CPSC Staff Statement on University of Cincinnati Report
"Toxicity Review for Tributyl Citrate (TBC)"[1]

June 2019

The U.S. Consumer Product Safety Commission (CPSC) contracted with the University of Cincinnati to conduct toxicology assessments for nine dialkyl o-phthalate (o-DAP) substitutes: phenyl esters of C10-C18 alkylsulfonic acid esters (ASE); glycerides, castor-oil-mono-, hydrogenated, acetates (COMGHA); dibutyl adipate (DBA) and di-isobutyl adipate (DiBA); di (2-ethylhexyl) sebacate (DEHS)/dioctyl sebacate (DOS); a mixture of 98% di-2-ethylhexyl terephthalate (DEHT) and 2% 2-ethylhexyl methyl terephthalate (2-EHMT); dibutyl sebacate (DBS); diisononyl adipate (DINA); epoxidized soybean oil (ESBO); and tributyl citrate (TBC). The reports will be used to inform staff's assessment of products that may contain these compounds and is the first step in the risk assessment process.

CPSC staff assesses a product's potential health effects to consumers under the Federal Hazardous Substances Act (FHSA). The FHSA is risk-based. To be considered a "hazardous substance" under the FHSA, a consumer product must satisfy a two-part definition. First, it must be "toxic" under the FHSA, or present one of the other hazards enumerated in the statute. Second, it must have the potential to cause "substantial personal injury or substantial illness during or as a proximate result of any customary or reasonably foreseeable handling or use." Therefore, exposure and risk must be considered in addition to toxicity when assessing potential hazards of products under the FHSA.

The first step in the risk assessment process is hazard identification, which consists of a review of the available toxicity data for the chemical. If it is concluded that a substance may be "toxic," then CPSC staff will pursue a quantitative assessment of exposure and risk to evaluate whether a specified product may be considered a "hazardous substance."

The toxicity review for TBC follows. Based on the research conducted by the University of Cincinnati, the animal data support the conclusion that TBC does not fit the designation of acutely toxic under the FHSA following single oral exposure. Data are not available to assess the acute toxicity of TBC under FHSA via the inhalation or dermal routes.

[1] This statement was prepared by the CPSC staff, and the attached report was produced by the University of Cincinnati for CPSC staff. The statement and report have not been reviewed or approved by, and do not necessarily represent the views of, the Commission.

TOXICITY REVIEW FOR
TRIBUTYL CITRATE
(TBC)

Contract No. CPSC-D-17-0001
Task Order 61320618F1002

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April 11, 2019

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1 Introduction

This report summarizes available data on the identity, physicochemical properties, manufacture, supply, use, toxicity, and exposure associated with tributyl citrate (TBC).

Literature searches for physico-chemical, toxicological, exposure, and risk information were performed in July 2018 using the CAS number and synonyms (see Appendix 1 for the full list of search terms), and using the following databases:

- EPA SRS
- PUBMED
- RTECS
- TSCATS (included in TOXLINE)
- TOXNET databases, including
    - TOXLINE
    - CCRIS
    - DART/ETIC
    - GENE-TOX
    - HSDB

Searches were conducted for studies indexed to PubMed and Toxline databases from all dates to the date of the search (July, 2018). Other databases and websites were also used to identify additional key information, particularly authoritative reviews. Authoritative reviews for general toxicity and physicochemical information were identified in the following databases using the CAS number for TBC and synonyms. Downloaded documents were saved as pdfs. The sites searched included:

