UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

March 11, 2011

MEMORANDUM

SUBJECT: Summary of Product Chemistry, Environmental Fate, and Ecotoxicity Data for the Chlorhexidine Derivatives Registration Review Decision Document.

Active Ingredients	PC Codes	CAS Nos.
Chlorhexidine diacetate	045502	56-95-1
Chlorhexidine digluconate	045504	18472-51-0
Chlorhexidine dihydrochloride	481700	3697-42-5

Case: 3038 **DP Barcode:** 383096

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Introduction

Products formulated with chlorhexidine diacetate as an active ingredient were registered in the United States as early as 1955 for use as a farm premises disinfectant/virucide. Currently, two manufacturing use products and three end-use products with chlorhexidine diacetate as an active ingredient are registered for use as hard surface-treatment disinfectant/non-food contact surface sanitizer (floors & walls)/bactericides/virucides. Chlorhexidine diacetate is used to control bacteria on agricultural premises and on equipment, egg handling and packing equipment, meat processing plants, and for veterinary or farm premises to control certain viruses.

A product (BioSURF) formulated with chlorhexidine gluconate as an active ingredient was registered in the United States in 1987 for use as a disinfectant for hard, non-porous surfaces

(wheelchairs, metal bed frames, exteriors of toilets, cuntertops, metal surfaces, imaging equipment surfaces, metal, glass, acrylic, and porcelain) in hospitals, restrooms, schools, offices, gyms, and homes. Also, Mint-A-Kleen® a ready-to-use liquid product containing chlorhexidine gluconate was registered in 2010 for cleaning and control of microbial contamination in dental unit waterlines.

There are three active ingredients in the chlorhexidine derivatives case 3038; however, one of these active ingredients, chlorhexidine dihydrochloride, does not have active registered products. This chemical is not being supported and is not addressed in this registration review. The chlorhexidine diacetate and chlorhexidine digluconate are the only active ingredients in the case with active products. For chlorhexidine diacetate a Reregistration Eligibility Decision (RED) was issued by EPA in September 1996 but no RED was issued by EPA for chlorhexidine digluconate.

Table 1. Registered Active Products of Chlorhexidine diacetate

Registration #	Registration Name	Company Name	Formulation Type	% of Active Ingredient
1117-30	Fort Dodge Nolvasan Solution	Fort Dodge Animal Health	Soluble Concentrate	2
1117-48	Fort Dodge Nolvasan S	Fort Dodge Animal Health	Soluble Concentrate	2
1117-62	Chlorhexidine Diacetate	Fort Dodge Animal Health	Technical	99.3
3573-74	Cougar	The Procter & Gamble Company	Soluble Concentrate	0.01
3573-94	Chlorhexidine Diacetate	The Procter & Gamble Company	Technical	99.3

Table 2. Registered Active Product of Chlorhexidine digluconate

Registration #	Registration Name	Company Name	Formulation Type	% of Active Ingredient
70467-3	BioSURF	Micrylium Laboratories	Liquid Spray	0.2
85298-2	Mint-A-Kleen®	Anodia Systems	Ready-to-use Liquid	0.12

Use Patterns

EPA Reg. No.1117-30
Nolvasan® Solution
Ch1orhexidine diacetate

Scented Disinfectant
Bactericide Virucide
For Animal Premises Use Only
Active Ingredient:
1,1'-Hexamethylenebis -5-(p-chlorophenyl) biguanide) diacetate 2%
For cleaning, disinfection, deodorizing inanimate surfaces
For disinfection of veterinary or farm premises
For use in federally inspected meat, poultry, rabbit and egg establishments
For dipping teats as an aid in controlling bacteria that causes mastitis.
For disinfection of inanimate objects to aid in control of bacteria and viruses

EPA Reg. No.1117-48
Nolvasan® S
Chlorhexidine diacetate
Scented Disinfectant
Bactericide Virucide
For Animal Premises Use Only
Active Ingredient:
1,1'-Hexamethylenebis [5-(p-chlorophenyl) biguanide] diacetate 2%
For cleaning, disinfection, deodorizing
For disinfection of veterinary or farm premises
For disinfection of inanimate objects to aid in control of bacteria and viruses

EPA Reg. No.1117-62
Chiorhexidine Diacetate Technical 99.3%
This is a manufacturing use product for the formulation of indoor use antimicrobial hard surface disinfectant products.

