Didecyl Dimethyl Ammonium Chloride
(DDAC)
Final Work Plan

Registration Review: Initial Docket
Case Number 3003

March 2017

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TERMS, ABBREVIATIONS AND SYMBOLS

AD	Antimicrobials Division
ADBAC	alkyl dimethyl benzyl ammonium chloride
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
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations
CHO	Chinese hamster ovary
CIP	Circulate in Place
CMA	Chemical Manufacturers Association
CO_2	carbon dioxide
COC	concentration-of-concern
cPAD	chronic population adjusted dose
DDAC	Didecyl Dimethyl Ammonium Chloride
DCI	data call-in
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
FCN	food contact notification
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FWP	Final Work Plan
g/mol	grams per mole
GLN	guideline number
HEC	Human Equivalent Concentration
HPV	high production volume
IDS	Incident Data System
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
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
PWR	potable water rinse
QSAR	quantitative structure-activity relationship
RED	Reregistration Eligibility Decision
RO	Reverse Osmosis
SAR	structure activity relationship
SF	safety factor
SSTS	Section Seven Tracking System
TEP	typical end-use product
TGAI	technical grade active ingredient
TMDL	total maximum daily loads
UF	uncertainty factor
UV/VIS	ultraviolet/visible light absorption
% w/w	percent weight per weight.
WP	wettable powder
WWTPs	wastewater treatment plants

Table of Contents

List of Tables

1 Introduction

This document is the United States Environmental Protection Agency's (USEPA, EPA or "the Agency") Final Work Plan (FWP) for the Didecyl Dimethyl Ammonium Chloride chemical case, also known as the aliphatic alkyl quaternary chemical case, herein referred to as DDAC. The FWP document explains what EPA's Office of Pesticide Programs (OPP) knows about DDAC, 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 a screening-level dietary risk assessment and an anticipated timeline for completing DDAC's review.

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 DDAC and what types of new data or other information would be helpful for the Agency to receive as it moves toward a decision on DDAC.

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://www2.epa.gov/pesticide-reevaluation.

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.

1.2 Updates to the Workplan

Since the publication of the Preliminary Work Plan (PWP), the Agency has made the following updates:

- Updated Section 1 to reflect the cancellation of the only remaining product from DDAC's PC Code 069146, and updated Table 5 to reflect the current number of EPA registered products that contain DDAC.

- Updated Section 1.7.1 to reflect the current number of human health incidents and to incorporate responses to the Weber (2016) article.
- Updated Section 2, "Anticipated Data Needs". In Table 10, a footnote was added to guideline numbers 850.3030, 850.3040, 875.2500, 860.1340, 860.1380, 860.1480, and Non-Guidelines: Tier I Honey bee larvae chronic oral toxicity, Tier I Honey bee adult chronic oral toxicity, and Tier II Semi-field testing for pollinators. Footnotes were deleted from Non-Guidelines: Tier I Honey bee adult acute oral toxicity, Tier I Honey bee larvae acute oral toxicity, Tier I Honey bee larvae chronic oral toxicity, Tier I Honey bee adult chronic oral toxicity, Tier II Semi-field testing for pollinators, and Tier III Field testing for pollinators. Test substances were added to 850.3300 and changed for Non-Guideline: Tier II Semi-field testing for pollinators. The timeframe was changed for guideline numbers 875.2100 and 875.2500. In Table 11, study statuses were updated and additional footnotes were added.
- Deleted the "Guidance for Commenters" Section.
- Updated Section 7, "Next Steps".
- Updated spelling and grammatical errors.

No public comments were received on the initial docket. No changes were made to the registration review schedule of DDAC. This document makes final the work plan for the DDAC registration review process.

1.3 Case Overview

The docket for DDAC (case 3003) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2015-0740. Documents associated with this registration review can be viewed in this docket. Tables 1 and 2 below summarize the assessments and data needs relevant to this registration review case and the anticipated registration review schedule. Data required for reregistration are summarized in Table 11.

Table 1 - Anticipated Risk Assessments for Registration Review

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 10 for details)
Dietary (food)	Yes	2006	Updated	Residue Data
Dietary (drinking water)	Yes[1]	N/A	New	Activated Sludge Sorption Isotherm (ASSI), WWTP Biodegradation, and Activated Sludge Respiration Inhibitor (ASRI)
Occupational Handler	Yes	2006	Updated	None
Occupational Post Application (Antimicrobial)	Yes	2006	Updated	None
Occupational Post Application (Conventional)	Yes	N/A	New	Dislodgeable Foliar Residue
Residential Handler	Yes	2006	Updated	None

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 10 for details)
Residential Post Application (Antimicrobial)	Yes	2006	Updated	Post Application Inhalation Exposure
Residential Post Application (Conventional)	Yes	2006	Updated	Turf Transferable Residue Dissipation
Aggregate	Yes	2006	Updated	None
Cumulative	No	N/A	None	None
Tolerance Review	Yes	2006	Updated	None
Ecological – antimicrobial and conventional uses	Yes	2006[2]	Updated	Chronic toxicity data for benthic invertebrates.

N/A = Not applicable
[1] If the Agency receives environmental fate data which demonstrate strong sorption to activated sludge and a lack of toxicity to WWTP microorganisms, the Agency would not anticipate conducting a drinking water risk assessment.
[2] For the Reregistration Eligibility Decision (RED), the antimicrobial uses assessed were once-through cooling towers and wood preservatives (antisapstain use) while the conventional uses assessed were applications to puddles, ornamental ponds, and pools.

Table 2 - Anticipated Registration Review Schedule

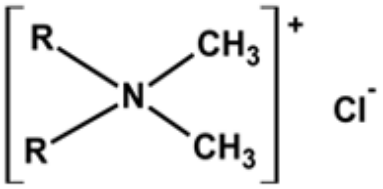
Anticipated Activity	Target Date*	Completion Date
Phase 1: Opening the Docket		
Open Docket and 60-Day Comment Period for Preliminary Work Plan	2016-09	2016-09
Close Public Comment Period	2016-11	2017-01
Phase 2: Case Development		
Issue Final Work Plan	2017-03	2017-03
Issue Data Call-In (DCI)	2018-03	
Receive Data to be Considered in Risk Assessment	2020-03	
Open 30-Day Public Comment Period for Preliminary Risk Assessment(s)	2021-09	
Close Public Comment Period	2021-10	
Phase 3: Registration Review Decision and Implementation		
Open 60-Day Public Comment Period for Proposed Decision	2022-03	
Close Public Comment Period	2022-05	
Issue Final Decision	2022-09	
Begin Post-Decision Follow-up	2022-09	
Total (years)	6	

*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).

1.4 Chemical Identification and Properties

Tables 3 and 4 present the chemical and physical properties of the active ingredient to be assessed in case 3003: DDAC. The DDAC chemical case is composed of 5 compounds (PC Codes: 069149, 069165, 069166, 069173, and 129012). The Agency will use Didecyl Dimethyl Ammonium Chloride (PC code 069149) as the model compound because this active ingredient has the highest number of active registrations and therefore, is expected to be the most representative compound for this case.

Table 3 – Chemical Identification of Representative DDAC Active Ingredient

Chemical Name	DDAC
Chemical Classification	Quaternary Amines
PC Code	069149
CAS Number	7173-51-5
Molecular Formula	$R_2C_2H_6NCl$ ($R=C_{10}$)
Molecular Weight (grams/mole)	362.08
Molecular Structure	

The DDAC product chemistry and physical property information relevant to risk assessment is summarized in Table 4 and the details of the environmental fate information are discussed in Appendix B.

Table 4 – Physical-Chemical Properties for DDAC (PC Code 069149)

Guideline No.	Parameter	Value	Source (MRID unless specified)
830.7000	pH	6.31	44520303
830.7050	UV/Visible Absorption	None in 290-800nm range	46588002
830.7300	Density (g/cm^3 at 25 °C)	0.9216	44520303
830.7370	Dissociation constant (pKa)	N/A	49740501
830.7550	Octanol-water partition coefficient at 25 °C (Log K_{ow})	4.66	EpiSuite v.4.11
830.7840	Solubility in water (mg/L)	Completely soluble	44520303
830.7950	Vapor pressure (mmHg) at 25 °C	$2.33x10^{-11}$	EpiSuite v.4.11
None	Boiling Point (°C)	534.70	EpiSuite v.4.00
None	Henry's law constant at 25 °C ($atm-m^3/mol$)	$6.85x10^{-10}$	EpiSuite v.4.11

$atm-m^3/mol$ = atmosphere cubic meter per mole; °C = degrees Celsius; mg/L = milligrams per liter; mmHg = millimeters of mercury

1.5 Use/Usage Description

1.5.1 Registrations

There are 279 EPA-registered products that contain DDAC as an active ingredient (a.i.), 278 of which are antimicrobial-registered products and 1 that is a conventional-registered product.

The conventional registered product (EPA Registration Number 1021-2559) is a ready to use household insecticidal product co-formulated with antimicrobial active ingredients. This product contains three insecticides (cypermethrin, pyrethrins and prallethrin) and four antimicrobial ingredients (1 ABDAC and 3 DDAC chemicals). This insecticidal product is also registered for use as a disinfectant and sanitizer on pre-cleaned non-porous, non-food surfaces. Cypermethrin, pyrethrins and prallethrin will be assessed separately from DDAC.

Of the 278 antimicrobial-registered products, 7 products also include conventional uses. These 7 products include 5 end-use-products and 2 technical products. One of these end-use-products (397-13) contains an insecticidal a.i. (phenothrin) and three antimicrobial a.i.s (DDAC, ADBAC and isopropyl alcohol). The remaining 4 end-use-products (9150-11, 81820-2, 10324-108 and 10324-117) contain only antimicrobial ingredients. The conventional uses of 9150-11 and 81820-2 include dipping applications for bulbs, seeds, roots, and foliar drench, or fogging in coolers to cut flowers and potted plants in greenhouses. According to the product label for 9150-11, bulb dip "treatment acts as a surface disinfectant for a variety of fungal and bacterial pathogens but will not control systemic pathogen events". The conventional uses of 10324-108 and 10324-117 include hard surface spray and floor drain treatment for the control of small fruit and drain flies.

Table 5 presents the DDAC chemical case's 5 structurally similar quaternary ammonium compounds (quats), CAS numbers, ingredient names, and active registrations (at the time of DDAC's FWP publication to the docket). The formulations include pressurized liquids, emulsifiable concentrates, soluble concentrates, ready-to-use solutions, aerosols, and impregnated materials (i.e. wipes). The product pesticide types include disinfectants, bacteriocides, bacteriostats, fungicides, fungistats, virucides, sanitizers, microbicides, microbiostats, algaecides, tuberculocides, antimicrobials, miticides, and insecticides. Many of the DDAC products contain multiple active ingredients including but not limited to: other DDAC chemical case compounds, Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) chemical case compounds[1], glutaraldehyde, isopropyl alcohol, chlorine dioxide, and pyrethroid insecticides.

[1] Documents relevant to the registration review of the Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) chemical case (case number 0350) can be accessed at http://www.regulations.gov in docket number EPA-HQ-OPP-2015-0737. The ADBAC case, which includes active ingredients structurally similar to DDAC active ingredients, is also being assessed through registration review.

Table 5 – Number of EPA Registered Products that contain DDAC Sorted by PC Code

PC code	CAS Number	Ingredient Name	Number of Active Antimicrobial Product Registrations as of 3/14/17 [1]	Number of Active Conventional Product Registrations as of 3/14/17 [1]
069149	7173-51-5	Didecyl dimethyl ammonium chloride	260	1
069165	32426-11-2	1-Decanaminium, N,N-dimethyl-N-octyl-, chloride	133	1
069166	5538-94-3	1-Octanaminium, N,N-dimethyl-N-octyl-, chloride	146	1
069173	68607-28-3	Oxydiethylenebis(alkyl* dimethyl ammonium chloride) *(as in fatty acids of coconut oil)	4	0
129012	61789-18-2	Alkyl* trimethyl ammonium chloride *(as in fatty acids of coconut oil)	1	0

[1] Several of DDAC's products contain multiple active ingredients. As a result, many products are recorded more than once under multiple DDAC PC Codes.

The individual exposure scenarios in DDAC assessments are developed by summing the total percent of DDAC active ingredients on a product's label.

1.5.2 Summary of Registered Uses

Table 6 presents a summary of the registered uses of DDAC that will be assessed in this registration review. This table also includes the application methods.

Table 6 – DDAC Registered Uses that will be Assessed During Registration Review

Use	Application Method	DDAC Concentration Range/ Application Rate[1]
Agricultural Premises and Equipment		
Hard Surface Sanitizer/Disinfectant Hoof Trimming Equipment Entryway Shoe Baths Hatchery Rooms Incubators and Hatchers	Spray, Mop, Sponge, Wipe Dip Shoe Bath Fog Fog	120 to 1200 ppm 72 to 792 ppm 72 to 792 ppm 1.1 to 2.9% 1760 to 6000 ppm
Aquatic Areas		
Decorative fountains and water displays	Open pour	2 ppm
Commercial, Industrial, Institutional, Premises and Equipment		
Cadavers - Cleansing Exterior Surfaces Hard Surface Sanitizer/Disinfectant Commercial Laundry	Sponge, Towel, Brush Spray, Mop, Sponge Open pour	281 to 800 ppm 100 to 15000 ppm[2] 387 to 390 ppm

Use	Application Method	DDAC Concentration Range/ Application Rate[1]
Wood, wallboard, urethane insulation, masonry Garbage trucks and equipment	Spray Spray	510 to 1000 ppm 270 ppm
Food Handling/Storage Establishments Premises and Equipment		
Hard Surface Sanitizer/Disinfectant Egg Shell Sanitation, Egg washing Dairies, beverage and food processing plants	Spray, Mop, Sponge Spray Fog	90 to 3780 ppm 90 to 282 ppm 720 ppm
Human Drinking Water (Sanitization of Interior Hard Surfaces of Equipment and Tanks)		
Ice Machines, Water holding tanks, Reverse Osmosis (RO) units	Open Pour, Spray, Circulate in Place (CIP)	90 to 120 ppm
Industrial Processes and Water Systems		
Cooling Water Systems, Recirculating Cooling Water Systems, Once Through Oil and gas drilling and fracturing fluids Paper Mill Processing Water (Whitewater) Wastewater Systems	Open pour Open pour Open pour Open pour Open pour	12 ppm 3.6 ppm 565 to 1,000 ppm 90 to 149 ppm 154 ppm
Material Preservative		
Paper Coatings, Pigments and Fillers	Open Pour	16 to 98 ppm
Medical/Dental/Veterinary Premises and Equipment		
Hard Surface Sanitizer/Disinfectant Salon/Barber instruments and tools	Spray, Mop, Sponge, Wipe Spray, immersion	90 to 15,000 ppm[2] 200 to 7600 ppm[3]
Residential and Public Access Premises		
Hard Surface Sanitizer/Disinfectant Carpet Cleaner Interior Building or Wall Surfaces Waterbed Water HVAC Units and Dehumidifiers Humidifier Water	Spray, Mop, Sponge, Wipe Spray, Truck Mounted Extraction Units Spray Open Pour Spray, Liquid Pour Liquid Pour	90 to 15,000 ppm[2] 204 to 6,200 ppm 4000 ppm 20 to 98 ppm 520 ppm 3.6 to 760 ppm[4]
Swimming Pools and Spas		
Pool and Spa Water Treatment	Open Pour Liquid or Place Solid	2 ppm
Wood Preservation		
Seasoned lumber (termite control) Fresh cut lumber (sapstain control) Existing wood shingle/shake roofs and siding	Pressure Treat/Double Vacuum Dip or Spray Brush or Spray	0.1 to 0.6 pcf 1.9 to 3.0% 0.5 to 3.0%
Conventional Uses		
Bulbs and Corms Broccoli/flower seed Ornamental Plants, Nursery Stock	Immersion Immersion Foliar Spray	900 ppm 1,200 ppm 230 ppm

Use	Application Method	DDAC Concentration Range/ Application Rate[1]
Root drench	Fertilizer Injector Pumps	300 ppm
Cut Flowers and Potted Plants in Coolers	Fog	300 ppm
Turf, Golf Course, Commercial, Residential	Spray	Unknown[5]
Restaurant/Food storage area surfaces/drains	Spray	0.5 oz/gal water

[1] Many products contain more than one DDAC a.i. and one or more ADBAC a.i. The concentration range/application rate is the sum of the DDAC a.i.s. The rate does not include the ADBAC a.i.s.

[2]The rate of 15,000 ppm is for EPA Reg. No. 6836-276. The rate for all other labels is 90 to 2100 ppm, 90 to 511 ppm, and 90 to 3000 ppm for commercial, medical, and residential uses, respectively.

[3]The rate of 7600 ppm is for EPA Reg. No. 46781-12.

[4] The rate of 3.6 ppm is from EPA Reg. No. 69741-2 and the rate of 760 ppm is from EPA Reg. No. 10324-72.

[5]The turf and golf course uses are included on four formulation intermediate labels (EPA Reg. Nos. 1839-63, 1839-77, 1839-135 and 1839-119). These labels do not include application rates. These uses are not included on any end-use product labels. The registrant, Stepan, has submitted label amendments to cancel the turf and golf course uses for all four of these registered products. The Agency is currently processing the submission and anticipates deleting the turf and golf course uses and data requirements from DDAC's FWP.

The Agency notes that some registered uses of DDAC will be removed from EPA product labels in accordance with the Reregistration Eligibility Decision (RED)[2]. Labeling changes were specified as part of the risk mitigation measures outlined in the August 2006 DDAC RED. "Table 13. Labeling Changes Summary Table" in the DDAC RED describes how language on labels containing DDAC active ingredients should be amended. One use, for example, was already removed from labels under the DDAC registration review case. The use on udders, flanks, and teats on dairy cows was removed from EPA product labels because the use was not supported at the time of the RED. Some DDAC uses will continue to be removed from EPA product labels through DDAC's post-RED label review process, as noted in section 1.5.

