, 200 and 500 ppm, equivalent to 207.5, 830 and 2075 mg/m³. The 5 male and 5 females which served as concurrent controls were exposed to air in the same manner. In order to accustom the rats to the exposure conditions, they were kept singly in wire cages in the whole-body exposure chambers and exposed to air for 6 hours per day as of day 2 before the beginning of exposure (day –2). Body weight development and food and water consumption were determined regularly. On study days –1, 6, 13 and 20, detailed clinical observations were carried out on all rats outside the inhalation chambers (open field observations). Ophthalmoscopic examinations were carried out in all animals of the 500 ppm group and the control group before the beginning of exposure (day –2) and

on day 25. Detailed passive observation of all rats under open field conditions, sensorimotor tests, reflex tests and motor activity measurements were carried out on the last day of the study (day 28, see Section 7.10). In addition, all animals were given a detailed examination with respect to haematology, clinical chemistry and urinalysis at the end of the exposure period. At study termination, all rats were necropsied. Absolute and relative weights of all major organs were determined. All gross lesions and 34 organs and tissues from all animals were fixed in 4-percent formaldehyde. The major organs from all 500 ppm rats and controls and the macroscopic lesions, nasal cavities (4 levels) and larynges (3 levels) from all test and control rats were histotechnically processed and examined by light microscopy. During the exposure period, the concentration levels of isopropenyl acetate were analytically determined by gas chromatography using a computer-controlled system in order to calculate mean concentrations for the entire study period.

Table 2. Concentrations of isopropenyl acetate as used in a 28-day inhalation study (BASF, 2002)

Target concentration		Measured concentration (mean ± standard deviation)	
mg/m³	ppm	mg/m³	ppm
0	0	0	0
207.5	50	209.1 ± 12.3	50.4
830	200	809.0 ± 22.4	195
2075	500	2011.0 ± 65.3	485

Except for low arousal noted in rats of the 500 ppm group, no differences were observed between test rats and concurrent controls with respect to clinical signs and findings, functional and behavioural tests, body weight development, ophthalmological examinations and neurofunctional tests. There were also no substance-related abnormal haematology, clinical chemistry or urinalysis findings. With the exception of significantly decreased absolute and relative epididymal weights in the 200 ppm group, the weights of all other organs from the exposed animals did not differ from those of the concurrent controls. The decreased epididymal weights in the 200 ppm group were assessed as being incidental as the rats were observed to have neither macroscopic nor light microscopic epididymal changes. Light microscopy revealed the following lesions of concentration-dependently in-

creasing severity in the upper respiratory tract of the treated animals: minimal to slight focal to multifocal inflammatory cell infiltration, in level I of the nasal cavity in 2 control animals (1 male, 1 female), in 2 male rats from the 50 ppm group, in 2 males and 4 females from the 200 ppm group, and in 3 male and 4 female rats from the 500 ppm-group, and in level II of the nasal cavity in one male and 2 females from the 500 ppm group. In addition, in the 500 ppm group, focal to multifocal minimal to slight degeneration of the olfactory epithelium was observed in level II of the nasal cavity in 3 male and all 5 female rats and in level III of the nasal cavity in 2 male rats and one female rat; and in 4 male and 4 female animals a multifocal minimal to slight hyperplasia of the nasal transitional epithelium was seen in level I of the nasal cavity. The level IV of the nasal cavity and all other organs and tissues showed no treatment-related histopathological changes. Under the conditions of the study, isopropenyl acetate caused clear irritation of the upper respiratory tract of rats at the top concentration level of 2075 mg/m³ (500 ppm) and moderate irritation of the upper respiratory tract at the mid and low concentrations. None of the isopropenyl acetate concentrations tested caused any signs of systemic toxicity. The *no observed adverse effect concentration* (NOAEC) for isopropenyl acetate was 2075 mg/m³ (500 ppm). The NOAEC for hyperplasia of nasal transitional epithelium and degeneration of olfactory epithelium was 830 mg/m³ (200 ppm). No NOAEC could be established for slight irritancy leading to minimal to slight inflammatory cell infiltration of the anterior nasal mucosa because even at the lowest test concentration of 207.5 mg/m³ (50 ppm) these lesions were observed only in 2 out of 5 male rats, but in none of 5 female rats in section level I of the nasal cavity (BASF, 2002). As minimal inflammatory cell infiltration in level I of the nasal cavity were found also in one male and one female control animal, the lowest concentration of 50 ppm can be regarded as *low observed adverse effect concentration* (LOAEL).

