

**GreenScreen™ Assessment for Tris(2-ethylhexyl) trimellitate (TEHTM)
(CAS #3319-31-1)**

GreenScreen™ Version 1.2 Verified Assessment

Date of Verification:	May 1, 2013
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Chemical Name: Tris(2-ethylhexyl) trimellitate

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Date: February 13, 2012; February 1, 2013; May 1, 2013

Confirm application of the *de minimus* rule¹: yes

Chemical Name (CAS #): Tris(2-ethylhexyl) trimellitate (TEHTM) (CAS #3319-31-1)

Also Called: 1,2,4-Benzenetricarboxylic acid, tris(2-ethylhexyl) ester; Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate; TOTM

Chemical Surrogates, analogs or moieties used in this assessment (CASs #):

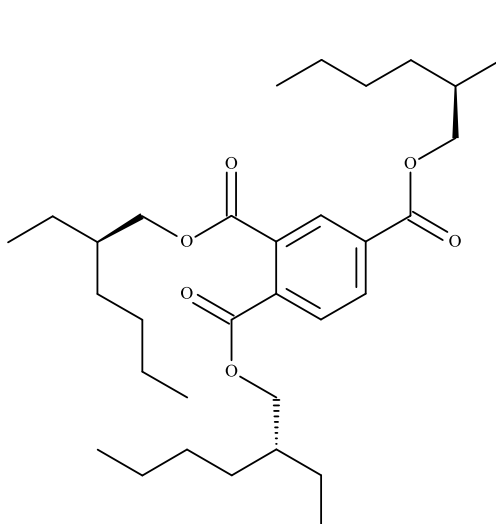
Based on the lack of data for TEHTM for several endpoints, ToxServices considered the inclusion of a chemical surrogate to address data gaps. However, there are insufficient peer-reviewed mechanistic data available in the published literature to justify the selection of a surrogate to model hazards identified as data gaps. Specifically, it is not known whether all high molecular weight aromatic esters share the same mechanism of action for the identified data gaps. Therefore, it is not justified to use toxicity data from surrogates to address data gaps without confirmation that the selected surrogate shares the same mechanism of action for a specific endpoint. As a result, no surrogate or analogs were selected. ToxServices considered the use of OncoLogic for estimation of TEHTM's

¹ Every chemical in a material or formulation should be assessed if it is:

1. intentionally added and/or
2. present at greater than or equal to 100 ppm.

carcinogenic potential, but TEHTM did not fall into any of the available chemical classes in the software. Modeling cannot address the remaining data gaps for endocrine activity, neurotoxicity or respiratory sensitization; therefore, the data gaps were left unfilled.

Structure of Chemical under Review:



Tris(2-ethylhexyl) trimellitate (TEHTM) (CAS #3319-31-1)

Notes related to production specific attributes²: No information disclosed by manufacturer or Green Chemistry and Commerce Council (GC3).

For Inorganic Chemicals and relevant particulate organics (if not relevant, list NA)

Define Properties:

1. Particle size (e.g. silica of respirable size) - NA
2. Structure (e.g. amorphous vs. crystalline) - NA
3. Mobility (e.g. Water solubility, volatility) - NA
4. Bioavailability - NA

Identify Applications/Functional Uses:

(e.g. Cleaning product, TV casing)

1. Plasticizer (UNEP 2002)
2. Electrical cable insulation and sheathing (UNEP 2002)

Green Screen Rating³: ToxServices assigned Tris(2-ethylhexyl) trimellitate (TEHTM) a GreenScreen™ Benchmark Score of U (unspecified) based on data gaps for two Group I Human Health Endpoints, Carcinogenicity (C) and Endocrine Activity (E). As outlined in CPA (2011c) Section III(1) (Benchmarking Chemicals With Data Gaps), permissible data gaps for Group I Human Health endpoints may only include Endocrine Activity and either Reproductive (R) or Developmental Toxicity. It should be noted that TEHTM was assigned a Moderate (M) for Reproductive (R) Toxicity. Based on this endpoint, TEHTM would be assigned a GreenScreen™ Benchmark score

² Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.