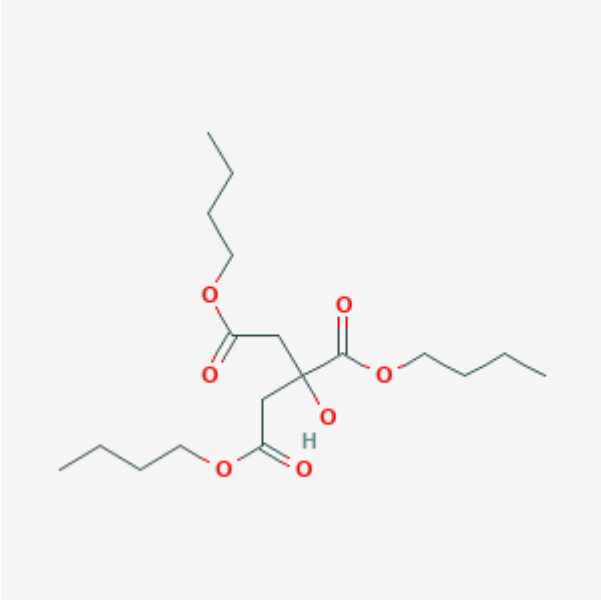
- ANSES Information on Chemicals (https://www.anses.fr/en)
- ChemIDPlus (https://chem.nlm.nih.gov/chemidplus/)
- ECHA Information on Chemicals (https://echa.europa.eu/information-on-chemicals)
- EFSA (https://www.efsa.europa.eu/)
- EPA chemistry dashboard (https://comptox.epa.gov/dashboard)
- EPA (https://www.epa.gov/)
- EPA IRIS (https://www.epa.gov/iris)
- FDA (https://www.fda.gov/)
- Health Canada (https://www.canada.ca/en/health-canada.html)
- IARC (https://www.iarc.fr/)
- INCHEM (http://www.inchem.org/)

- JEFCA (http://www.who.int/foodsafety/areas_work/chemical-risks/jecfa/en/)
- NICNAS (https://www.nicnas.gov.au/)
- NTP (https://ntp.niehs.nih.gov/)
- OECD (http://www.oecd.org/)
- WHO (http://www.who.int/en/)

2 Physico-Chemical Characteristics

2.1 Physical-Chemical Properties

Table 1: Physical and chemical properties

Chemical Name	Tributyl Citrate
Synonyms	2-Hydroxy-1,2,3-propanetricarboxylic acid, tributyl ester; Butyl citrate; Butyl citrate; Citric acid, tributyl ester; n-butyl citrate; Citroflex 4 (ChemIdPlus, 2019)
CAS Number	77-94-1 (PubChem, 2018)
Structure	 (PubChem, 2018)
Chemical Formula	$C_{18}H_{32}O_7$ (PubChem, 2018)
Molecular Weight	360.447 g/mol (PubChem, 2018)
Physical State	Liquid (PubChem, 2018)
Color	Colorless (U.S. EPA, 2018a)
Melting Point	-20.0ºC (PubChem, 2018)
Boiling Point	362ºC (predicted average)
Vapor Pressure	1.09×10^{-7} to 2.64×10^{-5} mmHg (predicted range)

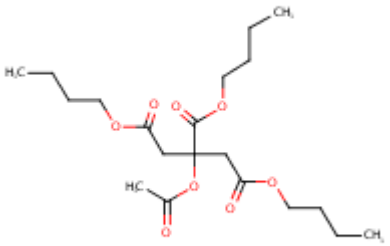
Water Solubility	7.59 x 10^{-5} to 1.84 x 10^{-3} mol/L (predicted range)
Log Kow	3.64 (predicted average)
Log Koc[1]	827 L/kg (predicted average)
Henry's Law	274 x 10^{-8} atm-m^3/mole (predicted average)
Flashpoint	121 - 200°C (predicted range)
Density	1.09 g/cm^3 (predicted average)
BCF	18.6 (predicted average)
Source	US EPA (2019a), unless otherwise stated)

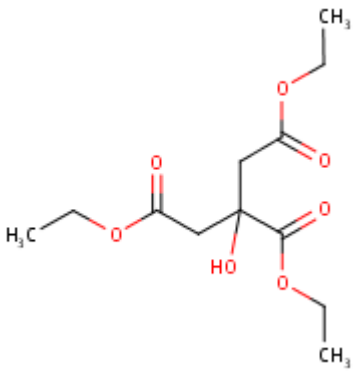
Log K_{ow} is the octanol-water partition coefficient. Henry's Law is Henry's Law Constant. Log Koc is soil adsorption coefficient. BCF is bioconcentration factor. See Appendix 2 for more details.

