

NTP NOMINATION HISTORY AND REVIEW

**2,4,6-TRIBROMOPHENOL**

CAS No. 118-79-6

NOMINATION HISTORY

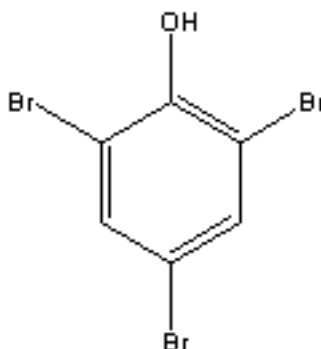
1. Nomination Source: NIEHS
2. Recommendations:
  - Carcinogenicity
  - Toxicology
3. Rationale/Comments:
  - Potential human exposure (environmental and consumer)
  - Evidence of mutagenic activity
  - Lack of carcinogenicity testing
4. Priority:
5. Date of Nomination:

SUMMARY OF DATA FOR CHEMICAL SELECTION

CHEMICAL IDENTIFICATION

<u>CAS Registry Number:</u>	118-79-6
<u>Chemical Abstracts Service Name:</u>	Phenol, 2,4,6-tribromo (9CI)
<u>Synonyms:</u>	Bromkal Pur 3; Bromol; Flammex 3BP
<u>Structural Class:</u>	Halogenated phenol

Structure, Molecular Formula and Molecular Weight:



C<sub>6</sub>H<sub>3</sub>Br<sub>3</sub>O

330.80

Chemical and Physical Properties:

<u>Description:</u>	Soft, white needles with a sweet taste and penetrating bromine odor (Lewis, 1993)
<u>Boiling Point:</u>	286°C (Lide, 1995)
<u>Melting Point:</u>	95.5°C (Lide, 1995)
<u>Density:</u>	2.55 at 20°C (Lide, 1995)
<u>Solubility:</u>	Slightly soluble in water (<0.1 g/100 g); soluble in benzene and diethyl ether; very soluble in ethanol (Lide, 1995)
<u>Volatility:</u>	Relative vapor density (air = 1), 11.4 (Great Lakes Chemical Corp., 1990)
<u>Octanol/water partition coefficient:</u>	log P = 3.96 (Hansch <i>et al.</i> , 1995)

Technical Products and Impurities: 2,4,6-Tribromophenol is commercially available with the following specifications: purity, 98% min.; bromine content, 71% min.; iron, 10 ppm max.; and water 0.3% max. (Great Lakes Chemical Corp., 1995). It is sold in bulk quantities less than 55 pounds up to a truckload of approximately 40,000 pounds (Great Lakes Chemical Corp., 1992).

The following impurities were determined in a 2,4,6-tribromophenol flame retardant preparation at the following levels (ppb): tribromodibenzodioxin, 1.5; tetrabromodibenzodioxin, 84.0; dibromodibenzofuran, 2.2; tribromodibenzofuran, 16.2; tetrabromodibenzofuran, 12.0; and pentabromodibenzofuran, 1.0 (Thoma *et al.*, 1986a).

## EXPOSURE INFORMATION

Production and Producers: 2,4,6-Tribromophenol is prepared by controlled bromination of phenol (Budavari, 1989).

2,4,6-Tribromophenol is listed in the EPA's TSCA Inventory (NLM, 1996). No quantitative information on annual production was found in the available literature. 2,4,6-Tribromophenol is listed as a chemical in commerce in the U.S. International Trade Commission (USITC) publication, *Synthetic Organic Chemicals, US Production and Sales, 1985-1992* (USITC, 1986-1994). The reporting company for each year was listed as Great Lakes Chemical Corp., but no production or sales quantities were included. According to the USITC, separate statistics were not published to avoid disclosure of individual company operations. Although no specific production data were reported, the USITC reporting guidelines specify that each company's report of a chemical represents manufacture of a quantity 4,500 kg [10,000 lbs] or sales \$10,000.

Use Pattern: 2,4,6-Tribromophenol is primarily used as a chemical intermediate and can be used as a flame retardant and an antifungal agent (with government approval) (Great Lakes Chemical Corp., 1995).

Human Exposure: There is potential for occupational, consumer, and environmental exposure to 2,4,6-tribromophenol (TBP).

### *Occupational*

The National Occupational Exposure Survey (NOES), which was conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983, estimated that 1,427 workers, including 734 female employees, were potentially exposed to TBP in the workplace. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemicals listed therein (NIOSH, 1990).