1.5.3 Usage Information

Production volume data for the years 2011 through 2014 indicate that no more than 45 million kilograms (99 million pounds) of DDAC are sold per year in the United States. Data for the years 2015 and 2016 were not used in this estimate since data collection is still in progress.

1.6 Regulatory History

In 1962, the first pesticide product containing a DDAC active ingredient was registered in the United States. The DDAC case is comprised of 5 structurally similar quaternary ammonium compounds (quats) characterized by having a positively charged nitrogen covalently bonded to two alkyl group substituents (at least one C8 or longer) and two methyl substituents. In finished form, these quats are salts with a positively charged nitrogen (cation) balanced by a negatively charged molecule (anion).

[2] The DDAC RED is located at http://www.regulations.gov in docket number EPA-HQ-OPP-2006-0338.

In 1988, the Agency issued PR Notice 88-2 outlining "Clustering of Quaternary Ammonium Compounds," in which structurally similar quats were clustered into 4 groups as follows:

Group I: The alkyl or hydroxyalkyl (straight chain) substituted Quats

Group II: The non-halogenated benzyl substituted Quats (including hydroxybenzyl, ethylbenzyl, hydroxyethylbenzyl, naphthylmethyl, dodecylbenzyl, and alkyl benzyl)

Group III: The di- and tri-chlorobenzyl substituted Quats

Group IV: Quats with unusual substitutes (charged heterocyclic compounds).

DDAC's chemical case was clustered into Group I and the Agency completed a Reregistration Eligibility Decision (RED) for DDAC in August 2006. The post-RED Generic Data Call-Ins (DCIs) and Product Specific DCIs were issued in May 2015[3]. The RED specified label changes to mitigate human health and environmental risks and the Agency acknowledges that there are existing labels not yet in compliance with these risk mitigation measures. Some of these mitigation measures will impact the risk assessments for the DDAC registration review, and the Agency is actively working to bring these labels into compliance prior to the development of the registration review risk assessments.

A consortium was formed by DDAC registrants to support the reregistration activities of the DDAC chemical case. The consortium, the DDAC Issues Steering Committee/Joint Venture, is comprised of the following registrants: Lonza Incorporated, Mason Chemical Company, and Stepan Company.

Since reregistration, several human health risk assessments have been completed to support new uses and label amendments. The most recent human health risk assessment for DDAC was completed on December 19, 2013 (D413897). The Agency's most recent ecological risk assessment for DDAC was completed on August 2, 2006 (prepared for RED).

1.6.1 Tolerance Information

EPA has established tolerance exemptions for indirect food uses (food-contact surfaces) for residues of some DDAC active ingredients. The end-use concentration of DDAC in solution is not to exceed 200 or 240 ppm. Therefore, the Agency has conducted a commercial dietary assessment assuming 240 ppm of DDAC. These exemptions are listed in Table 7 and are located in 40 CFR part 180.940. DDAC is also approved for food and non-food use as an inert ingredient with an exemption from the requirement of a tolerance under 40 CFR parts 180.910, 180.920, and 180.930.

[3] DDAC's post-RED Generic Data Call-Ins (GDCIs) and Product Specific Data Call-Ins (PDCIs) are located at http://www.regulations.gov in docket number EPA-HQ-OPP-2006-0338.

Table 7 – Tolerance Exemption under 40 CFR Part 180.940

Chemical Name	PC Code	CAS No.	Tolerance Exemption
Didecyl dimethyl ammonium chloride	069149	7173-51-5	When ready for use, the end-use concentration is not to exceed 200 ppm of active quaternary compound.
Quaternary ammonium compounds, di-n-Alkyl (C_8-C_{10}) dimethyl ammonium chloride, average molecular weight (in amu), 332 to 361	069165 069166 069173	32426-11-2 5538-94-3 68607-28-3	When ready for use, the end-use concentration of this specific quaternary compound is not to exceed 240 ppm within the end-use total concentration that is not to exceed 400 ppm active quaternary compound.

DDAC PC Code 129012 does not include food contact product labels and therefore does not require a tolerance or tolerance exemption.

DDAC has been listed as a food contact substance by the FDA under FFDCA Section 409. There are no food contact notifications[4] (FCNs) for DDAC; however, DDAC has been listed as an indirect food additive (Table 8) under 21 CFR parts 176 and 178. There are no direct additive FDA clearances.

Table 8 – Summary of DDAC Indirect Food Additives

CFR Section	Use	Maximum Residue Level
21 CFR 178.1010	Sanitizing solutions	An aqueous solution containing n -alkyl (C12-C16) benzyl-dimethylammonium chloride and didecyldimethylammonium chloride.
21 CFR 176.300	Slimicides	None indicated

1.7 Incidents

1.7.1 Human Health

Since the 2006 RED, 781 individual human health incidents have been reported for DDAC in OPP's Incident Data System (IDS) for the time period spanning from August 1, 2006 to March 3, 2017. A summary of the incidents is given in Table 9. The largest number of incidents are associated with liquid concentrate products (577 incidents) followed by ready to use (RTU) solutions (58 incidents) and RTU Trigger sprayer products (51 incidents).

The liquid concentrate products are used to prepare dilute working solutions that can be applied by a variety of methods including spray, mop, wipe or fog. To determine if the incident was caused by handling of the liquid concentrate during preparation of the working solution or if the incident was caused by the application of the working solution, it would be necessary to review each of the 577 liquid concentrate incidents. These incidents will be reviewed during the registration review process as needed to characterize and mitigate risks.

[4] More information about food contact notifications (FCNs) can be found at http://www.accessdata.fda.gov/scripts/fdcc/?set=fcn and http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=iaListing&page=30.

In terms of severity, most of the incidents (724) were rated as HC (human moderate), followed by 35 rated as HB (human major), 16 rated as HD (human minor), five rated as HA (human fatality) and one rated as HE (severity unknown). The circumstances leading to the five HA incidents are listed below:

- A maintenance worker at a gas station used an ADBAC/DDAC disinfectant product. Another worker there was allegedly exposed to it and developed respiratory distress and ultimately died. She previously had chronic obstructive pulmonary disease.
- An airline employee developed respiratory distress resulting in death. Chemical exposure to an ADBAC/DDAC product and three other cleaning products was the potential cause. No other details were provided.
- A person deliberately inhaled a fabric and air deodorizer. This person had a history of inhalant abuse.
- A 68-year dementia patient in a nursing home ingested an ABDAC/DDAC disinfectant product that was being used to clean wheelchairs during the overnight shift.
- An individual ingested an ADBAC/DDAC powder product along with another non-pesticidal cleaning product in a correctional facility.

Table 9 – Summary of DDAC Human Health Incidents Since the RED

Type of Product (RTU = Ready to Use)	Number of Incidents					
	Human Fatality	Human Major	Human Moderate	Human Minor	Severity Unknown	Total
Powder or Solid	1	0	0	0	0	1
RTU Insecticide	0	0	2	0	0	2
RTU Pool Treatment Solution	0	0	2	0	0	2
RTU Wipe	0	0	15	0	0	15
RTU Aerosol Can	0	1	17	0	0	18
RTU Toilet Bowl Disinfectant	0	2	21	0	0	23
RTU Foam	0	0	34	0	0	34
RTU Trigger Sprayer	1	3	46	1	0	51
RTU Solution	0	4	54	0	0	58
Liquid Concentrate	3	25	533	15	1	577
Total of Above	5	35	724	16	1	781

In addition to the incidents reported in individual reports discussed above, there are 4,096 incidents that were reported in quarterly aggregate incident summaries. In terms of severity, most of the aggregate incidents (4,056) were rated as HD and the remainder (40) were rated as HE.

The Agency will assess human health incidents in DDAC's registration review risk assessment.

Epidemiology Studies and Incidents Reported in the Literature

There are reports in the literature of work-related asthma associated with exposure to cleaning agents and disinfectants and some of these reports relate to the use of the quaternary ammonium compounds (QACs). The earliest reports include a case of a laundry worker who developed asthma after using a disinfectant containing QACs (Innocenti, 1978), a pharmacist who had asthma attacks when contacting a floor cleaning solution containing QACs (Burge, 1994) and a

worker who had occupational asthma caused by prolonged exposure to cleaning agents containing QACs (Berstein, 1994). Three more cases were reported in Purohit (2000) of nurses who experienced asthma symptoms when preparing a 10% solution of disinfectant containing QAC, cleaning surgical instruments in a tray with a QAC disinfectant, and entering a room where a solution of disinfectant containing 40% QAC was kept. In a multistate report of 401 cases of pesticide related illness of health care workers (Mehler et al, 2010), QACs were involved in the most cases (151) followed by glutaraldehyde (101) and sodium hypochlorite (71). In terms of occupation, janitors and housekeepers had the most cases (95), followed by nursing/medical assistants (64) and health technicians (59).

In Gonzalez (2013), the association between disinfection with QACs and asthma in health care workers was investigated. This investigation was conducted in a cohort of 543 workers, which consisted of registered nurses (37.1%), auxiliary nurses (16.4%), cleaners (17.3%) and administrative staff (32.8%). Of the 543 workers, 335 were exposed to QACs as part of their normal workday. Registered and auxiliary nurses and cleaners reported a significantly higher risk of reported physician diagnosed asthma and nasal symptoms than administrative staff. This risk was particularly marked during disinfection tasks and when exposed to QACs. Exposure to QACs significantly increased the risk of reported physician diagnosed asthma with an adjusted odds ratio of 7.56 (95% CI = 1.84 – 31.05) compared to an adjusted odds ratio of 1.0 for persons not exposed. Exposure to QACs also increased the incidences of nasal symptoms at work with an odds ratio of 3.21 (95% CI = 1.42-7.22). No significant association was found with other exposures such as latex gloves, chlorinated products/bleach or glutaraldehyde. The highest risk was associated with tasks involving dilution of disinfection products by manual mixing. An editorial on this study (Heedrick, 2014) concluded that "Initiatives are needed in particular to improve education and labeling of products and to reduce exposure to disinfectants and cleaning agents."

In response to the increasing evidence that chemicals used for environmental surface cleaning in health care can cause respiratory illnesses such as asthma, the Cleaning and Disinfecting in Health Care (CDHC) Working Group was established to provide a more integrated approach to effective environmental surface cleaning and disinfection while protecting the respiratory health of health care personnel. This working group is part of the National Institutes of Safety and Health (NIOSH) National Occupational Research Agenda (NORA) and includes experts in inhalation toxicology, industrial hygiene, epidemiology, and infection control. This group recently published an article (Quinn, 2015) that discusses the potential hazards of the chemicals used for cleaning and disinfection, including quats, and how those hazards could be reduced by a better understanding of the efficacy of cleaning and disinfecting products and procedures. In particular, through improved guidance to assist health care institutions in determining if cleaning is sufficient for non-clinical public spaces and floors and whether to reduce the amount of disinfectant used to reduce worker exposures. The article also notes that asthma symptoms or exacerbations have been associated with the use of sprays.

In contrast to the CDHC Working Group, Weber (2016) concludes that dermatitis and respiratory symptoms (e.g., asthma) as a result of chemical exposures, including low-level disinfectants, (which include DDAC) are "exceedingly rare". The authors examined the medical records for an occupational health clinic that serves the employees of the University of North (UNC) Carolina

Hospital. Over the time period studied, 2003-2012, UNC Hospital employed 69,075 full-time work years, which constituted 144 million person days of exposure. Injuries or illnesses caused by chemical exposures were uncommon. Overall, 70 of 128 chemical exposures were caused by a known germicide (i.e., antiseptic, high-level disinfectant, low-level disinfectant), including alcohol 17, quaternary ammonium compound 18, germicide (not specified) 12, glutaraldehyde 7, peracetic acid 6, hypochlorite (bleach) 5, phenol 3, and chlorhexidine 2. Other chemicals included floor strippers, cleaning agents, formaldehyde, xylene, toilet disinfectants, and miscellaneous. The authors acknowledge that unprotected exposures to high-level disinfectants may cause dermatitis and respiratory symptoms and they recommend the use of engineering controls (e.g., closed containers, adequate ventilation) and personal protective equipment (e.g., gloves) to minimize exposure to high-level disinfectants. As noted above, DDAC is considered to be a low level disinfectant and therefore is not included in this author's recommendation for engineering controls.

In response to the Weber (2016) article, a letter was written by Pechter and Rosenman (2016) to the editor of the publishing journal. This letter states that the conclusion of Weber (2016) is not supported by the occupational health clinic data or the literature review. Over 40 articles have documented the association of cleaning products, and specifically disinfectants used in hospitals, with asthma. Workers in cleaning occupations do not frequently report their work-related illnesses because of discouragement by employers, job insecurity and marginalization of the occupational category. The letter concludes that: "failing to recognize the hazards of disinfectants along with the blanket advice to continue to disinfect environmental surfaces leads to overuse and overexposure of hospital staff to these antimicrobial pesticides".

In response to Pechter and Rosenman (2016), Weber (2017) disagreed with many of the issues and criticisms raised. Weber's response discusses the substantial morbidity and mortally associated with healthcare-associated infections (HAIs) and how daily disinfection can reduce HAIs. Weber notes that disinfectant use is only recommended for the decontamination of environmental surfaces in contact with patients and is not recommended for non-patient areas such as offices. Weber also states that most of the literature is focused on the risks of asthma from high-level disinfectant uses and that there are fewer studies on low-level disinfectant uses. In addition, Weber states that the 40 articles mentioned in the letter were not based on clinical trials or prospective cohort studies. Weber agrees with Pechter and Rosenman that additional research is needed and suggests that prospective studies with appropriate clinical tests (i.e. pulmonary function tests and human challenge studies) are needed to document possible allergies to low-level disinfectants and disinfectant-precipitated asthma. Weber also agrees that training and PPE should be provided to minimize exposures.

The EPA plans to consider all available incident and epidemiological information in the DDAC registration review risk assessment.

1.7.2 Ecological

A search in August 2016 of OPP's Incident Data System (IDS) resulted in 4 reports of "minor" plant damage resulting from BARDAC®, a group of formulation intermediates of DDAC (EPA Registration Numbers 6836-18 and 6836-51). The incidents took place between March and June, 2009, according to the report submitted by the registrant.

2 Anticipated Data Needs

The studies listed in Table 10 are expected to be needed for the registration review of DDAC. Data requirements outstanding from the August 2006 DDAC Reregistration Eligibility Decision (RED) are outlined in Table 11. The Agency anticipates reviewing data received in response to the post-RED DCIs as well as data required for this registration review prior to conducting the registration review risk assessments for DDAC.

Table 10 – Antimicrobial and Conventional Studies Anticipated as Needed for the Registration Review of DDAC

Guideline Number (GLN)	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
835.1110[1,2]	Activated Sludge Sorption Isotherm (ASSI)	TGAI	12	Ecological and Drinking Water	Antimicrobial uses: Recirculating cooling towers, air washer systems, wood preservatives, and swimming pools Conventional uses: Waste water from turf, golf courses, ornamentals, and bulb, root, seed, and leaf drench treatments in greenhouses	Ecological
835.3110, 835.3220, 835.3240, or 835.3280[1,3]	Wastewater Treatment Plant (WWTP) Biodegradation Studies	TGAI	12	Ecological and Drinking Water		Ecological
850.3300[3,4,5]	Activated Sludge Respiration Inhibition (ASRI)	EUP, PAI, TGAI	12	Ecological and Drinking Water		Ecological
Non-Guideline[6,7,8,9]	Whole sediment: chronic freshwater invertebrates (with an amphipod, for example, *Hyalella azteca*)	TGAI	24	Ecological	Antimicrobial and conventional uses	Ecological
Non-Guideline[7,8,10]	Whole sediment: chronic marine/estuarine invertebrates (with an amphipod, for example, *Leptocheirus plumulosus*)	TGAI	24	Ecological	Antimicrobial and conventional uses	Ecological
850.2100[11,12]	Avian Acute oral (with a passerine species)	TGAI	12	Ecological	Turf and golf courses	Ecological
850.2300[12]	Avian Reproduction	TGAI	24	Ecological	Turf and golf courses	Ecological
850.4100 and 850.4225[13,14]	Tiers I and II Terrestrial plant toxicity-Seedling emergence	TEP	12	Ecological	Turf and golf courses	Ecological
850.4150 and 850.4250[14,15]	Tiers I and II Terrestrial plant toxicity-Vegetative vigor	EUP, TGAI	12	Ecological	Turf and golf courses	Ecological
Non-Guideline[12,16]	Tier I Honey bee adult acute oral toxicity	TGAI	12	Ecological	Turf and golf courses	Ecological
Non-Guideline[12,17]	Tier I Honey bee larvae acute oral toxicity	TGAI	12	Ecological	Turf and golf courses	Ecological
Non-Guideline[8,12,18]	Tier I Honey bee larvae chronic oral toxicity	TGAI	12	Ecological	Turf and golf courses	Ecological

Non-Guideline[8,12,19]	Tier I Honey bee adult chronic oral toxicity	TGAI	12	Ecological	Turf and golf courses	Ecological
850.3030[8,12,20]	Tier I Honey bee toxicity of residues on foliage	TEP	12	Ecological	Turf and golf courses	Ecological
Non-Guideline[8,12,21,22,23]	Tier II Semi-field testing for pollinators	TGAI	24	Ecological	Turf and golf courses	Ecological
850.3040[8,12,24,25,26]	Tier III Field testing for pollinators	TGAI	24	Ecological	Turf and golf courses	Ecological
860.1340[8]	Residue analytical method for data collection	ROC	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
860.1380[8]	Storage stability	TEP or ROC	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
860.1480[8]	Meat, Milk, Poultry, Eggs	TGAI	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
875.2100[27]	Foliar Dislodgeable Residue Dissipation	TEP	12	Occupational Post Application	Conventional uses: Greenhouse foliar sprays (cut flowers, ornamentals, nursery stock)	Dermal
875.2100[28]	Turf Transferable Residue Dissipation	TEP	12	Residential Post-application	Conventional use: Turf	Dermal and Incidental Oral
875.2500[8,29]	Inhalation Exposure – Post Application	TEP	24	Residential Post-application	Antimicrobial use: Humidifier water	Inhalation

TGAI = Technical Grade Active Ingredient; EUP = End-Use Product; PAI = Pure Active Ingredient; TEP = Typical End-Use Product; ROC = Residue of Concern

Footnotes

[1] Additional WWTP tests such as biodegradation simulation tests (835.3110, 835.3220, 835.3240, or 835.3280) may be required if DDAC does not demonstrate a strong potential to sorb to activated sludge.