[1]It appears that this value is actually the Koc, not the Log Koc, based on its magnitude.

2.2 Potential Analogs for Read Across

Table 2: Analogs for potential read-across

Chemical Name	CAS No.	Structure and SMILE Notation
Acetyltributylcitrate [identified by ECHA as a structural analog]	77-90-7	CCCCOC(=O)CC(CC(=O)OCCCC)(C(=O)OCCCC)OC(=O)C 
Triethyl citrate	77-93-0	O=C(OCC)C(O)(CC(=O)OCC)CC(=O)OCC

		
acetyl-tri-(2-ethylhexyl)-citrate [identified by ECHA, 2018 as a structural analog]	144-15-0	CCCCC(CC)COC(=O)CC(CC(=O)OCC(CC)CCCC)(C(=O)OCC(CC)CCCC)OC(=O)C
Source	U.S. EPA 2018a unless otherwise stated	

The EPA's Analogue Information Methodology (AIM) (U.S. EPA, 2018a) was used to identify potential analogues that could be used to fill data gaps for TBC. However, most of the potential analogues were considered inappropriate, due to the presence of additional functional groups that could affect toxicity. Triethyl citrate is structurally very similar to TBC, but Finkelstein and Gold (1959) found that the toxicity of triethyl citrate, while still low, was substantially higher than that of TBC (triethyl citrate LD_{50} about 7 mL/kg, vs. >30 mL/kg for TBC; see Section 5). This higher toxicity of triethyl citrate was attributed to its higher solubility in water. Another potential analogue is acetyl-tri-(2-ethylhexyl)-citrate, but this compound would hydrolyze to a 2-ethylhexyl alcohol moiety, which has toxicity different from that of butanol. Based on these considerations, the most appropriate potential analogue is acetyl tributyl citrate (ATBC) (see Risk Science Center, 2018), which can hydrolyze to TBC, among other metabolites. ECHA (2018) used ATBC as an analogue for TBC in much of its assessment. Similarly, ANSES[1] (2016) considered the potential for read across from ATBC to TBC on an endpoint-by-endpoint basis, and concluded that a read across from ATBC would be appropriate for several endpoints. ANSES (2016) rejected the suggestion of a category approach with additional citrate compounds, due to the lack of supporting toxicokinetic data.

3 Manufacture, Supply, and Use

Manufacture and Supply

TBC is a high production volume chemical with U.S. manufacture and imports reported to be between one and 10 million pounds (500 to 5000 tons) per year for 2015 (U.S. EPA, 2018b).

[1] ANSES is the Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'environnement et du travail, or the French Agency for Food, Environmental and Occupational Health & Safety.

The overall production and/or imported volume in Europe is between 1000 and 10,000 tons per year (ECHA, 2018).

Use

TBC is a substitute for diethylhexyl phthalate (DEHP) and is used primarily to plasticize vinyl resins in applications such as toys, pacifiers, medical devices, and packaging films (ANSES, 2016). It is used in building and construction materials, adhesives and sealants, plastic and rubber products, paints and coatings, perfumes, paint removers, ink and toners, and personal care products (ANSES, 2016; PubChem, 2018). Additional uses include washing machine liquids/detergents and automotive care products (ECHA, 2018). According to ANSES (2016), the Danish EPA lists colored textiles and light sticks as registered products containing TBC. The Household Products Database lists dozens of products containing TBC, primarily personal care products and specifically hair coloring products (Household Products Database, 2018).

TBC is an indirect additive used in food contact substances (FDA, 2018) and is an FDA-approved pharmaceutical plasticizer (Sui et al., 2015).