7.3 Skin and mucous membrane effects

Application of undiluted isopropenyl acetate to the clipped abdominal skin of 5 rabbits caused no skin irritation (no further details; Smyth et al., 1949).

The skin of 2 Pirbright White Hsd/Win:DH guinea pigs showed no signs of irritation after 48-hour occlusive application of undiluted (99.5% pure) iso-

propenyl acetate (pilot study to the sensitisation study discussed below; see Section 7.4; no further details; Medcon, 1995 c).

In a mucous membrane irritation study of isopropenyl acetate, conducted in accordance with OECD guideline No. 405 and Directive 92/69/EEC, 3 New Zealand rabbits received an instillation of 0.1 ml undiluted compound (99.5% pure) into the conjunctival sac of one eye. One hour after treatment, all animals were noted to have moderate redness of the conjunctivae and one animal exhibited slight swelling of the conjunctivae. At 24 hours, only one animal still exhibited mild redness of the conjunctivae, and 48 hours after treatment all animals were without abnormal findings. On the basis of Directive 93/21/EEC and the German Hazardous Substances Ordinance ("Gefahrstoffverordnung") and based on the results of the trial, isopropenyl acetate was evaluated as not irritating to the eye (Medcon, 1995 b).

Application of 0.5 ml undiluted isopropenyl acetate to the cornea of the rabbit eye caused mild irritation (no further details; Carpenter and Smyth, 1946; Smyth et al., 1949).

7.4 Sensitisation

The skin sensitisation potential of isopropenyl acetate (99.5% pure) was assessed in 10 male and 10 female Pirbright White Hsd/Win:DH guinea pigs using the Magnusson and Kligman maximisation test in accordance with Directive No. 92/69/EEC and OECD guideline No. 406. Intradermal induction was accomplished with a 5-percent dilution of the test article in peanut oil and with a 5-percent dilution of the test article in water and Freund's complete adjuvant. One week after intradermal induction, the skin was pretreated with 10% sodium lauryl sulphate in petrolatum in order to cause mild irritation 24 hours prior to dermal induction by means of a 48-hour occlusive application of undiluted compound. Dermal challenge with undiluted isopropenyl acetate (24-hour occlusive application), which was carried out 14 days after the second induction treatment, elicited no positive skin reactions in any of the 20 guinea pigs treated. Thus, isopropenyl acetate did not cause skin sensitisation in this test (Medcon, 1995 c).

7.5 Subchronic and chronic toxicity

No information available.

7.6 Genotoxicity

7.6.1 In vitro

Isopropenyl acetate (99.96% pure) was tested for mutagenic potential on *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 at concentration levels ranging from 1.23 to 100.00 µg/plate by means of the standard plate test conducted in accordance with OECD guideline No. 471. With an independent repeat assay, 3 plates were used per concentration and strain in the absence and presence of metabolic activation (S-9 mix from Aroclor 1254-induced rat liver). The highest concentration (100 mg/plate) had a slightly toxic effect on all strains. No mutagenic effect was observed either in the presence or absence of metabolic activation (TNO-CIVO, 1988).