[2] EPA has published a final guideline for this study: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0003.

[3] The results of the ASRI, GLN 850.3300, will determine which of the four biodegradation tests would be expected 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, GLN 835.3280 or (ii) Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units, GLN 835.3240, or (iii) the Porous Pot Test, GLN 835.3220 would be expected to be required. If the ASRI test EC_{50} is greater than 20 mg/L, then the Agency would expect to require the registrant to conduct either: (i) Ready Biodegradability (GLN 835.3110) 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 (i) Biodegradation in Activated Sludge, or (ii) Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units, or (iii) the Porous Pot study would be expected to be required.

[4] EPA published draft guidance under guideline 850.6800 and has since published final guidance for this study under guideline 850.3300: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0021.

[5] OECD Test Guideline 209 can also be used as guidance for this study, available online at http://www.oecd-ilibrary.org/content/book/9789264070080-en.

[6] The anticipated DCI will require conduct of the study according to ORD Study Method EPA 600/R-099-064 but with 12 replicates per treatment (4 for 28-d survival and growth and 8 for the remainder of the test) with 10 neonates per replicate.

[7] The guidance for the formulated sediment can be found in OECD 218 Sediment-Water Chironomid Toxicity Test using Spiked Sediment.

[8] The anticipated DCI will require that a protocol be approved by the Agency prior to the initiation of the study.

[9] The guideline is partially fulfilled. Testing on one additional freshwater species is needed.

[10] The anticipated DCI will require conduct of the study according to ORD Study Method: EPA 600/R-099-020 but with 10 replicates per treatment with 20 neonates per replicate.

[11] OECD TG 233 using the "LD50- slope test" or "limit dose test" can be used instead of OCSPP 850.2100 for certain species and conditions (e.g., causes no delayed effects, causes no regurgitation). Details on the species and conditions under which TG 233 would not fulfill the data requirement are described at https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-classifying-studies-conducted-using-oecd.

[12] The study must be conducted on turf and golf course uses only.

[13] In a Federal Register Notice dated June 27, 2012, test guidelines 850.4100 and 850.4225 were merged and harmonized into OCSPP 850.4100. See “Final Test Guidelines; OCSPP 850 Series; Notice of Availability” 77 FR 38282, June 27, 2012. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0028.

[14] Guideline studies are required to assess the impact on non-target plants resulting from runoff and drift of the end-use products. The anticipated data are intended to provide an understanding of the relative sensitivity of a wide-range of terrestrial plants and are not intended to be specific to the actual target crop. Data are required for six species of dicots from at least four families, one species of which is soybean (*Glycine max*). Data are required for four species of monocots from at least two families, one species which is corn (*Zea mays*). At least one of either the monocot or dicot species must be a root crop.

[15] In a Federal Register Notice dated June 27, 2012, test guidelines 850.4150 and 850.4250 were merged and harmonized into OCSPP 850.4150. See “Final Test Guidelines; OCSPP 850 Series; Notice of Availability” 77 FR 38282, June 27, 2012. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0028.

[16] See the OECD 213: OECD Guidelines for the Testing of Chemicals. Honeybees, Acute Oral Toxicity Test. 213. http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en.

[17] OECD Test Guideline 237 may be used to develop a protocol for this study (OECD. 2013 Guidelines for Testing Chemicals. Honey bee (Apis mellifera) larval toxicity test, single exposure.) See: http://www.oecd-ilibrary.org/environment/test-no-237-honey-bee-apis-mellifera-larval-toxicity-test-single-exposure_9789264203723-en.

[18] OECD has not yet finalized test guidelines for chronic studies with honey bee larvae. OECD draft guidance has is being developed, see OECD 2013b. OECD Draft Guidance Document Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeated Exposure. http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf.

[19] OECD has not yet finalized test guidelines for chronic studies, and efforts are underway to develop standardized guidelines for assessing the effects from chronic exposure to adult and larvae in the laboratory. Discussion of the study design elements for the 10-day adult toxicity test can be found in Appendix O of the European Food Safety Authority (EFSA) guidance document: EFSA. Guidance on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus spp.* and solitary bees). EFSA Journal 2013;11(7):3295, 266 pp. doi:10.2903/j.efsa.2013.3295. Available online at: https://www.efsa.europa.eu/en/efsajournal/pub/3295.

[20] USEPA. 2012b. “Honey Bee Toxicity of Residues on Foliage.” Ecological Effects Test Guidelines OCSPP 850.3030. EPA 712-C-018. Data are required when the product formulation contains one or more active ingredient(s) having an acute LD50 of < 11 micrograms per bee as determined in the honey bee acute contact study and the use pattern(s) indicate(s) that honey bees may be exposed to the pesticide.

[21] The need for a semi-field test for pollinators (i.e., either a field-feeding test or a tunnel test) will be determined based upon lower-tiered tests and/or other lines of evidence, and the need for a refined pollinator risk assessment.

[22] Formal guidelines for semi-field tests do not yet exist; however, information that can help guide the development of either a semi-field tunnel test protocol can be found at OECD 75, see: OECD. 2007. Series on Testing and Assessment Number 75. Guidance document on the honey bee (*Apis mellifera L.*) brood test under semi-field conditions. Environmental Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. ENV/JM/MONO(2007)22. 31-Aug-2007. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2007)22&doclanguage=en.

[23] For field-feeding studies see: Oomen et al. 1992: Oomen, P. A. A. DeRuijter and J. Van der Steen. 1992. Method for honey bee brood feeding tests with insect growth-regulating insecticides. Bul OEPP/EPPO Bulletin 22: 613 – 616.
[24] The need for a field test for pollinators will be determined based upon lower-tiered tests and/or other lines of data and the need for a refined pollinator risk assessment.
[25] See information and guidance identified in the EPA documents, (i) USEPA. 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation; (ii) 2014 Guidance for Assessing Pesticide Risks to Bees. Office of Pesticide Programs United States Environmental Protection Agency, Health Canada Pest Management Regulatory Agency, California Department of Pesticide Regulation. June 19, 2014. http://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf.
[26] USEPA. 2012c. "Field Testing for Pollinators." Ecological Effects Test Guidelines OCSPP 850.3040. EPA 712-C-017.
[27] Available labels do not provide application rates in a format that allows for estimation of foliar surface residues. Thus, assuming an application range of 100 to 1000 gallons of solution per acre, risk estimates are not of a magnitude that would render a residue study unnecessary for risk assessment. Therefore, the anticipated data requirement remains.
[28] Available labels do not provide application rates, which can potentially be used to determine the necessity of the data for risk assessment purposes. Therefore, the anticipated data requirement remains.
[29] A post application inhalation exposure study for ADBAC treated humidifier water (MRID 47222901) was submitted after the RED, however, the LOQ of 0.026 mg/m^3 is not low enough to permit comparison to the HEC of 0.018 mg/m^3 which has a target MOE of 100. A new study needs to be conducted with an LOQ of 0.00018 mg/m^3 to allow for this comparison. In addition, the application rate of 100 ppm used in the study is less than the maximum application rate of 760 ppm allowed by the labels.

Table 11 – Antimicrobial Data Required through the May 2015 post-RED Generic Data Call-Ins (GDCIs) for DDAC

GLN	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario	Status[1]
850.1300	Daphnid chronic toxicity test	TGAI	12	Ecological	All	All	Acceptable DP Barcode: 435338
850.1400[2]	Fish early-life stage toxicity test	TGAI	12	Ecological	All	All	Acceptable DP Barcode: 435338
850.3020	Honey bee acute contact toxicity	TGAI	12	Beneficial insects	Wood treatment	Wood treatment	Deficiencies / Data Gap DP Barcode: 435338
850.4225[3]	Seedling emergence, Tier II	TEP	12	Ecological	All	Data are needed only for rice (*Oryza sativa*).	Waived
850.4250[3]	Vegetative vigor, Tier II	TEP	12	Ecological	All	Data are needed only for rice (*Oryza sativa*).	Waived
850.4400[4]	Aquatic plant toxicity test using *Lemna spp.* Tiers I and II	TGAI	12	Aquatic plants	All	All	Deficiencies / Data Gap DP Barcode: 435338
850.4500[3,5]	Algal toxicity, Tier II	TGAI	12	Ecological	All	All	Deficiencies / Data Gap DP Barcode: 435338
850.4550[3,5]	Algal toxicity, Tier II	TGAI	12	Ecological	All	All	Acceptable DP Barcode: 435338
870.3465[6]	90-day inhalation toxicity	TGAI	24	Toxicology	All	All	Acceptable DP Barcode: 414494
875.1100[7,8]	Dermal Exposure - Outdoor	TEP	24	Occupational and Residential Handler	See Footnote 7	See Footnote 7	Partially Satisfied[9,10,11]
875.1200[7,8]	Dermal Exposure - Indoor	TEP	12	Occupational and Residential Handler	See Footnote 7	See Footnote 7	Partially Satisfied[9,10,11]
875.1300[7,8]	Inhalation Exposure – Outdoor	TEP	24	Occupational and Residential Handler	See Footnote 7	See Footnote 7	Partially Satisfied[9,10,11]
875.1400[7,8]	Inhalation Exposure - Indoor	TEP	24	Occupational and Residential Handler	See Footnote 7	See Footnote 7	Partially Satisfied[9,10,11]
875.2300[12]	Indoor Surface Residue Dissipation	TEP	12	Residential Post Application	See Footnote 12	See Footnote 12	Partially Satisfied[13]

GLN	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario	Status[1]
875.2800	Description of Human Activity	N/A	24	Occupational Post Application	All	All	Satisfied[14]
Special Study-DDAC[15]	Dietary Residue in Food from Treating Hard Surfaces with DDAC	TEP	12	Dietary	Hard surface products in commercial areas.	Hard surface products in commercial areas.	Acceptable DP Barcode: 435265

TGAI = Technical Grade Active Ingredient; TEP = Typical End-Use Product; N/A = Not Applicable

Footnotes
[1] Status of the DDAC Issues Steering Committee/Joint Venture, GDCI response.
[2] Data are required on the freshwater species that is most acutely sensitive to DDAC.
[3] In response to the post-RED Generic Data Call-In for DDAC issued May 2015, the Agency concurred with the Task Force's request to bridge DDA carbonate/bicarbonate studies to DDAC for rice (850.4225 and 850.4250), cyanobacteria (850.4550), and freshwater diatom (850.4500).
[4] Data are required if algal studies show toxicity at less than 1 ppm.
[5] Data are required on 4 species: *Anabaena flosaquae*, *Navicula pelliculosa*, *Skeletonema costatum*, and *Selenastrum capricornutum*.
[6] A 28-day inhalation toxicity study was approved in lieu of a 90-day inhalation toxicity study.
[7] The GDCI required exposure studies for the following scenarios: Indoor hard surfaces (mop, wipe, trigger pump spray, aerosol spray, and liquid pour); Air deodorization (aerosol spray); carpets (low pressure spray); uses requiring liquid pour of formulated products; dehumidifiers; low and high pressure sprays for disinfectants (such as vehicle treatment); non-pressure treatment of wood (e.g., industrial sapstain treatments, airless sprayer of wood for existing structures); and pressure treatment of wood.
[8] A protocol was due to the Agency for approval prior to the start of the study. The draft protocol was due to the Agency within 90 days of receipt of this DCI.
[9] Data needs for the following scenarios are satisfied: Indoor hard surfaces (mop, wipe, trigger pump spray, aerosol spray, and liquid pour); uses requiring liquid pour of formulated products; pressure treatment of wood, and non-pressure treatment of wood (industrial sapstain treatments).
[10] Data needs for the following scenarios are not satisfied: Non-pressure treatment of wood (airless sprayer of wood for existing structures), low and high pressure sprays for disinfectants (such as vehicle treatment), and carpets (low pressure spray). These studies are within the scope of the Antimicrobial Exposure Assessment Task Force (AEATF) study plan.
[11] The AEATF has conducted an aerosol spray study using a surface spray product; however, this study might not be representative of exposures that occur when using a space spray product for air deodorization. Information regarding the droplet sizes released would be needed for an air deodorization product to determine if exposures could be evaluated using the AEATF aerosol study.
[12] The GDCI required surface residue studies for the following uses: Carpets, flooring, textiles (laundered clothing/diapers), treated wood; and musical instruments (mouthpiece/reed).
[13] The submitted study addresses hard surfaces, which include flooring. Studies are still needed for carpets, textiles (laundered clothing/diapers), treated wood and musical instruments (mouthpiece/reed). Without these studies, EPA will default to 100 percent of the application rate as the amount of residue transferred.
[14] The submitted Antimicrobial Exposure Joint Venture (AEJV) National Antimicrobial and Health Care surveys address consumer and medical hard surface uses, respectively. The Health Care Survey could also be used to address hard surface uses in the other commercial, industrial, and institutional market sectors such as food service and food processing.
[15] A residue transfer protocol was due to the Agency for approval prior to the start of the study. The draft protocol was due to the Agency within 90 days of receipt of this DCI.

3 Human Health Risk Assessment

The Agency anticipates the need to conduct a human health risk assessment for DDAC. The Agency also anticipates requiring human health data during registration review (as shown in Table 10) and will review data required by the RED DCIs.

3.1 Existing Toxicological Endpoints

EPA has re-examined the existing toxicological endpoints as part of this registration review. Table 12 presents the revised endpoints selected. Based on the memo from the Hazard and Science Policy Council (HASPOC) meeting on March 3, 2016 (TXR# 0052128[5]), the acute neurotoxicity, subchronic neurotoxicity and the immunotoxicity studies were waived. Table 12 includes the new inhalation endpoint, and these data will be used in the revised risk assessment. A 28-day inhalation toxicity study was approved in lieu of a 90-day inhalation toxicity study. The new inhalation study was not used in the exposure section, but is shown here to indicate what the endpoint will be for the risk assessment. A detailed description of the toxicity studies is provided in Appendix A.

Table 12 – Existing Toxicological Endpoints

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE or UF, Special FQPA SF for Risk Assessment	Study and Toxicological Effects
Acute Dietary (general)	NOAEL = 10 mg/kg/day aPAD=aRfD = 0.1 mg/kg/day	FQPA SF=1 UF=100 (10x inter-species extrapolation, 10x intra-species variation)	Acute Oral Study – Rat MRID 42296101 LOEL = 20 mg/kg/day based on clinical signs (urine and fecal stains, saliva discharge, red stains on muzzle, shallow respiration, slight/severe depression, viscous red blood like discharge from the mouth, piloerection, ataxia, tremors, labored and shallow breathing, bloated appearance of the abdomen and spasms of the abdominal area) following single dose exposure
Acute Dietary (Females 13-50			
Chronic Dietary (All populations)	NOAEL = 10 mg/kg/day cPAD=cRfD = 0.1 mg/kg/day	FQPA SF=1 UF=100 (10x inter-species extrapolation, 10x intra-species variation)	Chronic Toxicity Study - Dog MRID 41970401 LOEL = 20 mg/kg/day based on increased incidence of clinical signs in males (emesis and soft/mucoid feces) and females and decreased total cholesterol in females

[5] The HASPOC memorandum (TXR# 0052128) titled *DDAC: Summary of Hazard and Science Policy Council (HASPOC) Meeting of March 3, 2016: Recommendation on the Requirement for Neurotoxicity (Acute and Subchronic) and Immunotoxicity Studies* can be found in the docket at www.regulations.gov, EPA-HQ-OPP-2015-0740.

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE or UF, Special FQPA SF for Risk Assessment	Study and Toxicological Effects
Incidental Oral (all duration)	NOAEL (maternal) = 1 mg/kg/day	MOE = 100 UF=100 (10x inter-species extrapolation, 10x intra-species variation)	Prenatal Developmental Toxicity – Rat[1] MRID 41886701 LOAEL = 10 mg/kg/day The LOEL is based on decreased body weight/weight gain.
Dermal (all duration)	NOAEL = 2 mg ai/kg/day (8 µg ai/cm^2)	MOE = 10 (3x inter-species extrapolation, 3x intra-species variation)	90-day Dermal Toxicity – Rat MRID 41305901 LOEL = 6 mg ai/kg/day based on increased clinical and gross findings (erythema, edema, exfoliation, excoriation, and ulceration)
Inhalation (short and intermediate term)	LOAEC < 0.08 mg/m^3 (HEC = 0.018 mg/m^3)	UF = 100 (3x inter-species extrapolation, 10x intra-species variation, 3X NOAEC to LOAEC conversion)	28-day inhalation toxicity – rat, MRID 48667903 LOAEC = 0.08 mg/m^3, based on ulceration of the nasal cavity, degeneration of the olfactory epithelium, increase in mucoid production and decreased body weight/weight gain in males
Inhalation (Long term)	LOAEC < 0.08 mg/m^3 (HEC = 0.018 mg/m^3)	UF = 1000 (3x inter-species extrapolation, 10x intra-species variation, 3X NOAEC to LOAEC conversion, 10X duration)	28-day inhalation toxicity – rat, MRID 48667903 LOAEC = 0.08 mg/m^3, based on ulceration of the nasal cavity, degeneration of the olfactory epithelium, increase in mucoid production and decreased body weight/weight gain in males
Cancer (oral, dermal, inhalation)	Classified as "Not Likely" to be a human carcinogen.[2]		

HEC = LOAEC (0.08 mg/m^3) * (6 hours/day Rat Exposure /8 hours/day Human Exposure) * RDDR (0.298)

[1] The prenatal developmental toxicity study, which used gavage dosing, is considered to be more appropriate for assessing incidental oral exposures because they can occur as bolus ingestions.
[2] Hazard Identification Assessment Review Committee (HIARC) determined that DDAC is not likely to be carcinogenic based on the lack of evidence of carcinogenicity in mice or rats (EPA, 2000).