4 Toxicokinetics

No standard toxicokinetic studies of TBC were located. However, some information on TBC metabolism is available from an *in vitro* study. In an unpublished technical report (Davis, 1991, as cited by ECHA, 2018), a single sample of human serum and a rat liver homogenate from a single adult rat were treated with 100 μg TBC/mL (252 nmoles/mL). In human serum, the half-life was reported as 4 hours, while the half-life in rat liver was estimated to be seconds, as the time-zero measurement detected only about 1/3 (35 μg/mL) of the administered dose. The level of TBC in human serum showed exponential and complete decline over the 24 hour time period, and the level of TBC in the rat liver homogenate showed complete metabolism in 15 minutes. Butanol was reported as a metabolite of TBC (apparently from the rat liver homogenate), with a maximal concentration at 1-2 hours. The authors concluded that 1.74 mole equivalents of butanol (of a theoretically possible 3 moles) are produced from 1 mole of TBC. The authors also suggested that the metabolites would include citric acid. Overall, the results support rapid metabolism of TBC in human serum and rat liver homogenate, with no bioaccumulation potential. ATBC was also evaluated in this study, and was noted to also hydrolyze to butanol, and presumably acetic and citric acid.

ANSES (2016) suggested that absorption of TBC would be expected to be high, based on its molecular weight, water solubility and Log P_{OW} (another term for the Log K_{OW}) and in comparison with ATBC. At least 67% of an oral dose of ATBC was reported to be absorbed in rats (Dow Chemical Company, 1992, as cited by U.S. EPA 2019b).

5 Hazard Information

5.1 Acute Single Dose Toxicity

Lethality of TBC by acute oral exposure is low. Groups of five Wistar rats were given a single gavage dose of TBC at dose levels ranging from 10 to 30 mL/kg (10,800-32,400 mg/kg, based on a density of 1.08 g/mL) (Finkelstein and Gold, 1959). All of the rats survived for the 21-day observation period with no clinical signs of toxicity (LD_{50} >32,400 mg/kg) (Finkelstein and Gold, 1959). Cats were also tested in this study. All 12 cats given a single gavage dose of TBC at dose levels ranging from 30 to 50 mL/kg survived through an 8-week observation period (Finkelstein and Gold, 1959). Shortly following dosing in this study, the dosing material began to leak from the rectums of both rats and cats, likely because of the very large dosing volume (current guidelines recommend no more than 1 mL/kg body weight for rats). Rats appeared sluggish following dosing but recovered during the observation period, and did not exhibit any other clinical signs of toxicity. Cats showed signs of nausea and developed diarrhea, which subsided in less than 24 hours following dosing. Hematology and urinalysis examinations conducted at 2-week intervals for 2 months on two cats receiving a single gavage dose of 50 mL/kg did not reveal any treatment-related changes (Finkelstein and Gold, 1959).

No other acute oral studies were located, and there were no acute studies of TBC conducted via the inhalation or dermal routes.

5.1.1 Irritation/Sensitization

No data were located on the potential for TBC to cause skin or eye irritation, or sensitization.

5.2 Repeated Dose Toxicity

Finkelstein and Gold (1959) performed a short-term feeding study in rats to evaluate the effect of oral exposure to TBC on growth, hematology, and pathology. Twenty-one day-old Wistar rats (mixed sex groups, 4/dose) were provided diets containing 0, 5%, or 10% TBC for up to 6 weeks. Based on a food factor of 0.151 for weanling Wistar rats (U.S. EPA, 1988), the doses were approximately 7500 and 15,100 mg/kg-day. Body weight gain among rats fed 5% TBC in diet showed no deleterious effects when compared to control. However, body weight was reduced by approximately 20% in rats fed the 10% TBC diet. High-dose rats also had frequent diarrhea, which may have contributed to the lower weight gain. In a separate experiment, groups of 4 (control) or 3 rats were fed 5% or 10% TBC in the diet (corresponding to approximately 4600 and 9200 mg/kg-day, based on a food factor of 0.092 for a subchronic study in Wistar rats). There was no effect on red or white blood cell count or differential cell count (measured prior to treatment and at 4 and 8 weeks), or on gross or microscopic pathology (40 tissues examined at the end of the 8-week study period). This study was limited by the small sample size and incomplete study protocols.

