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

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: **June 23, 2020**

SUBJECT: **Registration Review Draft Risk Assessment for Polixetonium Chloride the Active Ingredient in Busan 77**

PC Code: 069183	DP Barcode: 455149
Decision No.: 557271	Docket No: EPA-HQ-OPP- 2004-0301
Regulatory Action: Registration Review	Case No.: 3034
Risk Assessment Type: DRA	CAS No.: 31512-74-0

TO: Peter Bergquist, Chemical Review Manager
Rose Kyprianou, Branch Chief
Regulatory Management Branch (RMB) II
Antimicrobials Division (7510P)
Office of Pesticide Programs

FROM: David Bays, Ph.D., Microbiologist
Jim Breithaupt, Agronomist
Timothy Dole, Industrial Hygienist
Jorge G. Muñiz Ortiz, Ph.D., DABT, Toxicologist
Siroos Mostaghimi, Ph.D., Senior Scientist
Risk Assessment and Science Support Branch
Antimicrobials Division (7510P)
Office of Pesticide Programs

THROUGH: Judy Facey, Ph.D., Human Health Risk Assessment Process Leader JUDY FACEY Digitally signed by JUDY FACEY Date: 2020.06.23 15:59:45 -04'00'
Diana Hsieh, Ecological Risk Assessment Process Leader
Timothy Leighton, Senior Human Health Scientist
Melissa Panger, Ph.D., Branch Chief
Risk Assessment and Science Support Branch
Antimicrobials Division (7510P)
Digitally signed by MELISSA PANGER Date: 2020.06.23 16:02:57 -04'00'

This document provides the draft human health and ecological risk assessment conducted in support of the antimicrobial pesticide active ingredient (a.i.) poly[oxyethylene (dimethyliminio) ethylene (dimethyliminio) ethylene dichloride) that is in the product Busan 77. This a.i. is also known as polixetonium chloride.

Table of Contents

List of Tables

1 EXECUTIVE SUMMARY

Busan 77 is the product name of the first product that contained the active ingredient poly (oxyethylene (dimethyliminio) ethylene (dimethyliminio) ethylene dichloride). This ingredient is also known by the synonym polixetonium chloride. Therefore, for the purposes of this draft risk assessment (DRA), the active ingredient in Busan 77 will be referred to as polixetonium chloride.

Polixetonium chloride is used as an algaecide, bacteriostat, fungicide, microbiocide/microbiostat, and molluscicide. Products containing polixetonium chloride are used in a variety of materials and processes including, air washer systems, cooling water systems, petroleum secondary recovery, metalworking fluids, pulp and paper manufacturing, and pulp and paper board mills, decorative fountains, swimming pools, and spas. End-use products that contain polixetonium chloride are formulated as liquid concentrates.

Human Health Risk Summary

Dietary Risks

There are no dietary or drinking water exposures associated with the currently registered uses of polixetonium chloride), due to its use profile (restricted to non-food paper uses) and environmental fate properties (strong sorption). Therefore, a dietary risk assessment is not needed for registration review.

Residential Risks

Residential handler inhalation and dermal exposures were assessed for open pour application of polixetonium chloride to swimming pools. The inhalation margin of exposure (MOE) of 770,000 is not of concern because it is greater than the level of concern (LOC) of 100. The dermal MOE is 3.6 when the application rate is 10 ppm for the winterizing treatment and the dermal MOE is 11 when the application rate is 3.2 ppm for the maintenance treatment. The MOE of 3.6 is of concern because it is less than the LOC of 10.

Dermal and incidental oral exposures were assessed for persons swimming in pools treated with polixetonium chloride. The dermal MOE of 670 is not of concern because it is greater than the LOC of 10. The incidental oral MOEs range from 1,900 to 4,800 and are not of concern because they are above the LOC of 100.

Aggregate Risks

Because there are no dietary or drinking water exposures associated with polixetonium chloride, an aggregate assessment is not needed for registration review.

Occupational Risks

The occupational handler inhalation MOEs of 11,000 and 25,000 are not of concern because they are greater than the LOC of 100.

Long term dermal and inhalation risks were assessed for machinists using metalworking fluids (MWF) treated with polixetonium chloride. The inhalation MOE of 360,000 is above the LOC of 1000 and is not of concern. The dermal MOE of 12 is less than the LOC of 100 and is of concern.

Ecological Risk Summary

Based on the current use patterns for polixetonium chloride, no terrestrial exposure is expected but several of the use patterns could result in aquatic exposure. Screening-level ecological assessments of polixetonium chloride used in cooling water towers and pulp and paper mills were performed using the Exposure and Fate Assessment Screening Tool (E-FAST, USEPA, 2014). Various scenarios were performed evaluating: (1) high-end (low stream-flow rate) and average (average stream flow rate) assessments, (2) moderate-sized and large-sized cooling water towers, and (3) high and low application rates in pulp and paper mills.

In general, these evaluations demonstrated that invertebrates (chronic exposure) were the most sensitive taxa; concentrations of concern (COCs) were exceeded for all rates and scenarios modeled, and exceedances were higher for low-flow stream scenarios than average-flow streams; the number of days per year COCs were exceeded was reduced with the size of cooling water towers and when paper mills used low (30 ppm) instead of high (180 ppm) application rates of polixetonium chloride. However, the sorption of polixetonium chloride to sediment is the predominant and only apparent dissipation process in the environment and is expected to reduce aqueous concentrations and aquatic risk.

The model used does not account for degradation or other chemical/fate properties. This chemical is expected to bind to sediments although the impact of this could not be quantified, but there is no apparent route of chemical or microbial degradation for polixetonium chloride in the environment. Therefore, based on the available data, the use pattern for polixetonium chloride is expected to result in risks to aquatic taxa (*i.e.*, non-listed aquatic plants, fish, and aquatic invertebrates) from the cooling water and paper mill uses.

No risk assessment was performed for estuarine/marine organisms or benthic invertebrates. Polixetonium chloride is expected to partition from water to soil and sediment in estuarine/marine environments. Based on the ecotoxicity endpoints, the Agency assumes the magnitude of risk to estuarine/marine organisms is comparable to freshwater organisms when used in cooling tower/paper mills and releasing blowdown and effluent into estuarine/marine environment of similar volume.