3.2 Dietary Exposure

The last dietary exposure assessment was conducted in 2006 for the DDAC RED. EPA anticipates the need to conduct revised dietary exposure (food and drinking water) assessments to support registration review of DDAC since there are multiple labeled uses that could result in both direct and indirect food contact, and the dietary exposure assessment policies have been updated since 2006. The registered antimicrobial uses of DDAC that result in dietary food exposure include: (1) as a sanitizer/disinfectant in/around agricultural premises and equipment; (2) a sanitizer/disinfectant for food contact surfaces in food handling establishments/food processing plants, residential areas, and commercial areas; (3) as a slimicide in paper production; and (4) as an egg wash. The registered antimicrobial uses of DDAC that result in human drinking water exposure include: (1) ice machines; (2) water holding tanks; and (3) reverse osmosis (RO)

units. The registered conventional uses of DDAC that could potentially result in human drinking water exposure include turf, golf course, and restaurant/food storage area surfaces/drains.

3.2.1 Food

Dietary exposure assessments will be conducted during registration review since currently registered antimicrobial uses of DDAC may result in dietary (food) exposure. Screening-level dietary assessments were conducted to determine anticipated data needed for the registration review of DDAC (see Table 10). The Agency has determined that none of the conventional uses of DDAC are likely to result in dietary (food) exposure.

Screening-level acute and chronic (food only) dietary exposure assessment were conducted for registration review using established toxicological points of departure (PODs). The acute and chronic population adjusted doses (aPAD and cPAD) are both 0.1 mg/kg/day.

A summary of the registered uses of DDAC with the potential to result in dietary (food only) exposure is provided in Table 13. A residue study is available that shows the reduction of DDAC residues from hard surfaces following a potable water rinse (PWR) (MRID 46870704). The results of the study indicate that after a DDAC solution is sprayed or wiped onto a hard surface as a disinfectant, the residues of DDAC are reduced by 60% from a PWR.

Additionally, a study is available that quantifies the transfer of DDAC residues to food when food (represented by apples, bread, and bologna) contacts hard surfaces treated with DDAC (MRID 46870703). The results of the study indicate that after treating a hard surface with DDAC, up to 44.3% of residues may transfer to food. This represents the most conservative estimate of transferability and was generated from the bologna food samples.

Therefore, the acute and chronic dietary exposure assessments were conducted using the maximum amount of refinement available based on chemical-specific residue estimates where appropriate (i.e., incorporating residue reductions with a PWR, as applicable, and incorporating a reduction to account for residue loss from transfer of DDAC from hard surfaces to food).

Table 13 – Summary of Registered DDAC Uses Expected to Result in Dietary (Food Only) Exposure

158W Use Site Category	Highest Labeled Concentration (ppm)	Representative EPA Reg. No.	PWR Adjustment[1]	Transferability Adjustment[4]
Food Handling/Storage Establishments, Premises and Equipment[3]	3780	67619-21	Yes	Yes
Commercial, Institutional and Industrial Premises and Equipment	15000	6836-276	Yes	Yes
Residential and Public Access Premises	15000	6836-276	Yes	Yes
Paper Manufacturing[5]	24 lb ai/ton paper[6]	1839-226	No[2]	No
Egg Wash	400	10324-115; 10324-67; 10324-81; 10324-117; 10324-177; 10324-194	No[2]	No

[1] Available study results indicate that 40% of DDAC residues will remain on surfaces following a potable water rinse after application. The highest maximum residue levels on all registered labels containing DDAC have been corrected for this reduction when applicable. Residue value (mg) = AoS (Active on Surface = 1 mg/cm^2 * µg/g * 1g/1,000,000 µg)* Area of Treated Surface (cm^2) * Fraction Remaining on the Surface (40%)
[2] Treatments not requiring a potable water rinse or for which a potable water rinse is not applicable.
[3] Dietary (food only) exposure assessment for food handling/storage establishments, premises and equipment is represented by the "commercial areas" dietary exposure assessment.
[4] Residue values adjusted for transferability data (MRID 46870703) indicating that up to 44.3% of DDAC residues may transfer to food from hard surfaces.
[5] Slimicide, whitewater uses, etc. Although several labels include paper coating applications, the use instructions indicate that they are for the manufacture of non-food contact papers; therefore, an assessment was not completed for these uses.
[6] The next highest application rate is 0.49125 lb ai/ton paper (EPA Reg. No. 10324-211).

Animal premises and equipment were listed as both non-food and food uses in the use site data tables provided by the DDAC Issues Steering Committee/Joint Venture. The Agency relied on the information provided by the Committee in this screening assessment. Several of the labels were checked for the uses identified as food uses, and language was included (as summarized below) that indicated that the uses would be considered non-food. The Agency considers uses on animal premises "non-food" if the labels state the following restriction:

Prior to use of this product, remove all animals {poultry} and feeds from [{premises} {areas to be treated}], animal transportation vehicles {trucks, cars}, and enclosures [{coops, crates, kennels, stables}]. Remove all litter, droppings and manure from floors, walls and surfaces of barns, pens, stalls, chutes and other surfaces of facilities and fixtures occupied or traversed by animals. Empty all troughs, racks and other feeding and watering appliances. Thoroughly clean surfaces with soap or detergent and rinse with water.

Registrants whose DDAC product labels do not currently bear the language above regarding animal premises and wish their products to be considered non-food must amend their labels accordingly with the Agency. DDAC registrants who do not take action to this change should anticipate that the Agency will assume that labels claiming an animal premise use are direct or indirect food use per the Antimicrobial Use Site Index (USI) (https://www.epa.gov/pesticide-registration/antimicrobial-pesticide-use-site-index). Product designations of direct or indirect food use may result in conservative assumptions in the risk assessment.

Although some labels allow active ingredient concentrations of up to 15,000 ppm on hard surfaces that may contact food, this concentration is greater than the currently established tolerance exemption of 200 or 240 ppm for food contact/hard surfaces in commercial areas. Therefore, for hard surfaces in commercial areas, in addition to using the label rates, the dietary exposure assessment was also conducted using the established tolerance exemption level of 240 ppm.

For dietary (food only) scenarios, a total estimated daily dietary intake (TEDDI) assessment is usually conducted to determine whether additional toxicity data (chronic/carcinogenicity studies) are required; however, there is an available and acceptable chronic/carcinogenicity study for DDAC. Therefore, an additional study is not required at this time and a TEDDI assessment has not been conducted for any dietary exposure scenarios.

Dietary Exposure Assessment – Residential Areas

Assuming the highest labeled rate, a PWR, and transfer data. The labels were assessed as having a PWR since no labels without a PWR were identified.

A residential dietary exposure assessment for hard surface products was conducted using the Tier 3 Indirect Dietary Residential Exposure Assessment Model (IDREAM). DDAC and ADBAC residue transfer data (MRID No. 46870703) for bologna (44.3%; translated to the IDREAM food categories of pieces, cheese, and semisolids), apples (37.4%; translated to the IDREAM food category of vegetables), and bread (0.89%; translated to the IDREAM food category of powders) were used to refine the residential IDREAM dietary assessment. Additionally, since the label indicated that a PWR was required, the Tier 3 assessment incorporated a reduction in DDAC residues of 60% (D435265). The acute exposure and risk estimates exceed the level of concern (LOC) at the 90th and 95th percentiles for various population subgroups. The chronic dietary (food only) exposure and risk estimates do not exceed the LOC [i.e., < 100% of the PAD] for the general U.S. population or any population subgroups.

Table 14 – Tier 3 Acute Exposure Assessment at the 90th Percentile for Use of DDAC in Residential Areas – IDREAM (15,000 ppm; with 60% Removal from PWR, and 0.89% to 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% aPAD
General U.S. Population	0.0941	94
All Infants (<1 year old)	0.209	210
Children 1-2 years old	**0.249**	**250**
Children 3-5 years old	0.211	210
Children 6-12 years old	0.131	130
Youth 13-19 years old	0.0892	89
Adults 20-49 years old	0.0794	79
Adults 50-99 years old	0.0672	67
Females 13-49 years old	0.0743	74

[1] Active on Surface (mg/cm^2) x surface area (2000 cm^2) x fraction transferred (100%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Table 15 – Tier 3 Acute Exposure Assessment at the 95th Percentile for Use of DDAC in Residential Areas – IDREAM (15,000 ppm; with 60% Removal from PWR, and 0.89% to 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% aPAD
General U.S. Population	0.122	120
All Infants (<1 year old)	**0.352**	**350**
Children 1-2 years old	0.309	310
Children 3-5 years old	0.261	260
Children 6-12 years old	0.164	160
Youth 13-19 years old	0.113	110
Adults 20-49 years old	0.0967	97
Adults 50-99 years old	0.0834	83
Females 13-49 years old	0.0934	93

[1] Active on Surface (mg/cm^2) x surface area (2000 cm^2) x fraction transferred (100%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Table 16 – Tier 3 Chronic Exposure Assessment for Use of DDAC in Residential Areas – IDREAM (15,000 ppm; with 60% Removal from PWR, and 0.89% to 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.0101	10
All Infants (<1 year old)	0.00766	7.7
Children 1-2 years old	**0.0283**	**28**
Children 3-5 years old	0.0242	24
Children 6-12 years old	0.0143	14
Youth 13-19 years old	0.00858	8.6
Adults 20-49 years old	0.00842	8.4
Adults 50-99 years old	0.00811	8.1
Females 13-49 years old	0.00804	8.0

[1] Active on Surface (mg/cm^2) x surface area (2000 cm^2) x fraction transferred (100%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Commercial Areas

Assuming the highest labeled rate, a PWR, and maximum transfer from treated hard surfaces to food (44.3%). The labels were assessed as having a PWR since no labels without a PWR were identified.

In commercial areas, the acute and chronic dietary (food only) exposure and risk estimates exceed the LOC [i.e., >100% of the PAD] for the general U.S. population and all population subgroups when using the Commercial Tier 1B model for food contact (hard surfaces). These assessments incorporate residue adjustments for the potable water rinse (60% removal of residues) and account for transfer of residues from treated hard surfaces to food by assuming a maximum transfer of 44.3%. The Agency notes that the exposure and risk estimates presented in Tables 17-22 assume the same consumption amounts for both the acute and chronic assessments. Since the acute and chronic endpoints are the same for DDAC, both the acute and chronic exposure estimates and the acute and chronic risk estimates are the same for these assessments.

Table 17 – Acute Exposure Assessment for Use of DDAC in Commercial Areas Assuming Highest Labeled Rate (15000 ppm, with 60% Removal from PWR, and 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% aPAD
General U.S. Population	0.151	150
All Infants (<1 year old)	**1.38**	**1400**
Children 1-2 years old	0.844	840
Children 3-5 years old	0.569	570
Children 6-12 years old	0.287	290
Youth 13-19 years old	0.158	160
Adults 20-49 years old	0.130	130
Adults 50-99 years old	0.131	130
Females 13-49 years old	0.146	150

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm) x PWR Adjustment (40%)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.
Calculated using the application rate from EPA Reg. No. 6836-276.

Table 18 – Chronic Exposure Assessment for Use of DDAC in Commercial Areas Assuming Highest Labeled Rate (15000 ppm, with 60% Removal from PWR, and 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.151	150
All Infants (<1 year old)	**1.38**	**1400**
Children 1-2 years old	0.844	840
Children 3-5 years old	0.569	570
Children 6-12 years old	0.287	290
Youth 13-19 years old	0.158	160
Adults 20-49 years old	0.130	130
Adults 50-99 years old	0.131	130
Females 13-49 years old	0.146	150

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm) x PWR Adjustment (40%)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.
Calculated using the application rate from EPA Reg. No. 6836-276.

Assuming the tolerance exemption of 240 ppm

In commercial areas, the acute and chronic dietary (food only) exposure and risk estimates are not of concern [i.e., <100% of the PAD] for the U.S. population and all population subgroups when using the Commercial Tier 1B model for food contact (hard surfaces) at the tolerance exemption level of 240 ppm. This assessment does not include a PWR, but it does assume a maximum transfer from hard surfaces to food of 44.3%.

Table 19 – Acute Exposure Assessment for Use of DDAC in Commercial Areas Assuming Tolerance Exemption (240 ppm)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% aPAD
General U.S. Population	0.00606	6
All Infants (<1 year old)	0.0552	55
Children 1-2 years old	0.0338	34
Children 3-5 years old	0.0227	23
Children 6-12 years old	0.0115	11
Youth 13-19 years old	0.00632	6
Adults 20-49 years old	0.00522	5
Adults 50-99 years old	0.00524	5
Females 13-49 years old	0.00583	6

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.

Table 20 – Chronic Exposure Assessment for Use of DDAC in Commercial Areas Assuming Tolerance Exemption (240 ppm)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.00606	6
All Infants (<1 year old)	0.0552	55
Children 1-2 years old	0.0338	34
Children 3-5 years old	0.0227	23
Children 6-12 years old	0.0115	11
Youth 13-19 years old	0.00632	6
Adults 20-49 years old	0.00522	5
Adults 50-99 years old	0.00524	5
Females 13-49 years old	0.00583	6

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Paper Production

There are multiple end-use products for DDAC use in paper production that may result in indirect food contact to DDAC. The results have been presented here for DDAC use as a slimicide during paper production.

Slimicide

The screening-level dietary risk assessment for DDAC as a slimicide during paper production at a rate of 24 lb ai/ton of paper (EPA Reg. No. 1839-226) indicates that acute and chronic dietary (food only) exposure and risk estimates are not of concern [i.e., <100% of the PAD] for the U.S. population and all population subgroups.

Table 21 – Acute Exposure Assessment for Use of DDAC as a Slimicide in Papermaking – 24 lb ai/ton Paper

Population Subgroup	BW (kg)	Total Food Consumed (g)	DC (µg ai/g food)	EDI (µg ai/ person/day)	DDD (mg/kg/day)	% aPAD
General U.S. Population	70.2	3910	0.246	962	0.0137	14
All Infants (<1 year old)	7.7	766		189	0.0245	24
Children 1-2 years old	12.6	1770		436	0.0346	**35**
Children 3-5 years old	18.7	1940		477	0.0255	26
Children 6-12 years old	37.1	2460		605	0.0163	16
Youth 13-19 years old	67.3	3050		751	0.0112	11
Adults 20-49 years old	81.5	4110		1011	0.0124	12
Adults 50-99 years old	81.2	3780		930	0.0115	11
Females 13-49 years old	72.9	3680		906	0.0124	12

BW = Bodyweight; Mean weights from NHANES WWEIA 2003-2008
DC = Dietary concentration
EDI = Estimated daily intake = DC*Total Food Consumed
DDD = Daily dietary dose = (EDI*1 mg/1000 µg)/BW
%aPAD = % acute Population-Adjusted Dose = (DDD/aPAD)*100%

Table 22 – Chronic Exposure Assessment for Use of DDAC as a Slimicide in Papermaking – 24 lb ai/ton Paper

Population Subgroup	BW (kg)	Total Food Consumed (g)	DC (µg ai/g food)	EDI (µg ai/ person/day)	DDD (mg/kg/day)	% cPAD
General U.S. Population	70.2	3910	0.246	962	0.0137	14
All Infants (<1 year old)	7.7	766		189	0.0245	24
Children 1-2 years old	12.6	1770		436	0.0346	**35**
Children 3-5 years old	18.7	1940		477	0.0255	26
Children 6-12 years old	37.1	2460		605	0.0163	16
Youth 13-19 years old	67.3	3050		751	0.0112	11
Adults 20-49 years old	81.5	4110		1011	0.0124	12
Adults 50-99 years old	81.2	3780		930	0.0115	11
Females 13-49 years old	72.9	3680		906	0.0124	12

BW = Bodyweight; Mean weights from NHANES WWEIA 2003-2008
DC = Dietary concentration
EDI = Estimated daily intake = DC*Total Food Consumed
DDD = Daily dietary dose = (EDI*1 mg/1000 µg)/BW
%cPAD = % chronic Population-Adjusted Dose = (DDD/cPAD)*100%

Dietary Exposure Assessment – Egg Wash

There are multiple products containing DDAC that allow use as an egg-shell sanitizer. Therefore, screening-level acute and chronic dietary (food-only) exposure analyses were completed to evaluate the direct treatment of egg shells using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16. This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA).

For an acute exposure assessment, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for analyses performed at all levels of refinement. However, for deterministic assessments, any significant differences in user vs. per capita exposure and risk are specifically identified and noted in the risk assessment.

For a chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food-commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

The maximum allowed residue on eggshells found on all registered DDAC labels based on information provided by the ADBAC/DDAC Issues Steering Committee/Joint Venture was 400 ppm. Therefore, a residue value of 400 ppm was entered into DEEM for all egg commodities. The screening-level dietary risk assessment indicates that acute and chronic dietary (food only) exposure and risk estimates are of concern for all population subgroups [i.e., >100% of the PAD].