³ For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

of 2 (“Use but Search for Safer Substitutes”). In a worst case scenario, if TEHTM received a High (H) for Carcinogenicity (C) or Endocrine (E) Activity, it would be assigned a GreenScreen™ Benchmark score of 1.

GreenScreen™ Hazard Ratings: Tris(2-ethylhexyl) trimellitate (TEHTM)																			
Group I Human					Group II and II* Human								Ecotox		Fate		Physical		
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeat*	single	repeat*										
DG	L	M	L	DG	L	M	L	L	DG	L	DG	L	L	L	L	M	vL	L	L

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values and lower confidence. Hazard levels in **BOLD** font reflect values based on test data (See Guidance).

Transformation Products and Ratings:

Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) and/or moieties of concern⁴

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List ⁵ ?	Green Screen Rating ⁶
n/a	End of Life	Hydrolysis	2-Ethylhexanol	104-76-7	Not present on the Red List of chemicals	n/a
n/a	End of Life	Hydrolysis	Trimellitic acid	528-44-9	Not present on the Red List of chemicals	n/a

Introduction

Tris(2-ethylhexyl) trimellitate (TEHTM) is a plasticizer used for high temperature applications, or when low volatility and high viscosity are important. TEHTM is a U.S. EPA High Production Volume chemical with an estimated global production of 40,000-100,000 tons/year (CPSC 2009). When trimellitate esters, such as TEHTM, are processed with PVC, their principle feature is low volatility, even under high temperatures. Consequently, TEHTM’s primary use is in electrical cable insulation and sheathing. In addition, as a branched molecule, TEHTM is more viscous than other available plasticizers, such as linear adipates and phthalates, and thus can be used where high viscosity is required. The extraction and migration resistance of trimellitates are also significantly improved relative to phthalate plasticizers, leading to TEHTM’s recent use in dishwasher gaskets, medical tubing and photograph storage (CPSC 2009).

PhysioChemical Properties of Tris(2-ethylhexyl) trimellitate (TEHTM)

Table 1: Physical and Chemical Properties of Tris(2-ethylhexyl) trimellitate (TEHTM)		
Property	Value	Reference
Molecular formula	C ₃₃ H ₅₄ O ₆	HSDB 2003
SMILES Notation	c1(c(ccc(c1)C(OC[C@H](CCCC)CC)=O)C(OC[C@H](CCCC)CC)=O)C(O	ChemIDplus 2013

⁴ A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

⁵ The CPA “Red List” refers to chemicals 1). flagged as Benchmark 1 using the GreenScreen™ List Translator, or 2). flagged as Benchmark 1 or 2 using the GreenScreen™ List Translator and further assessed and assigned as Benchmark 1. The most recent version of the GreenScreen™ List Translator should be used.

⁶ The way you conduct assessments for transformation products depends on the Benchmark Score of the parent chemical (See Guidance).

Table 1: Physical and Chemical Properties of Tris(2-ethylhexyl) trimellitate (TEHTM)		
Property	Value	Reference
	C[C@@H](CCCC)C(=O)	
Molecular weight	546.79 g/mol	UNEP 2002
Physical state	Liquid	ECHA 2013
Appearance	Pale Yellow	ECHA 2013
Melting point	-43°C	ECHA 2013
Vapor pressure	6.8E-10 hPa at 25°C	ECHA 2013
Water solubility	0.13 mg/L (25°C) (OECD 105)	UNEP 2002
Dissociation constant	Not identified	
Density/specific gravity	0.987-0.990 g/cm ³ (20°C)	UNEP 2002
Partition coefficient	Log K _{OW} = 4.35-5.94 (25°C)	EC 2000, UNEP 2002