Due to low potential for exposure based on the registered use patterns for polixetonium chloride, risk to terrestrial organisms (including pollinators) is not expected.

2 INTRODUCTION

The active ingredient in Busan 77, poly (oxyethylene (dimethyliminio) ethylene (dimethyliminio) ethylene dichloride), henceforth referred to by its synonym polixetonium chloride, is used as an industrial preservative for the protection of a variety of materials and processes, including air washer systems, cooling water systems, petroleum secondary recovery, decorative fountains, swimming pools, metalworking fluids, pulp and paper manufacturing, and pulp and paper board mills. End-use products that contain polixetonium chloride are formulated as liquid concentrates.

2.1 Case Overview

The docket for polixetonium chloride (case 3034), has been established at http://www.regulations.gov in docket number EPA-HQ-2015-0256. Documents associated with this registration review can be viewed in this docket.

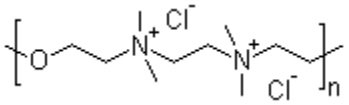
2.2 Regulatory History

Busan 77 was the first product containing polixetonium chloride as an active ingredient and was registered in the United States in 1971. The Agency completed a Reregistration Eligibility Decision (RED) for the a.i. in 2007. The post-RED Data Call-In (GDCI-069183-30193) was issued in September 2011. Products containing polixetonium chloride were previously registered for use in textiles, however, this use has been cancelled.

2.3 Ingredient Profile and Chemical Identity

Table 1 presents the active ingredient to be assessed in case 3034: polixetonium chloride (PC Code 069183), and Table 2 presents the physical-chemistry and fate properties for polixetonium chloride.

Table 1. Chemical Identification of Polixetonium Chloride

Chemical Name	**Poly[oxy-1,2-ethanediyl(dimethyliminio)-1,2-ethanediyl(dimethyliminio)-1,2-ethanediyl dichloride (1:2)]**
Chemical Classification	Polymeric quaternary ammonium
PC Code	069183
CAS Number	31512-74-0
Molecular Formula	$C_{10}H_{25}N_2O$ (monomer without chlorines)
Molecular Weight	189.32 grams/mol (monomer without chlorines)[1] 259.22 grams/mol (monomer with chlorines) 4,142-4,695 grams/mol (polymer with chlorines, N=16-18) 3,368 grams/mol (polymer without chlorines, N=16-18)[2]
Molecular Structure	
Smiles Code	CCOCCN(C)(C)CCN(C)(Cl)(Cl) [includes 2 chlorines as counter ions]

[1] EPI-Suite 4.11
[2] MRID 46276202

Table 2. Physical-Chemical and Environmental Fate Properties for Polixetonium Chloride

Guideline No./ Study Type	Results	Reference/Comments (MRID unless specified)
Water Solubility (mg/L) at 25 °C	10,000	Assumed based on miscibility
830.7050 UV/visible absorption	N/A	49176301 Compound has no double bonds to absorb UV light
830.7370 Dissociation constant	Waived	47120304 and 42372401
830.7550 Partition coefficient (Log Kow)	Waived	47120304 and 42372401 Not applicable for polar, water-soluble active ingredients
830.7950 Vapor pressure	N/A	47120304 The a.i. is a polymer, therefore vapor pressure is negligible
Henry's Law Constant (atm m^3 mol^{-1}) at 25°C	8.5 x 10^{-12}	Volatility from water not likely to occur given the high MW, solubility, and positive charges that will enhance sorption to solids.

2.4 Registered Products and Uses

Polixetonium chloride is currently registered in end-use products used as an algaecide, bacteriostat, fungicide, microbiocide/microbiostat and molluscicide. Products containing polixetonium chloride are used in swimming pools, spas, whirlpools, hot tubs, metalworking fluids, fire water protection systems, cooling water towers, petroleum secondary recovery systems, paper mill process water, air washer water systems, and ornamental ponds.

Table 3 presents a summary of the registered uses of polixetonium chloride that will be assessed in this registration review. Products containing polixetonium chloride can be applied by liquid pour and liquid pump.

Table 3. Summary of Registered Uses for Polixetonium Chloride

Use	Application Method	Application Rate (ppm a.i.)
Industrial Processes and Water Systems		
Air washer systems	Liquid Pour or Pump	6.0-48.0
Air washers and industrial scrubbing systems	Liquid Pour or Pump	15.6-26.0
Recirculating cooling and process water systems	Liquid Pour or Pump	6.0-36.0
Once through cooling systems	Liquid Pour or Pump	1.2-12
Petroleum secondary recovery	Liquid Pour or Pump	6.0-48.0
Fire water protection systems	Liquid Pour or Pump	12.0-48.0
Paper manufacture	Liquid Pour or Pump	15-150
Aquatic Areas		
Decorative fountains	Liquid Pour	4.7-9.4
Ponds	Liquid Pour	0.5-0.94
Non-potable industrial freshwater systems	Liquid Pour	0.6-6.0

Use	Application Method	Application Rate (ppm a.i.)
Swimming Pools		
Swimming pools, and spas[A]	Liquid Pour	5.1-8.0 (Initial) 1.2-3.2 (Maintenance) 5.1-10 (Winterizing)
Exterior spas, whirlpools and hot tubs	Liquid Pour	5.9-9.0
Material Preservatives		
Metalworking fluids systems, cutting fluids or oils	Liquid Pour or Pump	12-600
Pulp and paper, and paperboard mills (non-food)	Liquid Pour or Pump	30-180

A. The initial treatments are for single slug or shock treatments that are applied when the pool is visibly contaminated. The maintenance treatments are applied repeatedly to maintain control during the swimming season. The winterizing treatments are applied once in the fall to prevent contamination when the pool is not being used.

2.5 Usage Information

Polixetonium chloride is listed as Busan 77 in the report: Specialty Biocides 2016: United States Market Analysis (Kline, 2017). It is only mentioned in the metal working section of the report which lists the top 14 biocides used in metal working fluids. Busan 77 is not in the top 14 but is included in the 15th spot which is the "others" category. The "others" category contains two other biocides and has a usage of 111,000 pounds per year.

3 Human Health Risk Assessment

3.1 Data Deficiencies

The are no data deficiencies for polixetonium chloride.