EPA Reg. No. 3573-74
Cougar
Active Ingredients:
Didecyl Dimethyl Ammonium Chloride 0.03%
Chlorhexidine Diacetate 0.01%
Sanitizer: For use on hard non-porous floors.
Sanitizing Cleaner.
With Cougar Antibacterial solution, 99.9% of the bacteria* on floors are eliminated/killed.
All In-One mopping system.
Antibacterial Cleaner
Cleans and kills/eliminates/removes 99.9% of bacteria* on dining area/cafeteria floors.
Cleans and kills/eliminates 99.9% of bacteria* on public/school floors.
Cleans, and removes bacteria*
Cleans and removes household bacteria*
Cleans and Sanitizes.
Cleans and sanitizes floors wall-to-wall.
For use on all washable floors
For use on/Great for vinyl glazed ceramic laminate, and finished wood floor surfaces.

For use on/Great for vinyl, glazed ceramic sealed marble laminate and finished wood floors.
For vinyl, glazed ceramic, laminate, and finished wood floors.
Great for! For Use on finished floors/glazed ceramic tile/vinyl surfaces.
Kills 99.9% of bacteria* and (helps) eliminate(s) odors (with fresh scent).
Kills 99.9% of bacteria* and (helps) eliminate(s) odors in the air (with fresh scent).
Kills and, prevents the spread of 99.9% of Enterobacter aerogenes/E. aerogenes on treated surfaces.
Kills and, prevents the spread of 99.9% of Staphylococcus aureus/S. aureus on treated surfaces.
Kills/Eliminates/Removes 99.9% Enterobacter aerogenes/E. aerogenes
Kills/Eliminates/Removes 99.9% of bacteria*
Kills/Eliminates/Removes 99.9% of bacteria* on public/guest/school floors
Kills/Eliminatès/Removes 99.9% of bactéria* on floor/public restroom/lobby floors
Kills/Eliminates/Removes 99.9% of household bacteria*
Kills Eliminates/Removes 99.9% Staphylococcus aureus/S. aureus

* Effective against/kllls/99.9% of Staphylococcus aureus and Enterobacter aerogenes.

EPA Reg. No. 3573-94
Chlorhexidine Diacetate Technical 99.3%
This product is a manufacturing use product for the formulation of indoor use antimicrobial hard surface disinfectant products.
This product is a manufacture use product for formulation use only.

EPA Reg. No. 70467-3
BioSURF
Active Ingredients
Ethanol 70.5%
Chlorhexidine gluconate 0.2%

Tuberculocidal Canine Parvovirucidal Pseudomonacidal

Hospital Hard Surface Disinfectant
BioSURF is a ready to use hard surface disinfectant for nonporous surfaces • One Step.
For use on hard, non-porous imaging equipment surfaces
Restrooms • Schools • The Office •The Gym •At Home.
BioSURF Can be used on countertops metal surfaces and toilet exteriors. May be used on wheelchairs, metal bed frames and exteriors of toilets. BioSURF may be used on nonporous hard surfaces (imaging equipment, metal, glass, acrylic, and porcelain).

EPA Reg. No. 85298-2
MINT-A-KLEEN®
Ready-to-use Liquid
Active Ingredient
Chlorhexidine digluconate 0.12%
Dental Unit Waterline Cleaner
For the cleaning and control of microbial contamination in dental unit waterlines. For use in any dental unit. Ready to Use. Do Not Dilute.

Science Findings

The Agency has conducted a review of the available product chemistry, environmental fate, and ecotoxicity data for chlorhexidine diacetate and chlorhexidine digluconate. The findings are summarized below.

All product chemistry data requirements have been satisfied for the active ingredients chlorhexidine diacetate and chlorhexidine digluconate.