Finkelstein and Gold (1959) also performed a short-term TBC feeding study on two cats. Each

cat received 50 mL/kg-day (54,000 mg/kg-day) TBC via gavage for 2 months. An additional two cats served as controls. Treated cats developed diarrhea and their final body weight at 2 months was reduced by 30% relative to controls. The authors reported no changes in the appearance and behavior of the cats, or in urine, blood chemistry, or blood count, although this assessment notes that white blood cell counts appeared elevated, both compared to the pre-exposure values and compared to the concurrent controls. However, the small group sizes and lack of information about variability in this study limit interpretation of these results.

Finkelstein and Gold (1959) suggested that the apparent lack of toxicity of TBC may be related to its insolubility in water and therefore lack of systemic absorption. However, as noted in Section 4, absorption of TBC is expected to be high. The overall percent absorption in the Finkelstein and Gold (1959) studies may have been decreased by the extraordinarily high doses tested, which were much higher than modern limit doses, but the actual absorbed dose would likely still have been very high.

5.3 Chronic Toxicity/Carcinogenicity

No studies were located that evaluated chronic exposure to TBC.

5.4 Reproductive Toxicity

No studies were located that evaluated the potential reproductive toxicity of TBC.

5.5 Prenatal, Perinatal, and Postnatal Toxicity

No studies were located that evaluated the potential developmental toxicity of TBC.

5.6 Genotoxicity

No studies were located that evaluated the genotoxic potential of TBC. ANSES (2016) found no alerts for mutagenicity of TBC using DEREK, the Danish QSAR database, and the OECD toolbox.

5.7 Mechanistic Studies

Sui et al. (2015) investigated the potential for TBC to activate the human pregnane X receptor (PXR) using a CYP3A4-luciferase reporter in *in vitro* transient transfection assays. PXR is of interest because it regulates xenobiotic metabolism in the liver and intestine. TBC was a potent PXR agonist and induced reporter gene activity in intestinal LS180 cells in a dose-responsive fashion at 5, 10, and 20 µM. Similarly, TBC induced PXR target genes (UGT1A1, MDR1) in LS180 intestinal cells and in mouse primary enterocytes, but not in HepaRG cells or primary mouse hepatocytes. Because TBC did not activate any of a panel of additional receptors, including the peroxisome proliferator-activated receptor (PPAR) α, PPAR γ, the constitutive adrostane receptor (CAR), or the estrogen receptor (ERα), the authors concluded that TBC is a

selective PXR agonist (Sui et al., 2015). Consistent with the *in vitro* results, expression of PXR target genes was induced compared to controls in the intestine but not in the liver of C57BL/6 mice treated with 10 mg/kg-day TBC via oral gavage in corn oil for 1 week (Sui et al., 2015). Similar results were seen following intraperitoneal injection, indicating that the intestinal specificity could not be explained by presumed low systemic absorption precluding the TBC from reaching the liver.

In the same study, gavage with 10 mg/kg-day TBC in corn oil for a week significantly increased total cholesterol levels and low density lipoprotein (LDL) cholesterol [but not high density lipoprotein (HDL) or very low density lipoprotein (VLDL) cholesterol] in wild type (WT) mice. No increase was seen in PXR-/- mice, suggesting that the hypercholesterolemia was mediated via TBC-activated PXR signaling in the intestine (Sui et al., 2015). Additionally, TBC stimulated gene expression of the intestinal lipid transporters CD36 and NPC1L1 and increased cholesterol uptake in primary enterocytes, but these effects were not seen with PXR-/- mice or in primary enterocytes from PXR-/- mice (Sui et al., 2015). TBC also increased cholesterol uptake by human intestinal cells. TBC was a more potent PXR agonist than ATBC. These results suggest that TBC may affect lipid metabolism in humans, an endpoint that is not generally evaluated in standard toxicity assays.

