ALDICARB

1. Exposure Data

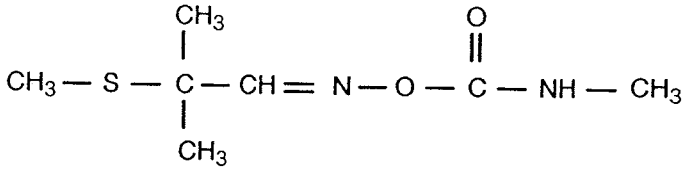
1.1 Chemical and physical data

1.1.1 *Synonyms, structural and molecular data*

Chem. Abstr. Serv. Reg. No.: 116-06-3

Chem. Abstr. Name: 2-Methyl-2-(methylthio)propanal, *O*-[(methylamino)carbonyl]-oxime

IUPAC Systematic Name: 2-Methyl-2-(methylthio)propionaldehyde *O*-methylcarbamoyloxime



$C_7H_{14}N_2O_2S$ Mol. wt: 190.30

1.1.2 *Chemical and physical properties*

(*a*) *Description*: Colourless crystals (Worthing & Walker, 1987)

(*b*) *Boiling-point*: Decomposes (Rhone-Poulenc Ag Co., 1987)

(*c*) *Melting-point*: 98-100°C (Worthing & Walker, 1987)

(*d*) *Spectroscopy data*: Infrared spectroscopy data have been reported (US Environmental Protection Agency, 1976).

(*e*) *Solubility*: Slightly soluble in water (6 g/l at 20°C); soluble in most organic solvents: at 25°C, acetone, 350 g/kg; dichloromethane, 300 g/kg; benzene, 150 g/kg; xylene, 50 g/kg; practically insoluble in heptane (Worthing & Walker, 1987)

(*f*) *Volatility*: Vapour pressure, 9.75×10^{-5} mm Hg [1.3×10^{-5} Pa] at 25°C (Worthing & Walker, 1987)

(*g*) *Stability*: Stable in neutral, acidic and weakly alkaline media; hydrolysed by concentrated alkalis; decomposes above 100°C; rapidly converted by oxidizing agents to the sulfoxide, which is more slowly oxidized to the sulfone (Worthing & Walker, 1987; Royal Society of Chemistry, 1989)

(*h*) *Conversion factor for airborne concentrations*[1]: $mg/m^3 = 7.78 \times ppm$

[1]Calculated from: mg/m^3 = (molecular weight/24.45) × ppm, assuming standard temperature (25°C) and pressure (760 mm Hg [101.3 kPa])

1.1.3 *Trade names, technical products and impurities*

Some common trade names are AI3-27 093, Aldicarb, ENT 27 093, OMS 771, Temik and UC 21149.

Aldicarb is available in the USA as a technical grade product with a purity of 98% (minimum) (Rhone-Poulenc Ag Co., 1987).

It is formulated in the USA and Europe as a granular product with the concentration of active ingredient ranging from 5 to 15%; some formulated products also contain gypsum and dichloromethane (Royal Society of Chemistry, 1986; Rhone-Poulenc Ag Co., 1990a,b; see IARC, 1987a). Aldicarb is also formulated as mixtures with pentachloronitrobenzene (see IARC, 1974, 1987b), 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole and lindane (see IARC, 1987c) (Royal Society of Chemistry, 1986; Rhone-Poulenc Ag Co., 1990c). The granular carrier material is impregnated with aldicarb and a bonding agent which helps prevent dustiness that may be caused by abrasion during shipping; dust is also removed during the manufacturing process to minimize inhalation exposure and hazards of direct handling (Baron & Merriam, 1988).

1.1.4 *Analysis*

Selected methods for the analysis of aldicarb in various matrices are given in Table 1. Several more methods and the environmental fate and transport of aldicarb and its metabolites have been reviewed (Moye & Miles, 1988).

Table 1. Methods for the analysis of aldicarb

Sample matrix	Sample preparation[a]	Assay procedure[a]	Limit of detection	Reference
Water	Filter; inject into reversed-phase HPLC column; separate analytes using gradient elution chromatography; hydrolyse with 0.05 N NaOH; react with *ortho*-phthalaldehyde and 2-mercaptoethanol	HPLC/FL	1.0 µg/l (2.0)[b]	US Environmental Protection Agency (1989a)
Drinking-water	Adsorb on Amberlite XAD-2 resin; elute with acetone	HPLC/UV	1 µg/l	Narang & Eadon (1982)
Crops, animal tissue	Extract with acetone/water (3:1); add peracetic acid to oxidize residues to sulfone; clean-up on activated Florisil column	GC/FPD[c]	0.01–0.05 ppm (mg/kg)	US Food and Drug Administration (1989a)
Milk	Precipitate solids with phosphoric acid and filter; add peracetic acid to oxidize residues to sulfone; extract into chloroform; clean-up on activated Florisil column	GC/FPD[c]	0.001 ppm (mg/l)	US Food and Drug Administration (1989a)
Cotton-seed	Grind sample; extract and oxidize with acetonitrile/peracetic acid solution; clean-up on activated Florisil column	GC/FPD[c]	0.02 ppm (mg/kg)	US Food and Drug Administration (1989a)

