GreenScreen™ Assessment for HallStar's Dioplex and Paraplex Series Polymeric Adipate Plasticizers

Also Called: [REDACTED]

Chemical Structures:

[REDACTED]

The following polymers comprise various mixtures of the chemicals assessed in this GreenScreen™ report:

- Polymer B
- Polymer C

For Polymers:
Identify Monomers and Corresponding Properties (All information was provided by A. Cesaretti , and is considered Proprietary/Confidential Business Information).

Polymer B:

1. % of Each Monomer
   a) Methyl Diol monomer: [REDACTED]
   b) Dicarboxylic Acid monomer: [REDACTED]
   c) Fatty Alcohol monomer: [REDACTED]
2. Are the monomers blocked: [REDACTED]
3. Molecular Weight (MW) of Polymer: [REDACTED]
4. % of Polymer with:
   a) MW <500: [REDACTED]
   b) MW <1,000: [REDACTED]
5. % Weight Residual Monomers: [REDACTED]
6. Solubility/Dispersability/Swellability: [REDACTED]
7. Particle Size: n/a
8. Overall Polymer Charge: No charge

Polymer C:

1. % of Each Monomer
   a) Diol monomer: [REDACTED]
   b) Dicarboxylic Acid monomer: [REDACTED]
   c) Fatty Alcohol monomer: [REDACTED]
   d) Butyl Diol monomer: [REDACTED]
2. Are the monomers blocked: [REDACTED]
3. Molecular Weight (MW) of Polymer: [REDACTED]
4. % of Polymer with:
   a) MW <500: [REDACTED]
   b) MW <1,000: [REDACTED]
5. % Weight Residual Monomers: [REDACTED]
6. Solubility/Dispersability/Swellability: [REDACTED]
7. Particle Size: n/a
8. Overall Polymer Charge: No charge

Table 1: Hazard Summary Table for HallStar's Proprietary Polymer Formulation

Chemical[1]	CAS RN	% In Ingredient	Group I Human Health					Group II and II* Human Health									Ecotoxicity		Fate		Physical		GS Benchmark Score (Chemical)[2]
			Carcinogenicity	Mutagenicity	Reproductive	Developmental	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic	Chronic Aquatic	Persistence	Bioaccumulation	Reactivity	Flammability	
									s	r*	s	r*											
Methyl Diol monomer	[REDACTED]	--	*L*	**L**	**L**	**L**	dg	**L**	dg	**L**	dg	dg	**L**	dg	**L**	**L**	**L**	*L*	**M**	*vL*	*L*	**L**	3
Dicarboxylic Acid monomers	[REDACTED]	--	*L*	**L**	*L*	*L*	dg	*L*	dg	*L*	dg	dg	**L**	dg	**L**	**H**	**M**	*L*	**vL**	*vL*	*L*	**L**	3
Fatty Alcohol monomer	[REDACTED]	--	*L*	*L*	dg	*M*	dg	*M*	dg	*L*	dg	dg	*L*	dg	*M*	*H*	*M*	*L*	*vL*	*vL*	*L*	*M*	2
Diol monomer	[REDACTED]	--	*L*	*L*	*L*	*L*	dg	*L*	dg	*L*	dg	dg	*L*	dg	*L*	*L*	*L*	*L*	*vL*	*vL*	*L*	*L*	3
Butyl Diol monomer	[REDACTED]	--	*L*	*L*	*L*	*L*	dg	*L*	dg	*L*	dg	dg	*L*	dg	*L*	*H*	*L*	*L*	*vL*	*vL*	*L*	*L*	3

s=single dose r=repeat dose
dg=not determined/unknown
L=Low Hazard **M**=Moderate Hazard **H**=High Hazard **vH**=very High Hazard-Endpoints in colored text (**L, M, H, and vH**) were assigned based on experimental data.
Endpoints in black italics (*L*, *M*, and *H*) were assigned using estimated values and professional judgment (Structure Activity Relationships)

[1] Redacted chemicals will be identified by their general chemical class and will indicate the presence and identity of metals and halogens.
[2] For inorganic chemicals with low human and ecotoxicity values across all hazard endpoints and low bioaccumulation, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

References

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

Clean Production Action (CPA). 2011c. The GreenScreen™ for Safer Chemicals v 1.2 Guidance for Hazard Assessment and Benchmarking Chemicals. 10/18/2011. http://www.cleanproduction.org/library/greenScreenv1-2/DRAFT_GreenScreen_v1-2_Guidance_2011_1018_v2.pdf

Formatted: No underline, Font color: Auto

GreenScreen™ Assessment for Methyl Diol Monomer

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this Green Screen Assessment

Chemical Name: Methyl Diol monomer

Green Screen Assessment Prepared By:
Name: Chris Schlosser, M.F.S.
Title: Associate Toxicologist
Organization: ToxServices, LLC
Date: February 10, 2012

Quality Control Performed By:
Name: Margaret Whittaker, PhD.,
M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices, LLC
Date: February 20, 2012

Confirm application of the *de minimus* rule[3]: Yes

Chemical Name (CAS #): Methyl Diol monomer

Also Called: [REDACTED]

Chemical Structure(s):

[REDACTED]

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Solvent
2. Emollient

GreenScreen™ Rating[4]: Methyl Diol monomer was assigned a GreenScreen™ Benchmark Score of 3 based on Moderate Persistence (P). This corresponds to GreenScreen™ benchmark classification 3a in CPA 2011a. Data gaps (dg) exist for Endocrine Activity (E), Neurotoxicity (N) (not listed, but not tested) and Respiratory Sensitization (SnR). As outlined in CPA (2011c) Section III(1)(Benchmarking Chemicals With Data Gaps), Methyl Diol monomer meets requirements for a GreenScreen™ Benchmark Score of 3, despite the hazard data gaps. In a worst-case scenario, if Methyl Diol monomer were assigned a High score for E, it would become a GreenScreen™ Benchmark 1 chemical.

GreenScreen™ Hazard Ratings: Methyl Diol Monomer																			
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*										
L	**L**	**L**	**L**	**DG**	**L**	**DG**	**L**	**DG**	**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).

[3] 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.

[4] 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.

Note: Please see Appendix A for a glossary of hazard acronyms.
Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[5]

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[6]?	GreenScreen™ Rating[7]
n/a	End	Combustion	Carbon Monoxide	630-08-0	Y	n/a
n/a	End	Combustion	Carbon Dioxide	124-38-9	N	n/a

Introduction

Methyl Diol monomer is used as a solvent, emollient, emulsifier and humectant in cosmetics. In addition, it is also used in the manufacturing of resins and coatings (HSDB 2005). Methyl Diol monomer is used as a monomer in one of the HallStar formulations.

[5] 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. Products that contain propanediol, 2-methyl monomers are often plastics, which are often disposed of via incineration. Therefore, health and environmental effects associated with combustion byproducts are of particular concern.
[6] 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 (CPA 2011b).
[7] GreenScreen™ reviews of transformation products depends on the GreenScreen™ Benchmark Score of the parent chemical (See Guidance).

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Carcinogenicity (C) Score (H, M or L): *L*
Methyl Diol monomer has been assigned a Low for carcinogenicity. Methyl Diol monomer has not been tested for carcinogenicity. However, it is not a known carcinogen and QSAR modeling indicates that Methyl Diol monomer is not expected to cause carcinogenicity via genotoxic or non-genotoxic mechanisms.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- Patlewicz et al. 2008 –
    - ToxTree Estimation software predicts that Methyl Diol monomer is not a carcinogenic via genotoxic or nongenotoxic mechanisms (Appendix C).

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Methyl Diol monomer was assigned a score of Low for mutagenicity based on negative mutagenicity and clastogenicity assays *in vitro*.

- ESIS 2000 –
    - A GLP compliant bacterial reverse mutation assay (Directive 84/449/EEC B.4) was conducted utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535 and TA1537 at concentrations of up to approximately 5,000 µg/plate (99% purity) in the presence and absence of metabolic activation. Methyl Diol monomer was reported as negative for mutagenicity under all tested conditions.
    - A GLP compliant chromosomal aberration assay (Directive 84/449/EEC B.10) was conducted utilizing cultured peripheral human lymphocytes at concentrations up to approximately 5,000 µg/L (99% purity) with and without metabolic activation. Methyl Diol monomer was reported as negative for clastogenicity under all tested conditions.
    - A GLP compliant mammalian cell gene mutation assay (Directive 2000/32/EEC B.17) was conducted utilizing V79 Chinese Hamster cells at concentrations of up to approximately 5,000 µg/ml in the presence and absence of metabolic activation. Methyl Diol monomer was reported as negative for mutagenicity under all tested conditions.

Reproductive Toxicity (R) Score (H, M, or L): L
Methyl Diol monomer was assigned a score of Low for reproductive toxicity based on no effects being identified following a two generation reproductive toxicity study, or a 90-day repeated dose toxicity study.

- ESIS 2000 –
    - A GLP compliant two generation reproductive toxicity study (EPA OPPTS 870.3800) was conducted using male and female Sprague-Dawley rats (30/sex/dose). Rats were administered doses ranging from 0 to approximately 1,000 mg/kg (98.67% purity) from 70 days pre-mating until termination. F1 groups were treated in utero until termination. No substance-related clinical findings were reported. Methyl Diol monomer did not affect reproductive performance in any sex at any dose level. Gestation length was unaffected by treatment and spermatogenic parameters were unaffected. No significant effects were observed at necropsy. No effects were reported on litter parameters, pup survival or anogenital distance. Organ weight changes were observed at the mid- and high-dose in the parental generation. Including absolute and relative ovary weights and adrenal weights in females. In the F1 generation significant increases in the absolute weight of the right testis (8%), left epididymis (10%) and right cauda epididymis (13%) were reported in males at the high dose, and increases in absolute kidney weights (6%) in females at the high dose. At mid dose, significant increases in absolute seminal vesicle and coagulating gland weights (18%), right and left testis weights (5%) and right and left epididymis and cauda epididymides (18 and 12%, respectively) was observed in males. In the low dose group, a significant increase in absolute weight of the left epididymis (7%), and left and right cauda epididymis (12%) was observed in males, and a significant increase in absolute kidney weight

(6%) in females. In the F1 generation, no weight changes were significant relative to body weight (except increase in right cauda epididymis weight at the mid dose), and no histopathological or morphological alterations accompanied weight changes. Therefore, the study director considered weight changes unrelated to treatment. Based on the available data, a NOAEL of the highest dose tested was established by study authors for the reproductive toxicity.

- No adverse effects were reported on organs (cervix, epdidymides, mammary gland, ovaries, prostate gland, seminal vesicle, testes, and vagina) following a 90-day toxicity study (details in the systemic toxicity section).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L
Methyl Diol monomer was assigned a score of Low for developmental toxicity based on no signs of developmental toxicity in rats or rabbits following GLP-compliant studies conducted under modern guidelines.

- ESIS 2000 –
  - A GLP compliant developmental toxicity study (Directive 87/302/EEC B.24) was conducted using female Wistar rats (30/dose). Rats were administered doses ranging from 0 to approximately 1,000 mg/kg via oral gavage daily on days 0 through 20 of gestation. No maternal toxicity was observed. Statistically significant increases in embryonic resorptions was noted in the top two doses, but fell within historical control values for the laboratory and were not considered to be of toxicological relevance. An independent reviewer confirmed that resorptions were not toxicologically relevant. There was no evidence of any effect of treatment on morphological development or skeletal ossification. Based on available data, A NOAEL of the highest dose tested was established by the study authors for developmental toxicity.
  - A GLP compliant developmental toxicity study (EPA OPPTS 870.3700) was conducted using female Wistar rats (25/group). Rats were administered doses ranging from 0 to approximately 1,000 mg/kg (98.7% purity) via oral gavage on days 0 to 19 of gestation. No maternal toxicity was observed at any dose level. Interuterine growth and survival was unaffected by treatment. No evidence of malformations or developmental variations was observed. Study authors reported a NOAEL of the highest dose tested for Methyl Diol monomer under the tested conditions.
  - A GLP compliant developmental toxicity study (EPA OPPTS 870.3700) was conducted using female New Zealand white rabbits (25/group). Rabbits were administered doses ranging from 0 to approximately 1,000 mg/kg (purity > 99.43%) of the test substance via oral gavage on days 9 through 28 of gestation. No treatment-related maternal toxicity was observed. One animal in the mid-dose and two in the high-dose died from improper gavage techniques. Interuterine growth and survival was unaffected by treatment. No statistically significant increases in skeletal variations were observed. Study authors reported a NOAEL of the highest dose tested for Methyl Diol monomer under the tested conditions.

Endocrine Activity (E) Score (H, M or L): dg
Methyl Diol monomer has been assigned a data gap for endocrine activity. Although it is not a known endocrine disruptor, endocrine disruption testing has not performed on the chemical.

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- 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 Methyl Diol monomer.

<u>Group II and II* Human Health Effects (Group II and II* Human)</u>
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.

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): L
Methyl Diol monomer was assigned a score of Low for acute mammalian toxicity based on oral, dermal, and inhalation values above the guidance values specified in the CPA GreenScreen 1.2 criteria (CPA 2011a).

- ESIS 2000 –
  - An acute Oral LD_{50} value of greater than 5,000 mg/kg was identified for Wistar rats.
  - An acute Inhalation LC_{50} value of greater than 5.1 mg/L was identified for Wistar rats.
  - An acute Dermal LD_{50} value of greater than 2,000 mg/kg was identified for New Zealand rabbits.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose: vH, H, M or L): dg
Methyl Diol monomer was assigned a data gap for systemic toxicity, single dose, as no relevant data were identified.

