

Chemical Information Profile

for

Tris(4-chlorophenyl)methanol

[CAS No. 3010-80-8]

and

Tris(4-chlorophenyl)methane

[CAS No. 27575-78-6]

**Supporting Nomination for Toxicological Evaluation by the
National Toxicology Program**

June 2009



NTP

National Toxicology Program

U.S. Department of Health and Human Services

National Toxicology Program
National Institute of Environmental Health Sciences
National Institutes of Health
U.S. Department of Health and Human Services
Research Triangle Park, NC
<http://ntp.niehs.nih.gov/>

**Data Availability Checklist for Tris(4-chlorophenyl)methanol [CAS No. 3010-80-8]
and Tris(4-chlorophenyl)methane [CAS No. 27575-78-6]**

Abbreviations: H = human; L = *Lepus* (rabbit); M = mouse; R = rat

Note: No judgement of whether the available data are adequate for evaluation of these endpoints in the context of human health hazard or risk assessment has been made.

ENDPOINT	H	M	R	L	ENDPOINT	H	M	R	L
ADME					Developmental Toxicity				
Absorption					Developmental abnormalities				
Distribution					Embryonic/fetal effects				
Metabolism					Newborn effects				
Excretion	X				Carcinogenicity				
Acute Toxicity (up to 1 week)					Dermal				
Dermal					Inhalation				
Inhalation					Oral				
Injection					Anticarcinogenicity				
Ocular					Anticarcinogenic effects				
Oral					Genotoxicity				
Subchronic Toxicity (1 to <26 weeks)					Cytogenetic effects				
Dermal					Microbial gene mutation			X	
Inhalation					Gene mutation <i>in vitro</i>				
Injection					Gene mutation <i>in vivo</i>				
Oral			X		Germ cell effects				
Chronic Toxicity (≥26 weeks)					Neurotoxicity				
Dermal					Behavioral activity				
Inhalation					Motor activity				
Injection					Immunotoxicity				
Oral					Immunotoxic effects			X	
Synergism/Antagonism					Cardiovascular Toxicity				
Synergistic effects					Cardiovascular effects				
Antagonistic effects					Mechanistic Data				
Cytotoxicity					Target Organs/Tissues	X			
Cytotoxic effects	X				Endocrine modulation	X		X	
Reproductive Toxicity					Effect on enzymes			X	
Fertility effects					Modes of action				
Maternal effects					Effect on metabolic pathways			X	
Paternal effects	X				Structure-Activity Relationships				
						X	X	X	X

The above table provides an overview of the data summarized in this profile. From left to right, column 1 and 6 list the endpoints and columns 2-5 and 7-10 identify the four species (human, rat, mouse, and rabbit) that were considered. An "X" is entered in each box that corresponds to an endpoint and species for which data are included in the profile. Blank cells indicate that no data were available in the literature.

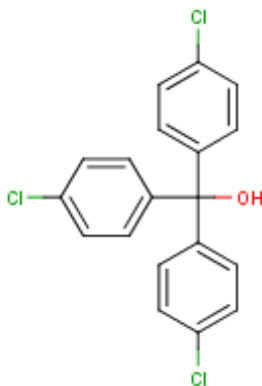
Tris(4-chlorophenyl)methanol [CAS No. 3010-80-8] and Tris(4-chlorophenyl)methane [CAS No. 27575-78-6] Nomination Summary

Chemical Name: Tris(4-chlorophenyl)methanol

CAS RN: 3010-80-8

Formula: C₁₉H₁₃Cl₃OH

Molecular Wt.: 363.66

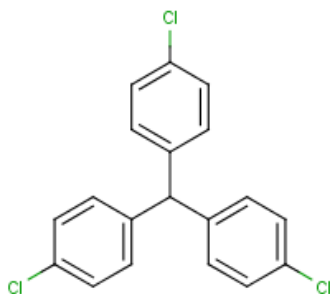


Chemical Name: Tris(4-chlorophenyl)methane

CAS RN: 27575-78-6

Formula: C₁₉H₁₃Cl₃

Molecular Wt.: 347.67



Basis for Nomination: Tris(4-chlorophenyl)methanol (TCPMOH) and tris(4-chlorophenyl)methane (TCPMe) were nominated by the National Institute of Environmental Health Sciences for toxicological characterization based on their widespread occurrence and persistence in the environment and limited availability of toxicity data. Both compounds are presumed to be bioaccumulative and have been found in human tissues. TCPMOH is a potent competitive inhibitor of human and rodent androgen receptors *in vitro*, at concentrations within an order of magnitude as that reported in human tissues. Further studies are needed to characterize the potential human health hazard of these environmentally persistent compounds.