Table 3. Chemical Identity

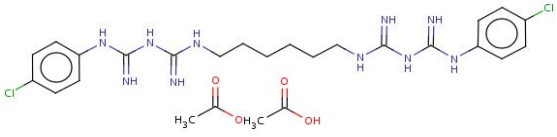
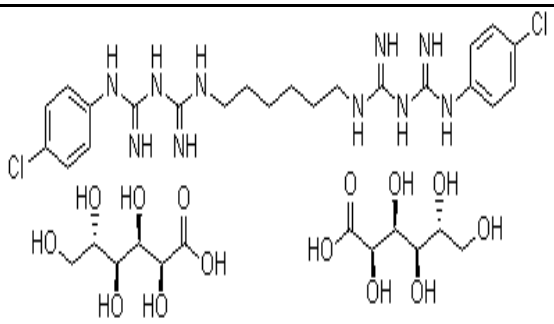
	Chlorhexidine diacetate	**Chlorhexidine digluconate**
Chemical Name	1,1'- hexamethylene bis [5-(p-chlorophenyl) biguanide] Diacetate 2,4,11,13-Tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino-, diacetate	1,1'-Hexamethylene bis(5-(4-chlorophenyl) biguanide) digluconate 2,4,11,13-Tetraazatetradecanediimidamide, N,N''-bis(4-chlorophenyl)-3,12-diimino, di-D-gluconate
Common Name	Chlorhexidine diacetate	Chlorhexidine digluconate
Synonyms	Chlorhexidine acetate	Chlorhexidine gluconate
Trade Names	Nolvasan, Arlacide A Bactigras, Hibitane acetate, Chlorhexidine acetate technical	Hibitane chlorhexidine gluconate
Molecular Weight	625.55 g/mol	897.8 g/mol
PC Code	045502	045504
CAS No.	56-95-1	18472-51-0
Molecular Formula	$C_{22}H_{30}Cl_2N_{10}\cdot 2(C_2H_4O_2)$	$C_{22}H_{30}Cl_2N_{10}\cdot 2(C_6H_{12}O_7)$
Molecular Structure:	 **Chlorhexidine diacetate**	 **Chlorhexidine digluconate**

Table 4. Product Chemistry Data Summary of Chlorhexidine diacetate and Chlorhexidine digluconate

Guideline No.	Physical and Chemical Properties	Chlorhexidine diacetate 99.9%	Chlorhexidine digluconate 20% w/v Aqueous solution (Technical)
830.1550	Product identity and composition	Refer to Table 3.	Refer to Table 3.
830.1600	Description of materials used to produce the product	CBI	CBI
830.1620	Description of production process	CBI	CBI
830.1650	Description of formulation process	CBI	CBI
830.1670	Discussion of formation of impurities	CBI	CBI
830.1700	Preliminary analysis	CBI	CBI
830.1750	Certified limits	CBI	CBI
830.1800	Enforcement analytical method	Polarographic methods	Polarographic methods
830.1900	Submittal of samples	N/A	NA
830.6302	Color	White or almost white	Clear, water white to amber liquid
830.6303	Physical State	Powdered Solid Microcrystalline powder	Liquid
830.6304	Odor	Odorless or almost odorless	Mild, practically odorless Mild medicinal odor It has a Bitter taste
830.6313	Stability to sunlight, normal and elevated temperature, metals/metal ions	Stable under ambient warehouse conditions to moisture and simulated sunlight. Stability data at temperatures of 25°C and 30°C over a 48 month period demonstrated that chlorhexidine acetate is stable in both amber glass bottles and in tin plate lever lid containers for a period of 48 months. Chlorhexidine acetate technical is transported in plastic bags inside fiberboard tin plate lever lid containers.	The product is stable.
830.6314	Oxidation/Reduction: Chemical Incompatibility	Chlorhexidine acetate is compatible with an oxidizing agent (potassium permanganate), a reducing agent (zinc powder), water and carbon dioxide. No significant increase in temperature was observed with any mixture tested although in the case of potassium permanganate, a rise in temperature of approximately 4°C was detected upon initial mixing but this returned to ambient within 1 hr.	N/A
830.6315	Flammability	N/A Flash point > 100 °C	N/A Flash point: 376.7 °C
830.6316	Explodability	N/A	N/A