Group II* Score (repeated dose: H, M, L): L
Methyl Diol monomer was assigned a score of Low for systemic toxicity/organ effects based on repeated exposure based on no effects being identified in rats at 1,000 mg/kg-bw following 14 and 90-day repeat dose studies.

- ESIS 2000 –
  - A GLP compliant 90-day toxicity study (Directive 87/302/EEC B.8) was conducted using male and female Wistar rats (10/sex/group). Rats were administered doses ranging from 0 to approximately 1,000 mg/kg (99% purity) of Methyl Diol monomer, daily, for 90 days. Rats were observed/monitored for body weight and food intake, clinical chemistry, hematology, necropsy and histopathology. No mortality, morbidity or clinical signs were observed. Alanaine tranasminase (ALAT) was significantly ($P < 0.05$) decreased in high-dose males Aspartate aminotransaminase (ASAT) was significantly ($P < 0.05$) in high-dose males. Total bilirubin was significantly ($P < 0.05$) increased in mid-dose males and phosphorus was significantly ($P < 0.05$) decreased in all dose groups. The study directed concluded that clinical chemistry changes were spontaneous and not directly related to treatment. Slight changes were observed in liver and kidney weights. However, these changes were did not establish a dose-response relationship and were inconsistent within and between sexes. Therefore, they were not considered to be directly related to treatment. The study authors concluded that no adverse effects were present and that a NOAEL of the highest dose tested can be established based on study results.
  - A 14-day toxicity study was completed under the same conditions as above. No effects were reported and a NOAEL of approximately1,000 mg/kg was reported by study authors.

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): dg
Methyl Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Methyl Diol monomer.

Group II* Score (repeated dose: H, M, L): dg
Methyl Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Methyl Diol monomer.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Methyl Diol monomer was assigned a score of Low for skin sensitization based data from human studies and a guinea pig maximization test indicating that Methyl Diol monomer is not classifiable as a skin sensitizer.

- ESIS 2000 –
  - A GLP compliant patch-test (method not reported) was conducted using human volunteers (n=110). Volunteers were induced with a 0.2 ml 50% aqueous dilution under occlusive epicutaneous conditions for 24 hours/3 days (M,W,F) a week for 10 applications. A challenge dose was applied two weeks

after the final application under the same conditions. Mild responses were seen in a number of subjects. It was unclear to study authors if the effects were irritant or allergic in nature.
    - Four further GLP compliant patch-tests (method not reported) were conducted using human volunteers (n=104). Volunteers were induced with a 0.2 ml 50% aqueous dilution under occlusive epicutaneous conditions for 24 hours/3 days (M,W,F) a week for 10 applications. A challenge dose was applied two weeks after the final application under the same conditions. During the induction phases sporadic skin responses consistent with minimal to mind irritation occurred in a low number of volunteers. No skin reactions occurred following the challenge phase and Methyl Diol monomer was reported as non-sensitizing under the tested conditions.
    - A GLP compliant guinea pig maximization test (Directive 96/54/EC B.6) was conducted using Himalayan albino guinea pigs (n=20). Guinea pigs were exposed to intradermal or epicutaneous inductions of 10% of the test substance followed by challenge doses of 25, 50, or 100%. A slight redness was reported in 3/20 (15%) animals in the 50% challenge group. GHS criteria state that chemicals will be categorized as dermal sensitizers if ≥ 30% of animals respond to the challenge dose. Under the study conditions, Methyl Diol monomer is not classifiable as a sensitizer under GHS criteria. Furthermore, there was no dose-response as only 1 animal in the 100% challenge exhibited a minimal redness.
- Based on the weight-of-evidence, sufficient data exist from human studies to support that Methyl Diol monomer is not sensitizing. Additionally, Methyl Diol monomer was not classified as a dermal sensitizer under GHS criteria following a guinea pig maximization assay.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg
Methyl Diol monomer has been assigned a data gap for respiratory sensitization as no relevant data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L
Methyl Diol monomer was assigned a score of Low for skin irritation/corrosivity based on GLP compliant studies in humans and guinea pigs reporting no skin irritation.
- ESIS 2000 –
    - A GLP compliant skin irritation study (method not reported) was conducted using New Zealand rabbits (sex not reported, n=6). The test substance was applied to two intact and abraded sites on each animal undiluted, under occlusive conditions. No abnormal signs, erythema, or edema was noted during the 24, 48, or 72-hr post observational periods. Methyl Diol monomer was reported as non-irritating under the tested conditions.
    - A GLP compliant skin irritation study (method not reported) was conducted using 25 human volunteers. Humans were exposed to 100% and a 50% aqueous dilution of Methyl Diol monomer under occlusive conditions for 24 hours/per day 5/days week for two weeks. All treated areas were reported as normal throughout the test, and Methyl Diol monomer was found to be non-irritating by study authors.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): L
Methyl Diol monomer was assigned a score of Low for eye irritation/corrosivity based on GLP compliant studies in rabbits reporting no eye irritation.
- ESIS 2000 –
    - A GLP compliant eye irritation study (method not reported) was conducted using female New Zealand rabbits (n=6). 0.1 ml of undiluted test substance was instilled into one eye of each rabbit for 24 hours. All 6 treated eyes appeared normal with no corneal, irridial, or conjunctival reactions at 24, 48, or 72 hours post observation. Methyl Diol monomer was reported as non-irritating under the tested conditions.
    - A GLP compliant eye irritation study (method not reported) was conducted using female New Zealand rabbits (n=3). 0.1 ml of undiluted test substance was instilled into one eye of each rabbit for 30 minutes. Only one rabbit had a slight conjunctival redness at 24 hours. No effects were reported 48 hours after treatment. Methyl Diol monomer was reported as non-irritating by the study authors.

Ecotoxicity (Ecotox)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L
Methyl Diol monomer was assigned a score of Low for acute aquatic toxicity based on L/EC_{50} values of greater than 1,000 mg/L identified for fish, invertebrates, and algae. Cutoff for Low aquatic toxicity following GreenScreen methodology is 100 mg/L (CPA 2011a).

- ESIS 2000 –
  - A reported LC_{50} value of greater than 1,000 mg/L was identified for *Cyprinus carpio* (fish, 96-hr).
  - A reported EC_{50} value of greater than 1,000 mg/L was identified for *Daphnia magna* (invertebrate, 48-hr).
  - A reported EC_{50} value of greater than 1,000 mg/L was identified for *Scenedesmus subspicatus* (algae, 72-hr).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *L*
No chronic aquatic toxicity data were identified for this chemical. The globally harmonized system (GHS) does not require a chronic aquatic toxicity hazard rating for substances which are both rapidly biodegradable and have a BCF < 500 and log K_{ow} < 4 (UN 2011)[8].

Environmental Fate (Fate)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Persistence (P) Score (vH, H, M, L, or vL): M
Methyl Diol monomer was assigned a score of Moderate for persistence based on reported and modeled data indicating a half-life between 16 and 60 days (CPA 2011a).

- ESIS 2000 –
  - A GLP compliant biodegradation test (Modified Strum Test) was conducted under aerobic conditions in activated domestic sludge. Methyl Diol monomer achieved approximately 50% biodegradation following 28 days.
  - A second biodegradation study with limited details was conducted and Methyl Diol monomer achieved greater than 50% biodegradation following 28 days.
- U.S. EPA 2011 –
  - Fugacity[9] modeling predicts approximately 60% partitioning to soil with a half-life of 17.3 days, approximately 40% partitioning to water with a half-life of 8.6 days and approximately 5% partitioning to air with a half-life of 22.5 hours (As shown in Appendix B).
- Based on modeled and reported data, a half-life between 16 and 60 days is expected for Methyl Diol monomer.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Methyl Diol monomer was assigned a score of Very Low for bioaccumulation based on a BCF below 100 (CPA 2011a).

- U.S. EPA 2011 –

[8] Table 4.1.1 of the Purple Book.
[9] Fugacity model predicts the partitioning and half-life of a chemical in sediment, water, soil and air. http://www.epa.gov/oppt/exposure/pubs/episuite.htm

- BCFBAF predicts a bioaccumulation factor (BCF) of less than 1based on a reported log K_{ow} of less than 0.25, which indicates a low likelihood that the chemical will bioaccumulate (As shown in Appendix B).

Physical Hazards (Physical)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Reactivity (Rx) Score (vH, H, M or L): *L*
Methyl Diol monomer 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.

- Methyl Diol monomer would not be classified as an oxidizing chemical as it structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, Methyl Diol monomer is not expected be explosive as it does not contain structural groups that would cause concern for explosion. Furthermore, the high flashpoint (approximately 200°C) further supports that Methyl Diol monomer is not a reactive chemical.

Flammability (F) Score (vH, H, M or L): L
Methyl Diol monomer was assigned a score of Low for flammability based on not being classified as a GHS Flammable Liquid.

- ESIS 2000 –
  - Methyl Diol monomer is reported as not flammable and has a flash point above the 93°C cut-off criteria to be classified as flammable by GHS (UN 2011)[10].

[10] Table 2.6.1 of the PurpleBook.

References

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

European Chemical Substances Information System (ESIS). 2000. IUCLID Dataset for Methyl Diol monomer. European Commission Joint Research Centre. Available: http://esis.jrc.ec.europa.eu/

Grandjean, P. and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

Hazardous Substances Data Bank (HSDB). 2005. Entry for Methyl Diol monomer. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

Patlewicz, G., N. Jeliazkova, R.J. Safford, A.P. Worth, and B. Aleksiev. 2008. An Evaluation of the Implementation of the Cramer Classification Scheme in the Toxtree Software. SAR QSAR Environ Res. 19(5-6):495-524. Available: http://toxtree.sourceforge.net

United Nations (UN). 2011. Globally Harmonized System of Classification and Labeling of Chemicals, Fourth Revised Edition.

United States Environmental Protection Agency (U.S. EPA). 2011. Estimation Programs Interface (EPI) Suite™ Web, v4.10, Washington, DC, USA.

Formatted: No underline, Font color: Auto

Formatted: No underline, Font color: Auto

Formatted: No underline, Font color: Auto

Field Code Changed

Field Code Changed

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**

APPENDIX B: EPISuite Results

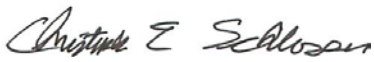
[REDACTED]

APPENDIX C: ToxTree Results

[REDACTED]

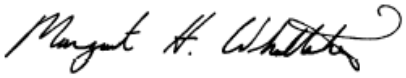
No structural concerns for carcinogenicity were identified.

Methyl Diol Monomer GreenScreen™ Evaluation Prepared By:



Christopher E. Schlosser, M.F.S.
Associate Toxicologist
ToxServices LLC

Methyl Diol Monomer GreenScreen™ Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

GreenScreen™ Assessment for Dicarboxylic Acid Monomer

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this GreenScreen™ Assessment

Chemical Name: Dicarboxylic Acid Monomer

GreenScreen™ Assessment Prepared By:
Name: Chris Schlosser, M.F.S.
Title: Associate Toxicologist
Organization: ToxServices LLC
Date: March 22, 2012

Quality Control Performed By:
Name: Margaret Whittaker, PhD.,
M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: April 5, 2012

Confirm application of the *de minimus* rule[11]: Yes

Chemical Name (CAS #): Dicarboxylic Acid monomer

Also Called: [REDACTED]

Chemical Structure(s):

[REDACTED]

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Food additive
2. Plasticizer
3. Monomer

GreenScreen™ Rating[12]: Dicarboxylic Acid monomer was assigned a GreenScreen™ Benchmark Score of 3 based on High Eye Irritation (IrE) and Moderate Acute Aquatic Toxicity (AA). This corresponds to GreenScreen™ benchmark classification 3b or 3c in CPA 2011a. Data gaps (dg) exist for Endocrine Activity (E), Neurotoxicity (N) and Respiratory Sensitization (SnR). As outlined in CPA (2011a), Dicarboxylic Acid monomer meets requirements for a GreenScreen™ Benchmark Score of 3. In a worst-case scenario, if Dicarboxylic Acid monomer were assigned a High score for E, it would become a GreenScreen™ Benchmark 1 chemical.

GreenScreen™ Hazard Ratings: Dicarboxylic Acid Monomer																	
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*										
L	**L**	*L*	*L*	dg	*L*	dg	*L*	dg	dg	**L**	dg	**L**	**H**	M	*L*	**vL**	*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).

[11] Every chemical in a material or formulation should be assessed if it is:
3. intentionally added and/or
4. present at greater than or equal to 100 ppm.

[12] 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.

Note: Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[13]

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[14]?	GreenScreen™ Rating[15]
n/a	End	Combustion	Carbon Monoxide	630-08-0	Y	n/a
n/a	End	Combustion	Carbon Dioxide	124-38-9	N	n/a

Introduction

Dicarboxylic Acid monomer is manufactured from a mixture of cyclohexanol and cyclohexanone by oxidative ring cleavage. Dicarboxylic Acid monomer is used in several consumer products and is important in the manufacture of nylon 66. It is also used in foodstuffs as an acidulating agent, or neutralizing agent (UNEP 2004).

[13] 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. Products that contain Dicarboxylic Acid monomer monomers are often plastics, which are often disposed of via incineration. Therefore, health and environmental effects associated with combustion byproducts are of particular concern.
[14] 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 (CPA 2011b).
[15] Green Screen reviews of transformation product(s) depend on the Green Screen Benchmark Score of the parent chemical and the intrinsic hazard of the transformation product(s) (See Guidance, CPA 2011c).