TCPMe is a byproduct of the reaction of chlorobenzene with chloral in the presence of fuming or concentrated sulfuric acid, a process that is used to produce dichlorodiphenyltrichloroethane (DDT). It also is produced by DDT reacting with aluminum chloride in the presence of chlorobenzene. TCPMOH is a presumed metabolite of TCPMe. Both TCPMe and TCPMOH are reported to be used in the

production of synthetic high polymers, lightfast dyes for acrylic fibers, and agrochemicals, indicating the potential for occupational exposure. The general population may also be exposed to TCPMe and/or TCPMOH from the consumption of food containing these compounds. Both TCPMe and TCPMOH have been found in tissues from a variety of animals, such as fish, birds, and marine mammals. TCPMe concentrations ranged from <6 µg/kg lipid in mussels up to 33,000 µg/kg lipid in white-tail sea eagles, and the concentration range for TCPMOH was 13 µg/kg lipid in mussels to 54,000 µg/kg lipid in white-tail sea eagles. One study reported evidence of TCPMe and TCPMOH in human adipose, liver, and bile. Both chemicals also have been identified in human breast milk. Oral exposure of rats to TCPMOH for 28 days increased liver/body weight ratios, urinary ascorbic acid, and Phase I and II enzyme activities as well as produced changes in liver cytoplasm, spleen, and blood counts. Evidence of reproductive and endocrine disrupting effects also was reported. TCPMOH dose-dependently altered motility, vitality, and acrosome reaction in human sperm; increased serum concentrations of follicle stimulating hormone in male rats; bound to rat prostate androgen receptors but not to bovine uterine estrogen receptors; and was antagonist to the human androgen receptor *in vitro*. TCPMe inhibited binding of 17-β estradiol to human estrogen receptor.

A. Chemical Information***Molecular Identification*****Chemical Name:** Tris(4-chlorophenyl)methanol [TCPMOH]**CAS RN:** 3010-80-8**Synonyms:** Benzenemethanol, 4,4',4''-Trichlorotriphenylmethanol; 4,4',4''-Trichlorotriptyl alcohol; 4-chloro- $\alpha\alpha$, α -bis (4-chlorophenyl)-; Methanol, tris(*p*-chlorophenyl) (6Cl, 7Cl, 8Cl); Tri-*p*-chlorophenyl carbinol; Tris (4-chlorophenyl) carbinol; Tris (*p*-chlorophenyl) methanol**Trade Names:** Not available**Hill Formula:** C₁₉H₁₃Cl₃O**Line Formula:** Not available**Smiles Notation:** C1=CC(=CC=C1C(C2=CC=C(C=C2)Cl)(C3=CC=C(C=C3)Cl)O)Cl**PubChem CID:** 76379 (PubChem, undated-a)**InChI:** 1/C19H13Cl3O/c20-16-7-1-13(2-8-16)19(23,14-3-9-17(21)10-4-14)15-5-11-18(22)12-6-15/h1-12,23H**Molecular Weight:** 363.66**Purity of Commercial Products:** 95% (Alfa Aesar, 2003; ChemExper, 2008)**Additives in Commercial Products:** Not available**Impurities in Commercial Products:** Not available**Mammalian Metabolites:** Not available**Biodegradation Products:** May decompose to hydrogen chloride (Alfa Aesar, 2003)**Environmental Transformation:** Not available***Physical-Chemical Properties*****Physical State:** Solid; white color (Alfa Aesar, 2003)**Specific Gravity or Density Value:** 1.366±0.06 gm/cm³ @ 20 °C [calculated] (Registry, 2008a)**Boiling Point:** 489.9±40.0 °C [calculated] (Registry, 2008a)**Melting Point:** 96-97 °C (Alfa Aesar, 2003)**Vapor Pressure:** 2.07×10⁻¹⁰ Torr @ 25 °C [calculated] (Registry, 2008a)**Solubility:** Insoluble in water (Alfa Aesar, 2003); 110 µg/L @ pH 1-10 @ 25 °C [calculated] (Registry, 2008a)**Log P = Log K_{ow}:** 6.372±0.371 @ 25 °C [calculated] (Registry, 2008a)**Bioconcentration Factor(s) (species):** 40932.49 @ pH 1-10 @ 25 °C [calculated] (Registry, 2008a); 14,000 [estimated using the PBT Profiler] (U.S. EPA, 2006)***Molecular Identification*****Chemical Name:** Tris(4-chlorophenyl)methane [TCPMe]**CAS RN:** 27575-78-6**Synonyms:** Benzene, 1,1',1''-methylidynetris (4-chloro-); Methane, 4, 4',4'' -trichlorotriphenyl-; Tris (*p*-chlorophenyl) methane**Trade Names:** Not available**Hill Formula:** C₁₉H₁₃Cl₃**Line Formula:** Not available**Smiles Notation:** C1=CC(=CC=C1C(C2=CC=C(C=C2)Cl)C3=CC=C(C=C3)Cl)Cl**PubChem CID:** 92256 (PubChem, undated-a)**InChI:** 1/C19H13Cl3/c20-16-7-1-13(2-8-16)19(14-3-9-17(21)10-4-14)15-5-11-18(22)12-6-15/h1-12,19H**Molecular Weight:** 347.67**Purity of Commercial Products:** Not available**Additives in Commercial Products:** Not available**Impurities in Commercial Products:** Not available**Mammalian Metabolites:** Not available**Biodegradation Products:** Not available**Environmental Transformation:** Not available

