HYDROGEN PEROXIDE

Data were last reviewed in IARC (1985) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 7722-84-1
Chem. Abstr. Name: Hydrogen peroxide
IUPAC Systematic Name: Hydrogen peroxide
Synonyms: Dihydrogen dioxide; hydrogen dioxide; hydrogen oxide; hydroperoxide; peroxide

1.1.2 *Structural and molecular formulae and relative molecular mass*

H_2O_2 Relative molecular mass: 34.0

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Colourless liquid with a bitter taste (Budavari, 1996; Lide, 997)
(*b*) *Boiling-point:* 150.2°C (Lide, 1997)
(*c*) *Melting-point:* –0.43°C (Lide, 1997)
(*d*) *Solubility:* Very soluble in water; soluble in diethyl ether; insoluble in petroleum ether (Budavari, 1996; Lide, 1997)
(*e*) *Vapour pressure:* 665 Pa at 30°C (American Conference of Governmental Industrial Hygienists, 1992)
(*f*) *Reactivity*: May decompose violently if traces of impurities are present; decomposed by many organic solvents (Budavari, 1996)
(*g*) *Conversion factor*: $mg/m^3 = 1.39 \times ppm$

1.2 Production and use

Production capacity of hydrogen peroxide in North America (including plants in the United States, Canada and Mexico) in 1995 was reported to be 547 thousand tonnes; that in the United States in 1992 was reported to be 348 thousand tonnes and, in Canada, 143

thousand tonnes. Worldwide capacity for hydrogen peroxide is estimated at 1800–1900 thousand tonnes per year (Anon., 1992, 1995; Hess, 1995).

Hydrogen peroxide is an oxidizing agent widely used for the bleaching or deodorizing of textiles, wood pulp, hair, fur and foods; in the treatment of water and sewage; as a disinfectant; as a component of rocket fuels; and in the manufacture of paper and pulp, foam rubber and many chemicals and chemical products. It has also been used in the synthesis of organic and inorganic peroxides; in the manufacture of glycerol, plasticizers and antichlors; in epoxidation, hydroxylation, oxidation, and reduction reactions; for viscosity control for starch and cellulose derivatives; for refining and cleaning metals; in dyeing and electroplating; and as a laboratory reagent, seed disinfectant and neutralizing agent in wine distillation (IARC, 1985; American Conference of Governmental Industrial Hygienists, 1992; Lewis, 1993).

Other uses for hydrogen peroxide in the United States are in the removal of hydrogen sulfide from the steam produced by geothermal power plants, during the mining and processing of uranium, pickling of copper and copper alloys, cleaning metals (germanium) and silicon semiconductors used in the electronics industry, and a variety of small-volume applications in photography, cosmetics (e.g., hair bleaches and dyes, mouthwashes), antiseptics and cleansing agents, food and wine processing and treatment of package liners in aseptic packaging (IARC, 1985).

The consumption pattern for hydrogen peroxide in the United States in 1995 was (%): pulp and paper, 50; environmental uses, including water treatment, 17; chemical synthesis, 15; textiles, 9; and miscellaneous, including mining, electronic, food and cosmetic uses, and the distributor market, 9 (Anon., 1995).

1.3 Occurrence

1.3.1 *Occupational exposure*

Occupational exposures may occur in the production of hydrogen peroxide, in wastewater treatment, metal cleaning, and chemical synthesis, and in the textile, pulp and paper, geothermal energy and mining industries (IARC, 1985).

1.3.2 *Environmental occurrence*

Gaseous hydrogen peroxide is a key component and product of the earth's lower atmospheric photochemical reactions, in both clean and polluted atmospheres. Atmospheric hydrogen peroxide is believed to be generated exclusively by gas-phase photochemical reactions (IARC, 1985). Low concentrations of hydrogen peroxide have been measured in the gas-phase and in cloud water in the United States (United States National Library of Medicine, 1998). It has been found in rain and surface water, in human and plant tissues, in foods and beverages and in bacteria (IARC, 1985).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 1.4 mg/m^3 as the 8-h time-weighted average threshold limit value for

occupational exposures to hydrogen peroxide in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for hydrogen peroxide in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

In the Montreal case–control study carried out by Siemiatycki (1991) (see the monograph on dichloromethane in this volume), the investigators estimated the associations between 293 workplace substances and several types of cancer. Hydrogen peroxide was one of the substances. About 0.7% of the study subjects had ever been exposed to hydrogen peroxide. Among the main occupations to which this exposure was attributed were hairdressers, textile bleachers and furriers. For all types of cancer examined (oesophagus, stomach, colon, rectum, pancreas, lung, prostate, bladder, kidney, skin melanoma, lymphoma), there was no indication of an excess risk due to hydrogen peroxide exposure. [The interpretation of the null results has to take into account the small numbers and possibly low exposure levels.]