3.2 Anticipated Exposure Pathways

Exposures to polixetonium chloride can occur via the oral (non-dietary), dermal, and inhalation routes. Dietary and drinking water exposures to polixetonium chloride are not anticipated because of its use profile (no food use) and environmental fate properties.

3.3 Hazard Characterization and Dose-Response Assessment

3.3.1 Toxicology Studies Available for Analysis

- 90-day oral toxicity study in rats (MRID 40025001)
- 90-day dermal toxicity study in rabbits (MRID 40170601)
- Prenatal developmental toxicity study in rabbits (MRID 41248001)
- Chronic oral toxicity study in dogs (MRID 41234501)
- Combined chronic/carcinogenicity study in rats (MRID 41809101)
- Dermal penetration study in rat (MRID 40139201)
- Carcinogenicity study in mice (MRID 41493401)
- Prenatal developmental toxicity study in rats (MRID 41423001)
- Reproduction and fertility effects toxicity study in rats (MRID 40578201)

- Reverse mutation assay in *Salmonella typhimurium* (MRID 41573701)
- Sex-linked recessive lethal test (MRID 00151205)
- Unscheduled DNA synthesis in mammalian cultured cells (MRID 40978701)
- Metabolism and pharmacokinetics (MRID 40268601)
- Dermal penetration study in rats (MRID 40139201)

The database for polixetonium chloride is complete. Based on a weight-of-evidence (WOE) approach, considering all the available hazard and exposure data for polixetonium chloride, the Agency concluded that the inhalation toxicity, neurotoxicity, genetic toxicity, and immunotoxicity studies for polixetonium chloride are not required and were recommended to be waived by the Hazard and Science Policy Committee (U.S. EPA, 2018). These studies were listed in generic data call-in (GDCI) 069183-1581. As these studies were all recommended to be waived, there are no outstanding data requirements, and, thus, no data gaps.

3.3.2 Summary of Toxicological Effects

The acute toxicity database for polixetonium chloride is complete. Polixetonium chloride is moderate for acute toxicity via the oral, dermal and inhalation routes of exposure (Toxicity Category III). For dermal irritation, polixetonium chloride has a low acute toxicity (Toxicity Category IV) and is not a dermal sensitizer. Polixetonium chloride is also identified to be a slight eye irritant. The acute toxicity data for polixetonium chloride is summarized in Appendix A.

Polixetonium chloride does not induce systemic effects in rats exposed to the chemical via the dermal route as a dermal penetration study performed in rats shows that 0.2% was absorbed (MRID 40139201). However, exposure to polixetonium chloride via the dermal route can cause dermatological changes consistent with chronic irritation and/or inflammation at 100 mg/kg/day. Irritation and inflammation caused by exposure to polixetonium chloride can be characterized as ulceration of the epidermis, chronic inflammation of the dermis, acanthosis, hyperkeratosis, parakeratosis, folliculitis, and epidermitis (MRID 40170601).

Kidney effects were observed in mice orally exposed to polixetonium chloride for 2 years (MRID 41494301). The weight of the right and left kidneys relative to body weight and relative to brain weights were significantly affected at the mid-dose (720 mg/kg/day) and the high-dose (1400 mg/kg/day) in females and at the high-dose in males. Other effects observed in female kidneys at the low-dose (360 mg/kg/day) from exposure to polixetonium chloride in this study consisted of enlarged kidney pelvis, diffuse rough kidney, and proteinaceous casts. In male kidneys, a dose-related increase in proteinaceous casts, and pelvic and tubular dilation were observed at the low-dose. The results from this study suggest that in mice, the kidney is a target organ of polixetonium chloride.

In a combined carcinogenic/oral chronic toxicity study performed in rats (MRID 41809101), reduced body weights and reduced body weight gains were observed at the mid-dose (180 mg/kg/day) in males (-15.9%). The same effects were observed in females, at the high-dose (540 mg/kg/day) (-38%).

Rabbits exposed to polixetonium chloride during pregnancy showed signs of emaciation and decreased defecation and decreased food consumption. In addition, an increase in dams that

aborted was observed at the highest dose tested of 75 mg/kg/day when compared to controls (3 dams aborted vs. 1 dam aborted; MRID 41248001). Even though pups showed an increase in the incidence of 13th rudimentary ribs (93.3% of litters at 75 mg/kg/day vs 52.6% at 0 mg/kg/day) and unossified sternebrae #5 and/or #6 (40% of litters at 75 mg/kg/day vs. 5.3% at 0 mg/kg/day), the incidences did not follow a dose response relationship and these effects are not considered adverse as they occur during normal development in rabbits. In addition, the incidences of these effects approximate the historical control incidence (13th rudimentary ribs 43.8% to 89.5% of litters and unossified sternebrae #5 and/or #6 12.5-36.8% of litters). Based on the toxicological database for polixetonium chloride, rabbits are the most sensitive species to the chemical and the kidney is the target organ.

The mutagenesis database for polixetonium chloride contains three studies (MRID 41573701, MRID 00151205, and MRID 40978701). MRID 41573701 is a reverse mutation assay performed in *Salmonella* and MRID 40978701 is an unscheduled DNA synthesis study. These two studies did not report the purity of the chemical. However, the results from these two studies concluded that polixetonium chloride is not genotoxic. A sex-linked recessive lethal test performed in *Drosophila* also demonstrated that polixetonium chloride is not genotoxic (MRID 00151205). The Agency has classified polixetonium chloride as a "Group D" carcinogen, as there is not enough data to determine its carcinogenic potential (U.S. EPA, 1994).

3.3.3 Safety Factor for Infants and Children (Special Sensitivity Safety Factor)

Exposures to polixetonium chloride via direct or indirect dietary routes are unlikely to occur; therefore, a special sensitivity safety factor does not need to be retained. The toxicology database for the polixetonium chloride demonstrates that the adverse effects in the developing fetus or offspring occur above doses at which maternal adverse toxicity effects are observed. Therefore, there is no susceptibility to the developing embryo or offspring.

3.3.4 Toxicity Endpoint and Point of Departure Selections

The point of departure for each exposure scenario accounts for the purity of the a.i. used in the studies reviewed. In the case of polixetonium chloride, the purity is 60%.