Table 23 – Acute Exposure Assessment for Use of DDAC as an Egg Wash (400 ppm)

Population Group	Exposure	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.708	700
All Infants (<1 year old)	0.835	840
Children 1-2 years old	**2.33**	**2300**
Children 3-5 years old	1.84	1800
Children 6-12 years old	1.08	1000
Youth 13-19 years old	0.635	640
Adults 20-49 years old	0.634	630
Adults 50-99 years old	0.584	580
Females 13-49 years old	0.602	600

The most highly exposed population subgroup is in bold.

Table 24 – Chronic Exposure Assessment for Use of DDAC as an Egg Wash (400 ppm)

Population Group	Exposure	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.161	160
All Infants (<1 year old)	0.123	120
Children 1-2 years old	**0.507**	**500**
Children 3-5 years old	0.380	380
Children 6-12 years old	0.215	210
Youth 13-19 years old	0.114	110
Adults 20-49 years old	0.133	130
Adults 50-99 years old	0.138	148
Females 13-49 years old	0.117	120

The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Conclusions

The acute and chronic dietary exposure assessments for the registered uses of DDAC at the maximum labeled rates are of concern, even when incorporating available data on transferability of residues from treated hard surfaces to food and data on reduction of residues following a potable water rinse, where applicable. The Agency does not plan to call in any additional data for indirect food uses at this time since chemical specific data representing a PWR as well as migration data have previously been submitted/reviewed and incorporated into the assessments herein. During the registration review process, additional refinements to the dietary exposure assessment may be performed to further refine estimated exposures from the indirect food uses of DDAC. The Agency notes that the product use rates assessed for commercial areas (15000 ppm with a PWR) are well-above the established tolerance exemption level for DDAC.

Because the use on eggs is considered a direct food use and the screening-level exposure analyses result in risks of concern, magnitude of the residue data on eggs are required (OCSPP Guideline 860.1480). The use on eggs will be reassessed when data are submitted. Supporting storage stability data (OCSPP Guideline 860.1380) as well as a residue analytical method for data collection (OCSPP Guideline 860.1340) are also required. These anticipated data needs are listed in Section 2, Table 10.

3.2.2 Drinking Water

A drinking water assessment was not conducted in 2006 as part of the RED for DDAC. The Agency determined at that time that the registered antimicrobial uses of DDAC were not expected to significantly impact surface or groundwater resources. The following uses of DDAC may result in drinking water exposure from surface water downstream of Waste Water Treatment Plants (WWTPs): cooling towers water systems, air washers, pulp and paper mills, and down-the-drain exposure from hospital and swimming pool uses, as well as waste water from conventional turf, golf course, ornamentals, and bulb, root, seed, and leaf drench treatments in greenhouses. In the absence of environmental fate data on sorption to activated sludge and toxicity to WWTP microorganisms, the Agency assumes that these uses can result in continuous exposure to surface water at low concentrations even though the primary route of dissipation of DDAC in the environment is sorption to sediment (bottom and suspended). If WWTP environmental fate and effects data required for registration review demonstrate high removal by sorption to sludge and a relatively low toxicity to WWTP microorganisms, the Agency does not anticipate conducting a drinking water risk assessment from DDAC in surface water downstream of WWTPs. However, in the absence of the WWTP studies or if the submitted data do not demonstrate high removal by sorption to sludge and a relatively low toxicity to WTTP microorganisms, the Agency will conduct a drinking water assessment.

Other potential sources of human exposure to drinking water are from registered antimicrobial uses of DDAC added to the interior of ice machines and the interior of water holding tanks, as well as application to reverse osmosis units in water holding tanks. The registered conventional uses of DDAC that could potentially result in human drinking water exposure include turf, golf course, and restaurant/food storage area surfaces/drains. A dietary risk assessment will include drinking water from these other potential sources and food uses.

3.3 Occupational and Residential Exposures

The Agency anticipates the need to revise the occupational and residential assessments conducted in support of the 2006 RED since the Margins of Exposure (MOEs) were calculated using toxicological point of departures (PODs) and exposure data that have since been updated. In particular, it will be necessary to reassess the inhalation exposures using the POD from the inhalation toxicity study that was submitted after the RED. In addition, DDAC's RED required label changes to mitigate occupational and residential exposures include the following:

- Add re-entry interval (REI) of 2 hours to all labels listing hatcheries fogging as a use.
- Add REI of 2 hours as well as a minimum of 4 air exchanges (ACH) per hour in the facility to all labels listing food processing plants fogging as a use.

- Add restriction that swimming pool/spa use products must not be applied when swimmers are in the immediate vicinity. Add REI of 15 minutes to all labels listing swimming pools/spas as a use.

The Agency anticipates that some mitigation measures may change due to changes in DDAC's toxicological endpoints. The exposure scenarios to be assessed during registration review are listed in Tables 25, 26, 27 and 28 for occupational handler, residential handler, occupational post application and residential post application exposures, respectively. These tables include exposure scenarios for both the antimicrobial and conventional uses of DDAC.

3.3.1 Occupational Handler Exposure

EPA anticipates the need to revise the occupational handler assessment conducted in support of the 2006 RED. In response to the need for indoor dermal and inhalation exposure data for antimicrobial chemicals, the Antimicrobial Exposure Assessment Task Force II (AEATF II) has completed exposure studies for several scenarios including liquid pour, solid pour, trigger spray and wipe, aerosol can application, mopping and pressure treatment wood preservation. These studies have been reviewed by the Agency in conjunction with the Human Studies Review Board and have been found to be ethically and scientifically acceptable for use in risk assessment. The data from these studies will be used to assess occupational and residential handler exposures for antimicrobial chemicals. In addition, two sapstain worker exposure studies (MRID 45524304 and 47618301) sponsored by the Sapstain Industry Group (SIG) were previously submitted to EPA and will be used to assess occupational handler dermal exposures during sapstain treatment. Unfortunately, the inhalation component of the SIG study was conducted for comparison to the inhalation toxicity endpoint that existed at the time of the study (the oral NOAEL of 8 mg/kg/day) and thus the LOD of 5.8 ug/m^3 for the study may not be low enough to allow comparison of exposures to the revised HEC of 0.018 mg/m^3 (18 ug/m^3) that is based on the inhalation toxicity study.

An occupational handler assessment will be conducted for conventional uses as indoor residential and commercial surface sprays, foliar greenhouse treatments, and root/bulb immersion and injection treatments. To assess occupational handler exposures for the conventional uses, the Agency will use the unit exposure data listed in the Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (US EPA, 2015). This table includes exposure data from the Agricultural Handler Exposure Task Force (AHETF) and the Outdoor Residential Exposure Task Force (ORETF).

It should be noted that data from the AHETF, ORETF, AEATF II and SIG are subject to data compensation. The occupational handler exposures to be assessed are presented in Table 25.

Table 25 – Occupational Handler Exposure Scenarios for DDAC

Exposure Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Open pour for material preservation, swimming pool treatment and industrial process and water systems treatment	Dermal, Inhalation	Short and Intermediate Term

Exposure Scenario	Exposure Routes	Duration
Wood Preservation – Pressure Treatment	Dermal, Inhalation	Short, Intermediate, and Long Term
Wood Preservation – Spray or dip treatment for sapstain control	Dermal, Inhalation	Short, Intermediate, and Long Term
Wood Preservation – Spray or brush treatment of existing shingle and shake structures	Dermal, Inhalation	Short and Intermediate Term
Hard surface disinfection using low pressure handwands, high pressure handwands, aerosol cans, trigger sprayers, mops and wipes.	Dermal, Inhalation	Short, Intermediate, and Long Term
Hard surface disinfection using handheld foggers or misters	Dermal, Inhalation	Short and Intermediate Term
Conventional Uses		
Immersion/dip treatment of bulbs and corms and broccoli/flower seed (fungicide)	Dermal, Inhalation	Short and Intermediate Term
Foliar sprays of greenhouse ornamentals, cut flowers, potted plants (handwands, handguns, foggers) (fungicide)	Dermal, Inhalation	Short and Intermediate Term
Root zone injections (fertilizer injector pumps, automatic dosing pumps or by hand) (fungicide)	Dermal, Inhalation	Short and Intermediate Term
Restaurants/kitchens/food storage area surface treatment and drain treatment with handwands, trigger spray bottles, sponges, pouring, or mopping (insecticide/fruit fly treatment)	Dermal, Inhalation	Short and Intermediate Term

3.3.2 Occupational Post Application Exposures

EPA anticipates the need to revise the occupational post application exposure assessment conducted in support of the 2006 RED. No data are anticipated to be needed to assess post application exposures for the antimicrobial uses. To assess post application exposures for the conventional uses, a dislodgeable residue (DFR) study (Guideline #875.2100) is anticipated to be needed. The occupational post application exposures to be assessed are presented in Table 26.

Table 26 – Occupational Post-Application Exposure Scenarios for DDAC

Exposure Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Post application exposure to fogging treatments	Inhalation	Short, Intermediate, and Long Term
Conventional Uses		
Post-application exposure for greenhouse foliar treatments (ornamentals, potted plants, cut flowers, etc.)	Dermal	Short, Intermediate Term

3.3.3 Residential Handler Exposures

EPA anticipates the need to revise the residential handler exposure assessment conducted in support of the 2006 RED. To assess residential handler exposures for the antimicrobial uses of DDAC, the Agency will use the data from AEATF as discussed in Section 3.3.1 for occupational handlers. To assess residential handler exposures for the conventional uses of DDAC, the Agency will use the unit exposures from the Standard Operating Procedures for Residential

Pesticide Exposure Assessment (US EPA, 2012). The residential handler exposures that will be assessed are listed in Table 27.

Table 27 – Residential Handler Exposure Scenarios for DDAC

Exposure Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Hard surface disinfection using aerosol cans, trigger sprayers, mops and wipes	Dermal, Inhalation	Short, Intermediate and Long Term
Soft surface sanitization of carpets using low pressure sprayers	Dermal, Inhalation	Short Term
Open pour for pool and spa treatment	Dermal, Inhalation	Short Term
Wood preservation – Spray and brush treatment of existing shingle and shake structures	Dermal, Inhalation	Short Term
Conventional Uses		
Lawn/turf spray	Dermal, Inhalation	Short Term

3.3.4 Residential Post-Application Exposures

EPA anticipates the need to revise the residential post-application exposure assessment conducted in support of the 2006 RED. To assess post application exposures for the antimicrobial uses, a post application inhalation exposure study (Guideline #875.2500) is anticipated to be needed. This study is needed to assess inhalation exposures resulting from the use of DDAC in humidifier water. To assess post application exposures for the conventional uses, a turf transferable residue (TTR) study (Guideline #875.2100) is anticipated to be needed. The residential post-application exposures that will be evaluated are listed in Table 28.

Table 28 – Residential Post-Application Exposure Scenarios for DDAC

Exposed Population	Exposure Scenario	Exposure Routes	Duration
Antimicrobial Uses			
Children	Mouthing DDAC treated laundry	Incidental Oral	Short and Intermediate Term
Children	Playing on decking and playground equipment	Dermal, Incidental Oral	Short and Intermediate Term
Children	Playing on treated floors and carpets	Dermal, Incidental Oral	Short and Intermediate Term
Children and Adults	Humidifier Water Treatment	Inhalation	Short and Intermediate Term
Children and Adults	Swimming in DDAC treated pools	Dermal, Incidental Oral	Short and Intermediate Term
Children and Adults	Wearing DDAC treated laundry	Dermal	Short and Intermediate Term

Conventional Uses			
Children and Adults	Playing on treated lawns/turf	Dermal	Short and Intermediate Term
Children	Playing on treated lawns/turf	Incidental Oral	Short and 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 2006 RED. Aggregate exposures will need to be assessed upon reevaluation of the aggregate assessment and toxicological endpoints, combined with the human health exposure assessments expected as a part of this registration review case. This assessment will include dietary (food and water) exposures and residential exposures.

3.4.2 Cumulative Exposures

In 2015, EPA's Office of Pesticide Programs released a guidance document entitled, Pesticide Cumulative Risk Assessment: Framework for Screening Analysis. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. In May 2016, a final version of this guidance document was released (U.S. EPA, 2016) stating that non-specific toxic effects, such as irritation, unless tied to a mode of action (MOA)/adverse outcome pathway (AOP) or testable hypothesis related to a potential MOA/AOP, would not support a candidate common mechanism group (CMG). This framework supplements the existing guidance documents for establishing common mechanism groups[6] and conducting cumulative risk assessments.[7]

The Agency has utilized this framework for DDAC and notes that irritation endpoints are not considered for cumulative assessments for DDAC and any other substances. Also, DDAC does not appear to produce a toxic metabolite produced by other substances. The Agency notes that the individual exposure scenarios in DDAC assessments are developed by summing the total percent of DDAC active ingredients on a product's label. For the purposes of this registration review, the Agency is not conducting a cumulative assessment. For information regarding the Agency'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/.

[6] Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (U.S. EPA, 1999)
[7] Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity (U.S. EPA, 2002)

4 Environmental Risk Assessment

The Agency anticipates the need to conduct an environmental risk assessment for DDAC. The Agency anticipates requiring ecological data during registration review (Table 10) and will review data required by the RED DCIs.

The Agency has not previously conducted a risk assessment that supports a complete endangered species determination for DDAC. The ecological risk assessment planned during registration review will allow the Agency to determine potential acute and chronic risks to aquatic organisms exposed to residues of DDAC that are transported from treatment sites into the aquatic environment. Such sites include cooling towers, wood preservative uses, and swimming pool/spa uses. There is potential for acute exposure in the water column because of the high solubility of DDAC in water (Table 4). However, bioconcentration in aquatic organisms is not expected despite the high log K_{ow} of 4.66 (>3) because DDAC is highly soluble in water and, being a positively-charged compound, is tightly sorbed to soil and sediment, which are typically negatively-charged. Chronic exposure to sediment-dwelling organisms from both antimicrobial and conventional uses is expected to occur based on the sorption potential from the positively-charged compound. Potential acute and chronic risks to terrestrial organisms will be assessed for the turf and golf course use only, as well as aquatic organisms.

The risk assessment also will allow the Agency to determine whether each use of DDAC has 'no effect' on, 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 Environmental Fate Assessment

DDAC is completely soluble in water, and based on the vapor pressure and Henry's Law value (Table 4), is not expected to partition from soil and water into air. DDAC is stable to hydrolysis at pH values of 5, 7, and 9 (MRID 41175801), with half lives of 368 days, 194 days, and 175 days, respectively. DDAC is stable to photodegradation in water at pH 7 (MRID 41175802); even in the presence of a photosensitizer (acetone), degradation in water is minimal with a calculated half-life of 227 days. DDAC was found to be stable in aerobic soils during a year-long metabolism study using sandy loam soil; the calculated half-life for aerobic soil degradation was 1,048 days (MRID 42253801).

Test data indicate that DDAC would be expected to be amenable to both sorption and biodegradation. The high log Kow of 4.66 (Table 4) indicates that DDAC is relatively hydrophobic, partitioning more to octanol than to water. Log Koc values of greater than 6 (MRID 41385301) indicate that DDAC would be expected to be immobile due to strong sorption to soil and sediment. In aqueous media offering the potential for both sorption and biodegradation, there is conflicting information about which of these processes would be expected to predominate. Based on results of aerobic and anaerobic aquatic metabolism studies (MRID 42253803 and 42253802), DDAC was stable to microbial degradation under aerobic conditions and anaerobic conditions in water and sediment, indicating that sorption would

predominate. In contrast, based on the results of MRID 47522212, 47522214, and 47522217, DDAC appeared to be readily biodegradable in the absence of clay, with 90% of DDAC biodegraded after 28 days, indicating that biodegradation would predominate.

A possible explanation of these apparently conflicting indications about whether sorption or biodegradation of DDAC would predominate is the difference between the test media used in the ready biodegradability study and the aquatic metabolism studies. The stability of DDAC in the aerobic and anaerobic aquatic metabolism studies can be attributed to strong sorption of DDAC to sediment present in a test medium that allows for both sorption and microbial degradation. In contrast, the finding of ready biodegradability of DDAC in the ready biodegradability study can be attributed to the influence of biodegradation which occurred in a medium in which microorganisms present are acclimated to experimental conditions that are typical of wastewater treatment plants. Consequently, these conditions would be expected to favor biodegradation over sorption of DDAC.

There is uncertainty about whether sorption or biodegradation of DDAC would predominate during wastewater treatment. In the absence of data on the extent for DDAC to sorb to sludge biomass during wastewater treatment, data from an Activated Sludge Sorption Isotherm (ASSI) study (GLN 835.1110) are needed. If the results from this study do not indicate a high potential for DDAC to sorb to sludge biomass and/or if the results from the ASRI study indicate high toxicity to activated sludge microorganisms (EC_{50} less than or equal to 20 mg/L), the Agency may require a wastewater treatment plant biodegradation simulation test rather than a ready biodegradability test.

In soil and sediment, DDAC is expected to be immobile based on the Freundlich K_{ads} values of 1,095-30,851 L/kg and K_{oc} values of 437,805 – 1,599,564 L/kg_{oc}[8] (MRID 41385301). Due to its strong adsorption to soils, DDAC is not expected to leach to ground water or be present in run-off water discharged to surface water, though it may be sorbed to eroded sediment transported in runoff. There are no major degradates of DDAC based on its stability to microbial metabolism in the environment.

4.1.1 Leaching [Treated Wood]

Leaching rates for DDAC from treated blocks were essentially proportional to the treatment rate of the wood. At the end of a 14-day period the total amount of DDAC leached ranged from 2.6-8.2%, with maximum leach rates of 1,219-13,330 $\mu g/cm^2$/day at 0.8-3.2 % w/w (MRID 49812403).

