C. I. Pigment Blue 15 (CAS# 147-14-8) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

Washington State Department of Ecology

Prepared by:

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October 14, 2014

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TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for C. I. Pigment Blue 15 (CAS #147-14-8)

C.I. Pigment Blue 15 is a pigment used in inks, paints, surface coatings, rubber, resins, linoleum, artist materials, leather cloth, paper, wallpaper, tinplate printing, wax compositions, cements, and textile printing. In addition to its use as a pigment, C.I. Pigment Blue 15 is used as a chemical intermediate in the synthesis of Direct Blue 86, Pigment Green 7, Pigment Green 36, Reactive Blue 7, and Vat Blue 29 (HSDB 2011).

C. I. Pigment Blue 15 was assigned a GreenScreen® Benchmark Score of 3 ("Use but Still Opportunity for Improvement") as it has Very High persistence (P). This corresponds to GreenScreen® benchmark classification 3a in CPA 2011. Data gaps (DG) exist for endocrine activity (E), and single and repeated dose neurotoxicity (Ns and Nr*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), C. I. Pigment Blue 15 meets requirements for a GreenScreen® Benchmark Score of 3 despite the hazard data gaps. In a worst-case scenario, if C. I. Pigment Blue 15 were assigned a High score for the data gaps E, Nr*, or SnR*, it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal, and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 3 ("Use but Still Opportunity for Improvement") is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for C. I. Pigment Blue 15

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	repeated*	single	repeated*										
L	**L**	**L**	**L**	DG	**L**	DG	**L**	DG	DG	*L*	DG	*L*	*L*	*L*	*L*	*vH*	**vL**	*L*	*L*

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Assessment for C. I. Pigment Blue 15 (CAS #147-14-8)

Method Version: GreenScreen® Version 1.2[1]
Assessment Type[2]: Certified

Chemical Name: C. I. Pigment Blue 15

CAS Number: 147-14-8

GreenScreen® Assessment Prepared By:
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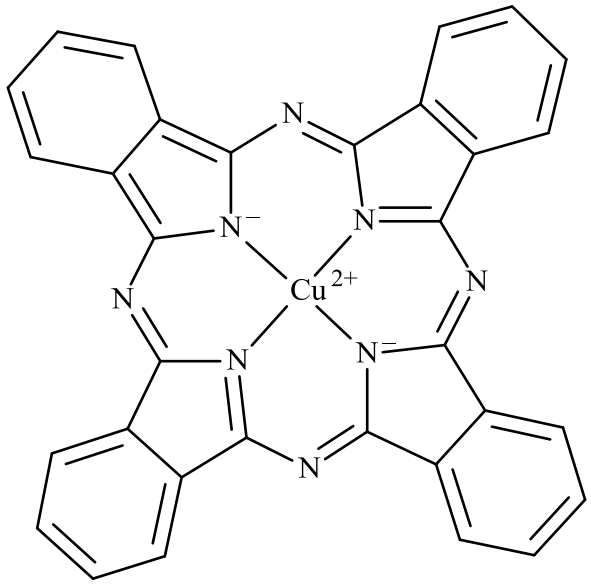
Title: Toxicologist
Organization: ToxServices LLC
Date: October 15, 2014
Assessor Type: Licensed GreenScreen® Profiler

Quality Control Performed By:
Name: Bingxuan Wang, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: October 16, 2014

Confirm application of the *de minimus* rule[3]: N/A

Chemical Structure(s):



Also called: Accosperse cyan blue GT; Aqualine blue; Bahama blue BC; Bermuda blue; Blue GLA; Blue phthalocyanine .alpha.-form; Blue pigment; Blue toner GTNF; BT 4651; Calcotone blue GP; Ceres blue BHR; Chromatex blue BN; Chromofine blue 4920; C.I. 74160; Congo blue B 4; Copper(II)

[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2

[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen® Verification Program)