5.8 Mode of Action

In light of the very low toxicity seen with TBC and the few reported adverse effects, no MOA evaluation is possible. However, the results of Sui et al. (2015) suggest that TBC can activate PXR and can affect lipid metabolism. The toxicological consequences of these results have not been investigated.

5.9 Lowest Hazard Endpoints by Organ System and Exposure Duration

The repeat dose toxicity data for TBC are extremely limited, and consist of studies with small numbers of rats and cats conducted prior to modern testing methods (Finkelstein and Gold, 1959), as well as a 1-week study in rats that evaluated a very limited set of endpoints related to lipid metabolism (Sui et al., 2015). None of these studies are adequate for identifying an effect level. However, these limited data suggest that the toxicity of TBC is very low. No mortality was seen at doses well above modern limit doses for acute lethality testing. In addition, although sensitivity was limited due to the small numbers of animals tested and the endpoints evaluated were not as extensive as under modern methods, a range of endpoints was evaluated (red and white blood cell counts, histopathology of 40 tissues) in rats treated with TBC at up to 10% of the diet, and the only adverse effect was decreased body weight gain. The decrease may have been due to diarrhea, which may have been related to the high dose of a lipophilic compound. Similarly, decreased weight gain was the only effect seen in cats treated with TBC by gavage at up to 50 mL/kg day for up to 2 months, despite the extraordinarily high gavage volume.

No data are available on the chronic toxicity, reproductive or developmental toxicity, or genetic toxicity of TBC, but read-across from the related compound ATBC may be possible.

5.10 Uncertainties and Data Gaps

The data gaps for TBC are substantial, since the only toxicity data obtained using standard methods are for acute exposure. Toxicokinetic data, particularly absorption data, on TBC are lacking, as well as studies on repeated-dose toxicity, chronic toxicity/carcinogenicity, reproductive toxicity, developmental toxicity, and genotoxicity. In addition, the studies that are available were generally reported with few details.

In light of the lack of systemic effects, there are no uncertainties related to interpretation of the hazard data.

6 Exposure

The use of TBC in consumer products has been described in Section 3 of this report. The general population may be exposed to TBC via dermal contact with consumer products (including cosmetics), via mouthing of products (e.g., children's toys), by the ingestion of food or beverages containing this compound, and by ingestion of foods stored in packaging containing TBC.

Several investigators have detected and measured TBC in toys and child care articles. Abe et al. (2012) measured plasticizers in 101 samples of PVC toys on the Japanese market. They found TBC in 35% of the "designated toys"[2] samples (mean concentration [detected samples only] of 1.6%), and in 15% of the "not-designated" toys samples (mean concentration [detected samples only] of 12%). The detection ratio and content of TBC were derived from unknown peaks. McCombie et al. (2017) tested 118 samples from 88 toys taken from the Swiss market in 2015 for compliance with a 0.1% restriction for phthalate content. TBC was found in eight of the samples in amounts over 0.1% (range 1 - 50.4% by weight). CPSC found one item containing TBC in a group of 63 toys and child care articles purchased in 2008 and analyzed for phthalates and phthalate substitutes (Dreyfus, 2010).

TBC is an indirect additive used in food contact substances (FDA, 2018). FDA estimated a cumulative estimated daily intake (CEDI) of 0.00035 mg/kg-day for TBC (FDA, 2012).

7 Discussion

7.1 Toxicity Under FHSA

[2] Japanese publication with abstract and tables only in English. We assumed "designated" refers to those toy types that are defined as "designated toys" in Article 78 of the Ordinance for Enforcement of the Food Sanitation Act (revised in March 2008) (https://www.jetro.go.jp/en/reports/regulations/pdf/foodext201112e.pdf). "Designated toys" include those toys intended to come into direct contact with an infant's mouth, infant jewelry, decal sticker toys, rolly-polies, masks, origami, rattles, intellectual development facilitating toys, wooden blocks, toy telephones, toy animals, dolls, clay, toy vehicles, balloons, toy building bricks, balls, housekeeping toys, and toys to be played with in combination to those types of toys listed.