4.1.2 Wastewater Treatment Plants (WWTPs)

DDAC has the potential to reach WWTPs from the registered uses. In the absence of clay, DDAC is expected to be readily biodegradable over time (MRID 47522214, 47522212 and 47522217). Data on activated sludge sorption isotherm (ASSI) and activated sludge respiration inhibition (ASRI) have not been submitted and are expected to be required. Additional WWTP tests such as biodegradation simulation tests (835.3220, 835.3240, or 835.3280) may be required

[8] Based on the Food and Agriculture Organization of the United Nations (FAO) soil classification of mobility, http://www.fao.org/docrep/003/x2570e/x2570e06.htm

if the results of the ASSI test on DDAC do not demonstrate strong sorption to activated sludge or if results from the ASRI test indicate high toxicity to activated sludge microorganisms (EC_{50} is less than or equal to 20 mg/L).

4.1.3 Water Quality

DDAC is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[9]. In addition, no Total Maximum Daily Loads (TMDL) have been developed for DDAC[10]. More information on impaired water bodies and TMDLs can be found at EPA's website[11].

4.2 Conceptual Models for Environmental Exposure Pathways

Based on the summary of registered uses of DDAC presented in Table 6, physical/chemical properties and environmental fate data presented in Table 4 and Appendix B, the Agency has developed conceptual model diagrams for exposure of ecological organisms to DDAC. Under environmental conditions where DDAC is likely to be released, DDAC is not likely to hydrolyze (MRID 41175801) or photolyze (MRID 41175802).

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 down-the-drain and from several hours to roughly a day following their discharge to subsequently be discharged from wastewater treatment plants to surface water. Since DDAC is stable to chemical degradation (hydrolysis and photodegradation), DDAC is expected to enter wastewater treatment plants as a result of down-the-drain discharges of DDAC. Sorption is expected to be the main pathway for removal of DDAC entering WWTPs but data supporting this assumption have not been submitted. Because of DDAC's expected stability in the aquatic environment, aquatic organisms in surface water downstream of both direct and indirect sources of DDAC would be expected to be exposed to DDAC and not its degradation products.

The Agency has created conceptual models for potential routes of environmental exposure which are included in "Conceptual Models for Environmental Exposure Pathways of Antimicrobial Pesticides", found in the docket at www.regulations.gov, EPA-HQ-OPP-2014-0638-0002.

Use sites and corresponding figures of conceptual model diagrams are as follows:

- Cleaning and laundry down-the-drain uses (slide 15)
- Cooling towers and air washer systems (slides 13 and 14)
- Pulp and paper mill use (slide 26)
- Swimming pool and spa use (slides 27 and 28)
- Wood preservative uses: industrial (slide 29); professional or amateur in-service (slides 30 and 31)

[9] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885
[10] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[11] http://www.epa.gov/owow/tmdl/

For the turf and golf course use only, ecological receptors that may potentially be exposed to DDAC include terrestrial and semiaquatic wildlife (*i.e.*, mammals, birds, amphibians and reptiles), terrestrial and semi-aquatic plants, and terrestrial and aquatic sediment invertebrates (including insect pollinators). Additionally, aquatic organisms (*i.e.*, freshwater and estuarine/marine fish and invertebrates, amphibians, and aquatic plants) are potential receptors in adjacent water bodies through the off-site transport of DDAC from the application site through erosion and spray drift (commercial turf and golf courses). Based on DDAC's sorption properties, it is not expected that off-site transport via runoff water discharged to surface water will be of concern.

4.3 Ecological Effects Assessment

4.3.1 Ecotoxicity Endpoints

Acute and chronic toxicity data from registrant-submitted studies (850 OCSPP Harmonized Test Guidelines) are used to evaluate the potential effects of the DDAC active ingredients to aquatic and terrestrial non-target organisms. Available ecotoxicity endpoints, data requirements, and data gaps for the DDAC active ingredients are presented in Appendix C. OPP uses the most sensitive of these endpoints for assessing risks to each receptor group. The endpoints currently selected for risk assessment are listed in Table 29.

Table 29 – Available Ecotoxicity Endpoints

Receptor Group	Test Material	Scenario	Toxicity Endpoint	Reference (MRID)
Freshwater fish	TGAI	Acute	LC_{50} = 190 µg ai/L (highly toxic)	47555301
		Chronic	NOAEC = 32 ai/L	--
Freshwater invertebrates	TGAI	Acute	EC_{50} = 18 µg ai/L (very highly toxic)	00147818
		Chronic	NOAEC = 10 µg ai/L	--
Estuarine/marine fish	TGAI	Acute	LC_{50} = 960 µg ai/L (highly toxic)	43620001
Estuarine/marine invertebrates	TGAI	Acute	EC_{50} = 69 µg ai/L (very highly toxic)	41578004
Benthic invertebrates, freshwater[1]	TGAI	Chronic	NOAEC = 260 mg/kg sediment	45821701
Benthic invertebrates, estuarine/marine	TGAI	Chronic	Data gap	--
Aquatic plants (vascular)	TGAI	--	Data gap	--
Aquatic plants (algal)	TGAI	--	EC_{50} = 11.3 µg ai/L NOAEC = 5.4 µg ai/L	46295803

Birds	TGAI	Acute	LD_{50} = 54.4 mg ai/kg bw (moderately toxic)	00148078
		Dietary	LC_{50} = 2625 ppm (slightly toxic)	ACC132486
		Chronic	Not required	--
Beneficial insects	TGAI	Acute	Data gap	--

[1] The guideline is partially fulfilled. Testing on one additional freshwater species is needed.

4.3.2 Deactivation Studies

Deactivation studies have been submitted using the fathead minnow (*Pimephales promelas*) exposed in the water column and midge (*Chironomus tentans*), mayfly (*Hexagenia limbata*), amphipod (*Hyalella azteca*), and *Daphnia magna* exposed in sediments containing various concentrations of DDAC. According to the registrant, these studies were submitted to ". . . show a substantial reduction in potential ecological risks, associated with DDAC, when clay deactivation is used in once-through cooling water systems treated with DDAC." Endpoints and citations for these ecotoxicity tests are provided in the data tables in Appendix C. Any relevant information from these tests will be used when the risk assessment is conducted.

4.3.3 Open Literature

The ECOTOXicology (ECOTOX) is a source for locating single chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The database will be searched when the risk assessment is conducted. Any acute or chronic endpoints more sensitive than what is currently available may be used in the risk assessment. Other relevant information also may be used to characterize risks. ECOTOX was created and is maintained by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory's (NHEERL's) Mid-Continent Ecology Division (MED).
https://cfpub.epa.gov/ecotox/

4.4 Exposure Analysis Plan

4.4.1 Screening Level Down-the-Drain Analysis

A screening level Down-the-Drain (DtD) analysis would be performed if all of DDAC's uses were released from residential, commercial, and institutional applications solely to domestic wastewater treatment plants. However, DDAC is also used in industrial applications that would lead to discharges to industrial wastewater treatment plants. Therefore, no screening level DtD analysis was performed for this FWP.

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 its reregistration decision for DDAC, 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), DDAC is 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. A second list of chemicals identified for EDSP screening was published on June 14, 2013[12] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.
For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[13]

6 Label Changes

As noted in section 1.6, the Agency is actively working to bring DDAC labels into compliance with risk mitigation measures from the DDAC RED. DDAC's PDCIs issued in May 2015 required revised labels be submitted according to requirements listed in the RED and Fact Sheet. If the Agency finds that DDAC's product-specific data and labels are not acceptable, the Agency may require the registrant to submit additional or amended information or proceed with suspension action. The Agency will continue to pursue label compliance through regulatory or other action during registration review, as the RED risk mitigation measures would impact the scope of DDAC's risk assessment.

[12] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[13] http://www2.epa.gov/endocrine-disruption

As indicated in Section 1.6.1, the Agency has established tolerance exemptions for residues of some uses of quaternary ammonium compounds in/on food (see Table 7). The end-use concentration of these specific quaternary ammonium compounds is not to exceed 200 or 240 ppm of active quaternary ammonium compound and the end-use concentration of all quaternary chemicals in the solution is not to exceed 400 ppm of active quaternary compound. These exemptions are listed under 40 CFR part 180.940. The Agency notes in Section 3.2.1. that some DDAC labels allow for end-use solution concentrations for food-contact hard surfaces greater than the established tolerance exemption of 200 or 240 ppm for DDAC; however, the Agency will use the end-use solution concentrations greater than 240 ppm for risk assessment and will evaluate the need for revisions to the product labels and/or to the existing tolerance exemptions.

The Agency invites any label amendments that could be considered to eliminate the anticipated need for EPA to require certain data, reduce the possibility that EPA's planned risk assessments overestimate risk due to reliance on conservative assumptions, and/or improve label clarity.

7 Next Steps

A DCI will be developed requiring generation and submission of the data listed under the "Anticipated Data Needs" Section of this document. The Agency expects to issue the DCI by March of 2018.

8 References

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Appendix A Toxicology Profile

Acute Toxicity for Product Labeling

DDAC was assigned Toxicity Category II in two acute oral toxicity studies in rats, MRIDs 41394404 [65% a.i.; LD_{50} = 262 mg/kg (combined)] and 42296101 [80% a.i.; LD_{50} = 238 mg/kg (combined)]. DDAC was assigned Toxicity Category III in two acute dermal toxicity studies in rabbits, MRIDs 42053801 [65% a.i.; LD_{50} = 2930 mg/kg (combined)] and 00071158 [50% a.i.; LD_{50} = 4350 mg/kg (combined)]. For acute inhalation toxicity (MRID 00145074), the LC_{50} of DDAC (purity not reported) was reported as 0.07 mg/L; Toxicity Category II was assigned. For primary eye irritation, DDAC was found to be corrosive (Toxicity Category I) in two primary eye irritation studies in rabbits, MRIDs 41394404 [65% a.i.] and 42161602 [80% a.i]. For primary dermal irritation, DDAC (80% a.i.) was found to be corrosive (Toxicity Category I) in a primary dermal irritation study in rabbits (MRID 42161601). A dermal sensitization study in guinea pigs using BARDAC 2280 80% a.i. (MRID 46367601) showed that DDAC is not a dermal sensitizer.

Table 30 – Acute Toxicity Studies for DDAC

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100/ Acute oral toxicity	41394404	LD_{50} =262 mg/kg (combined) LD_{50} =331 mg/kg (males) LD_{50} =238 mg/kg (females)	II
	42296101	LD_{50} =238 mg/kg (combined)	
870.1200/ Acute dermal toxicity	42053801	LD_{50} =2930 mg/kg (combined) LD_{50} =3140 mg/kg (males) LD_{50} =2730 mg/kg (females)	III
870.1300/ Acute inhalation toxicity	00145074	LC_{50} (combined) = 0.07 mg/L	II
870.2400/ Acute eye irritation	41394404	Corrosive	I
870.2500/ Acute dermal irritation	42161601	Corrosive	I
870.2600/ Skin sensitization	46367601	Not a sensitizer	N/A

N/A=Not available

Subchronic Toxicity

The database for subchronic toxicity of DDAC is considered complete. For oral toxicity, the database includes two studies, a 90-day oral toxicity test in rats (MRID 40966302) and a 90-day oral study in dogs (MRID MRID 40262901). For dermal toxicity, there are two 21-day dermal studies using DDAC formulations, one in the rat (MRID 45656601) and one in the guinea pig

(MRIDs 40565301 and 41105801) and there is a 90-day dermal toxicity study using DDAC, technical grade, in rats (MRID 41305901). There is a 28 day inhalation study using DDAC (50.79%) in rats (MRID 48667903).

870.3100 Subchronic (Oral) Toxicity - Rat

In a 90-day rat feeding study (MRID 40966302), male and female rats were given diets containing 0, 100, 300, 600, 1000, and 3000 ppm (respective mg/kg/day equivalents; 0, 6.2, 18.5, 36.8, 60.7 and 175 for males; 0, 7.5, 22.3, 44.4, 74.3 and 225.5 for females) DDAC for 13 weeks. High-dose animals showed increased mortality, decreased mean body weights, body weight gain and food consumption, and increased incidence of gross pathological observations and non-neoplastic lesions, including a higher incidence of glycogen depletion in the liver and contracted spleens. Additionally, high-dose females showed sinus erythrocytosis and lymphoid hyperplasia of mesenteric lymph nodes.

From the results of this study, the NOAEL is 60.7 mg/kg/day for males and 74.3 mg/kg/day for females. The LOAEL is 175.4 mg/kg/day for males and 225.5 mg/kg/day for females. The LOAEL is based on increased mortality, decreased mean body weights, body weight gain and food consumption, and increased incidences of gross pathological lesions.

This study is classified as acceptable.

870.3150 Subchronic (Oral) Toxicity - Dog

DDAC at doses of 0, 5, 15 and 50 mg/kg/day. High-dose animals experienced marked decrease in body weight gain, food consumption and food efficiency. Clinical chemistry, hematology, urinalysis, and pathological results did not reveal any treatment-related effects.

Based on decreased body weight gain, food consumption and food efficiency, for both males and females, the NOAEL is 15 mg/kg/day, and the LOAEL is 50 mg/kg/day.

This study is classified as acceptable.

870.3250 Subchronic (21-day dermal) Toxicity – Guinea pig

In a 21day dermal toxicity study (MRIDs 40565301 and 41105801), a 1:5 dilution of HS sanitizing carpet shampoo (containing 6% didecyl dimethyl ammonium chloride and 4% alkyl dimethyl benzyl ammonium chloride) was applied to a 2 inch square area of the shaved dorsal trunk of 5 male and 5 female guinea pigs at doses of 500 and 1000 mg/kg, five days a week, for 21 days. Actual doses to the skin based on 6% DDAC in the formulation were calculated to be 30 and 65 mg/kg a.i. (communication from registrant). There was no mortality or signs of clinical toxicity noted. Signs of skin irritation were noted during the second week of treatment and the report stated that the response intensified during the third week of treatment. Body weight was decreased in treated males and females by 7% and 11% vs untreated animals at week 3. Results of hematology and clinical chemistry measurements indicated a slight elevation of basophils and eosinophils as well as a slight elevation of SGPT and SGOT but statistics were not

performed on these data. Histologically, the skin irritation was described as sloughing of the stratum corneum as a result of defatting.

Although this study was identified with several deficiencies (HED document 007757, from the 1/31/90 review by Pamela Hurley, Ph.D.), the data are useful for determining a level of concern for dermal irritation and systemic effects after shortterm exposure to ADBAC. In this case, the 500 mg/kg dose level (30 mg/kg a.i.) produced no significant dermal or systemic effects, and is considered a NOAEL for the study for dermal irritation and systemic effects.

870.3200 Subchronic (21-day dermal) Toxicity – Rat

In a 21-day dermal toxicity study (MRID 456566-01), SS0853.01 (100% pure) was administered directly to the skin of CD [Crl:CD (SD) IGS BR] rats (10/sex/group) at doses of 100, 500, and 1000 mg/kg-day. The dermal route of exposure was chosen because it is a possible route of human exposure. Doses for this study were determined by the Sponsor to achieve a gradient of toxic effects. The high-dose level was selected per OPPTS 870-3200 and was considered to show signs of toxicity. The mid-dose level was selected as an additional dose in order to evaluate any potential toxicological effects.

No treatment-related effects on clinical observations (including expanded clinical observations), motor activity, dermal irritation, ophthalmic observations, body weights or body weight changes, food consumption, clinical pathology parameters, terminal body weights, mean absolute or relative organ weights, or macroscopic or microscopic observations were observed. Analyses of hindlimb strength, food consumption, hematology and clinical chemistry parameters, and relative organ weights showed significantly reduced hindlimb strength in female rats at 500 and 1000 mg/kg/day. However, there were no other indications of effects on motor function in male or female rats at any dose tested. Numerous microscopic changes in the liver were observed, but were noted to be test system-related due to the torso wrapping procedure. The systemic NOAEL for SS0853-01 is 1000 mg/kg-day in this study, and the systemic LOAEL is > 1000 mg/kg/day.

This study is classified as acceptable.

870.3250 Subchronic (90-day dermal) Toxicity – Rat

In a 90-day rat dermal study (MRID 41305901), Sprague-Dawley rats (15/sex/group) received repeated dermal dosing of the test compound at 0, 2, 6, and 12 mg/kg/day for 6 hours/day, 5 days/week for 13 weeks. No treatment-related effects were noticed in mortality, weight gain, food consumption, or systemic toxicity. Toxicity was limited to treated skin of mid-dose females and high-dose males and females. The clinical and gross findings (erythema, edema, exfoliation, excoriation and ulceration) were confirmed by histopathological examination, where increased incidence of hyperkeratosis, acanthosis, epidermitis, dermatitis and ulceration were noted.

The systemic NOAEL is gr**e**ater than 12 mg/kg/day (highest dose tested). The dermal LOAEL for dermal toxicity is 6 mg/kg/day. The dermal NOAEL is 2 mg/kg/day.

This study is classified as acceptable.

TG412 Subchronic (28-day inhalation) Toxicity – Rat

In a subchronic inhalation toxicity study (MRID 48667903), Didecyl dimethyl ammonium chloride (DDAC) (50.79%, 00503J5) was administered to 5 Sprague-Dawley rats/sex/concentration by dynamic nose-only exposure at concentrations of 0, 0.08, 0.5, and 1.5 mg/m^3 (0.00008, 0.0005, 0.0015 mg/L) for 6 hours/day, 5 days/week for a total of 20 or 21 days depending on necropsy time. There were two additional groups of 5 rats/sex exposed to 0 or 1.5 mg/m^3 which had a 2-week recovery period before necropsy.