Hazard Classification Summary Section:
Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): DG

Tris(2-ethylhexyl) trimellitate has been assigned a data gap for carcinogenicity. Although it is not a known carcinogen, appropriate carcinogenicity testing has not been performed on the chemical.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- UNEP 2002
 - A report with very limited study detail indicated that mice (strain not identified) administered TEHTM (route not identified) at a dose of 1,400 mg/kg (possibly per day) did not produce evidence of carcinogenicity. Positive control animals administered urethane demonstrated evidence of carcinogenicity. No further details were provided for this study so the study was not considered to be of sufficient scientific rigor to assign a score for this endpoint.

Mutagenicity/Genotoxicity (M) Score (H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for mutagenicity based on negative test results for mutagenicity, clastogenicity and unscheduled DNA synthesis (UDS), both *in vitro* and *in vivo*.

- UNEP 2002
 - *In vitro* - A GLP-compliant Bacterial Reverse Mutation assay (OECD Guidelines 471 and 472) was conducted utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537, and *E. coli* tester strain WP2 UVY A in the presence and absence of metabolic activation (S9-mix) at concentrations of 0, 313, or 5,000 µg/plate TEHTM (99.0% purity). The chemical did not induce gene mutations under the test conditions. TETHM was determined to be negative for mutagenicity.
 - *In vitro* - An Ames assay (GLP compliance and test guideline were not reported) was conducted utilizing *Salmonella typhimurium* tester strains TA97, TA97, TA100 and TA1537 in the presence and absence of metabolic activation (S9-mix) at concentrations of 0, 100, 333, 1,000, 3,333, or 10,000 µg/plate TEHTM (purity not reported). No evidence of mutagenic activity was reported by the study authors.
 - *In vitro* - Two further Ames assays were identified by the SIDS dossier with very limited data. Both reported TETHM to be negative for mutagenicity.
 - *In vitro* - A GLP-compliant Cytogenetics assay (Guidelines for Screening Mutagenicity Testing of Chemicals (Japan)) was conducted utilizing Chinese Hamster Lung (CHL/IU) cells in the presence and absence of metabolic activation at concentrations of 0, 0.005, 1.3, 2.5, or 5.0 mg/L TEHTM (99.0% purity). The chemical did not induce structural chromosomal aberrations or polyploidy under the tested conditions. TEHTM was found to be negative for clastogenicity.
 - *In vitro* - A GLP-compliant Hypoxanthine-Guanine Phosphoribosyltransferase (HPGRT) assay (test method not reported) was conducted utilizing Chinese Hamster Ovary (CHO) cells in the presence and absence of metabolic activation at concentrations ranging from 5 to 200 nl/ml TEHTM (purity not reported). In the non-activated 50 nl/ml group a statistical increase in mutant frequencies were reported. However, the result was not repeated under a duplicate assay and was considered to represent

a statistical failure. In the activated 200 nl/ml, both duplicate assays showed a statistical increase in mutant frequencies. A repeated trial was conducted and did not confirm the response. The evaluation stated that TEHTM was found to be non-mutagenic. SIDS authors also report that HGPRT assays show that TEHTM is not mutagenic.

- *In vitro* – A GLP-compliant Unscheduled DNA Synthesis (UDS) assay (test method not reported) was conducted utilizing primary rat hepatocytes in the absence of metabolic activations at concentrations ranging from 250 to 5,000 nl/ml TEHTM (purity not reported). Authors reported that the stability in cell numbers and normal morphological appearance indicated that hepatocyte cultures were in good metabolic condition. No significant changes were reported and the test substance was found to be negative for UDS.
- *In vivo* – A Dominant Lethal assay (GLP status not reported and test method not reported) was conducted using male Swiss mice (number not reported). Mice were administered doses (method of administration not reported) of 1,400 mg/kg TEHTM (purity not reported) for an unknown number of doses. The authors reported that TEHTM was not mutagenic when compared to positive controls.