Dietary (acute or chronic)

Dietary points of departure or endpoints are not being established for polixetonium chloride as there are no direct or indirect food exposures to the chemical. There are also no drinking water exposures anticipated for polixetonium chloride.

Incidental oral (short-, intermediate-, and long-term)

A prenatal developmental study performed in rabbits (MRID 41248001) was reviewed to establish an incidental oral short- (1-30 days) and intermediate-term (1-6 months) point of departure based on a NOAEL of 27 mg/kg/day and a LOAEL of 75 mg/kg/day based on increased incidence of abortions and clinical signs (reduced defecation and emaciation). The uncertainty factors (UF) to be implemented to estimate the margins of exposure (MOEs) for incidental exposures of short- and intermediate-term duration total 100x (10x for interspecies extrapolation (UF_A) and 10x for human to human variation (UF_H)). For long-term incidental oral

exposures, a UF_S of 10x is included for using a developmental toxicity study to establish a long-term POD for a total of 1000x for margin of exposure calculations.

Dermal (short- and intermediate-term)

A 90-day dermal toxicity study performed in New Zealand white rabbits (MRID 40170601) was reviewed and selected to establish a point of departure (POD) of 6 mg/kg/day NOAEL and a LOAEL of 60 mg/kg/day based on dermatological changes consistent with chronic irritation and/or inflammation. The skin lesions observed in the rabbits consisted of one or more combinations of ulceration of the epidermis, chronic inflammation of the dermis, acanthosis, hyperkeratosis, parakeratosis, folliculitis, and epidermitis. The uncertainty factors (UF) to be implemented to estimate the margins of exposure (MOEs) for dermal exposures total 10x (3x for interspecies extrapolation (UF_A) and 3x for human to human variation (UF_H)).

Because the dermal POD was based on irritation effects that can be localized to the area of contact, the dermal POD was converted from a dose of 6 mg/kg/day to a dermal loading of 72 µg/cm^2. This conversion was done using the following formula:

$$Dermal\ Loading\ = \frac{(Dermal\ Dose * BW * 1000\ \mu g\ per\ mg)}{Area\ Dosed * BSA}$$

Where:

- The dermal dose is 6 mg/kg/day.
- The body weight (BW) is 2.27 kg based on the week zero weight of the female rabbits in the 6 mg/kg/day dose group. The body weights in this dose group ranged from 2.27 kg for week zero females to 3.46 kg for week 14 males.
- The area dosed is 10 percent of the Body Surface Area (BSA) based on the study report.
- The BSA is 1900 cm^2 (0.19 m^2) for the 2.27 kg rabbit based on the Meeh's formula for New Zealand white rabbits from Itoh (2018). This formula is as follows:

$$100 \text{ x BSA } (m^2) = 11.0 \text{ x BW } (kg)^{2/3}$$

Inhalation (short-, intermediate-, and long-term)

A prenatal developmental study performed in rabbits was reviewed to establish inhalation short- (1-30 days) and intermediate- (1-6 months), and long-term exposures points of departure based on a NOAEL of 27 mg/kg/day and a LOAEL of 75 mg/kg/day based on increased incidence of abortions and clinical signs (reduced defecation and emaciation). The uncertainty factors (UF) to be implemented to estimate the margins of exposure (MOEs) for incidental exposures of short- and intermediate-term duration total 100x (10x for interspecies extrapolation (UF_A) and 10x for human to human variation (UF_H)). For long-term inhalation exposures, a UF_S of 10x is included for using a developmental toxicity study to establish a long-term POD for a total of 1000x for margin of exposure calculations. A 10x for the lack of an inhalation study is not being implemented for this route of exposure as the Agency has waived the need for such study (U.S. EPA, 2018).

Table 4. Summary of Toxicological Doses and PODs for Polixetonium Chloride

Exposure/ Scenario	Point of Departure (POD)	Uncertainty Factors (UFs)	Level of Concern (LOC) for the MOE	Study and Toxicological Effects
Incidental Oral Short-Term (1-30 days)/ Intermediate-Term (1-6 months)	NOAEL= 27 mg/kg/day	UF_A= 10x UF_H=10x	LOC for MOE = 100	Prenatal developmental toxicity study in rabbits (MRID 41248001) Maternal LOAEL = 75 mg/kg/day based on increased incidence of abortions, clinical signs (reduced defecation and emaciation).
Incidental Oral Long-Term (>6 months)	NOAEL= 27 mg/kg/day	UF_A= 10x UF_H=10x UF_S = 10x	LOC for MOE = 1000	Prenatal developmental toxicity study in rabbits (MRID 41248001) Maternal LOAEL = 75 mg/kg/day based on increased incidence of abortions, clinical signs (reduced defecation and emaciation).
Dermal Short- /Intermediate- term	NOAEL= 6 mg/kg/day (72 µg/cm^2)	UF_A= 3x UF_H=3x	LOC for MOE = 10	90-day dermal toxicity study in rabbits (MRID 40170601) LOAEL = 60 mg/kg/day based on treatment related changes consistent with chronic irritation/inflammation.
Dermal Long-term	NOAEL = 6 mg/kg/day (72 µg/cm^2)	UF_A= 3x UF_H=3x UF_S = 10x	LOC for MOE = 100	90-day dermal toxicity study in rabbits (MRID 40170601) LOAEL = 60 mg/kg/day based on treatment related changes consistent with chronic irritation/inflammation.
Inhalation Short- and Intermediate-Term	NOAEL= 27 mg/kg/day	UF_A= 10x UF_H=10x	LOC for MOE = 100	Prenatal developmental toxicity study in rabbits (MRID 41248001) Maternal LOAEL = 75 mg/kg/day based on increased incidence of abortions, clinical signs (reduced defecation and emaciation).
Inhalation Long-Term	NOAEL= 27 mg/kg/day	UF_A= 10x UF_H =10x UF_S = 10x	LOC for MOE = 1000	Prenatal developmental toxicity study in rabbits (MRID 41248001) Maternal LOAEL = 75 mg/kg/day based on increased incidence of abortions, clinical signs (reduced defecation and emaciation).
Cancer (oral, dermal, inhalation)	Polixetonium chloride has been classified as a "Group D" carcinogen (not classifiable as to human carcinogenicity: agents without adequate data either to support or refute human carcinogenicity).			