Table 1 (contd)

Sample matrix	Sample preparation[a]	Assay procedure[a]	Limit of detection	Reference
Grapes, potatoes	Extract with methanol; clean-up by liquid-liquid partitioning and column chromatography	LC/FL	Not reported	Association of Official Analytical Chemists (1985)
Formulations	Extract and dilute with dichloromethane; measure absorbance at 5.75 μm and compare with standard	IR	Not reported	Romine (1974); Williams (1984)

[a]Abbreviations: GC/FPD, gas chromatography/flame photometric detection; HPLC/FL, high-performance liquid chromatography/fluorescence detection; HPLC/UV, high-performance liquid chromatography/ultraviolet detection; IR, infrared spectroscopy; LC/FL, liquid chromatography/fluorimetric detection
[b]Estimated limit of detection for aldicarb sulfone and aldicarb sulfoxide
[c]Total residues of aldicarb and its carbamate metabolites are determined as aldicarb sulfone

1.2 Production and use

1.2.1 *Production*

Aldicarb was first prepared by Payne and Weiden (1965) and was first made available as a commercial product in 1970, following its registration in the USA for use on cotton (Romine, 1974).

Aldicarb is synthesized by reacting nitrosyl chloride with isobutylene to obtain 2-chloro-2-methyl-1-nitrosopropane dimer, which is further reacted with methyl mercaptan and sodium hydroxide to obtain 2-methyl-2-(methylthio)propionaldoxime. Aldicarb is obtained by reaction of the oxime with methyl isocyanate (Romine, 1974).

Aldicarb is currently produced in the USA and in France (Meister, 1990). Production in the USA in 1979-81 was estimated at 2000 tonnes per annum (US Environmental Protection Agency, 1987).

1.2.2 *Use*

Aldicarb acts as a systemic insecticide, acaricide and nematicide and is applied to soil under cotton, potatoes, sugar beets, peanuts, soya beans, ornamental plants, sweet potatoes, pecans, citrus (grapefruit, lemons, limes and oranges only), dry beans, sorghum and sugar-cane (Rhone-Poulenc Ag Co., 1989; Meister, 1990). In the USA during 1979-81, annual usage of aldicarb (active ingredient) was estimated as follows (tonnes; %): cotton, 520 (29%); potatoes, 430 (25%); peanuts, 250 (14%); soya beans, 205 (12%); pecans, 180 (10%); ornamental plants (lilies, roses, holly), 45 (3%); sugar beets, 45 (3%); citrus, 34 (2%); sweet potatoes, 22 (< 1%); and tobacco, 6 (< 1%) (Holtorf, 1982). In Finland, 132 kg aldicarb (active ingredient) were sold in 1988 (Hynninen & Blomqvist, 1989). In the USA in 1989, about 1000-1500 tonnes aldicarb are believed to have been used. Aldicarb use is restricted in certain areas in various parts of the world, usually because of its potential to leach to groundwater (IRPTC/UNEP, 1990).

1.3 Occurrence

1.3.1 *Air*

Few studies are available on the stability or migration of aldicarb in air over or near treated fields. Laboratory studies with ^{14}C-labelled aldicarb in various soil types resulted in its loss, which could be explained only on the grounds that aldicarb or its decomposition products had been transferred to the vapour phase. Subsequent experiments showed that transfer of radioactivity to the atmosphere was inversely proportional to the depth of application in the soil (Coppedge *et al.*, 1977). Little aldicarb was released from a clay soil treated with this pesticide and placed in a volatilizer (Supak *et al.*, 1977).

1.3.2 *Water*

Aldicarb has been detected in ground- and drinking-water in 15 states in the USA at levels ranging from traces to 500 μg/kg (WHO, 1991).

It was detected in water in Suffolk County, NY, in August 1979: a monitoring programme for aldicarb in water indicated that 1121 (13.5%) of 8404 wells examined exceeded the State recommended guideline of 7 μg/l. Of the contaminated wells, 52% contained between 8 and 30 μg/l, 32% between 31 and 75 μg/l and 16% contained more than 75 μg/l (Zaki *et al.*, 1982). Following the banning of aldicarb in Suffolk County in 1979, approximately 74% of all wells sampled in the County in 1981 contained no detectable level of aldicarb. Of the 27% of wells (2054 samples) that did, residue levels were 1-10 μg/l in 56%, 11-100 μg/l in 40% and > 100 μg/l in 4% (US Environmental Protection Agency, 1988). Data derived from monitoring of all drinking-water wells in Suffolk County in which contamination had occurred are shown in Table 2.