3. Studies of Cancer in Experimental Animals

Hydrogen peroxide had been tested for carcinogenicity in mice, by oral administration in drinking-water, by skin application and by subcutaneous administration. Adenomas and carcinomas of the duodenum were reported following its oral administration. The other studies were inadequate for an evaluation of carcinogenicity. One study by skin application indicated that hydrogen peroxide has no promoting activity (IARC, 1985).

3.1 Topical administration

Hamster: Groups of 25 male and 25 female Syrian golden hamsters, 8–10 weeks of age, were administered hydrogen peroxide at a concentration of 0.75% in dentifrice introduced into the buccal cheek pouches five times per week for 20 weeks. The hydrogen peroxide-containing dentifrice induced no neoplasms in 37 animals surviving to 20 weeks (Marshall *et al*., 1996). [The Working Group noted the unusual vehicle and the short duration of the study.]

3.2 Administration with known carcinogens

3.2.1 *Hamster*

Groups of 30–40 male and female Syrian golden hamsters, eight weeks of age, were administered hydrogen peroxide [purity unspecified] by topical application to the cheek pouch of 20 μL of a 30% solution on five days per week for 24 weeks, after which they

were maintained for up to 16 months. Another group received hydrogen peroxide for 24 weeks after an initiating dose of 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone, after which they were also maintained for up to 16 months. In the group given hydrogen peroxide after initiation, 1/31 animals developed a cheek pouch adenoma, compared with 1/15 with initiator alone (Padma *et al*., 1989).

3.2.2 *Trout*

Groups of 52–93 Shasta rainbow trout embryos, 23 days of age, were exposed to *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine to initiate hepatic carcinogenesis and four weeks after hatching were administered hydrogen peroxide [purity unspecified] at 0, 600 or 3000 ppm [mg/kg] in diets containing two levels of vitamin E for 10 months. Hydrogen peroxide increased the incidence of liver tumours, mainly mixed hepatocholangiocellular carcinomas, in a dose-related manner, especially in fish given the higher level of vitamin E, from about 15% in fish exposed only to the initiator to about 25% with low-dose hydrogen peroxide and to about 45% with high-dose hydrogen peroxide ($p < 0.02$) (Kelly *et al*., 1992). [The Working Group noted the complexity of oral administration in the diet and the presence of other variables in the diets.]

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

Glutathione peroxidase, responsible for decomposing hydrogen peroxide, is present in normal human tissues. Hydrogen peroxide has been detected in serum and in intact liver (IARC, 1985).

4.1.2 *Experimental systems*

Hydrogen peroxide is formed intracellularly by mitochondria, endoplasmic reticulum, peroxisomes and soluble enzymes, where it results from oxidase-catalysed reactions or superoxide dismutase-catalysed superoxide breakdown. It is decomposed by catalase or glutathione peroxidase. Levels of hydrogen peroxide are particularly high in rat kidney, reflecting the high peroxisomal content, and polymorphonuclear leukocytes during phagocytosis (IARC, 1985). These levels are markedly increased in rat liver homogenates after in-vivo administration of peroxisome proliferators (Tamura *et al*., 1990).

The presence of oxygen bubbles in the tongue and jugular veins following sublingual application of 3–30% hydrogen peroxide solutions to dogs, cats and rabbits suggests that significant amounts of hydrogen peroxide were absorbed. Ingested hydrogen peroxide can increase the oxygen content of blood, also indicating absorption by the intestine. It can penetrate the epidermis and mucous membranes and decomposes in the underlying

tissues. Within 1 h, 33% of the ^{18}O of a 19% solution of $H_2{}^{18}O_2$ was recovered in expired air following sublingual application to cats (IARC, 1985).

4.2 Toxic effects

The toxicity of hydrogen peroxide has been reviewed (Li, 1996).