Physical-Chemical Properties

Physical State: Solid

Specific Gravity or Density Value: 1.294±0.06 gm/cm³ @ 20 °C [calculated] (Registry, 2008b)

Boiling Point: 441.6±40.0 °C [calculated] (Registry, 2008b)

Melting Point: 80 °C (Registry, 2008b)

Vapor Pressure: 1.29x10⁻⁰⁷Torr @ 25 °C [calculated] (Registry, 2008b)

Solubility: 2.5 µg/L @ pH 1-10 @ 25 °C [calculated] (Registry, 2008b)

Log P = Log Kow: 7.8 (Ikemoto et al., 2008 [PMID:18313720]); 7.474±0.261 @ 25 °C [calculated] (Registry, 2008b)

Bioconcentration Factor(s) (species): 282046.28 @ pH 1-10 @ 25 °C [calculated] (Registry, 2008b); 25,000 [estimated using the PBT Profiler] (U.S. EPA, 2006)

B. Exposure Potential

U.S. Annual Production

1986-2002: No reports for TCPMOH or TCPMe (U.S. EPA, 2009 [U.S. EPA IUR database])

Worldwide Annual Production

Not available

Production Processes

TCPMOH: Not available

TCPMe: Reaction of dichlorodiphenyltrichloroethane (DDT) with aluminum chloride in the presence of chlorobenzene; byproduct from the production of DDT via reaction of chlorobenzene with chloral in the presence of fuming or concentrated sulfuric acid with gentle agitation (Buser, 1995).

Uses

Production of synthetic high polymers and lightfast dyes for acrylic fibers (de Boer, 2000).

Occupational Exposure

Exposure may occur during manufacture of synthetic high polymers, lightfast dyes for acrylic fibers, anthelmintic drugs, and agrochemical formulations (e.g., DDT) (de Boer, 2000).

General Population Exposure

Foods and Beverages, Cosmetics, etc.

TCPMOH and TCPMe were found in aquatic animals (e.g., mussels and trout) that may be consumed (de Boer et al., 1996 [PMID:15091367]; Fisk et al., 1998).

Ambient Environment

Air Limit: Not available

Water Limit(s): Not available

Soil Limit: Not available

Environmental Exposure in the United States: Not available

Levels in Tissues, Body Fluids, and Excreta

- TCPMOH concentrations in human adipose, liver, and bile samples collected in Japan ranged from <0.28-31, <4-38, and <10 ng/g lipid weight, respectively. TCPMe concentrations ranged from 2.5-44, 1.1-20, and <5-62 ng/g lipid weight, respectively. The TCPMOH and TCPMe concentrations in adipose tissues correlated with those of DDT and its metabolites (Minh et al., 2000, 2001). TCPMe plasma concentrations ranged from <0.1-8.1 ng/g lipid weight (Minh et al., 2006 [PMID:16783626]).
- TCPMOH and TCPMe were found in human breast milk sampled from a variety of geographic regions including Europe, China, and Indonesia (Kunisue et al., 2004a [PMID:15195813], 2004b [PMID:15261401]; Minh et al., 2004 [PMID:15016464]; Sudaryanto et al., 2004). TCPMOH and TCPMe concentrations reported for samples collected from European women were 2.0 and 1.6 ng/g milk fat, respectively (Rahman et al., 1993). In Cambodia, TCPMe concentrations ranged from 2.9-70 ng/g lipid weight (Kunisue et al., 2004a [PMID:15195813]) and in Indonesia, the concentrations ranged from <0.03-15 ng/g lipid weight (mean 3.4) (Sudaryanto et al., 2008