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Carcinogenicity (C) Score (H, M or L): *L*
Dicarboxylic Acid monomer has been assigned a score of Low for carcinogenicity based on a limited 2-year study indicating no increases in tumors or signs of carcinogenic activity.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- [REDACTED] –
    - A (GLP status not reported) two-year chronic/carcinogenicity toxicity study (method not reported) was conducted using (strain not reported) male rats (20/group) and female rats (10-19/group). Rats were administered doses ranging from 0 to approximately 4,000 mg/kg (purity not reported) of Dicarboxylic Acid monomer to males, and from 0 to approximately 750 mg/kg to females for 2 years. Animals that died during treatment and those scarified at termination did not have an increased number of tumors when compared to controls. However, this study is limited and does not follow current guidelines. A lower number of animals were used and microscopic evaluation was only conducted on 15 tissues.

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Dicarboxylic Acid monomer was assigned a score of Low for mutagenicity based on no mutagenic or clastogenic following both *in vitro* and *in vivo* genotoxicity assays.

- [REDACTED] –
    - Dicarboxylic Acid monomer was not mutagenic or cytotoxic following (GLP status not reported) bacterial reverse mutation assays (similar to OECD 474) utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537 and TA1538 and *E. coli* tester strain WP2 at concentrations up to 10 mg/plate (purity not reported) with and without metabolic activation. No increases in revertants were reported under any of the tested conditions.
- [REDACTED] –
    - Dicarboxylic Acid monomer was negative following a gene mutation assay (method not reported) utilizing *Saccharomyces cerevisiae* tester strains D3with metabolic activation at concentrations up to approximately 200 mg/L (purity not reported).
    - A non-GLP compliant chromosomal aberration assay (method not reported) was conducted using male Sprague-Dawley rats (15/dose). Rats were administered doses ranging from 0 to approximately 400 mg/kg (purity not reported) via oral gavage either in a single dose or five doses administered 24 hours apart. No statistically significant increases in aberrations were observed under the tested condition and Dicarboxylic Acid monomer was reported as negative for clastogenicity by the study authors.
    - A non-GLP compliant dominant lethal assay (method not reported) was conducted using male Sprague-Dawley rats (10/dose). Rats were administered doses ranging from 0 to approximately 400 mg/kg (purity not reported) via oral gavage either in a single dose or five doses administered 24 hours apart. Rats administered a single dose showed significant decreases in average implantations at weeks 1 and 4, and corpora lutea at weeks 4 and 7 in the mid dose group. However, no dose-response relationship was established and no effects were reported at the higher doses. No statistically significant dominant lethal effects were identified in animals receiving multiple doses. Based on the available data, the study authors reported Dicarboxylic Acid monomer as not genotoxic under the tested conditions.

Reproductive Toxicity (R) Score (H, M, or L): *L*
Dicarboxylic Acid monomer was assigned a score of Low for reproductive toxicity as no toxic effects were observed in animals following chronic feeding or developmental toxicity studies and a long history of use as an approved food additive by the U.S. FDA.

- Specific reproductive toxicity studies have not been conducted on Dicarboxylic Acid monomer. However, in a two-year feeding study no effects were observed reproductive organs (testes, ovaries, and uterus) following

administration of approximately 3,500 mg/kg Dicarboxylic Acid monomer to male rats and approximately750 mg/kg of Dicarboxylic Acid monomer to female rats. SIDS authors concluded that based on available data and long history of use Dicarboxylic Acid monomer is unlikely to cause reproductive toxicity (UNEP 2004). Available data from humans and animals show that Dicarboxylic Acid monomer is readily absorbed from the alimentary tract and primarily metabolized through oxidation to carbon dioxide. Unchanged Dicarboxylic Acid monomer is rapidly excreted in the urine (U.S. FDA 2006). Dicarboxylic Acid monomer caused no harmful in animals in long-term studies in which it was added to the diet and available evidence suggests metabolism is similar in both humans and animals (U.S. FDA 2006). The Select Committee on GRAS Substances (SCOGS) concluded that no available evidence on Dicarboxylic Acid monomer demonstrates, or suggests grounds to suspect a hazard to the public when used at current levels (U.S. FDA 2006).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): *L*
Dicarboxylic Acid monomer was assigned a score of Low for developmental toxicity based on no developmental toxicity effects reported following developmental toxicity studies in rats and rabbits.

- U.S. FDA 1972 –
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female Wistar rats (25/group). Rats were administered doses ranging from 0 to approximately 400 mg/kg of Dicarboxylic Acid monomer (purity not reported) for 10 days (gestation days 6-15) by oral gavage. The administration of approximately 300 mg/kg for 10 days had no discernible effect on nidation or maternal and fetal survival. The number of abnormalities seen did not differ from control groups. A NOAEL of greater than 300 mg/kg was established by the study authors for developmental toxicity.
- U.S. FDA 1974 –
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female Dutch rabbits (number not reported). Rabbits were administered doses ranging from 0 to approximately 250 mg/kg of Dicarboxylic Acid monomer (purity not reported) for 13 days (gestation days 6-18) by oral gavage. The administration of the high dose for 13 days had no discernible effect on nidation (early embryo implantation) or on maternal and fetal survival. The number of abnormalities seen did not differ from control groups. The reported maternal and developmental NOAEL for this study was established as greater than the highest dose tested by the study authors.

Endocrine Activity (E) Score (H, M or L): dg
Dicarboxylic Acid monomer has been assigned a data gap for endocrine activity. Although it is not a known endocrine disruptor, endocrine disruption testing has not performed on the chemical.

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- 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 Dicarboxylic Acid monomer.

<u>Group II and II* Human Health Effects (Group II and II* Human)</u>
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.

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): *L*
Dicarboxylic Acid monomer was assigned a score of Low for acute mammalian toxicity based on an acute oral LD_{50} of above the cutoff value for low acute toxicity. GHS criteria categorize substances with a LD_{50} between 2,000 and 5,000 mg/kg as a Category 5 acute toxicant (UN 2011). Following GreenScreen™ criteria, a GHS category 5 receives a hazard rating of Low (CPA 2011a).

- BASF 1978 –
  - An oral LD_{50} value greater than 5,000 mg/kg was established in (strain not reported) rats (similar to OECD 401).
- ChemIDplus 2012 –
  - An oral LD_{50} value greater than 10,000 mg/kg was identified for (strain not reported) rats.
  - An oral LD_{50} value greater than 10,000 mg/kg was identified for (strain not reported) rabbits.
- [REDACTED] –
  - An oral LD_{50} value of approximately 2,000 mg/kg (1640 to 2200 mg/kg, limits of error) was established in (strain not reported) mice. The study reported distention of the stomach and small intestine along with irritation and hemorrhage of the intestines in all treated animals that died (U.S. EPA 2012). The reported effects could be the result of improper gavage techniques and not directly related to the test substance. Furthermore, the EPA also classified this study as of medium reliability as a suboptimal design was used (U.S. EPA 2012).
- Solutia Inc. 1975 –
  - An oral LD_{50} value of greater than 5,000 mg/kg was established in (strain not reported) rats.
  - A dermal LD_{50} value of approximately 8,000 mg/kg was established in (strain not reported) rabbits.
- BASF 1981 –
  - An inhalation LC_{50} value of greater than 7 mg/L was established in (strain not reported) rats.
- Based on the weight of evidence following rat, mouse and rabbit oral LD_{50} values Dicarboxylic Acid monomer is not expected to cause acute oral toxicity. Dicarboxylic Acid monomer is reported as having very low acute toxicity by the SIDS authors and all modern studies identified LD_{50} values significantly above 2,000 mg/kg (UNEP 2004).

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose: vH, H, M or L): dg
Dicarboxylic Acid monomer was assigned a data gap for systemic toxicity, single dose, as no relevant data were identified.

Group II* Score (repeated dose: H, M, L): *L*
Dicarboxylic Acid monomer was assigned a score of Low for systemic toxicity/organ effects based on a NOAEL and LOAEL of approximately 750 and 2,000 mg/kg identified in a 2 year chronic toxicity study.

- [REDACTED] –
  - A (GLP status not reported) two-year chronic toxicity/carcinogenicity study was conducted using (strain not reported rats) male (20/group) and female rats (10-19/group). Rats were administered doses ranging from 0 to approximately 4,000 mg/kg (purity not reported) of Dicarboxylic Acid monomer to males and 0, or approximately 750 mg/kg to females for 2 years. No body weight differences were identified in female rats. Significantly decreased body weights were reported in the top two doses in male rats. At necropsy no treatment related effects were observed and no effects on organs were reported following microscopic examinations. A NOAEL of approximately 750 mg/kg was reported by the study authors based on decreased body weights in male rats. It should be noted that this study did not follow current guide-lines and only limited microscopic evaluations were conducted.
- [REDACTED] –
  - A non-GLP compliant 33 week toxicity study (method not reported) was conducted using male and female (strain not reported) rats (13-15/group). Rats were administered doses ranging from 0 to approximately 3,000 mg/kg (purity not reported) in the diet for 33 weeks. The administration of the mid dose had no effect on weight gain and general behavior of animals. Histopathological examination revealed slight effects on the liver and inflammation of the intestine at the mid dose. However, limited details were available. No NOAEL or LOAEL may be established from this study.
  - A non-GLP compliant 19 week toxicity study (method not reported) was conducted using male (strain not reported) rats (8-10/group). Rats were administered doses ranging from 0 to approximately 3,000 mg/kg (purity not reported) in a protein deficient diet for 19 weeks. Reduced weight gain was observed in rats in the top dose group. Unspecified liver and intestine effects were also observed in the top dose group. Additionally, only 5-7 animals (including controls) survived the duration of the study. As limited details are available, no relevant NOAEL or LOAEL may be established from this study.

- [REDACTED] –
    - A (GLP status not reported) limited three month toxicity study (method not reported) was conducted using male (strain not reported) rats (n=4). Rats were administered doses ranging from 0 to approximately 2,000 mg/kg of the test substance. The purpose of the study was aimed at investigating peroxisome proliferation. No differences were observed compared to controls in general behavior, liver size, peroxisome proliferation, hepatic activities of catalase and carnitine acetyltransferase, and no hypolipidemia was observed.
- [REDACTED] –
    - A 15-day repeat dose inhalation study was identified in rats. No effects were reported at the maximum concentration tested of approximately 125 µg/L. However, this study was not of sufficient design, and limited details were provided. Therefore, no relevant LOAEL or NOAEL may be established from this study.

Neurotoxicity (N): dg
Dicarboxylic Acid monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Dicarboxylic Acid monomer.

Group II* Score (repeated dose: H, M, L): dg
Dicarboxylic Acid monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Dicarboxylic Acid monomer.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Dicarboxylic Acid monomer was assigned a score of Low for skin sensitization based on negative skin sensitization data in guinea pigs.

- [REDACTED] –
    - Dicarboxylic Acid monomer (99.99% purity) was applied to the intact skin of 10 Albino Guinea Pigs in a 50% and 25% suspension in Diol monomer. To test for sensitization a series of four sacral intradermal injections were given, 1 each week for 3 weeks. Following a two week rest period the skin was challenged again by application of 50% and 25% suspension and compared to a control group. No sensitization effects were observed. It was reported that Dicarboxylic Acid monomer is mildly irritating and not sensitizing to the skin of guinea pigs.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg
Dicarboxylic acid monomer was assigned a data gap for respiratory sensitization as no relevant data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L
Dicarboxylic Acid monomer was assigned a score of Low for skin irritation/corrosivity based on data supporting that Dicarboxylic Acid monomer is not classifiable as a GHS skin irritant.

- BASF 1978 –
    - A (GLP status not reported) skin irritation study (method not reported) was conducted using rabbits (strain/sex not reported, n=6). A 50% aqueous suspension of 500 mg of Dicarboxylic Acid monomer (99.8%) was applied to the intact and scarified skin of six rabbits for 24 hours. Redness was observed at 24 hours (score 2-3). This effect was fully reversible at 72 hours. Mild to severe reddening and edema was observed in scarified skin at 24 hr (score 2-3). At 72 hours scores were between 0 and 2. All effects were fully reversible in 1 week. This chemical is not classified as a GHS Skin irritant based on the available data. GHS requires a score of ≥ 1.5 at 24, 48, and 72 hours to classify a chemical a minor irritant. Furthermore, modern guidelines require a 4-hour exposure period; a 24-hour exposure period may be considered a worst-case scenario.

  - In a second (GLP status not reported) irritation study (method not reported) an 80% aqueous paste of Dicarboxylic Acid monomer (99.8%) was applied to the back and the ears of 2 rabbits, for 20 hours. All irritation was fully reversible (Scored of 0) at 72 hours.
- [REDACTED] –
  - Dicarboxylic Acid monomer (99.99% purity) was applied to the intact skin of 10 Albino Guinea Pigs in a 50% and 25% suspension in polyethylene glycol. To test for sensitization a series of four sacral intradermal injections were given, 1 each week for 3 weeks. Following a two week rest period the skin was challenged again by application of 50% and 25% suspension and compared to a control group. No sensitization effects were observed. It was reported that Dicarboxylic Acid monomer is mildly irritating and not sensitizing to the skin of guinea pigs.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): H
Dicarboxylic Acid monomer was assigned a score of High for eye irritation/corrosivity based on classification as a GHS Category 2A eye irritant.