No early mortality was observed in any of the dose groups. At all concentrations in males and at the 0.5 and 1.5 mg/m^3 concentrations in females, lower body weight was observed. In males, these body weights were 6.1%, 9.9% and 20.5% lower respectively in males and 4.0% and 8.5% lower respectively in females. This was statistically significant in 1.5 mg/m^3 dosed males. Lower body weight was correlated with statistically significant lower food consumption. In the 1.5 mg/m^3 group, females and males had increased body weight gain during recovery, leading to full resolution of body weight reduction in females and partial resolution in males.

Concentration-related higher lung weights per 100 grams of body weight occurred in the 1.5 mg/m^3 group males and 0.5 and 1.5 mg/m^3 group females. These changes were reversible. Ulceration of the stratified squamous epithelium in the nasal cavity in the 1.5 mg/m^3 group male and females and degeneration of the olfactory epithelium of the nasal cavity in the 0.5 and 1.5 mg/m^3 group males and 1.5 mg/m^3 group females also occurred.

The bronchoalveolar lavage fluid (BALF) analysis indicated that at the high dose (for most measures the only dose examined other than control) that neutrophils and eosinophils increased with a concomitant decrease in macrophages. In males, there was an increase in cell count and total protein across all doses. In females there was a dose-dependent increase in LDH across all doses, while in males there were increases but the size of some standard deviations made determining dose dependence difficult. This increase was consistent with an increase in lung inflammation. Statistical significance was difficult to assess with the small sample size of 5 animals per group, but trends towards changes in these parameters was clear.

Ulceration and increase in mucus production was most pronounced in the rostral section of the nasal cavity. DDAC produced ulceration of the nasal vestibule lined with stratified squamous epithelium and increased mucus production. There was also degeneration of the olfactory epithelium along with squamous metaplasia in nasal sections II and III. These regions are especially susceptible to injury, as they represent the most rostral extension of the olfactory epithelium. There were increases in mucus respiratory epithelium in a dose and severity dependent fashion. There were also changes in nasal cavity hemorrhage. These effects generally change in severity with dose.

The LOAEC is 0.08 mg/m^3/day based on increases in relative lung weight (males), changes in LDH, BALF total protein, BALF cell count (males only), increase in mucus in the respiratory epithelium, increase in hemorrhage, increase in mucoid exudate. These effects are observed to

occur in a dose dependent fashion. The changes in BAL fluid are consistent with inflammatory effects in the lung. There was also the start of a trend towards lower body weights in males at this dose. There is no NOAEC established in this study.

These findings and conclusions were made using the available information within the report.

This study was missing histopathology of numerous major organ groups as required by the guideline, including but not limited to heart, thymus, spleen, thyroid, bone, testes and stomach. Although these measurements were not made, per guideline, this study is considered acceptable as this study was designed to examine route specific (primarily respiratory) effects.

The study is well designed and provides scientifically sound information. The study is classified as acceptable.

Developmental Toxicity

Adequacy of database for Prenatal Developmental Toxicity: The database includes 2 developmental studies, one in the rat (MRID 41886701) and another in the rabbit (MRID 41018701).The database includes 2 developmental studies, one in the rat (MRID 41886701) and another in the rabbit (MRID 41018701).

870.3700 Prenatal Developmental Toxicity (Gavage) Study – Rat

In a developmental toxicity study (MRID 41886701) DDAC (80.8% a.i.) was administered to 25 female Sprague Dawley rats/dose by gavage at dose levels of 0, 1, 10 or 20 mg a.i./kg/day from days 6-15 of gestation, inclusive.

Compound related and dose dependent maternal toxicity was observed at 10 and 20 mg/kg/day. It manifested as significantly increased clinical signs (audible respiration and/or gasping) at both dose level as well as decreased food efficiency. There were decreases in body weight gains in the 20 mg/kg/day group.

The maternal LOAEL is 10 mg/kg bw/day, based on clinical signs, including audible respiration. The maternal NOAEL is 1 mg/kg bw/day.

There were no signs of developmental effects. The developmental LOAEL is > 20 mg/kg bw/day. The developmental NOAEL is ≥20 mg/kg bw/day.

This is a revision of the existing DER for this chemical. Based on an updated review of the study and effects, the previously noted developmental effects (increased incidence of skeletal variations) were determined to be equivocal and not dose dependent. Therefore the developmental endpoint is revised as above.

This study is classified as acceptable.

870.3700 Prenatal Developmental Toxicity (Gavage) Study – Rabbit

In a developmental toxicity study (MRID 41018701) DDAC (80.8% a.i.), 16 New Zealand White rabbits per dose were administered DDAC daily via gavage at dose levels of 0, 1, 3, or 10 mg/kg bw/day on gestational days (GDs) 6-18, inclusively.

There was an increased incidence of mortality in maternal rabbits at 10 mg/kg bw/day. Hypoactivity (1/16), labored respiration (4/16), audible respiration (7/16) and decreased body weight gain during the period (60% of control) were present at 10 mg/kg bw/day.

The maternal LOAEL is 3 mg/kg bw/day, based on clinical signs, including hypoactivity, labored and/or audible respiration and decreased body weight gain during the dosing period. The maternal NOAEL is 1 mg/kg bw/day.

There was a decrease in fetal body weights at the highest dose tested (10 mg/kg/day). The developmental LOAEL is 10 mg/kg bw/day based on decreased fetal body weights. The developmental NOAEL is 3 mg/kg bw/day.

NOTE: This is a revision of the existing DER for this chemical (TXR 010689). Based on a re-review of the study and effects, it was determined that there was an insufficient number of does available to make the determination that the increase in dead fetuses at the 10 mg/kg bw/day dose level was a real effect, rather than a statistical artifact. Therefore the developmental endpoint is revised as above.

Reproductive Toxicity

Adequacy of database for Reproductive: The database for reproductive toxicity of DDAC is considered complete. The database includes an acceptable 2-generation reproduction toxicity study in rats, MRID 41804501.

870.3800 Reproduction and Fertility Effects – Rat

In a two-generation reproduction study (MRID 418045-01), 28/sex/dose (both F0 and F1) Sprague-Dawley CD Rats were fed a diet containing DDAC (80.8% a.i.) at dosage levels of 0, 300, 750, and 1500ppm (during premating, for both sexes = 22, 56, and 113 mg/kg/day, for males = 20, 50, and 103 mg/kg/day and for females = 24, 61, and 122 mg/kg/day). No compound-related mortalities were observed in either sex or generation. No compound-related clinical signs were observed in either sex or generation.

Based on decreased body weight/weight gain and food consumption, the parental Toxicity NOAEL = 750ppm (56 mg/kg/day); LOAEL = 1500ppm (113 mg/kg/day) . Based on decreased pup body weight/weight gain, the reproductive toxicity NOAEL = 750ppm (56 mg/kg/day); LOAEL = 1500ppm (113 mg/kg/day).

This study is classified as acceptable.

Chronic Toxicity

Adequacy of database for Chronic Toxicity: The database for chronic toxicity of DDAC is considered adequate, including a chronic oral toxicity study in dogs (MRID 41970401).

870.4100 Chronic Toxicity (Oral feed) – Dog

In a chronic, 1-year toxicity study (MRID 41970401), males and female beagle dogs were administered DDAC (80.8% a.i.) at dosage levels of 0, 3, 10 and 20/30 mg/kg/day (dosing at 30 mg/kg/day was not tolerated well and was discontinued on day 31; dosing was resumed at day 36 at 20mg/kg/day). No treatment-related deaths occurred during the study. The treatment-related clinical signs (soft/mucoid feces, emesis) were observed frequently in high-dose animals. Hematology or urinalysis results were normal. Total cholesterol levels were significantly decreased in high-dose females. Gross and histopathological findings did not reveal any treatment-related effects.

Based on increased incidence of clinical observations (emesis and soft/mucoid feces) in males and females and decreased total cholesterol levels in females, the NOAEL for both male and females is 10 mg/kg/day, and the LOAEL is 20 mg/kg/day.

This study is classified as acceptable.

Carcinogenicity

Adequacy of database for Carcinogenicity: The database for the carcinogenicity of DDAC is considered adequate. The database for carcinogenicity includes two combined chronic/carcinogenicity studies, one in the rat (MRID 41965101) and one in the mouse (MRID 41802301).

870.4300 Combined Chronic /Carcinogenicity (Oral) – Rat

In a two-year rat carcinogenicity study (MRID 41965101), 60 Sprague-Dawley CD rats per sex per group were fed diets containing DDAC (80.8% a.i.) at 0, 300, 750 or 1500 ppm (mg/kg/day equivalents: 0, 13, 32, and 64 for males and 0, 16, 41, and 83 for females) for two years. High-dose animals showed significant, but slight (<10%) decreases in mean body weight during the study. Treatment related effects consisted of increased incidence of sinusoidal blood, hemosiderosis and histiocytosis in the mesenteric lymph nodes of high dose animals. In addition, an increase in the incidence of interstitial cell adenomas in testes was reported. In this study, the incidences of this tumor for control and treated animals are: Control 1 (5%, 3/60); Control 2 (5% 3/60), 300ppm (12.5%, 1/8), 750ppm (17.9%, 5/28), and 1500ppm (11.7%, 6/60). However, because the incidence was within the historical incidence range, this effect was not considered treatment related. (See Table 31)

Table 31 – Incidence of Testicular Interstitial Adenomas in Male Sprague-Dawley Rats for the Studies conducted at Bushy Run Research Center since 19871,2

Study	Dates of In-Life Phase	Group[3]				
DDAC	06/3/88 to 06/19/90	3/60	3/60	1/18	5/28	7/60
Historical Control #1	03/22/88 to 03/27/90	3/59	1/60	-	-	-
Historical Control #2	03/08/89 to 03/13/91	4/59	7/60	-	-	
Historical Control #3	04/29/91 to 05/04/93	1/60	6/60	-	-	-

[1] Data provided by Bushy Run Research Center (1995, MRID 43613801).
[2] All rats were from Charles River Breeding Laboratories, Portage MI.
[3] C_1 - Control Group 1; C_2 - Control Group 2; L - Low-dose Group; M - Mid -dose Group; and H- High-dose group.

The NOEL for both sexes is 750 ppm. The LOEL for both sexes is 1500 ppm, based on increased incidence of non-neoplastic lesions in the mesenteric lymph nodes.

This study is classified as acceptable.

870.4300 Combined Chronic/Carcinogenicity (Oral) – Mouse

In a 78-week mouse feeding carcinogenicity study (MRID 41802301), 60 CD-1 mice per sex per group were fed diets containing DDAC (Batch # B-1889, 80.8% a.i.) at levels of 0, 100, 500 or 1000 ppm (mg/kg/day equivalents:0, 15.0, 76.3, and 155.5 for males and 0, 18.6, 93.1, and 193.1 for females). No treatment-related effects were noted in the incidence of clinical signs, deaths, gross and histopathological observations. Hematological values were comparable among all study groups.

The NOAEL for both male and females is 500 ppm (76.3 mg/kg/day for males and 93.1 mg/kg/day for females), and the LOAEL is1500ppm (155.5 mg/kg/day for males; 193.1 mg/kg/day for females). The LOAEL is based on decreases in mean body weights and body weight gains.

At the dose level tested, DDAC was not carcinogenic.

This study is classified as acceptable.

Mutagenicity

In the Ames test, with or without the microsomal activation (S-9 fraction), DDAC was not mutagenic to *Salmonella typhimurium* tester strains (MRID 40282201 and supplemental information MRID 44005801).

In a forward gene mutation assays (MRID 93014008, reformat of 40895202) demonstrated that DDAC was negative for induction of gene mutations in CHO cells at the HGPRT locus, with levels of DDAC ranging from 1-10 µg/ml without S9 induction and 1-26 µg/ml with S9

induction. Severe toxicity was demonstrated at doses of ≥10 µg/ml (-S9) and ≥ **25** µg/ml (+S9).

In an *in vitro* chromosome aberration test (MRID 41252601), DDAC failed to induce chromosome aberrations in Chinese hamster ovary (CHO) cells harvested 26 hours after exposure to DDAC at concentrations of 1-8 µg/ml without microsomal fraction (S9) induction or DDAC at concentrations of 2-8 µg/ml with S9 induction. Cytotoxic effects were observed at DDAC concentrations 16 µg/ml (with or without S9).

In an *in vitro* mutagenicity test (MRID 93014007, reformat of 40895201), DDAC did not induce unscheduled DNA Synthesis (UDS) in primary rat hepatocytes treated with DDAC at doses up to 2.00 µg/ml. Higher concentrations (4.0 µg/mL) of DDAC were severely cytotoxic.

Other Toxicological Effects

Requirement of immunotoxicity, acute and subchronic neurotoxicity studies were waived (HASPOC memo TXR# 0052128).

In a rat pharmacokinetics/ metabolism study (MRID 41617101 and addendum 41385101), single oral doses of ^{14}C-DDAC (5 or 50 mg/kg) or repeated dose (34 ppm of DDAC in the diet for 14 days and then one single dose of 5 mg/kg of ^{14}C-DDAC) were given to both male and female rats. DDAC was mostly excreted in the feces within 3 days principally as parent compound and metabolites. The elimination pattern and metabolic profile was not substantially altered by the dose or exposure duration. Male and female rats showed similar elimination patterns, but females metabolized DDAC more extensively than males. Four major metabolites were identified as oxidation products with oxidation confined to the decyl side chains.

Appendix B Environmental Fate

Environmental Fate and Transport Properties of DDAC

DDAC is completely soluble in water, and, based on the vapor pressure and Henry's Law value (Table 4), is not expected to partition from soil and water into air. DDAC is stable to hydrolysis at pH values of 5, 7, and 9 (MRID 41175801), and stable to aqueous photodegradation at pH 7 (MRID 41175802).

Test data indicate that DDAC would be expected to be amenable to both sorption and biodegradation. The high log Kow of 4.66 (Table 4) indicates that DDAC is relatively hydrophobic, partitioning more to octanol than to water. Log Koc values of greater than 6 (MRID 41385301) indicate that DDAC would be expected to be immobile due to strong sorption to soil and sediment. In aqueous media offering the potential for both sorption and biodegradation, there is conflicting information about which of these processes would be expected to predominate. Based on results of aerobic and anaerobic aquatic metabolism studies (MRID 42253803 and 42253802), DDAC was indicated to be stable to microbial degradation under aerobic conditions and anaerobic conditions in water and sediment, indicating that sorption would predominate. In contrast, based on the results of ready biodegradability studies (MRID 47522212, 47522214, and 47522217), DDAC appeared to be readily biodegradable in the absence of clay, with 90% of DDAC biodegraded after 28 days, indicating that biodegradation would predominate.

A possible explanation of these apparently conflicting indications about whether sorption or biodegradation of DDAC would predominate is the difference between the test media used in the ready biodegradability study and the aquatic metabolism studies. The stability of DDAC in the aerobic and anaerobic aquatic metabolism studies can be attributed to strong sorption of DDAC to sediment present in a test medium that allows for both sorption and microbial degradation. In contrast, the finding of ready biodegradability of DDAC in the ready biodegradability study can be attributed to the influence of biodegradation which occurred in a medium in which microorganisms present are acclimated to experimental conditions that are typical of wastewater treatment plants. Consequently, these conditions would be expected to favor biodegradation over sorption of DDAC.

There is uncertainty about whether sorption or biodegradation of DDAC would predominate during wastewater treatment. In the absence of data on the extent for DDAC to sorb to sludge biomass during wastewater treatment, data from an Activated Sludge Sorption Isotherm (ASSI) study (GLN 835.1110) are needed. If the results from this study do not indicate a high potential for DDAC to sorb to sludge biomass and/or if the results from the ASRI study indicate high toxicity to activated sludge microorganisms (EC_{50} less than or equal to 20 mg/L), the Agency may require a wastewater treatment plant biodegradation simulation test rather than a ready biodegradability test.

DDAC was found to be stable in aerobic soils during a year-long metabolism study using sandy loam soil; the calculated half-life for aerobic soil degradation was 1,048 days (MRID 42253801). In soil and sediment, DDAC is expected to be immobile based on the Freundlich K_{ads} values of 1,095-30,851 L/kg and K_{oc} values of 437,805 – 1,599,564 L/kg (MRID 41385301). Because of its strong sorption to soils, DDAC is not expected to leach to ground water or run off in dissolved form to surface water. Table B1 contains a summary of environmental fate data for DDAC.

DDAC has the potential to reach WWTPs from the registered uses. Data from activated sludge sorption isotherm (ASSI) and activated sludge respiration inhibition (ASRI) studies have not been submitted and are required.

Water and Sediment

Hydrolysis

In a hydrolysis study (MRID 41175801) DDAC was essentially stable with half-lives of 368 days at pH 5, 194 days at pH 7 (TRIS), 175 days at pH 7 (HEPES) and 506 days at pH 9 at 25^{o}C ± 1^{o}C.

Aqueous Photolysis

In a photodegradation in water study (MRID 41175802) DDAC was essentially stable to photodegradation in sterile buffered solutions and sensitized solutions at pH 7; the calculated half-life was 227 days at 25^{o}C ± 1^{o}C.

Octanol-Water Partition Coefficient and Bioconcentration in Fish

The log K_{ow} of DDAC is 4.66 (Table 4), which is above the level of concern for potential bioconcentration in fish (>3). However, the bioconcentration in fish study (MRID 42480701) submitted demonstrated limited bioconcentration factors of 38X (edible tissue), 140X (non-edible tissue), and 81X for whole fish. The limited bioconcentration is consistent with the miscibility of DDAC in water (Table 4). No additional data are required for bioconcentration in fish.

