

## INTRODUCTION

In 1971 the International Agency for Research on Cancer (IARC) began a programme to prepare monographs on the evaluation of the carcinogenic risk of chemicals to humans (1). The objectives of the Monographs Programme are to examine critically the data relating to carcinogenicity for chemicals to which humans are known to be exposed; to evaluate these data with the help of experts in chemical carcinogenesis, epidemiology, and related fields; and to make this information available for the primary prevention of cancer. Selection of chemicals for evaluation is based on two criteria: firstly, there are data related to carcinogenicity in humans or experimental animals; and secondly, there is evidence of human exposure (2).

In the first sixteen volumes of the monographs the assessments of carcinogenicity in humans and experimental animals were made separately. No attempt was made to estimate carcinogenic risk to humans on the basis of data from experimental animals. However, most of the chemicals evaluated in the monographs had only data from animal studies; specifically, more than 350 chemicals were evaluated in Volumes 1-16, while human data were available for only 48 (14%) of them. In cases where there was no information available from studies in humans, the IARC was asked repeatedly to consider making an assessment of the carcinogenic risk for humans which was based only on animal data.

An *ad hoc* Working Group met in October 1977 to review the criteria for the assessment of the carcinogenic risk of chemicals to humans (3). The group drafted guidelines for subsequent Working Groups which standardize the evaluations of carcinogenicity studies both in humans and in animals. More importantly, they recommend that in the absence of adequate data in humans it is reasonable, for practical purposes, to regard chemicals for which there is *sufficient evidence* of carcinogenicity (i.e. a causal association) in animals *as if they presented a carcinogenic risk for humans*. The use of the expressions "for practical purposes" and "as if they presented a carcinogenic risk" indicates that at the present time a correlation between carcinogenicity in animals and possible human risk cannot be made on a scientific basis, but rather only pragmatically, with the intent of helping regulatory agencies in making decisions related to the primary prevention of cancer.

These guidelines were adopted starting with Volume 17 of the Monographs. However, since these criteria were not used for Volumes 1-16, a further *ad hoc* Working Group was convened to re-evaluate the data from animal studies for substances evaluated in those volumes, and to identify those for which there is *sufficient evidence* of carcinogenicity (4).

This Working Group did not consider chemicals or industrial processes for which epidemiological data or case reports suggested an association with the occurrence of cancer in humans (5).

By the end of 1978, twenty volumes of Monographs had been prepared. Of the 442 chemicals and industrial processes evaluated therein, there is *sufficient evidence* of carcinogenicity in experimental animals for 142 (32%) of them. These chemicals are listed in Table 1. Case reports or epidemiological studies have been published for only 60 of the 442 (14%). Because of time limitations, six compounds with limited data on human carcinogenicity were not considered by the Working Group. These compounds are listed in Table 2, and summaries of the animal and human evidence (without evaluations) are given at the end of the appendix. The Group also did not consider sex hormone preparations (with the exception of diethylstilboestrol), since they had recently been re-evaluated for volume 21. There were thus 54 chemicals and industrial processes with data on carcinogenicity from human and animal studies reviewed by the Working Group.

Table 1. Chemicals evaluated in *IARC Monographs*, Volumes 1-20 for which there is *sufficient evidence* of carcinogenicity in experimental animals<sup>1</sup>

Compound	IARC Monograph volume and page number
<u>A</u>	
<i>Acrylonitrile</i> <sup>1</sup>	19, 73
Actinomycins	10, 29
<i>Aflatoxins</i>	10, 51
<i>ortho</i> -Aminozotoluene	8, 61
<i>4</i> -Aminobiphenyl	1, 74
2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole	7, 143
<i>Amitrole</i>	7, 31
Aramite	5, 39
<i>Asbestos</i>	14
Azaserine	10, 73
<u>B</u>	
Benz[ <i>a</i> ]anthracene	3, 45
<i>Benzidine</i>	1, 80
Benzo[ <i>b</i> ]fluoranthene	3, 69
Benzo[ <i>a</i> ]pyrene	3, 91
Benzyl violet 4B	16, 153
<i>Beryllium</i>	1, 17
Beryllium oxide	1, 17
Beryllium phosphate	1, 17
Beryllium sulphate	1, 17
<i>Bis(chloromethyl) ether</i>	4, 231
$\beta$ -Butyrolactone	11, 225

<sup>1</sup> Chemicals with data on cancer in humans appear in italics.

Compound	IARC Monograph volume and page number
<u>C</u>	
<i>Cadmium</i>	2, 74; 11, 39
Cadmium chloride	2, 74; 11, 39
Cadmium oxide	2, 74; 11, 39
Cadmium sulphate	2, 74; 11, 39
Cadmium sulphide	2, 74; 11, 39
Calcium chromate	2,100
<i>Carbon tetrachloride</i>	1, 53; 20
<i>Chlorambucil</i>	9,125
Chlordecone (Kepone)	20
Chloroform	20
<i>Chromium</i>	2,100
Citrus red no. 2	8,101
Cycasin	1,157; 10,121
<i>Cyclophosphamide</i>	9,135
<u>D</u>	
Daunomycin	10,145
N,N'-Diacetylbenzidine	16,293
4,4'-Diaminodiphenyl ether	16,301
2,4-Diaminotoluene	16, 83
Dibenz[ <i>a,h</i> ]acridine	3,247
Dibenz[ <i>a,j</i> ]acridine	3,254
Dibenz[ <i>a,h</i> ]anthracene	3,178
7H-Dibenzo[ <i>c,g</i> ]carbazole	3,260
Dibenzo[ <i>a,e</i> ]pyrene	3,201
Dibenzo[ <i>a,h</i> ]pyrene	3,207
Dibenzo[ <i>a,i</i> ]pyrene	3,215
1,2-Dibromo-3-chloropropane	15,139; 20
<i>3,3'-Dichlorobenzidine</i>	4, 49
3,3'-Dichloro-4,4'-diaminodiphenyl ether	16,309
1,2-Dichloroethane	20
Diepoxybutane	11,115
1,2-Diethylhydrazine	4,153
<i>Diethylstilboestrol</i>	6, 55; 20
Diethyl sulphate	4,277
Dihydrosafrole	1,170; 10,233
3,3'-Dimethoxybenzidine ( <i>ortho</i> -Dianisidine)	4, 41
<i>para</i> -Dimethylaminoazobenzene	8,125
<i>trans</i> -2[(Dimethylamino)methylimino]-5-[2-(5-nitro-2-furyl)vinyl]-1,3,4-oxadiazole	7,147
3,3'-Dimethylbenzidine ( <i>ortho</i> -Tolidine)	1, 87
<i>Dimethylcarbamoyl chloride</i>	12, 77
1,1-Dimethylhydrazine	4,137
1,2-Dimethylhydrazine	4,145
<i>Dimethyl sulphate</i>	4,271
1,4-Dioxane	11,247