[PMID:17482735]). The concentrations of both compounds were typically lower than those of other organochlorines (Kunisue et al., 2004a [PMID:15195813], 2004b [PMID:15261401]; Minh et al., 2004 [PMID:15016464]; Sudaryanto et al., 2008 [PMID:17482735]). A correlation between TCPMe and DDT concentrations was reported (Kunisue et al., 2004a [PMID:15195813], 2004b [PMID:15261401]).

Environmental Occurrence

- The source(s) for entry of TCPMOH and TCPMe into the environment is(are) unknown but suggested to result from the limited reported industrial uses and from the presence of TCPMe as an impurity in DDT technical formulations (Buser, 1995).
- More than 40 studies have reported that TCPMOH and/or TCPMe is found in a variety of animal wildlife (e.g., fish, birds, and marine mammals). For example, TCPMOH concentrations were 13 µg/kg lipid weight in mussels, 14-54,000 µg/kg lipid weight in white-tail sea eagles, 52-333 µg/kg lipid weight in beluga whale blubber, and 4000-6800 µg/kg lipid weight in polar bear liver. TCPMe concentrations of <6 µg/kg lipid weight in mussels, 9-33,000 µg/kg lipid weight in white-tail sea eagles, and 42-1450 µg/kg lipid weight in beluga whale blubber were reported (de Boer, 2000).
- TCPMOH and TCPMe were found in the blubber of seals from the Caspian Sea at concentrations ranging from 7.3-9900 ng/g and 1.0-950 ng/kg, respectively, following mass deaths in 2000-2001. TCPMOH concentrations were higher in male seals from Azerbaijan and TCPMe was higher in male seals from Iran than that seen in female seals. TCPMOH concentrations were significantly higher in samples taken during the spring/summer season compared to those from the autumn/winter season due to reduced total fat in the seals (Kajiwara et al., 2008a [PMID:17900768]). The TCPMOH concentrations in blubber of melon-headed whales stranded in mass along the Japanese coasts since the 1980s ranged from 9.6 (mature female) to 67 (immature male) ng/g lipid weight. TCPME concentrations ranged from 1.9 (fetus) to 23 (mature male) ng/g lipid weight (Kajiwara et al., 2008b [PMID:18272274]).
- Bioaccumulation potential of both chemicals is proposed to be high. Marine TCPMOH concentrations suggest a biomagnification in the order of 10- to 100-fold (de Boer, 2000). In samples of phytoplankton, crustaceans, and some fish species collected from the Mekong Delta in South Vietnam, TCPMe was measured at concentrations ranging from not detectable to 0.26 ng/g. Positive biomagnification through the food web was reported based on the increased concentration of TCPMe relative to the stable nitrogen ratio ($\delta^{15}\text{N}$) for wet-, dry-, and lipid-weight (Ikemoto et al., 2008 [PMID:18313720]).
- The following half-lives (in days) were calculated using the PBT Profiler: 2.3 (air, TCPMe), 3.2 (air, TCPMOH), 180 (water), 360 (soil), and 1600 (sediment) (U.S. EPA, 2006).

Natural Occurrence: Not applicable

U.S. Environmental Releases: Not available

Concentrations in Environmental Media

Surface Water: Not available

Groundwater: Not available

Industrial Wastewater: Not available

Municipal Waste/Sewage: TCPMOH and TCPMe were below the level of detection in sludge collected from wastewater treatment facility in Gdansk, Poland (Falandysz and Strandberg, 2004).

Ambient Air: Not available

Soils: TCPMOH and TCPMe concentrations in sediment samples from the Baltic Sea, Vistula River, St. Lawrence (Canada) estuary and gulf, and Rhine estuary ranged from not detectable to ≤ 3 ng/g dry weight (de Boer et al., 1996 [PMID:15091367]; Falandysz and Strandberg, 2004; Falandysz et al., 1999; Lebeuf et al., 1998).