Guideline No.	Physical and Chemical Properties	Chlorhexidine diacetate 99.9%	Chlorhexidine digluconate 20% w/v Aqueous solution (Technical)
830.6317	Storage Stability	Stability data at temperatures of 25° and 30°C over a 48 month period demonstrated that chlorhexidine acetate is stable in both amber glass bottles and in tin plate lever lid containers for a period of 48 months	Shelf-life is three years at 2-8°C. Storage Temp: 2-8°C.
830.6319	Miscibility	N/A	Miscible with water
830.6320	Corrosion Characteristics	Stability studies have shown that the physical condition of the product in tin plate lever lid containers is satisfactory. There is no evidence to suggest that product pack interaction would be a problem.	Non-corrosive in presence of glass.
830.6321	Dielectric breakdown voltage	N/A	N/A
830.7000	pH	6.8 (in 1% solution) 7 in solution	20% solution (w/v) 6.0 – 6.8 (1% soln/water): Neutral.
830.7050	UV/Visible Absorption	Not Reported.	Not Reported.
830.7100	Viscosity	N/A	NR
830.7200	Melting point	158.7ºC	N/A
830.7220	Boiling point	N/A	The lowest known value is 100°C (212°F) (Water).
830.7300	Density	Density: 1.2 g/cm^3	Sp Gr: 1.06 at 20°C Density: 1.06 g/mL at 25°C (lit.)
830.7370	Dissociation Constant	N/A pKa = 10.78 in water	1
830.7550	Partition coefficient (*n*-octanol/water)	N/A Octanol/acetate buffer (pH 5) Log D=0.08	N/A -0.33 (EPI Suite)
830.7840	Solubility in water	Solubilizes 1.9 g/100 mL (20 ºC)	Soluble in water. Easily soluble in cold water. Fully miscible. Miscible with water.
830.xxxx	Solubility in organic solvents	Ethanol..... 6.7 gm/100 ml Glycerol.... slightly soluble Propane..... slightly soluble	Soluble in ethanol & acetone. Soluble in polar solvents such as lower alcohols, glycols and other polyols.
830.7950	Vapor pressure	N/A Chlorhexidine acetate is a solid which melts above 100 °C, vapor pressure is therefore not applicable.	The highest known value is 17.535 mm of Hg (@ 20°C (Water).

N/A = Not applicable; TGAI=Technical Grade Active Ingredient; CBI= Confidential Business Information

Environmental Fate Summary

No definitive environmental fate assessment can be made because no data have been submitted regarding the chemical degradation, microbial metabolism or mobility of chlorhexidine derivatives.

The Agency did not conduct an environmental fate assessment for chlorhexidine derivatives because of lack of data. However, the Agency needs to conduct an environmental fate assessment for disinfectant/sanitizers used in animal premises that may potentially pass through waste water treatment plants (WWTPs) and may be discharged into terrestrial and aquatic environments. For this assessment the Agency anticipates needing those data outlined on page 11 of this document.

Water Quality

Chlorhexidine derivatives are not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885 . In addition, no Total Maximum Daily Loads (TMDL) have been developed for chlorhexidine derivatives, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES . More information on impaired water bodies and TMDLs can be found at http://www.epa.gov/owow/tmdl/. The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process* (see: http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

Ecological Effects Summary

The registrant has submitted ecological effects studies for both terrestrial and aquatic animals. These data are adequate to provide the Agency with sufficient information to determine appropriate label precautions, and may be seen in Tables 5 and 6 below.

a. Toxicity to Terrestrial Animals

(1) Birds, Acute and Subacute

Chlorhexidine diacetate is slightly toxic to practically nontoxic to avian species on an acute oral and subacute dietary basis.

Chlorhexidine digluconate is slightly toxic to avian species on an acute oral and subacute dietary basis.

b. Toxicity to Aquatic Animals

(1) Freshwater Fish

Chlorhexidine diacetate is moderately toxic to cold water fish and highly toxic to warm water fish.

Chlorhexidine digluconate is highly toxic to both cold and warm water fish.

(2) Freshwater Invertebrates

Chlorhexidine diacetate is highly toxic to aquatic invertebrates.

Chlorhexidine digluconate is highly toxic to aquatic invertebrates.

c. Toxicity to Aquatic Plants

(1) Freshwater Algae

No algal toxicity data have been submitted. For the ecological risk assessment, including an endangered species assessment for all uses, the Agency anticipates needing the algal toxicity data outlined on page 11 of this document.