Compound	IARC Monograph volume and page number
<u>E</u>	
Ethinylloestradiol	6, 77
Ethylene dibromide	15,195
Ethylenethiourea	7, 45
Ethyl methanesulphonate	7,245
<u>F</u>	
2-(2-Formylhydrazino)-4-(5-nitro-2-furyl) thiazole	7,151
<u>G</u>	
Glycidaldehyde	11,175
<u>H</u>	
Hexachlorobenzene	20
Hexamethylphosphoramide	15,211
Hydrazine	4,127
<u>I</u>	
Indeno[1,2,3- <i>cd</i> ]pyrene	3,229
<i>Iron dextran</i>	2,161
Isosafrole	1,169; 10,232
<u>L</u>	
Lasiocarpine	10,281
Lead acetate	1, 40
Lead phosphate	1, 40
Lead subacetate	1, 40
<u>M</u>	
<i>Melphalan</i>	9,167
Merphalan	9,167
Mestranol	6, 87
2-Methylaziridine	9, 61
Methylazoxymethanol acetate	1,164; 10,131
4,4'-Methylene bis(2-chloroaniline)	4, 65
4,4'-Methylene bis(2-methylaniline)	4, 73
Methyl iodide	15,245
Methyl methanesulphonate	7,253
N-Methyl-N'-nitro-N-nitrosoguanidine	4,183
Methylthiouracil	7, 53
Mirex	5,203; 20

Compound	IARC Monograph volume and page number
Mitomycin C	10,171
Monocrotaline	10,291
5-(Morpholinomethyl)-3-[(5-nitro- furfurylidene)-amino]-2-oxazolidinone	7,161
<u>N</u>	
<i>2-Naphthylamine</i>	4, 97
<i>Nickel</i>	2,126; 11, 75
Nickel subsulphide	2,126; 11, 75
Niridazole	13,123
5-Nitroacenaphthene	16,319
1-[(5-Nitrofurfurylidene)amino]-2- imidazolidinone	7,181
N-[4-(5-Nitro-2-furyl)-2-thiazolyl]acetamide	1,181; 7,185
Nitrogen mustard and its hydrochloride	9,193
Nitrogen mustard N-oxide and its hydrochloride	9,209
N-Nitrosodi- <i>n</i> -butylamine	4,197; 17, 51
N-Nitrosodiethanolamine	17, 77
N-Nitrosodiethylamine	1,107; 17, 83
N-Nitrosodimethylamine	1, 95; 17,125
N-Nitrosodi- <i>n</i> -propylamine	17,177
N-Nitroso-N-ethylurea	1,135; 17,191
N-Nitrosomethylethylamine	17,221
N-Nitroso-N-methylurea	1,125; 17,227
N-Nitroso-N-methylurethane	4,211
N-Nitrosomethylvinylamine	17,257
N-Nitrosomorpholine	17,263
N-Nitrosornicotine	17,281
N-Nitrosopiperidine	17,287
N-Nitrosopyrrolidine	17,313
N-Nitrososarcosine	17,327
<u>O</u>	
Oestradiol-17 $\beta$	6, 99
Oestrone	6,123
Oil orange SS	8,165
<u>P</u>	
<i>Polychlorinated biphenyls</i>	18, 43
Ponceau MX	8,189
Ponceau 3R	8,199
1,3-Propane sultone	4,253
$\beta$ -Propiolactone	4,259
Propylthiouracil	7, 67

Compound	IARC Monograph volume and page number
<u>S</u>	
Safrole	1,169; 10,231
<i>Soots, tars and oils</i>	3, 22
Sterigmatocystin	1,175; 10,245
Streptozotocin	4,221; 17,337
<u>T</u>	
Testosterone	6,209
Thioacetamide	7, 77
Thiourea	7, 95
Toxaphene	20
<i>Tris(aziridinyl)phosphine sulphide</i> <i>(thiotepa)</i>	9, 85
Tris(2,3-dibromopropyl)phosphate	20
Trypan blue (commercial grade)	8,267
<u>U</u>	
Uracil mustard	9,235
Urethane	7,111
<u>V</u>	
<i>Vinyl chloride</i>	7,291; 19,377

Table 2. Chemicals from IARC Monographs Volumes 1-20 with evidence from human studies which were not considered by the Working Group.

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*ortho*- and *para*-Dichlorobenzene  
Dichlorobenzidine  
Phenylbutazone  
2,3,7,8-Tetrachlorodibenzo-*para*-dioxin (TCDD)  
*ortho*- and *para*-Toluidine  
Vinylidene chloride

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