Reproductive Toxicity (R) Score (H, M, or L): M

Tris(2-ethylhexyl) trimellitate was assigned a score of Moderate for reproductive toxicity based on limited data that classifies this compound as a GHS Category 2 reproductive toxicant. Chemicals that are assigned to GHS Category 2 for reproductive toxicity are assigned a hazard score of moderate (CPA 2011a).

- UNEP 2002
 - A GLP-compliant OECD Preliminary Reproductive Screening test was conducted using male and female Sprague-Dawley rats (numbers not reported). Rats were administered oral doses of 0, 100, 300, or 1,000 mg/kg TEHTM (99.0% purity) via gavage for 46 days in males, and from 14 days before mating to day 3 of lactation in females. In adult males, histopathological examination of the testes demonstrated decrease of spermatocytes and spermatids in the 300 and 1,000 mg/kg groups. No effects on general appearance, body weight, food consumption, autopsy findings, or weight of reproductive organs were reported. In adult females, no effects were reported on general appearance, body weight, food consumption, autopsy findings, and weight of reproductive organs. In the offspring, no effects were reported on reproductive ability, organ weights, viability, general appearance, body weights or autopsy findings. On the basis of the findings, a reproductive LOAELs of 300 mg/kg for males and a NOAEL of 1,000 mg/kg for females and offspring were established. The GHS criteria state that evidence from screening studies may be used to classify a material, but are recognized as less reliable than a full reproductive toxicity study. Furthermore, GHS Category 1B states that it requires clear evidence of reproductive toxicity to animals, while GHS Category 2 states that it requires some evidence (UN 2011). Therefore, in the absence of further data on the historical occurrence of these effects in rats, along with the absence of statistical evaluations and a full reproductive toxicity study, ToxServices classifies TEHTM as a GHS Category 2 reproductive toxicant.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for developmental toxicity based on a GLP-compliant study that showed no developmental toxicity induced by TEHTM.

- HLS 2002 –
 - A GLP-compliant Developmental toxicity study was conducted in female Sprague-Dawley rats (35/group). Rats were administered oral doses of 0, 100, 500, or 1,050 mg/kg TEHTM via gavage on gestation days 6-19 for pre-natal teratology and on gestation day 6 through lactation day 20 for postnatal developmental evaluation. No significant effects on maternal body weights or gravid uterus weights were observed. No significant effects were reported on developmental parameters including number of implantations, post-implantation loss, gestation length and index, litter size, fetal body weights, or offspring survival. The only significant effect reported was an increase in the number of male offspring from high-dose dams with retained areolar regions. However, this effect was no longer present by post-natal day 13 when compared to controls. This effect was not considered to be toxicologically significant by researchers. Therefore, a NOAEL of 1,050 mg/kg was identified for both maternal and developmental toxicity.

Endocrine Activity (E) Score (H, M or L): DG

Tris(2-ethylhexyl) trimellitate was assigned a data gap for endocrine activity. Although it is not known to have endocrine activity, testing for endocrine activity has not been performed on TEHTM. It is not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors or on the lists of chemicals generated by the U.S. EPA's Endocrine Disruptor Screening Program (EDSP).

- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Not listed as a potential endocrine disruptor on the Red List of Chemicals (CPA 2011b).
- No relevant data were identified for Tris(2-ethylhexyl) trimellitate.

Group II and II* Human Health Effects (Group II and II* Human)

Note: Group II and Group II endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.*

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for acute mammalian toxicity based on oral and dermal LD₅₀ values being greater than 2,000 mg/kg, the cut off for low acute mammalian toxicity (CPA 2011a). Although one dermal LD₅₀ fell just below the 2,000 mg/kg cutoff, weight of evidence suggests this compound to be of low acute toxicity.