Industrial hygiene surveys were conducted in the Semi-Works unit of the Beaumont, TX plant of Velsicol Chemical Corp. to determine possible employee exposure to 2,4,6-tribromophenol. The surveys were conducted in May and June 1979. Due to sampling and analytical difficulties, it could not be determined if employee exposures exceeded the internal Velsicol limit of 0.1 mg/m<sup>3</sup> of air (Velsicol Chemical Corp., 1979).

*Consumer*

There is the potential for consumer exposure to TBP through the consumption of foods (e.g., fish) and beverages (e.g., drinking water) that may contain TBP.

*Environmental*

There is the potential for environmental exposure to TBP through its occurrence in ambient air (from combustion sources) and wastewater.

Environmental Occurrence:

*Air*

Brominated aromatic compounds were identified in automotive emissions from leaded gasoline containing dibromoethane. 2,4,6-Tribromophenol ( $1-5 \mu\text{g}/\text{m}^3$ ) was among the major compounds identified; it was also detected on snow ( $1.1$  to  $3.7 \text{ ng}/\text{m}^2$ ) collected near a highway (Müller & Buser, 1986).

2,4,6-Tribromophenol production from combustion was measured at an industrial waste treatment and disposal facility in Sweden. Varying levels of 2,4,6-tribromophenol were produced depending on the bromine levels in the source materials and the operating conditions. 2,4,6-Tribromophenol was produced during the combustion of both municipal solid waste and peat (Öberg *et al.*, 1987).

*Water*

Effluent samples taken from at the Jessup and Freedom Districts wastewater treatment plants at Sykesville, MD in 1981 where bromine chloride treatment was used, were analyzed to determine concentrations of brominated compounds. 2,4,6-Tribromophenol was found in all of the bromine chloride disinfected effluent samples at concentrations ranging from 100 to 2,400 ppt. 2,4,6-Tribromophenol was also detected in all of the untreated effluent samples at concentrations ranging from 10 to 12 ppt, which was at the estimated limit of detection of 10 ppt. The source of this 2,4,6-tribromophenol was not known (Dow Chemical Co., 1982).

Discharge water and suspended matter samples from three freshwater-cooled power plants were collected from Redondo Beach, CA. 2,4,6-Tribromophenol concentrations ranged from 20 to 150 ng/l in solvent extracted filtered discharge water samples; concentrations ranged from 0.05 to 9.6 ng/l on suspended matter samples (Bean *et al.*, 1985).

Halogenated phenols were determined in raw and treated water samples of Canadian drinking water supplies. 2,4,6-Tribromophenol was determined in one treated water sample at a concentration of 5 ng/l (Sithole *et al.*, 1986). They were also determined in water samples from 40 potable water treatment plants in Canada. Mean concentrations of 2,4,6-tribromophenol ranged from 0.2 to 0.6 ng/l (max., 10-13 ng/l) in raw water samples and from 0.2 to 1.3 ng/l (max., 4-22 ng/l) in treated water samples (Sithole & Williams, 1986).

Surface water was halogenated by the addition of: (i) chloroperoxidase (CPO), hydrogen peroxide, and chloride or bromide; (ii) hydrogen peroxide and chloride or bromide; (iii) hypochlorite. Water samples were collected from a peat bog in southern Sweden. After the addition of hydrogen peroxide and bromide at pH 1.2, 2,4,6-tribromophenol was present at a concentration of approximately 300 ng/l. In CPO-mediated experiments with a high chloride concentration, the addition of KCl may have resulted in a bromide concentration approaching 0.1 mM; the GC analysis showed the 2,4,6-tribromophenol was formed in higher concentrations (>100 ng/l) than any other halogenated phenol (Hodin *et al.*, 1991).

#### *Fish*

Non-migratory fish from the mouths of tributaries to Lake Ontario and from the Niagara River and its tributaries were analyzed for anthropogenic organic compounds by gas chromatography-mass spectrometry. 2,4,6-Tribromophenol was identified at a concentration of 130 ng/g fish fat in fish collected from the Genesee River, a tributary of Lake Ontario (Jaffe & Hites, 1986).

The carcass and gut contents of 10 species of fish caught along the eastern coast of Australia were analyzed for a range of bromophenols, including 2,4,6-tribromophenol, which are the cause of iodoform-like off-flavors in seafoods. The concentrations of 2,4,6-tribromophenol in the whole gut samples of the fish ranged from <0.05 to 170 ng/g; concentrations in the carcass samples ranged from <0.05 to 3.4 ng/g (Whitfield *et al.*, 1995).