Table 2. Numbers of wells containing aldicarb residues in Suffolk County, NY, 1980-85[a]

Year	No. of samples	No. of wells containing aldicarb	
		> 8 μg/l	1-7 μg/l
1980	8595	1193	1167
1981	677	190	275
1982	2905	380	265
1983	4659	804	661
1984	3974	670	546
1985	4022	942	688

[a]From US Environmental Protection Agency (1988)

Extensive monitoring studies in the USA have mostly been related to potato and citrus production. Relatively high percentages (5–> 50%) of positive findings occurred in Wisconsin and north-eastern states (New York, Massachusetts, Rhode Island, Connecticut, Maine). There was substantial evidence for leaching to shallow groundwater associated with citrus production in Florida (US Environmental Protection Agency, 1988; WHO, 1991).

1.3.3 *Soil*

Numerous studies have been carried out with aldicarb under field and laboratory conditions to study its translocation, persistence and degradation (WHO, 1991). It has a half-time in soil of approximately 30 days; this can vary depending on microbial populations, soil composition, moisture, temperature and farming practices (Meister, 1990). Its half-time in the root zone varied from one week to over two months. The primary mode of degradation in this zone is oxidative metabolism by microorganisms, although some hydrolysis may occur. Warm soil temperatures, high moisture content and high organic contents may result in more rapid degradation (US Environmental Protection Agency, 1988; WHO, 1991).

Aldicarb is mobile in most types of soil, with adsorption coefficients typically of < 1.0 and often 0.1. Incidents of groundwater contamination have primarily been associated with sandy soils, to which aldicarb residues are poorly bound (US Environmental Protection Agency, 1988).

Aldicarb has been used extensively since 1979-80 to control cotton whitefly in the Sudan, reaching a maximum of nearly 84 000 ha in 1984-85. When uptake and distribution were studied and the maximum uptake recorded two weeks after application of aqueous treatments and four weeks after application of granular formulations, no aldicarb or its sulfoxide or sulfone metabolites were detected in plant tissues or in soil at harvest (El-Zorgani *et al.*, 1988).

1.3.4 *Food*

In a market-basket survey carried out in the USA in 1983-85 on 491 samples of raw agricultural commodities, 76 (72 of white potatoes, two of sweet potatoes, one peach and one collard green) contained aldicarb residues. The mean residue level in potato samples taken in 1984 and 1985 was 200 µg/kg, while that taken in 1983 was 720 µg/kg (US Environmental Protection Agency, 1988).

In 1984-85 to 1988-89 in Canada, aldicarb residues were found in 13 of 30 samples of potatoes, at 0.02-0.78 mg/kg (mean, 0.13 mg/kg). No residue was detected in samples of bananas, oranges, cucumbers or wine (Government of Canada, 1990).

In 1978, national monitoring of potatoes treated at 3 kg/ha active ingredient in the Netherlands found total residues (expressed as the sulfone) in 23 samples, ranging from < 0.03 to 0.38 mg/kg, 100-205 days after broadcast application (mean, 0.11 mg/kg). Monitoring in 1982 of potatoes treated similarly showed residues of < 0.03-0.25 mg/kg (mean, 0.06 mg/kg) (FAO/WHO, 1986).

In a total diet study in 1986-88, 3737 domestic and imported food samples were analysed in the USA. Of these, 3656 (98%) contained no detectable residue. Potatoes (312) were included and residues found in 18% of samples, the highest level being 0.71 mg/kg. No residue was found in 98% of bananas sampled (55); one sample contained 0.12 mg/kg (US Food and Drug Administration, 1989b).

1.4 Regulations and guidelines

Limits for residues of aldicarb in foods in various countries or regions are given in Table 3.

Table 3. National or regional residue limits for aldicarb in foods[a]

Country or region	Residue limit (mg/kg)	Commodities
Australia	0.2	Potatoes, strawberries
	0.05[b]	Cottonseed
	0.02[b]	Cereal grain, sugar-cane
	0.01[b]	Citrus
Austria	0.05[c]	All foodstuffs of vegetable origin
	0.01[c]	All foodstuffs of animal origin
Belgium	0.05[d]	Brussels sprouts, potatoes
	0[e] (0.02)	Other foodstufs of vegetable origin
Brazil	1.0	Potatoes
	0.3	Bananas
	0.2	Citrus fruit
	0.1	Cottonseed, coffee (raw beans)
	0.05	Peanuts
	0.02	Beans, sugar-cane, tomatoes
Canada	0.5[f]	Potatoes
Denmark	0.2[d]	Citrus fruit, potatoes
	0.5[d]	Bananas
	0.05[d]	Onions
Finland	0.2[d]	Citrus fruit
	0.05[d]	Other foodstuffs (except cereal grains)
Germany	0.5[c]	Potatoes
	0.3[c]	Citrus fruit
	0.1[c]	Beans, citrus juices, cottonseed, raw coffee
	0.05[c]	Maize, onions, peanuts, soya beans, sugar beets, strawberries
	0.01[c]	All foodstuffs of animal orign
Hungary	0.05	Sugar beets
	0.01	Sugar
Israel	0.1	Cottonseed
Italy	0.05	Sugar beets
Kenya	0.1	Cottonseed
Mexico	1.0	Cotton, potatoes
	0.6	Citrus fruit (processed), tomatoes (processed)
	0.5	Nuts, sorghum forage
	0.3	Pecans
	0.1	Beans, coffee
	0.05	Peanuts, sorghum grain
	0.02	Soya beans, sugar-cane and sweet potatoes (negligible)
Netherlands	0.5[d]	Bananas, pecan nuts, potatoes
	0.2[d]	Sorghum
	0.1[d]	Beans (dry), coffee beans, cottonseed, sweet potatoes
	0.05[g]	Brussels sprouts, onions, peanuts
	0.01[g]	Meat, milk
	0 (0.02)[h]	Other crops or food