Ecotoxicity data are adequate to provide the Agency with sufficient information to determine appropriate label precautions.

Table 5. Ecotoxicity Data Summary for Chlorhexidine diacetate

GUIDE LINE	COMMON NAME	TAXONOMIC NAME	TEST TYPE	% AI	STUDY TIME	DOSE TYPE	TOXICITY	TOX LEVEL	NOEL	STUDY STATUS	TOX CATEGORY	MRID
Avian Acute Oral Toxicity												
850.2100	Bobwhite quail	*Colinus virginianus*	O	100	14 D	LD_{50}	2013	MGK	292	Acceptable	Slightly toxic	42197501
Avian Subacute Dietary Toxicity												
850.2200	Bobwhite quail	*Colinus virginianus*	D	100	8 D	LC_{50}	>5620	PPM	1780	Acceptable	Practically nontoxic	42197502
850.2200	Mallard duck	*Anas platyrhynchos*	D	100	8D	LC_{50}	>5620	PPM	5620	Acceptable	Practically nontoxic	42197503
Freshwater Fish Acute Toxicity												
850.1075	Rainbow trout	*Oncorhynchus mykiss*	S	100	96 hr	LC_{50}	1871	PPB	900	Acceptable	Moderately toxic	42197504
850.1075	Bluegill sunfish	*Lepomis macrochirus*	S	100	96 hr	LC_{50}	600	PPB	300	Acceptable	Highly toxic	42197505
Freshwater Invertebrate Acute Toxicity												
850.1010	Water flea	*Daphnia magna*	S	100	48 hr	EC_{50}	63	PPB	32	Acceptable	Very highly toxic	42197506

Table 6. Ecotoxicity Data Summary for Chlorhexidine digluconate

GUIDE LINE	COMMON NAME	TAXONOMIC NAME	TEST TYPE	% AI	STUDY TIME	DOSE TYPE	TOXICITY	TOX LEVEL	NOEL	STUDY STATUS	TOX CATEGORY	MRID
Avian Acute Oral Toxicity												
850.2100	Mallard duck	*Anas platyrhynchos*	O	20.0 Tech	14 D	LD_{50}	>2510 Eq to 502 mg/kg ai	MGK		Supplemental	Slightly toxic	00030213
Avian Subacute Dietary Toxicity												
850.2200	Mallard duck	*Anas platyrhynchos*	D	20.0 Tech	8 D	LC_{50}	>10000 Eq to 2000 ppm ai	PPM	4640	Supplemental	Slightly toxic	124744
850.2200	Bobwhite quail	*Colinus virginianus*	D	20.0 Tech	8D	LC_{50}	>10000 Eq to 2000 ppm ai	PPM	>10000	Supplemental	Slightly toxic	126034
Freshwater Fish Acute Toxicity												
850.1075	Rainbow trout	*Oncorhynchus mykiss*	S	20.0 Tech	96 hr	LC_{50}	2.3	PPM	1.21	Acceptable	Highly toxic	00124743
850.1075	Bluegill sunfish	*Lepomis macrochirus*	S	20.0 Tech	96 hr	LC_{50}	0.51	PPM	0.21	Acceptable	Highly toxic	00124743
Freshwater Invertebrate Acute Toxicity												
850.1010	Water flea	*Daphnia magna*	S	20.0 Tech	48 hr	EC_{50}	0.42 Eq to 84 ppb	PPM		Acceptable	Very highly toxic	241539 045504

Adverse Ecological Incidents

There are no reported incidents in the Agency' s Ecological Incident Information System (EIIS) regarding chlorhexidine derivatives. The absence of documented incidents does not necessarily mean that such incidents did not occur.

Ecological Effects Risk Assessment

An ecological risk assessment was not conducted on the chlorhexidine derivatives's disinfectant/sanitizer use patterns described in this document. Chlorhexidine derivatives uses in animal premises and dental unit water lines that have potential for environmental exposure are down the drain disinfectant/sanitizer discharges. The Agency needs to conduct environmental fate and ecological risk assessments for disinfectant/sanitizers used in animal premises and dental unit water lines that potentially pass through waste water treatment plants (WWTPs) and may be discharged into terrestrial and aquatic environments. For this ecological risk assessment, including an endangered species assessment for all uses, the Agency anticipates needing the algal toxicity data outlined on page 11 of this document.