Analysis of sexually immature saltwater Pacific salmon identified 2,4,6-tribromophenol at a concentration of 33.2 ng/g in chinook salmon, 32.1 ng/g in pink salmon, 7.4 ng/g in sockeye salmon, and 5.1 ng/g in coho salmon; but the compound was virtually absent in

spawning run ocean and prime condition Great Lakes freshwater salmon. Analysis of marine fish, crustaceans, and molluscs identified 2,4,6-tribromophenol at concentrations ranging from not detected to 18.9 ng/g for crustaceans, 0.9 to 2.1 ng/g for molluscs, 3.7 to 13.5 ng/g for marine fish, and 18.2 ng/g of unrefined sea salt. Only sporadic, low concentrations of 2,4,6-tribromophenol were found in freshwater fish (Boyle *et al.*, 1992).

#### *Sediment*

Sediment samples exposed to discharge plumes from three freshwater-cooled power plants were collected from Redondo Beach, CA. 2,4,6-Tribromophenol was found at only one site at concentrations ranging from 0.3 to 0.8 µg/kg (Bean *et al.*, 1985).

River and marine sediment samples were collected from Osaka, Japan, to determine the environmental levels of brominated phenols. 2,4,6-Tribromophenol was found in nearly all the samples analyzed (occurrence: 10/12) with concentrations ranging from 0.8 to 36 µg/kg dry weight. The authors considered it an ubiquitous environmental contaminant (Watanabe *et al.*, 1985).

Estuarine sediment samples were collected from the Rhône River in France, to determine the environmental levels of brominated phenols. 2,4,6-Tribromophenol was found in all the samples analyzed with concentrations ranging from 26 to 3,690 ng/g dry weight Tolosa *et al.*, 1991).

#### *Other Environmental Concerns*

Purified 2,4,6-tribromophenol was pyrolyzed at 700°C, 800°C, and 900°C. Di-, tri-, tetra- (up to 89.6%), penta-, and hexabromodibenzodioxins and di-, tri-, tetra-, and pentabromodibenzofurans were formed from 2,4,6-tribromophenol. The results showed that brominated dioxins and furans are formed much easier from tribromophenol than from the corresponding chlorinated compounds (Thoma *et al.*, 1986b).

Regulatory Status: No standards or guidelines have been set by NIOSH or OSHA for occupational exposure to or workplace maximum allowable levels of 2,4,6-tribromophenol. The American Conference of Governmental Industrial Hygienists (ACGIH) has not recommended a Threshold Limit Value (TLV) or Biological Exposure Index (BEI) for this compound.

## EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the association of exposure to 2,4,6-tribromophenol and cancer risk in humans were identified in the available literature.

### Animal Data:

#### *Acute*

Acute oral toxicity of 2,4,6-tribromophenol was evaluated in 6 groups of 10 Spartan rats (5 male; 5 female) administered a single dose by gavage at dose levels of 1,585, 2,512, 3,980, 6,308, 10,000, and 15,848 mg/kg. A 14-day observation period followed dosing. In each of the 3 highest dosing groups 9 rats died by the third observation day. In the 1,585, 2,512, and 3,980 mg/kg dose groups, respectively, 0, 1, and 1 rats died. The oral LD<sub>50</sub> for males and females was calculated to be 5,012 mg/kg. All survivors showed normal weight gain. Clinical signs of toxicity included: nasal discharge, lacrimation, and decreased motor activity at all dose levels; ocular discharge, tachypnea, and tachycardia in all but the lowest dose group; ataxia and tremors in dose groups 6,308 mg/kg and above; flaccidity, prostration, and cyanosis were each observed in 1 of the 2 highest dose groups. Gross necropsy revealed a dose-related increase in lung, stomach, and liver congestion (International Research and Development Corp., 1974a).

Acute oral toxicity of 2,4,6-tribromophenol was evaluated in 6 groups of 10 Charles River CD rats (5 males; 5 females) administered a single dose by gavage as a suspension in corn oil at dose levels of 631, 1,000, 1,585, 2,512, 3,980, and 6,308 mg/kg. The use of controls was not reported. A 14-day observation period followed dosing. A single mortality was observed in a female rat in the 1,595 mg/kg dose group, and all rats in the 3 highest dose groups died by the end of the first day of the observation period. The oral LD<sub>50</sub> was reported to be 1,995, 1,819, and 1,905 mg/kg for males, females, and all rats, respectively. Survivors gained weight during the observation period. No clinical signs of toxicity or pathology were reported (International Research and Development Corp., 1978).