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
South Africa	1.0[c]	Potatoes
	0.5[c]	Bananas
	0.2[c]	Citrus (except lemons), grapes, tomatoes
	0.1[c]	Cottonseed, sugar-cane
	0.05[c]	Macadamia nuts, mealies (green), pecan nuts
Spain	5.00[c]	Tobacco
	1.00[c]	Beetroot tops
	0.50[c]	Potatoes
	0.30[c]	Bananas
	0.20[c]	Citrus fruit
	0.10[c]	Cottonseed
	0.05[c]	Other plant products
Sweden	0.2[c]	Citrus fruit
	0.05[c]	Potatoes
Switzerland	0.02[f]	Maize
	0.01	Sugar beets
Taiwan	0.5	Fruit vegetables, root vegetables, tropical fruit
	0.2	Citrus fruit
	0.1	Beans (dry)
USA	1[f]	Potatoes, sugar beets (tops)
	0.6	Dried citrus pulp (feed)
	0.5	Peanuts (hulls), pecans, sorghum (fodder), sorghum bran (feed)[i]
	0.3	Bananas, cottonseed hulls (feed), grapefruit, lemons, limes, oranges
	0.2	Sorghum (grain)
	0.1	Beans (dry), coffee beans, cottonseed, sugar-cane (fodder, forage), sweet potatoes, sorghum bran[i]
	0.05	Peanuts, sugar beets
	0.02	Soya beans, sugar-cane
	0.01	Cattle, goats, hogs, horses and sheep (fat, meat and meat by-products)
	0.002	Milk
Yugoslavia	0.05[f]	Sugar beets

[a]From Health and Welfare Canada (1990); US Environmental Protection Agency (1989b,c)

[b]The maximum residue limit has been set at or about the limit of analytical determination.

[c]Sum of aldicarb, aldicarb sulfoxide and aldicarb sulfone (total calculated as aldicarb)

[d]Sum of aldicarb, its sulfoxide and its sulfone

[e]The figure in parentheses is the lower limit for determining residues in the corresponding product according to the standard method of analysis.

[f]Including the metabolites aldicarb sulfoxide and aldicarb sulfone

[g]A pesticide may be used on an eating or drinking ware or raw material without a demonstrable residue remaining; the value listed is considered the highest concentration at which this requirement is deemed to have been met.

[h]Residues shall be absent; the value in parentheses is the highest concentration at which this requirement is still deemed to have been met.

[i]Interim tolerance

The FAO/WHO Joint Meeting on Pesticide Residues evaluated aldicarb at meetings in 1979, 1982, 1985 and 1988 (FAO/WHO, 1980, 1983a, 1986, 1988). In 1982, an acceptable daily intake in food of 0.005 mg/kg bw was established (FAO/WHO, 1983b).

Maximum residue levels have been established by the Codex Alimentarius Commission for aldicarb (sum of aldicarb, its sulfoxide and its sulfone, expressed as aldicarb) in or on the following commodities (in mg/kg): maize forage, 5; sugar beets (leaves or tops), 1; bananas, dry sorghum (straw and fodder), pecans, potatoes, 0.5; citrus fruit, sorghum, 0.2; coffee beans, dry beans, cottonseed, sweet potatoes, 0.1; maize, onion (bulb), peanuts, sugar beets, 0.05; dry soya beans, 0.02; meat, milk, 0.01 (Codex Commission on Pesticide Residues, 1990).

The Office of Drinking Water of the US Environmental Protection Agency established a Health Advisory Level of 10 ppb (μg/l) for residues of aldicarb in drinking-water (US Environmental Protection Agency, 1984), with a proposed revision of 3 ppb (μg/l) (US Environmental Protection Agency, 1991). Aldicarb was included in the 1987 Canadian guidelines for drinking-water quality, with a maximum acceptable concentration of 9 μg/l (Minister of National Health and Welfare, 1987).