NOAEL = no observed adverse effect level.
LOAEL = lowest observed adverse effect level.
UF_A = extrapolation from animal to human (interspecies).
UF_H = potential variation in sensitivity among members of the human population (intraspecies).
UF_S = use of a short-term study for long-term risk assessment.
MOE = margin of exposure.
µg/cm^2 = Dermal Dose (10 mg/kg/day) * BW (2.27 kg) * 1000 µg/mg / Area Dosed (10% BSA) * BSA (1900 cm^2)

3.4 Human Health Incidents

A search of the Agency's Incident Data System (IDS) on April 22, 2020, indicated that there were three incidents that involved polixetonium chloride within the past 5 years. All three incidents were associated with the use of pool products and resulted in health effects classified as of moderate severity. In incident #27823-23, a person accidentally ingested some of the product. In incident #27929-22, a child experienced respiratory irritation after swimming in a pool treated with the product. In incident #29020-06, a consumer got the product on their hands which caused skin irritation.

3.5 Dietary Exposure and Risk Assessment

There are no dietary exposures associated with the currently registered uses of polixetonium chloride; therefore, a dietary risk assessment is not needed for registration review. Dietary exposure via drinking water is also expected to be minimal because the parent compound sorbs tightly to soil and sediment (MRIDs 00157906, 00157907). Further, paper uses are restricted to non-food applications.

3.6 Residential (Non-Dietary) Exposure/Risk Characterization

3.6.1 Residential Handler Exposure

There is the potential for residential handler exposure when applying products that contain polixetonium chloride to swimming pools. This exposure is short term in duration because these applications are made at weekly intervals during the pool season. The assessment of swimming pool risks are protective of exposure from spas and fountains because residential swimming pools have a large water volume than residential pools and spas.

Residential Handler Inhalation MOE

An MOE of 770,000 for residential handler inhalation exposure to polixetonium chloride was calculated as outlined in Table 5. This MOE is not of concern because it is greater than the LOC of 100.

Table 5. Residential Handler Inhalation MOEs for Polixetonium Chloride

Scenario	Application Rate[A] (ppm a.i.)	Amount of Pool Water Treated[B]	Amount a.i. Handled (lb/day)[C]	Unit Exposure[D] (mg/lb a.i.)	Inhalation Exposure[E] (mg/day)	Inhalation Dose[F] (mg/kg/day)	MOE[G] (LOC =100)
Open pour liquids for pool treatment	10	20,000 gallons	1.67	0.0017	0.0028	0.000035	770,000

A. Winterizing treatment rate from EPA Reg. No. 46978-4.
B. Standard assumption used for residential pool application of AD chemicals.
C. Amount a.i. Handled (lb/day) = [Application Rate (ppm) / 1,000,000 ppm] x Amount Pool Water Treated * 8.35 lb/gal.
D. Conventional pour unit exposure from AEATF II human exposure liquid pour study (MRID 48917401).
E. Inhalation Exposure (mg/m^3) = Amount a.i. Handled (lb/day) * Unit Exposure (mg/lb a.i.)
F. Inhalation Dose (mg/kg/day) = Inhalation Exposure (mg/day) / BW (80 kg)
G. MOE = POD (27 mg/kg/day) / Inhalation Dose (mg/kg/day).

Residential Handler Dermal MOE

The MOEs for residential handler dermal exposure to polixetonium chloride were calculated as outlined in Table 6 using a hand surface of 820 cm^2 from US EPA, 1996. The MOE is 3.6 when the application rate is 10 ppm for the winterizing treatment and the MOE is 11 when the application rate is 3.2 ppm for the maintenance treatment. The MOE of 3.6 is of concern because it is less than the LOC of 10.

Table 6. Residential Handler Dermal MOE for Polixetonium Chloride

Scenario	Application Rate (ppm a.i.)	Amount of Pool Water Treated per Day[C]	Amount a.i. Handled (lb/day)[D]	Unit Exposure (mg/lb a.i.)	Dermal Exposure[F] (mg/day)	Dermal Loading[G] (µg/cm^2)	MOE[H] (LOC = 10)
Open pour liquids for pool treatment	10[A]	20,000 gallons	1.67	10[E]	16.7	20.2	**3.6**
	3.2[B]		0.53		5.3	6.4	11

A. Winterizing treatment rate from EPA Reg. No. 46978-4.
B. Maximum maintenance treatment rate from EPA Reg. No. 46978-4.
C. Standard assumptions used for residential exposure assessments of AD chemicals.
D. Amount of a.i. Handled (lb/day) = [Application Rate (ppm) / 1,000,000 ppm] x Amount Pool Water Treated (gal) x Water Density (8.35 lb/gal)
E. Conventional pour value from AEATF II human exposure liquid pour study (MRID 48917401). Hands = 99%.
F. Dermal Exposure (mg/day) = Amount a.i. Handled (lb/day) * Unit Exposure (mg/lb a.i.)
G. Dermal Loading (ug/cm^2) = [Dermal Exposure (mg/day) *Hand Exposure (%/100) *1000 µg/mg] / Hand Area (820 cm^2)
H. MOE = POD (72 µg/cm^2) / Dermal Loading (µg/cm^2)

3.6.2 Residential Post Application Exposure

There is the potential for dermal and incidental oral exposures to polixetonium chloride to persons swimming in treated swimming pools. Adults and children ages 11 to <16 and 6 to <11 years are the relevant age groups for this exposure scenario. The exposures are assumed to be short- and intermediate-term in duration because polixetonium chloride is primarily used in outdoor pools.

Dermal Exposures and MOEs for Persons Swimming in Treated Pools

An MOE of 670 for dermal exposure was calculated as shown in Table 6 by comparing the swimming pool water concentration of polixetonium chloride to the concentration of the a.i. applied to the animals in the dermal toxicity study. This MOE is greater than the LOC of 100 and is not of concern.

