

Solvents in pesticides

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PETRELLI G, SIEPI G, MILIGI L, VINEIS P. Solvents in pesticides. *Scand J Work Environ Health* 1993;19:63-5. Solvents are extensively used in pesticide formulations. This study concerns the solvents notified to the Italian Registry of Pesticides, which has information on approximately 8000 pesticide formulations. Solvents with evidence of carcinogenicity in humans or animals, including benzene, chloroform, carbon tetrachloride, 1,2-dichloroethane, 1,4-dioxane, and 2-nitropropane, have been notified for use in pesticides. Exposure to such solvents could partly explain some of the reported excesses of leukemia and non-Hodgkin's lymphoma among farmers.

Key terms: 1,2-dichloroethane, 1,4-dioxane, 2-nitropropane, benzene, chloroform, carbon tetrachloride, farmers, leukemia, non-Hodgkin's lymphoma.

Occupational handling and spraying of pesticides involves exposure to the active compound, but also to several different chemicals which are used as additives and solvents. Organic, and particularly chlorinated, solvents have been extensively used in the past in technical formulations. Since exposure levels are highest among mixers and loaders of pesticides, it is likely that these jobs are also associated with high levels of exposure to solvents (1). The presence of organic solvents in pesticides is highly relevant to cancer risk. Benzene and other solvents have been causally linked with leukemia (2). Leukemia and non-Hodgkin's lymphoma have also been found to have a high incidence among farmers (3) and subjects occupationally exposed to some pesticides (3, 4). However, none of the studies reporting risks associated with pesticide exposure have given information on the solvents used.

In this presentation we report information on the solvents notified to the National Registry of Pesticides at the Italian National Institute of Health.

Materials and methods

The National Registry of Pesticides has been operating at the Italian National Institute of Health since 1984. According to Italian law, the marketing of a pesticide must be authorized by the Ministry of

Health. The Registry receives information on all of the technical formulations of pesticides and their single active ingredients or additives which are notified to the Ministry of Health. The information registered is the tradename, the active ingredient(s), the solvents used, and the name of the producer (5). The Registry has information on about 8000 technical formulations proposed for use in Italy between 1970 and 1990. The fact that a specific pesticide (and its ingredients) has been notified to the Registry does not imply that it has been actually used in Italy.

Results

We analyzed the information concerning solvents notified to the Registry for use in pesticide formulations. Overall, we identified 71 different solvents (table 1). Many of them were known to be actually present in technical formulations (eg, xylene in 924), while others were only notified for use with no knowledge of actual use. The solvents were then classified according to the degree of evidence of carcinogenicity, as assessed within the monograph program of the International Agency for Research on Cancer (IARC) (2, 6). Table 1 presents the degree

Table 1. Solvents notified to the Registry of Pesticides of the Italian National Institute of Health for use in pesticide formulations according to the number of technical formulations in which they were known to be present and evidence of carcinogenicity according to the IARC monograph program (6).

Chemical name	Technical formulations (N)	Evidence of carcinogenicity ^a	
		Humans	Animals
Aniline	4	I	L
Aromatic hydrocarbon	5	NE	NE
2-Bentanol	1	NE	NE
Benzene	3	S	S
Butyl alcohol	66	NE	NE

(continued)

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Table 1. Continued.