Acute inhalation toxicity was evaluated in Spartan albino rats (5 rats/sex) receiving whole-body exposure to micronized tribromophenol at a concentration of 50 mg/l, for 4 hours, in a dynamic airflow chamber. During the exposure period, rats exhibited decreased motor activity, eye squint, slight dyspnea, erythema, and ocular porphyrin



discharge. During the 14-day observation period following exposure, rats exhibited diarrhea, ocular porphyrin discharge, clear nasal discharge, and slight dyspnea. The treatment had no adverse effects with respect to mortality rate or body weight gain. Based on the results obtained, the acute inhalation toxicity in albino rats for 2,4,6-tribromophenol is greater than 50 mg/l (International Research and Development Corp., 1974b).

Acute dermal toxicity of 2,4,6-tribromophenol was evaluated in 2 male and 2 female New Zealand White rabbits exposed once to 8,000 mg/kg on clipped (also abraded for 1 male and 1 female) skin. After a 24-hour exposure period, the site of exposure was rinsed with water, and the animals were observed for 14 days. No deaths occurred. No clinical signs of toxicity were observed, and body weight changes were described as "normal." Gross necropsy revealed scattered hemorrhaging in subcutaneous tissue at the site of application. Based on the results obtained, the acute dermal toxicity of 2,4,6-tribromophenol in male and female albino rats is greater than 8,000 mg/kg (International Research and Development Corp., 1974c).

Acute dermal sensitization of 2,4,6-tribromophenol was evaluated in 8 male albino guinea pigs. 2,4,6-Tribromophenol, at a concentration of 0.1% in 0.9% sodium chloride solution, was injected intradermally into a prepared area on the back and flanks of the animals every other day, 3 times each week, until a total of 10 sensitizing doses had been given. The injection sites were read and scored for diameter and intensity of erythema (flare) and height of edema (wheal) at 24 and 48 hours following each injection. Two weeks following the tenth sensitizing dose a challenge dose was given. Four of the eight guinea pigs responded to the challenge dose. Based on the results obtained, the test compound would be considered a possible sensitizing agent in man which could produce slight sensitization in the occasionally susceptible individual (International Research and Development Corp., 1975).

Eye irritation of 2,4,6-tribromophenol was evaluated in 6 (3 male, 3 female) New Zealand white (albino) rabbits. One hundred milligrams of 2,4,6-tribromophenol was instilled into the conjunctival sac of the right eye of each rabbit. Examinations were made at 24, 48, 72 hours and at 7 days. Examination at 72 hours with sodium fluorescein and ultraviolet light revealed that there was slight corneal damage in five of the six rabbits tested. Based on the results obtained, 2,4,6-tribromophenol would be considered an eye irritant (International Research and Development Corp., 1974d).

Primary skin irritation of 2,4,6-tribromophenol was evaluated in New Zealand white (albino) rabbits (3 male, 3 female). Five hundred milligrams of 2,4,6-tribromophenol was applied to the back of each rabbit. Examinations were made at 24 and 72 hours. Based on the computed primary irritation score of 0.3, 2,4,6-tribromophenol was not considered a primary skin irritant, nor did it present a corrosive hazard to the skin (International Research and Development Corp., 1974e).

#### *Subacute*

2,4,6-Tribromophenol was evaluated in a 21-day subacute dust inhalation toxicity study. Three groups of Charles River albino rats (5 rats/sex) were exposed to 2,4,6-tribromophenol dust at dose levels of 0, 0.10, or 0.92 mg/l for 6 hours/day, 5 days/week for 3 weeks, for a total of 15 exposures. There were no deaths in the low dose group; one high dose male died after 10 exposures and one high dose female died after 11 exposures. Adverse reactions noted in both treated groups included hypoactivity, salivation, lacrimation, and red nasal discharge. One high dose animal exhibited hyperpnea on day 11 of treatment. Body weight gains for the low dose males compared favorably with controls. However, low dose females and both high dose groups exhibited lower weight gains compared to controls. There were no significant differences between test and control animals with respect to hematologic, clinical blood chemistry, or urinalysis values obtained during the investigation. Gross and histopathologic changes involving the liver and kidneys were noted in the high dose animals (Industrial Bio-Test Laboratories, Inc., 1990a).

