TETRAKIS(HYDROXYMETHYL)PHOSPHONIUM SALTS

Data were last evaluated in IARC (1990).

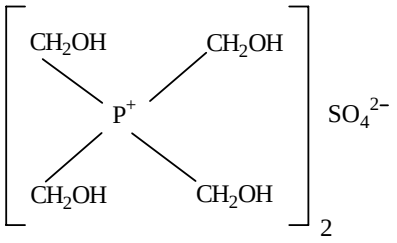
1. Exposure Data

1.1 Chemical and physical data

Tetrakis(hydroxymethyl)phosphonium sulfate

Chem. Abstr. Serv. Reg. No.: 55566-30-8

Chem. Abstr. Name: Phosphonium, tetrakis(hydroxymethyl)-, sulfate (2:1) (salt)

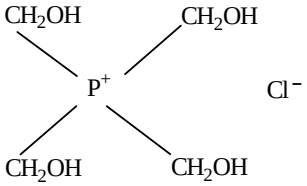


$C_8H_{24}O_{12}P_2S$ Relative molecular mass: 406.28

Tetrakis(hydroxymethyl)phosphonium chloride

Chem. Abstr. Serv. Reg. No.: 124-64-1

Chem. Abstr. Name: Phosphonium, tetrakis(hydroxymethyl)-, chloride

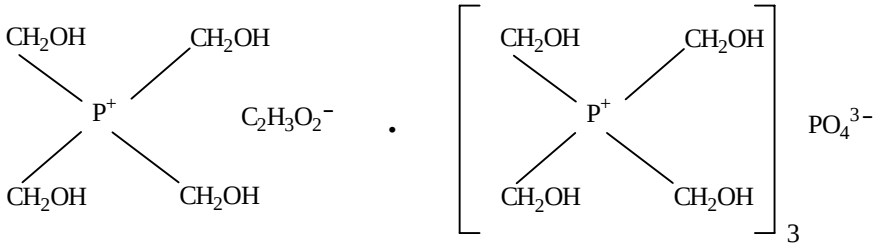


$C_4H_{12}ClO_4P$ Relative molecular mass: 190.56

Tetrakis(hydroxymethyl)phosphonium acetate/phosphate

Chem. Abstr. Serv. Reg. No.: 55818-96-7

Chem. Abstr. Name: Phosphonium, tetrakis(hydroxymethyl)-, acetate (salt), mixture with tetrakis(hydroxymethyl)phosphonium phosphate (3:1) (salt)



$C_4H_{12}O_4P$. $C_2H_3O_2$/$(C_4H_{12}O_4P)_3$. PO_4 Relative molecular mass: 214.16/560.30

1.2 Production and use

Tetrakis(hydroxymethyl)phosphonium salts are used to produce crease-resistant and flame-retardant finishes on textile fabrics, including children's nightwear. No data on occupational exposure levels were available (IARC, 1990).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Tetrakis(hydroxymethyl)phosphonium sulfate was tested for carcinogenicity by oral administration in one strain of mice and one strain of rats. No dose-related increase in the incidence of any tumour was observed, but in males receiving the low dose there was an increased incidence of malignant lymphomas in mice and of mononuclear-cell leukaemia in rats.

Tetrakis(hydroxymethyl)phosphonium chloride was tested for carcinogenicity by oral administration in one strain of mice and one strain of rats. No dose-related increase in the incidence of any tumour was observed; however, in male rats receiving the low dose, there was an increased incidence of mononuclear-cell leukaemia. Tetrakis(hydroxymethyl)-phosphonium chloride did not show significant promoting activity in a two-stage skin carcinogenicity test in mice.

A mixed acetate/phosphate salt of tetrakis(hydroxymethyl)phosphonium base showed weak promoting activity in a two-stage skin carcinogenicity study (IARC, 1990).

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

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Tetrakis(hydroxymethyl)phosphonium chloride can be absorbed through the skin (Ulsamer *et al.*, 1980).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

During 90-day gavage studies, hepatocyte vacuolar degeneration was seen in rats and mice receiving tetrakis(hydroxymethyl)phosphonium sulfate or chloride. Neurotoxicity was also caused by the latter salt (IARC, 1990).

In two-year studies, lesions attributed to administration of the sulfate salt in rats included liver cystic degeneration in males and hepatocyte cytoplasmic vacuolization in animals of each sex. No lesion was reported in treated mice. When treated with the chloride salt, mice and rats showed hepatocyte cytoplasmic vacuolization. Moreover, male rats showed liver cystic degeneration, female mice displayed thyroid follicular-cell hyperplasia and female rats spleen haematopoeisis (IARC, 1990).

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*

Tetrakis(hydroxymethyl)phosphonium chloride and sulfate salts were not mutagenic to bacteria in either the presence or absence of an exogenous metabolic system. In single studies, the sulfate salt induced mutations in mouse lymphoma L5178Y cells *in vitro* at the *tk* locus and, in mouse bone marrow *in vivo*, it caused a marginal increase in the frequency of chromosomal aberrations, but did not induce micronuclei (IARC, 1990).

Tetrakis(hydroxymethyl)phosphonium chloride was not mutagenic to bacteria in either the presence or absence of an exogenous metabolic system. It induced sister chro-

matid exchanges and chromosomal aberrations in Chinese hamster ovary cells *in vitro* and, in a single study, it induced mutations in mouse lymphoma L5178Y cells *in vitro* at the *tk* locus (IARC, 1990).

5. Evaluation

No epidemiological relevant to the carcinogenicity of tetrakis(hydroxymethyl)-phosphonium salts were available.

There is *inadequate evidence* in experimental animals for the carcinogenicity of tetrakis(hydroxymethyl)phosphonium salts.

Overall evaluation

Tetrakis(hydroxymethyl)phosphonium salts are *not classifiable as to their carcinogenicity to humans (Group 3).*

6. References

Grasselli, J.G. & Ritchey, W.M., eds (1975) *CRC Atlas of Spectral Data and Physical Constants for Organic Compounds*, Vol. 4, Cleveland, OH, CRC Press, p. 120

IARC (1990) *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans*, Volume 48, *Some Flame Retardants and Textile Chemicals, and Exposures in the Textile Manufacturing Industry*, Lyon, pp. 95–107

Ulsamer, A.G., Osterberg, R.E. & McLaughlin, J., Jr (1980) Flame-retardant chemicals in textiles. *Clin. Toxicol.*, **17**, 101–131