Table 7. Dermal MOE for Swimmer Exposure to Polixetonium Chloride

Application Rate[A]	NOAEL for Dermal Effects	Dose Concentration Applied at NOAEL[B]	MOE[C] (LOC = 100)
9 ppm a.i.	6 mg/kg/day	6,000 ppm	670

A. Based on several labels that contain polixetonium chloride.
B. Based on 5 grams of polixetonium chloride, which contains 60% a.i., added to 500 ml of water for the 10 mg/kg/day dose group.
C. MOE = POD (Dose Concentration Applied at NOAEL (6,000 ppm) / Application Rate (9 ppm)

Incidental Oral Exposures for Persons Swimming in Pools Treated with Polixetonium Chloride

There is potential for post-application incidental oral exposures to polixetonium chloride when products containing this a.i. are used to treat swimming pools. Adults and children ages 11 to <16 and 6 to <11 years are the relevant age groups for this exposure scenario. The index life-stage for other scenarios, children 1 to < 2 years old, is not appropriate in this case, because this age group is less likely to engage in the activity that results in exposure. The exposures for recreational swimmers are assumed to be short- and intermediate-term in duration and the exposures for competitive swimmers are assumed to be long-term in duration.

Incidental oral exposures are assessed using the formulas from SWIMODEL 3.0. This model was developed by EPA as a screening tool to conduct exposure assessments of pesticides found in swimming pools and spas. Information regarding this model can be found at https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/swimmer-exposure-assessment-model-swimodel. Some of the inputs and parameters have been updated for this risk assessment based on information provided in the 2011 edition of the EPA Exposure Factors Handbook (U.S. EPA, 2011).

The equation below, taken from SWIMODEL 3.0, is used to calculate post application ingestion exposures to polixetonium chloride added to swimming pools.

$$PDD = \frac{Cw \times IgR \times ET}{BW}$$

Where:

PDD = Potential daily dose, (mg/kg/day),
Cw = Chemical concentration in pool water (mg/L),
IgR = Ingestion rate of pool water (L/hr),
ET = Exposure time (hrs/day),
BW = Body weight (kg)

Assumptions

- Cw: Chemical concentration in pool water (mg/L) is 9.0 based on several labels that contain polixetonium chloride.
- IgR: The ingestion rates for non-competitive swimmers is 0.05 liters/hour for adult, 11 to < 16 year-old, and 6 to < 11 year-old swimmers, respectively. This value is from the Superfund Exposure Assessment Manual (EPA, 1988). The ingestion rates for competitive swimmers are 0.025, 0.025 and 0.05 liters/hour for adult, 11 to < 16 year-old, and 6 to < 11 year-old swimmers, respectively. These rates are based on the opinion of swim coaches interviewed during a survey (Wright, 2006) that competitive swimmers ingest half as much water as non-competitive swimmers.
- ET: The exposure time for competitive swimmers is based on a survey (Wright, 2006) and the exposure time for non-competitive/ recreational swimmers is based on Table 16 of the Exposure Factors Handbook (EPA, 2011). The exposure time for competitive swimmers is 3, 2, and 1 hours per day for adult, 11 to < 16 year-old, and 6 to < 11 year-old swimmers, respectively. The exposure time for noncompetitive and/or

recreational swimmers is one hour per day based on National Human Activity Pattern (NHAPs) data (U.S. EPA, 1996a).

- BW (Adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights listed in Exposure Factors Handbook (EPA, 2011).
- BW (Child): The average body weight is 57 kg for children ages 11 to <16 years, and 32 kg for children age 6 to <11. These are the recommended values from the Exposure Factors Handbook (EPA, 2011).

Swimming Pool Incidental Oral MOEs

The MOEs for incidental oral exposure to polixetonium chloride are included in Table 8. The MOEs range from 1,900 to 4,800 and are not of concern because they are above the LOC of 100.

Table 8. Incidental Oral MOEs for Swimmer Exposure to Polixetonium Chloride

Competitive Swimmers	**Adult**	**Child 11 to <16**	**Child 6 to <11**
Water Concentration in a.i.	9.0 mg/liter[A]		
Ingestion Rate (liters/hour)	0.025	0.025	0.025
Exposure Time (hours/day)	3	2	1
Daily Exposure[B] (mg/day)	0.675	0.45	0.225
Body Weight (kg)	80	57	32
Daily Dose[C] (mg/kg/day)	0.0084	0.0079	0.0070
Incidental Oral MOE[D]	3,200	3,400	3,900
Non-Competitive Swimmers	**Adult**	**Child 11 to <16**	**Child 6 to <11**
Water Concentration in a.i.	9.0 mg/liter[A]		
Ingestion Rate (liters/hour)	0.05	0.05	0.05
Exposure Time (hours/day)	1	1	1
Daily Exposure[B] (mg/day)	0.45	0.45	0.45
Body Weight (kg)	80	57	32
Daily Dose[C] (mg/kg/day)	0.0056	0.0079	0.014
Incidental Oral MOE[D]	4,800	3,400	1,900

A. Based on several labels that contain polixetonium chloride.
B. Exposure = Water Concentration (mg/liter) * Ingestion Rate (0.050 liter/hour) * Exposure Time (1 hour)
C. Dose = Exposure (mg/day)/Body weight (kg)
D. MOE = NOAEL (27 mg/kg/day)/Dose (mg/kg/day)

3.7 Aggregate Exposure/Risk Characterization

There are no dietary or drinking water exposures associated with the uses of polixetonium chloride to combine with the one residential use; therefore, an aggregate assessment is not needed for registration review.

3.8 Cumulative Exposure/Risk Characterization

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to polixetonium chloride and any other substances and polixetonium chloride does not appear to produce a toxic metabolite produced by other substances. For the purposes of this action,

therefore, EPA has not assumed that polixetonium chloride has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. 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. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[1] and conducting cumulative risk assessments (CRA)[2].

3.9 Occupational Exposure/Risk Characterization

There is the potential for occupational handler exposure when polixetonium chloride is open poured to treat the use sites listed in Table 3. There is also the potential for occupational post application exposure when using metalworking fluids that are preserved with polixetonium chloride.

3.9.1 Occupational Handler Exposures

Occupational handler exposures were assessed separately for open pour applications for swimming pools and all other use sites, which in includes the aquatic, industrial process and water treatment and material preservation use sites listed in Table 3. The exposures for swimming pools was calculated using a use site specific application rate and amount treated. The exposure for all of the other use sites is based on the assumption that a maximum of 20 gallons of product containing the maximum amount of a.i. (60 %) would be open poured. Twenty gallons is the maximum amount of product that was handled during the AEATF II human exposure liquid pour study (MRID 48917401). It is assumed that larger amounts would be metered in rather than open poured.