- UNEP 2002 –
 - Oral LD₅₀ (Sprague-Dawley rat) > 2,000 mg/kg TEHTM (> 99.0% purity) (OECD 401)
 - Oral LD₅₀ (rat) > 3,200 mg/kg TEHTM (No further details available)
 - Oral LD₅₀ (mouse) > 3,200 mg/kg TEHTM (No further details available)
 - Dermal LD₅₀ (rabbit) > 1,970 mg/kg TEHTM (98.95% purity) (modified OECD 402)
 - Dermal LD₅₀ (guinea pig) > 19,700 mg/kg TEHTM (No further details available)
- ECHA 2013 –
 - Inhalation LD₅₀ (Sprague-Dawley rat) > 2,600 mg/m³ TEHTM (98.95%) (4-hour exposure, GLP compliant, OECD 403).

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

Group II Score (single dose: vH, H, M or L): M

Tris(2-ethylhexyl) trimellitate was assigned a score of Moderate for systemic toxicity/organ effects (single dose) based on the lack of pathological findings after single oral and dermal exposures and the observation of reddened patches on the lungs of animals administered a single inhalation exposure. The toxicological significance of this effect is not clear but it is likely transient and would result in the classification of TEHTM as a GHS Specific Target Organ Toxicity (STOT): Single Exposure Category 3 (Transient Target Organ Effects) compound which leads to an assigned hazard score of Moderate.

- UNEP 2002 –
 - No gross pathological changes or clinical signs of toxicity were observed during the observation periods following a single oral dose of 2,000 mg/kg in Crj:CD rats or a single dermal dose of 2 mL/kg applied for 24-hours in New Zealand White rabbits.
- ECHA 2013 –
 - Inhalation – Sprague-Dawley rats were administered a single inhalation exposure of 2,600 mg/m³ (2.6 mg/L) TEHTM (4 hours, 98.95% purity). After a 15-day observation period, surviving animals were necropsied and evaluated for gross pathologies. Five of five male animals and three of five female animals exhibited reddened patches on the lungs. No further data is provided and no microscopic evaluations were performed.

Group II* Score (repeated dose: H, M, L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for systemic toxicity/organ effects (repeated dose). As no 90-day repeat dose studies are available for this chemical, the reference values for oral repeat dose toxicity studies, as provided in the GHS guidance (UN 2011), were adjusted by a factor of 3: from ≤10 to < 30 mg/kg/day for Category 1 and from >10 -100 to >30-300 mg/kg/day for Category 2. Based on the available data, TEHTM is

not categorized as a GHS Category 1 or 2 chemical as the studies reviewed below have NOAEL and/or LOAEL values greater than 300 mg/kg/day. Furthermore, the primary liver effects observed in the rodent studies, namely peroxisome proliferation, are of questionable relevance to human beings. The weight of evidence is that TEHTM has a low potential to cause toxicity after repeated-dose exposures. Low scores for systemic toxicity/organ effects (repeated dose) are assigned when adequate negative studies are available and the LOAELs exceed 100 mg/kg/day or 300 mg/kg/day after adjustment from a 28-day exposure period to a 90-day exposure period (CPA 2011a, UN 2011).