2,4,6-Tribromophenol was evaluated in a 28-day subacute dermal toxicity study. Four groups of 8 New Zealand albino rabbits (4 rabbits/sex) were dermally exposed to 2,4,6-tribromophenol (50% (w/v) in 1.0% aqueous methylcellulose) at dose levels of 0, 100, 300 or 1,000 mg/kg/day, 5 days/week for 4 weeks, for a total of 20 applications. One high-dose male rabbit died after receiving 15 dermal applications but the cause of death was not evident from an examination of the tissues. No pharmacotoxic symptoms were observed at any time during the study. 2,4,6-Tribromophenol was slightly irritating to the skin upon repeated exposure. There were no consistent, significant, exposure-related differences between treated and control animals in the following: body weight, hematology, clinical blood chemistry, and urinalysis. Treatment and dose-related microscopic changes observed included minimal to moderate, focal or multifocal to diffuse

epidermal acanthosis with hyperkeratosis accompanied by multifocal to diffuse dermal inflammatory infiltrates (Industrial Bio-Test Laboratories, Inc., 1977, 1990b).

2,4,6-Tribromophenol was applied to the inner surface of the rabbit (strain not identified) ear 5 times/week for 4 weeks at a dose of 0.1 ml/day. 2,4,6-Tribromophenol did not produce a positive chloracne response (Dow Chemical Co., 1970).

#### *Chronic/Carcinogenicity*

No 2-year carcinogenicity studies of 2,4,6-tribromophenol in animals were identified in the available literature.

Short-Term Tests: 2,4,6-Tribromophenol (TBP) was not mutagenic with or without metabolic activation (S9) in the *Salmonella typhimurium* standard plate assay when tested at doses up to 333 µg/plate in strains TA98, TA100, TA1535, TA1537, and TA1538 (NCI, 1996); and in the *Salmonella typhimurium* preincubation assay when tested at doses up to 333 µg/plate in strains TA98, TA100, TA1535, and TA1537 (Zeiger *et al.*, 1987).

2,4,6-Tribromophenol was evaluated for mutagenicity by plate assay in two microorganisms, *Saccharomyces cerevisiae*, strain D4, and *Salmonella typhimurium*, strains TA98, TA100, TA1535, TA1537, and TA1538, both in the presence and absence of Aroclor 1254-induced rat liver homogenate (S9). Positive (chemicals not identified) and solvent (DMSO) controls were utilized. Test concentrations ranged from 1.0 to 1,000 µg/plate; the low dose was less than that which demonstrated any toxic effect, and the high dose produced quantitative or qualitative evidence of some chemically-induced physiological effects. No evidence of mutagenic activity from 2,4,6-tribromophenol was seen in any of the assays conducted (Litton Bionetics Inc., 1978).

TBP induced mutagenic responses at the *tk* locus in the mouse lymphoma cell forward mutation assay in the absence of S9 at concentrations in the range of 80-120 µg/ml; there was a negative mutagenic response in the presence of S9 at concentrations in the range of 5-35 µg/ml (NCI, 1996).

Metabolism: The absorption, distribution, and elimination of radiolabelled 2,4,6-tribromophenol were examined in 5 groups of male or female Holzman's albino rats (2 or 3 per group) orally administered doses ranging from 4.04 to 5.34 mg/kg. The

post-dosing monitoring period lasted from 8 to 96 hours, followed by sacrifice and tissue sampling. The proportion of the administered radiocarbon remaining in each of 11 tissues after 48 hours did not exceed 0.005%, and only kidney, liver and lungs retained detectable residues. The retention half-life of radiocarbon in the blood was 2.03 hours, and ranged from 1.45 to 2.30 hours for the other tissues. After 48 hours, the total excretion of radiocarbon in the urine ranged from 50.3 to 91.2% of the dose. During the same period, between 3.90 and 13.74% of the administered radiocarbon was eliminated in the feces (Velsicol Chemical Corp., 1978).

Other Biological Effects:

*Reproductive Effects/Teratology*

In a pilot study, reproductive toxicity was evaluated in 6 groups of 5 pregnant Charles River CD female rats receiving 2,4,6-tribromophenol via oral gavage at dose levels of 10, 30, 100, 300, 1000, and 3,000 mg/kg/day on gestation days 6 through 15. No effects were noted on maternal behavior or appearance for the groups that received 1,000 mg/kg/day or less. Total mortality was observed at the 3,000 mg/kg/day dose after one day of treatment. There were no treatment-related effects on maternal body weights, food consumption, number of corpora lutea, viable or nonviable fetuses, resorptions, or implantations at dose levels of 300 mg/kg/day or less. At 1,000 mg/kg/day, decreased body weight gain, increased post-implantation loss, and a slight decrease in the number of viable fetuses occurred (International Research and Development Corp., 1973).