- BASF 1978 –
  - A (GLP status not reported) eye irritation study (method not reported) was conducted using rabbits (sex/strain not reported, n=6). A 0.1 ml instillation of Dicarboxylic Acid monomer (99.8% purity) was found to be highly irritating to the eye of 6 rabbits. Symptoms were not reversible within the 8 day observation period and a score of 41.5 on a scale of 100 was reported.
- LPT 2004 –
  - A GLP compliant eye irritation/corrosion study (OECD 405) was conducted. Species and number of animals was not specified in the summary. Severe irritation occurred after the instillation of 100 mg of Dicarboxylic Acid monomer. Corneal opacity and irritation of the iris was observed in all animals with scores of 3 and 2, respectively. Effects were reversible after 16 days.
- Following GHS criteria, Dicarboxylic Acid monomer is classified as a Category 2A eye irritant as all effects were reversible within a 21-day period (UN 2011).

Ecotoxicity (Ecotox)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): M
Dicarboxylic Acid monomer was assigned a score of Moderate for acute aquatic toxicity based on reported EC_{50} values that fall between 10 and 100 mg/L. Acute toxicity values between 10 and 100 mg/L are classified as Moderate in the GreenScreen™ criteria.

- [REDACTED] –
  - An LC_{50} value just below 100 mg/L was identified for *Pimephales promelas* (fish, 96-hr).
- BASF 1980 –
  - An LC_{50} value greater than 200 mg/L was identified for *Leuiscus idus* (fish, 96-hr).
- Bayer 1991 –
  - An LC_{50} value of greater than 1,000 mg/L was obtained for *Danio rerio* (fish, 96-hr).
- BASF 1988 –
  - An EC_{50} value just below 100 mg/L was identified for *Daphnia manga* (daphnid, 48-hr).
- BASF 1996 –
  - An EC_{50} value of less than 50 mg/L was identified for *Desmodesmus subspicatus* (algae, 72-hr).
- UNEP 2004 –
  - Acute aquatic toxicity tests in *Pimephales promelas*, *Leuiscus idus* and *Daphnia magna* were conducted with pH ranges between reaching as low as 3.8. Therefore, pH effects cannot be ruled out as causes for the first two values and these studies are not appropriate for risk assessment. Furthermore, Dicarboxylic Acid monomer is not a strong acid, and pH effects are unlikely to occur in the environment. The study in *Danio rerio* was conducted with a pH range of 7.4 to 7.7, and the study

with *Desmodesmus subspicatus* ranged from 6.0 to 8.2. Therefore, a <50 mg/L EC_{50} for algae will be considered the appropriate value for assessment in the GreenScreen™.

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *L*
Dicarboxylic Acid monomer was assigned a score of Low for chronic aquatic toxicity based on being readily biodegradable and having a low potential for bioaccumulation.

- Dicarboxylic Acid monomer is not classifiable for chronic toxicity following GHS criteria as it is expected to be readily biodegradable and not expected to bioaccumulate in aquatic species (UN 2011).

Environmental Fate (Fate)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Persistence (P) Score (vH, H, M, L, or vL): vL
Dicarboxylic Acid monomer was assigned a score of Very Low for persistence based on meeting OCED ready biodegradable criteria.

- UNEP 2004 –
  - Several OECD guideline biodegradation studies have been conducted on Dicarboxylic Acid monomer including: 301B, 301C, 301D, 301E, and 303A. Biodegradation ranged from approximately 60-90% after 14 days, and from approximately 80 to 95% at 28 days following readily biodegradable (301) criteria. Following OECD 303A Dicarboxylic Acid monomer achieved 99% biodegradation after 1 day. Based on the available data, Dicarboxylic Acid monomer is expected to meet the 10-day ready biodegradability criterion.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Dicarboxylic Acid monomer was assigned a score of Very Low for bioaccumulation based on a predicted BCF below 100 (CPA 2011a).

- U.S. EPA 2011 –
  - BCFBAF predicts a bioconcentration factor of less than 1and a log K_{ow} of less than 4 indicating that this chemical is not likely to bioaccumulate.

Physical Hazards (Physical)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Reactivity (Rx) Score (vH, H, M or L): *L*
Dicarboxylic Acid monomer 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.

- Dicarboxylic Acid monomer would not be classified as an oxidizing chemical as it structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, Dicarboxylic Acid monomer is not expected be explosive as it does not contain structural groups that would cause concern for explosion. Furthermore, the high flashpoint (approximately 200°C) and ignition temperature (greater than 400°C) further support that Dicarboxylic Acid monomer is not a reactive chemical.

Flammability (F) Score (vH, H, M or L): L
Dicarboxylic Acid monomer was assigned a score of Low for flammability based on a high flashpoint and high ignition temperature, indicating that Dicarboxylic Acid monomer is not readily combustible.

- UNEP 2004 –

- Dicarboxylic Acid monomer has a flashpoint of approximately 200°C and ignition temperature of approximately 400°C. GHS criteria states that flammable substances are those that are easily ignited or may cause fire through friction (UN 2011)[16]. Based on the available data, Dicarboxylic Acid monomer is not expected to have high flammability.

[16] Section 2.7.1 of the GHS Purple Book.

References

BASF. 1978. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

BASF. 1980. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

BASF. 1981. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

BASF. 1988. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

BASF. 1996. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

Bayer. 1991. Unpublished test data for Dicarboxylic Acid monomer (As cited in UNEP 2004)

ChemIDplus. 2012. Online entry for Dicarboxylic Acid monomer. Available: http://chem.sis.nlm.nih.gov/chemidplus/

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2: Guidance for Hazard Assessment and Benchmarking Chemicals. October 18, 2011. http://www.cleanproduction.org/library/greenScreenv1-2/DRAFT_GreenScreen_v1-2_Guidance_2011_1018_v2.pdf

[REDACTED]. The Subacute Inhalation Toxicity of 109 Industrial Chemicals. Brit. J. Industr. Med. [REDACTED] (As cited in UNEP 2004)

Grandjean, P. and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

[REDACTED]. Haskell Data Report [REDACTED]. (As cited in UNEP 2004).

[REDACTED]. Safety of Dicarboxylic Acid monomer as Compared with Citric and Tartaric Acid. (As cited in UNEP 2004)

[REDACTED]. Biochem. Z. [REDACTED]. (As cited in UNEP 2004)

[REDACTED]. Mutagenic Evaluation of compound FDA 71-50, Dicarboxylic Acid monomer. Report No. [REDACTED]. (As cited in UNEP 2004)

Laboratory of Pharmacology and Toxicology (LPT). 2004. Eye Irritation Study in Rabbits. Unpublished Report. (As cited in UNEP 2004).

[REDACTED]. Acute Toxicity of Selected Organic Compounds to Flathead Minnows. U.S. EPA Report No. [REDACTED]. (As cited in UNEP 2004)

[REDACTED]. Hepatic Peroxisome Proliferation in Rats fed Plasticizers and Related Compounds. Toxicol. Appl. Pharmacol. 45:497-504 (As cited in UNEP 2004)

[REDACTED]. Microbial Mutagenesis Testing of Substances. Final Report. Project [REDACTED] (As cited in UNEP 2004)

[REDACTED]. Bacterial Mutagenicity Testing of 49 Food Ingredients Gives Very Few Positive Results. Mutat. Res. [REDACTED] (As cited in UNEP 2004)

[REDACTED]. The Results of Microbial Mutation Test for Forty-Three Industrial Chemicals. Jpn. J. Ind. Health. [REDACTED] (As cited in UNEP 2004)

Solutia Inc. 1975. Robust Summary for Dicarboxylic Acid Category. (As cited in UNEP 2001)

United Nations (UN). 2011. Globally Harmonized System of Classification and Labeling of Chemicals, Fourth Revised Edition.

United Nations Environmental Programme (UNEP). 2004. Screening Information Dataset (SIDS) for Dicarboxylic Acid monomer. Organisation for Economic Development (OECD). Available: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

United States Environmental Protection Agency (U.S. EPA). 2011. Estimation Programs Interface (EPI) Suite™ Web, v4.10, Washington, DC, USA.

United States Environmental Protection Agency (U.S. EPA). 2012. High Production Volume Information System (HPVIS) online entry for Dicarboxylic Acid monomer. Available: http://www.epa.gov/hpvis/index.html

United States Food and Drug Administration (U.S. FDA). 1972. Teratologic Evaluation of FDA-71-50. Report No. [REDACTED]. (As cited in UNEP 2004)

United States Food and Drug Administration (U.S. FDA). 1974. Teratologic Evaluation of FDA-71-50. Report No. [REDACTED]. (As cited in UNEP 2004)

United States Food and Drug Administration (U.S. FDA). 2006. Database of Select Committee on GRAS Substances (SCOGS) Reviews for Dicarboxylic Acid monomer. Available: http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=scogsListing

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

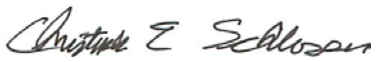
(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: EPISuite Results

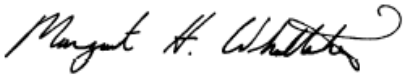
[REDACTED]

Dicarboxylic Acid Monomer GreenScreen™ Evaluation Prepared By:



Christopher E. Schlosser, M.F.S.
Associate Toxicologist
ToxServices LLC

Dicarboxylic Acid Monomer GreenScreen™ Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

GreenScreen™ Assessment for Fatty Alcohol Monomer

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this GreenScreen™ Assessment

Chemical Name: Fatty Alcohol monomer

GreenScreen™ Assessment Prepared By:
Name: Chris Schlosser, M.F.S.
Title: Associate Toxicologist
Organization: ToxServices LLC
Date: February 10, 2012

Quality Control Performed By:
Name: Margaret Whittaker, PhD.,
M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: February 17, 2012

Confirm application of the *de minimus* rule[17]: yes

Chemical Name (CAS #): Fatty Alcohol monomer

Also Called: [REDACTED]

Chemical Structure(s):

[REDACTED]

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Plasticizer

GreenScreen™ Rating[18]: Fatty Alcohol monomer was assigned a GreenScreen™ Benchmark Score of 2 based on Moderate Developmental toxicity (D). This corresponds to GreenScreen™ benchmark classification 2e in CPA 2011a. Data gaps (dg) exist for Reproductive Toxicity (R), Endocrine Activity (E), Neurotoxicity (N) (not listed, but not tested) and Respiratory Sensitization (SnR). As outlined in CPA (2011c) Section III(1)(Benchmarking Chemicals With Data Gaps), Fatty Alcohol monomer meets requirements for a GreenScreen™ Benchmark Score of 2, despite the hazard data gaps. In a worst-case scenario, if Fatty Alcohol monomer were assigned a High score for E, it would become a GreenScreen™ Benchmark 1 chemical.

GreenScreen™ Hazard Ratings: Fatty Alcohol Monomer																		
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*										
L	*L*	*dg*	*M*	*dg*	*M*	*dg*	*L*	*dg*	*dg*	*L*	*dg*	*M*	**H**	*M*	*L*	*vL*	*vL*	*L*	*M*

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).
Note: Please see Appendix A for a glossary of hazard acronyms.

[17] Every chemical in a material or formulation should be assessed if it is:
5. intentionally added and/or
6. present at greater than or equal to 100 ppm.

[18] 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.

Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[19]

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[20]?	GreenScreen™ Rating[21]
n/a	End	Combustion	Carbon Monoxide	630-08-0	Y	n/a
n/a	End	Combustion	Carbon Dioxide	124-38-9	N	n/a

Introduction

Fatty Alcohol monomer is used as a solvent for dyes, oils and resins as well as a plasticizer for PVC resins and wetting agent (HSDB 2003). Fatty Alcohol monomer is used as a monomer in one of the HallStar formulations.

[19] 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.
[20] 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 (CPA 2011b).
[21] GreenScreen™ reviews of transformation products depends on the GreenScreen™ Benchmark Score of the parent chemical (See Guidance).

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Carcinogenicity (C) Score (H, M or L): *L*
Fatty Alcohol monomer was assigned a score of Low for carcinogenicity based on no evidence of carcinogenic effects following two year or eighteen month carcinogenicity studies.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- ESIS 2000 –
    - A GLP compliant 2 year chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female Fischer 344 rats (50/sex/group). Rats were administered doses ranging from 0 to approximately 500 mg/kg of the test substance (99.8% purity) via oral gavage (vehicle: 0.005% aqueous cremophor EL) for 2 years. Fatty Alcohol monomer was not carcinogenic under the tested conditions. In both sexes the sum of primary tumors, malignant tumors, and benign tumors was lower than the control groups.
    - A GLP compliant 18 month chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female $B6C3F_1$ mice (50/sex/group). Mice were administered doses ranging from 0 no approximately750 mg/kg of the test substance (99.8% purity) via oral gavage for 18 months. Fatty Alcohol monomer was not carcinogenic in the mouse. A slight increase in tumors occurred when compared to the control group dosed with the emulsion vehicle. However, this increase was not significant when compared to the control group dosed with water. No significant increases occurred in male rats. Fatty Alcohol monomer was reported as not carcinogenic under the tested conditions by study authors.

Mutagenicity/Genotoxicity (M) Score (H, M or L): *L*
Fatty Alcohol monomer was assigned a score of Low for mutagenicity based on negative results for mutagenicity and clastogenicity both *in vivo* and *in vitro*.