- UNEP 2002 –
 - In a GLP-compliant 28-day toxicity study (test method not reported), male and female Fischer 344 rats (5/sex/group) were administered oral doses of 0, 184, 650, or 1,826 mg/kg TEHTM (98.2% purity) daily in feed. Body weights and food intake were monitored, tissue samples were examined from top and control groups, liver samples were examined microscopically. Male and female rats in the 650 mg/kg/day group has slightly increased liver weights and increased activities of liver enzymes (including palmitoyl CoA and carnitine acetyl transferase). Hematological effects include reduced erythrocytes, increased leucocytes and raised cholesterol at 650 mg/kg/day in both sexes. However, reduced blood cell counts were slight and a dose-response relationship could not be established. Slight peroxisome proliferation was seen in rats receiving the highest dose. A NOAEL and LOAEL of 184 and 650 mg/kg/day based on hematological effects and increased liver weights were established by study authors, respectively. The CPSC (2009) established a NOAEL of 1,826 mg/kg/day upon full review of the study. The liver changes reported in this study were found by the CPSC to be due to peroxisome proliferation, which is a rodent specific effect with questionable relevance to humans.
 - In a GLP-compliant 28-day toxicity study (Guidelines for 28-day Repeated Dose Toxicity Testing of Chemicals (Japan)), male and female Sprague-Dawley rats (5/sex/group) were administered oral doses of 0, 100, 300, or 1,000 mg/kg TEHTM (> 99% purity) daily in feed. No adverse effects to clinical signs, body weights, food consumption, hematology, blood chemistry, urinalysis and pathological examination were reported. A NOAEL of 1,000 mg/kg/day was reported by the authors.
 - In a GLP-compliant 28-day toxicity study (test method not reported), male Fischer 344 rats (5/group) were administered doses of 0 or 1,000 mg/kg TEHTM (98.95% purity) via oral gavage 5 times a week for 4 weeks. A slight non-significant increase in liver weight was reported, along with significantly decreased blood triglyceride levels. However, as reported by the CPSC (2009), the toxicological significant of this finding is unclear. Based on the decreased triglyceride levels, a LOAEL of 1,000 mg/kg/day was established.
 - In a GLP-compliant 21-day toxicity study (test method not reported), male and female Fischer 344 rats (5/sex/group) were administered doses of 0, 200, 700, or 2,000 mg/kg TEHTM (purity not reported) daily via oral gavage. Relative liver weights were significantly increased in female rats at all dose levels, although no dose-response relationship could be established. Males in the top dose group showed a slight increase in hepatic peroxisomes compared to controls. Various hepatic enzyme activities (palmitoyl-CoA/lauric acid 12-hydroxylate) were increased in males at 200 mg/kg/day and in females at 2,000 mg/kg/day. The CPSC (2009) concluded that a NOAEL of 2,000 mg/kg/day could be established for this study as peroxisome proliferation appears to be the key affect, as discussed in the study above.

Neurotoxicity (N)

Group II Score (single dose: vH, H, M or L): L

TEHTM has been assigned a score of Low for neurotoxicity (single dose) based on the lack of clinical behavioral effects following acute toxicity studies. A score of low is awarded for neurotoxicity (single dose) when adequate negative studies are available (CPA 2011a).

- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2011b).
- ECHA 2013a
 - No clinical behavioral signs of toxicity were observed during the observations periods following a single oral dose of 2,000 mg/kg in Crj:CD rats, a single inhalation dose of 2,600 mg/m³ (4-hours) in Sprague-Dawley rats, or a single dermal dose of 2 mL/kg applied for 24-hours in New Zealand White rabbits.

Group II* Score (repeated dose: H, M, L): DG

Tris(2-ethylhexyl) trimellitate was assigned a data gap for neurotoxicity (repeated dose). Although it is not a known neurotoxicant, neurotoxicity testing has not performed on this chemical.

- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2011b).
- No relevant data were identified for Tris(2-ethylhexyl) trimellitate.

Skin Sensitization (SnS) Group II* Score (H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for skin sensitization based on negative results in both human and animal studies.

- UNEP 2002 –
 - The skin sensitization potential of TEHTM (98.95% purity) was tested in a GLP-compliant Buehler Test (Following OECD 406) using guinea pigs (number/sex/strain not reported). Guinea pigs were exposed to TEHTM under covered contact for 24 hours on alternate days for 10 applications. A challenge application was made after a 2 week rest period. No sensitization was observed in any of the 10 tested animals. The authors reported TEHTM to be non-sensitizing to guinea pigs.
- David et al. 2003
 - Two to three hundred human volunteers were tested for skin sensitization of TEHTM. Dermal applications were applied 3 times week for 3 weeks, followed by a challenge dose two weeks later. The overall conclusion by the authors was that TEHTM demonstrated no evidence of sensitization.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): DG

Tris(2-ethylhexyl) trimellitate was assigned a data gap for respiratory sensitization.