A further Salmonella/microsome test on *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 also revealed no mutagenic potential for isopropenyl acetate, either in the absence or presence of metabolic activation. Isopropenyl acetate (purity not specified) was tested in the standard plate test conducted in accordance with the EPA, FDA and OECD guidelines at concentration levels of 100 to 10000 µg/plate (3 plates/concentration and strain) both without metabolic activation and in the presence of S-9 mix from Aroclor 1254-induced rat and hamster liver. The top concentration of 10000 µg/plate was associated with precipitation of the test substance. Isopropenyl acetate caused no bacteriotoxicity in the concentration range tested (Microbiological Associates, 1994 a).

The mutagenic potential of isopropenyl acetate (purity not specified) was also investigated in the L5178Y TK+/– mouse lymphoma cell line in the absence and presence of metabolic activation (S-9 mix from Aroclor 1254-induced rat liver). Cytotoxicity studies demonstrated that treatment of cultures with a concentration of 5000 µg/ml resulted in 62% toxicity in the absence of metabolic activation while toxicity was 100% in cultures treated in the presence of metabolic activation. An initial mutagenesis assay was conducted in the absence and presence of S-9 mix at treatment concentration levels from 500 to 5000 µg/ml but was invalidated due to excessive toxicity. A second mutagenesis assay was conducted in the absence and presence of S-9 mix over respective treatment level ranges of 500 to 4000 µg/ml and 1000 to 2000 µg/ml but yielded only partial results. The cultures

activated with S-9 mix exhibited a complete lack of cytotoxicity, and therefore the data generated from that portion of the assay were not reported. The portion of the assay that was conducted without S-9 mix demonstrated concentration-dependent cytotoxicity and genotoxicity. Compared with the solvent controls, there was a 4.2-fold increase in mutant frequency in association with 75% toxicity following treatment with 3500 µg/ml. At 4000 µg/ml "total growth" was below 3% and therefore that concentration was so toxic as to render any calculation of mutant frequency futile. In a third mutagenesis assay, cells were treated with concentrations in the range from 3000 to 5000 µg/ml in the absence of S-9 mix. Toxicity ("suspension growth"), according to the text of the investigators' report, was in the range from 49 to 92%. According to the data given in the tables, toxicity ranged from 53 to 78% (mean values of duplicate assays for each concentration) in the absence of any apparent concentration-dependence. The "total growth" data were concentration-independently spread across ranges from 41 to 80% (all individual values) and 47.5 to 62.5% (mean values of duplicate assays for each concentration). No concentration-dependent increase in mutant frequency was noted. The assays carried out with positive control substances yielded marked increases in mutant frequency. The investigators concluded that treatment of the cells with test substance concentrations of 500 to 4000 µg/ml in the absence of S-9 mix resulted in mutant induction, i.e. the test substance was mutagenic, while treatment of the cells with 3000 to 5000 µg/ml in the presence of S-9 mix produced only an equivocal response because those concentrations were below the cytotoxic range (Microbiological Associates, 1994 b). It should be noted, however, that no details of assay conduct or duration of treatment were reported. The experimental data presented in tabular form in the report are incomplete. The summary text discusses data evaluation in a little-differentiated and partly inaccurate manner. In the absence of S-9 mix, the data from one experiment demonstrate the presence of a concentration-dependent mutagenic effect extending into the range of concentrations with acceptable cytotoxicity. However, no independent repeat assay was carried out. In the presence of S-9 mix, the recommendation of the OECD guideline was not met according to which the highest concentration tested should have a "low level of survival", i.e. cause marked toxicity. Under this premise, the assay was not carried out in an adequate manner and thus the evaluation of the data as representing an equivocal response, as stated in the report, is not sufficiently well founded. In conclusion, the report on the mouse lymphoma assay

does not provide sufficient basis for a well-founded judgement on the mutagenic potential of isopropenyl acetate with respect to gene mutations. At most, the reported data permit the conclusion that the test substance showed a tendency to induce gene mutations in the absence of S-9 mix.