Occupational Handler Inhalation Exposures

The MOEs for occupational handler inhalation exposures to polixetonium chloride were assessed as outlined in Table 9. The MOEs are not of concern because they are greater than the LOC of 100.

Table 9. Occupational Handler Inhalation MOEs for Polixetonium Chloride

Scenario	Application Rate (ppm a.i.)	Amount of Water Treated per Day (gallons)	Amount a.i. Handled (lb/day)	Unit Exposure[G] (mg/lb a.i.)	Inhalation Dose[H] (mg/kg/day)	MOE[I] (LOC =100)
Open pour liquids for swimming pool treatment	10[B]	660,000[C]	55.1[E]	0.0017	0.0011	25,000
Open pour liquids for all other use sites[A]	Not Applicable[D]		115[F]	0.0017	0.0024	11,000

A. All other aquatic, industrial processes and water treatment, and material preservation use sites listed in Table 3.
B. Winterizing treatment rate from EPA Reg. No. 46978-4.
C. Based on an Olympic sized swimming pool.

[1] *Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)
[2] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

D. It is assumed that a maximum of 20 gallons of a product would be open poured based on the AEATF II human exposure liquid pour study (MRID 48917401). It is assumed that larger amounts would be metered in rather than open poured.
E. Amount of a.i. Handled (lb/day) = [Application Rate (ppm) / 1,000,000 ppm] x Amount Water Treated (gal) x Density of Water (8.35 lbs/gal).
F. Is the amount of a.i. in 20 gallons of EPA Reg. No. 1448-42 that contains 60% a.i. and has a density of 9.6 lb/gallon.
G. Conventional pour unit exposure from AEATF II human exposure liquid pour study (MRID 48917401).
H. Inhalation Dose (mg/kg/day) = [Amount a.i. Handled (lb/day) * Unit Exposure (mg/lb a.i.)] / BW (80 kg)
I. MOE = POD (27 mg/kg/day) / Inhalation Dose (mg/kg/day).

Occupational Handler Dermal Exposures

Although dermal exposures can occur during open pouring, these exposures do not need to be assessed for polixetonium chloride because the repeat dose dermal toxicity study indicated that dermal irritation was the only observed effect. This effect can be prevented by the chemical resistant gloves that are required by the label.

3.9.2 Occupational Post Application Exposures

Polixetonium chloride is registered for use in metalworking fluids (MWFs); therefore, there is the potential for machinists to be exposed when using treated MWFs. Both dermal and inhalation exposures are anticipated.

Machinist Inhalation MOEs

The inhalation MOE of 360,000 was calculated as outlined in Table 10. This MOE is not of concern because it is greater than the LOC of 1000 for long-term exposure.

Table 10. Inhalation MOE for Machinists Using MWF Treated with Polixetonium Chloride

Application Rate[A]	MWF Air Concentration (mg/m^3)	Polixetonium Chloride Air Concentration (mg/m^3)	Breathing Rate (m^3/hr)	Daily Exposure (mg/day)	Daily Dose (mg/kg/day)	Inhalation MOE[F] (LOC = 1000)
600 ppm	1.0[B]	0.0006[C]	1.25	0.006[D]	0.000075[E]	360,000

A. Maximum application rate for cutting fluids listed on EPA Reg No. 5383-199.
B. Average 8 hr TWA for oil mist air (n=544 samples) measured by OSHA (2000 to 2009) corrected for 25% volatilization loss based on McAneny (1995) and Park (2003).
C. Polixetonium Chloride Air Concentration = Application Rate (ppm) / 1,000,000 ppm * MWF Air Concentration (1.0 mg/m^3).
D. Daily Exposure (mg/day) = Polixetonium Chloride Air Concentration (mg/m^3) * Breathing Rate (m^3/hr) * Exposure Time (8 hrs/day)
E. Daily Dose (mg/kg/day) = Daily Exposure (mg/day) / Body Weight (80 kg)
F. MOE = POD (27 mg/kg/day) / Daily Dose (mg/kg/day)

Machinist Dermal Exposure and MOE

The dermal exposure of machinists to MWFs treated with polixetonium chloride was assessed by using the thin film approach for comparison to the POD which is expressed as the amount of a.i. per given area of skin. This approach using the following equation:

$$\text{Dermal Loading } (\mu g/cm^2) = WF \text{ (Application Rate/1,000,000) x } Qu\ (mg/cm^2) \text{ x 1,000 } \mu g/mg$$

The following assumptions were used in this assessment:

- WF: The weight fraction is based on the application rate of 600 ppm.
- Qu: The quantity remaining on the skin is 10.3 mg/cm^2 based on the hand immersion with no wiping results for mineral oil reported in Cinalli (1992). This value is used to evaluate dermal irritation effects because these effects can be localized.
    - It is not feasible for machinists to wear chemical resistant gloves because they interfere with the fine motor skills needed to operate the metalworking machines and measure the materials that being machined.

The dermal MOE of 12 was calculated as outlined in Table 11 and is of concern because it is less than the LOC of 100.

Table 11. Dermal MOE for Machinists Using MWF Treated with Polixetonium Chloride

Application Rate[A]	Weight Fraction[B]	Qu (mg/cm^2)	Dermal Loading[D] (µg/cm^2)	Dermal MOE[E] (LOC = 100)
600 ppm a.i.	0.0006	10.3[C]	6.2	12

A. Maximum application rate for cutting fluids listed on EPA Reg No. 5383-199.
B. Weight Fraction = Application Rate (600 ppm) / 1,000,000 ppm
C. Standard value used by AD based on hand immersion and wiping experiments reported in Cinalli, 1992.
D. Dermal Loading = Weight Fraction x Qu (mg/cm^2) x 1000 µg/mg
E. MOE = Dermal POD (72 µg/cm^2) / Dermal Loading (µg/cm^2).

4 ENVIRONMENTAL RISK ASSESSMENT

Risks to terrestrial taxa (including pollinators) are not expected from the currently registered uses of polixetonium chloride due to low exposure potential. However, there is a potential for aquatic exposures to polixetonium chloride from several use patterns, with the highest exposures expected from the following uses: pulp and paper mill, recirculating cooling towers, and once through cooling systems. All of the other registered uses would have lower exposures than the pulp and paper mill, recirculating cooling tower, and once through cooling tower uses, therefore, risks associated with these uses would be higher than for the other uses.