- No relevant data identified for this compound.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for skin irritation/corrosivity as it is not classified as a GHS Skin Irritant/Corrosive chemical.

- UNEP 2002 –
 - The acute dermal irritation/corrosiveness of TEHTM was tested in rabbits (2/sex, strain not reported) following OECD Guideline 404 in two separate studies (not GLP-compliant). Rabbits were exposed to doses of 0.5 ml of TEHTM (purity not reported) under an occlusive patch. The animals demonstrated slight erythema 30 to 60 minutes after removal of patches, and in one study a single rabbit showed slight erythema remaining after 72 hours. No animals were affected at 7 days after removal of the patch. Both studies reported the test substance as being non-irritating following EC classification.
 - In a second GLP-compliant acute dermal irritation/corrosiveness study, rabbits (n=6) and male guinea pigs (n=10) were exposed to 0.5 ml of TEHTM (98.95% purity) for 24 hours following an unspecified test guideline. Limited details were provided for this study and the authors reported that TEHTM was not a primary skin irritant to rabbits or guinea pigs.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for eye irritation/corrosivity as no irritation or corrosion was observed following administration of the substance.

- UNEP 2002 –
 - The acute ocular irritation/corrosion of TEHTM (98.96% purity) was tested in New Zealand White rabbits (n=6) in a GLP-compliant study, following an unspecified method. Rabbits were exposed to single instillations of 0.1 ml of the test substance and examined on days 1, 2, 3, 4, and 7 following treatment. Limited data were available for the study results, and the authors concluded that TEHTM was not a primary eye irritant.
 - In a second study, the acute ocular irritation of TEHTM was tested in rabbits (2/sex/strain not reported) following OECD 405 “Acute Eye Irritation” (not GLP-compliant). Rabbits were exposed to single instillations of 0.1 ml of the test material into the conjunctival sac of the left eye. After 72 hours no abnormalities were seen. The study authors reported TEHTM to be non-irritating following EC classification.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for acute aquatic toxicity based on its low water solubility and L/EC₅₀ values greater than 100 mg/L, the cut off for low acute aquatic toxicity (CPA 2011a).

- UNEP 2002 -
 - TEHTM has reported L/EC₅₀ values of > 100 mg/L (*Oryzias latipes*, fish, 96-hr) (OECD 203), > 180 mg/L (*Daphnia magna*, Daphnia, 48-hr) (OECD 202), and > 100 mg/L (*Selenastrum capricornutum*, algae, 72-hr) (OECD 201).
 - As these values are several orders of magnitude above the water solubility of TEHTM (0.13 mg/L), no acute toxicity to aquatic organisms is expected at saturation.

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for chronic aquatic toxicity based on its low water solubility and NOEC values greater than 10 mg/L, the cutoff for low chronic aquatic toxicity (CPA 2011a).

- UNEP 2002 -
 - TEHTM has reported chronic NOEC values of 75 mg/L (*Oryzias latipes*, fish, 14-day) (OECD 204) and 55.6 mg/L (*Daphnia magna*, daphnia, 21-day) (OECD 211).
 - As these values are several orders of magnitude above the water solubility of TEHTM (0.13 mg/L), no acute toxicity to aquatic organisms is expected at saturation.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): M

Tris(2-ethylhexyl) trimellitate was assigned a score of Moderate for persistence based on a hydrolysis half-life of 17.5 days at pH 7 and the results of biodegradability tests indicating this substance has a half-life between 16 and 60 days, the range for moderate persistence (CPA 2011a).