C. Regulatory Information

U.S. Regulations

None available (EPA, FDA, OSHA)

Exposure Limits (Standards and Criteria)

ACGIH TLV: Not available

NIOSH REL: Not available

OSHA PEL: Not available

European Union Scientific Committee Regulations

None available

Canadian Domestic Substances List (DSL) and Non Domestic Substances List (NDSL)

TCPMOH and TCPMe are both not specified on the DSL or the NDSL. They are, however, subject to the New Substances Notifications Regulations of the Canadian Environmental Protection Act, 1999 (Environment Canada, 2009).

D. Toxicological Information

General Toxicity

Human Studies: TCPMOH may cause skin, eye, and respiratory tract irritation (Alfa Aesar, 2003).

Animal Studies: No effect on body weight or clinical signs of toxicity were observed in rats of both sexes after 4-week dietary exposure to 1-100 ppm TCPMOH (Foster et al., 1999 [PMID:10448550]; Poon et al., 1997 [PMID:9011026]).

Chemical Disposition, Metabolism, and Toxicokinetics

Absorption and Clearance: Not available

Human Studies: Biliary excretion rate of TCPMe was estimated to be 0.11% (Minh et al., 2001).

Animal Studies: Studies in four seal species showed that lipid normalized concentrations of TCPMOH and TCPMe were comparable in different organs and tissues, with the highest concentration appearing in blubber (Watanabe et al., 1999). In mature male and female melon-headed whales, body burdens were 1.3 and 0.21 mg for TCPMOH, respectively; for TCPMe, the body burdens were 0.39 and 0.23 mg, respectively. The estimated transfer rates of the body load during the reproductive cycle (gestation and lactation) were 84% and 41% for TCPMOH and TCPMe, respectively. In addition, placental transfer was observed in the whales; the transfer rates from pregnant females to their fetuses were 3.3-5.3% for TCPMOH and 0.55-1.2% for TCPMe (Kajiwara et al., 2008b [PMID:18272274]).

Acute Exposures

Not available assessment

Subchronic Exposures

Route: oral (via food)
Species: rat (Sprague Dawley, 5 male and 5 female/dose)
Dose/Duration: 1, 10, and 100 ppm TCPMOH/day for 28 days
Observation Time: not provided

Effects:

- Increased spleen/body weight ratio in males at 10 and 100 ppm and in females at 100 ppm and increased liver/body weight ratio in both sexes at 100 ppm;
- Increased Phase-I and II enzyme activities in both sexes at doses ≥ 10 ppm;
- Increased urinary ascorbic acid in both sexes at 10 and 100 ppm (1 week) and 100 ppm (4 weeks);
- Increase in the percentage of lymphocytes in males and of blood cell and lymphocyte counts in females at doses ≥ 10 ppm;
- Decrease in the percentage of monocytes in males at 100 ppm;
- Liver cytoplasmic and splenic changes in both sexes at doses ≥ 10 ppm; and
- Increase in apoptosis in hepatocytes of males at 100 ppm.

- Source:
- LOAEL = 10 ppm (equivalent to 1.2 mg/kg/day)
Poon et al. (1997 [PMID:9011026])

Chronic Exposures

Not available

Synergistic/Antagonistic Effects

Not available

Cytotoxicity

TCPMOH was cytotoxic to MCF-7-AR1 human mammary adenocarcinoma cells, PC-3 human prostate adenocarcinoma cells, and Chinese hamster ovary cells at $\geq 10 \mu\text{M}$ (Körner et al., 2004).

Reproductive and Developmental Toxicity

Human Studies: TCPMOH *in vitro* dose dependently altered human sperm motility, vitality, and acrosome reaction; very high cytotoxic concentrations modulated acrosome reaction and motility (Pflieger-Bruss et al., 2006 [PMID:16529574]).

Animal Studies:

TCPMOH

- In sexually mature (age not provided) male Sprague-Dawley rats, 1, 10 or 100 ppm in the diet for 28 days (5 animals/dose group) did not affect the concentration of luteinizing hormone (LH), testosterone (T), or the T/LH ratio, but did increase serum concentrations of follicle stimulating hormone at the highest dose. There was no significant treatment-related effect on testicular morphology or occurrence of apoptotic figures. An NOAEL for reproductive effects of 10 ppm was determined from the intake of 1.2 mg/kg/day (Foster et al., 1999 [PMID:10448550]).
- 16 and 32 μM inhibited intracellular cAMP concentrations in single adherent bovine oviductal cells (Pöhland and Tiemann, 2003 [PMID:12781216]).
- 16-64 μM inhibited gap junction formation and connexin43 protein expression in bovine granulosa cells (Tiemann, 2008 [PMID:18434086]).