- ESIS 2000 –
    - Multiple Ames bacterial reverse mutation assays were identified for Fatty Alcohol monomer utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537, and TA1538 at concentrations of up to approximately 5,000 µg/plate with and without metabolic activation. Fatty Alcohol monomer was reported as negative for mutagenicity under all tested conditions.
    - A (GLP status not reported) bacterial gene mutation assay utilizing *Bacillus subtilis* tester strain H17/M45 was conducted at concentration of up to approximately 500 µg/plate. Fatty Alcohol monomer was reported as negative for mutagenicity under the tested conditions. No further details were provided.
    - A GLP compliant HGPRT assay (method not reported) was conducting using Chinese Hamster Ovary (CHO) cells at concentrations of up to approximately 400 nl/ml (purity not reported) with and without metabolic activation. Fatty Alcohol monomer was reported as negative for mutagenicity under the tested conditions by study authors.
    - A GLP compliant mouse lymphoma assay (method not reported) was conducted utilizing L5178Y TK +/- cells at concentrations up to approximately 0.25 µl/ml (> 99.7% purity) in the presence and absence of metabolic activation. Fatty Alcohol monomer was reported as negative for mutagenicity under the tested conditions by study authors.
    - A GLP compliant *in vivo* cytogenetic assay (method not reported) was conducted using male Fischer 344 rats (5/group). Rats were administered doses ranging from 0.01 to approximately 0.2 ml/kg (> 99.7% purity) for 5 days. No significant increases in chromatid and chromosome breaks or structural rearrangements were reported. Fatty Alcohol monomer was reported as negative for clastogenicity under the tested conditions by study authors.
    - A GLP compliant *in vivo* dominant lethal assay (method not reported) was conducted using male and female ICR mice (number not reported). Mice were administered doses ranging from 0 to

approximately 1,000 mg/kg (> 99.7% purity) for 5 days. The fertility indices and average number of dead and total implants per pregnancy were within normal ranges. Fatty Alcohol monomer was reported as negative for genotoxicity under the tested conditions.

Reproductive Toxicity (R) Score (H, M, or L): dg
Fatty Alcohol monomer was assigned a data gap for reproductive toxicity as no relevant data were identified.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): *M*
Fatty Alcohol monomer was assigned a score of Moderate for developmental toxicity based on being categorized as a GHS category 2 reproductive toxicant.

- ESIS 2000 –
  - A GLP compliant developmental toxicity study (87/302/EEC) was conducted using female Wistar rats (10/group). Rats were administered doses ranging from 0 to approximately 1,500 mg/kg via oral gavage on gestation days 6 through 15. At the high dose, significantly reduced food consumption was reported in all parental dose groups. Severe clinical symptoms were observed including abdominal or lateral position, unsteady gait and apathy. Discoloration of the liver, lung edema, and emphysema were also reported in parental animals of the top dose group. An increased number of resorptions and markedly increased post implantation loss, along with increased resportions, decreased fetal body weights and increased incidence of fetuses with dilated renal pelvis and/or skeletal malformations. At the mid-high dose the only reported maternal effects were two dams with piloerection. Pups displayed a reduction in mean fetal body weights and increased frequency of fetuses with skeletal variations and retardations. At mid-low dose no substance related effects were reported. Based on available data, ToxServices established a NOAEL and LOAEL of mid-low dose and the mid-high due to reduced fetal body weights and increased skeletal variations in pups.
  - A (GLP status not reported) developmental toxicity study (method not reported was conducted using female Wistar rats (number not reported). Rats were administered doses ranging from 0 to approximately 1,500 mg/kg of the test substance (purity not reported) on day 12 of gestation. At the mid dose, slight increases (2%) in malformed fetuses were reported. At the high dose, mean fetal body weights were reduced (22%) and increased fetal malformation were observed including hydronephrosis (7.8%), tail anomalies (4.9%), and anomalies of the extremities (9.7%). Based on available data, ToxServices established a NOAEL and LOAEL of the mid dose and the high dose.
  - A GLP compliant developmental toxicity study (method not reported) was conducted using female CD-1 mice (n=50). Mice were administered does of 0 and approximately 1,000 mg/kg on days 7 through 14 of gestation. Results from this test are not applicable to the developmental toxicity endpoint. One dose was administered, which resulted in severe maternal toxicity including the death of ~30% of the test animal. Due to severe maternal toxicity the results of this study are not relevant as it is not possible to determine if toxic effects are primary, or secondary to maternal toxicity.
  - A GLP compliant developmental toxicity study (method not reported) was conducted using female F344 rats (25/group). Rats were exposed to doses ranging from 0 to approximately 2,000 mg/kg (> 99.7% purity) via occluded cutaneous application on days 6 to 15 of gestation. No developmental toxicity or increased incidence of malformation was reported at any dose. A NOEAL of less than the high-dose was reported for developmental toxicity by the study authors. No further details were available.
  - A (GLP status not reported) developmental toxicity study (method not reported) was conducted using female Sprague-Dawley rats (number not reported). Rats were exposed to concentrations of 0, and slightly less than 1.00 mg/L of the test substance (> 99% purity) via inhalation on days 1 to 19 of gestation. Fatty Alcohol monomer reduced maternal feed intake. No fetal toxicity or increased malformations were reported. A NOAEL of the highest dose tested was established by the study authors. No further details were available.
- Based on data in Wistar rats from a GLP compliant study following EEC guidelines a significant increase in pup body weights and skeletal variations occurred in the absence of maternal toxicity. Therefore, ToxServices categorizes Fatty Alcohol monomer as a GHS category 2 reproductive toxicant.

Endocrine Activity (E) Score (H, M or L): dg
Fatty Alcohol monomer has been assigned a data gap for endocrine activity. Although it is not a known endocrine disruptor, endocrine disruption testing has not performed on the chemical.

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- 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 Fatty Alcohol monomer.

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.

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint

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

Fatty Alcohol monomer was assigned a score of Moderate for acute mammalian toxicity based on oral LD_{50} values that fall between 300 to 2,000 mg/kg. Chemicals with oral LD_{50} values less than 2,000 mg/kg but greater than 300 mg/kg are designated as having moderate acute toxicity (CPA 2011a).

- ESIS 2000 –
    - Oral LD_{50} values of >1,500 to 7,000 mg/kg were identified in (strain not reported) rats.
    - Oral LD_{50} values of approximately 2,500 to approximately 4,500 mg/kg were identified in (strain not reported) mice.
    - Oral LD_{50} values of >1,000 to <1,500 mg/kg were identified in (strain not reported) rabbits.
    - Oral LD_{50} values of >500 to <3,000 mg/kg were identified (strain not reported) guinea pigs.
    - A Dermal LD_{50} value of greater than 3,000 mg/kg was identified in (strain not reported) rats.
    - Dermal LD_{50} values of <2,000 to >3,000 mg/kg were identified in (strain not reported) rabbits.
    - Insufficient data were provided to assess acute inhalation toxicity.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose: vH, H, M or L): dg

Fatty Alcohol monomer was assigned a data gap for systemic toxicity, single dose, as no relevant data were identified.

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

Fatty Alcohol monomer was assigned a score of Low for systemic toxicity/organ effects based on repeated exposure as it was not classified as a GHS specific target organ toxicant.

- ESIS 2000 –
    - A non-GLP compliant 3 month oral toxicity study (method not reported) was conducted using male and female Wistar rats (10/sex/group). Rats were administered doses ranging from 0 approximately 1,000 mg/kg in males and 0 to approximately 1,500 mg/kg in females daily in the diet for 3 months. In the top dose group increased liver weights, cortical degeneration of the kidney (in males), focal liver congestion and/or swelling (in females). In the top two dose groups an increased incidence and distribution of transitory hepatic diffuse cloudy swelling and cloudy swelling of the proximal convoluted kidney tubule was observed. No further details were provided. Based on reported data, ToxServices established a NOAEL and LOAEL of the mid-low dose and mid-high dose.
    - A GLP compliant 3 month oral toxicity study (method not reported) was conducted using male and female Fischer 344 rats (10/sex/dose). Rats were administered doses ranging from 0 to approximately 500 mg/kg (> 99.8% purity) 5 days/week for 3 months via oral gavage. The oral administration of Fatty Alcohol monomer led to reduced food consumption and body weight gain in male and female rats in the top dose group. In addition, increased relative liver and stomach weights (both sexes), increased absolute stomach weight (females) decrease in alanine-aminotransferase, glucose, and cholesterol (both sexes), decrease in alkaline phosphatase (males), single or multiple elevated foci in

the mucosa of the fore-stomach (both sexes), and focal or multifocal acanthosis in the mucosa of the fore-stomach in both sexes. At the mid-high dose, increased relative liver weights in both sexes, increased relative stomach weights in females, decreases in alkaline phosphatase and glucose in males, and a decrease in alanine-aminotransferase in females. A NOAEL and LOAEL of the mid-low dose and mid-high dose were reported by the study authors.

- A GLP compliant 3 month oral toxicity study was conducted using B6C3F$_1$ mice (10/sex/group). Mice were administered doses ranging from 0 to approximately 500 mg/kg (purity not reported) 5 days/week for 3 months via oral gavage. Limited details were available for this study. Increased weights and slight focal and multifocal acanthosis in the mucosa of the fore-stomach were reported in the top dose of both sexes, and in the mid-high dose males. No further details were provided for this study. A NOAEL and LOAEL of mid-low dose and mid-high dose were reported.

- Fatty Alcohol monomer is not classified as a GHS specific target organ toxicant as no effects were reported within the 10 to 100 mg/kg recommended guidance values (UN 2011). Furthermore, a consistent target organ was not identified and it was not clear or reported if improper gavage techniques may have played a role on reported stomach effects.

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): dg
Fatty Alcohol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Fatty Alcohol monomer.

Group II* Score (repeated dose: H, M, L): dg
Fatty Alcohol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Fatty Alcohol monomer.

Skin Sensitization (SnS) Group II* Score (H, M or L): *L*
Fatty Alcohol monomer was assigned a score of Low for skin sensitization based on not being sensitizing following a human repeat patch test.

- ESIS 2000 –
  - A non-GLP compliant human patch test (method not reported) was conducting using male and female human volunteers (n=29). Subjects were administered five 48-hour patch tests within a 10-day period using a 4% concentration in a petrolatum. No positive reactions were shown during the induction phase, or when challenged 10-14 days later. Fatty Alcohol monomer was reported as non-sensitizing by the study authors.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg
Fatty Alcohol monomer was assigned a data gap for respiratory sensitization as not relevant data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): *M*
Fatty Alcohol monomer was assigned a score of Moderate for skin irritation/corrosivity based on being classified as a GHS Category 2 skin irritant.

- ESIS 2000 –
  - A non-GLP compliant acute dermal irritation/corrosion study (OECD 404) was conducted using (strain not reported) rabbits (n=3). Rabbits were exposed to (concentration not reported) Fatty Alcohol monomer under occlusion for 4 hours. An irritation index of 3.33 for redness and 4.00 for erythema is reported. Following GHS criteria a chemical with a score of between 2.3 and 4.0 is classified as a Category 2 Irritant (UN 2011).
  - Several other irritation studies were identified and reported Fatty Alcohol monomer as moderately to highly irritating.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): *H*
Fatty Alcohol monomer was assigned a score of High for eye irritation/corrosivity based on being classified as a GHS Category 2A Eye Irritant.

- ESIS 2000 –
  - A non-GLP compliant acute eye irritation/corrosion study (OECD 405) was conducted using (strain not reported) rabbits (number not reported). Scores of 1.44 were reported for corneal opacity and 2.56 for conjunctival redness. Following GHS criteria, a score of above 1 for corneal opacity and above 3 for conjunctival redness classifies this chemical as a Category 2A eye irritant.
  - Multiple other studies were reported in the IUCLID document, and reports ranged from minimally to highly irritating. Very limited details were provided.

Ecotoxicity (Ecotox)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): *M*
Fatty Alcohol monomer was assigned a score of Moderate for acute aquatic toxicity based on L/EC_{50} values identified between 10 and 100 mg/L, the cutoffs for Moderate acute aquatic toxicity (CPA 2011a).

- ESIS 2000 –
  - An LC_{50} value of approximately 30 mg/L was identified for *Pimephalas promelas* (fish, 96-hr).
  - An LC_{50} value of >20 mg/L was identified for *Leuciscus idus meanotus* (fish, 96-hr).
  - An LC_{50} value of approximately 35 mg/L was identified for *Salmo gairdneri* (fish, 96-hr).
  - An EC_{50} value of approximately 40 mg/L was identified for *Daphnia magna* (invertebrate, 48-hr).
  - An EC_{50} value of approximately 20 mg/L was identified for *Artemia salina* (invertebrate, 24-hr).
  - An EC_{50} value ranging from10 to 50 mg/L was identified for *Chlorella emersonii* (algae, 48-hr).
  - An EC_{50} value of approximately 10 mg/L was identified for *Scenedesmus subspicatus* (algae, 72-hr).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *L*
Fatty Alcohol monomer was assigned a score of Low for chronic aquatic toxicity based on being readily biodegradable and having a low potential for bioaccumulation.

- Fatty Alcohol monomer is not classifiable for chronic toxicity following GHS criteria as it is expected to be readily biodegradable and not expected to bioaccumulate in aquatic species (UN 2011)[22].

Environmental Fate (Fate)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint

Persistence (P) Score (vH, H, M, L, or vL): *vL*
Fatty Alcohol monomer was assigned a score of Very Low for persistence based on modeled data indicating this data is expected to meet the 10-day window.