4.2.1 *Humans*

A characteristic whitening of the skin occurs after topical application of hydrogen peroxide, which is believed to be the result of oxygen bubbles acting microembolically in the capillaries. Human erythrocytes exhibit increased osmotic fragility when incubated with hydrogen peroxide; this is related to lipid peroxidation. Erythrocytes from individuals with enzyme deficiencies related to oxygen radical metabolism, such as those with acatalasaemia, favism, paroxysmal nocturnal haemoglobinuria, erythropoietic protoporphyria or thalassaemia, or with glutathione-metabolizing enzyme or vitamin E deficiencies, are unusually sensitive to hydrogen peroxide-induced haemolysis (IARC, 1985).

4.2.2 *Experimental systems*

Hydrogen peroxide, administered extrinsically or produced intrinsically, generates hydroxyl radicals and induces lipid peroxidation and may lead to DNA damage and cell death. In in-vitro studies, these effects may be prevented by antioxidants or iron chelators (IARC, 1985). In line with these findings, hydrogen peroxide evoked a dose-dependent increase in dichlorofluorescein fluorescence intensity in Hep G_2 cells, and this effect was completely blocked by catalase or a water-soluble vitamin E (Trolox C) (Wu *et al*., 1997). Low (10^{-8} mol/L), but not high ($\geq 10^{-5}$ mol/L) concentrations of hydrogen peroxide stimulated the growth of immortalized hamster BHK-2 cells, H-*ras* transformed RFAGT1 rat cells (Burdon *et al*., 1990) and BHK-21 fibroblasts *in vitro* (Burdon *et al*., 1996).

Hydrogen peroxide induced squamous metaplasia in hamster tracheal explants at concentrations of 50–100 μmol/L, while cytotoxicity was observed only at concentrations ≥ 500 μmol/L. Squamous metaplasia was prevented by exogenous addition of catalase (Radosevich & Weitzman, 1989).

At a concentration of 700 μmol/L, hydrogen peroxide induced necrosis of immortalized rat embryo fibroblasts, while at a concentration of 150 μmol/L, it induced apoptosis (Guénal *et al*., 1997). In primary human diploid fibroblasts, low concentrations (50–100 μmol/L) of hydrogen peroxide induced a senescence-like state, while higher concentrations (300–400 μmol/L) induced apoptosis (Bladier *et al*., 1997). Apoptosis was also observed in BHK-21 fibroblasts at hydrogen peroxide concentrations of ≥ 100 μmol/L (Burdon *et al*., 1996).

Hydrogen peroxide (50 μmol/L) induced transcription of the early growth response 1 gene (*EGR*1) in a human HL-525 myeloid leukaemia cell line; this was prevented by *N*-acetyl-L-cysteine (Datta *et al*., 1993).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

Hydrogen peroxide induced DNA damage in bacteria and mutation in *Salmonella typhimurium* and *Escherichia coli* in the absence of exogenous metabolic activation. It was not mutagenic in *S. typhimurium* in the presence of exogenous metabolic activation. It induced forward mutation in *Saccharomyces cerevisiae* and was mutagenic to *Aspergillus nidulans* and *Neurospora crassa*. In a single study, sex-linked recessive lethal mutations were not induced in *Drosophila* following larval injections with 3% hydrogen peroxide.

Hydrogen peroxide induced DNA damage in Chinese hamster cell cultures. It induced a weak mutagenic response at the *hprt* locus in one study using L5178Y mouse lymphoma cell sublines (LY-R and LY-S). Only one of six studies reviewed reported that hydrogen peroxide induced gene mutation in Chinese hamster V79 cells at the *hprt* locus. Hydrogen peroxide induced sister chromatid exchanges in Chinese hamster cell cultures (Chinese hamster ovary CHO or lung V79) and inhibited gap junctional intercellular communication in WB-Fischer 344 rat liver epithelial cells. It did not bind covalently to DNA in mouse keratinocytes *in vitro*. It did induce chromosomal aberrations in Chinese hamster cells and in ascites tumour cells of mice treated *in vivo*. In a single study *in vivo*, hydrogen peroxide did not increase the frequency of chromosomal aberrations in rat bone marrow.

DNA single-strand breaks and fragmentations were observed in human lymphocytes and respiratory tract epithelial cells and in cultures of transformed human cells. Hydrogen peroxide induced unscheduled DNA synthesis and chromosomal aberrations in human fibroblast cells *in vitro*. It induced sister chromatid exchanges or chromosomal aberrations in human lymphocyte cultures and gave inconclusive results for induction of aneuploidy.