Carcinogenicity

Not available

Anticarcinogenicity

Not available

Genetic Toxicity

Microbial Gene Mutation: Inconclusive in Ames test for TCPMOH and TCPMe (de Boer, 2000)

Human Studies (*in vitro* and *in vivo*): Not available

Animal Studies (*in vitro* and *in vivo*): Not available

Gene Mutation: Not available

Cytogenetic Effects: Not available

Germ Cell Effects: Not available

Neurotoxicity

Not available

Immunotoxicity

Not available

E. Mechanistic Data

Target Organs/Tissues

Human: Eyes, skin, and respiratory system (Alfa Aesar, 2003)

Animal: Not available

Endocrine Modulation

Human:

- TCPMOH and TCPMe inhibited binding of 17- β estradiol to human estrogen receptor but did not induce receptor/steroid receptor coactivator-1 interactions (Lascombe et al., 2000).

- TCPMOH did not induce cellular proliferation or block estradiol induced cellular proliferation of MCF-7 cells (Foster et al., 1999 [PMID:10448550]; Körner et al., 1997).
- TCPMOH was an antagonist at human androgen receptor *in vitro* (Körner et al., 2004; Schrader and Cooke, 2002 [PMID:12368053]).
- TCPMOH induced proliferation of MFM-223 cells (androgen receptor positive human breast cancer cell), with a maximum stimulation of 49% above control at 5 μ M, and blocked the antiproliferative effects of 5 α -dihydrotestosterone and Mibolerone (Körner et al., 1997, 2004).

Animal:

TCPMOH

- increased 4-hydroxylation of estradiol in liver microsomes of male, but not female, Sprague Dawley rats given 138 μ mol/kg i.p. x 3 days (Segura-Aguilar et al., 1997 [PMID:9169096]).
- competitively bound to rat prostate androgen receptors (Foster et al., 1999 [PMID:10448550]).
- did not bind to bovine uterine estrogen receptors (Kramer and Giesy, 1999 [PMID:10492903]).

Effect on Enzymes

Human: Not available

Animal: See "Effect on Metabolic Pathways" below.

Modes of Action

Human: Not available

Animal: Proposed that accumulation in the lipid layer leads to decreased membrane fluidity and altered gap-junctional conductance (Tiemann, 2008 [PMID:18434086]).

Effect on Metabolic Pathways:

Activation:

- Liver microsome P450 activity involved in hydroxylation of estradiol increased in rats injected with 138 μ mol/kg TCPMOH for 3 days (Segura-Aguilar et al., 1997 [PMID:9169096]).
- Dietary exposure to 10 and 100 ppm TCPMOH for 28 days increased hepatic Phase I and Phase II metabolic enzyme activities in Sprague Dawley rats (Poon et al., 1997 [PMID:9011026]).

Perturbation: Not available

Structure-Activity Relationships

Two congeners, triphenylmethane and triphenylmethanol, were selected since both contain the basic triphenylmethyl moiety that is found in TCPMOH and TCPMe. The difference between the congeners and the TCP-chemicals is the presence of a chlorine atom on each of the phenyl rings. Additionally, two chemicals from which TCPMOH or TCPMe may arise, DDT and Dicofol, were also evaluated.

Isomers: Not applicable

Congeners:

Triphenylmethane (CAS No. 519-73-3; PubChem CID: [10614](#) [PubChem, undated-a])

- Negative in *S. typhimurium* strains TA97, TA98, TA100, and TA104, TA1537, and TA1538 (CCRIS, 1993).
- Inactive in NCI *in vivo* anticancer drug screen in CD2F1 mice and yeast anticancer drug screen (stage 0) (PubChem, undated-b).
- Inhibited 3-methyl-cholanthrene-induced neoplastic transformation of 10T1/2 cells (Cooney et al., 1992).
- Inhibited GAP junctional intercellular communication in argininosuccinate synthetase-deficient human fibroblasts co-cultured with argininosuccinate lyase-deficient fibroblasts at concentrations that were at least 12-fold lower than concentrations that were cytotoxic (Davidson et al., 1985 [PMID:3931694]).