The Agency has not conducted a risk assessment that supports a complete endangered species determination. The ecological risk assessment planned during registration review will allow the Agency to determine whether chlorhexidine derivatives's use has "no effect or "may affect" federally listed threatened or endangered species (listed species) or their designed 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.

Environmental Fate and Ecotoxicity Data Gaps and Anticipated Work

Environmental fate and ecological risk assessments have not been conducted for chlorhexidine derivatives. The Agency needs to conduct environmental fate and ecological risk assessments for disinfectant/sanitizers used in animal premises and dental unit water lines that may potentially pass through waste water treatment plants (WWTPs) and may be discharged into terrestrial and aquatic environments. Therefore, the Agency anticipates needing the proposed environmental fate and ecotoxicity data for chlorhexidine derivatives and/or any of its major degradation products that are of potential concern for all registered uses of chlorhexidine derivatives. The following environmental fate and ecotoxicity data are needed to conduct an environmental fate and ecological risk assessment:

- The Agency anticipates needing the following data to conduct a complete environmental fate assessment for animal premises and dental unit water lines uses:

    - (GLN 835.2120) Hydrolysis;
    - (GLN 835.2240) Photodegradation in water;
    - (GLN 850.6800) Modified Activated Sludge Respiration Inhibition;
    - (GLN 835.1110) Activated Sludge Sorption Isotherm; and
    - (GLN 835.3110) Ready Biodegradability.

- The Agency anticipates needing the following data in order to conduct a complete ecological risk assessment, including an endangered species assessment:

    - (GLN 850.5400) algal toxicity (Tier II) using freshwater green alga, *Selenastrum capricornutum.*

Appendix A. Environmental Fate Guideline Study Justifications

Guideline Number: 835.2120
Study Title: Hydrolysis

Practical Utility of the Data

1) What is the value of the study?
Data characterizing the rate of hydrolytic degradation of chlorhexidine derivatives and/or the formation and decline of degradates is important in determining the persistence and concentrations of chlorhexidine derivatives and potential degradates over time in various aquatic environments. For outdoor uses, chlorhexidine derivatives can reach surface water through direct contact or discharge to WWTPs. Chlorhexidine derivatives may also reach surface water or groundwater through run-off or leaching processes. The Agency will evaluate the potential risks of concern.

2) How would the data be used?
The data would establish the significance of chemical hydrolysis as a route for degradation and identify, if possible, the hydrolytic transformation products formed that may adversely affect non-target organisms and may contaminate water and food source of aquatic organisms. The data would also help establish the hydrolytic half-life of chlorhexidine derivatives and possibly degradates, and assist in developing a degradation pathway.

3) How could the data affect the risk assessment?
The results of hydrolysis data would indicate if chlorhexidine derivatives is persistent or if it degrades into other products that may adversely affect nontarget organisms and may contaminate their food and water and possibly soil.

4) What is triggering the need for this data?
Hydrolysis data is needed to conduct the fate assessment to support material preservatives uses for chlorhexidine derivatives.

Guideline Number: 835.2240
Study Title: Photodegradation in water

Practical Utility of the Data

1) What is the value of the study?
Biocides introduced into aqueous systems in the environment can undergo photolytic transformation by sunlight. Results from the photolysis study will indicate the stability and persistence of chlorhexidine derivatives and potential degradates in an aquatic environment when exposed to sunlight. The Agency will evaluate the potential risks of concern.

2) How would the data be used?
The data would establish the significance of chemical photolysis as a route for degradation and identify, if possible, the photolytic degradation products formed that may adversely affect non-target organisms and may contaminate water and food source of aquatic organisms. The data would also help establish the photolytic half-life of chlorhexidine derivatives and possibly degradates, and assist in developing a degradation pathway.

3) How could the data affect the risk assessment?
The results of photolysis data would indicate if chlorhexidine derivatives are persistent or if they degrade into other chemical products that may adversely affect nontarget organisms by contaminating their food supply. The results of the photolysis data would expand the understanding of the results of the hydrolysis data since environmental aquatic conditions usually involve exposure to sunlight.