[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

phthalocyanine; Copper phthalocyanin; Copper .beta.-phthalocyanine; Copper(2+) phthalocyanine; .alpha.-Copper phthalocyanine; .eta.-Copper phthalocyanine; Copper phthalocyanine blue Copper tetrabenzoporphyrazine; Cromofine blue 4950 Cromophtal blue 4G; Cupric phthalocyanine; Cyan blue BNC 55-3745; Cyanine blue BB and others; Cyan peacock blue G; Dainichi cyanine blue B; Daltolite fast blue B; Duratint blue 1001; EM blue NCB; Euvinyl blue 702; Fastogen blue 5007; Fastolux blue; Fastolux peacock blue; Fenalac blue B disp; Franconia blue A 4431; Graphtol blue BL; Helio blue B; Helio fast blue B; Heliogen blue and others; Hostaperm blue AFN; Irgalite blue BCA; Irgalite blue LGLD; Irgalite fast brilliant blue BL; Irgaplast blue RBP; Isol fast blue B; Copper, (29H,31H-phthalocyaninato(2-)-kappaN29,kappaN30,kappaN31,kappaN32)-, (SP-4-1)-; Copper, (29H,31H-phthalocyaninato(2-)-N29,N30,N31,N32)-, (SP-4-1)- (9CI); Tetrabenzo-5,10,15,20-diazaporphyrinephthalocyanine; Copper, (phthalocyaninato(2-))-; Copper, (29H,31H-phthalocyaninato(2-)-N29,N30,N31,N32)-; Copper phthalocyanine blue; Copper, (phthalocyaninato(2-))- (UNEP 2005; ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
A sufficient dataset was available for C.I. Pigment Blue 15; therefore, a surrogate was not used in this GreenScreen®.

Identify Applications/Functional Uses: (HSDB 2011)
1. Pigment
2. Chemical Intermediate

GreenScreen® Summary Rating for C. I. Pigment Blue 15[4]: C. I. Pigment Blue 15 was assigned a GreenScreen® Benchmark Score of 3 ("Use but Still Opportunity for Improvement") as it has Very High persistence (P). This corresponds to GreenScreen® benchmark classification 3a in CPA 2011, 2012a. Data gaps (DG) exist for endocrine activity (E), and single and repeated dose neurotoxicity (Ns and Nr*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), C. I. Pigment Blue 15 meets requirements for a GreenScreen® Benchmark Score of 3 despite the hazard data gaps. In a worst-case scenario, if C. I. Pigment Blue 15 were assigned a High score for the data gaps E, Nr*, or SnR*, it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for C.I. Pigment Blue 15

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	repeated*	single	repeated*										
L	**L**	**L**	**L**	DG	**L**	DG	**L**	DG	DG	*L*	DG	*L*	*L*	*L*	*L*	*vH*	**vL**	*L*	*L*

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e. vH, H, M, and L) instead of three (i.e. H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

[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.

Transformation Products and Ratings:

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[5]

No data were identified on the transformation products. The rate of hydrolysis for C.I. Pigment Blue 15 is negligible and it does not biodegrade (U.S. EPA 2009).

Introduction

C.I. Pigment Blue 15 is a pigment used in inks, paints, surface coatings, rubber, resins, linoleum, artist materials, leather cloth, paper, wallpaper, tinplate printing, wax compositions, cements, and textile printing. In addition to its use as a pigment, C.I. Pigment Blue 15 is used as a chemical intermediate in the synthesis of Direct Blue 86, Pigment Green 7, Pigment Green 36, Reactive Blue 7, and Vat Blue 29 (HSDB 2011).

ToxServices assessed C.I. Pigment Blue 15 against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.69 (GreenScreen® Hazard Assessment) (ToxServices 2013).

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b) and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for C. I. Pigment Blue 15 can be found in Appendix C and a summary of the results can be found below:

PBT

DSL: DSL Substances that are Persistent

PhysicoChemical Properties of C.I. Pigment Blue 15

C.I. Pigment Blue 15 is a non-volatile solid with a melting point of 600 ºC. It is not soluble in water. Its partition coefficient indicates that it may bioaccumulate.

Table 1: Physical and Chemical Properties of C.I. Pigment Blue 15 (CAS #147-14-8)

Property	Value	Reference
Molecular formula	C32-H16-Cu-N8	ChemIDplus 2014
SMILES Notation	c1ccc2=C3N=C4c5ccccc5C6=N4[Cu+2]78[N-]3C(=c2c1)N=C9N7=C(c1c9cccc1)N=C1[N-]8C(=N6)c2c1cccc2	ChemIDplus 2014
Molecular weight	578.0962	ChemIDplus 2014
Physical state	Solid	UNEP 2005
Appearance	Bright blue microcrystals with	UNEP 2005

[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.

Table 1: Physical and Chemical Properties of C.I. Pigment Blue 15 (CAS #147-14-8)		
Property	**Value**	**Reference**
	purple luster	
Melting point	600ºC	UNEP 2005
Vapor pressure	0.000295 mm Hg at 384ºC	UNEP 2005
Water solubility	Not Soluble	UNEP 2005
Dissociation constant	N/A	
Density/specific gravity	1.62	UNEP 2005
Partition coefficient	Log K_{ow} = 6.6 (Estimated)	ESIS 2000

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): *L*
C. I. Pigment Blue 15 was assigned a score of Low for carcinogenicity based on carcinogenicity studies in mice and its lack of bioavailability. Confidence in this endpoint was reduced due to the lack of study details. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - In an eight-month carcinogenicity study, mice were subcutaneously treated with 0.5 mg/animal C.I. Pigment Blue 15 (approximately equivalent to 15.77 mg/kg in male mice and 17.39 mg/kg in female mice[6]). It is unclear how frequently animals were dosed. Treatment produced no tumors.
- UNEP 2005
  - In an eight month carcinogenicity study, mice were orally exposed to C.I. Pigment Blue 15 for eight months. No tumors were found after the treatment period. No further details were provided.
- ECHA 2014
  - National Toxicology Program (NTP) decided not to conduct a long term carcinogenicity study based on the absence of toxic effects in 90-day studies in mice and rats. They also stated that based on the insolubility of C.I. Pigment Blue 15 and minimal changes in tissue copper residues following repeated exposure, C.I. Pigment Blue 15 is not bioavailable.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L
C. I. Pigment Blue 15 was assigned a score of Low for mutagenicity/genotoxicity based on negative findings in *in vitro* and *in vivo* mutagenicity tests. GreenScreen® criteria classify chemicals as a Low

[6] Average weight of male mouse: (0.0261 kg + 0.0373 kg)/2 = 0.0317 kg
Approximate dose = 0.5 mg / 0.0317 kg = 15.77 mg/kg
Average weight of female mouse: (0.0222 kg + 0.0353 kg)/2 = 0.02875 kg
Approximate dose = 0.5 mg / 0.02875 kg = 17.39 mg/kg
(Weight values for male and female mice, chronic studies, obtained from http://www.tera.org/Tools/ratmousevalues.pdf)

hazard for mutagenicity/genotoxicity when adequate data are available and negative for both chromosomal aberrations and gene mutations, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- UNEP 2005
  - C.I. Pigment Blue 15 was negative in an Ames reverse mutation assay in *S. typhimurium* tester strains TA97, TA98, TA100, and TA102, in the presence and absence of metabolic activation. The concentrations of C.I. Pigment Blue 15 were not reported.
  - C.I. Pigment Blue 15 was negative in an Ames reverse mutation assay in *S. typhimurium* tester strains TA1535 and TA1538 in the presence and absence of metabolic activation. The concentrations of C.I. Pigment Blue 15 were not reported.
  - C.I. Pigment Blue 15 was negative in an Ames reverse mutation assay in *S. typhimurium* tester strains TA98 and TA100 in the presence and absence of metabolic activation. The concentrations of C.I. Pigment Blue 15 were not reported.
  - C.I. Pigment Blue 15 was negative in an *in vitro* chromosomal aberration assay in Chinese lung hamster cells in the presence and absence of metabolic activation at concentrations between 750 and 3,000 µg/mL.
- ECHA 2014
  - C.I. Pigment Blue 15 was negative in an Ames reverse mutation assay in *S. typhimurium* tester strains TA98, TA100, TA1535, and TA1537 in the presence and absence of metabolic activation at concentrations between 20 and 5,000 µg/plate.
  - C.I. Pigment Blue 15 was negative in an Ames reverse mutation assay in *E. coli* strain WP_2 *uvr*A in the presence and absence of metabolic activation at concentrations between 20 and 5,000 µg/plate.
  - C.I. Pigment Blue 15 was negative in an *in vitro* chromosomal aberration assay in Chinese hamster lung cells in the presence and absence of metabolic activation at concentrations between 0.75 – 3 mg/mL.
  - C.I. Pigment Blue 15 was negative in an *in vivo* chromosome aberration assay in male and female Chinese hamsters (3/sex/dose). Animals received 1,250, 2,500, or 5,000 mg/kg C.I. Pigment Blue 15 via oral gavage once daily on two consecutive days. Bone marrow was harvested 24 hours after the second treatment.
  - C.I. Pigment Blue 15 was negative in an *in vivo* mouse spot test in female C57/Bl/6 mice. Animals received a single dose of 1,250, 2,500, or 5,000 mg/kg C.I. Pigment Blue 15 via intraperitoneal injection. Treatment was not mutagenic.

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

C. I. Pigment Blue 15 was assigned a score of Low for reproductive toxicity based on the findings of a combined reproductive/developmental toxicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ECHA 2014; UNEP 2005; JECDB Undated
  - In a combined reproductive/developmental toxicity study male and female Crj:CD (SD) rats (12/sex/dose) received 0, 40, 200, or 1,000 mg/kg/day C.I. Pigment Blue 15 via oral gavage.

The duration of testing was 42-days for male rats; 14-days before mating to day 3 of lactation for female rats. The only effects reported were blue discoloration of feces in groups receiving > 40 mg/kg, and blue-green or grayish-blue discoloration of contents of the stomach and intestines were noted in a few of the 200 mg/kg animals and in almost all animals in the 1,000 mg/kg dose group. Treatment had no adverse effects on the reproductive ability of males or females. There were no changes in the oestrous cycle, the occurrence of copulation and gestation, fertility, implantation, delivery and nursing indices, weight of the testes and epididymis, delivery, or maternal behavior. The authors found no histopathological changes of the reproductive organs. The reproductive NOAEL was 1,000 mg/kg/day (highest dose tested).

- U.S. EPA 2009
    - A NOAEL of 1,000 mg/kg/day was identified in a combined oral reproductive/developmental toxicity study in rats. No further details were provided.

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

C. I. Pigment Blue 15 was assigned a score of Low for developmental toxicity based on the findings of a combined reproductive/developmental toxicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* not on any authoritative lists
    - *Screening:* not on any screening lists
- ECHA 2014; UNEP 2005; JECDB Undated
    - In the previously described combined reproductive/developmental toxicity study, male and female Crj:CD (SD) rats (12/sex/dose) received 0, 40, 200, or 1,000 mg/kg/day C.I. Pigment Blue 15 via oral gavage. The duration of testing was 42-days for male rats; 14-days before mating to day 3 of lactation for female rats. Treatment had no effect on the rate of live/dead pups born. There were no changes in fetal clinical signs, body weight, or autopsy findings. The F1 NOAEL was 1,000 mg/kg/day (highest dose tested).
- U.S. EPA 2009
    - A NOAEL of 1,000 mg/kg/day was identified in a combined oral reproductive/developmental toxicity study in rats. No further details were provided.

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

C. I. Pigment Blue 15 was assigned a score of Data Gap for endocrine disruption based on a lack of data for this endpoint. Authoritative and Screening Lists

- *Authoritative:* not on any authoritative lists
- *Screening:* not on any screening lists

- 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.
- No data were identified.

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

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

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

C. I. Pigment Blue 15 was assigned a score of Low for acute toxicity based on oral and dermal LD_{50} values in rats and rabbits. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when the oral and dermal LD_{50} are greater than 2,000 mg/kg (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - Oral LD_{50} = > 6,400 mg/kg (rats)
  - Oral LD_{50} = > 10,000 mg/kg (rats)
  - Oral LD_{50} = > 15,000 mg/kg (rats)
  - Oral LD_{50} = > 10,000 mg/kg (rats)
  - Oral LD_{50} = > 16,000 mg/kg (rabbits)
- ECHA 2014
  - Dermal LD_{50} = > 5,000 mg/kg (rats)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

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

C. I. Pigment Blue 15 was assigned a score of Data Gap for systemic toxicity (single dose) based on a lack of data for this endpoint.

Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- No data were identified.

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

C. I. Pigment Blue 15 was assigned a score of Low for systemic toxicity (repeated dose) based on 90-day oral NOAEL values greater than 200 mg/kg/day in mice and rats. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when oral NOAEL values are greater than 200 mg/kg/day (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ECHA 2014; UNEP 2005; JECDB Undated
  - In a 28-day study in Wistar rats (10/group/sex), rats were given the test compound at doses of 0, 40, 200, or 1,000 mg/kg/day via oral gavage. A slight but statistically significant drop in red blood cell count (RBC), hemoglobin (Hb), and packed cell volume (PCV) was found in the 200 mg/kg and 1,000 mg/kg male groups. After a recovery period of 14 days, a slight but statistically significant increase in erythroblasts was found in the 1,000 mg/kg/day females. At 1,000 mg/kg/day, increased weights of lung, spleen adrenals and salivary glands were also observed. No histopathological changes were reported. A NOAEL of 200

mg/kg/day and a LOAEL of 1,000 mg/kg/day was established based on the effect on the differentiation of red blood cells. *As the guideline values are tripled from 90-day studies to 28-day studies (i.e. to 30 and 300 mg/kg/day), there is insufficient data to determine if adverse effects would occur at 300 mg/kg/day.*

- ECHA 2014
  - In an oral 13-week study, male and female Fischer 344 rats (10/sex/dose) received 0.3, 0.6, 1.25, 2.5, or 5.0% C.I. Pigment Blue 15 in their diet. No mortality was reported. Treatment did not significantly alter food consumption or weight gain. No adverse clinical signs were reported. No clinical chemistry, hematology, or urinalysis was performed and organs were not weighed. No treatment related macroscopic or microscopic changes were reported. The authors reported a high incidence of pulmonary lesions in both controls and the high-dose treated animals. They associated the pulmonary lesions with a Sendai virus infection. The authors identified a NOAEL of 5% (4,500 mg/kg/day) C.I. Pigment Blue 15 based on the absence of treatment-related effects.
  - In an oral 13-week study, male and female B6C3F1 mice (10/sex/dose) received 0.3, 0.6, 1.25, 2.5, or 5.0% C.I. Pigment Blue 15 in their diet. Four male mice from different treatment groups died during weeks 3, 7, and 10, while 3 control female mice died during week 3. Treatment did not significantly alter food consumption or weight gain. No adverse clinical signs were reported. No clinical chemistry, hematology, or urinalysis was performed and organs were not weighed. No treatment related macroscopic or microscopic changes were reported. The authors identified a NOAEL of 5% (16,000 mg/kg/day in males and 18,700 mg/kg/day in females) C.I. Pigment Blue 15 based on the absence of treatment-related effects.
- UNEP 2005
  - In an oral 13-week feeding study, mice (strain not reported) received 5,000 mg/kg/day C.I. Pigment Blue 15. No toxic effects or pathological changes were reported. ToxServices identified a NOAEL of 5,000 mg/kg/day (only dose tested).
  - In an oral 13-week feeding study, rats and mice (stain/sex not reported) received 0.3 – 5% C.I. Pigment Blue 15 (equivalent to 288 – 4,800 mg/kg/day in male and female rats and 591 – 9,850 mg/kg/day in male and female mice[7]).
- U.S. EPA 2009
  - C.I. Pigment Blue 15 is not a repeat-dose toxicant. A NOAEL of 250 mg/kg/day (highest dose tested) was identified in 90 day dietary studies in mice and rats. No toxic effects were reported. No further details were provided.
- Based on the weight of evidence, a score of Low was assigned. A 28-day oral study in rats identified a NOAEL of 200 mg/kg/day and a LOAEL of 1,000 mg/kg/day based on the differentiation of red blood cells in rats. While, oral NOAEL values greater than 200 mg/kg/day were identified in mice and in rats in 90-day oral studies. No significant toxic effects were reported. Based on NOAEL values greater than 200 mg/kg/day and the absence of significant toxic effects in 90-day oral studies in rats and mice, a score of Low was assigned.

Neurotoxicity (N)
***Group II Score (single dose)* (vH, H, M, or L):** DG
C. I. Pigment Blue 15 was assigned a score of Data Gap for neurotoxicity (single dose) based on a lack of data for this endpoint.

[7]5% = 50,000 mg/kg food * 0.096 kg food/kg bw/day = 4,800 mg/kg/day for male and female rats
5% = 50,000 mg/kg food * 0.197 kg food/kg bw/day = 9,850 mg/kg/day for male and female mice
(food factor values for male and female Wistar rats, subchronic study, obtained from http://www.tera.org/Tools/ratmousevalues.pdf)

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- No data were identified.

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

C. I. Pigment Blue 15 was assigned a score of Data Gap for neurotoxicity (repeated dose) based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- No data were identified.

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

C. I. Pigment Blue 15 was assigned a score of Low for skin sensitization based on negative skin irritation studies. Confidence in this endpoint was reduced due to the lack of study details. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - A mixture of several paint compounds which contained C.I. Pigment Blue 15 was not sensitizing in a modified Draize repeated insult patch test in humans. No further details were provided.
- HSDB 2011
  - C.I. Pigment Blue 15 was not sensitizing in rabbits. No further details were provided.
- U.S. EPA 2009
  - C.I. Pigment Blue 15 is not sensitizing in rats. No further details were provided.
- Sigma-Aldrich 2014
  - C.I. Pigment Blue 15 was not sensitizing in a guinea pig maximization test (OECD 406). No further details were provided.
- ECHA 2014
  - *The test material used in this study was CT-BX 121. The REACH Dossier indicated that it is the same as C.I. Pigment Blue 15, however CT-BX 121 is not listed as a synonym on ChemIDPlus (2014) or the SIDS Dossier (OECD 2005).* CT-BX 121 was not sensitizing in a GLP-compliant mouse local lymph node assay conducted according to OECD Guideline 429. Mice were treated with 5, 10, or 25% CT-BX 121 on the dorsal surface of each ear for 3 consecutive days. A stimulation index less than 3 was reported for all concentrations.
  - *The test material used in this study was KET BLUE Ex-8. The REACH Dossier indicated that it is the same as C.I. Pigment Blue 15, however KET BLUE Ex-8is not listed as a synonym on ChemIDPlus (2014) or the SIDS Dossier (OECD 2005).* KET BLUE Ex-8 was not sensitizing in a GLP-compliant guinea pig maximization test conducted according to OECD Guideline 406. Mice were intradermally induced with a 7.5% (w/v) KET BLUE Ex and challenged with 25% and 50% (w/v) KET BLUE Ex. No positive skin reactions were reported.

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG
C. I. Pigment Blue 15 was assigned a score of Data Gap for respiratory sensitization based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- No data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): *L*
C. I. Pigment Blue 15 was assigned a score of Low for skin irritation/corrosivity based on negative findings in dermal irritation studies. Confidence in this endpoint was reduced due to the lack of study details. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - C.I. Pigment Blue 15 did not cause irritation in two dermal irritation studies in rabbits. No further details were provided.
- UNEP 2005
  - C.I. Pigment Blue 15 did not cause irritation in a dermal irritation study. No further details were provided.
- HSDB 2011
  - C.I. Pigment Blue 15 did not cause dermal irritation in rabbits. No further details were provided.
- U.S. EPA 2009
  - C.I. Pigment Blue 15 is not a dermal irritant in rabbits. No further details were provided.
- Sigma-Aldrich 2014
  - Dermal exposure to C.I. Pigment Blue 15 for 4 hours did not cause irritation in a dermal irritation study in rabbits (OECD 404). No further details were provided.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): *L*
C. I. Pigment Blue 15 was assigned a score of Low for eye irritation/corrosivity based on negative findings in eye irritation studies. Confidence in this endpoint was reduced due to the lack of study details. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when adequate data are available and negative, there are no structural alerts, and they are not GHS classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - C.I. Pigment Blue 15 did not cause irritation in an ocular irritation study in rabbits. No further details were provided.
  - C.I. Pigment Blue 15 did not cause irritation in two ocular irritation studies. No further details were provided.
- HSDB 2011
  - C.I. Pigment Blue 15 did not cause ocular irritation in rabbits. No further details were

provided.
- U.S. EPA 2009
    - C.I. Pigment Blue 15 is not an ocular irritant in rabbits. No further details were provided.
- Sigma-Aldrich 2014
    - Ocular exposure to C.I. Pigment Blue 15 for 24 hours did not cause irritation in an ocular irritation study in rabbits (OECD 405). No further details were provided.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): *L*
C. I. Pigment Blue 15 was assigned a score of Low for acute aquatic toxicity based on measured data. Confidence in this endpoint was reduced due to the use of data from an SDS. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute toxicity values are greater than 100 mg/L (CPA 2012a).
- Authoritative and Screening Lists
    - *Authoritative:* not on any authoritative lists
    - *Screening:* not on any screening lists
- UNEP 2005
    - 48h LC_{50} = > 100 mg/L (*Oryzias latipes,* fish)
- Sigma-Aldrich 2014
    - 96h LC_{50} = > 100 mg/L (*Danio rerio,* fish)
    - 96h LC_{50} = > 100 mg/L (*Cyprinus carpio,* fish)
    - 48h EC_{50} = > 500 mg/L (*Daphnia magna,* daphnia)
    - 72h EC_{50} = > 100 mg/L (*Desmodesmus subspicatus,* algae)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *L*
C. I. Pigment Blue 15 was assigned a score of Low based on being insoluble in water and not bioavailable in mammalian repeated dose toxicity studies. Confidence level was reduced due to lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when ChVs are greater than 10 mg/L or there are no effects at saturation (CPA 2012a).
- Authoritative and Screening Lists
    - *Authoritative:* not on any authoritative lists
    - *Screening:* not on any screening lists
- ECHA 2014
    - National Toxicology Program (NTP) decided not to conduct a long term carcinogenicity study based on the absence of toxic effects in 90-day studies in mice and rats. They also stated that based on the insolubility of C.I. Pigment Blue 15 and minimal changes in tissue copper residues following repeated exposure, C.I. Pigment Blue 15 is not bioavailable.
    - Water solubility of C.I. Pigment 15 is measured to be 4.9 µg/L using the Analytical Expert Meeting of ETAD 2005 guideline.
- Based on the weight of evidence, a score of Low was assigned. Although copper is very toxic to the aquatic environment, data indicate that it is not bioavailable from the matrix of C.I. Pigment Blue 15. Copper has a Predicted No Effect Concentration (PNEC) 1.92 µg/L in the aquatic/marine environment (NIVA 2007), while only 0.54 µg/L copper can be released from C.I. Pigment Blue in the soluble fraction[8], assuming that copper is bioavailable from the compound. Therefore, even if

[8] The solubility of C.I. Pigment Blue 15 is 4.9 µg/L. The amount of copper in 4.9 µg C.I. Pigment Blue 15 = 4.9 µg x MW(Cu)/MW(C.I. Pigment Blue) = 4.9 µg x 64/578 = 0.54 µg.

copper can be released from C.I. Pigment Blue 15 in the water, the level would be too low to be toxic to aquatic/marine life.

Environmental Fate (Fate)

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

C. I. Pigment Blue 15 was assigned a score of Very High for persistence based on classification on Environment Canada's DSL. GreenScreen® criteria classify chemicals as a Very High hazard for persistence when classified as Persistent on the DSL (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* DSL: DSL substances that are Persistent
- ESIS 2000
  - C.I. Pigment Blue 15 was not biodegradable in a modified MITI test with < 1% degraded after 28 days.
  - C.I. Pigment Blue 15 was not biodegradable in a MITI test with 0% degraded after 14 days.
- Based on the weight of evidence, a score of Very High was assigned. As indicated by the studies above, C.I. Pigment Blue 15 is not readily biodegradable and modeling is not appropriate due to the presence of copper in C.I. Pigment Blue 15. It is classified as Persistent on Environment Canada's DSL, with corresponds to a score of High – Very High. ToxServices considered C.I. Pigment Blue 15 to be persistent and assigned conservatively assigned a Very High score. Confidence in this endpoint was reduced because it is based on a screening list and no data on the half-life of C.I. Pigment Blue 15 was available.

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

C. I. Pigment Blue 15 was assigned a score of Very Low for bioaccumulation based on measured BCF values. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the BCF is less than 100 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ESIS 2000
  - A BCF of < 0.33 – 11 was measured in a bioaccumulation study (OECD 305C) where *Cyprinus carpio* were exposed to 0.6 mg/L C.I. Pigment Blue 15 for 42 days at 25ºC.
  - A BCF of < 3.6 was measured in a bioaccumulation study (OECD 305C) where *Cyprinus carpio* were exposed to 0.06 mg/L C.I. Pigment Blue 15 for 42 days at 25ºC.
  - A BCF of < 0.33 - 11 was measured in a bioaccumulation study (OECD 305C) where *Oryzias latipes* were exposed to 0.6 mg/L C.I. Pigment Blue 15 for 42 days at 25ºC.
  - A BCF of < 3.6 was measured in a bioaccumulation study (OECD 305C) where *Oryzias latipes* were exposed to 0.06 mg/L C.I. Pigment Blue 15 for 42 days at 25ºC.
  - Log K_{ow} = 6.6 (estimated). Although the estimated partition coefficient indicates that C.I. Pigment Blue 15 may bioaccumulate, the authors noted that it will not due to its very low water solubility.