- ESIS 2000 -
  - A GLP compliant modified strum test (Directive 84/449/EEC, C.5, similar to OECD 301B) was conducted under aerobic conditions in domestic activated sludge. Fatty Alcohol monomer was reported as reaching approximately 50% to 70% biodegradation after 17 days.

[22] Table 4.1.1 of the Purple Book.

  - A non-GLP compliant Inherent biodegradability: Modified Zahn-Wellens tests (OECD 302B) was conducted under aerobic conditions using industrial activated sludge. Fatty Alcohol monomer was reported as approximately 95 to 100% biodegradable after 5 days.
- U.S. EPA 2011 –
  - Test data do not specify if Fatty Alcohol monomer meets the 10-day biodegradation window. However, BIOWIN[23] modeling indicates that this chemical is likely to meet the 10-day biodegradation window (as shown in Appendix B).

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Fatty Alcohol monomer was assigned a score of Very Low for bioaccumulation based on a BCF of less than 100, which is the cut-off value for a Very Low classification following GreenScreen™ criteria (CPA 2011a).
- ESIS 2000 –
  - Fatty Alcohol monomer has a reported BCF of approximately 25 based on calculations from water solubility indicating that it is unlikely to bioaccumulate. No further details were provided.

Physical Hazards (Physical)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint

Reactivity (Rx) Score (vH, H, M or L): *L*
Fatty Alcohol monomer 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.
- Fatty Alcohol monomer would not be classified as an oxidizing chemical as it structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, Fatty Alcohol monomer is not expected be explosive as it does not contain structural groups that would cause concern for explosion.

Flammability (F) Score (vH, H, M or L): *M*
Fatty Alcohol monomer was assigned a score of Moderate for flammability based on being classified as a GHS Category 4 Flammable Liquid. Category 4 Flammable Liquids are assigned a score of Moderate following GreenScreen™ criteria (CPA 2011a).
- ESIS 2000 –
  - Fatty Alcohol monomer has a flashpoint between 73 and 82°C. Following GHS criteria, chemicals with a flashpoint between 60 and 93°C are considered a Category 4 flammable liquid (UN 2011)[24].

[23] BIOWIN estimates the probability of rapid aerobic and anaerobic biodegradation of an organic compound in the presence of mixed populations of environmental microorganisms.
[24] Table 2.6.1 of the GHS Purple Book.

References

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

European Chemical Substances Information System (ESIS). 2000. IUCLID Dataset for Fatty Alcohol monomer. European Commission Joint Research Centre. Available: http://ecb.jrc.ec.europa.eu/esis/

Grandjean, P. and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

Hazardous Substances Data Bank (HSDB). 2005. Entry for Fatty Alcohol monomer. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

United Nations (UN). 2011. Globally Harmonized System of Classification and Labeling of Chemicals, Fourth Revised Edition.

United States Environmental Protection Agency (U.S. EPA). 2011. Estimation Programs Interface (EPI) Suite™ Web, v4.10, Washington, DC, USA.

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

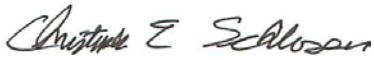
(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: EPISuite Results

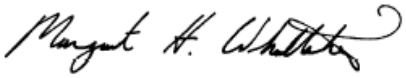
[REDACTED]

Fatty Alcohol Monomer GreenScreen™ Evaluation Prepared By:



Christopher E. Schlosser, M.F.S.
Associate Toxicologist
ToxServices LLC

Fatty Alcohol Monomer GreenScreen™ Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

GreenScreen™ Assessment for Diol Monomer

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this GreenScreen™ Assessment

Chemical Name: Diol monomer

GreenScreen™ Assessment Prepared By:
Name: Chris Schlosser, M.F.S.
Title: Associate Toxicologist
Organization: ToxServices, LLC
Date: February 10, 2012

Quality Control Performed By:
Name: Margaret Whittaker, PhD., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: February 20, 2012

Confirm application of the *de minimus* rule[25]: Yes

Chemical Name (CAS #): Diol monomer

Also Called: [REDACTED]

Chemical Structure(s):

[REDACTED]

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Solvent
2. Polymer production

GreenScreen™ Rating[26]: Diol monomer was assigned a GreenScreen™ Benchmark Score of 3 based on data gap analysis. Data gaps (dg) exist for Endocrine Activity (E), Neurotoxicity (N) (not listed, but not tested) and Respiratory Sensitization (SnR). As outlined in CPA (2011c) Section III(1)(Benchmarking Chemicals With Data Gaps), Diol monomer does not meet requirements for a GreenScreen™ Benchmark Score of 4 due to data gaps. In a worst-case scenario, if Diol monomer were assigned a High score for E, it would become a GreenScreen™ Benchmark 1 chemical.

GreenScreen™ Hazard Ratings: Diol Monomer																			
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*										
L	*L*	*L*	*L*	dg	*L*	dg	*L*	dg	dg	*L*	dg	*L*	*L*	*L*	*L*	*vL*	*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).
Note: Please see Appendix A for a glossary of hazard acronyms.

[25] Every chemical in a material or formulation should be assessed if it is:
7. intentionally added and/or
8. present at greater than or equal to 100 ppm.

[26] 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.

Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[27]

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[28]?	GreenScreen™ Rating[29]
n/a	End	Combustion	Carbon Monoxide	630-08-0	Y	n/a
n/a	End	Combustion	Carbon Dioxide	124-38-9	N	n/a

Introduction

Diol monomer is used for the production of antifreeze, deicing products, polymer compounds, laundry detergents, paint, food additives, pharmaceuticals, pet foods, and tobacco processing (UNEP 2001). Diol monomer is used as a monomer in one of the HallStar formulations.

[27] 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. Products that contain Diol monomer monomers are often plastics, which are often disposed of via incineration. Therefore, health and environmental effects associated with combustion byproducts are of particular concern.
[28] 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 (CPA 2011b).
[29] GreenScreen™ reviews of transformation products depends on the GreenScreen™ Benchmark Score of the parent chemical (See Guidance).

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Carcinogenicity (C) Score (H, M or L): *L*
Diol monomer was assigned a score of Low for carcinogenicity based on no evidence of carcinogenic effects following two year studies in rats and dogs.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- UNEP 2001 –
    - A non-GLP compliant 2 year chronic toxicity/carcinogenicity study (method not reported) was conducted using male and female CD rats (number not reported). Rats were administered doses of up to approximately 2,000 mg/kg of the Diol monomer (purity not reported) daily for 2 years. No evidence of any treatment related tumors were reported under the test conditions. Limited details were available for this study.
    - A non-GLP compliant 2 year chronic toxicity/carcinogenicity study (method not reported) was conducted using male and female Beagle dogs (number not reported). Dogs were administered doses of up to approximately 5,000 mg/kg of Diol monomer daily for 2 years. Tumor incidences were unchanged in male and female dogs when compared to the controls. No further details were provided for this study.

Mutagenicity/Genotoxicity (M) Score (H, M or L): *L*
Diol monomer was assigned a score of Low for mutagenicity based on lack of evidence of genotoxic effects following *in vitro* and *in vivo* assays.

- UNEP 2001 –
    - A (GLP status not reported) bacterial reverse mutation assay (method not reported) was conducted utilizing *Salmonella typhimurium* tester strains TA92, TA94, TA98, TA100, TA1535 and 1537 in the presence of metabolic activation at concentrations up to approximately10 mg/plate. No increase in revertants was observed and Diol monomer was reported as negative for mutagenicity under the tested conditions.
    - A (GLP status not reported) bacterial reverse mutation assay (method not reported) was conducted utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535 and TA1537 at concentrations of up to approximately 300 µmol/plate in the absence of metabolic activation. No increase in revertants was observed and Diol monomer was reported as negative for mutagenicity under the tested conditions.
    - A GLP compliant chromosomal aberration test (OECD 473) was conducted utilizing cultured human lymphocytes at concentrations of up to approximately 3,000 µg/ml with and without metabolic activation. Diol monomer showed no evidence of clastogenic effects under all tested conditions and was reported as negative for genotoxicity.
    - A (GLP status not reported) chromosomal aberration test (method not reported) was conducted utilizing Chinese Hamster Lung (CHL) fibroblasts at concentrations of up to approximately 30 mg/ml in the absence of metabolic activation. Cells at approximately 30 mg/ml (~400 mM) showed a 38% increase in structural aberrations. However, at approximately 30 mg/ml significant cytotoxicity was reported, and this concentration is above the 10 mM maximum concentration recommended by modern guidelines. Therefore, the results of this study are inconclusive as cytotoxic and osmotic destabilizing effects could cause the study results to be unreliable. In addition, the lower two doses tested showed no signs of cytogenic activity.
    - A non-GLP compliant cytogenetic assay (method not reported) was conducted using male Sprague-Dawley rats (15/group). Rats were administered a single dose ranging from 0 to approximately 5,000 mg/kg then sacrificed at 6, 24, or 48 hours following treatment. Increases in chromosomal aberrations were reported in the mid and high-dose group. However, these effects were well within historic ranges.

Reproductive Toxicity (R) Score (H, M, or L): *L*
Diol monomer was assigned a score of Low for reproductive toxicity based on no evidence of reproductive toxicity following a two generation study in mice at doses of up to approximately 10,000 mg/kg.

- UNEP 2001 –
    - A (GLP status not reported) two generation toxicity study (method not reported) was conducted using male and female CD-1 mice (20/sex/group). Mice were administered doses ranging from 0 to approximately 10,000 mg/kg from 7 before mating and 98 days following mating in drinking water. Slight increases in water consumption were observed in all parental dose groups. Body weights were unaffected. Necropsy of F1 adults revealed no effects on mating, fertility or the number, weight or viability of F2 pups. The study authors reported a NOAEL of approximately10,000 mg/kg based on no effects at the top dose.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): *L*
Diol monomer was assigned a score of Low for developmental toxicity based on no evidence of developmental toxicity following studies in rats, rabbits, mice, and hamsters.

- UNEP 2001 –
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female Wistar rats (25/dose). Rats were administered does ranging from 0 to approximately 1,500 mg/kg on days 6 to 15 of gestation via oral gavage. No effects were reported on live litters, total or average number of implant sites, total and partial resorptions, the total and average number of five fetuses and their sex ratio, and the number of dead fetuses or fetal weight. Based on the available data, a NOAEL of approximately 1,500 mg/kg was reported by the study authors.
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female Dutch-belted rabbits (n=15 to 20). Rabbits were administered doses ranging from 0 to approximately 1,200 mg/kg of the test substance on days 6 to 18 of gestation via oral gavage. No effects were reported on live litters, total or average number of implant sites, total and partial resorptions, the total and average number of five fetuses and their sex ratio, and the number of dead fetuses or fetal weight. Based on the available data, a NOAEL of approximately 1,200 mg/kg was reported by the study authors.
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female CD-1 mice (n=25 to 28). Mice were administered doses ranging from 0 to approximately 1,500 mg/kg of the test substance on days 6 to 15 of gestation via oral gavage. No effects were reported on live litters, total or average number of implant sites, total and partial resorptions, the total and average number of five fetuses and their sex ratio, and the number of dead fetuses or fetal weight. Based on the available data, a NOAEL of approximately1,500 mg/kg was reported by the study authors.
    - A non-GLP compliant developmental toxicity study (method not reported) was conducted using female (strain not reported) Hamsters (n=24 to 27). Hamsters were administered doses ranging from 0 to approximately 1,500 mg/kg of the test substance on days 6 to 10 of gestation via oral gavage. No effects were reported on live litters, total or average number of implant sites, total and partial resorptions, the total and average number of five fetuses and their sex ratio, and the number of dead fetuses or fetal weight. Based on the available data, a NOAEL of approximately1,500 mg/kg was reported by the study authors.

Endocrine Activity (E) Score (H, M or L): dg
Diol monomer has been assigned a data gap for endocrine activity. Although it is not a known endocrine disruptor, endocrine disruption testing has not performed on the chemical.

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- 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 Diol monomer.

<u>Group II and II* Human Health Effects (Group II and II* Human)</u>
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.

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): *L*
Diol monomer was assigned a score of Low for acute mammalian toxicity based on Oral and Dermal LD_{50} value exceeding the 2,000 mg/kg cutoff for moderate toxicity (CPA 2011a).

- UNEP 2001 -
  - An Oral LD_{50} value of approximately20,000 mg/kg in (strain not reported) rats.
  - An Oral LD_{50} value of approximately 25,000 mg/kg in (strain not reported) mice.
  - An Oral LD_{50} value of approximately 20, 000 mg/kg in (strain not reported) guinea pigs.
  - A Dermal LD_{50} value of approximately20,000 mg/kg in (strain not reported) rabbits.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose: vH, H, M or L): dg
Diol monomer has been assigned a data gap for systemic toxicity, single exposure, as no relevant data were identified.

Group II* Score (repeated dose: H, M, L): *L*
Diol monomer was assigned a score of Low for systemic toxicity/organ effects based on repeated exposure as it is not classified as a GHS Specific Target Organ Toxicant.