The technical product aldicarb has been classified as 'extremely hazardous' by WHO (1990).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Oral administration

Mouse

Groups of 50 male and 50 female B6C3F_1 mice, six weeks old, were fed aldicarb (approximately 99% pure) at 2 or 6 mg/kg of diet for 103 weeks. A control group of 25 males and 25 females was available. Survival at 90 weeks was 21/25 control, 48/50 low-dose and 45/50 high-dose males and 19/25 control, 45/50 low-dose and 44/50 high-dose females. No reduction in body weight was observed in treated animals, and there was no treatment-related increase in tumour incidence at any site. The authors stated that the dietary concentrations of aldicarb used were too low to be considered a maximum tolerated dose (US National Cancer Institute, 1979).

Rat

Groups of 50 male and 50 female Fischer 344/N rats, eight weeks of age, were fed aldicarb (approximately 99% pure) at 2 or 6 mg/kg of diet for 103 weeks. A control group of 25 males and 25 females was available. Survival at 90 weeks was 18/25 control, 44/50 low-dose and 39/50 high-dose males and 24/25 control, 44/50 low-dose and 46/50 high-dose females. No reduction in body weight was observed in treated animals, and there was no treatment-related increase in tumour incidence at any site. The authors stated that the

dietary concentrations of aldicarb used were too low to be considered a maximum tolerated dose (US National Cancer Institute, 1979).

4. Other Relevant Data

The toxicity of aldicarb has been reviewed (FAO/WHO, 1980, 1983a; Risher *et al.*, 1987; Baron & Merriam, 1988; WHO, 1991).

4.1 Absorption, distribution, metabolism and excretion

The metabolism of aldicarb is shown in Figure 1 (Risher *et al.*, 1987).

4.1.1 *Humans*

Most carbamate insecticides are readily absorbed from the gastrointestinal tract. They may also be absorbed to varying degrees through the skin (Feldman & Maibach, 1970; Sterling, 1983).

Reports on the toxicity of aldicarb in humans (section 4.2.1) suggest that it enters the human body following skin contact, inhalation and ingestion. It is metabolized to aldicarb sulfoxide and aldicarb sulfone. Aldicarb derivatives (aldicarb, aldicarb sulfoxide and aldicarb sulfone) were found in the tissues of a 20-year-old man run over by a tractor following overexposure for about 2 h without adequate protection. The levels found were 482 µg/l in blood, 187 µg/kg in liver, 683 µg/kg in kidney and 823 µg/kg in skin from the hand. Aldicarb itself was not detected in blood, but aldicarb sulfoxide was present at 108 ppb [µg/l] and aldicarb sulfone at 374 ppb [µg/l], indicating an almost complete two-step oxidation process. The same trend was seen in the liver and kidney, while aldicarb occurred at the highest level in the skin. The total body burden of aldicarb was estimated at 18.2 mg (equivalent to 0.275 mg/kg bw) (Lee & Ransdell, 1984).