Aerobic Aquatic Metabolism

In an aerobic aquatic metabolism study (MRID 42253803) DDAC was essentially stable with a half-life of 180 days. There are indications that strong sorption to sediment contributed to this apparent stability.

Anaerobic Aquatic Metabolism

In an anaerobic aquatic metabolism study DDAC was stable with a half-life of 261 days (MRID 42253802). There are indications that strong sorption to sediment contributed to this apparent stability.

Leachability from Treated Wood

A study done on DDAC (MRID 49812403) demonstrated leaching rates for DDAC from treated blocks were essentially proportional to the treatment rate of the wood. At the end of a 14-day period the total amount of DDAC leached ranged from 2.6-8.2%, with maximum leach rates of 1,219-13,330 ug/cm^2/day at 0.8-3.2 % w/w.

Another study was performed with didecylmethyl ammonium carbonate (DDACarb, MRID 45524305). Leaching rates for DDACarb were inversely related to the treatment rate of the treatment rate of wood. The maximum, minimum, and average leaching rates ranged from 624 - 2,174, 74 – 179, and 198 – 585 ug/cm^2/day at 0.8-3.2% w/w. The total amount of DDACarb leached ranged from 1.5%-2.0%

Data from the DDAC study may be used to bridge to the other aliphatic alkyl quaternary chemicals, while data from the DDACarb study may be used to satisfy DDACarb data requirements only.

Soil

Soil Leaching/Adsorption/Desorption Batch Equilibrium

The Freundlich K_{ads} value range from 1,095-30,851 L/kg and $K_{oc\ values}$ of 437,805 – 1,599,564 L/kg for DDAC. DDAC is expected to be immobile based on its Freundlich K_{ads} and K_{oc} values (MRID 41385301). Additional soil leaching data are not anticipated to be required.

Photodegradation on Soil

In a photodegradation on soil study (MRID 42480701) the half-life of DDAC was reported to be 169 days and DDAC is thus considered stable to photolysis on soil.

Aerobic Soil Metabolism

In an aerobic soil metabolism study (MRID 42253801) DDAC was stable with a calculated half-life of 1,084 days.

Anaerobic Soil Metabolism

DDAC is not expected to degrade in anaerobic soil based on the stability observed in the aerobic soil metabolism study (MRID 422538001), aerobic aquatic metabolism study (MRID 42253803) and anaerobic aquatic metabolism study (MRID 42253802). Anaerobic soil metabolism data are not anticipated to be required.

Fate and Transport in WWTP

Activated Sludge Respiration Inhibition

ASRI data are anticipated to be required because the registered uses of DDAC can result in exposure to microorganisms in WWTPs.

Activated Sludge Sorption Isotherm

ASSI data are anticipated to be required because the registered uses of DDAC can result in releases to WWTPs, the log K_{ow} value is ≥3, results of the adsorption/desorption study indicate high sorption potential, and DDAC is a quaternary ammonium compound that would be expected to sorb to sludge because of its positive electrical charge.

Activated Sludge Biodegradation

The Agency has received four ready biodegradability studies for DDAC (MRID 47522214, 47522212, 47522217, and 46865701). These studies provide conflicting supplemental data.

DDAC was reported to be not readily biodegradable in MRID 46865701, however, there is low confidence in this study because a decline in cumulative CO_2 was measured during the study with no explanation provided. This suggests some type of sampling error occurred during the study; normally cumulative CO_2 shows a steady increase until it plateaus.

The remaining three studies submitted (MRID 47522214, 47522212, and 47522217) suggest that DDAC is readily biodegradable. DDAC is reported to be readily biodegradable in MRID 47522214 with 71% biodegradation after day 6 and 90% after 28 days. This study was considered supplemental, however, due to errors and omissions in their methods and materials used.

MRID 47522212 reported 81% theoretical CO_2 ($ThCO_2$) evolution and 85% theoretical dissolved organic carbon (DOC) removal at 28 days. However, it could not be determined if the required threshold values of 60% $ThCO_2$ evolution and 70% removal of DOC occurred within a 10 day window because the sampling intervals were insufficient. Similarly, MRID 47522217 reported 77.5% $ThCO_2$ evolution at 28 days, however, it could not be determined if this occurred within a 10-day window due to insufficient sampling intervals. These studies also contained a separate clay treatment to sorb DDAC. The clay treatments demonstrated that DDAC was not readily biodegradable likely due to DDAC sorption to clay.

Based on the weight of evidence, the Agency believes DDAC to be readily biodegradable under circumstance in which sorption is not a competing process, however, additional WWTP tests, such as biodegradation simulation tests (835.3220, 835.3240, 835.3280), may be required if DDAC does not demonstrate strong sorption to activated sludge and/or if results from the ASRI test indicate high toxicity to activated sludge microorganisms (EC_{50} less than or equal to 20 mg/L).

Table B1. Environmental Fate Properties of DDAC

Guideline No.	Parameter	DDAC	MRID
Leaching-Adsorption/Desorption			
835.1240	K_f/K_{oc} (L/kg) (sand, sandy loam, silty clay loam, silt loam)	K_f (K_{oc}) 1,095 ($4.4x10^5$), 8,179 ($9.1x10^5$), 32,791 ($1.6x10^6$), 30,851 ($1.5x10^6$)	41385301
Persistence in Water (half-life)			
835.2120	Hydrolysis at 25 ºC (days) pH 5, pH 7 (TRIS), pH 7 (HEPES), pH 9	368 d, 194 d, 175 d, 506 d	41175801
835.2240	Aqueous photolysis at 25 ºC (days)	227 d	41175802
835.4300	Aerobic aquatic metabolism (days)	180 d	42253803
835.4400	Anaerobic aquatic metabolism half-life (days)	261 d	42253802
Persistence in soil (% removed)			
835.2410	Photodegradation in Soil	169 d	42480701
835.4100	Aerobic soil metabolism	1,048 d	42253801
835.4200	Anaerobic soil metabolism	No data	Assumed stable based on aquatic metabolism studies
Persistence in WWTP (% removed)			
835.3110	Ready Biodegradability	Readily Biodegradable in absence of clay 90% by 28 d	47522214 47522212 47522217

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Appendix C Ecotoxicology Profile

Toxicity to Terrestrial Animals

Birds, Acute and Dietary

Results of the available acute oral (850.2100) and dietary (850.2200) toxicity studies are provided in Table C1. No additional avian toxicity data are needed for the antimicrobial uses. To support the conventional use, turf and golf courses, an avian acute oral toxicity study with a passerine species (850.2100) and avian reproduction toxicity studies on an upland game species and a waterfowl species (850.2300) are anticipated to be required.

Table C1. Acute Oral and Dietary Toxicity of DDAC to Birds

Species	% ai	Toxicity	Toxicity Category	Status/ MRID
Northern bobwhite (*Colinus virginianus*	50	LD_{50} = 54.4 mg ai/kg bw	Moderately toxic	Acceptable 00148078
	80.8	LD_{50} = 217 mg ai/kg bw	Moderately toxic	Acceptable 41785803
	33	LD_{50} = 542 mg ai/kg bw	Slightly toxic	Acceptable 40696501
	50	LC_{50} = 2625 ppm	Slightly toxic	Acceptable ACC132486
	80.8	LC_{50} >5620 ppm	Practically nontoxic	Acceptable 41785801
	50	LC_{50} >5620 ppm	Practically nontoxic	Acceptable 00148079
	33	LC_{50} >5000 ppm	Practically nontoxic	Acceptable 40696502
Mallard (*Anas platyrhynchos*)	50	LD_{50} = 186 mg ai/kg bw	Moderately toxic	Acceptable ACC232249
	50	LD_{50} = 240 mg ai/kg bw	Moderately toxic	Acceptable ACC232249
	50	LC_{50} = 5000 ppm	Slightly toxic	Acceptable ACC132436
	80.8	LC_{50} >5620 ppm	Practically nontoxic	Acceptable 41785802
	50	LC_{50} >5620 ppm	Practically nontoxic	Acceptable 00148077
	33	LC_{50} >5000 ppm	Practically nontoxic	Acceptable 40696503

Nontarget Insects - Honeybees

Honey bee acute contact toxicity data (850.3020) was submitted; however, there is still outstanding post-RED data that must be submitted to support DDAC antimicrobial uses.

In addition, data are anticipated to be required to support a DDAC conventional use on turf and golf courses. These data include acute oral toxicity to adult honey bees (non-guideline), acute oral toxicity to larval honey bees (non-guideline) and chronic toxicity to adult honey bees (non-guideline). Higher-tier colony level studies may be required pending the outcome of the screening level assessment using laboratory-based acute (single dose) and chronic (repeat dose) toxicity studies with adult and larval bees (all with TGAI). These higher-tier studies include field trial of residues in pollen and nectar (850.3030), semi-field testing for pollinators (TGAI) and field testing for pollinators (TGAI). In addition, although the acute contact toxicity to adult honey bees study (850.3020) was submitted, there is still outstanding data that must be submitted.

Terrestrial Plants

No data for terrestrial plants are available for DDAC. Tier I and Tier II seedling emergence (850.4100 and 850.4225) and vegetative vigor data (850.4150 and 850.4250) with the TEP are anticipated to be required to support the turf and golf courses.

Toxicity to Aquatic Animals

Freshwater Fish, Acute

Results of acute testing with cold-water and warm-water freshwater fish (850.1075) and freshwater invertebrates (850.1010) are presented in Table C2. No additional data are anticipated to be required for the antimicrobial or conventional uses. Five additional studies were submitted to determine if toxicity of DDAC to fish is reduced by adding either bentonite clay or humic acid to the test solutions.

Table C2. Acute Toxicity of DDAC to Freshwater Fish

Species	% ai	96-h LC_{50} (µg/L)	Toxicity Category	Status/ MRID
Bluegill sunfish (*Lepomis macrochirus)*	Tech.	270	Highly toxic	Acceptable 00133803
	41.2	320	Highly toxic	Acceptable 41578001
	Tech.	590	Highly toxic	Supplemental 00133803
	100	600	Highly toxic	Acceptable 00147818
	36	900	Highly toxic	Acceptable 41468301
	33	1900	Moderately toxic	Acceptable 40666717
	50	5900	Moderately toxic	Acceptable ACC221510
Rainbow Trout	36	600	Highly toxic	Acceptable 41468302

Species	% ai	96-h LC_{50} (µg/L)	Toxicity Category	Status/ MRID
(*Oncorhynchus mykiss)*	50	700	Highly toxic	Supplemental 00134444
	Tech.	1100	Moderately toxic	Acceptable 2053541
	33	2300	Moderately toxic	Acceptable 40872901
	100	2800	Moderately toxic	Acceptable 00147818
	82 (with 450 ppm bentonite clay)	>45,500	Not determined	Supplemental 47522205
Coho Salmon (*Oncorhynchus kisutch*)	41.2	1000	Highly toxic	Acceptable 41578003
Fathead minnow (*Pimephales promelas*)	80.5	190	Highly toxic	Acceptable 47555301
	80.5 (with 10 mg/L humic acid)	770	Highly toxic	Acceptable 47555301
	80.5 (with 20 mg/L humic acid)	1200	Moderately toxic	Acceptable 47555301
	82 (with 12.5 to 25 ppm bentonite clay)	>2500	Not determined	Supplemental 47522206
	82 (with 450 ppm bentonite clay)	7-d LC50 >45,500	Not determined	Supplemental 47522208
	50	5200	Moderately toxic	Acceptable ACC221510
Channel catfish (*Ictalurus punctatus*)	50	11,200	Slightly toxic	Acceptable ACC221510

Freshwater Invertebrates, Acute

Results of the studies submitted for guideline 850.1010 are provided in Table C3. No additional data are anticipated to be required for the antimicrobial or conventional uses.

Table C3. Acute Toxicity of DDAC to Freshwater Invertebrates

Species	% Active Ingredient	48-h EC_{50} (µg/L)	Toxicity Category	Status/ MRID
Waterflea (*Daphnia magna)*	100	18	Very highly toxic	Acceptable 00147818
	41.2	94	Very highly toxic	Acceptable 41578002
	50	100	Highly toxic	Acceptable ACC232249
	33	280	Highly toxic	Acceptable 40666720
	36	1700	Moderately toxic	Acceptable 41446803

Estuarine and Marine Organisms, Acute

The available data for estuarine/marine fish (850.1075), bivalves (850.1055), and shrimp (850.1035) are presented in Table C4. No additional data are anticipated to be required for the antimicrobial or conventional uses.

Table C4. Acute Toxicity of DDAC to Estuarine/Marine Organisms

Species	% ai	LC_{50} or EC_{50} (µg/L)	Toxicity Category	Status/ MRID
Sheepshead minnow (*Cyprinodon variegatus*)	80.5	960	Highly toxic	Acceptable 43620001
Eastern oyster (*Crassostrea virginica*)	84.6	94	Very highly toxic	Acceptable 43260003
	50	3000	Moderately toxic	Acceptable 00120301
	50	10,500	Moderately toxic	Acceptable 00120301
Mysid shrimp (*Mysidopsis bahia)*	41.2	690	Very highly toxic	Acceptable 41578004

Aquatic Organisms, Chronic

Chronic toxicity tests are available for freshwater fish (early life stage, 850.1400) and freshwater invertebrate (life cycle, 850.1300) (Table C4). No additional testing is anticipated to be required for the antimicrobial or conventional uses.

Table C5. Chronic Toxicity of DDAC to Fish and Aquatic Invertebrates

Species	% ai	NOAEC and LOAEC (µg/L)	Endpoints Affected	Status/ MRID
Zebra fish (*Brachydanio rerio*)	51.4	NOAEC = 32 LOAEC = 100	Survival, Weight, Condition	Acceptable 49812405
Waterflea (*Daphnia magna*)	51.4	NOAEC = 10 LOAEC = 18	Survival	Acceptable 49812404

Benthic Invertebrates, Chronic

One standard chronic sediment toxicity study for a midge has been submitted for DDAC (Table C6). This study partially fulfills the need for chronic sediment testing. Based on environmental fate data indicating that the DDACs will occur and persist in sediment/soil (K_{ads} >1000), chronic studies with a freshwater amphipod and an estuarine/marine amphipod also are anticipated to be required. There is no guideline number for this study. Four additional shorter-term studies also were submitted in which bentonite clay was added to the sediment to determine if the clay would reduce the toxicity of DDAC to benthic organisms. Those studies provide some supplemental information indicating that the clay itself, even in the absence of DDAC, can adversely affect growth of benthic invertebrates.

Table C6. Chronic Toxicity of DDAC to Freshwater Benthic Invertebrates

Species	% ai	Endpoints (mg/kg sediment)	Status/ MRID
Midge (*Chironomus tentans*)	82	28-d NOAEC = 260 28-d LOAEC = 530 (emergence)	Supplemental 45821701
	50 (10:1 bentonite clay:DDAC complex)	10-d LC_{50} >90,000 ppm DDAC in 900,000 ppm clay Note: larval wt adversely impacted when the bentonite clay concentration exceeded 10% of the complex; clay alone, without any DDAC, adversely affect growth when comprising ≥30% of the sediment complex	Supplemental 47522201
Mayfly (*Hexagenia limbata*)		21-d LC_{50} = 126 ppm DDAC with 1260 ppm clay 21-d NOAEC = 27 ppm DDAC with 270 ppm clay 21-d LOAEC (growth) = 90 ppm DDAC with 900 ppm clay	Supplemental 47522202
Amphipod (*Hyalella azteca*)		10-d LC_{50} = 3492 ppm DDAC with 34,920 ppm clay	Supplemental 47522203

Species	% ai	Endpoints (mg/kg sediment)	Status/ MRID
Waterflea (*Daphnia magna*)		10-d LC_{50} >90,000 ppm DDAC with 900,000 ppm clay Note: reproduction was impacted when the bentonite clay concentration exceeded 10% of the complex	Supplemental 47522204

Toxicity to Plants

Some data for DDAC and DDA carbonate are available (Table C7). In response to the post-RED Generic Data Call-In for DDAC issued May 2015, the Agency concurred with the Task Force's request to bridge DDA carbonate/bicarbonate studies to DDAC for rice (850.4225 and 850.4250), cyanobacteria (850.4550), and freshwater diatom (850.4500). However, testing is required with an aquatic vascular plant (*Lemna gibba*) and marine diatom (*Skeletonema costatum*). The post-RED guidelines (850.4400 and 850.4500) are not satisfied. Registrants can satisfy those guidelines either by submitting *Lemna* and *Skeletonema* studies for DDAC or by bridging the data available for DDA carbonate/bicarbonate (see RASSB 2012).

Table C7. Toxicity of DDAC to Plants

Species	% ai	Endpoints (µg/L)	Status/ MRID
Green algae (*Selanastrum capricornutum*)	81	96-h EC_{50} = 26 NOAEC = 14	Acceptable 45896402
	81	96-h EC_{50} = 73.2 NOAEC = 27	Supplemental 459074011
Freshwater diatom (*Navicula pelliculosa*)	49.85 (DDA carbonate)	96-h EC_{50} = 11.3 NOAEC = 5.4	Acceptable 46295803
Cyanobacteria (*Anabaena flos-aquae*)	49.85 (DDA carbonate)	96-h EC_{50} = 58 NOAEC = 40	Acceptable 46295801
Rice (*Oryza sativa*)	49.1 (DDA carbonate)	Emergence: 21-d EC_{25} = 55.4 mg/kg (dry wt) NOAEC = 39.1 mg/kg (dry wt) Vegetative vigor: 21-d EC_{25} = 2% ai NOAEC = 1% ai	Supplemental 46375401 and 46414501

Appendix C References

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Appendix D Screening Level Down-the-Drain Analysis

No screening level Down-the-Drain (DtD) assessment was performed for this FWP. A rationale is provided in Section 4.4.1.