2,4,6-Tribromophenol, 5 µl of 200 mM solution in DMSO added to 2 ml culture, decreased the viability and glycogenolytic activity of rat hepatocytes, which indicated that TBP may inhibit metabolic activity of hepatocytes. The authors also noted there was no cancer promotion activity, as assessed by morphological change of HL-60 cells, using 5 µl of 200 mM solution in DMSO added to 1 ml media (Utsumi *et al.*, 1992).

Structure Activity Relationships: Four structurally related chemicals were selected for evaluation of relative biological effects. No carcinogenicity or mutagenicity data were found on three of the related compounds: 2,4-dibromophenol [615-58-7]; 2,6-dibromophenol [608-33-3]; and 2,4,6-tribromoresorcinol [2437-49-2]. 2,4,6-Trichlorophenol was tested in a 2-year bioassay for possible carcinogenicity by administering the test chemical in feed to F344 rats and B6C3F1 mice. It was concluded that under the conditions of the bioassay, 2,4,6-trichlorophenol was carcinogenic in male F344 rats, inducing lymphomas or leukemias; and was also carcinogenic in both sexes of B6C3F1 mice, inducing

hepatocellular carcinomas or adenomas (NCI, 1979). 2,4,6-Trichlorophenol has also been shown to be mutagenic in several test systems. A summary of information found in the available literature is presented in Table 1.

**Table 1. Summary of Information on 2,4,6-Tribromophenol and Structurally Related Compounds**

Chemical [CAS No.]	Carcinogenicity data	Mutagenicity data
2,4,6-Tribromophenol [118-79-6]	NDF <sup>a</sup>	<p>negative in <i>S. typhimurium</i> standard plate assay in TA98, TA100, TA1535, TA1537, and TA1538 with and without S9 activation (NCI, 1996)</p> <p>negative in <i>S. typhimurium</i> preincubation assay in TA98, TA100, TA1535, and TA1537 with (rat and hamster) and without S9 activation (Zeiger <i>et al.</i>, 1987)</p> <p>positive in mouse lymphoma L5178Y cells without S9 activation; negative with S9 activation (NCI, 1996)</p> <p>negative in <i>Saccharomyces cerevisiae</i> strain D4 and <i>S. typhimurium</i> TA98, TA100, TA1535, TA1537, and TA1538 with and without S9 activation (Litton Bionetics Inc., 1978)</p>
2,4,6-Trichlorophenol [88-06-2]	<p>limited evidence for the carcinogenicity of occupational exposure to chlorophenols in humans (IARC, 1986)</p> <p>sufficient evidence for carcinogenicity to animals (IARC, 1987)</p> <p>positive in male rats and in male and female mice in a 2-year feed study, inducing lymphomas or leukemias in male F344 rats; and inducing hepatocellular carcinomas or adenomas in male and female B6C3F1 mice (NCI, 1979)</p> <p>negative in female rats in a 2-year feed study (NCI, 1979)</p>	<p>positive in <i>S. typhimurium</i> TA97, TA98, and TA104 with S9 activation (Strobel &amp; Grummt, 1987)</p> <p>negative in <i>S. typhimurium</i> TA97, TA98, TA100, and TA104 without S9 and in TA100 with S9 activation (Strobel &amp; Grummt, 1987)</p> <p>negative in <i>S. typhimurium</i> TA98, TA100, TA1535, and TA1537 with (hamster and rat) and without S9 activation (Haworth <i>et al.</i>, 1983)</p> <p>positive in mouse lymphoma L5178Y cells without S9 activation (McGregor <i>et al.</i>, 1988)</p> <p>positive in Chinese hamster V-79 cells without activation; negative with cell-mediated activation (Hattula &amp; Knuutinen, 1985)</p> <p>positive for hyperdiploidy and micronuclei in Chinese hamster V-79 cells without exogenous metabolic activation (Jansson &amp; Jansson, 1992)</p> <p>negative at the <i>hprt</i> locus to TG resistance and for CAs in Chinese hamster V-79 cells without exogenous metabolic activation (Jansson &amp; Jansson, 1986, 1992)</p> <p>negative for CAs and SCEs in Chinese hamster ovary (CHO) cells with and without S9 activation (Galloway <i>et al.</i>, 1987)</p>

<sup>a</sup> NDF, no data found

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