Guideline Number: 835.2240
Study Title: Photodegradation in water

4) What is triggering the need for this data?
Aqueous photodegradation data is needed to conduct the fate assessment to support material preservative uses for chlorhexidine derivatives.

Guideline Number: 850.6800
Study Title: Modified Activated Sludge Respiration Inhibition

Rationale for Requiring the Data

The modified activated sludge, respiration inhibition test is needed to identify whether this pesticide could harm microorganisms found in biological wastewater treatment systems. The Agency will utilize these data to conduct the environmental fate assessment and to determining the potential impact of this chemical on waste water treatment plants (WWTPs) via effects on WWTP microbes. This test is also necessary to enable EPA to establish correct concentrations for use in the ready biodegradability test.

Practical Utility of the Data

1. How will the data be used?
The data will be used to assess exposure and risk to non-target endangered and non-endangered species. Exposure data are integral parts of the risk equation for determining the impact of pesticides to beneficial non-target organisms through direct exposure from their food sources and habitat.

In addition, the data will be used to determine whether or not additional studies and/or label restrictions are needed. The study will identify the inhibitory effect of this chemical on the treatment plant's microorganisms' respiration at a particular concentration and will identify the EC_{50}, the effective concentration at which the respiratory rate is reduced by 50%. EPA will use the data to determine the chemical's potential to directly harm the non-target organisms and/or the microbial treatment processes present in a WWTP. The data will also determine suitable non-inhibitory concentrations to be used in biodegradability tests.

2. How could the data impact the Agency's future decision-making?
If the data show a high degree of respiratory inhibition, higher-tiered environmental fate studies may be required and the risk assessments for this chemical may need to be revised to address the impact of the potential risk. The risk assessment may result in the Agency requiring label restrictions that would be necessary for the products to meet the "no unreasonable adverse effects" requirements of FIFRA (e.g., changes to the directions for disposal).

In addition, EPA is required by section 7(a)(2) of the ESA to ensure that any action it authorizes or takes "…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat" and to use the best scientific data available" in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by the ESA as to whether continued registration of a pesticide is not likely to jeopardize the species or its critical habitat. Absent this data EPA may not be able to conclude that this pesticide will not harm endangered species and may therefore need to consider other limitations on the use of the pesticide in order to fulfill the Agency's statutory obligations under the ESA. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with the ESA and could result in use restrictions which are unnecessarily severe.

Guideline Number: 835.1110
Study Title: Activated Sludge Sorption Isotherm

Rationale for Requiring the Data

Data from this study are needed to determine the sorption potential of activated sludge for the removal of specific chemical compounds in biological wastewater treatment plants (WWTPs). If the chemical is not sorbed or biodegraded, then it would pass through a biological treatment system unaffected, potentially contaminating surface and drinking waters where it may then have the potential to adversely affect nontarget organisms. EPA needs activated sludge sorption study data to assess the distribution of the antimicrobial chemical among the solid, aqueous, and vapor phases of WWTPs. Specifically, this study identifies those chemicals which sorb to sludge biomass.

Practical Utility of the Data

1. How will the data be used?

The data will be used to assess exposure and risk to non-target endangered and non-endangered species. Exposure data are integral parts of the risk equation for determining the impact of pesticides to beneficial nontarget organisms through direct exposure from their food sources and habitat.

In addition, the data will be used to determine whether or not additional studies and/or label restrictions are needed. If the data indicate that the chemical does not sorb to sludge and instead partitions more readily to water, then the chemical has the potential to pass through the WWTP and therefore could be discharged in to the aquatic environment. This determination could trigger further data requirements to assess the chemical's impact upon release.

2. How could the data impact the Agency's future decision-making?

If the data show that the chemical negatively impacts the aquatic environment or the effectiveness of the WWTP, then the risk assessments for this chemical may need to be revised to reflect the magnitude of potential risk derived from the new data. The risk assessment may result in the Agency requiring label restrictions that would be necessary for the products to meet the "no unreasonable adverse effects" requirements of FIFRA (e.g., changes to the directions for disposal).