7.6.2 In vivo

Isopropenyl acetate (99.45% pure) was tested in accordance with OECD guideline No. 474 and Directive 92/69/EEC by means of a micronucleus assay in bone marrow cells from male and female NMRI mice with respective mean initial weights of 33.6 and 26.8 g. A single dose of isopropenyl acetate, dissolved in deionised water, was administered by oral gavage in the dose-finding study and the main study (volume administered: 10 ml/kg body weight). In the preliminary study, groups of 2 male and 2 female mice received isopropenyl acetate at dose levels of 500, 1000, 1500 or 2000 mg/kg body weight. In these amounts, the substance was well tolerated during the 2-day observation period, apart from mild transient clinical signs (reduction of spontaneous activity, apathy and eyelid closure). The main study was carried out in groups of 6 male and 6 female mice and encompassed 4 test groups (200, 670, 2000 and 2000 mg isopropenyl acetate/kg body weight), a water control group and a positive control group (given 40 mg cyclophosphamide/kg body weight). In the main study, all test and control mice, except those in the second group treated with 2000 mg/kg, were killed for examination of bone marrow cells 24 hours after treatment. The 12 mice from the second 2000 mg/kg group were sacrificed 48 hours after isopropenyl acetate administration. For 5 male and 5 female mice per group, 2000 polychromatic erythrocytes per animal were analysed for micronuclei. In order to describe a cytotoxic effect, the ratio of polychromatic to normochromatic erythrocytes was determined and presented as the number of normochromatic erythrocytes/2000 polychromatic erythrocytes. The mice in the groups treated with 2000 mg/kg body weight showed mild signs of toxicity (no further details). The mean number of normochromatic erythrocytes/2000 polychromatic erythrocytes was not elevated in any of the test groups relative to the water control group, indicating that isopropenyl acetate had no cytotoxic effect on the bone marrow of mice. The substance used as a positive control, cyclophosphamide, induced a statistically significant increase in the number of micronucleated polychromatic ery-

throcytes. However, the mean values of micronucleated polychromatic erythrocytes were smaller in all 4 test groups as compared with the concurrent solvent control group. Therefore, under the conditions of the study, isopropenyl acetate did not induce micronuclei in the bone marrow of mice (RCC, 1999).

7.7 Carcinogenicity

No information available.

7.8 Reproductive toxicity

No information available.

7.9 Effects on the immune system

No information available.

7.10 Neurotoxicity

In the context of a 28-day whole-body inhalation study in which rats were exposed to isopropenyl acetate at target concentrations of 0 (controls), 50, 200 or 500 ppm (see Section 7.2), test and control rats were examined by means of a series of specific neurotoxicity tests on the last day of the study. They began with a phase of passive observation of the animals in their cages. Subsequently, each rat was placed under passive observation in a standard environment under open field conditions for 2 minutes, then subjected to sensorimotor and reflex tests and finally assessed for motor activity. The following sensorimotor reflexes were tested: approach response and touch response, visual placing response, pupillary reflex, winking reflex and pinna reflex, startle response, olfaction, catalepsy (descending from box), coordination of movements (righting response), behaviour during handling, vocalisation, pain perception (tail pinch) and grip strength of forelimbs and hindlimbs. Motor activity measurements were performed in the dark using the Multi-Varimex System with 4 infrared beams per cage. For each animal, the numbers of beam interrupts were counted over 12 intervals, each lasting 5 minutes. Except for low arousal noted in rats of the

500 ppm group relative to the concurrent controls, no differences were observed between test and concurrent control rats with respect to clinical signs and findings, functional and behavioural tests and neurofunctional tests (BASF, 2002).

7.11 Other effects

One source states that isopropenyl acetate is a narcotic in high concentrations (no further details; Budavari et al., 1989).

8 Experience in humans

No information available.

9 Classifications and threshold limit values

In the Federal Republic of Germany, the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area ("MAK-Kommission") of the Deutsche Forschungsgemeinschaft has established a MAK value (maximum workplace concentration) for isopropenyl acetate on the suggestion of BG Chemie. It was set in the List of MAK and BAT Values 2004 at 10 ml/m³ (ppm, equivalent to 46 mg/m³; DFG, 2004).

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