Hydrogen peroxide transformed mouse myeloid progenitor cells (FDC-P1) from interleukin-3 dependence to factor independence, but only at cytotoxic concentrations (≥ 12/5 μmol/L). Such a transformation was not induced by non-specific insults to the cells, such as sodium fluoride or heat shock treatment. The transformed cells produced tumours when injected into pre-irradiated mice (Crawford & Greenberger, 1991). Hydrogen peroxide (10 μmol/L) induced overexpression of the proto-oncogene c-*jun* in hamster tracheal epithelial (HTE) cells; c-*jun* overexpression led to proliferation and increased growth rate, as well as increased anchorage-independence of HTE cells (Timblin *et al*., 1995).

Table 1. Genetic and related effects of hydrogen peroxide

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
PRB, Prophage, induction/SOS response/strand-breaks/or cross-links	+	NT	0.5	Müller & Janz (1993)
PRB, Prophage, induction/SOS response/strand-breaks/or cross-links	+	NT	1	Northrop (1958)
PRB, Prophage, induction/SOS response/strand-breaks/or cross-links	+	NT	45	Nakamura *et al*. (1987)
BRD, *Escherichia coli*, differential toxicity	+	NT	20	Hartman & Eisenstark (1978)
BRD, *Escherichia coli*, differential toxicity	+	NT	340	Ananthaswamy & Eisenstark (1977)
SAF, *Salmonella typhimurium* BA13, forward mutation	+	NT	0.2	Ariza *et al*. (1988)
SAF, *Salmonella typhimurium* (SV50), forward mutation	+	NT	0.22	Xu *et al*. (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	NT	340	Stich *et al*. (1978)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	NT	136	Norkus *et al*. (1983)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	0.9	Xu *et al*. (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	NT	5	Fujita *et al*. (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	–	5780	Kensese & Smith (1989)
SA2, *Salmonella typhimurium* TA102, reverse mutation	(+)	–	5780	Kensese & Smith (1989)
SA2, *Salmonella typhimurium* TA102, reverse mutation	(+)	NT	20.4	Abu-Shakra & Zeiger (1990)
SA4, *Salmonella typhimurium* TA104, reverse mutation	+	NT	10	Abu-Shakra & Zeiger (1990)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	+	–	4046	Kensese & Smith (1989)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	(+)	–	5780	Kensese & Smith (1989)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	NT	340	Stich *et al*. (1978)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	0.9	Xu *et al*. (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	–	5780	Kensese & Smith (1989)
SAS, *Salmonella typhimurium* hisC3108, reverse mutation	+	NT	30	Ames *et al*. (1981)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
SAS, *Salmonella typhimurium* TA96, reverse mutation	+	NT	50	Levin *et al*. (1982)
SAS, *Salmonella typhimurium* TA97, reverse mutation	(+)	–	2890	Kensese & Smith (1989)
SAS, *Salmonella typhimurium* TA97, reverse mutation	+	NT	4.25	Abu-Shakra & Zeiger (1990)
SAS, *Salmonella typhimurium* SB1106p, reverse mutation	+	NT	5.1	Abu-Shakra & Zeiger (1990)
SAS, *Salmonella typhimurium* SB1111, reverse mutation	(+)	NT	10	Abu-Shakra & Zeiger (1990)
SAS, *Salmonella typhimurium* SB1106, reverse mutation	+	NT	10	Abu-Shakra & Zeiger (1990)
ECF, *Escherichia coli* (excluding K12), forward mutation	+	NT	3	Abril & Pueyo (1990)
ECR, *Escherichia coli* WP2, reverse mutation	+	NT	2160	Demerec *et al*. (1951)
BSM, *Bacillus subtilis*, multigene test	+	NT	7.2	Sacks & MacGregor (1982)
MAF, *Micrococcus aureus*, forward mutation	+	NT	6	Clark (1953)
SCF, *Saccharomyces cerevisiae ade2*, forward mutation	+	NT	100	Thacker (1976)
SCF, *Saccharomyces cerevisiae ade2*, forward mutation	+	NT	2000	Thacker & Parker (1976)
SGR, *Streptomyces griseoflavus*, reverse mutation	–	NT	1440	Mashima & Ikeda (1958)
ANR, *Aspergillus chevalieres*, reverse mutation	(+)	NT	1440	Nanda *et al*. (1975)
NCF, *Neurospora crassa*, forward mutation	(+)	NT	9180	Han (1997)
NCR, *Neurospora crassa*, reverse mutation	+	NT	7140	Dickey *et al*. (1949)
NCR, *Neurospora crassa*, reverse mutation	+	NT	6800	Jensen *et al*. (1951)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	–		43200 inj	Dipaolo (1952)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
DIA, DNA single-strand breaks, Chinese hamster lung V79 cells *in vitro*	(+)[c]	NT	12	Bradley *et al*. (1979)
DIA, DNA single-strand breaks, rat hepatocytes *in vitro*	+	NT	3.4	Olson (1988)
DIA, DNA single-strand breaks, Chinese hamster ovary CHO cells *in vitro*	+	NT	3.4	Cantoni *et al*. (1989)
DIA, DNA single-strand breaks, Chinese hamster lung V79-379A fibroblasts *in vitro*	+	NT	0.34	Prise *et al*. (1989)
DIA, DNA single-strand breaks, Chinese hamster ovary CHO cells *in vitro*	+	NT	0.85	Cantoni *et al*. (1992)