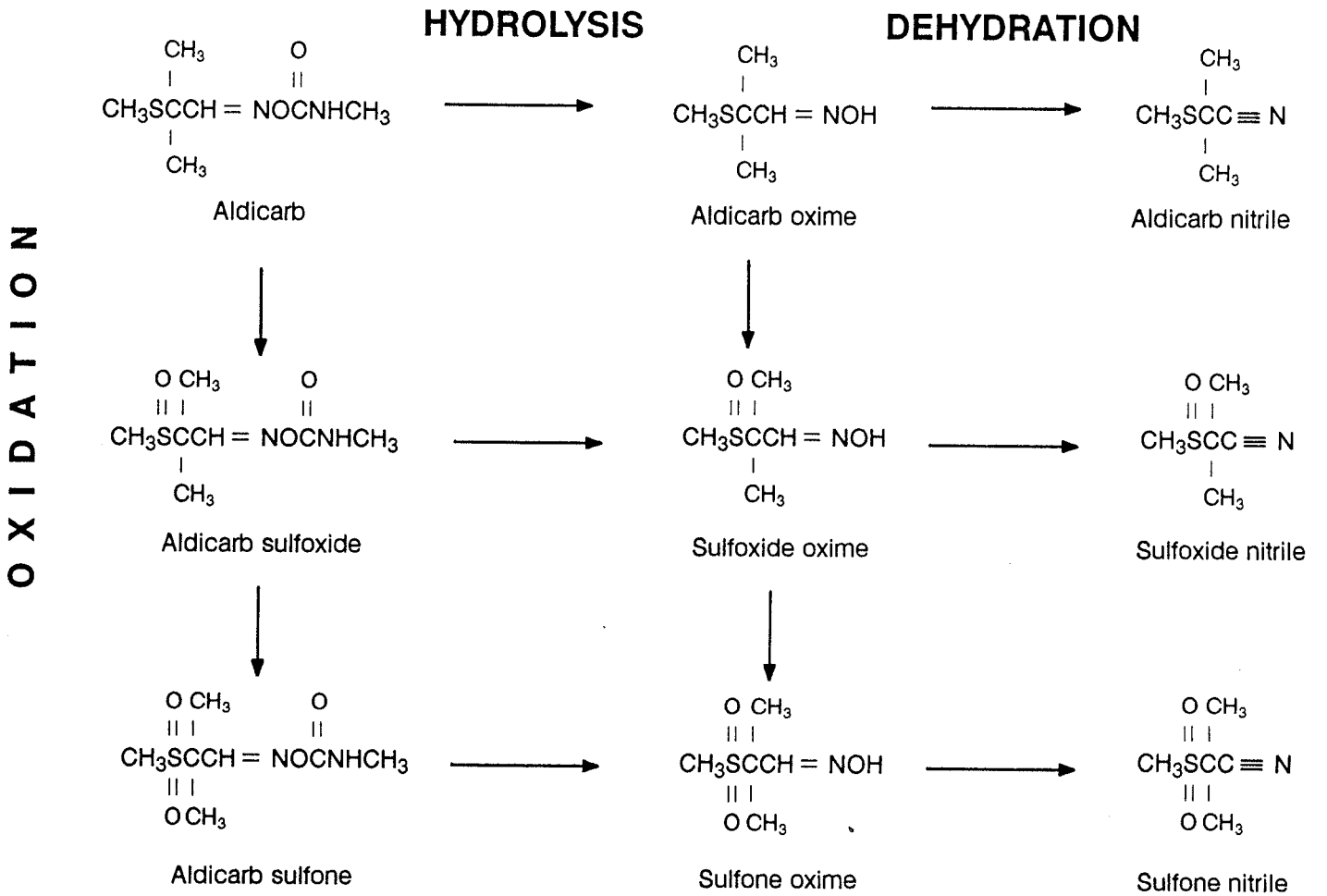
4.1.2 *Experimental systems*

Aldicarb is readily absorbed through the gut in rats and cows and through the skin in rats and rabbits. It is rapidly metabolized and excreted within 24 h of exposure, almost all of the toxic and nontoxic metabolites being excreted in urine (Risher *et al.*, 1987). Signs of poisoning were reported to occur only a few minutes after administration of higher doses in rats given aldicarb at up to 0.1 mg/kg bw by intubation (Cambon *et al.*, 1979). In rats administered radiolabelled aldicarb orally, 80% of the label was excreted in the urine within 24 h; less than 0.4% consisted of unchanged aldicarb (Andrawes *et al.*, 1967). Almost complete absorption *via* the gut was observed in cows (Dorough & Ivie, 1968; Dorough *et al.*, 1970).

Analysis of tissue samples taken from rats one to four days following oral administration of radiolabelled aldicarb indicated general distribution and elimination (Andrawes *et al.*, 1967).

The metabolism of aldicarb in rats involves both hydrolysis of the carbamate ester and oxidation of the sulfur to the sulfoxide and sulfone derivatives (Andrawes *et al.*, 1967). While the hydrolysis results in compounds with little or no insecticidal activity or toxicity to other organisms, the sulfoxide and sulfone metabolites are active cholinesterase inhibitors (Bull *et*

Fig. 1. Metabolic pathways of aldicarb in rats (from Risher *et al.*, 1987)



al., 1967; Risher *et al.*, 1987). In rats, the sulfoxide and the oxime sulfoxide constitute the major urinary metabolites, at 40% and 30%, respectively (Knaak *et al.*, 1966).

4.2 Toxic effects

4.2.1 *Humans*

Aldicarb is one of the most toxic pesticides known (Marshall, 1985). Its toxicity is based on a transient inhibition of acetylcholinesterase. Carbamates form unstable complexes with chlolinesterases by carbamoylation of the active sites of the enzymes (Done, 1979; Mortensen, 1986). Unlike the relatively irreversible anticholinesterase activity of the organophosphorus insecticides, the carbamoylation process which produces the esterase inhibition is quickly reversible.

Several reports on the acute and chronic toxicity of aldicarb are summarized in Table 4. In most exposure situations, the clinical symptoms observed were consistent with the known mechanism of action (inhibition of acetylcholinesterase). In some of the studies, the dose has been estimated. Cholinesterase measurements have been of additional use in characterizing dose or extent of exposure.

4.2.2 *Experimental systems*

The acute toxicity of alidcarb is high, with oral LD_{50}s in rats and mice generally below 1 mg/kg bw. Depression of cholinesterase activity has been reported in rats administered aldicarb, its sulfoxide or its sulfone. The relative order of inhibition of cholinesterase was plasma > red blood cells > brain (DePass *et al.*, 1985; studies reported by Risher *et al.*, 1987).

After a review of several studies, Risher *et al.* (1987) concluded there was no effect of subchronic and chronic oral feeding to rats of aldicarb at 0.3 mg/kg bw/day; of aldicarb sulfoxide at 0.3 mg/kg bw/day; of aldicarb sulfone at 2.4 mg/kg bw/day; or of 1:1 aldicarb sulfoxide:sulfone mixture at 0.6 mg/kg bw/day. The latter was tested owing to the observation that residues found in drinking-water are generally present as this mixture.