In addition, EPA is required by section 7(a)(2) of the ESA to ensure that any action it authorizes or takes "…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat" and to use the best scientific data available" in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by the ESA as to whether continued registration of a pesticide is not likely to jeopardize the species or its critical habitat. Absent this data EPA may not be able to conclude that this pesticide will not harm endangered species and may therefore need to consider other limitations on the use of the pesticide in order to fulfill the Agency's statutory obligations under the ESA. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with the ESA and could result in use restrictions which are unnecessarily severe.

Guideline Number: 835.3110
Study Title: Ready Biodegradability

Rationale for Requiring the Data

For antimicrobial chemicals that go down-the-drain and reach a WWTP, as part of its screening-level environmental fate assessment, EPA will analyze the potential impact of the antimicrobial chemical on the microorganisms in the biological treatment processes of a WWTP. Biodegradation is an important environmental pathway in which the antimicrobial is broken down by bacteria. This study supplies information on the rate of breakdown and the completeness of the degradation to carbon dioxide and water. A ready biodegradability study would allow the Agency to determine whether the chemical achieves ‘‘pass levels’’ for ready biodegradability (e.g., 70% removal of dissolved organic carbon).

Practical Utility of the Data

1. How will the data be used?

The data will be used to assess exposure and risk to non-target endangered and non-endangered species. Exposure data are integral parts of the risk equation for determining the impact of pesticides to beneficial non-target organisms through direct exposure from their food sources and habitat.

In addition, the data will be used to determine whether or not additional studies and/or label restrictions are needed. If the chemical does not achieve a ‘‘pass level’’ for ready biodegradability, then the Agency would determine that the chemical has the potential to pass through the WWTP and therefore may be discharged in to the aquatic environment potentially resulting in exposure to non-target species. This determination would trigger further data requirements to assess the chemical’s impact on the aquatic environment upon release.

2. How could the data impact the Agency’s future decision-making?

If the chemical is found to be readily biodegraded, then impact on WWTP would be identified as minimal and most likely no further studies or label restrictions would be required. If a low rate of biodegradability is identified, then higher-tiered environmental fate studies may be triggered and the risk assessments for this chemical may need to be revised to reflect the magnitude of potential risk derived from the chemical’s lack of biodegradability. The risk assessment may result in the Agency requiring label restrictions that would be necessary for the products to meet the “no unreasonable adverse effects” requirements of FIFRA (e.g., changes to the directions for disposal).

In addition, EPA is required by section 7(a)(2) of the ESA to ensure that any action it authorizes or takes “…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat” and to use the best scientific data available” in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by the ESA as to whether continued registration of a pesticide is not likely to jeopardize the species or its critical habitat. Absent this data EPA may not be able to conclude that this pesticide will not harm endangered species and may therefore need to consider other limitations on the use of the pesticide in order to fulfill the Agency’s statutory obligations under the ESA. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with the ESA and could result in use restrictions which are unnecessarily severe.

Appendix B: Ecological Guideline Study Justifications

Guideline Number: 850.5400
Study Title: Algal toxicity (Tier II) using freshwater green alga, *Selenastrum Capricornutum*

Practical Utility of the Data

1) What is the value of the study?
As part of an initial risk assessment, one indicator plant species is tested for phytotoxicity. This study would allow the Agency to categorize chlorhexidine derivatives as toxic or non-toxic to plants. If toxic, additional higher tier plant tests would be needed. An endangered species assessment for endangered or threatened plants is not possible without this study.

2) How would the data be used?
This study would be used to evaluate the toxicity of chlorhexidine derivatives to non-target plants in terrestrial and aquatic ecosystems.

3) How could the data affect the risk assessment?
Adverse effects to non-target plants in terrestrial and aquatic ecosystems may result in mitigation to protect species at risk. Mitigation might include reduced label dosages, neutralization of effluents prior to discharge into water, restrictions on use in sensitive ecosystems or where endangered species are present, or other mitigation measures.

4) What is triggering the need for this data?
Increased concern from state regulators and the public to evaluate impacts on WWTP operations, endangered species, and persistence in the environment, since initial registration, have triggered the need for this study. Green algae are critical to ecosystem health and productivity.