DIA, DNA single-strand breaks, Chinese hamster ovary CHO cells *in vitro*	+	NT	0.68	Iliakis *et al*. (1992)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	–	NT	12	Bradley *et al*. (1979)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	–	NT	20	Bradley & Erickson (1981)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	–	NT	3.4	Tsuda (1981)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	–	NT	7	Nishi *et al*. (1984)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	–	NT	13.6	Speit (1986)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	+	NT	17	Ziegler-Skylakakis & Andrae (1987)
G9O, Gene mutation, Chinese hamster lung V79 cells, ouabain resistance *in vitro*	–	NT	3.4	Tsuda (1981)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
G51, Gene mutation, mouse lymphoma L5178Y cell subline LY-R, *hprt* locus *in vitro*	(+)	NT	0.17	Kruszewski *et al*. (1994)
G51, Gene mutation, mouse lymphoma L5178Y cell subline LY-S, *hprt* locus *in vitro*	(+)	NT	0.34	Kruszewski *et al*. (1994)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	(+)	NT	12	Bradley *et al*. (1979)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	NT	0.13	MacRae & Stich (1979)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	(+)	NT	17	Wilmer & Natarajan (1981)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	+	NT	3.4	Speit *et al*. (1982)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	+	(+)	0.34	Mehnert *et al*. (1984a)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	(+)	0.34	Mehnert *et al*. (1984a)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	(+)	NT	7	Nishi *et al*. (1984)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	+	NT	0.68	Speit (1986)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO AU × 91 cells *in vitro*	+	NT	1.4	Tucker *et al*. (1989)
MIA, Micronucleus test, C57BL/6J mouse splenocytes *in vitro*	–	NT	0.68	Dreosti *et al*. (1990)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	(+)	NT	10	Stich *et al*. (1978)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
CIC, Chromosomal aberrations, Chinese hamster DON-6 cells *in vitro*	+	NT	34	Sasaki *et al*. (1980)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO-K1 cells *in vitro*	+	NT	3.4	Tsuda (1981)
CIC, Chromosomal aberrations, Chinese hamster lung V79 cells *in vitro*	+	NT	3.4	Tsuda (1981)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	(+)	NT	340	Wilmer & Natarajan (1981)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	(+)	NT	1	Hanham *et al*. (1983)
CIM, Chromosomal aberrations, newborn BALB/c mouse back-skin cells *in vitro*	+	NT	0.34	Tsuda (1981)
CIS, Chromosomal aberrations, Syrian hamster lung cells *in vitro*	+	NT	3.4	Tsuda (1981)
DIH, DNA single-strand breaks, transformed human WI-38 & XP cells *in vitro*	(+)	NT	3.4	Hoffmann & Meneghini (1979)
DIH, DNA single-strand breaks, human D98/AH2 cells *in vitro*	+	NT	2	Wang *et al*. (1980)
DIH, DNA single-strand breaks, human epithelioid P3 cells *in vitro*	+	NT	0.21	Peak *et al*. (1991)
DIH, DNA single-strand breaks, human cells *in vitro*	+	NT	0.85	Meyers *et al*. (1993)
DIH, DNA single-strand breaks, human leukocytes *in vitro*	+	NT	17	Rueff *et al*. (1993)
DIH, DNA damage, human bronchial epithelium (HBEI) cells *in vitro*	+	NT	1.7	Spencer *et al*. (1995)
DIH, DNA damage, human bronchial epithelium (BEAS and NHBE) cells *in vitro*	+	NT	0.68	Lee *et al*. (1996)
DIH, DNA damage, human lymphobastoid (GM1899A) cells *in vitro*	+[d]	NT	0.34	Duthie & Collins (1997)
UHF, Unscheduled DNA synthesis, human fibroblasts *in vitro*	+	NT	20	Stich *et al*. (1978)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
UHF, Unscheduled DNA synthesis, human fibroblasts *in vitro*	+	NT	9	Coppinger *et al*. (1983)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	(+)	2.7	Mehnert *et al*. (1984b)
CHF, Chromosomal aberrations, human fibroblasts *in vitro*	+	NT	0.07	Parshad *et al*. (1980)
CHL, Chromosomal aberrations, human lymphocytes *in vitro*	–	NT	0.17	Smith *et al*. (1990)
CIH, Chromosomal aberrations, human embryonic fibroblasts *in vitro*	+	NT	0.34	Oya *et al*. (1986)
CIH, Chromosomal aberrations, human lymphocytes *in vitro*	+	NT	510	Rueff *et al*. (1993)
AIH, Aneuploidy, human lymphocytes *in vitro*	?	NT	0.17	Smith *et al*. (1990)
CBA, Chromosomal aberrations, rat bone-marrow cells *in vivo*	–		NG	Kawachi *et al*. (1980)
CVA, Chromosomal aberrations, mouse ascites tumour cells *in vivo*	+		340 µg/mouse	Schöneich (1967)
CVA, Chromosomal aberrations, mouse ascites tumour cells *in vivo*	+		170 µg/mouse	Schöneich *et al*. (1970)
BID, DNA binding (covalent), 8-hydroxydeoxyguanosine, BALB/c mouse keratinocytes *in vitro*	–	NT	680	Beehler *et al*. (1992)
ICR, Inhibition of cell communication, WB-Fischer 344 rat liver epithelial cells *in vitro*	+	NT	3.4	Upham *et al*. (1997)