Animal data support the conclusion that **TBC does not fit the designation of acutely toxic under the Federal Hazardous Substances Act (FHSA) (16 CFR§1500.3(c)(2)(i)(A))** following single oral exposures. The acute LD_{50} value for TBC in rats was >32,400 mg/kg (Finkelstein and Gold, 1959). Although the study was not conducted according to modern methods, the absence of lethality at such a high dose was sufficient to conclude that TBC is not acutely toxic under FHSA. Data are not available to assess the acute toxicity of TBC under FHSA via the inhalation or dermal routes.

Data are also not available to determine whether TBC is irritating to the skin or eyes. ANSES (2016) suggested that TBC may be more reactive than ATBC at the site of contact, but did not provide further information.

No data were available on the repeated dose toxicity of TBC, or on its potential to cause reproductive or developmental toxicity, genotoxicity, or cancer. Read-across from the related compound ATBC may be possible for these endpoints.

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APPENDIX 1

Search Terms Used

Toxline: "Tributyl citrate" OR "tributyl ester 2-hydroxy-1,2,3-Propanetricarboxylic acid" OR "1,2,3-tributyl ester 2-Hydroxy-1,2,3-propanetricarboxylic acid" OR "Butyl citrate" OR "tributyl ester citric acid" OR "Citroflex 4" OR "Citric acid, tributyl ester" OR "n-Butyl citrate" OR "Tri-n-butyl citrate" OR "Tributyl 2-hydroxy-1,2,3-propanetricarboxylate" OR (77-94-1)

Pubmed: "Tributyl citrate" OR "n-Butyl citrate" OR "Tri-n-butyl citrate" OR (77-94-1)

APPENDIX 2

Explanation of Physico-chemical Parameters

The organic carbon normalized solid-water partition coefficient (K_{oc}), also known as the organic carbon adsorption coefficient, is defined as the ratio of the chemical's concentration in a state of sorption (i.e. adhered to soil particles) and the solution phase (i.e. dissolved in the soil water). K_{oc} is crucial for estimating a chemical compound's mobility in soil and the prevalence of its leaching from soil. For a given amount of chemical, the smaller the K_{oc} value, the greater the concentration of the chemical in solution. Thus, chemicals with a small K_{oc} value are more likely to leach into groundwater than those with a large K_{oc} value (http://www.acdlabs.com/products/phys_chem_lab/logd/koc.html).

Henry's law, one of the gas laws formulated by William Henry, states that "at a constant temperature, the amount of a given gas dissolved in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid (http://en.wikipedia.org/wiki/Henry's_law)." Henry's Law Constants characterize the equilibrium distribution of dilute concentrations of volatile, soluble chemicals as the ratio between gas and liquid phases.

The octanol/water partition coefficient (K_{ow}) is defined as the ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system. In recent years, this coefficient has become a key parameter in studies of the environmental fate of organic chemicals. It has been found to be related to water solubility, soil/sediment adsorption coefficients, and bioconcentration factors for aquatic life. Because of its increasing use in the estimation of these other properties, K_{ow} is considered a required property in studies of new or problematic chemicals (http://www.pirika.com/chem/TCPEE/LOGKOW/ourlogKow.htm).

The bioconcentration factor (BCF) is the concentration of a particular chemical in a tissue per concentration of chemical in water (reported as L/kg). This property characterizes the accumulation of pollutants through chemical partitioning from the aqueous phase into an organic phase, such as the gill of a fish. The scale used to determine if a BCF value is high, moderate or low will depend on the organism under investigation. The U.S. EPA generally defines a high potential BCF as being greater than 5,000; a BCF of moderate potential as between 5,000 and 100; a low potential BCF as less than 100 (http://en.wikipedia.org/wiki/Bioconcentration_factor; http://sitem.herts.ac.uk/aeru/footprint/en/Quest/ecotox.htm).