Triphenylmethanol (CAS No. 76-84-6; PubChem CID: [6457](#) [PubChem, undated-a])

- Inactive in the NCI *in vivo* anticancer drug screen in CD2F1 mice and yeast anticancer drug screen (stage 0); inconclusive results using B6D2F1 mice (PubChem, undated-b).
- Negative in the tetrahymena-pyriiformis population growth impairment assay (Schultz et al., 1993 [PMID:8288847]).

- Inhibited 3-methyl-cholanthrene-induced neoplastic transformation of 10T1/2 cells (Cooney et al., 1992).

DDT (CAS No. 50-29-3; PubChem CID: 3036 [PubChem, undated-a])

Numerous studies and international reports have described the toxicological properties of DDT (e.g., CCRIS, 2006a; ChemIDPlus, undated-a; HSDB, 2005; IPCS, 2000; NTP, 2008a). Results from some of these reports are provided below:

- LD₅₀ values: < 250 mg/kg (oral; rat, mouse, rabbit, guinea pig, monkey)
>5 g/kg (oral; hamster)
< 2 g/kg (dermal; rat, rabbit, guinea pig) (ChemIDPlus, undated-a).
- Short-term studies in rats indicated that oral exposure increased para-nitroanisole *O*-demethylase activity and DNA synthesis accompanied by increased hepatocyte mitotic activity (IPCS, 2000).
- Long-term rodent studies indicated that DDT induced hepatic lesions including hepatocellular adenomas, carcinomas, and benign liver tumors. DDT administered orally was neurotoxic, hepatotoxic, and produced estrogenic effects in monkeys (IPCS, 2000).
- Technical-grade DDT administered via feed to male and female Osborne-Mendel rats and B6C3F1 mice was not carcinogenic (NTP, 2008a). However, other studies have reported that DDT induced liver carcinomas and adenomas in mice and rats (CCRIS, 2006a; IPCS, 2000).
- Multigenerational studies of DDT in rodents reported that fertility and gonadal weights, the number of implantations, and the average litter size decreased while the length of the estrous cycle, the rate of embryo mortality, and the length of gestation increased. In a three-generation rat study, the mortality rate for offspring increased at all doses tested (IPCS, 2000).
- In most studies, DDT was not genotoxic or mutagenic *in vitro* or *in vivo* (CCRIS, 2006a; IPCS, 2000; NTP, 2008a).
- DDT induced neurotoxic and hormonal effects, as well as immune responses (IPCS, 2000).
- In humans, a TD_{Lo} of 5-16 mg/kg (oral, adult); LD_{Lo} of 150 mg/kg (oral; infant), 550 mg/kg (oral, adult) and 221 mg/kg (route unknown, adult) were reported; adverse effects included convulsions, arrhythmia, acute pulmonary edema, nausea, and vomiting (ChemIDPlus, undated-a).

Dicofol (CAS No. 115-32-2; PubChem CID: 8268 [PubChem, undated-a])

Numerous studies and international reports have summarized and discussed the toxicological properties of Dicofol (e.g., ChemIDPlus, undated-b; CCRIS, 2006b; HSDB, 2006; IPCS, 1996; NTP, 2008b). Results from some of these reports are provided below:

- LD₅₀ values: <2 g/kg (oral; rat, mouse, rabbit, guinea pig)
<2 g/kg (dermal; rat, rabbit)
>5 g/kg (inhalation; rat) (ChemIDPlus, undated-b)
- Short-term studies in mice, rats, and dogs reported that dietary administration reduced body-weight, increased hepatic mixed function oxidase activity, and reduced cortisol response to adrenocorticotrophin. NOAELs ranged from 0.07-2.1 mg/kg/day (IPCS, 1996).
- Long-term carcinogenicity studies in rats and mice reported species and gender specific results. Dicofol was not carcinogenic in female mice or in male or female rats but increased the incidence of liver adenomas and adenomas/carcinomas in male mice (IPCS, 1996; NTP, 2008b).
- An NOAEL for maternal toxicity in rats and rabbits of 0.25 and 4 mg/kg/day, respectively, was reported in a teratogenicity study. The NOAEL for embryo-fetal toxicity in rats and rabbits was 25 and 4 mg/kg/day, respectively (IPCS, 1996).
- A decrease in offspring viability was seen in two-generation reproductive study in rats given concentrations ≥125 mg/kg diet. The NOAEL for reproductive parameters was 25 mg/kg diet (equal to 2.1 mg/kg/day) (IPCS, 1996).
- Dicofol was not genotoxic or mutagenic in most studies *in vitro* or *in vivo* (IPCS, 1996; NTP, 2008b).