Suppressed humoral immune response (splenic plaque-forming cell assay) has been reported after exposure of mice to aldicarb in drinking-water for up to 34 days. Suppression on day 34 was significant, however, only at 1 ppb [µg/l] water and was less pronounced and not significant at 10, 100 or 1000 µg/l water (Olson *et al.*, 1987). In a similar study in mice exposed to aldicarb in drinking-water at levels of 0.1-1000 ppb [µg/l] for 34 days, using a variety of immunological endpoints including that used by Olson *et al.*, no significant effect on the immunological system was noted (Thomas *et al.*, 1987). Shirazi *et al.* (1990), however, performed a follow-up experiment using the same assay and aldicarb at 0.01-1000 µg/l in drinking-water but prolonging the study time up to 180 days. After extensive statistical analysis, the authors concluded that there was a stimulatory effect at 30 and 60 days and an inhibitory effect at 90 and 180 days. Dean *et al.* (1990) reported that aldicarb given intraperitoneally to mice at doses of 0.01-100 ng per mouse (0.1 ml of a 0.1, 1, 10, 100 or 1000 ppb solution) decreased the stimulatory function of macrophages without affecting T-lymphocyte function. There was no clear dose-response relationship.

Table 4. Acute and chronic toxicity of aldicarb in human populations

Type of exposure/population studied	No. of cases	Clinical symptom reported[a]	Estimated dose	Other endpoints/ comments	Reference
Foreman running mechanical bagging machine for one day	1	+	NR[b]	Decrease in plasma and red blood cell AChE[c]	US Environmental Protection Agency (1975)
California, USA, 1974-76 Acute occupational intoxication as reported by physicians; dermal and inhalation exposure	38	+	NR	Not reported	Peoples *et al.* (1978)
Florida, USA, 1981 Interview survey of 436 citrus growers	1	+	NR	Intoxication confirmed by unspecified laboratory tests	Griffith & Duncan (1985)
Farm worker exposed ~2 h without adequate protection	1	–	0.275 mg/kg bw	Incapacitation due to intoxication thought to contribute to death in an accident	Lee & Ransdell (1984)
Woman ate leaf of spearmint growing near roses sprayed three weeks previously	1	+	NR	NR	Marshall (1985)
Nebraska, USA, 1977 and 1978 Two incidents of intoxication following ingestion of cucumbers; aldicarb contamination identified in later incident	14	+	(0.025–0.041 mg/kg bw)[d]	No abnormal blood chemistry	Goes *et al.* (1980)
Vancouver, Canada, 1985 Ingestion of cucumbers contaminated with aldicarb	140	+	0.01–0.03 mg/kg bw	NR	Hirsch *et al.* (1987)

Table 4 (contd)

Type of exposure/population studied	No. of cases	Clinical symptom reported[a]	Estimated dose	Other endpoints/ comments	Reference
Oregon and California, USA Ingestion of watermelon					
Oregon, aldicarb residues in 10/16 melons eaten by definite cases	61 definite, 43 suspected 264 reported	+		NR	Green *et al.* (1987)
California, aldicarb sulfoxide residues in 10/250 melons	690 probable of 1350 reported	+	0.002–0.06 mg/kg bw	NR	Jackson & Goldman (1986); Jackson *et al.* (1986)
Suffolk County, NY, USA, 1981 Questionnaire survey of 1500 households with well-water aldicarb levels > 7 ppb (μg/l)	641 individuals evaluated from 204 question-naires	–	NR	Trend in neurological syndromes reported with increasing aldicarb con-centration	Sterman & Varma (1983)
Portage County, WI, USA, 1985 37 women from households supplied by well-water screened for aldicarb and 13 from households supplied with muni-cipal water	23 exposed to detectable levels of aldi-carb, 27 controls	–	0.3–48 μg/day	Increased number of T8 cells; increased % of total lymphocytes as T8 cells; decreased ratio T4:T8 cells in exposed *versus* controls	Fiore *et al.* (1986)

[a]Clinical symptoms reported consistent with inhibition of acetylcholinesterase, +; no such symptom reported, –

[b]NR, none reported and no details given to estimate dose

[c]AChE, acetylcholinesterase

[d]Dose estimated by Jackson & Goldman (1986)

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Few data are available on the reproductive and developmental effects of aldicarb. In two studies described in a review by Risher *et al.* (1987), there was reported to be no evidence of toxicity in the offspring of rats treated with aldicarb in the feed at doses as high as 1 mg/kg bw [near the LD_{50}] throughout pregnancy and lactation, and offspring of rabbits treated with aldicarb by gavage at doses of up to 0.5 mg/kg bw on days 7-27 of gestation were reported to exhibit no developmental toxicity. Rats investigated in a three-generation study in which aldicarb was incorporated into the diet were also reported to exhibit no significant difference in any parameter assessed compared to control animals.