- UNEP 2001 –
  - A non-GLP compliant 2 year chronic toxicity/carcinogenicity study (method not reported) was conducted using male and female CD rats (number not reported). Rats were administered doses of up to approximately 2,000 mg/kg of the Diol monomer (purity not reported) daily for 2 years. No systemic effects were reported under the test conditions. Limited details were available for this study.
  - A non-GLP compliant 2 year chronic toxicity/carcinogenicity study (method not reported) was conducted using male and female Beagle dogs (number not reported). Dogs were administered doses of up to approximately5,000 mg/kg of Diol monomer daily for 2 years. Minor red blood cell changes (significance not reported) were the only reported effect. No further details were provided for this study.
  - Several other repeat dose studies were identified with limited details available. No significant effects were reported except for species specific formation of Heinz bodies in cats administered approximately 500 mg/kg of Diol monomer.
- Based on the available data, Diol monomer is not classifiable as specific target organ toxicant as no clear effects within the 10 to 100 mg/kg guidance values were identified. In addition SIDS authors report that Diol monomer is well tolerated, with low toxicity to laboratory animals (UNEP 2001).

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): dg
Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Diol monomer.

Group II* Score (repeated dose: H, M, L): dg
Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Diol monomer.

Skin Sensitization (SnS) Group II* Score (H, M or L): *L*
Diol monomer was assigned a score of Low for skin sensitization based on not sensitizing effects reported following studies using human volunteers.

- UNEP 2001 –
  - A GLP compliant repeat insult patch test (method not reported) was conducted using human volunteers (n=104). Approximately 0.2 ml of a 50% aqueous dilution of Diol monomer was applied under semi-occlusive dressing to humans for 24 hours, 3 days a week, for 3 weeks. A challenge dose was applied 2 weeks after the final treatment. No effects were reported following the challenge dose and Diol monomer was reported as negative for skin sensitization.
  - A second non-GLP compliant patch test (method not reported) was conducted using human volunteers (n=204). Ten consecutive induction applications of 0.5g in a 12% dilution were applied to the lateral portion of the arm under occlusive conditions. A challenge dose (conditions not specified) was applied following a two week rest period and no reactions were observed. Diol monomer was reported as negative for skin sensitization by the study authors.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg
Diol monomer was assigned a data gap for respiratory sensitization as no relevant data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): *L*
Diol monomer was assigned a score of Low for skin irritation/corrosivity based on not being classified as a GHS Skin Irritant.

- UNEP 2001 –
  - A (GLP status not reported) acute dermal irritation/corrosion study (OECD 404) was conducted using female New Zealand rabbits (n=6). Rabbits were exposed to 0.5 ml of Diol monomer (purity not reported) for an unreported amount of time. Animals were examined at 1, 24, 48, and 72 hours following patch removal. An average score of 0.1 was reported for erythema. Diol monomer was reported as not irritating to the skin of rabbits by the study authors. An average score of greater than 1.5 at 24, 48, and 72 hours is required for classification as a GHS skin irritant.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): *L*
Diol monomer was assigned a score of Low for eye irritation/corrosivity based on no effects following an OECD guideline eye irritation study.

- UNEP 2001 –
  - A (GLP status not reported) acute eye irritation/corrosion study (OECD 405) was conducted using New Zealand white rabbits (sex not reported, n=6). 0.1 ml of an undiluted Diol monomer was instilled into the eyes of rabbits for an unreported amount of time. Rabbits were examined at 4, 24, 48, 72, and 96 hours. There were no signs of chemosis, corneal opacity, or surface corneal damage at all doses. Diol monomer was reported as non-irritating to the eyes of rabbits by the study authors.

Ecotoxicity (Ecotox)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): *L*
Diol monomer was assigned a score of Low for acute aquatic toxicity based on L/EC_{50} values above 100 mg/L, the cutoff for a low toxicity classification (CPA 2011a).

- UNEP 2001 –
  - An LC_{50} value of >50,000 mg/L was identified in *Oncorhynchus mykiss* (fish, 96-hr) (OECD 203).
  - An LC_{50} value of approximately 50,000 mg/L was identified in *Pimephalas promelas* (fish, 96-hr) (OECD 203).

- An LC_{50} value of approximately 40,000 mg/L was identified in *Daphnia magna* (invertebrate, 48-hr) (OECD 202).
- An LC_{50} value of approximately 20,000 mg/L was identified in *Mysidopsis bahia* (invertebrate, 96-hr).
- An LC_{50} value of approximately 20,000 mg/L was identified in *Ceriodaphnia sp.* (invertebrate, 48-hr).
- An EC_{50} value of approximately 20,000 mg/L was identified in *Selenastrum capricornutum* (algae, 96-hr) (OECD 201).
- An EC_{50} value of approximately 20,000 mg/L was identified in *Skeletonema costatum* (algae, 96-hr) (OECD 201).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *L*
The globally harmonized system (GHS) does not require a chronic aquatic toxicity hazard rating for substances that are both rapidly biodegradable and have a BCF < 500 and log K_{ow} < 4.

Environmental Fate (Fate)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Persistence (P) Score (vH, H, M, L, or vL): *vL*
Diol monomer was assigned a score of Very Low for persistence based on meeting the 10-day biodegradation window.

- UNEP 2001 –
  - A non-GLP compliant biodegradation study (method not reported) was conducted under aerobic conditions in activated domestic sludge. Diol monomer was reported as approximately 70% biodegradable after 10 days and approximately 80% biodegradable at 20 day and was reported as readily biodegradable under the tested conditions.
  - A (GLP status not reported) biodegradation study (method not reported) was conducted under aerobic conditions using soil microcosm. Diol monomer was reported as 100% degradable after 12 days.
  - A (GLP status not reported) biodegradation study was conducted under aerobic conditions using unadapted and adapted sludge. Diol monomer reached approximately 85-95% biodegradation within 24 hours and was reported as readily biodegradable.
- While no studies following modern guidelines have been reported, the weight-of-evidence supports that Diol monomer is expected to be readily biodegradable.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Diol monomer was assigned a score Very Low for bioaccumulation based on a BCF below 100 (CPA 2011a).

- UNEP 2001 -
  - A BCF of approximately 1 was calculated based on the log K_{ow} of <1.00, indicating this chemical is not likely to bioaccumulate in aquatic species. No further details were provided.

Physical Hazards (Physical)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Reactivity (Rx) Score (vH, H, M or L): *L*
Diol monomer 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.

- Diol monomer would not be classified as an oxidizing chemical as it structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, Diol monomer is not

expected be explosive as it does not contain structural groups that would cause concern for explosion. Furthermore, the high flashpoint (>100°C) further supports that Diol monomer is not a reactive chemical.

Flammability (F) Score (vH, H, M or L): *L*
Diol monomer was assigned a score of Low for flammability based on classified as a GHS Flammable Liquid.

- UNEP 2001 –
  - A flash point of >100°C was reported for Diol monomer. Following GHS criteria, Diol monomer is not classified as a flammable liquid (UN 2011)[30].

[30] Table 2.6.1 of the GHS Purple Book.

References

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

Grandjean, P. and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

United Nations (UN). 2011. Globally Harmonized System of Classification and Labeling of Chemicals, Fourth Revised Edition.

United Nations Environmental Programme (UNEP). 2001. Screening Information Dataset (SIDS) for Diol monomer. Organisation for Economic Development (OECD). Available: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

Formatted: No underline, Font color: Auto, French (France)

Formatted: French (France)

Field Code Changed

Formatted: French (France)

Formatted: No underline, Font color: Auto, French (France)

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

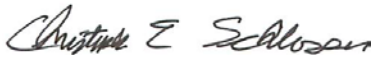
(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

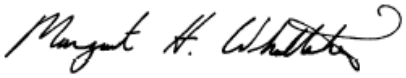
(ST) Systemic/Organ Toxicity

Diol Monomer GreenScreen™ Evaluation Prepared By:



Christopher E. Schlosser, M.F.S.
Associate Toxicologist
ToxServices LLC

Diol Monomer GreenScreen™ Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

GreenScreen™ Assessment for Butyl Diol Monomer

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this GreenScreen™ Assessment

Chemical Name: Butyl Diol monomer

GreenScreen™ Assessment Prepared By:
Name: Chris Schlosser, M.F.S.
Title: Associate Toxicologist
Organization: ToxServices, LLC
Date: February 10, 2012

Quality Control Performed By:
Name: Margaret Whittaker, PhD., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: February 17, 2012

Confirm application of the *de minimus* rule[31]: yes

Chemical Name (CAS #): Butyl Diol monomer

Also Called: [REDACTED]

Chemical Structure(s):

[REDACTED]

Identify Applications/Functional Uses:
(e.g. Cleaning product, TV casing)
1. Manufacture of Plasticizer

GreenScreen™ Rating[32]: Butyl Diol monomer was assigned a GreenScreen™ Benchmark Score of 3 based on High Eye Irritation/Corrosion (IrE). This corresponds to GreenScreen™ benchmark classification 3c in CPA 2011a. Data gaps (dg) exist for Endocrine Activity (E), Neurotoxicity (N) (not listed, but not tested) and Respiratory Sensitization (SnR). As outlined in CPA (2011c) Section III(1)(Benchmarking Chemicals With Data Gaps), Butyl Diol monomer meets requirements for a GreenScreen™ Benchmark Score of 3, despite the hazard data gaps. In a worst-case scenario, if Butyl Diol monomer were assigned a High score for E, it would become a GreenScreen™ Benchmark 1 chemical.

GreenScreen™ Hazard Ratings: Butyl Diol Monomer																			
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*										
L	*L*	*L*	*L*	dg	*L*	dg	*L*	dg	dg	*L*	dg	*L*	H	*L*	*L*	*vL*	*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).

[31] Every chemical in a material or formulation should be assessed if it is:
9. intentionally added and/or
10. present at greater than or equal to 100 ppm.

[32] 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.

Note: Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings:
Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[33]

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[34]?	GreenScreen™ Rating[35]
n/a	End	Combustion	Carbon Monoxide	630-08-0	Y	n/a
n/a	End	Combustion	Carbon Dioxide	124-38-9	N	n/a

Introduction

Butyl Diol monomer is used in the polymer industry as well as in cosmetics and pharmaceuticals (HSDB 2003). Butyl Diol monomer is a monomer in the HallStar formulations.

[33] 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. Products that contain butanediol monomers are often plastics, which are often disposed of via incineration. Therefore, health and environmental effects associated with combustion byproducts are of particular concern.
[34] 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 (CPA 2011b).
[35] GreenScreen™ reviews of transformation products depends on the GreenScreen™ Benchmark Score of the parent chemical (See Guidance).

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Carcinogenicity (C) Score (H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for carcinogenicity based on chronic toxicity/carcinogenicity assays in rats and dogs not identifying increases in tumors. The endpoint is assessed as low confidence as limited details were provided for the studies.

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- [REDACTED] –
    - A (GLP status not reported) 2-year chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female Sprague-Dawley rats (30/sex/group). Rats were administered doses ranging from 0 to approximately 10.0% of Butyl Diol monomer (99.98% purity) daily in the feed for 2 years. No increases in tumors were identified.
    - A (GLP status not reported) 2-year chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female Beagles dogs (4/sex/group). Dogs were administered doses ranging from 0 to approximately 3.0% of Butyl Diol monomer (99.98% purity) daily in the feed for 2 years. No increases in tumors were identified.

Mutagenicity/Genotoxicity (M) Score (H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for mutagenicity based on assays that show no genotoxicity bacterial strains or rats.

- [REDACTED] –
    - A (GLP status not reported) bacterial reverse mutation assay (OECD 471 and 472) was conducted by utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535, and TA1537, and *E.coli* tester strain WP2 uvrA at concentrations of up to approximately 5,000 µg/plate with and without metabolic activation. No increase in histidine revertants was observed and Butyl Diol monomer was reported as negative for mutagenicity.
- [REDACTED] –
    - A (GLP status not reported) cytogenetic assay/dominant lethal assay (method not reported) was conducted by using male and female Wistar rats (2/sex/group). Rats from the parental, F1 and F2 generations of a reproductive toxicity study were examined for cytogenic analysis, and dominant lethal effects. No increases in chromosomal aberrations or dominant lethal effects were observed and Butyl Diol monomer was reported as negative for genotoxicity.

Reproductive Toxicity (R) Score (H, M, or L): *L*
Butyl Diol monomer was assigned a score of Low for reproductive toxicity based on no clear evidence of reproductive toxicity at relevant dose levels. Due to minimal study details and lack of GLP compliance and modern test guidelines this endpoint will be assessed as low confidence.

- [REDACTED] –
    - A (GLP status not reported) two generation continuous breeding reproductive toxicity study (method not reported) was conducted using male and female Wistar rats (25/sex/group). Rats were administered doses ranging from 0 to approximately 24% (approx. 0 to 25,000 mg/kg[36]) of Butyl Diol monomer in the diet. Five successive mating cycles were achieved with F1 rats over 77 weeks. The

[36] Dose conversion estimates are based on default female Wistar rat food consumption and body weight values from http://www.tera.org/Tools/ratmousevalues.pdf:

5% in the diet: $\frac{0.05 \times 16{,}000 \text{ mg/kg}}{0.156 \text{ kg}}$ = ~4,800 mg/kg

pregnancy rates of F1A rats decreased during the five successive mating trials. Decreases in fertility index (92, 64, 60, 40, 20 at the mid dose level and 76, 52, 44, 28, 0 in the high dose level) suggest a cumulative effect over time. No significant treatment-related effects were noted on examination of testes, ovaries, or pituitary glands. No further effects were reported. Based on available data, ToxServices assigned a NOAEL and LOAEL of the mid dose and high dose.