- In humans, a TD_{Lo} of 0.8 mL/kg (oral; women) was reported; adverse effects included diarrhea, gastrointestinal hypermotility, and excitement. Other symptoms of exposure included sinus congestion, dizziness, nausea, vomiting, disorientation, confusion, lethargy, and headaches (ChemIDPlus, undated-b).

Reactive Moieties: Not available

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PubChem. Undated-a. Compound Summary for the following:

- Tris(4-chlorophenyl)methanol; CID: 76379. Internet address: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=76379&loc=ec_rcs.
- 27575-78-6; CID: 92256. Internet address: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=92256&loc=ec_rcs.
- Triphenylmethane; CID: 10614. Internet address: <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=10614>.
- Triphenylcarbinol; CID: 6457. Internet address: <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=6457>.
- DDT; Clofenotane; CID: 3036. Internet address: <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=3036>.
- Dicofof; CID: 8268. Internet address: <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=8268>.

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PubChem. Undated-b. BioActivity Analysis: Summary for the following:

- Triphenylmethane. Internet address: <http://pubchem.ncbi.nlm.nih.gov/assay/assay.cgi?q=cids&reqid=137319133762642620>
- Triphenylcarbinol. Internet address: <http://pubchem.ncbi.nlm.nih.gov/assay/assay.cgi?reqid=463719084899757874&q=cids>

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Search Strategy

STN International files MEDLINE, AGRICOLA, CABA, EMBASE, BIOTECHNO, IPA, ESBIODBASE, BIOSIS, TOXCENTER, FSTA, FROSTI, PASCAL, and NTIS were searched simultaneously and CAPLUS was searched separately for environmental occurrence information on May 23, 2008. The edited history of the search session is shown below.

```
L1          413 S (TRIS OR TRI) (W) (4 OR P OR PARA) (W) CHLOROPHENYL (W) (METHANOL
OR METHANE OR CARBINOL)
L2          185 S (4 (W) 4 (W) 4 OR P (W) P (W) P OR PARA (W) PARA (W) PARA) (W)
TRICHLOROTRITYL (W) ALCOHOL OR 3010-80-8 OR 27575-78-6
L3          420 S L1 OR L2
SET DUPORDER FILE
L4          102 DUP REM L3 (318 DUPLICATES REMOVED)
L5          102 SORT L4 1-102 AU
SAVE L3 X540NAMES/A
SAVE L5 X540BIOMED/A
FILE 'CAPLUS' ENTERED AT 11:42:32 ON 23 MAY 2008
L6          49 S 27575-78-6/POL
L7          46 S 3010-80-8/POL
```


Chemical Information Profile for Tris(4-Chlorophenyl)methanol and Tris(4-Chlorophenyl)methane

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L9          115 S 3010-80-8
L10         29 S (L9 OR 2757-78-6) AND (59/SC OR 60/SC OR 61/SC)
L11         60 S L6 OR L7 OR L10
L12         60 DUP REM L11 (0 DUPLICATES REMOVED)
L16         60 SORT L11 1-60 AU
           SAVE L16 X540POLLU/A
```

Due to the CAS No. error in query L10, only the CAS No. for TCPMOH was combined with CAPLUS sections known to cover literature on environmental media. However, this was a redundant strategy to the use of the correct CAS No. for TCPMe with the pollutant "role." A total of 37 records was selected for full-record download (MEDLINE, 2; BIOSIS, 4; TOXCENTER, 17; CABA, 3; AGRICOLA, 1; EMBASE, 3; AND CAPLUS, 7). Searches on various Internet sites, including TOXNET, Google Scholar, IPCS INCHEM, and U.S. EPA, were conducted using chemical names and/or CAS RNs with and without specific search terms.

The same basic strategy (L1-L5) previously used was repeated in the biomedical databases on May 21, 2009 and the CAS Nos. were searched separately. The results accounted for all of the hits in L2 which was searched on May 23, 2008. Adding "Trichlorotriphenylmethanol OR trichlorotriphenylmethane" to the 2009 L2 query did not produce additional hits. Seven records were found when the search results were limited to publication years 2008 and 2009, four of which were new records from TOXCENTER that originated from CAPLUS. The remaining three were duplicates or previously considered.