[a] +, positive; (+), weakly positive; –, negative; NT, not tested; ?, inconclusive

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; inj, injection; NG, not given

[c] Negative for DNA–DNA and DNA–protein cross-links

[d] Positive at 50 µM (1.7 µg/mL) for HeLa, CaCo-2 colon cells and HepG2 liver cells.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Hydrogen peroxide is produced in moderately high volume and is widely used. Its primary uses are as a chemical intermediate, as a bleaching agent in the textile and paper and pulp industry and in water treatment operations. It occurs naturally at low levels in the air and water, in human and plant tissues and bacteria, and in food and beverages.

5.2 Human carcinogenicity data

No adequate data on the carcinogenicity of hydrogen peroxide were available to the Working Group.

5.3 Animal carcinogenicity data

Hydrogen peroxide was tested in mice by oral administration, skin application and subcutaneous administration and in hamsters by topical application to oral mucosa. In mice, adenomas and carcinomas of the duodenum were found following oral administration. The other studies in mice and the study in hamsters were inadequate for evaluation. One study in mice and one study in hamsters showed no promoting activity of hydrogen peroxide.

5.4 Other relevant data

Hydrogen peroxide is formed intracellularly as a result of certain enzymatic reactions. Hydrogen peroxide, either from this source or externally applied, generates hydroxyl radicals that initiate lipid peroxidation chain reactions within exposed cells and can lead to DNA damage and cell death. DNA damage has been demonstrated in bacteria and in cultured mammalian cells. In addition, hydrogen peroxide induced mutations in bacteria, yeast and other fungi and there is some evidence that it can do so in Chinese hamster V79 and mouse lymphoma L5178Y cells at the *hprt* locus. Chromosomal aberrations and sister chromatid exchanges are induced in both human and other mammalian cells *in vitro*, but it did not induce chromosomal aberrations in the bone-marrow cells of exposed rats.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of hydrogen peroxide.

There is *limited evidence* in experimental animals for the carcinogenicity of hydrogen peroxide.

Overall evaluation

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

6. References

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