Chemical name	Technical formulations (N)	Evidence of carcinogenicity ^a	
		Humans	Animals
Butylglycol	—	NE	NE
Carbon tetrachloride ^b	16	I	S
Chloroform	2	I	S
Chloropentane	1	NE	NE
Cresol	—	NE	NE
Cyclohexanol	—	NE	NE
Cyclohexanone	186	ND	I
Dibromomethane	—	NE	NE
1,2-Dichlorobenzene	—	I	I
1,1-Dichloroethane	—	NE	NE
1,2-Dichloroethane	2	ND	S
Dichloroethylene	—	NE	NE
1,1-Dichloroethylene	—	NE	NE
1,2-Dichloropropane	—	ND	L
Diethylbenzene	1	NE	NE
Dimethyl carbonate	—	NE	NE
N,N-Dimethylformamide	17	L	I
1,4-Dioxane	2	I	S
Ethanol	2	NE	NE
Ethylbenzene	—	NE	NE
Ethylene glycol	221	NE	NE
Ethylglycol	24	NE	NE
Formol	1	NE	NE
Furfuryl alcohol	4	NE	NE
Isophorone	32	NE	NE
Isopropylglycol	—	NE	NE
Kerosene	2	NE	NE
Mesityl oxide	3	NE	NE
Mesitylene	8	NE	NE
Methanol	17	NE	NE
2-Methoxypropanol	—	NE	NE
Methylmetacrylate	—	ND	I
Methylcyclohexanol	—	NE	NE
Methylcyclohexanone	—	NE	NE
Methylglycol	10	NE	NE
Methylisobutylcarbinol	—	NE	NE
N-Methylpyrrolidone	—	NE	NE
Monochlorobenzene	17	NE	NE
Naphtha	41	NE	NE
Nitrile acetic acid	4	NE	NE
Nitrobenzene	—	NE	NE
1-Nitropropane	1	NE	NE
2-Nitropropane	1	ND	S
Oil of turpentine	—	NE	NE
O-Chlorotoluene	1	NE	NE
Paraffin	—	NE	NE
Pentachloroethane	—	ND	L
Phenol	1	NE	NE
Propylbenzene	—	NE	NE
Propylbromide	—	NE	NE
Propyl chloride	—	NE	NE
Propylene glycol	59	NE	NE
Pyridine	—	NE	NE
Styrene	—	I	L
Tetrabenzylphenol	—	NE	NE
1,1,2,2-Tetrachloroethane	—	I	L
Tetrachloroethylene	4	I	L
Tetrahydrofuran	—	NE	NE
Tetrahydronaphthalene	1	NE	NE
Toluene	4	I	I
1,1,1-Trichloroethane	14	ND	I
1,1,2-Trichloroethane	1	ND	L
Trichloroethylene	1	I	L
Trimethylbenzene	9	NE	NE
Vinyltoluene	—	NE	NE
Xylene	924	I	I

^a I = inadequate evidence, L = limited evidence, ND = no data available, NE = data not evaluated, S = sufficient evidence.

^b Used as an active ingredient.

Table 2. Active ingredients of the technical formulations containing solvents with sufficient evidence of carcinogenicity in humans or animals.

Solvent	Active ingredient of the pesticide formulation ^a
Benzene	Cypermethrin (10%)
Benzene + xylene	Alachlor (30%)
Benzene + xylene + cyclohexanol	Dimethoate (38%)
Carbon tetrachloride	Used as active ingredient
Chloroform	Dichlorvos (25%)
1,2-Dichloroethane	Glycerophthalic resin (50%) Polyglycerylphthalate (—)
1,4-Dioxane + 2-nitropropane	Metalddehyde (5%)
1,4-Dioxane + cyclohexanol	Binapacryl (80%)

^a Concentration percentage of the solvent in parentheses.

of evidence of carcinogenicity in humans and experimental animals for each solvent which has been considered in IARC monographs 1 through 53. For each solvent, the table also reports the number of technical formulations in which it was known to be present.

For solvents with sufficient evidence of carcinogenicity, either in humans or in animals, table 2 presents the names of the active ingredients of the technical formulations in which they were used.

Discussion

Through an examination of about 8000 pesticide formulations registered in the Registry of Pesticides at the Italian National Institute of Health, we have identified 71 different solvents notified for use. Some of these solvents have "sufficient" evidence of carcinogenicity in humans or animals or both, including benzene and other chlorinated compounds. The presence of such chemicals in pesticides indicates that the exposure of farmers and applicators could occur; exposure would be particularly high in the case of mixers and loaders.

Several studies among farmers have found excess risks for leukemia and non-Hodgkin's lymphoma (3). One study in particular has reported elevated relative risks for leukemia among subjects exposed to crotoxyphos, dichlorvos, famphur, pyrethrins, and metoxychlor (4). According to our survey, dichlorvos, extensively used in Italy in the past, contains chloroform (a carcinogen in animals), xylene, 1,1,1-trichloroethane, butyl alcohol, and aliphatic hydrocarbons. Although there is clear evidence of carcinogenicity for only one of these chemicals, the presence of chlorinated solvents in many pesticides might at least partly explain some of the leukemia excesses.

Future epidemiologic studies on the risk of cancer among farmers should consider solvents as one of the relevant exposures. This goal could be attained, for example, by the use of pesticide-solvent matrices in case-referent studies.

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