- [REDACTED] –
  - A (GLP status not reported) three generation toxicity study (test method not reported) was conducted using male and female (strain/number not reported) rats. Very limited details were provided for this study, animals were administered one dose approximately 20% (~20,000 mg/kg, based on above study) and no effects on fertility or reproductive parameters were reported. No further details or specific endpoints analyzed were provided.
- Based on available data, Butyl Diol monomer is not classifiable as a reproductive toxicant following GHS criteria (UN 2012). Doses which caused toxicity were not identified below the OECD recommended maximum dose level of 10%. Doses at this level are likely to cause maternal toxicity and/or significant decreases in the nutritional intake of dams. In addition, a slight decrease in control animals was observed over the 5 generations (72, 44, 64, 60, 40) suggesting effect not related to the test material.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for developmental toxicity based on not being classifiable as a GHS developmental toxicant.

- [REDACTED] –
  - A (GLP status not reported) developmental toxicity study (method not reported) was conducted using female Long-Evans rats (10/group). Rats were administered doses ranging from 0 to approximately 7,000 mg/kg of Butyl Diol monomer (purity not reported) daily on days 6 through 15 of gestation. A significant decrease in pup body weights was observed during organogenesis, only in the high dose group. A dose related increase in malformed pups per dam was reported (1.6, 2.1, 2.7, and 3.0) thought not analyzed for statistical significance. Maternal sedation was noted at mid and high doses.
- [REDACTED] –
  - A (GLP status not reported) developmental toxicity study (method not reported) was conducted using female Wistar rats (14-15/group). Rats were administered doses ranging from 0 to approximately 25% (approx. 0 to 25,000 mg/kg[37]) of Butyl Diol monomer (purity not reported) in the feed on days 0 to 19 of gestation. Limited details were provided for this study. Maternal toxicity was not reported, but lower maternal body weight gain was suspected. Limited fetotoxicity was reported including delayed ossification of sternebrae was reported in the mid and top dose groups. Study authors reported a NOAEL and LOAEL of the mid dose and the high dose under the tested conditions.
- Butyl Diol monomer is not classifiable as a GHS reproductive toxicant as significant increases skeletal variations occurred at doses at or above the recommended maximum dose level (10%) for developmental toxicity studies and reported effects could be confounded by secondary or maternal toxicity.

Endocrine Activity (E) Score (H, M or L): dg
Butyl Diol monomer has been assigned a data gap for endocrine activity. Although it is not a known endocrine disruptor, endocrine disruption testing has not performed on the chemical.

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- 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 Butyl Diol monomer.

[37] Dose conversion estimates are based on default female Wistar rat food consumption and body weight values from http://www.tera.org/Tools/ratmousevalues.pdf:

5% in the diet: $\frac{0.05 \times 16{,}000 \text{ mg/kg}}{0.156 \text{ kg}}$ = ~4,800 mg/kg

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.

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

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

Butyl Diol monomer was assigned a score of Low for acute mammalian toxicity based on not being classified as a GHS acute toxicant with oral LD_{50} values above 2,000 mg/kg (UN 2011).

- U.S EPA 2012 –
  - An Oral LD_{50} value of approximately 20,000 was identified in (strain not reported) rats.
  - An Oral LD_{50} value of approximately 10,000 mg/kg was identified in (strain not reported) mice.
  - An Oral LD_{50} value of approximately 10,000 mg/kg was identified in (strain not reported) guinea pigs.
  - An inhalation toxicity study identified no deaths at saturated atmospheres of Butyl Diol monomer.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

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

Butyl Diol monomer was assigned a data gap of systemic toxicity, single dose, as no relevant data were identified.

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

Butyl Diol monomer was assigned a score of Low for systemic toxicity/organ effects based on not being classifiable as a GHS specific target organ toxicant.

- [REDACTED] –
  - A (GLP status not reported) 2-year chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female Sprague-Dawley rats (30/sex/group). Rats were administered doses ranging from 0 to approximately 10.0% of Butyl Diol monomer (99.98% purity) daily in the feed for 2 years. Mortality, body weight gain, blood parameters, urine parameters, organ weights, incidence of neoplasm, and organ histopathology were unaffected by the two-year treatment. Limited details were available.
  - A (GLP status not reported) 2-year chronic toxicity/carcinogenicity assay (method not reported) was conducted using male and female Beagles dogs (4/sex/group). Dogs were administered doses ranging from 0 to approximately 3.0% of Butyl Diol monomer (99.98% purity) daily in the feed for 2 years. Mortality, body weight gain, blood parameters, urine parameters, organ weights, incidence of neoplasm, and organ histopathology were unaffected by the two-year treatment. Limited details were available.
- U.S. EPA 2012 –
  - A (GLP status not reported) 13-week sub-chronic toxicity study (method not reported) was conducted using male and female Beagles dogs (4/sex/group). Dogs were administered doses ranging from 0 to approximately 12,000 mg/kg of Butyl Diol monomer (purity not reported) daily in the feed for 13-weeks. Reduction in body weight gain was observed in the top two dose groups of both sexes. Increased platelets were observed in the top two doses, and an increased level of methemoglobin at the top dose level of both sexes. A dose-related increase in free fatty acids was observed, but only reached significance in the top dose. Relative organ weights of liver kidney, brain, adrenals and lung were increased, and relative thymus and spleen weights were decreased in the top dose group. However, no histopathological effects were reported that corresponded to organ weight changes. Epileptic-like seizures were reported in a dose-dependent manner in both sexes. Study authors reported a NOAEL and LOAEL of the mid dose tested and the high dose tested.
- Butyl Diol monomer is not classifiable as a GHS toxicant as no clear toxic effects were present within GHS guidance values of 10 to 100 mg/kg for a category 2 specific target organ toxicant.

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): dg
Butyl Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Butyl Diol monomer.

Group II* Score (repeated dose: H, M, L): dg
Butyl Diol monomer has been assigned a data gap for neurotoxicity. Although it is not a known neurotoxicant, neurotoxicity testing has not performed on the 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 Butyl Diol monomer.

Skin Sensitization (SnS) Group II* Score (H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for skin sensitization based on no evidence of sensitization following a human repeat patch test.

- ESIS 2000 –
    - A (GLP status not reported) human patch-test (method not reported) was conducted using 200 human volunteers. Volunteers were induced with 15 24-hour covered patch exposures spread over a 5-week period and challenged two weeks later with a 24-hour patch. No sensitization was observed. Minimal study details were provided.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg
Buty Diol monomer was assigned a data gap for respiratory sensitization as no relevant data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for skin irritation/corrosivity based on not being classified as a GHS skin irritant.

- ESIS 2000 –
    - Three irritation studies were identified with limited to no details. Butyl Diol monomer was found to be non-irritating to humans under occluded and semi-occluded conditions for 24 hours. No irritation was produced in rabbits following a French cosmetic testing guideline, details not reported. Minimal irritation was reported to rabbits patch tested for 24 hours. However, modern guidelines recommend a maximum of 4-hour exposure. Therefore, the weight-of-evidence supports that Butyl Diol monomer is not irritating to the skin.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): *H*
Butyl Diol monomer was assigned a score of High for eye irritation/corrosivity based on causing immediate and severe pain to humans upon instillation into the eye.

- ESIS 2000 –
    - The IUCLID dataset identified four eye irritation studies. However, limited to no details were provided for each study. Therefore, insufficient data is present to classify this chemical.
- HSDB 2003 –
    - A single drop of Butyl Diol monomer to the eyes of humans causes immediate and severe pain.

Ecotoxicity (Ecotox)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for acute aquatic toxicity based on not being classified as GHS acute aquatic toxicant with LD_{50} values above 100 mg/L (UN 2011).

- ESIS 2000 –
  - An EC_{50} value of greater than 1,000 mg/L was reported for *Selenastrum capricornutum* (algae, 72-hr) (OECD 201).
- U.S. EPA 2011a (as shown in Appendix C)–
  - A LC_{50} value of approximately 10,000 mg/L is estimated for fish (96-hr).
  - An EC_{50} value of approximately 4,000 mg/L is estimated for daphnid (48-hr).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for chronic aquatic toxicity based on not being classified as GHS chronic aquatic toxicant with ChV values above 1 mg/L (UN 2011).

- U.S. EPA 2011a (as shown in Appendix C) –
  - A ChV of >500 mg/L is estimated for fish.
  - A ChV of >200 mg/L is estimated for daphnid.
  - A ChV of >100 mg/L is estimated for algae.

Environmental Fate (Fate)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Persistence (P) Score (vH, H, M, L, or vL): *vL*
Butyl Diol monomer was assigned a score of Very Low for persistence based on modeled data indicating that this chemical is likely to meet the 10-day biodegradation window (CPA 2011a).

- U.S. EPA 2011b –
  - BIOWIN[38] modeling indicates that this chemical is expected to be readily biodegradable with a predicted biodegradation time of days to weeks. Fugacity[39] modeling predicts approximately 60% partitioning to soil with a half-life of 17.3 days and approximately 30% partitioning to water with a half-life of 8.66 days. Based on modeled data, this chemical is predicted to meet 10-day readily biodegradable guidelines (as shown in Appendix B).

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Butyl Diol monomer was assigned a score of Very Low for persistence based on predicted BCF value below 100 (CPA 2011a).

- U.S. EPA 2011b –
  - BCFBAF predicts a bioconcentation factor (BCF) of <1 and a log K_{ow} of <1 indicating that this chemical is not likely to bioaccumulation in aquatic species (As shown in Appendix B).

[38] BIOWIN estimates the probability of rapid aerobic and anaerobic biodegradation of an organic compound in the presence of mixed populations of environmental microorganisms.
[39] Fugacity model predicts the partitioning and half-life of a chemical in sediment, water, soil and air.

Physical Hazards (Physical)

Complete copies of toxicological studies or extended abstracts (or primary references) were not available for review by ToxServices. For some endpoints, only limited quantitative details (e.g., statistical significance, organ weight values, and percent changes in measured endpoints) were provided/disclosed. Therefore, a low confidence rating has been assigned for those endpoint, as reflected by italics for each hazard endpoint.

Reactivity (Rx) Score (vH, H, M or L): *L*
Butyl Diol monomer 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.

- Butyl Diol monomer would not be classified as an oxidizing chemical as it structure does not contain a halogen and oxygen atoms present are only bonded to carbon or hydrogen (UN 2011). In addition, Butyl Diol monomer is not expected be explosive as it does not contain structural groups that would cause concern for explosion. Furthermore, the high flashpoint (>100°C) further supports that Butyl Diol monomer is not a reactive chemical.

Flammability (F) Score (vH, H, M or L): *L*
Butyl Diol monomer was assigned a score of Low for flammability based on not being classified as a GHS Flammable Liquid.

- ScienceLab 2010 –
    - A flashpoint of >100 °C (closed cup) and >120°C (open cup) were identified, which is above the 93°C cut-off criteria to be classified as flammable by GHS (UN 2011)[40].

[40] Table 2.6.1 of the GHS Purple Book.

References

Clean Production Action (CPA). 2011a. The GreenScreen™ for Safer Chemical Version 1.2. Available: http://www.cleanproduction.org/Greenscreen.v1-2.php

Clean Production Action (CPA). 2011b. Red List of Chemicals. Available: http://www.cleanproduction.org/library/greenScreenv1-2/GS_v_1_2_Benchmark_1_Lists.pdf

[REDACTED]. Fedn Proc. Fedn Am. Socs exp. Biol. [REDACTED] (As cited in U.S. EPA 2012)

European Chemical Substances Information System (ESIS). 2000. IUCLID Dataset for Butyl Diol monomer. European Commission Joint Research Centre. Available: http://ecb.jrc.ec.europa.eu/esis/

Grandjean, P. and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

Hazardous Substances Data Bank (HSDB). 2003. Entry for Butyl Diol monomer. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

[REDACTED]. J. Appl. Toxicol. [REDACTED] (As cited in U.S. EPA 2012)

[REDACTED]. Testing Reports of Environmental Chemicals. [REDACTED] (As cited in U.S. EPA 2012)

[REDACTED]. Birthweight Depression in Male Rats Contiguous to Male Siblings in Utero Exposed to High Doses of Butyl Diol monomer During Organogenesis. J. Am. Coll. Toxicol. [REDACTED]

[REDACTED]. Toxic. Appl. Pharmax. [REDACTED]. (As cited in U.S EPA 2012)

ScienceLab. 2010. Material Safety Data Sheet (MSDS) for [REDACTED]. Available: http://www.sciencelab.com/

United Nations (UN). 2011. Globally Harmonized System of Classification and Labeling of Chemicals, Fourth Revised Edition.

United States Environmental Protection Agency (U.S. EPA). 2011. Estimation Programs Interface (EPI) Suite™ Web, v4.10, Washington, DC, USA.

United States Environmental Protection Agency (U.S. EPA). 2012. High Production Volume Information System (HPVIS) online entry for Butyl Diol monomer. Available: http://www.epa.gov/hpvis/index.html

Formatted: No underline, Font color: Auto, French (France)

Formatted: French (France)

Field Code Changed

Formatted: French (France)

Formatted: No underline, Font color: Auto, French (France)

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

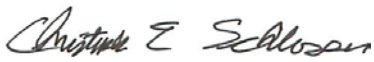
APPENDIX B: EPISuite Results

[REDACTED]

APPENDIX C: ECOSAR Results:

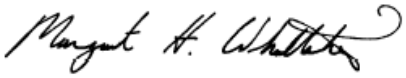
[REDACTED]

Butyl Diol Monomer GreenScreen™ Evaluation Prepared By:



Christopher E. Schlosser, M.F.S.
Associate Toxicologist
ToxServices LLC

Butyl Diol Monomer GreenScreen™ Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC