Sodium and Potassium Dimethyldithiocarbamate Salts
Preliminary Work Plan

Registration Review: Initial Docket
Case Number 8100

September 2013

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ABBREVIATIONS AND SYMBOLS

AD	Antimicrobials Division
A.I. or a.i.	active ingredient
aPAD	acute population adjusted dose
ASRI	activated sludge respiration inhibition
atm-m^3/mole	atmospheric pressure-cubic meter per mole
BCF	bioconcentration factor
°C	degrees Celsius
$CaSO_4$	calcium sulfate
$CaSO_3$	calcium sulfite
CAS	Chemical Abstracts Service
CCA	chromated copper arsenate
CFR	Code of Federal Regulations
CHO	Chinese hamster ovary
CMA	Chemical Manufacturers Association
CO_2	carbon dioxide
COC	concentration-of-concern
cPAD	chronic population adjusted dose
CS_2	carbon disulfide
DCI	data call-in
DEA	diethanol amine
DMA	dimethylamine
DDC	dimethyldithiocarbamate
EC_{50}	median (or 50 percent) effect concentration
EC_{05}	5 percent effect concentration
ECOTOX	ECOTOXicology
EDI	estimated daily intake
EDSP	Endocrine Disruptor Screening Program
E-FAST	Exposure and Fate Assessment Screening Tool
EPI Suite	Estimation Program Interface Suite
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FGD	flue-gas desulfurization
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FWP	Final Work Plan
g/mol	grams per mole
GLN	guideline number
HPV	high production volume
IDS	Incident Data System
KDDC	potassium dimethyldithiocarbamate
Koc	organic carbon normalized soil-water partition coefficient
Kd	soil-water partition coefficient
Kow	octanol-water partition coefficient
LC_{50}	median (or 50 percent) lethal concentration
LD_{50}	median (or 50 percent) lethal dose
LOAEC	lowest-observed-adverse-effect-concentration
LOEC	lowest-observed-effect-concentration
LOAEL	lowest-observed-adverse-effect-level

Log K_{ow}	logarithm of the octanol-water partition coefficient
µg	microgram
ml/g	milliliter per gram
mg/kg	milligram per kilogram
mg/kg/day	milligram per kilogram per day
mg/L	milligram per liter
mm Hg	millimeter of mercury
MOE	margin of exposure
MRID	Master Record Identification Number
MRL	maximum residue limit
N/A	not applicable
NaDDC	sodium dimethyldithiocarbamate salt
nm	nanometers
NOAEC	no-observed-adverse-effect-concentration
NOAEL	no-observed-adverse-effect-level
OCSPP	Office of Chemical Safety and Pollution Prevention
OECD	Organization for Economic Co-operation and Development
OPP	Office of Pesticide Programs
PAD	population adjusted dose
PAI	pure active ingredient
PDM	Probabilistic Dilution Model
%	percent
PC Code	Pesticide Chemical Code
PCF	pounds per cubic foot
pH	power of hydrogen or power of the concentration of the hydrogen ion
PHED	Pesticide Handler's Exposure Data
PIS	primary irritation score
pKa	power of the acid dissociation constant or negative base-10 logarithm of the acid dissociation constant of a solution
ppb	parts per billion
ppm	parts per million
PWP	Preliminary Work Plan
QSAR	quantitative structure-activity relationship
RED	Reregistration Eligibility Decision
SAR	structure activity relationship
SF	safety factor
SSTS	Section Seven Tracking System
SO2	sulfur dioxide
TEP	typical end-use product
TGAI	technical grade active ingredient
TMDL	total maximum daily loads
TMTDS	tetramethylthiuram disulfide (Thiram)
TMTMS	tetramethyl thiomonosulfide
TMTU	tetramethyl thiourea
UF	uncertainty factor
UV/VIS	ultraviolet/visible light absorption
% w/w	percent weight per weight.
WP	wettable powder
WWTPs	wastewater treatment plants

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1 Introduction

This document is the United States Environmental Protection Agency's (USEPA, EPA or "the Agency") Preliminary Work Plan (PWP) for Sodium and Potassium Dimethyldithiocarbamate Salts, herein referred to as dimethyldithiocarbamate or DDC salts. The PWP document explains what EPA's Office of Pesticide Programs (OPP) knows about dimethyldithiocarbamate, highlighting anticipated data and assessment needs, identifying the types of information that would be especially useful to the Agency in conducting the review, and providing an anticipated timeline for the dimethyldithiocarbamate review. This PWP document does not include disodium ethylene bis dithiocarbamate (Nabam which is also a dimethyldithiocarbamate). Nabam was included in its own Registration Eligibility Decision (RED) rather than the 2009 Dimethyldithiocarbamate RED Amendment and is being addressed in a separate Registration Review case (docket number EPA-HQ-OPP-2012-0339). Additionally, Nabam produces ethylene thio urea (ETU) as a degradate whereas DDC salts do not.

The registration review process was designed to include a public participation component to solicit input from interested stakeholders. The Agency intends, by sharing this information in the docket, to inform the public of what it knows about dimethyldithiocarbamate and what types of new data or other information would be helpful for the Agency to receive as it moves toward a decision on dimethyldithiocarbamate. The Agency encourages all interested stakeholders to review the PWP and to provide comments and additional information that will help the Agency's decision-making process for this chemical.

1.1 Statutory and Regulatory Authority

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides distributed or sold in the United States generally must be registered by the USEPA based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at http://www.epa.gov/oppsrrd1/registration_review/.

The Agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The regulations governing registration review begin at 40 CFR 155.40. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial

comment period, the Agency will develop and commit to a Final Work Plan (FWP) and anticipated schedule for the Sodium and Potassium Dimethyldithiocarbamate Salts Case.

Documents associated with this registration review can be viewed at http://www.regulations.gov in docket EPA-HQ-OPP-2013-0245. Below is a summary of the issues relevant to this registration review case.

Table 1 – Summary of Anticipated Risk Assessments and Data Needs: Dimethyldithiocarbamate

Risk Assessment	Assessment Necessary to Support Registration Review	Date of Most Recent Assessment	Type of Assessment Required (New/Updated)	Data Anticipated as Needed (See Table 6 for details)
Dietary (food)	Yes	7/14/2009	Updated	Migration Studies[1]
Dietary (drinking water)	Yes	7/8/2009	Updated	None
Occupational and Residential Handler	Yes	3/3/2009	Updated	Inhalation Toxicity – 90 Day Reproduction and Fertility Effects Chronic Toxicity/Carcinogenicity[3, 4] Dermal Exposure Inhalation Exposure Product Use Information
Residental Post Application - Incidental Oral and Dermal	Yes	3/3/2009	Updated	Surface Residue Data[3]
Aggregate	Yes	N/A	New	Reproduction and Fertility Effects Chronic Toxicity/Carcinogenicity[3,4]
Cumulative	No (see 3.4.2)	N/A	None	None
Tolerance Review (EPA)	No (see 1.5.2)	7/14/2009	N/A	None
Ecological Effects and Environmental Fate	Yes	2009	New[2] Updated for wood preservative	Fish (chronic); Aquatic invertebrates (chronic); Aquatic and semi-aquatic plants; Beneficial Insect Studies[3] Aerobic soil metabolism[3] Leaching from treated wood[3] Activated Sludge Respiration Inhibition or Modified Activated Sludge Respiration Inhibition Ready biodegradability test or one of three biodegradation in activated sludge simulation tests

[1] Residue chemistry data are anticipated to be needed to determine dietary exposure to DDC as a result of food contact with components of food packaging such as coatings, adhesives, paper-making additives, and paper made from treated pulp
[2] Commercial/Industrial Cooling Water, Pulp/Paper Mill Water Systems, Gas/Oil operations
[3] EPA has received a request to cancel the only product with a wood preservative use. When the cancellation order becomes effective, this anticipated data requirement should no longer be needed
[4] EPA has received a request to cancel the only product with a metal working fluid use. When the cancellation order becomes effective, this anticipated data requirement should no longer be needed

Table 2 – Anticipated Registration Review Schedule

Anticipated Activity	Target Date*	Completion Date
Phase 1: Opening the Docket		
Open Docket and 60-Day Comment Period for Preliminary Work Plan	2013-09	2013-09-18
Close Public Comment Period	2013-11	
Phase 2: Case Development		
Issue Final Work Plan	2014-03	
Issue Data Call-In (DCI)	2016-03	
Receive Data to be Considered in Risk Assessment	2019-03	
Open 30-Day Public Comment Period for Preliminary Risk Assessment(s)	2020-09	
Close Public Comment Period	2020-10	
Phase 3: Registration Review Decision and Implementation		
Open 60-Day Public Comment Period for Proposed Decision	2021-03	
Close Public Comment Period	2021-05	
Issue Final Decision	2021-09	
Begin Post-Decision Followup	2021	
Total (years)	8	

*The anticipated schedule will be revised as necessary (*e.g.*, need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

1.2 Case Overview

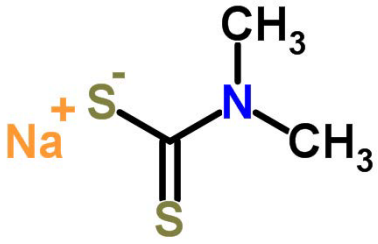
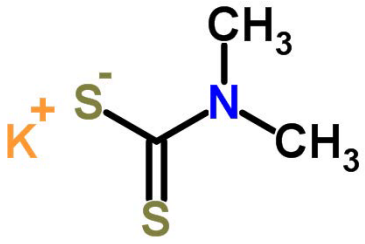
The docket for the Sodium and Potassium Dimethyldithiocarbamate Salts Case (Case 8100) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2013-0245.

1.3 Chemical Identification and Properties

Table 3 presents the active ingredients to be assessed in Case 8100: Sodium Dimethyldithiocarbamate Salt (NaDDC, PC Code 034804); and Potassium Dimethyldithiocarbamate Salt (KDDC, PC Code 034803). These chemicals are herein referred to as dimethyldithiocarbamate or DDC salts.

Table 3 – Chemical Identification of Dimethyldithiocarbamate Sodium and Potassium Salts

Chemical Name	Sodium dimethyldithiocarbamate	Potassium dimethyldithiocarbamate
Abbreviation	NaDDC	KDDC
Classification	Dithiocarbamate	Dithiocarbamate
PC Code	034804	034803
CAS No.	128-04-1	128-03-0
Molecular Formula	$C_3H_6NNaS_2$	$C_3H_6NKS_2$
Molecular Weight	143.21 grams per mole	159.31 grams per mole
Purity	40 percent (%) weight per weight[A] (w/w) as aqueous solution	50% w/w as aqueous solution

Chemical Name	Sodium dimethyldithiocarbamate	Potassium dimethyldithiocarbamate
Molecular Structure		

[A] % w/w is the number of grams of solute per 100 grams of solutions.

NaDDC and KDDC salts product chemistry information (source: MRIDs 41586303, 41609403, 41651301, 42510401, and 41609407 and EPI Suite v4.1) relevant to risk assessment is summarized in Table 4 and details of the environmental fate properties are discussed in Appendix B and product chemistry information in Appendix D.

Table 4 – Physical-Chemical and Fate Properties for Dimethyldithiocarbamate Salts

Guideline No.	Physical and Chemical Properties	NaDDC	KDDC
830.7000	pH	As measured 13.3 at 20 degrees Celsius (°C) 10.1 (1% aqueous solution) - HPV 12.6 (32% aqueous solution) - HPV	9-14 (50% solution)
830.7050	Ultraviolet (UV)/Visible Absorption	NaDDC was identified by UV/VIS spectra recorded at different pH values. Result at pH < 2: > 200 nanometers (nm), ε = 0 l mol^{-1} cm^{-1} Result at pH 7: 254 nm, ε = 12792 l mol^{-1} cm^{-1} 279 nm, ε = 13127 l mol^{-1} cm^{-1} 295 nm, ε = 1863 l mol^{-1} cm^{-1} Result at pH > 11: 254 nm, ε = 13388 l mol^{-1} cm^{-1} 279 nm, ε = 13687 l mol^{-1} cm^{-1} 295 nm, ε = 1803 l mol^{-1} cm^{-1}	KDDC was identified by UV/VIS spectra recorded at different pH values. Result at pH < 2: 207 nm, ε = 12713 l mol^{-1} cm^{-1} Result at pH 7: 253 nm, ε = 26409 l mol^{-1} cm^{-1} 279 nm, ε = 28187 l mol^{-1} cm^{-1} 495 nm, ε = 3562 l mol^{-1} cm^{-1} Result at pH > 11: 254 nm, ε = 12714 l mol^{-1} cm^{-1} 279 nm, ε = 13120 l mol^{-1} cm^{-1}
830.7200	Melting point	PAI: > 300 °C with decomposition.	PAI: > 300 °C with decomposition.
830.7220	Boiling point	Not required since PAI is solid Boiling point of 32% solution: 102°C	Not required since PAI is solid. Boiling point of 50% solution: >100°C
830.7300	Density	1.17 g/ml (40% solution)	1.25 g/ml (50% solution)

Guideline No.	Physical and Chemical Properties	NaDDC	KDDC
830.7370	Dissociation Constant in water	pKa = 5.4 for the organic portion/ Estimated/(40% w/w aqueous solution). 6.5 x 10^{-8} at 20°C. Performed on PAI. pKa value: Not applicable; product decomposes below pH 8. – HPV	pKa = 5.4 for the organic portion/ Estimated/(40% w/w aqueous solution). 6.5 x 10^{-8} at 20°C. Performed on PAI.
830.7550	Partition coefficient (*n*-octanol/water)	Performed on PAI. Estimated to be less than 1 based on solubility at 20°C. −2.41 (EPI Suite v4.1)	−1.43 (EPI Suite v4.1)
830.7840	Solubility in water	Complete 132 g/100 ml of water at 20 °C Performed on PAI.	Complete. Easily soluble in water.
830.7950	Vapor pressure	Solid: 4.17 x 10^{-9} mm Hg at 25°C (EPI Suite v4.1).	Solid: 8.15 x 10^{-10} mm Hg at 25°C (EPI Suite v4.1).
N/A	Henry's Law Constant	7.857 x 10^{-16} atm-m^3/mole (EPI Suite v4.1)	2.01 x 10^{-16} atm-m^3/mole (EPI Suite v4.1).

PAI - Pure active ingredient
HPV – High production volume

1.4 Use/Usage Description

1.4.1 Registrations

There are 18 registered KDDC products and 13 registered NaDDC products. There are no inert uses and no pending registrations.

1.4.2 Summary of Registered Uses

Table 5 presents a summary of the registered uses of DDC salts that will be assessed in this registration review. Per label directions, products that contain only DDC salts can be open poured or metered into the system being treated or the product being preserved. Some products also contain the active ingredient Nabam and these products require closed system loading for certain uses such as industrial cooling towers, oil drilling fluids, paper mills, beet sugar mill and cane sugar mills. These requirements are based on label specifications in the Nabam RED[1].

Several product labels have been amended since the 2009 RED Amendment to voluntarily delete uses. Deleted uses include sapstain treatment, paints and coatings, metalworking fluids, cotton fabrics, wood veneers and alginate pastes. There are still some labels that include some of these uses, and the labels are noted in Table 5.

[1] PC Code 014503, http://www.epa.gov/oppsrrd1/REDs/0641.pdf

Table 5 – Summary of the Registered Uses of Dimethyldithiocarbamate

Use Site	Application Rate in Terms of Active Ingredient (A.I.)	Labels (EPA Registration no.)
Industrial Processes and Water Systems		
Air Washer Water Systems	6 to 29 ppm	Several labels.
Beet and Cane Sugar Mills	3 ppm	Several labels.
Beet Sugar Mills	12 ppm	One label (45728-29)
Coal Slurry Systems	75 ppm	One label (34688-76)
Commercial/Industrial Cooling Water Systems	6 to 59 ppm	Several labels.
Evaporative Condenser Water Systems	6 to 59 ppm	Several labels.
Food Processing Water Systems	3 to 12 ppm	Several labels.
Oil Recovery Drilling Muds and Packer Fluids	77 to 1214 ppm	Several labels.
Oil Recovery Injection Water, Secondary	4 to 394 ppm	Several labels.
Pulp and Paper Mill Water Systems	113 to 250 ppm	Several labels[1]
Reverse Osmosis Water Systems	10 to 51 ppm	Several labels.
Sewage Systems	5 to 14 ppm	Two labels (1448-70, 34688-77)
Material Preservative		
Adhesives, Coatings, Emulsions	1000 ppm	One label (1022-563)[2]
Fuels and Oils Bottom Water	58 ppm	One label (1022-563)[2]
Metal Working Fluids	1000 ppm	One label (1022-563)[2]
Paints and varnish (applied film)	1000 ppm	One label (1022-563)[2]
Papermaking Additives (Alum solutions, pigment slurries, coating formulations etc.)	200 ppm	Two labels (1022-563[1,2], 1448-70)
Wood Preservative		
Wood, Pressure Treatment	1 pound per cubic foot	One Label (1022-577)[2]

[1] Includes indirect food uses.
[2]EPA has received a product cancellation request for 1022-563, 1022-577, and 1022-574. A cancellation order is anticipated to be issued in late 2013.

1.4.3 **Usage Information**

According to the Specialty Biocides North America Report 2004-2005 (Kline, 2006) the dithiocarbamates, which include Nabam (disodium ethylene bis dithiocarbamate), and dimethyldithiocarbamate**,** are used primarily for paper production and industrial cooling water treatments, and to a lesser extent, for leather production. The report does not distinguish the use patterns for Nabam and dimethyldithiocarbamate. With respect to wood preservation, the report indicates that dimethyldithiocarbamate is not used.

Production volume data in the EPA Section Seven Tracking System (SSTS) for the years 2004 through 2008 indicate that no more than 2,000,000 kilograms of dimethyldithiocarbamate are sold per year in the United States[2].

1.5 Regulatory History

The Dimethyldithiocarbamate Salts were previously included in RED Case 2180, with PC Codes 034801, 034803, 034804, 034805, and 034806. KDDC (034803) and NaDDC (034804) have been split from Case 2180 and moved into Case 8100 for registration review; case 8100 consists

[2] As per EPA's Section Seven Tracking System, data pulled on 3/12/13.

of only these two chemicals. The Agency completed an Amended RED for DDC salts in 2009. Ziram (034805) and Ferbam (034801) each had individual REDs in 2003 and 2005, respectively; registration review dockets for these conventional chemicals are scheduled to open in FY 2015. Zinc dimethyldithiocarbamate (034806) was canceled in 1992.

The first product containing NaDDC was registered in 1949, and the first product containing KDDC was registered in 1980.

NaDDC and KDDC are registered for use as material preservatives for fuels, metalworking fluids, paints, coatings, adhesives, cloth, and paper/paperboard; they are also registered for use as antifoulants/slimicides in a variety of liquids including industrial/commercial cooling water, air washer water, sugar mill pulp/process water, marine heat exchangers, gas/oil recovery fluid, industrial wastewater treatment systems, industrial water purification systems, reverse osmosis water systems, and pasteurizer cooling water. Their main uses reportedly are as antifoulants in industrial cooling and air washer water systems, as well as pulp and paper mills and gas/oil drilling muds.

1.5.1 **Recent/Pending Regulatory Actions**

Several uses of dimethyldithiocarbamate are pending termination/cancellation as of the publication of this document, including all wood-preservative/ pressure treatment, as well as preservation of adhesives/coatings/emulsions, fuels and oils bottom water, metal working fluids, and paints and varnish (EPA registration numbers 1022-563, 1022-574, and 1022-577). EPA anticipates issuing the Registration Review generic-data call-in (GDCI) as noted in the anticipated schedule in Table 2.

1.5.2 **Tolerance Information**

EPA has not established a tolerance or exemption from the requirement of a tolerance for residues of dimethyldithiocarbamate in food. The Food & Drug Administration (FDA) has established a number of food additive regulations for NaDDC. No food additive regulations have been established for KDDC. In the case of NaDDC, regulations have been established as a (an):

- Chemical for controlling microorganisms in cane-sugar and beet-sugar mills (21 CFR 173.320);

- Slimicide used in the manufacture of paper and paperboard that contact food (21 CFR 176.300);

- Adhesive used as components of articles intended for use in packaging, transporting, or holding food (21 CFR 175.105);

- Rubber article intended for repeated use, used in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food (21 CFR 177.2600)

1.6 Incidents

1.6.1 **Human Health**

There have been no incidents reported in the OPP Incident Database System for the period 6/30/2009, when the RED Amendment was signed, to the present (search conducted on 6/18/2013).

1.6.2 **Ecological**

As of August 6, 2013, no incidents have been reported in the Incident Data System (v. 1.8).

2 Anticipated Data Needs

Table 6 presents a summary of the data anticipated as being needed to support this registration review.

Table 6 – Studies Anticipated as Needed for the Registration Review of Dimethyldithiocarbamate

OCSPP GLN	Study Name	Test Substance	Time Frame[1] (Months)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Studies Anticipated to be Required through the Registration Review DCI						
835.3110[4] 835.3220[5] 835.3240[6] 835.3280[7]	Ready biodegradability test or one of three biodegradation in activated sludge simulation tests	TGAI	12	Activated sludge microorganisms	All uses	Transport to Industrial wastewater treatment plant
835.4100[3,16]	Aerobic soil metabolism	Ethanolamine (degradate)	24	Wood Preservatives	Treated wood in terrestrial environments	Terrestrial exposure
OECD 209 or 850.3300[8]	Activated Sludge Respiration Inhibition or Modified Activated Sludge Respiration Inhibition	TGAI	12	Activated sludge microorganisms	All uses	Transport to Industrial wastewater treatment plant
850.1300	Aquatic invertebrate life-cycle toxicity, freshwater	TGAI	24	Aquatic organisms	Industrial process water; Pulp and paper; Gas/oil, wood preservative[3]	Transport to the aquatic environment
850.1350	Aquatic invertebrate life-cycle toxicity, estuarine/marine	TGAI	24	Aquatic organisms	Industrial process water; Pulp and paper; Gas/oil, wood preservative[3]	Transport to the aquatic environment
850.1400	Fish early-life stage, freshwater	TGAI	12	Aquatic organisms	As above	Transport to the aquatic environment
850.3020[3]	Honeybee, acute contact toxicity	TGAI	12	Wood preservatives	Wood preservatives	Treated wood
850.3030[3]	Honeybee, toxicity of residues	TGAI	12	Wood preservatives	Wood preservatives	Treated wood
850.4100[9]	Seedling emergence, Tier II rice	TGAI	12	Aquatic organisms	Industrial process water; Pulp and paper; Gas/oil, wood preservative[3]	Transport to the aquatic environment
850.4150[15]	Vegetative vigor, Tier II rice	TGAI	12	Aquatic organisms	Gas/oil	Transport to the aquatic environment
850.4400	Aquatic Plant Testing using *Lemna* sp., Tier II	TGAI	12	Aquatic organisms	As above	Transport to the aquatic environment
850.4500	Algal Toxicity Tier II –marine diatom, freshwater diatom, and green algae	TGAI	12	Aquatic organisms	As above	Transport to the aquatic environment
850.4550	Algal Toxicity Tier II - Cyanobacteria	TGAI	12	Aquatic organisms	As above	Transport to the aquatic environment

OCSPP GLN	Study Name	Test Substance	Time Frame[1] (Months)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
870.2345	Inhalation Toxicity – 90 Day	TGAI	24	Occupational/ Residential Exposure	All Use Sites	As listed[10]
870.3800[11]	Reproduction and Fertility Effects	TGAI	36	Human Health	All Use Sites	As listed[10] Dietary and drinking water exposures.
870.4300	Combined Chronic Toxicity/Carcinogenicity	TGAI	36	Human Health	All Use Sites	MWF and Wood Preservation[12]. Dietary and drinking water exposures.
870.5395	Mammalian Erythrocyte Micronucleus Test	TGAI	12	Human Health	All Use Sites	All exposure scenarios.
870.7800	Immunotoxicity	TGAI	12	Human Health	All Use Sites	All exposure scenarios
875.1200[13,14]	Indoor Dermal Exposure	TGAI	24	Occupational/ Residential Handler	All Use Sites	As Listed[10]
875.1400[13,14]	Indoor Inhalation Exposure	TGAI	24	Occupational/ Residential Handler	All Use Sites	As Listed[10]
875.1700	Product Use Information	TGAI	12	Human Health	All Use Sites	All exposure scenarios.
875.2300[3]	Indoor Surface Residues	TGAI	12	Residential Exposure	Wood Preservative	Toddlers on Decks and Playsets
AWPA E11-06[3]	Leaching from treated wood	TGAI	12	Wood preservatives	Treated wood in terrestrial environments	Terrestrial exposure
Special Study	Migration Studies	TEP	24	Dietary and Aggregate	Cane sugar and beet sugar Mills; Coatings, adhesives, paper-making additives, and pulp/paper mill slimicide use	Dietary/Tier II

Data Needs No Longer Anticipated to be Required from the 2009 RED

GLN	Study Name	Test Substance	Time Frame[1] (Months)	Reason the Study is No Longer Anticipated to be Required
835.2240	Photodegration in Water	TGAI	12	Data were available from active ingredient Thiram, a dimer of DDC acid (MRID 45651201)
835.2410	Photodegradation on Soil	TGAI	12	Data were available from active ingredient Thiram, a dimer of DDC acid (MRID 45724501)
835.4100	Aerobic Soil Metabolism	TGAI	24	Data were available from active ingredient Thiram, a dimer of DDC acid (MRID 43734901)
835.6100	Terrestrial Field Dissipation	TGAI	24	The Agency has reviewed the need for these data and determined that the aerobic soil metabolism half-life of approximately two days indicates limited potential for leaching to ground water or runoff to surface water. In addition, the 158 W regulations do not require 835.6100 data ([1] 40 CFR § 158.2282).
875.1100	Outdoor Dermal Exposure	TGAI	24	Exposure scenarios were added to the indoor studies.
875.1300	Outdoor Inhalation Exposure	TGAI	24	Exposure scenarios were added to the indoor studies.
875.1600	Application exposure monitoring data reporting	TGAI	12	This study will be addressed in the submission of the remaining anticipated exposure data requirements

OCSPP GLN	Study Name	Test Substance	Time Frame[1] (Months)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
875.2700	Product Use Information	TGAI	12	This study will be addressed in the submission of the Product Use Information Study 875.1700		
875.2800	Description of Human Activity	TGAI	12-24	This study will be addressed in the submission of the Product Use Information Study 875.1700		
875.2900	Data Reporting and Calculations	TGAI	12	This study will be addressed in the submission of the remaining anticipated exposure data requirements		

[1]The timeframe will be measured from the receipt of the anticipated DCI.

[2]MRID 40220701 was submitted and found to be acceptable for parent compound, but degradates were not identified. As a result, another study is anticipated to be required to assess the formation and decline of degradates.

[3] EPA has received a request to cancel the only product with a wood preservative use. When the cancellation order becomes effective, this anticipated data requirement should no longer be needed.

[4] EPA has a published final guideline for this study: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0017. The biodegradation study anticipated to be required is based on results of an Activated Sludge Respiration Inhibition test.

[5] EPA has a published final guideline for this study: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0024. The biodegradation study anticipated to be required is based on results of an Activated Sludge Respiration Inhibition test.

[6] EPA has a published final guideline for this study: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0034. The biodegradation study anticipated to be required is based on results of an Activated Sludge Respiration Inhibition test.

[7] The results of the ASRI test will determine which of these four biodegradation tests is/are anticipated to be required. If the ASRI test EC_{50} is less than or equal to 20 mg/L, then either the (i)Biodegradation in Activated Sludge Study or (ii) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units or (iii) the Porous Pot Test is expected to be required. If the ASRI test EC_{50} is greater than 20 mg/L, then the registrant would likely be required to conduct either: (i) Ready Biodegradability or (ii) a) Biodegradation in Activated Sludge or b) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units or c) the Porous Pot Test. If the Ready Biodegradability study is conducted and passes, then no further testing would be expected to be required. If, however, the antimicrobial fails the Ready Biodegradability study, then the a) Biodegradation in Activated Sludge or b) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units, or c) the Porous Pot study would likely be required.

[8]The anticipated DCI will provide that 850.3300 may be used in place of OECD 209 if the test substance is not sufficiently soluble to allow preparation of a concentrated stock solution in water.

[9]Test guidelines 850.4100 and 850.4225 were merged and harmonized into OCSPP 850.4100 in a Federal Register Notice dated June 27, 2012 (FRL-9333-1).

[10]Indoor exposure scenarios include Open Pour Liquids, Open Pour Wettable Powder, Brush/Roller Application, Airless Spray Application, Wood Pressure Treatment and Using Treated MWF.

[11]Results from a multi-generation (EPA guideline 870.3800) or an extended one-generation reproductive and fertility effects study using OECD Test Guideline 443 (http://www.oecd-ilibrary.org/environment/test-no-443-extended-one-generation-reproductive-toxicity-study_9789264185371-en) will satisfy this requirement.

[12] Only the metal working fluid and wood preservation uses may result in long term exposures to workers.

[13] Data reporting and calculations are anticipated to be required when handler exposure data are submitted

[14] EPA has received requests to cancel the only products with a paints and coatings use and a metal working fluid use. When the cancellation orders become effective, this anticipated data requirement should no longer be needed for the brush/roller paint, airless sprayer paint and metal working fluid indoor exposure scenarios that are listed in footnote 10.

[15] Test guidelines 850.4150 and 850.4250 were merged and harmonized into OCSPP 850.4150 in a Federal Register Notice dated June 27, 2012 (FRL-9333-1).

[16] The registrant submitted MRID 43685901 for diethanolamine, a surrogate compound for the dimethylamine (DMA) degradate of NaDDC and KDDC. Until this study is reviewed and classified as appropriate for use in the risk assessment, it is included as an anticipated data requirement for use in conducting the risk assessment.

3 Human Health Risk Assessment

The Agency anticipates the need to conduct a human health risk assessment for DDC salts. The Agency expects to require additional data for use in conducting the registration review.

3.1 Existing Toxicological Endpoints

EPA anticipates the need to revise the existing toxicological endpoints as part of this registration review. Table 7 presents a summary of the endpoints used in EPA's most recent human health risk assessment in support of the 2009 RED Amendment. As previously stated, toxicological studies were identified as data gaps in the 2009 RED Amendment and identified in the registration review as anticipated data needs based on currently registered uses. All available information including existing toxicology studies, valid scientific literature, and the studies that are expected to be required for registration review will be considered in establishing the endpoints to be used in the registration review risk assessment. A summary listing of all of the available toxicity studies is provided in Appendix A .

Table 7 –Toxicological Endpoints Used for the Dimethyldithiocarbamate RED

Exposure Scenario	Dose, UF	Study and Toxicological Effects
Dietary Exposures		
Acute Dietary (Females 13-50)	**Oral NOAEL =** 13 mg/kg/day UF = 100[A]	**Rabbit developmental study (MRID 40995101)** LOAEL = 38 mg/kg/day based on clinical signs (reddish-colored material in cage trays) and possible increased maternal death and abortions.
Acute Dietary (General population)	**Oral NOAEL =** 20 mg/kg UF = 100[A]	**Co-critical studies:** **Acute neurotoxicity study (MRID 43544201)** LOAEL = 790 mg/kg/day based on clinical signs of toxicity, numerous functional observational battery parameter effects, and decreased motor activity. NOAEL = 20 mg/kg/day **Sub-chronic neurotoxicity study (MRID 43550501)** LOAEL = 99 mg/kg/day based on salivation, oral staining and decreased body weight. NOAEL = 2.0 mg/kg/day
Chronic Dietary (All populations)	**Oral NOAEL** = 2 mg/kg/day UF = 1000[B]	**90-day subchronic oral study (MRID 42047201)** LOAEL = 100 mg/kg/day and NOAEL = 2 mg/kg/day based on decreased erythrocyte counts, increased glucose concentration, and increased alkaline phosphatase activity in females, and exocrine pancreatic atrophy with fibrosis in males. Note: This study had a very wide dose range of 0, 0.2, 2 and 100 mg/kg/day which resulted in the 50 fold difference between the LOAEL of 100 mg/kg/day and the NOAEL of 2 mg/kg/day.
Occupational and Residential Exposures		
Incidental oral (Short-Term)	**Oral NOAEL** = 2 mg/kg/day UF = 1000[B]	**90-day subchronic oral study (MRID 42047201)** Same study used for the chronic dietary scenario above.

Exposure Scenario	Dose, UF	Study and Toxicological Effects
Incidental Oral (Intermediate-Term)	**Oral NOAEL** = 2 mg/kg/day UF = 1000[B]	**90-day subchronic oral study (MRID 42047201)** Same study used for chronic dietary above.
Dermal (Short, intermediate and long-term)	**Dermal NOAEL** = 60 mg/kg/day UF = 1000[B]	**90-Day Dermal toxicity study (MRID 40140101)** LOAEL = 120 mg/kg/day Based on decreased leukocyte and platelet counts.
Inhalation (Short, intermediate and long-term)	**Oral NOAEL** = 2 mg/kg/day UF = 1000[B]	**90-day subchronic oral study (MRID 42047201)** Same study used for chronic dietary above.
A. Uncertainty Factor (UF) includes 10X for interspecies extrapolation and 10x for intraspecies variation. B. UF includes 10X for interspecies extrapolation, 10x for intraspecies variation and 10x for database uncertainty.		

3.2 Dietary Exposure

The Agency anticipates the need to revise the previous dietary risk assessment conducted in 2009[3]. Uses of NaDDC and KDDC salts that may result in indirect dietary exposure include their use as slimicide in paper mill pulp slurries, material preservatives (including adhesives, coatings, and papermaking additives that have the potential to be in food-contact packaging), and their use in water process systems for beet sugar mills and cane sugar mills. Additionally, drinking water exposure may occur as a result of DDC salts' use in various industrial process water systems and in wood pressure treatment.

Dietary risk is characterized in terms of the Population Adjusted Dose (PAD), which reflects the reference dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA Safety Factor (SF). This calculation is performed for each population subgroup for which an endpoint exists. A risk estimate that is less than 100% of the acute or chronic PAD is not of concern. Acute and chronic dietary risks for DDC salts will be assessed by comparing dietary exposure estimates expressed in mg/kg/day to the acute Population Adjusted Dose (aPAD) and chronic Population Adjusted Dose (cPAD), respectively.

The Agency also anticipates the need to conduct an aggregate risk assessment.

3.2.1 **Food**

NaDDC is considered to be a food additive by the U.S. Food and Drug Administration (FDA) under 21 CFR, when used in raw cane and sugar beets. Use limitations for the additive are 3.0 ppm on a raw cane basis combined with disodium ethylenebisdithiocarbamate for control of microorganisms in cane sugar mills and 3.0 ppm on a raw cane or sugar beets basis when combined with disodium ethylene bisdithiocarbamate and ethylenediamine for control of microorganisms in cane sugar and beet sugar mills (21 CFR §173.320)[4]. The Agency anticipates reassessing dietary risks attributable to the sugar cane and sugar beet uses of NaDDC. The Agency anticipates the need to require migration studies in order to refine the risk assessment.

[3] *Dietary Risk Assessment for Potassium Dimethyldithiocarbamate for the RED Process*," dated July 14, 2009.
[4] 21 CFR §173.320

In 2009, the Agency assessed the risks associated with the use of DDC salts in adhesives and coatings that have the potential to be in food-contact packaging. FDA guidance for migration from food contact surfaces was adapted in the risk assessment[5]. Based on this guidance, a DDC salts dietary concentration of 7 ppb was assumed in calculating the Estimated Daily Intake (EDI). The Agency anticipates updating the dietary (food) risk assessments for food-contact paper/paperboard, paper additives and coatings. The Agency anticipates the need to require migration studies in order to refine the risk assessment. Dietary exposures will be incorporated into the aggregate risk assessment.

3.2.2 **Drinking Water**

EPA expects to conduct a Tier I screening-level drinking water analysis to estimate dietary exposure from uses that are expected to result in DDC salts passing through WWTPs (see Appendix B). Any drinking water risks will be incorporated into the aggregate risk assessment.

3.3 Occupational and Residential Exposures

The occupational and residential exposures to dimethyldithiocarbamate were last assessed in D359537 (EPA, 2009b) which was written for the 2009 RED Amendment. The Agency anticipates the need to revise the occupational and residential assessments conducted in support of the 2009 RED Amendment since the Margins of Exposure (MOE)s were calculated using unit exposure data and transferable residue data that have underlying limitations and will need to be reassessed using updated values.

3.3.1 **Occupational Exposures**

EPA anticipates the need to revise the occupational exposure assessment conducted in support of the 2009 RED Amendment. There is the potential for both dermal and inhalation exposures during the open pouring of dimethyldithiocarbamate liquid and wettable powder (WP) formulations. There is a much lower potential for exposure during metering pump addition of liquids and water soluble package addition of WP because these addition methods are considered to be closed systems. The risks from closed system addition methods were assumed to be mitigated by label language and were not assessed quantitatively in the 2009 RED Amendment. The Chemical Manufacturers Association (CMA) unit exposure data were used for the open pour liquid handling scenarios and the Pesticide Handlers Exposure Database (PHED) unit exposure data were used for the open pour WP scenarios. The dermal and inhalation MOEs for handling liquid formulations of dimethyldithiocarbamate were all greater than the target MOE of 1000 and were not of concern. The dermal MOEs for handling wettable powder formulations ranged from 1 to 6000 and were of concern for most of the scenarios. The inhalation MOEs for handling wettable powder formulations ranged from <1 to 2000 and were also of concern.

Machinist Exposure to Dimethyldithiocarbamate Treated Metal Working Fluids

[5] FDA. *Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations.* December 2007. http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm081818.htm#aii8

DDC salts may be used to treat metal working fluids in accordance with one label (EPA reg. number 1022-563). There is a potential for dermal and inhalation exposure when machinists use metalworking fluids treated with DDC salts. The dermal exposure was estimated in the 2009 RED Amendment using the film thickness approach and the resulting dermal MOE was 1200. The inhalation exposure was estimated in the 2009 RED Amendment using the OSHA PEL approach by adjusting the oil mist concentration by the a.i. concentration and the resulting MOE was 2800. EPA has received a product cancellation request for EPA registration number1022-563. A cancellation order is anticipated to be issued in late 2013.

Pressure Treatment Worker Exposures

DDC salts may be used to pressure treat wood used for decks, buildings, fences, poles, etc., in accordance with one label (EPA reg. number 1022-577). These exposures were assessed in the 2009 RED Amendment using data from a chromated copper arsenate (CCA) exposure study (MRID 455021-01) that was sponsored by Arsenical Wood Preservative Task Force of the American Chemistry Council. The arsenic portion of the results from this study was used as a surrogate to assess DDC salts exposures and these results were normalized to extrapolate the measured exposures in the CCA study (monitored at 0.438 to 0.595% arsenic in the CCA solution) to the maximum DDC salts treatment solution concentration (10% ai in solution). The resulting inhalation MOEs ranged from 400 to 7,600 and were of concern for two scenarios because they were less than the target MOE of 1000. The dermal MOEs ranged from 19 to 2200 and were of concern for most of the scenarios because they were less than the target MOE of 1000. EPA has received a voluntary cancellation request for EPA registration number 1022-577. A cancellation order is anticipated to be issued in late 2013.

Occupational Risk Characterization

Scenarios that Need to be Assessed During Registration Review

All of the handler scenarios that were assessed in the 2009 RED Amendment will need to be revised during registration review upon receipt of the unit exposure data that is anticipated to be required to supplement or replace the unit exposure data that were used in the 2009 RED Amendment. Occupational handler scenarios to be assessed are presented in Table 8.

Table 8 – Occupational Exposure Scenarios for the Dimethyldithiocarbamate Salts

Handler Scenarios	**Exposure Route(s)**	**Duration**
Open Pour Liquids for treatment of Cooling Water, Drilling Muds, Drilling Fluids, Paints and Coatings.	Dermal Inhalation	Intermediate Term
Open Pour Wettable Powder for treatment of Cooling Water, Drilling Muds, Drilling Fluids and Pulp and Papers	Dermal Inhalation	Intermediate Term
Using Treated Metal Working Fluids	Dermal Inhalation	Long Term
Pressure Treatment of Wood	Dermal Inhalation	Long Term
Airless Sprayer and Brush Roller Application of Treated Paints	Dermal Inhalation	Intermediate Term

3.3.2 **Residential Exposures**

EPA anticipates the need to revise the residential exposure assessments conducted in support of the 2009 RED Amendment. There is one product (EPA reg. number 1022-563) that is labeled for use as an in-can preservative of water thinned paints and coatings. There is one product (EPA reg. number 1022-577) labeled for pressure treatment wood preservation. EPA has received a voluntary cancellation request for both products. A cancellation order is anticipated to be issued in late 2013.

Residential Handler Exposures for Painting

There is the potential for residential handler exposure during the brush/roller and airless sprayer application of paints treated with dimethyldithiocarbamate. Both dermal and inhalation exposures are anticipated and are assumed to be primarily short term because painting is done on an episodic basis. The risks were assessed in the 2009 RED Amendment using PHED data and an application rate of 1000 ppm. The dermal MOEs were 910 and 350 for brush/roller and airless sprayer application, respectively, and were less than the target MOE of 1000 which means that the risks were of concern. The inhalation MOEs were 25,000 and 1,100, respectively, and were greater than the target MOE of 1000.

Residential Post Application Exposures from Pressure Treated Wood

There is a potential for child exposure to dimethyldithiocarbamate residues when playing on dimethyldithiocarbamate-treated wood structures such as decks and children's playsets. Both dermal and incidental oral exposures are anticipated. These exposures were assessed in the 2009 RED Amendment using an assumed transferable residue value of 1.0 ug/cm^2 that was higher than the maximum residue seen for chromium and non-chromium based wood preservatives (D330159, EPA, 2006). The dermal MOE was 440 and the incidental oral MOE was 360, both of which were less than the target MOE.

Scenarios that Need to be Assessed During Registration Review

The residential handler scenario that was assessed in the 2009 RED Amendment will need to be revised during registration review upon receipt of the unit exposure data that is anticipated to be required to supplement or replace the unit exposure data that were used in the 2009 RED Amendment. The post application scenario will need to be revised during registration review upon receipt of the transferable residue data that are anticipated to be required to verify the assumption that was used in the 2009 RED Amendment. A listing of residential exposure scenarios to be assessed is included in Table 9.

Table 9 – Residential Exposure Scenarios for DDC Salts

Scenario	Exposure Route(s)	Duration
Handler Exposures		
Application of Preserved Paint (Brush/Roller and Airless Spray)	Dermal Inhalation	Short Term
Post Application Exposures		
Toddlers Playing on Pressure Treated Decking and Playground Equipment	Dermal Incidental Oral	Intermediate Term

3.4 Aggregate and Cumulative Exposure

3.4.1 Aggregate Exposures

EPA anticipates the need to revise the aggregate assessment conducted in support of the 2009 RED Amendment. Upon a reevaluation and selection of toxicological endpoints, combined with the human health exposure assessments expected as a part of this registration review case, aggregate exposures will need to be assessed. This assessment will include dietary (food) exposures and residential exposures.

3.4.2 Cumulative Exposures

With respect to cumulative exposure, unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, the Agency made a 2001 final determination that there is insufficient data to show a common mechanism of toxicity with other substances and dimethyldithiocarbamate does not appear to produce a toxic metabolite produced by other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see http://www.epa.gov/pesticides/cumulative/.

4 Environmental Risk Assessment

A risk assessment was conducted for the Amended RED[6] (EPA 2009) that assessed acute risks to fish and aquatic invertebrates from the use of sodium dimethyldithiocarbamate salt as a wood preservative. LOCs were exceeded for acute risk to aquatic organisms for some applications. However, in April, 2013, EPA received a request to cancel the only product with a wood preservative use. The product cancellation order is expected to be issued in late 2013. For currently registered uses, the ecological risk assessment planned during registration review will allow the Agency to determine potential acute and chronic risks to aquatic organisms exposed to dimethyldithiocarbamate salts that are transported from treatment sites into the aquatic environment. Such uses include commercial/industrial cooling water, pulp/paper mill water systems, and gas/oil operations. The Agency has not conducted a risk assessment that supports a complete endangered species determination for DDC salts. The ecological risk assessment planned during registration review will allow the Agency to determine whether DDC salts' use has 'no effect' or 'may affect' federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use 'may affect' a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services), as appropriate.

4.1 Water Quality

Sodium and potassium dimethyldithiocarbamate salts are not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[7]. In addition, no Total Maximum Daily Loads (TMDL) have been developed for sodium and

[6] http://www.epa.gov/oppsrrd1/REDs/DDCsalts-red-amended.pdf
[7] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

potassium dimethyldithiocarbamate salts[8]. More information on impaired water bodies and TMDLs can be found at EPA's website[9].

4.2 Environmental Conceptual Model Exposure Pathways

NaDDC and KDDC salts are active ingredients in antimicrobials that can be used in water process systems (air washer, reverse osmosis, and industrial, cane and beet sugar mills in cane juice and beet pulp press water, commercial/industrial cooling water, industrial wastewater, pulp/paper mills (pulp), gas and oil (drilling muds/packer fluids, recovery injection water, fracturing fluids, workover and completion fluids), and coal powered plant flue gas desulfurization thickeners).

Antimicrobials with the above uses will eventually be released to wastewater treatment plants (WWTPs) whose effluents will reach surface water and aquatic organisms. The exposure to parent compounds is limited because of ready disassociation of the sodium and potassium cations from the acid of the DDC salts. The initial exposures will be from a mixture of parent compounds and degradates which are impurities because the major degradates were present at the beginning of the aerobic aquatic metabolism study.[10] The primary and major ($\geq$10 % of applied parent compound) degradates include dimethylamine (DMA), carbon disulfide ($CS_{2)}$, tetramethylthiuram disulfide (TMTDS), tetramethyl thiomonosulfide (TMTMS), and tetramethyl thiourea (TMTU). The oil and gas uses can create environmental exposure of ground water to impurities and degradates if well casing is not intact or to surface water if treated water fracking water is released into streams. The flue gas desulfurization use is associated with coal-burning power plants and there are two forms of waste, water which goes to a WWTP and sludge which goes to a landfill.[11] As a result, the Agency is assessing the WWTP exposure from the desulfurization use but not the landfill disposal because it is assumed that landfills are lined and will not create exposure.[12]

Except as noted, the environmental fate properties of DDC salts and its degradates were based on the results of submitted studies. Degradation of DDC salts and its degradates occur by both abiotic[13] and biotic means[14]. Parent DDC salts and its degradates are water soluble and will be associated with water in the presence of soil, sediment, and sewage sludge. While most DDC salts compounds have limited potential to volatilize from water based on estimated values using the EPI-Suite 4.1[15] Henry's Law constants of 10^{-10} to 10^{-9} atm m^3 mol^{-1}, DMA and CS_2 degradates have Henry's Law constants of 10^{-5} to 10^{-2} atm m^3 mol^{-1} and are likely to volatilize from water and create aerial exposure, especially from the cooling tower use (Table B1).

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[8] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES

[9] http://www.epa.gov/owow/tmdl/

[10] MRID 40365702

[11] http://water.epa.gov/scitech/wastetech/guide/steam-electric/upload/Steam-Electric_Detailed-Study-Report_2009.pdf , EPA 821-R-09-008

[12] http://www.epa.gov/osw/nonhaz/municipal/landfill/criteria/landbig.pdf

[13] Hydrolysis (MRID 43180801) and photolysis in water (MRID 40220701)

[14] Aquatic metabolism, MRIDs 43865901 and 40365702

[15] http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

For all the following conceptual exposure models for DDC salts and its degradates, the Agency is using solid lines to signify that surface water exposure and attribute changes can occur, but the potential for bioconcentration and secondary exposure is unlikely or insignificant as indicated by the dashed lines.

Figure 1 contains the conceptual model for the environmental exposure from the cooling tower use of DDC salts. Based on the lack of data on the persistence in cooling towers and chemical and physical properties[16] of DDC salts and its degradates, all lines in Figure 1 are solid with the exception of ingestion and bioconcentration in aquatic organisms. Water from cooling towers will eventually be released to surface water directly or to a WWTP where it will be present in water and not be sorbed to the sludge. Treated water from a WWTP will then be released to surface water.

Figure 2 contains the conceptual model for environmental exposure of DDC salts from the water system and flue-gas desulfurization (FGD) uses. The water system and FGD uses involve scrubbing of SO_2 gas from the smokestacks of steam electric power plants that consume fossil fuels (e.g. coal). The waste water will eventually pass through a WWTP where it will reach surface water. The solid waste (sludge) will be placed in a landfill or other surface impoundment or applied to land as a fertilizer and consists of ash (including some heavy metals), $CaSO_4$, and $CaSO_3$. The water system and FGD uses contain air washers, reverse osmosis, and industrial wastewater systems.[17]

The conceptual models for the oil and gas uses may be seen in Figures 3 and 4. These uses include potential for waste water to be used in irrigation and exposure of terrestrial plants. The conceptual model for the wood preservative uses of DDC salts is attached in Figure 5. The wood preservative use is based on the sole remaining registered label[18] that includes wood preservation.

[16] Water solubility, log Kow, and low potential for sorption

[17] EPA 821-R-09-008. October, 2009. Steam Electric Power Generating Point Source Category: Final Details Study Report. http://water.epa.gov/scitech/wastetech/guide/steam-electric/upload/Steam-Electric_Detailed-Study-Report_2009.pdf

[18] http://www.epa.gov/pesticides/chem_search/ppls/001022-00577-19960423.pdf

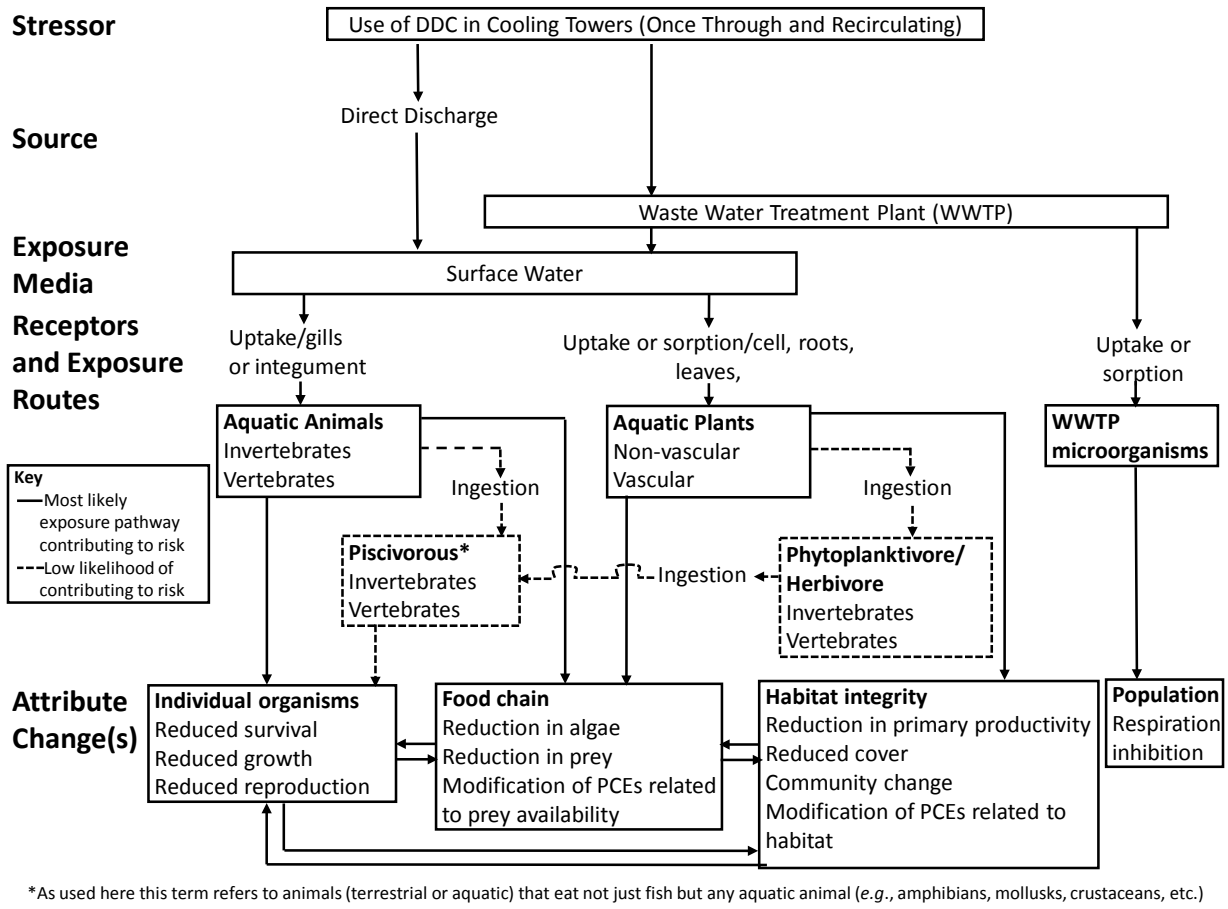


Figure 1 – Conceptual Model for Cooling Tower Use of DDC Salts and Ecological Exposure and Effects of DDC Salts to Aquatic and Terrestrial Organisms

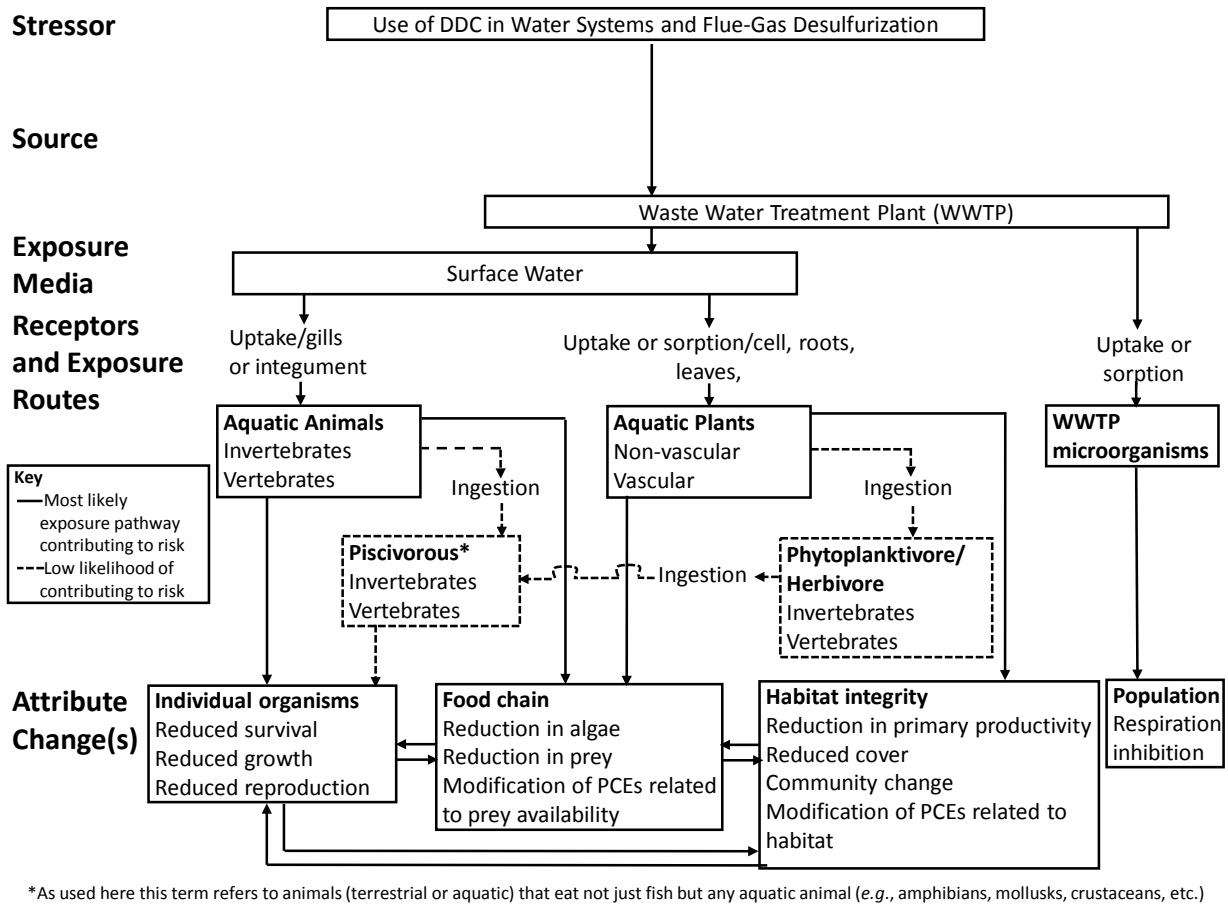
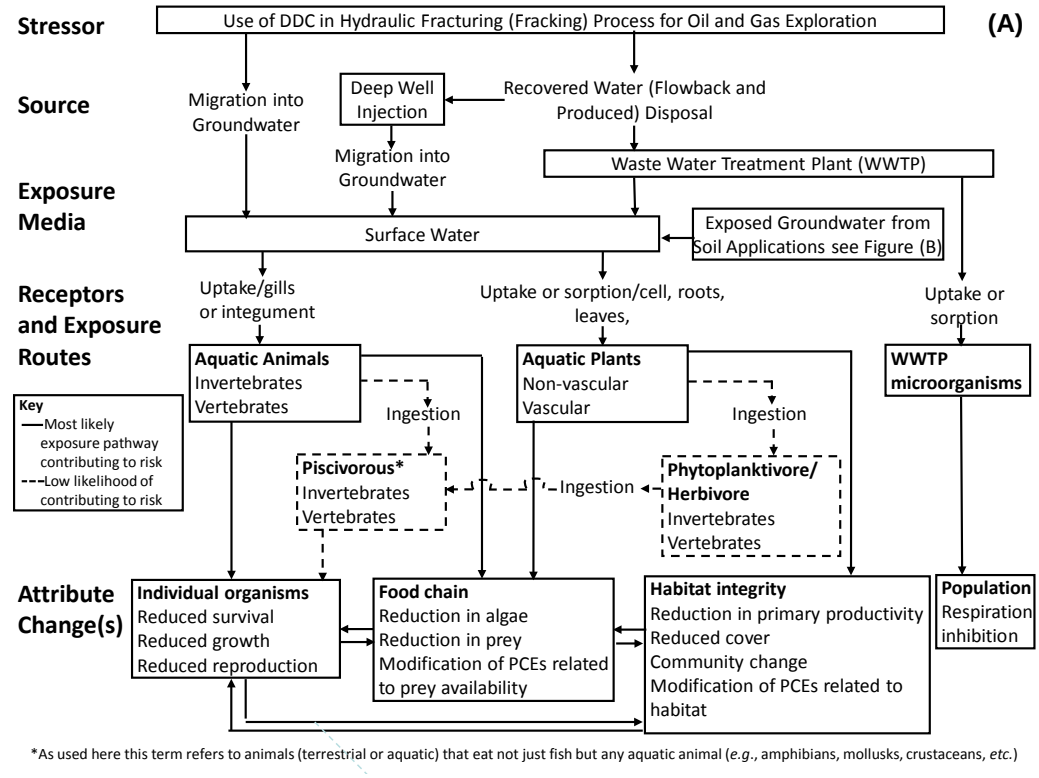


Figure 2 - Conceptual Model for Environmental Exposure of DDC Salts from Water System and Flue-Gas Desulfurization (FGD) to Aquatic and Terrestrial Organisms



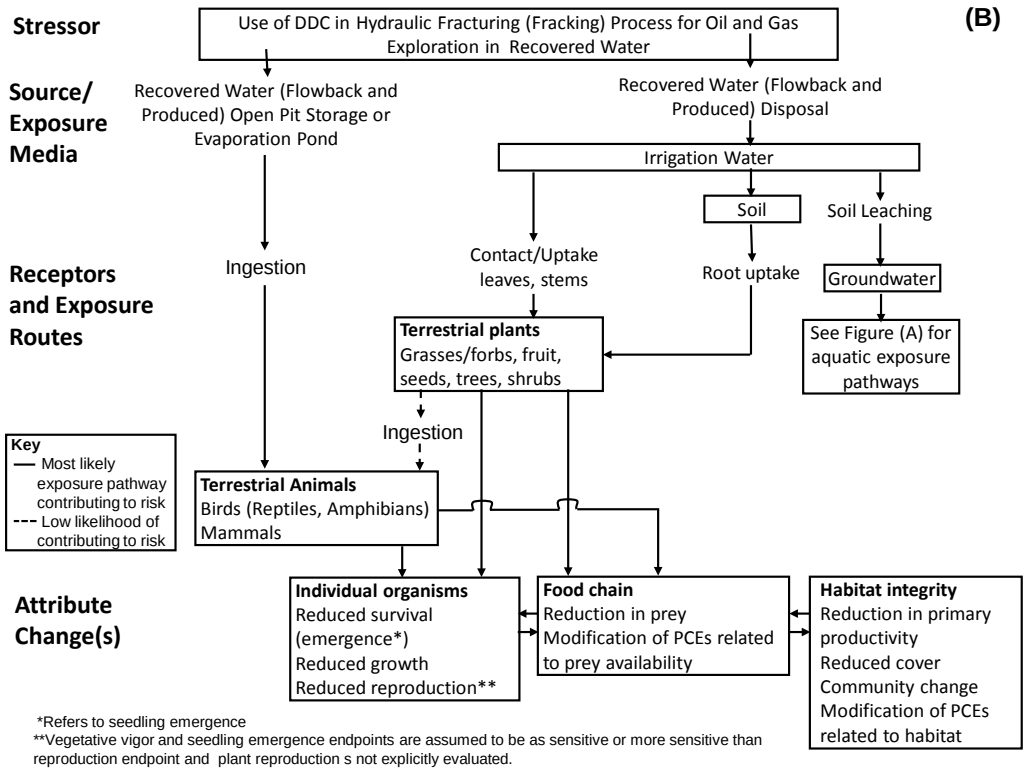


Figure 3 – Conceptual Model for Aquatic (A) and Terrestrial (B) Environmental Exposure of DDC Salts in Recovered Water from Oil and Gas Use

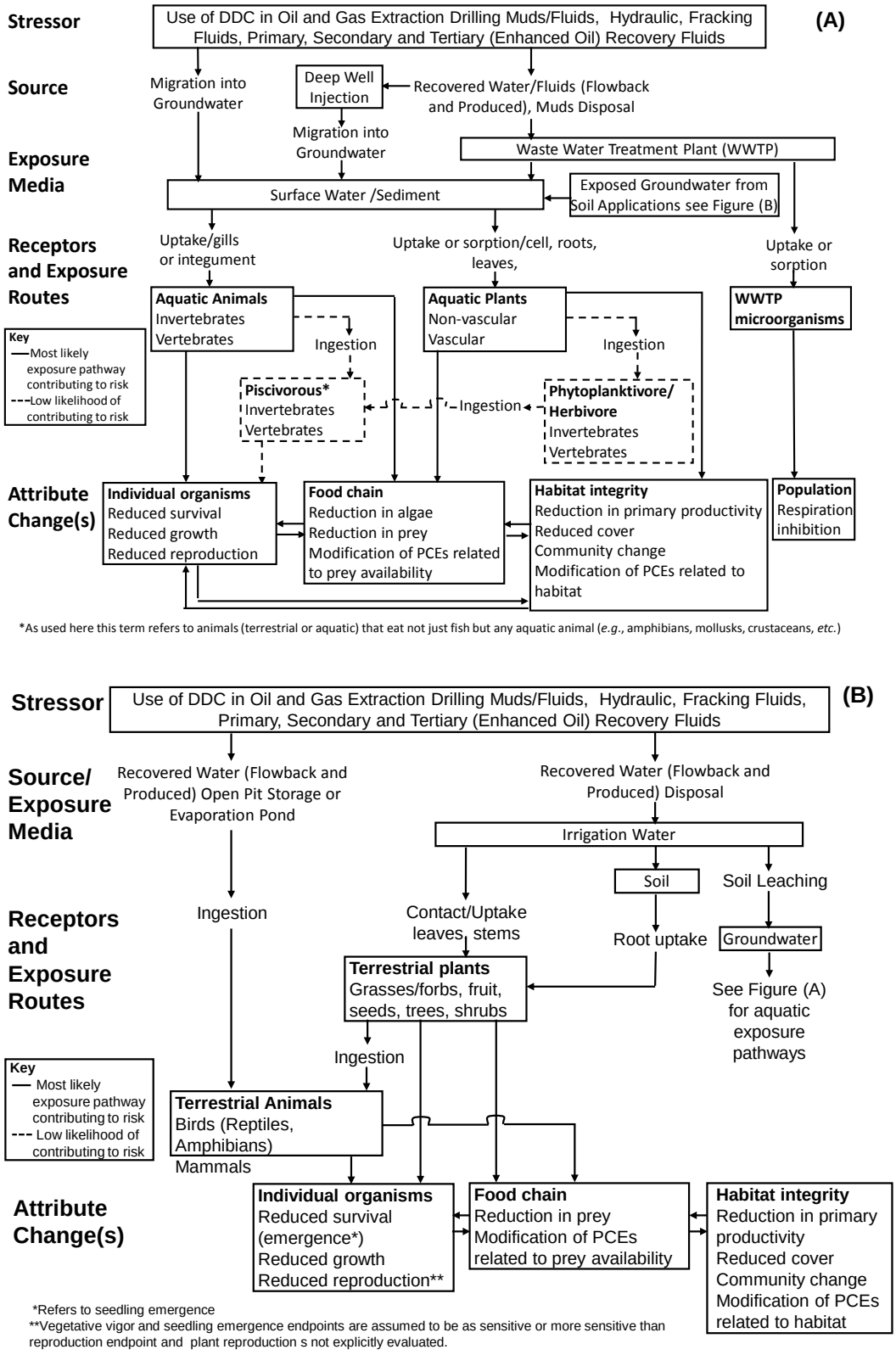


Figure 4 - Conceptual Model for Aquatic (A) and Terrestrial Environmental Exposure (B) of DDC Salts from Use in Oil and Gas Extraction, Drilling Muds/Fluids, Hydraulic Fracturing Fluids, and Primary, Secondary, and Tertiary (Enhanced Oil) Fluids

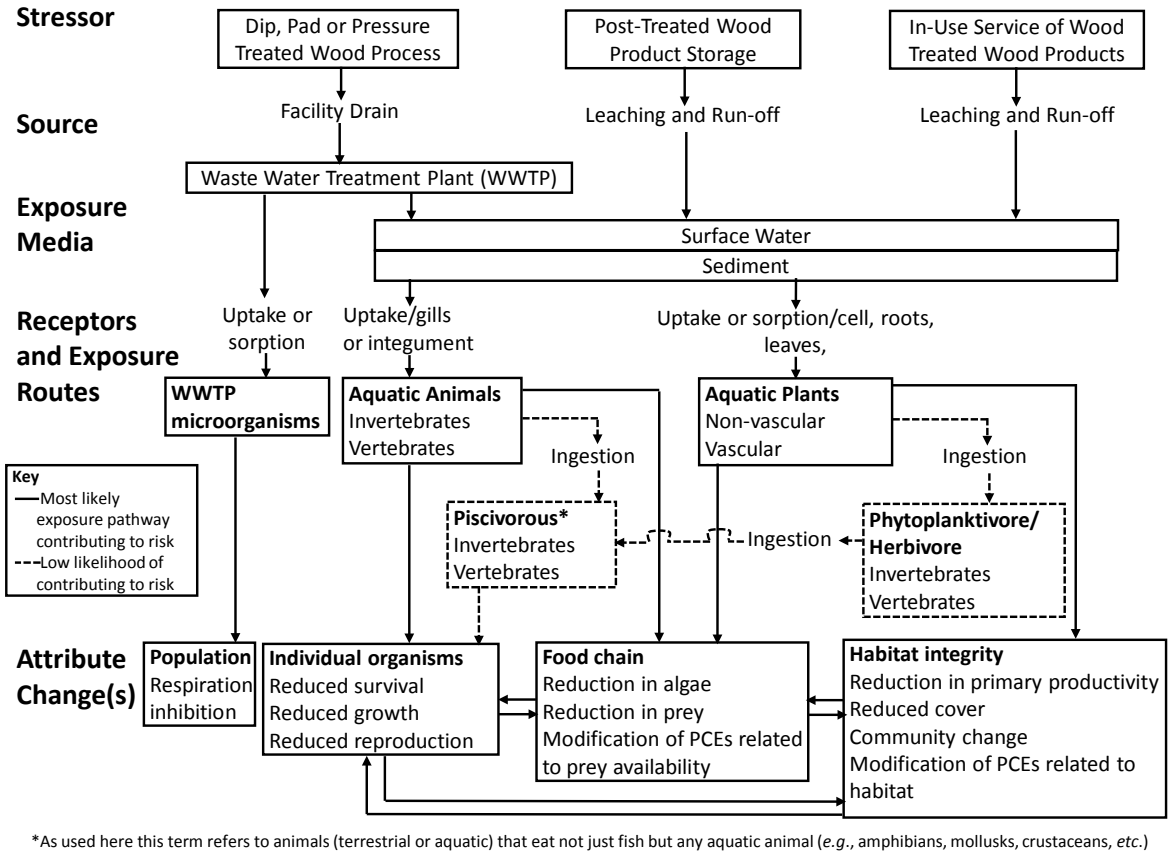


Figure 5 - Conceptual Model for Aquatic Environmental Exposure of DDC Salts from Use in Pressure Treated Wood

4.3 Ecological Effects Assessment

4.3.1 **Mode of Action**

NaDDC and KDDC are synthetic broad-spectrum antimicrobial agents. Dithiocarbamate fungicides inhibit sulfhydryl (-SH) groups in amino acids, proteins and enzymes of fungal and bacterial cells. While these salts are a subgroup of the carbamate pesticides, the Agency made a 2001 final determination that in animals they do not share a common mechanism of toxicity[19]. The dithiocarbamates all release carbon disulfide (CS_2), under acidic conditions, which is toxic to the central and peripheral nervous systems.

4.3.2 **Measures of Effect (Ecotoxicology Endpoints)**

Ecological effects data are used as measures of direct and indirect effects to aquatic and terrestrial organisms. Acute and chronic toxicity data from registrant-submitted studies will be used to evaluate the potential direct and indirect effects of the DDC salts and degradates to plants

[19] http://epa.gov/pesticides/cumulative/

and animals. The ecotoxicity data requirements and all available ecotoxicity endpoints from studies submitted by registrants are tabulated in Appendix C .

OPP uses the most sensitive toxicity values for assessing risk to each receptor group. The endpoints that will be used for the DDC salts ecological risk assessment are presented in Table 11. Anticipated data gaps for the TGAI also are indicated. Data also are included for thiram, a major reaction product and also a registered active ingredient (PC Code 079801).

Table 11. Selected Ecological Effects Endpoints for Risk Assessment

Receptor Group	Surrogate Species	Test material	Risk Scenario	Toxicity Endpoint	EPA ID
Freshwater fish	Fathead minnow	KDDC	Acute	96-h LC_{50} = 60 µg ai/L	240946
			Chronic	Data gap	N/A
	Bluegill	Thiram	Acute	96-h LC_{50} = 42 µg ai/L	070801
		Thiram estimated using ACR	Chronic	NOAEC = 0.36 µg ai/L	See Appendix C
Freshwater invertebrates	Waterflea	NaDDC	Acute	48-h EC_{50} = 52 µg ai/L	42504802
			Chronic	Data gap	N/A
		Thiram	Acute	48-h EC_{50} = 210 µg ai/L	164662
			Chronic	Under Review	N/A
Estuarine/marine fish	Sheepshead minnow	NaDDC	Acute	96-h LC_{50} = 59,000 µg ai/L	41984701
			Chronic	Not a data gap: Mysid is more acutely sensitive	N/A
		Thiram	Acute	96-h LC_{50} = 540 µg ai/L	42514401
			Chronic	Not a data gap: Mysid is more acutely sensitive	N/A
Estuarine/marine invertebrates	Mysid	NaDDC	Acute	LC_{50} = 88 µg ai/L	42561901
			Chronic	Data gap	N/A
		Thiram	Acute	LC_{50} = 3.36 µg ai/L	42488302
			Chronic	Will use generated ACRs	N/A
Aquatic non-vascular plants	Green algae, Freshwater diatom, Estuarine/marine diatom, and Cyanobacteria	DDC salts	IC_{50} and NOAEC	Data gap	N/A
	Green algae	Thiram	Non-listed	IC_{50} = 45 µg a.i/L	42646001
			Listed	NOAEC <57 µg a.i/L (will calculate IC_{05})	
Aquatic vascular plants	*Lemna* sp.	TGAI	IC_{50} and NOAEC	Data gap	N/A
		Thiram	Non-listed	IC_{50} = 1,600,000 µg a.i/L	45441202

Receptor Group	Surrogate Species	Test material	Risk Scenario	Toxicity Endpoint	EPA ID
			Listed species	NOAEC <57,000 µg a.i/L (will calculate IC_{05})	
Semi-aquatic plants (seedling emergence)	Rice	TGAI	IC_{50} and NOAEC	Data gap	N/A
Vegetative Vigor	Multiple species	TGAI	IC_{50} and NOAEC	Data gap	N/A
Birds	Northern bobwhite	NaDDC (40)	Acute	LD_{50} = 391 mg ai/kg bw	00159788
	Ring-necked pheasant	Thiram (99)	Acute	LD_{50} = 673 mg ai/kg bw	00160000
	Mallard	Thiram (97.5)	Chronic	NOAEC = 9.6 ppm	45441201
Beneficial insects	Honeybee	TGAI	Acute	Data gap	NA

4.4 Exposure Analysis Plan

4.4.1 Aquatic and Terrestrial Wildlife Exposure Estimates

In order to address the risk hypothesis, the potential for adverse effects on the environment will be estimated. For down-the-drain (DtD) risk estimates, an approach that estimates the number of days a concentration-of-concern (COC) is exceeded, also referred to as a probabilistic dilution model (PDM) approach is used to assess risk to aquatic organisms.

4.4.2 Screening Level Down-the-Drain Analysis

The Industrial Releases Module of the E-FAST (Exposure and Fate Assessment Screening Tool) will be used to determine the potential for aquatic organisms downstream of the industrial wastewater treatment plants that receive discharges from the end-use of KDDC and NaDDC to be exposed these chemicals or their degradates. NaDDC and KDDC salts are used in industrial water systems such as commercial/industrial cooling water, industrial wastewater, pulp/paper mills, etc. Antimicrobials with these uses will eventually be released to industrial wastewater treatment plants whose effluents will reach surface water and aquatic organisms. The primary and major ($\geq$10 % of applied parent compound) degradates include the DMA, CS_2, TMTDS, TMTMS, and TMTU. Chemicals that are released down-the-drain can typically take from a few to several hours to reach wastewater treatment plant intakes following their discharge and from several hours to roughly a day following their discharge down-the-drain to subsequently be discharged from industrial wastewater treatment plants to surface water. The half-life of both KDDC and NaDDC are long enough to enter the industrial wastewater treatment plants and subsequently be discharged to surface waters.

This analysis plan will be revisited and may be revised depending upon a full review of the data available in the open literature and the information submitted by the public in response to the opening of the Registration Review docket. The Agency does not anticipate requiring additional data to assess down-the-drain exposures for this registration review.

4.5 Effects Analysis Plan

Additional open literature studies will be identified through EPA's ECOTOXicology (ECOTOX) database[20], which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The ECOTOX database will be searched when the risk assessment for the DDC salts is prepared. Open literature studies will be reviewed that potentially provide data for missing endpoint values or provide values more sensitive than available from the anticipated registrant-submitted studies. ECOTOX was created and is maintained by the USEPA, Office of Research and Development, and the National Health and Environmental Effects Research Laboratory's Mid-Continent Ecology Division.

5 Endocrine Disruptor Screening Program (EDSP)

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of the 2009 Amended RED, for DDC salts, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), DDC salts are subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. NaDDC and KDDC are not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Accordingly, as part of registration review, EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for NaDDC and KDDC.

[20] http://cfpub.epa.gov/ecotox/

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

6 Guidance for Commenters

6.1 Preliminary Work Plan

The public is invited to comment on EPA's Preliminary Work Plan and rationale. The Agency will carefully consider all comments as well as any additional information or data provided in a timely manner prior to issuing a final work plan for the Sodium and Potassium Dimethyldithiocarbamate Salts registration review case.

6.1.1 Trade Irritants

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. The Agency will work to harmonize tolerances and international maximum residue limits (MRLs) and may modify tolerance levels to do so, when possible. **Stakeholders are asked to comment** on any trade irritant issues resulting from lack of MRLs or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

6.1.2 Water Quality

See section 4.1. **The Agency invites submission of water quality data for this pesticide.** To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process*[21] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

6.1.3 Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to sodium and potassium dimethyldithiocarbamate salts compared to the general population. **Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.**

6.1.4 Structure Activity Relationships

EPA must rely upon information of appropriate quality and reliability for each decision made by the Agency. In the Office of Pesticide Programs (OPP), the evaluation process for a pesticide

[21] http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm

chemical traditionally begins with the applicant's submission of a set of studies conducted with the specific pesticide chemical of interest. The use of the results of such testing (measured data) is a logical, scientifically rigorous process that identifies the physical, chemical, and environmental fate properties of the pesticide, as well as the dose and endpoints at which an adverse effect can occur in various animal species.

Today, there is significant interest in alternative techniques, i.e., techniques other than data generation that could significantly inform the Agency's decision-making process. Recently, OPP has made increasing use of structure activity relationship (SAR) as part of its regulatory decision-making process. In the SAR process, a chemical's molecular structure is compared to that of other chemicals for which data are available. These structural similarities are then used to make predictive judgments about a chemical's physical, chemical, and biological properties. Thus, the chemical's physical, chemical, and biological properties are a function of (or directly related to) the chemical's molecular structure. Quantitative SAR is referred to as QSAR. To develop a QSAR, a selected set of measured data on a single physical, chemical, or biological property is used to derive a model (an equation) to predict the value of that property.

Since SAR assessments and QSAR modeling are another set of tools that are available to Agency scientists, OPP has begun a process shift that envisions shifting from the current study-by-study approach to an approach in which the use of predicted data, generated using validated models, is considered along with information from open literature and studies specifically generated under Part 161 requirements. All relevant information would be considered as part of a weight-of-the-evidence evaluation.

At this time, EPA believes that for certain endpoints, especially physical/chemical and fate properties, that SAR and QSAR might be effectively utilized to fulfill these data requirements for many antimicrobial pesticide chemicals. When considering biological properties, at this time, EPA believes that SAR and QSAR can be most effectively utilized in the evaluation of chemicals that exhibit lower toxicity for human health and/or ecotoxicity parameters. This is appropriate because the risk assessment for lower toxicity chemicals can be stream-lined, i.e., a screening-level assessment procedure rather than multiple tiers of assessments with progressively more data requirements.

If stakeholders believe that submission of predicted data can fulfill one of the data needs for the Sodium and Potassium Dimethyldithiocarbamate Salts Case, then the Agency invites submission of this information. The submitter would be expected to supply a rationale describing the utility of the information and provide documentation on the scientific validity of the information. The determination that the predicted data fulfills the data requirement would be at the sole discretion of the Agency. Pre-submission consultation with the Agency is encouraged.

6.1.5 **Additional Information**

Stakeholders are also specifically asked to provide available information and data that will assist the Agency in refining its risk assessments, including any species-specific ecological effects determinations. The Agency is interested in receiving the following information:

1. Confirmation on the following label information:

A. Sites of application
B. Formulations
C. Application methods and equipment
D. Maximum application rates
E. Frequency of application, application intervals and maximum number of applications
F. Geographic limitations on use

2. Use or potential use distribution
3. Use history
4. Usage/use information for non-agricultural uses (e.g., materials preservation)
5. Typical application interval
6. State or local use restrictions
7. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
8. Monitoring data

7 Next Steps

After the 60-day comment period closes in November 2013, the Agency will review and respond to any comments received in a timely manner, and then issue a Final Work Plan for the Sodium and Potassium Dimethyldithiocarbamate Salts case.

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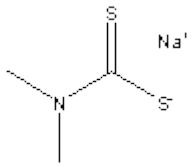
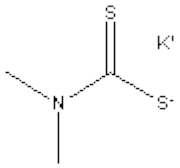
Appendix A Toxicology Profile for Dimethyldithiocarbamate

I. BACKGROUND

Both sodium dimethyldithiocarbamate and potassium dimethyldithiocarbamate react with water readily and decompose into their respective salts. Due to their structural and chemical similarities as shown in Table 1, the bridging of their toxicological databases was ascertained. A consensus was reached on bridging the repeat exposure database of both sodium dimethyldithiocarbamate and potassium dimethyldithiocarbamate in the ADTC endpoint selection meeting (US EPA, 2009). However, the acute toxicological database could not be bridged due to lack of data on the technical active ingredient on each of the chemicals.

Table 1. Chemical structures

Sodium dimethyldithiocarbamate	Potassium dimethyldithiocarbamate
	

Adapted from RED, Table 1. p. 1

II. Acute Toxicity

A. Sodium dimethyldithiocarbamate

The acute toxicity summary for sodium dimethyldithiocarbamate is provided in Table 2. Sodium dimethyldithiocarbamate is corrosive to the eye and causes mild or slight irritation to skin. The toxicity study with sodium dimethyldithiocarbamate yielded a Toxicity Category II with dermal route of exposure and a Toxicity Category IV with inhalation route of exposure study. There were no acceptable acute oral toxicity studies available; however, an unacceptable / guideline-upgradeable study's (MRID 00160993, 00160994) results were considered. An acute oral study for the sodium salt is anticipated to be required for the product specific data call in (PDCI).

Table 2. Acute toxicity database for sodium dimethyldithiocarbamate

Guideline No.	Study Type	MRID number (s)	Results	Toxicity Category
81-1	Acute Oral	No acceptable study available.	LD_{50} (M) = 2100 mg/kg LD_{50} (F) = 2500 mg/kg	**III**
81-2	Acute Dermal	00160995, 92043009	LD_{50} (M) = 1450 mg/kg LD_{50} (F) = 1020 mg/kg	**II**
81-3	Acute Inhalation	00159769, 42327801, 92043010	LC_{50} (M) > 2.22 mg/L LD_{50} (F) > 2.22 mg/L	**IV**
81-4	Primary Eye Irritation	00161185, 92043011	Corrosive	**I**
81-5	Primary Skin Irritation	00159782, 43481501, 92043012	Mild or slight	**IV**
81-6	Dermal Sensitization	00159783, 92043013	Negative	

Adapted from RED (2009), Table 5, p. 9

B. Potassium dimethyldithiocarbamate

The acute toxicity summary table for potassium dimethyldithiocarbamate is provided in Table 2. Potassium dimethyldithiocarbamate is a dermal sensitizer and causes moderate dermal irritation. The primary eye irritation study was assigned a Toxicity Category of III with the corneal involvement reversible within 7 days. A Toxicity Category III was assigned to both acute oral and dermal toxicity studies. No inhalation study was provided. An acute inhalation toxicity study for the potassium dimethyldithiocarbamate is anticipated to be required for the PCDI.

Table 3. Acute toxicity database for potassium dimethyldithiocarbamate

Guideline No.	Study Type	MRID (s)	Results	Toxicity Category
81-1	Acute Oral	00132382, 92039001 00143448*	LD_{50} (M) = 2196 mg/kg (LD_{50} (F) = 1867 mg/kg	**III**
81-2	Acute Dermal	00146768, 92039002 00132381* 00143449*	LD_{50} (M) = 2990 mg/kg	**III**
81-3	Acute Inhalation	No study available		
81-4	Primary Eye Irritation	00105157, 92039003	PIS: 32.2/110 unwashed, PIS: 40.7/110 washed	**III****
81-5	Primary Skin Irritation	00105157, 92039004	Primary Irritation Index: 3.08 after 72 hours	**III**
81-6	Dermal Sensitization	00132380, 92039005	Positive	

Adapted from RED, Table 6, p. 10

* MRIDs 00143448, 00132381, and 00143449 not included in the table, but included in toxicology profile

** An unacceptable primary eye irritation study (MRID 00143448) was assigned a Toxicity Category II.

III. Repeat Dose Toxicity

The toxicological database of repeat dose studies for dimethyldithiocarbamate is listed in Table 3. All of these studies were included in the hazard assessment that was written for the RED (US EPA, 2009). No new studies have been submitted since the publication of the RED, and no data are anticipated to be required. Summaries of the toxicity profiles for Sodium dimethyldithiocarbamate and Potassium dimethyl-dithiocarbamate are included in Tables 4 and 5, respectively.

Table 4. Toxicological Database of Repeat Dose Studies for Dimethyldithiocarbamate

Guideline Number	Study	Required	Satisfied	MRID Number(s) (Chemical)
870.3100	90-Day Oral - Rats	Yes	Yes	42047201 (NaDDC)
870.3250	90-Day Dermal -Rats	Yes	Yes	40830801 (KDDC)
870.3250	90-Day Dermal -Rabbit	Yes	Yes	40140101 (NaDDC)
870.3700a	Developmental Toxicity- Rats	Yes	Yes	40140102 (NaDDC), 41005501 (KDDC)
870.3700b	Developmental Toxicity- Rabbits	Yes	Yes	40165804 (NaDDC), 40995101 (KDDC)
870.3800	Reproduction and Fertility Effects	Yes	No	42905, 82096*
870.4100a	Chronic Toxicity – Rats	Yes	No	82096*
870.4100b	Chronic Toxicity – Dogs	No	No	82905*
870.5100	Bacterial Reverse Mutation Test	Yes	Yes	159688 (NaDDC), 40631103 (KDDC)
870.5300	In vitro Mammalian Cell Gene Mutation Test	Yes	Yes	159779 (NaDDC), 4089901 (KDDC)
870.5375	In vitro mammalian chromosome aberration test	Yes	Yes	159681 (NaDDC)
870.5550	Unscheduled DNA Synthesis in Mammalian Cell Culture	Yes	Yes	40631101 (KDDC)
870.5900	In vitro Sister Chromatid Exchange Assay	Yes	Yes	159778 (NaDDC), 40631102 (KDDC)
870.6200	Neurotoxicity Screening Battery	Yes	Yes	43544201 (NaDDC)
870.6200	Neurotoxicity Screening Battery	Yes	Yes	43550501 (NaDDC)

Adapted from RED, Table 4, p. 7.

*MRID numbers not in references or profile

Table 5. Toxicity Profile of Sodium Dimethyldithiocarbamate (excluding acute studies)

Guideline No./ Study Type	MRID No./ Study Classification	Animals Tested and Dose Administered	Results
Subchronic Toxicity			
870.3100 90-Day Oral Subchronic (Rat)	MRID 42047201 Acceptable Core-Minimum	10 Sprague-Dawley rats/sex/dose Gavage dose at 0.2, 2, or 100 mg/kg/day for 13 weeks.	**LOAEL = 100 mg/kg/day,** based on decreased erythrocyte counts, increased glucose concentration, and increased alkaline phosphatase activity in females, and exocrine pancreatic atrophy with fibrosis in males. **NOAEL = 0.2 mg/kg/day**
870.3250 90-Day Dermal (Rabbit)	MRID 40140101 Acceptable/ Guideline	10 New Zealand White rabbits/sex/dose Dermal dose to the clipped unabraded dorsal surfaces at 0, 20, 60, or 120 mg/kg/day, 6 hours/day, 5 days/week for 13 weeks.	Systemic Toxicity **LOAEL = 120 mg kg/day**, based on decreased leukocyte and platelet counts. **NOAEL = 60 mg/kg/day** Dermal Irritation **LOAEL = 20 mg/kg/day,** based on redness, edema, and/or desquamation at the treatment site. **NOAEL Not Determined**
Developmental Toxicity			
870.3700a Developmental Toxicity (Rat)	MRID 40140102 Acceptable	22 Female Sprague-Dawley rats/dose Gavage in water at 0, 2, 20, or 200 mg/kg/day on gestation days 6-15, inclusive. On GD 20, dams were sacrificed and necropsied.	Maternal Toxicity **LOAEL = 2 mg /kg/day** based on decreased corrected body weights. **NOAEL Not Determined** Developmental Toxicity **LOAEL Not determined** **NOAEL ≥ 200 mg/kg/day** No treatment related effects
870.3700b Developmental Toxicity (Rabbit)	MRID 40165804 Acceptable	18 New Zealand White rabbits/dose Administered by gavage in distilled water at doses of 0, 0.4, 4, or 40 mg/kg/day on gestation days 7-19, inclusive. On GD 29, surviving does were sacrificed and necropsied.	Maternal Toxicity **LOAEL = 40 mg/kg/day**, based on decreased body weights. **NOAEL = 4 mg/kg/day** Developmental Toxicity **LOAEL Not Determined** **NOAEL ≥ 40 mg/kg/day** There were no treatment related effects
Mutagenicity			
870.5100 Bacterial Reverse Mutation Test	MRID 00159688 Acceptable	Concentrations of 4, 40, 133, 400 or 1333 µg ai/plate.	**Positive** Positive results (frequencies of revertants greater than twice solvent control) were registered in three strains (TA100, TA1535, and TA1537), both with/without metabolic activation at non-cytotoxic dose levels (lowest dose levels at which effects occurred: 4 or 40 µg/plate ± S9).

870.5300 In Vitro Mammalian Cell Gene Mutation Test	MRID 00159779 Acceptable	Chinese Hamster Ovary Cells	Negative
870.5375 In Vitro mammalian chromosome aberration test	MRID 00159681 Acceptable	Chinese Hamster Ovary Cell Cultures	Positive in the presence of S9
870.5900 In Vitro Sister Chromatid Exchange Assay	MRID 00159778 Acceptable	Chinese Hamster Ovary Cell Cultures	Negative
Neurotoxicity			
870.6200 Neurotoxicity Screening Battery	MRID 43544201 Acceptable	17 Sprague-Dawley rats/sex/dose Single gavage doses of 0, 20, 400, or 790 mg/kg/day.	Neurotoxicity **NOAEL = 20 mg /kg/day** **LOAEL = 400 mg /kg/day** based on clinical signs of toxicity, numerous FOB parameter effects and decreased motor activity ChE Inhibition **NOAEL= 790 mg /kg/day (HDT)** There were no test material-related effects on plasma, RBC, or brain ChE activity for males or females at any dose level.
870.6200 Neurotoxicity Screening Battery	MRID 43550501 Acceptable	15 Sprague-Dawley rats/sex/dose Gavaged at daily doses of 0, 0.2, 2, or 99 mg/kg/day for 13 weeks.	Systemic (Clinical) Toxicity **NOAEL = 2 mg/kg/day.** **LOAEL = 99 mg/kg/day** based on Salivation, oral staining and decreased body weight. Neurotoxicity **NOAEL > 99 mg/kg/day,** except for minor clinical effects at the HDT (salivation; wet-mouth staining; decreased body weight of 2% - 8% in males; 2% to 6% in females), no significant neurotoxic or other systemic effects were recorded.

Adapted from RED, Table A3, p. 46

Table 6. Toxicity Profile of Potassium Dimethyldithiocarbamate (excluding acute studies)

Guideline No./ Study Type	MRID No./ Classification	Dosing and Animal Information	Results
Subchronic Toxicity			
870.3200 21-Day Dermal (Rat)	MRID 40747003 Supplementary A pilot study for 90-day dermal study (MRID	Sprague-Dawley Rat (5/sex/dose) Doses of 0, 51.3, 128, 257, 385, or 513 mg/kg/day, respectively were applied 5 days/week for 3	Dermal Irritation **NOAEL: 257 mg/kg/day** **LOAEL: 385 mg/kg/day**, based on slight dermal irritation in 2-3 females but not males. In addition, at 1000 mg/kg/day 3/5

	40830801)	weeks. A gauze patch was applied to the dosing area for 6 hours per day.	males and 5/5 females exhibited slight dermal irritation Systemic Effects **NOAEL: 257 mg/kg/day** **LOAEL: 385 mg/kg/day** based on female body weight gain decrement and reduced food efficiency.
870.3250 90-Day Dermal (Rat)	MRID 40830801 Acceptable Core-Minimum	10 Sprague Dawley Rats/sex/dose Doses of 0, 38.5, 180, or 385 mg/kg/day for 6 hr/day, 5 d/wk for 13 weeks.	Dermal Irritation **LOAEL = 180 mg/kg/day,** based on mild to moderate acanthosis, partial eschar, and ulceration, with ulceration occurring at 385 mg a.i./kg/day **NOAEL: 38.5 mg/kg//day** Systemic Effects **LOAEL = 385 mg/kg/day,** based on reduced body weight in males, decreased erythrocyte count and hematocrit in males, and hemosiderosis in the spleens of both sexes. **NOAEL = 180 mg a.i./kg/day**
Developmental Toxicity - Teratogenicity			
870.3700a Developmental Toxicity (Rat)	MRID 40747001 Supplementary - Pilot Study for the main study MRID 41005501	8 Sprague-Dawley Rats/dose Doses via gavage to pregnant rats at 0, 51.3, 103, 205, 308, 410 mg/kg/day respectively from gestation days 6 through 15.	Developmental Toxicity **NOAEL = 51 mg/kg/day** **LOAEL = 205 mg/kg/day**, based on post-implantation loss and fetal weight decrements at 600 mg/kg/day and above Maternal Toxicity **NOAEL < 51 mg/kg/day** **LOAEL <51 mg kg/day**, based on body weight gain decrements. Salivation at 103 mg ai/kg/day and above.
870.3700a Developmental Toxicity (Rat)	MRID 41005501 Acceptable	28 Sprague-Dawley Rats/dose Doses via gavage in water at 0, 0, 12.8, 77, or 205 mg/kg/day, on gestation days 6-15, inclusive. On GD 20, dams were sacrificed and necropsied.	Maternal Toxicity **LOAEL: 77 mg/kg/day,** based on reduced body weights and body weight gains and reduced food consumption. **NOAEL: 12.8 mg/kg/day** Developmental Toxicity **NOAEL: ≥ 205 mg/kg/day(HDT)** At 205 mg a.i./kg/day, mean fetal weight was marginally decreased.
870.3700a Developmental Toxicity (Rabbit)	MRID 40747002 Supplementary – **Pilot** Study for the main study MRID 40995101	6 female rabbits/dose. Dose was via gavage to pregnant rats at doses of 0, 12.8, 26.6, 77, 154, or 256 mg/kg/day from gestation days 6 through 18.	Developmental Toxicity **NOAEL: 75 mg/kg/day** **LOAEL: 77 mg/kg/day** based on post-implantation loss and fetal weight decreases. Maternal Toxicity **NOAEL: 26.6 mg/kg/day** **LOAEL: 77 mg/kg/day** based on body weight gain decrements. Death occurred at 154 and 256 mg/kg/day

870.3700a Developmental Toxicity (Rabbit)	MRID 40995101 Acceptable	20 inseminated female Rabbits/dose Dose by gavage in water at 0, 0, 12.8, 38, or 77 mg/kg/day on GD 6-18, inclusive. On GD 29, the does were sacrificed and necropsied.	Maternal Toxicity **LOAEL: 38 mg/kg/day,** based on clinical signs (reddish-colored material in cage trays), and possible increased maternal death and abortions. **NOAEL: 12.8 mg /kg/day** Developmental Toxicity **LOAEL: 38 mg /kg/day,** based on malalignment of sternebrae, increased early and total implantation losses, and decreased fetal weights. **NOAEL: 12.8 mg /kg/day**
Mutagenicity			
870.5100 Bacterial Reverse Mutation Test (Rat)	MRID 40631103 Acceptable	*S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538	Positive
870.5300 In Vitro Mammalian Cell Gene Mutation Test	MRID 40899001 Acceptable	Chinese Hamster Ovary K1-BH4 (CHO) Cells	Positive
870.5550 Unscheduled DNA Synthesis in Mammalian Cell Culture	MRID 40631101 Acceptable	Rat hepatocyte cultures	Negative
870.5900 In Vitro Sister Chromatid Exchange Assay	MRID 40631102 Acceptable	Chinese Hamster Ovary Cells	Negative

Adapted from RED, Table A4, p. 53

VI. Additional Data Gaps

A multi-generation reproduction study, 90-day inhalation toxicity study, and combined chronic toxicity/carcinogenicity study conducted with sodium dimethyldithiocarbamate were identified as data gaps and are anticipated to be required studies for an adequate risk characterization. Structure activity relationship (SAR) analysis may be used to address the cancer study concern. If the industry is interested in the SAR approach, a complete and valid SAR analysis should be submitted by the registrant, and the Agency will consider the validity of the approach.

An *in vivo* mutagenicity study such as an erythrocyte micronucleus assay is anticipated to be required.

An immunotoxicity study is a data requirement for all antimicrobial pesticide chemicals under 40 CFR Part 158W, Data Requirements for Antimicrobial Pesticides. The registrant can address this data requirement by submitting a study according to the OCSPP 870.7800 guideline, citing information from the scientific literature that addresses immunotoxicity of DDC salts, or submitting a request for waiver of this study using the Agency's published guidance, available at: http://www.epa.gov/pesticides/regulating/part158-tox-data-requirement.pdf.

References for Appendix A

US EPA, 2009. Hazard Assessment for the Reregistration Eligibility Decision (RED) Document of Sodium Dimethyldithiocarbamate and Potassium Dimethyldithiocarbamate. February 5, 2009

Appendix B Environmental Fate

NaDDC and KDDC salts are active ingredients in antimicrobials that can be used as material preservatives in water systems (air washer, reverse osmosis, and industrial), commercial/industrial cooling water, industrial wastewater, pulp/paper mills, gas and oil (drilling muds/packer fluids, recovery injection water, fracturing fluids, workover and completion fluids), flue gas desulfurization thickeners in smokestacks at coal-fired power plants, and sugar mills (cane and beet).

The half-lives in environmental fate studies indicate that both parent NaDDC and its degradates can reach WWTPs where they will be associated with water instead of sludge based on their water solubilities (260,000-1.63 million mg/l)[22], log Kow values (-0.38-1.94) of less than 3, and limited sorption to soil (Koc values of 312-445 ml/g)[23]. Although the half-lives for NaDDC and its degradates in water are relatively short (ranging up to 6.7 days), these estimates of persistence are not short enough to prevent residues from entering WWTPs. Data on the half-life of NaDDC and its degradates in environmental media do not provide specific information on the potential for these compounds to be removed during the wastewater treatment process in which conditions are present that tend to promote removal of chemical substances from WWTPs, particularly via processes such as biodegradation and sorption.[24] Table B1 and Table B2 contain the chemical, physical, and environmental fate properties of the DDC salts and degradates.

Abiotic

Hydrolysis

Parent NaDDC is composed of DMA and CS_2 moieties. When hydrolyzed it forms DMA, CS_2, a re-combination of DMA and CS_2 called TMTU, TMTDS, which is also known as thiram, and TMTMS. A hydrolysis study[25] in buffered aqueous solutions demonstrated that abiotic hydrolysis of NaDDC is pH dependant. The rate of hydrolysis and the relative amounts of major degradates DMA and CS_2 increased with decreasing pH. Hence acidic conditions will favor the decomposition of the DDC anion into DMA and CS_2. Formation of oxidative degradates such as the disulfide appears to be more predominant in alkaline as opposed to acidic or neutral conditions. The estimated abiotic hydrolysis half-lives of NaDDC are 16.5 min, 29.4 hours and 42.8 days at pH 5, 7 and 9, respectively.

Photodegradation

A registrant-submitted study for photodegradation of NaDDC in water[26] did not track degradates. The photolytic half-lives at pH 5, 7 and 9 were 26 minutes, 17.6 hours and 21.2 hours, respectively. Two degradation products were observed in all samples and a third

[22] http://www.epa.gov/opptintr/exposure/pubs/episuite.htm
[23] MRID 00164056
[24] MRIDs 43180801, 40220701, 40365701, and 40365702
[25] MRID 43180801
[26] 835.2240, MRID 40220701

degradate was observed in all pH 7 and pH 9 samples. Though these degradates were not identified , the photodegradation in water study is satisfied with the combination of MRIDs 40220701 and 45651201[27], which is an acceptable study for the active ingredient Thiram. Thiram is a dimer of the DDC acid and therefore any degradates present are expected to be the same as for NaDDC. In MRID 45651201, parent Thiram photodegraded in water with a half-life of 6.6 hours and formed four degradates that reached significant ($\geq$10 % of applied parent Thiram) concentrations. Three of the four degradates were intact Thiram dimers with substitutions of oxygen for sulfur and additions of oxygens to sulfur. Thiram sulfone (addition of two oxygen molecules) reached up to 31 % of applied parent compound by 24 hours (end of study). Thiram oxo (oxygen substituted for a sulfur) reached 11 % of applied parent compound by 24 hours. Thiram oxo sulfone (both oxo and sulfone groups) reached up to 15.3 % by 12 hours and decreased to 9 % by 24 hours. The fourth degradate was a mixture of sulfonic acid monomers of DDC in either an oxo form or a thio (sulfur-containing) form. The sum of these sulfonic acid degradates increased to 17-21 % of applied thiram by 24 hours. Table B2 below contains the chemical and physical properties of these four degradates. No additional data are anticipated to be required.

Data on photodegradation on soil[28] were not submitted for either NaDDC or KDDC salts. However, acceptable data on photodegradation on soil were submitted in MRID 45724501 for the active ingredient Thiram. The half-lives of parent Thiram were 0.72 days for the irradiated treatment and 1.78 days for the dark control treatment, with a dark-control adjusted half-life of 1.2 days. CO_2 was the only significant (formed at $\geq$10 % of applied Thiram) degradate. The only current use that requires photodegradation on soil data is wood preservation, and that use is expected to be cancelled. No additional data are expected to be required.

Soil Adsorption/Desorption (Kd) and Octanol-Water Partition Coefficient (Koc)

In an adsorption/desorption study[29] on agricultural soils, the change in concentration of an aqueous NaDDC solution was determined for four soil types: Plainfield sand, California sandy loam, Plano silt loam and Hagerstown silty clay loam. At approximately 25°C adsorption values (Kd) were observed to be 6.0, 12.6, 6.5 and 1.45 mL/g, respectively. Corresponding Koc values were 343, 367, 445 and 312 mL/g, respectively. Desorption of adsorbed DDC salts generally ranged from 0-25% but no desorption values were calculated. Sorption of DDC salts to soil particles increases with increasing organic carbon (OC) content ($r^2 = 0.98$) and pH ($r^2 = 0.56$). No additional data are anticipated to be required.

Sludge Adsorption/Desorption

No data on sludge sorption (OCSPP GLN 835.1110) have been submitted. Sorption to sludge is not a likely route of dissipation because the log Kow is less than three (3). Therefore data are not anticipated to be required. [30]

[27] 45651201, 835.2240
[28] 835.2410
[29] 835.1230, MRID 00164056
[30] Final 158 W regulations, 40 CFR Part 158.2282, test note 19, at 78 FR 26991.

Biotic

Aquatic Metabolism

Aerobic and anaerobic aquatic metabolism also degrade NaDDC. In an aerobic aquatic metabolism study (MRID 40365701), rapid degradation of NaDDC was observed with an estimated half-life of 6 days. Three major unidentified degradates (Peaks A, B, & C) which are most likely to be TMTMS, TMTDS, and TMTU, respectively, were detected using high performance liquid chromatography (HPLC). Under anaerobic conditions, NaDDC degraded into the same three degradates as seen under aerobic metabolism with TMTDS being the major degradate identified. Non-linear half lives for TMTDS and TMTMS were 67 days and 15 days, respectively under the conditions of the study. Complete mineralization of the parent compound was evident under both aerobic and anaerobic conditions as indicated by the amount of carbon dioxide (CO_2) formed, 38% and 36%, respectively. No additional data are anticipated to be required.

Soil Metabolism

No aerobic soil metabolism data were submitted for parent NaDDC. However, an acceptable aerobic soil metabolism study (MRID 43734901) was submitted for Thiram which degraded with a non-linear half-life of 2.1 days in sandy loam soil. TMTU, TMU, TMTM, and CS_2 were minor (<10 % of applied Thiram) degradates. Evolved CO_2 accounted for 9.0% of the applied radioactivity at 2 days post-treatment and increased to a maximum of 75% by 205 days. The DT_{50}, DT_{75}, and DT_{90} for thiram were approximately 1.7, 4.8, and 9.8 days, respectively. No additional data are anticipated to be required for parent NaDDC.

The Agency also received registrant- submitted aerobic soil metabolism (OCSPP GLN 835.4100, MRID 43685901) and aerobic aquatic metabolism (OCSPP GLN 835.4300, MRID 43685902) studies for DEA, a surrogate compound for the degradate DMA. The half-lives of DEA in the studies were 1.7 and 11 days, respectively. No major degradates were formed in the studies. While DEA is an appropriate surrogate compound for DMA, there is no record of review for these studies. These studies will be formally reviewed prior to the risk assessment. Until these studies are reviewed and classified as appropriate for use in the risk assessment, they are included as anticipated data requirements.

Terrestrial Field Dissipation

Data on terrestrial field dissipation (OCSPP GLN 835.6100) were not submitted for either NaDDC or KDDC salts. The Agency has reviewed the need for these data and determined that the aerobic soil metabolism half-life of approximately two days indicates limited potential for leaching to ground water or runoff to surface water. No additional data are anticipated to be required.

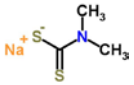
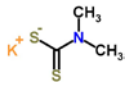
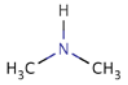
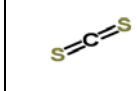
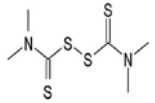
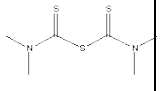
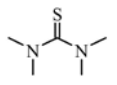
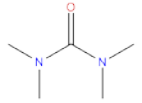
Leaching from Treated Wood

Data on leaching from treated wood were not submitted for either NaDDC or KDDC salts. This study is anticipated to be required. The preferred methods are AWPA E11-06 and E20-06 (see justification below). However, the only current use that requires data for leaching from treated wood is wood preservation, and that use is expected to be cancelled. If the use in wood preservation is cancelled, then this data requirement will no longer likely be needed.

Metabolism in Sewage Sludge and Activated Sludge Respiration Inhibition (ASRI)

No data on ASRI or on degradation in sewage sludge have been submitted but are anticipated to be required. The results of the ASRI test determine which of four tests are required and determines the extent of impacts to WWTP organisms. If the ASRI test EC_{50} is equal to or less than 20 mg/L, then one of three simulation tests would be anticipated to be required: OCSPP GLNs 835.3220, 835.3240, or 835.3280. If the ASRI test IC_{50} is greater than 20 mg/L, then the applicant can choose to conduct a ready biodegradability test (OCSPP GLN 835.3110) or one of the three simulation tests (*i.e.*, OCSPP GLNs 835.3220, 835.3240, or 835.3280). Pass criteria for the ready biodegradability study are: 70 percent removal of dissolved organic carbon and 60 percent removal of theoretical oxygen demand or theoretical CO_2 production for respirometric methods. These pass levels should be reached in a 10-day window within the 28-day period of the test. If the antimicrobial passes the ready biodegradability study, then no further testing is anticipated to be required. If the antimicrobial fails the ready biodegradability study, then the applicant should conduct one of the three biodegradation in activated sludge simulation tests mentioned previously.

Table B1 – Physical-Chemical and Fate Properties for Sodium and Potassium Dimethyldithiocarbamate Salts and Degradates

Test Guideline	Parent Compounds[31]		Degradates[32]						
	NaDDC	**KDDC[33]**	***Dimethylamine (DMA)***	***Carbon disulfide (CS_2)***	***TMTDS (Thiram)[34]***	***TMTMS[35]***	***TMTU[36]***	***TMU[37]***	**Reference (MRID for Parent Compounds unless Stated, EPI-Suite for Degradates)**
CAS Number	128-04-1	128-03-0	124-40-3	75-15-0	137-26-8	97-74-5	2782-91-4	632-22-4	EPI-Suite 4.11
Molecular Formula	$C_3 H_6 N_1 S_2 Na_1$	$C_3 H_6 N_1 S_2 K_1$	$C_2 H_7 N_1$	$C_1 S_2$	$C_6 H_{12} N_2 S_4$	$C_6 H_{12} N_2 S_3$	$C_5 H_{12} N_2 S_1$	$C_5 H_{12} N_2 O_1$	EPI-Suite 4.11
Molecular weight	143.20	159.31	45.08	76.13	240.42	208.36	132.22	116.16	EPI-Suite 4.11
Chemical Structure									N/A
Physical-Chemical Properties									
Melting Point (°C)	N/A[38]	N/A[39]	-92.2	-111.5	107	109.5	79.3	-1.2	EPI-Suite 4.11
Boiling Point (°C)	102	>100	6.8	46	339	301.3	245	176.5	EPI-Suite 4.11
Water Solubility (mg/L)	1.32×10^6	Easily soluble	1×10^6	2,160	30	1×10^6	350,000	1×10^6	EPI-Suite 4.11
Dissociation Constant in Water (pKa)	7.2	7.2	No data	No data	No data	No data	No data	No data	41609403 EPI-Suite 4.11
Octanol-water Partition Coefficient (Log K_{ow})	-2.41 (EPI-Suite 4.1)	-1.43 (EPI-Suite 4.1)	-0.38	1.94	1.73	0.75	0.49	0.19	EPI-Suite 4.11

[31] Chemical and physical properties of parent compounds relative to environmental risk assessment are listed in Table 4 above. Values in this Table B1 are copied from Table 4.
[32] Major degradates were formed at ≥10 % of applied parent compound. Minor degradates were formed at <10 % of applied parent compound.
[33] Environmental fate data were submitted for NaDDC but not KDDC. Both compounds are salts and therefore will readily disassociate in water to form the Na or K cations and the DDC anion. As a result, NaDDC is an acceptable surrogate for KDDC.
[34] DDC anion forms a cross-linked dimer TMTDS, which is joined by two (2) sulfur molecules. This dimer is the active ingredient Thiram (PC Code 079801).
[35] Cross-linked DDC anions joined by one (1) sulfur instead of two sulfurs.
[36] Tetramethyl thiourea (TMTU)
[37] Tetramethyl urea (TMU)
[38] Not applicable
[39] Not applicable

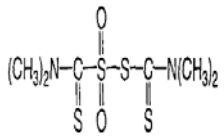
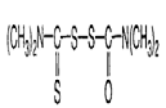
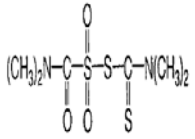
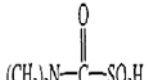
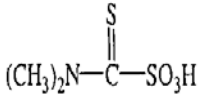
Test Guideline	Parent Compounds[31]		Degradates[32]						
	NaDDC	**KDDC[33]**	***Dimethylamine (DMA)***	***Carbon disulfide (CS_2)***	***TMTDS (Thiram)[34]***	***TMTMS[35]***	***TMTU[36]***	***TMU[37]***	**Reference (MRID for Parent Compounds unless Stated, EPI-Suite for Degradates)**
K_{oc} (ml/g)	312-445	No data[40]	4.7	48	676	337.3	25.7	8.6	00164056 EPI-Suite 4.11
Soil adsorption/ desorption (ml/g)	1.5-12.6	No data[41]	3.2	No data	No data	No data	No data	No data	00164056 EPI-Suite 4.11
Sludge adsorption/ desorption (%)	<1.9	<1.9	1.74	0.6	1.6	1.5	0.63	0.62	EPI-Suite 4.11
Bioconcentration Factor (BCF)	No data	No data	3.2	8.9	6.4	3.2	3.2	3.2	EPI-Suite 4.11
Vapor Pressure (mm Hg)	4.2×10^{-9}	8.2×10^{-10}	$1.5 \times 10^{+3}$	359	1.7×10^{-5}	2.7×10^{-4}	1.1×10^{-2}	$1.4 \times 10^{+1}$	EPI-Suite 4.11
Henry's Law Constant (atm-m^3/mole)	7.9×10^{-16}	2.0×10^{-16}	4.5×10^{-5}	1.2×10^{-2}	3.8×10^{-10}	8×10^{-10}	5.2×10^{-9}	5.0×10^{-5}	EPI-Suite 4.11
Abiotic Degradation Half-lives (days unless specified)									
Hydrolysis 835.2120	17 min (pH 5) 29 hours (pH 7) 43 days (pH 9)	No data	Stable, did not decline	Stable	Minor degradate	Minor	Not formed	Not formed	43180801
Photodegradation in water 835.2240[42]	3 hours (pH 5) 2.1 days (pH 7) 1.7 days (pH 9)	No data	No data	No data	No data	No data	No data	No data	40220701
Photodegradation in water 835.2240[43] for Thiram	No data	No data	No data	No data	6.6 hours (parent compound)	No data	No data	No data	45651201
Photodegradation on soil 835.2410[43], for Thiram	No data	No data	No data	No data	1.2 days (parent compound)	No data	No data	No data	45724501

[40] Data for NaDDC were used as a surrogate for KDDC
[41] Data for NaDDC were used as a surrogate for KDDC
[42] Unknown degradate was formed at up to 22-28 % of applied parent compound by 19 minutes, and declined to 1.4-3.3 % by 77 minutes. The 5/14/2009 environmental fate memorandum required another photodegradation in water study.
[43] Thiram data used as a surrogate for NaDDC and KDDC

Test Guideline	Parent Compounds[31]		Degradates[32]						
	NaDDC	**KDDC[33]**	***Dimethylamine (DMA)***	***Carbon disulfide (CS_2)***	***TMTDS (Thiram)[34]***	***TMTMS[35]***	***TMTU[36]***	***TMU[37]***	**Reference (MRID for Parent Compounds unless Stated, EPI-Suite for Degradates)**
Biotic Degradation Half-lives (days unless specified)									
Aerobic soil metabolism 835.4100 for Thiram	No data	No data	No major degradate formed	No major degradates formed	2.1 days (parent compound)	No major degradates formed	No major degradates formed	No major degradates found	43734901
Aerobic soil metabolism for **diethanolamine** (DEA)[44] 835.4100	No data	No data	1.7 day (diethanolamine)	No major degradates formed	No major degradates formed	No major degradates formed	No major degradates formed	No major degradates formed	43685901
Anaerobic soil metabolism 835.4200	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not applicable
Aerobic aquatic metabolism 835.4300	5.6 days	No data	Not formed	Not formed	7 days	Stable, did not decline	24 % at day zero, <4.3 % after	Not formed	40365702
Aerobic aquatic metabolism of Diethanolamine[45] 835.4300	No data	No data	7 days (diethanolamine)	No major degradates formed	No major degradates formed	No major degradates formed	No major degradates formed	No major degradates formed	43685902
Anaerobic aquatic metabolism 835.4400	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not applicable
Biodegradation half-life in sludge (days)	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not submitted	Not applicable

[44] Aerobic soil metabolism data on diethanolamine (MRID 43685901) were submitted as a surrogate for the dimethylamine (DMA) degradate.
[45] Aerobic aquatic metabolism data on diethanolamine (MRID 43685902) were submitted as a surrogate for the dimethylamine (DMA) degradate.

Table B2 – Physical-Chemical and Fate Properties for Degradates of Sodium and Potassium Dimethyldithiocarbamate Salts from Photodegradation in Water[46]

Test Guideline	*Thiram sulfone*	*Thiram oxo*	*Thiram oxo sulfone*	*DDC sulfonic acid monomer (oxo)*	*DDC sulfonic acid monomer (thio)*	Reference (MRID for Parent Compounds unless Stated, EPI-Suite for Degradates)
CAS Number	None	None	None	None	None	EPI-Suite 4.11
Molecular Formula	$C_6H_{13}N_2S_4$	$C_6H_{12}N_2OS_3$	$C_6H_{18}N_2O_3S_3$	$C_6H_7NO_4S$	$C_6H_7NO_3S_2$	EPI-Suite 4.11
Molecular weight	241.42	224.36	262.40	153.15	169.21	EPI-Suite 4.11
Chemical Structure						45651201
Melting Point (°C)	190.38	110.35	155.43	101.39	98.02	EPI-Suite 4.11
Boiling Point (°C)	452.44	344.70	428.80	325.94	320.06	EPI-Suite 4.11
Water Solubility (mg/L)	1×10^6	4.41×10^4	1×10^6	1×10^6	1×10^6	EPI-Suite 4.11
Dissociation Constant in Water (pKa)	N/A	N/A	N/A	N/A	N/A	EPI-Suite 4.11
Octanol-water Partition Coefficient (Log K_{ow})	-2.5	1.03	-1.58	-3.14	-2.47	EPI-Suite 4.11
K_{oc} (ml/g)	113.5	57.02	16.9	7.7	1	EPI-Suite 4.11
Soil adsorption/ desorption (ml/g)	No data	No data	No data	No data	No data	EPI-Suite 4.11
Sludge adsorption/ desorption (%)	1.75	1.80	1.75	1.75	1.75	EPI-Suite 4.11
Bioconcentration Factor (BCF)	3.16	2.21	3.16	3.16	3.16	EPI-Suite 4.11
Vapor Pressure (mm Hg)	7.9×10^{-9}	2.55×10^{-5}	1.85×10^{-10}	4.55×10^{-6}	7.22×10^{-6}	EPI-Suite 4.11
Henry's Law Constant (atm-m^3/mole)	2.51×10^{-15}	1.71×10^{-10}	6.38×10^{-17}	9.17×10^{-13}	1.61×10^{-12}	EPI-Suite 4.11
Abiotic Degradation Half-lives (days unless specified)						
Hydrolysis 835.2120	No data	No data	No data	No data	No data	No data

[46] Based on MRID 45651201, Photodegradation in water study for Thiram, a dimer of DDC acid.

Test Guideline	*Thiram sulfone*	*Thiram oxo*	*Thiram oxo sulfone*	*DDC sulfonic acid monomer (oxo)*	*DDC sulfonic acid monomer (thio)*	Reference (MRID for Parent Compounds unless Stated, EPI-Suite for Degradates)
Photodegradation in water 835.2240[47]	Stable, did not decline	Stable, did not decline	Stable, did not decline	Slight decline	Slight decline	45651201
Photodegradation on soil 835.2410	No data	No data	No data	No data	No data	Not applicable
Biotic Degradation Half-lives (days unless specified)						
Aerobic soil metabolism for **diethanolamine** (DEA)[48] 835.4100	Not formed	Not formed	Not formed	Not formed	Not formed	43685901
Aerobic soil metabolism 835.4100	No data	No data	No data	No data	No data	Not applicable
Anaerobic soil metabolism 835.4200	No data	No data	No data	No data	No data	Not applicable
Aerobic aquatic metabolism 835.4300	No data	No data	No data	No data	No data	Not applicable
Aerobic aquatic metabolism of Diethanolamine[49] 835.4300	Not formed	Not formed	Not formed	Not formed	Not formed	43685902
Anaerobic aquatic metabolism 835.4400	No data	No data	No data	No data	No data	Not applicable
Biodegradation half-life in sludge (days)	No data	No data	No data	No data	No data	Not applicable

[47] Unknown degradate was formed at up to 22-28 % of applied parent compound by 19 minutes, and declined to 1.4-3.3 % by 77 minutes. The 5/14/2009 environmental fate memorandum required another photodegradation in water study.
[48] Aerobic soil metabolism data on diethanolamine (MRID 43685901) were submitted as a surrogate for the dimethylamine (DMA) degradate.
[49] Aerobic aquatic metabolism data on diethanolamine (MRID 43685902) were submitted as a surrogate for the dimethylamine (DMA) degradate.

Appendix C Ecotoxicology Profile

Toxicity to Terrestrial Receptors

Avian acute-oral and dietary

Avian acute-oral and dietary toxicity data for the northern bobwhite (*Colinus virginianus*) and mallard (*Anas platyrhynchos*) categorize both DDC salts as being slightly to practically nontoxic to birds. Thiram, a degradate, is slightly to practically nontoxic based on acute-oral and dietary toxicity data for the northern bobwhite (*C. virginianus*) and mallard (*A. platyrhynchos*), Japanese quail (*Coturnix japonica*) and ring-necked pheasant (*Phasianus colchicus*). There are two avian reproduction studies with thiram, one with the northern bobwhite (*C. virginianus*) and one with the mallard (*A. platyrhynchos*). No additional avian data are anticipated to be required.

Avian Toxicity of Sodium and Potassium DDC Salts and Degradate

Study Type	Species	Test material (% ai)	Toxicity	Toxicity Classification	MRID & Status
Acute – Avian Oral GLN 850.2100	Northern bobwhite	NaDDC (40)	LD_{50}: 391 mg a.i./kg-bw/day (991mg ts/kg-bw/day)	Moderately toxic	00159788 Acceptable
		KDDC (50)	LD_{50}: 627 mg a.i./kg-bw (1255mg ts/kg-bw/day)	Slightly toxic	00105155 Acceptable
	Mallard	Thiram (99)	LD_{50}: >2800 mg/kg-bw/day	Practically nontoxic	00160000 Acceptable
	Red-winged black bird	Thiram (99)	LD_{50}: >100 mg/kg-bw/day	Unknown	00073683 Supplemental
	Ring-necked pheasant	Thiram (99)	LD_{50}: 673 mg/kg-bw/day	Slightly toxic	00160000 Supplemental
	Starling	Thiram (95)	LD_{50}: >5000 mg/kg-bw/day	Practically nontoxic	00022923 Acceptable
Subacute – Avian Dietary GLN 850.2200	Northern bobwhite	KDDC (50)	LC_{50}: >2600 ppm a.i. (>5200 ppm ts)	ts Practically nontoxic	00109244 Acceptable
		NaDDC (40)	LC_{50}: >2248 ppm a.i. (>5620 ppm ts)	ts Practically nontoxic	00159786 Supplemental
	Mallard	KDDC (50)	LC_{50}: >2500 ppm a.i. (>5000 ppm ts)	ts Practically nontoxic	00105156 Acceptable
		NaDDC (38.9)	LC_{50}: >2475 ppm a.i. (>6363 ppm ts)	ts Practically nontoxic	42561802 Acceptable
		NaDDC (40)	LC_{50}: 1874 ppm a.i. (4688 ppm ts)	ts Slightly toxic	00159787 Supplemental
		Thiram (95)	LC_{50}: 3950 ppm	Slightly toxic	00022923 Supplemental
		Thiram (95)	LC_{50}: 5000 ppm	Slightly toxic	00022923 Supplemental
	Japanese quail	Thiram (95)	LC_{50}: >5000 ppm	Practically nontoxic	00022923 Acceptable
	Ring-necked pheasant	Thiram (95)	LC_{50}: >5000 ppm	Practically nontoxic	00022923 Acceptable
Reproduction – Avian	Northern bobwhite	Thiram (97.5)	NOAEL: 500 ppm	NA	43612502 Acceptable

Study Type	Species	Test material (% ai)	Toxicity	Toxicity Classification	MRID & Status
GLN 850.2300	Mallard	Thiram (97.5)	NOAEL: 9.6 ppm	NA	45441201 Acceptable
		Thiram (97.5)	NOAEL <50 ppm	NA	43612501 Supplemental

ts: test substance

Beneficial Insects

No data are available for the DDC salts, there is an acute dermal contact study with the degradate thiram. Data (OCSPP GLNs 850.3020, 850.3030) are expected to be required for the wood preservative use of the DDC salts. If the use in wood preservation is cancelled, then this data requirement will no longer likely be needed.

Species, Age or size	% Purity	Design Exposure Type/ pH/ hardness/ temperature	Endpoint	Toxicity Category	MRID & Status
Honey bee (Apis mellifera), N.R. GLN 850.3020	Thiram Tech	Dermal contact	48-h LD_{50} = 74 µg/bee	Slightly toxic	00036935 Supplemental

Toxicity to Aquatic Receptors

Freshwater Fish, acute

Acute toxicity data for freshwater fish are available for rainbow trout (*Oncorhynchus mykiss*), bluegill (*Lepomis macrochirus*), and fathead minnow (*Pimephales promelas*). The potassium DDC salt is categorized as being highly to very highly toxic and the sodium DDC salt as slightly to moderately toxic. The combination of sodium DDC salt and Nabam is moderately toxic, and thiram, a degradate, is very highly toxic. No additional data are anticipated to be required.

Freshwater Fish Acute Toxicity of Sodium and Potassium DDC Salts and Degradate

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Toxicity Classification	MRID & Status
Acute - Freshwater Fish GLN 850.1075	Rainbow trout	NaDDC (40.9)	96-hr LC_{50}: 6700	Moderately toxic	42247901 Acceptable
		NaDDC (15) and Nabam (15)	96-hr LC_{50}: 1700 (as formulation)	Moderately toxic	00104057 Supplemental
		KDDC (50)	96-hr LC_{50}: 360	Highly toxic	00134589 Acceptable
		Thiram (99)	96-hr LC_{50}: 126	Highly toxic	McCann 1976 Test Number 1001 Acceptable
		Thiram (99)	96-hr LC_{50}: 46	Highly toxic	46249301 Supplemental
		Thiram (75)	96-hr LC_{50}: 320 (as formulation)	Highly toxic	Supplemental

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Toxicity Classification	MRID & Status
	Bluegill sunfish	NaDDC (40.5)	96-hr LC_{50}: 38,500	Slightly toxic	42504801 Acceptable
		NaDDC (15) and Nabam (15)	96-hr LC_{50}: 3400 (as formulation)	Moderately toxic	00104057 Supplemental
		Thiram (99)	96-hr LC_{50}: 42	Very highly toxic	00070801 Acceptable
		Thiram (75)	96-hr LC_{50}: 280 (as formulation)	Highly toxic	00090294 Supplemental
	Fathead minnow	KDDC (50)	96-hr LC_{50}: 60	Very highly toxic	ACC240946 Acceptable
	Harlequin fish	Thiram (80) formulation	96-hr LC_{50}: 7	Very highly toxic	05020144 Supplemental

Freshwater Fish, chronic

No data are available for the DDC salts. However, a flow-through life-cycle toxicity test with the fathead minnow (*Pimephales promelas*) is available for thiram. Time to hatch of the F1 generation and 4-week survival of the F1 generation were as sensitive as reproductive effects (reduced egg production and reduced spawning frequency). An early-life stage study (850.1400) with the DDC salts is anticipated to be required for assessing chronic risk to fish. For thiram, as the more sensitive acute fish was the bluegill sunfish, an acute-to-chronic ratio (ACR) method was used to calculate a chronic value for the bluegill sunfish. The Web-based Interspecies Correlation Estimation (Web-ICE[50]), version 3.2.1, application was first used to estimate acute toxicity of thiram to the fathead minnow from existing rainbow trout and bluegill sunfish data (results are provided at the end of this appendix). Web-ICE predicted a fathead minnow acute value for thiram 140 ppb based on the rainbow trout data; the rainbow trout correlation was used because it has a higher correlation than that for the bluegill sunfish, Comparing this fathead minnow acute value to the NOAEC from the fathead minnow full life cycle study provides an ACR of 127. Applying this ACR to the rainbow trout acute data provides an estimated NOAEC of 0.36 ppb thiram.

Freshwater Fish Chronic Toxicity of Thiram

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Endpoints	MRID & Status
Chronic – Freshwater Fish GLN 850.1500	Fathead minnow	Thiram (98.7)	NOAEC = 1.1 LOAEC = 2.2	F_0 egg production; F_0 % spawning frequency; F_1 4-week survival; F_1 time to hatch	47824101 Acceptable

[50] http://epa.gov/ceampubl/fchain/webice/

Freshwater Invertebrates, acute

Acute toxicity data for the water flea (*Daphnia magna*) categorize the sodium DDC salt as being very highly toxic and the potassium DDC salt as highly toxic. The degradate Thiram also is highly toxic. No additional data are anticipated to be required.

Freshwater Invertebrate Acute Toxicity of Sodium and Potassium DDC Salts and Degradate

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Toxicity Classification	MRID & Status
Acute – Freshwater Invertebrate GLN 850.1010	Water flea	NaDDC (40.5)	48-hr EC_{50}: 52	Very highly toxic	42504802 Acceptable
		KDDC (50)	48-hr EC_{50}: 340	Highly toxic	00105154 Acceptable
		Thiram (98)	48-hr EC_{50}: 210	Highly toxic	00164662 Acceptable

Freshwater Invertebrates, chronic

No data are available for the DDC salts. However, a thiram chronic study (MRID 47495001) is currently under review. A life cycle study (850.1300) is anticipated to be required for assessing chronic risk to aquatic invertebrates with the DDC salts.

Estuarine/Marine Fish and Invertebrates

Acute data are available for fish (sheepshead minnow, *Cyprinodon variegatus*) and the following invertebrates: Eastern oyster (*Crassostrea virginica*), mysid shrimp (*Mysidopsis bahia*), blue crab (*Callinectes sapidus*), and grass shrimp (*Palaemonetes pugio*). The data categorize sodium DDC salt as slightly toxic to fish and as highly to very highly toxic to invertebrates. The combination of sodium DDC salt and Nabam is moderately to very highly toxic. The degradate thiram is highly to very highly toxic. No additional data are anticipated to be required.

Estuarine/marine Acute Toxicity of Sodium DDC Salt and Degradate

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Toxicity Classification	MRID & Status
Acute – Saltwater Fish GLN 850.1075	Sheepshead minnow	NaDDC (48.3)	96-hr LC_{50}: 59,000	Slightly toxic	41984701 Acceptable
		NaDDC (16) and Nabam (15)	96-hr LC_{50}: 122 (as ts)	Highly toxic	00100706 Acceptable
		Thiram (98)	96-hr LC_{50}: 540	Highly toxic	42514401 Acceptable
Acute – Saltwater Invertebrate GLNs 850.1025/1055 850.1035	Eastern oyster	NaDDC (39.6)	96-hr EC_{50}: 760	Highly toxic	42561902 Acceptable
		NaDDC (16) and Nabam (15)	96-hr EC_{50}: 300 (as ts)	Highly toxic	00100704 Supplemental
		Thiram (98.3)	IC_{50} = 4.7 (embryo/larval development)	Very highly toxic	42488301 Acceptable

Study Type	Species	Test material (% ai)	Toxicity (µg ai/L)	Toxicity Classification	MRID & Status
	Mysid	NaDDC (39.6)	96-hr LC_{50}: 88	Very highly toxic	42561901 Acceptable
		Thiram (98.3)	LC_{50}: 3.36	Very highly toxic	42488302 Acceptable
	Grass shrimp	NaDDC (16) and Nabam (15)	LC_{50}: 17 (as ts)	Very highly toxic	00100705 Supplemental
	Blue crab	NaDDC (16) and Nabam (15)	LC_{50}: 9100 (as ts)	Moderately toxic	00100703 Supplemental

ts: test substance

Aquatic and terrestrial plants

Plant toxicity data are anticipated to be required for the DDC salts uses. Testing for aquatic plants is conducted with one species of aquatic vascular plant (duckweed, *Lemna gibba*) and four species of algae: (1) freshwater green alga, *Selenastrum capricornutum*, (2) marine diatom, *Skeletonema costatum*, (3) freshwater diatom, *Navicula pelliculosa*, and (4) bluegreen cyanobacteria, *Anabaena flos-aquae.* A seedling emergence test (OCSPP GLN 850.4100) also is anticipated to be required for rice (*Oryza sativa*), representing a rooted aquatic macrophyte. Data are not available for the DDC salts. Green algae and duckweed data are available for thiram.

A vegetative vigor study (OCSPP GLN 850.4150) is anticipated to be required to support an assessment of risk from exposure to residual biocides in waste water used for irrigation and from uses resulting in spray drift. Use patterns, such as the oil and gas uses, have the potential for waste water from the process to be used in irrigation. There are no vegetative vigor data for thiram or DDC salts. Uses that potentially result in spray drift, such as an anti-sapstain spray application, may result in exposure of non-target plants.

Aquatic Plants

Test Species	Test Material (% ai)	Toxicity Endpoint (µg ai/L)	EPA Study ID
Aquatic plants – vascular Duckweed, *Lemna gibba* GLN 850.4400	Thiram (98.7%)	IC_{50} = 1,600,000 NOAEC < 57,000	45441202 Acceptable
Aquatic plants - green algae, *Selenastrum capricornutum* GLN 850.4500	Thiram (99%)	IC_{50} = 45 NOAEC < 57 (will calculate IC_{05})	42646001 Acceptable
	Thiram (99%)	IC_{50} = 140 IC_{05} = NR	44086101 Acceptable

Mesocosm

A mesocosm study was conducted to simulate the potential impact of Thiram 80 WG (a water dispersible formulation containing 81.2% of the a.i. Thiram) contamination via spray drift from agricultural applications on a freshwater ecosystem under field conditions. There were seven treatment levels consisting of nominal Thiram 80 WG concentrations of 1.25, 4.0, 12.5, 40, 125,

400, and 1250 ppb Thiram 80 WG, which correspond to 1.0, 3.2, 10, 32, 100, 320, and 1000 ppb a.i. The mesocosm study design included three replicate mesocosm ponds for the negative control group and a single replicate mesocosm pond per treatment group. Four applications, simulating direct over-spray or spray drift, were made at 7-day intervals with identical application rates. Thiram quickly degraded in the water/sediment systems with a half-life ranging from 0.7 to 1.9 days.

In general, phytoplankton (at the community level) taxa abundance, diversity (based on the Shannon-Weaver index), evenness, and similarity (Steinhaus' and Stander's similarity indices) were reported to be significantly reduced during the treatment period at the two highest treatment levels tested; i.e, nominal 320 and 1000 ppb a.i. No significant treatment-related reductions in any individual phytoplankton taxa were meaningfully identified during the treatment period. However, these significant reductions in the above community parameters were attributed by the authors to treatment related reductions in zooplankton grazers and the subsequent rapid population growths, as supported by significant phytoplankton biomass, of those phytoplankton taxa with the most rapid population development/growth rates at the nominal 320 and 1000 ppb a.i. Therefore, true treatment-related negative effects as a result of Thiram 80 WG application on the phytoplankton community can be excluded with high probability at least up to and including the nominal 100 ppb a.i. treatment level. Consequently, the NOAEC for individual phytoplankton taxa and the community as a whole was concluded to be 106.5 ppb a.i. (measured; nominally 100 ppb a.i.). Periphyton biomass was significantly reduced also at the nominal 320 and 1000 ppb a.i. treatment levels. Treatment-related effects on specific taxa were never discussed within the study report.

Due to the significant negative concentration-effect relationship in zooplankton taxa abundance during the treatment period, the NOAEC for zooplankton taxa abundance was 2.1 ppb a.i. (measured; nominally 3.2 ppb a.i.). Zooplankton community diversity (based on ShannonWeaver Index) and evenness were not significantly affected during the treatment period. Similarity analysis of the treated zooplankton communities was compared to the control ponds using Steinhaus' and Stander's indices. The NOAEC value for zooplankton community similarity during the treatment period was <1.0 ppb a.i. (measured; nominally <1.0 ppb a.i.); i.e. less than the lowest treatment concentration tested.

Test material concentrations were not measured in all treatment ponds following each application and did not allow for an exact determination of what concentrations the mesocosm flora and fauna were exposed. The overall short duration of the study, less than 1 year for the in-life portion of the study, also prevented the assessment of chronic effects of Thiram 80 WG and did not allow for the comparison of the treated community structure compared to the structure from untreated or post-treatment years. This study provides only supplemental data because only five of the seven treatment levels were actually analytically verified during the study and because this study does not fulfill any current US EPA OPP guideline requirement. Additionally there was no true replication of treatment levels. Conclusions, provided in this study may be useful for characterization.

Test Species	Test Material (% ai)	Toxicity Endpoint	EPA Study ID
Mesocosm: Multiple species Non-Guideline	Thiram 80 WG (80)	Zooplankton community similarity NOAEC < 1.0 ppb a.i. *Hexarthra mira/intermedia* NOAEC was < 1.0 ppb a.i. (measured)	Supplemental

WebICE Results for Estimating Fathead Minnow Acute using Rainbow Trout

Surrogate Species: Rainbow trout (*Oncorhynchus mykiss*)

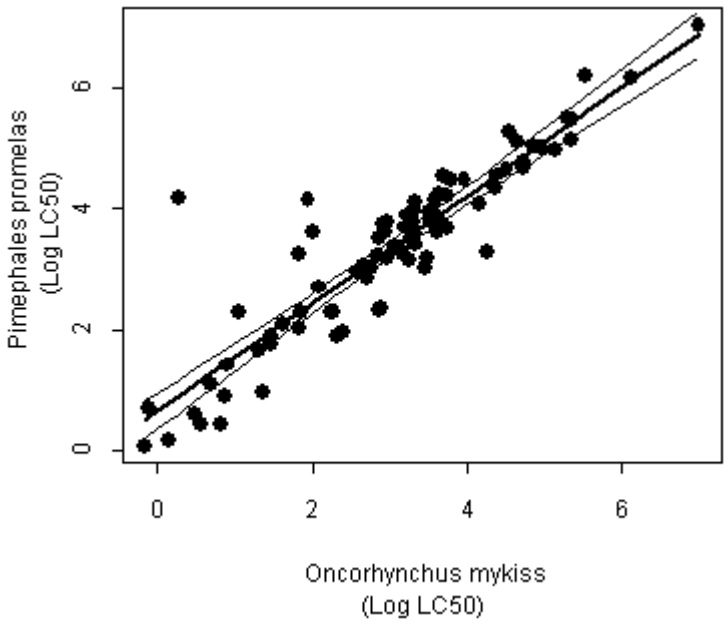
Predicted Species: Fathead minnow (*Pimephales promelas*)

Surrogate Acute Toxicity (log value)	Predicted Acute Toxicity (log value)	
46 µg/L (1.66)	140.16 µg/L (2.14)	
Select Confidence Interval:	**Lower Limit**	**Upper Limit**
95%	92.35 µg/L	212.71 µg/L

Model Information

Intercept:	0.669768
Slope:	0.888200
Degrees of Freedom (N-2):	79
R^2:	0.825954
p-value:	0.000000
Average value of surrogate (log value):	1077.24 (3.03)
Minimum value of surrogate (log value):	0.671479 (-0.172967)
Maximum value of surrogate (log value):	9800000.00 (6.99)
Mean Square Error (MSE):	0.372276
Sum of Squares (S_{xx}):	176.91

Cross-validation Success (%):	82.71
Taxonomic Distance:	4



WebICE Results for Estimating Fathead Minnow Acute using Bluegill Sunfish

Surrogate Species: Bluegill (*Lepomis macrochirus*)

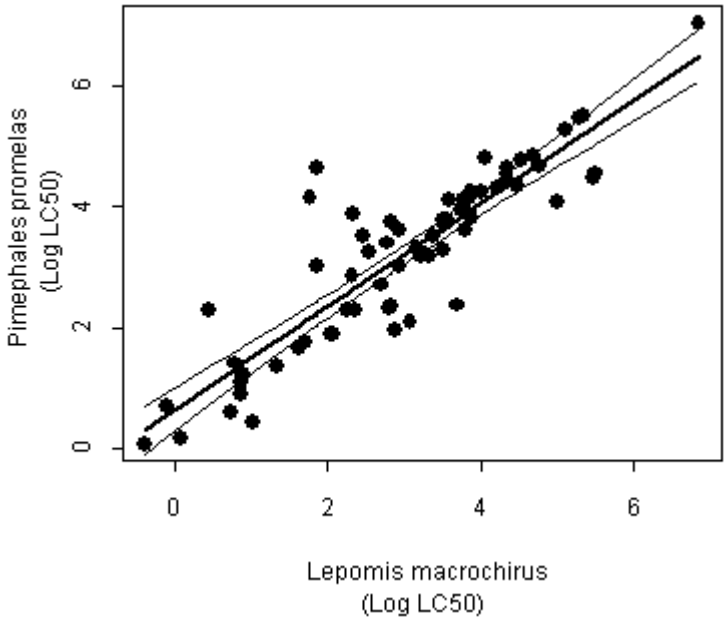
Predicted Species: Fathead minnow (*Pimephales promelas*)

Surrogate Acute Toxicity (log value)	Predicted Acute Toxicity (log value)	
42 µg/L (1.62)	109.55 µg/L (2.03)	
Select Confidence Interval:	**Lower Limit**	**Upper Limit**
95%	66.32 µg/L	180.97 µg/L

Model Information

Intercept:	0.663875
Slope:	0.847538

Degrees of Freedom (N-2):	66
R^2:	0.790938
p-value:	0.000000
Average value of surrogate (log value):	1174.34 (3.06)
Minimum value of surrogate (log value):	0.407815 (-0.389536)
Maximum value of surrogate (log value):	7100000.00 (6.85)
Mean Square Error (MSE):	0.431786
Sum of Squares (S_{xx}):	150.09
Cross-validation Success (%):	75.00
Taxonomic Distance:	4



Appendix D Product Chemistry

Sodium dimethyldithiocarbamate and Potassium dimethyldithiocarbamate salts product chemistry information is summarized in Table E1 (source: MRIDs 41586303, 41609403, 41651301, 42510401, and 41609407 and EPI Suite v4.1).

Table E1 – Product Chemistry of Sodium and Potassium Dimethyldithiocarbamate Salts

Guideline No.	Physical and Chemical Properties	Sodium dimethyldithiocarbamate	Potassium dimethyldithiocarbamate
830.1550	Product identity and composition	Refer to Table 3.	Refer to Table 3.
830.1600	Description of materials used to produce the product	Confidential Business Information (CBI)	CBI
830.1620	Description of production process	CBI	CBI
830.1650	Description of Formulation Process	CBI	CBI
830.1670	Discussion of formulation of impurities	CBI	CBI
830.1700	Preliminary analysis	CBI	CBI
830.1750	Certified limits	CBI	CBI
830.1800	Enforcement analytical method	Purity of dimethyldithiocarbamate is determined by acidic decomposition	Purity of dimethyldithiocarbamate is determined by acidic decomposition
830.1900	Submittal of samples	CBI	CBI
830.6302	Color	Yellow-green to amber liquid	Pale yellowish green liquid. Clear light amber liquid.
830.6303	Physical State	Liquid	Liquid
830.6304	Odor	Mild characteristic of sulfur-containing compounds	Mild characteristic of sulfur-containing compounds. Slight sulfur odor. Pungent, ammoniacal odor.
830.6313	Stability to normal and elevated temperature, metals/metal ions	Stable under recommended storage conditions. Stable up to 70 °C for extended periods.	Stable under recommended storage conditions. Stable up to 50 ± 2 C for a 30 day period.
830.6314	Oxidation/Reduction: Chemical Incompatibility	Does not contain an oxidizing or reducing agent. Incompatible with strong acids, strong oxidizing agents. (40% w/w aqueous solution)	Does not contain an oxidizing or reducing agent. Incompatible with strong acids, strong oxidizing agents. (50% w/w aqueous solution)
830.7000	pH	As measured 13.3 at 20°C. 10.1 (1% aqueous solution) -HPV 12.6 (32% aqueous solution) -HPV	9-14 (50% solution)

Guideline No.	Physical and Chemical Properties	Sodium dimethyldithiocarbamate	Potassium dimethyldithiocarbamate
830.7050	UV/Visible Absorption	Sodium dimethyldithiocarbamate was identified by UV/VIS spectra recorded at different pH values. Result at pH < 2: > 200 nm, ε = 0 l mol^{-1} cm^{-1} Result at pH 7: 254 nm, ε = 12792 l mol^{-1} cm^{-1} 279 nm, ε = 13127 l mol^{-1} cm^{-1} 295 nm, ε = 1863 l mol^{-1} cm^{-1} Result at pH > 11: 254 nm, ε = 13388 l mol^{-1} cm^{-1} 279 nm, ε = 13687 l mol^{-1} cm^{-1} 295 nm, ε = 1803 l mol^{-1} cm^{-1}	Potassium dimethyldithiocarbamate was identified by UV/VIS spectra recorded at different pH values. Result at pH < 2: 207 nm, ε = 12713 l mol^{-1} cm^{-1} Result at pH 7: 253 nm, ε = 26409 l mol^{-1} cm^{-1} 279 nm, ε = 28187 l mol^{-1} cm^{-1} 495 nm, ε = 3562 l mol^{-1} cm^{-1} Result at pH > 11: 254 nm, ε = 12714 l mol^{-1} cm^{-1} 279 nm, ε = 13120 l mol^{-1} cm^{-1}
830.7100	Viscosity	20.2 centipoise (cps) at 20°C	20.2 cps at 20°C
830.7200	Melting point	Not applicable. It is a liquid. MP Performed on PAI: > 300 °C with decomposition.	Not applicable. It is a liquid. MP Performed on PAI: > 300 °C with decomposition.
830.7220	Boiling point	Not required since PAI is solid Boiling point of 32% solution: 102°C	Not required since PAI is solid. Boiling point of 50% solution: >100°C
830.7300	Density	1.17 g/ml (40% solution)	1.25 g/ml (50% solution)
830.7370	Dissociation Constant in water	pKa = 5.4 for the organic portion/ Estimated/(40% w/w aqueous solution). 6.5 x 10^{-8} at 20°C. Performed on PAI. pKa value: Not applicable; product decomposes below pH 8. – HPV	pKa = 5.4 for the organic portion/ Estimated/(40% w/w aqueous solution). 6.5 x 10^{-8} at 20°C. Performed on PAI.
830.7520	Particle size, fiber length, & diameter distribution	Not Applicable; soluble in water	Not Applicable; soluble in water
830.7550	Partition coefficient (*n*-octanol/water)	Performed on PAI. Estimated to be less than 1 based on solubility at 20°C. −2.41 (EPI Suite v4.1)	−1.43 (EPI Suite v4.1)
830.7840	Solubility in water	Complete 132 g/100 ml of water at 20 °C Performed on PAI.	Complete. Easily soluble in water.
830.7860	Solubility in organic solvents	Methanol 89 g/100 g at 20°C Glycol 94 g/100 g at 20°C Performed on PAI.	Not reported (Not required).
830.7950	Vapor pressure	Solid: 4.17 x 10^{-9} mm Hg at 25°C (EPI Suite v4.1). 40% w/w as aqueous solution: 13 mm Hg at 25°C.	Solid: 8.15 x 10^{-10} mm Hg at 25°C (EPI Suite v4.1).