Cambon *et al.* (1979, 1980) evaluated the effects of administering a single dose of aldicarb (0-0.1 mg/kg bw) on gestation day 18 on acetylcholinesterase activity in maternal and fetal tissue of Sprague-Dawley rats. Maternal blood acetylcholinesterase activity was reduced at doses greater than 0.001 mg/kg, and fetal blood acetylcholinesterase activity was reduced at doses of 0.001 mg/kg and above in samples taken > 1 h after dosing. The effect persisted for up to 24 h at doses of 0.01 mg/kg and above. Tissues were stored overnight at 4°C before analysis. Acetylcholinesterase was assayed in maternal and fetal brain homogenates 1 h after administration of 0.1 mg/kg bw aldicarb, and isoenzymes were analysed using polyacrylamide electrophoresis. Both maternal and fetal brain acetylcholinesterase levels were decreased by aldicarb; the levels of two of three cholinesterase isozymes were decreased in fetal brain and that of only one of the cholinesterase isozymes was decreased in maternal brain.

4.4 Genetic and related effects (see Table 5 and Appendices 1 and 2)

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems*

Aldicarb induced differential toxicity in *Salmonella typhimurium* but not in strains of *Escherichia coli*. Aldicarb was not mutagenic to bacteria, whereas mutations were induced in cultured mammalian cells. Gene mutation, sister chromatid exchange and chromosomal aberrations were induced by aldicarb in cultured human cells. In a single study, no DNA strand breakage was observed in human cells.

In vivo, aldicarb induced chromosomal aberrations in cells of rat bone marrow.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Aldicarb is a moderately persistent systemic insecticide, acaricide and nematicide formulated as granules. It was first used in 1970 and is applied mainly on cotton and potatoes.

Exposure to aldicarb may occur during its production and application and, at lower levels, *via* contamination of groundwater and consumption of food containing residues.

Table 5. Genetic and related effects of aldicarb

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SAD, *Salmonella typhimurium* TA1538/1978, differential toxicity	+	0	1000.0000	Rashid & Mumma (1986)
ERD, *Escherichia coli* WP2, differential toxicity	–	0	2000.0000	Rashid & Mumma (1986)
ERD, *Escherichia coli* K12, differential toxicity	–	0	2000.0000	Rashid & Mumma (1986)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
SA0, *Salmonella typhimurium* TA100 reverse mutation	–	–	5000.0000	Zeiger *et al.* (1988)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	5000.0000	Zeiger *et al.* (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	5000.0000	Zeiger *et al.* (1988)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
SA9, *Salmonella typhimurium* TA98 reverse mutation	–	–	5000.0000	Zeiger *et al.* (1988)
SAS, *Salmonella typhimurium* TA97, reverse mutation	–	–	5000.0000	Zeiger *et al.* (1988)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	–	–	5000.0000	Dunkel *et al.* (1985)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	+	0	2600.0000	Caspary *et al.* (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	+	+	1300.0000	Mitchell *et al.* (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	–	+	1000.0000	Myhr & Caspary (1988)
DIH, DNA strand breakage, human skin fibroblasts *in vitro*	–	0	1.9000	Blevins *et al.* (1977)
GIH, Gene mutation, human lymphoblastoid TK6 cells, *tk* locus	+	0	1600.0000	Caspary *et al.* (1988)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	+	0.0000	Debuyst & Van Larebeke (1983; abstract)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	(+)	+	40.0000	Cid & Matos (1984)
CHL, Chromosomal aberrations, human lymphocytes *in vitro*	(+)	+	350.0000	Cid & Matos (1987)
CBA, Chromosomal aberrations, rat bone-marrow *in vivo*	+	0	0.0012 × 5 i.p.	Sharaf *et al.* (1982)

[a] +, positive; (+), weak positive; –, negative; 0, not tested
[b] In-vitro tests, μg/ml; in-vivo tests, mg/kg bw

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Aldicarb has not been tested adequately for carcinogenicity in experimental animals.

5.4 Other relevant data

Aldicarb is highly acutely toxic: it is one of the most potent cholinesterase-inhibiting carbamate insecticides.

No data were available on the genetic and related effects of aldicarb in humans.

Aldicarb induced chromosomal aberrations in rat bone-marrow cells *in vivo*. It induced various kinds of chromosomal damage and gene mutation in cultured human cells and induced gene mutation in rodent cells. It did not cause mutation in bacteria.

5.5 Evaluation[1]

No data were available from studies in humans.

There is *inadequate evidence* for the carcinogenicity of aldicarb in experimental animals.

Overall evaluation

Aldicarb *is not classifiable as to its carcinogenicity to humans (Group 3).*

6. References

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[1]For definition of the italicized terms, see Preamble, pp. 26-28.

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