Physical Hazards (Physical)

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

C. I. Pigment Blue 15 was assigned a score of Low for reactivity based on its HMIS reactivity rating. Confidence in this endpoint was reduced due to a lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are not explosive or self-reactive (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- ECHA 2014
  - Not explosive
- Sigma-Aldrich 2014
  - C.I. Pigment Blue 15 has an HMIS physical hazard rating of 0. An HMIS physical hazard rating of 0 corresponds to "Materials that are normally stable, even under fire conditions, and will NOT react with water, polymerize, decompose, condense, or self-react. Non-Explosives" (Paint.org 204).

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

C. I. Pigment Blue 15 was assigned a score of Low for flammability based on its NFPA and HMIS flammability ratings. Confidence in this endpoint was reduced due to the lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for flammability when they are not flammable solids (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not on any authoritative lists
  - *Screening:* not on any screening lists
- HSDB 2011
  - C.I. Pigment Blue 15 has an NFPA flammability rating of 0. An NFPA flammability rating of 0 corresponds to "Materials that will not burn under typical fire conditions, including intrinsically noncombustible materials such as concrete, stone, and sand".
- Sigma-Aldrich 2014
  - C.I. Pigment Blue 15 has an HMIS flammability rating of 0. An HMIS flammability rating of 0 corresponds to "Materials that will not burn" (Paint.org 204).

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(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: Results of Automated GreenScreen® Score Calculation for C.I. Pigment Blue (CAS #147-14-8)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	C.I. Pigment Blue 15	147-14-8	*L*	L	L	L	DG	L	DG	L	DG	DG	*L*	DG	*L*	*L*	*L*	*L*	*vH*	vL	*L*	*L*

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	No	No	No
3	Yes	No	No	No			
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
C.I. Pigment Blue 15	3

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
C.I. Pigment Blue 15	3

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2												
3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		3
4												

APPENDIX C: Pharos Output for C.I. Pigment Blue (CAS #147-14-8)

C.I. PIGMENT BLUE 15

CAS RN: 147-14-8

Synonyms: Accosperse cyan blue GT; copper phthalocyanine

Detailed Direct Hazard Listings — Quickscreen

PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified (LT-U)
EXEMPT	German FEA - Substances Hazardous to Waters (VwVwS) Non-Hazardous to Water (Water Hazard Class 0 NWG) - Not included in GreenScreen

Sources to Check for GreenScreen® Hazard Assessment

Note: For a GreenScreen® Hazard Assessment, data queries should be initially limited to the following references. If data gaps exist after these references have been checked, additional references may be utilized.

U.S. EPA High Production Volume Information System (HPVIS):
http://www.epa.gov/hpvis/index.html

UNEP OECD Screening Information Datasets (SIDS):
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

OECD Existing Chemicals Database: http://webnet.oecd.org/hpv/ui/SponsoredChemicals.aspx

European Chemical Substances Information System IUCLID Chemical Data Sheets:
http://esis.jrc.ec.europa.eu/index.php?PGM=dat

National Toxicology Program: http://ntp.niehs.nih.gov/

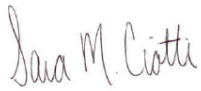
International Agency for the Research on Cancer:
http://monographs.iarc.fr/ENG/Classification/index.php

Human and Environmental Risk Assessment (HERA) on ingredients of household cleaning products:
http://www.heraproject.com/RiskAssessment.cfm

European Chemicals Agency (ECHA) REACH Dossiers: http://echa.europa.eu/

Licensed GreenScreen® Profilers

C. I. Pigment Blue 15 GreenScreen® Evaluation Prepared by:



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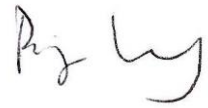

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