- UNEP 2002 -
 - Following OECD 302C “Inherent Biodegradability: Modified MITI Test (II)” (non GLP-compliant), TEHTM (purity not reported) was found to have 4.2% biodegradation after 28 days.
 - Following OECD 301C “Ready biodegradability: Modified MITI Test” (GLP-compliant), TEHTM (purity not reported) was found to have 3.4% biodegradation after 28 days.
 - Following a 28-day shake flask method (GLP-compliant), ¹⁴C-labeled TEHTM (purity not reported) was found to be inherently biodegradable with 68% biodegradation occurring in 28 days.
 - The stability of TEHTM (purity 98.5%) in water was evaluated in a GLP compliant, OECD 111 “Hydrolysis as a Function of pH” test. TEHTM was stable at pH 4 and 50 °C, had a half-life of 17.5 days at pH 7 and 25 °C, and a half-life of 11.9 days at pH 9 and 25 °C.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL

Tris(2-ethylhexyl) trimellitate was assigned a score of Very Low for Bioaccumulation (B) based on measured bioconcentration factor (BCF) values less than 100. Chemicals that have bioconcentration factors less than 100 are assigned very low scores for bioaccumulation (CPA 2011a).

- UNEP 2002 -
 - The bioaccumulation of TEHTM was evaluated in a non-GLP compliant test conducted according to OECD 305C “Degree of Bioconcentration in Fish.” Carp (*Cyprinus carpio*) were exposed to either 0.2 or 2 mg/L TEHTM with a solubilizer (not identified). Controls were exposed to the solubilizer alone. After 42 days of exposure, the bioconcentration factor (BCF) for the 0.2 mg/L group was 1-2.7 while that for the 2 mg/L group was 0.1-0.23.
 - Although the concentrations tested exceeded the water solubility (0.13 mg/L) of TEHTM, the use of an unidentified solubilizer likely adjusted the water solubility so that the accessibility of TEHTM to the fish was increased.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L

TEHTM was assigned a score of Low for reactivity based on not having any chemicals or functional groups expected to contain high energy bonds or oxidizing species which may cause reactivity.

- TEHTM would not be classified as an oxidizing chemical as its structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, TEHTM is not expected to be explosive as it does not contain structural groups that would cause concern for explosion. Furthermore, the high flashpoint (> 225°C) further supports that TEHTM is not a reactive chemical.

Flammability (F) Score (vH, H, M or L): L

Tris(2-ethylhexyl) trimellitate was assigned a score of Low for flammability based on not being classified as a GHS Flammable Liquid.

- UNEP 2001 –
 - TEHTM has a flash point of greater than 225°C, which is above the 93°C cut-off criteria to be classified as a flammable liquid by GHS (UN 2011).

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

- (AA) Acute Aquatic Toxicity**
- (AT) Acute Mammalian Toxicity**
- (B) Bioaccumulation**
- (C) Carcinogenicity**
- (CA) Chronic Aquatic Toxicity**
- (Cr) Corrosion/ Irritation (Skin/ Eye)**
- (D) Developmental Toxicity**
- (E) Endocrine Activity**
- (F) Flammability**
- (IrE) Eye Irritation/Corrosivity**
- (IrS) Skin Irritation/Corrosivity**
- (M) Mutagenicity and Genotoxicity**
- (N) Neurotoxicity**
- (P) Persistence**
- (R) Reproductive Toxicity**
- (Rx) Reactivity**
- (SnS) Sensitization- Skin**
- (SnR) Sensitization- Respiratory**
- (ST) Systemic/Organ Toxicity**

Original Tris(2-ethylhexyl) trimellitate (Version 1.0 and Revised 1.2) GreenScreen™ Evaluations Prepared By:



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Tris(2-ethylhexyl) trimellitate Updated to GreenScreen™ Version 1.2 By:



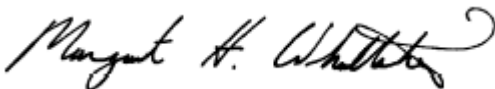
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