4.1 Environmental Fate

Polixetonium chloride is miscible in water (Table 2) and is not expected to degrade by either abiotic processes (MRIDs 41407401, 41420901, 41451419, 41561411) or biotic processes (MRIDs 40334101, 40165201, 40165202). Movement from water or soil into air is also not expected to occur for most uses based on the lack of vapor pressure and Henry's Law values (Table 2), but the air washer use has the potential to create aerial exposure because the cationic active ingredient, polixetonium chloride dissolved in water can volatilize with the water. Bioconcentration in aquatic organisms is also not expected, because polixetonium chloride is a polar compound that is miscible in water (Table 2).

Sorption to soil, sediment, and sludge is expected to be the primary route of dissipation, based on the fact that polixetonium chloride is a quaternary ammonium compound that has a positive electrical charge. Polixetonium chloride has the potential to reach wastewater treatment plants (WWTPs) from the registered uses. While activated sludge sorption isotherm data have not been submitted, activated sludge respiration inhibition data (MRID 50510601) indicate that polixetonium chloride is not toxic to WWTP microorganisms with an IC_{50} value of 76 mg/L (*i.e.*, >20 mg/L). WWTP biodegradability studies (OCSPP 835.3110, 835.3220, 835.3240, and 835.3280) are also normally required for chemicals that have the potential to reach WWTPs based on the registered uses. A ready biodegradability study (MRID 50510602, OCSPP 835.3110) demonstrated stability to microbial degradation in a WWTP, which is consistent with the results of other non-WWTP microbial degradation. Therefore, for polixetonium chloride, there is no apparent route of chemical or microbial degradation.

Table 12 below contains the results of environmental fate data for polixetonium chloride.

Table 12. Environmental Fate Data for Polixetonium Chloride

Guideline (OCSPP No.)	Study Result	Reference (MRID)/Comments
Hydrolysis (835.2120)	Stable at 25 °C	41407401, 41461409
Photodegradation in water (835.2240)	Stable at 25 °C	41420901
Photodegradation on soil (835.2410)	Stable at 25 °C	41561411
Aerobic soil metabolism[1] (835.4100)	Stable at 23-25 °C	40165202 41561412 Based on soil thin-layer-chromatography (TLC) study
Aerobic aquatic metabolism (835.4300)	Stable at 23-25 °C	40334101
Anaerobic aquatic metabolism (835.4400)	Stable at 23-25 °C	40165201

Guideline (OCSPP No.)	Study Result	Reference (MRID)/Comments
Leaching-adsorption-desorption (835.1230)	Tightly sorbed to soil at room temperature(unspecified)	00157906 00157907 Soil column leaching studies (835.1240 submitted)
Ready biodegradability (835.3110)	Stable at 22 ± 2 °C	50510602
Activated sludge sorption isotherm (835.1110)	No data	N/A (Use of sorption data for soil and sediments not appropriate for sludge)
Activated sludge respiration inhibition (ASRI, 850.3300)	IC_{50} = 76 mg/L at 20.4-20.6 °C	50510601
Higher-Tier WWTP biodegradation studies (835.3220, .3240, .3280)	No data	Not required because of overall stability of compound in fate studies

4.1.1 Available Fate Data and Uncertainties

The registrant has submitted acceptable data that demonstrate stability of the polixetonium chloride molecule and sorption in the environment (Table 12). However, data have not been submitted for the Activated Sludge Sorption Isotherm (ASSI) (OCSPP 835.1110) study. Data on sorption to sludge would allow refinement of possible aquatic exposure from effluent coming from WWTPs, and lack of the data creates an uncertainty in the risk assessment.

4.1.2 Degradates of Potential Concern

There are no degradation products of potential concern for polixetonium chloride because it is stable to degradation.

4.1.3 Water Quality – Total Maximum Daily Load (TMDL)

Based on a February 11, 2020 search, polixetonium chloride is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act.[3] In addition, no Total Maximum Daily Loads (TMDL) have been developed for polixetonium chloride.[4] More information on impaired water bodies and TMDLs can be found at EPA's website.[5]

The Water Quality Portal[6] was searched on May 7, 2020 but does not include monitoring data for polixetonium chloride.

4.2 Ecotoxicity Data

Ecotoxicity endpoint data are used as measures of the effects to aquatic and terrestrial organisms. Available ecotoxicity endpoints submitted by registrants, federal laboratory data, or from the public literature are provided in Appendix B along with the data requirements and data gaps. The most sensitive values for each receptor group are used for the risk assessment are provided in Table 13.

[3] http://iaspub.epa.gov/tmdl_watersdfmn, 10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885
[4] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[5] http://www.epa.gov/owow/tmdl/
[6] https://www.waterqualitydata.us/

Table 13. Ecological Effects Endpoints Selected for Assessing Risks from Polixetonium Chloride

Receptor Group	Surrogate Species	Risk Scenario	Toxicity Endpoint	Reference (MRID)
Freshwater fish	Rainbow trout	Acute	96-h LC_{50} = 0.047 mg/L	41352001
	Fathead minnow	Chronic	NOAEC = 0.019 mg/L	49362401
Freshwater invertebrates	*Daphnia magna*	Acute	48-h EC_{50} = 0.28 mg/L	41352003
		Chronic	NOAEC = 0.015 mg/L	49606601
Estuarine/marine fish	Sheepshead minnow	Acute	96-h LC_{50} = >360 mg/L	40139202
		Chronic	Not required[1]	--
Estuarine/marine invertebrates	Quahog clam	Acute	48-hr EC_{50} = 0.21 mg/L	40334201
	Mysid Shrimp	Acute	96-hr LC_{50} = 7.8 mg/L	40139203
		Chronic	Not required[1]	--
Algae	Freshwater diatom	N/A	96-hr EC_{50} = 0.083 mg/L NOAEC = 0.044 mg/L	42013303
Aquatic marine invertebrate/sediment	Maine invertebrate	Acute	LC_{50} = >1000 mg/kg NOAEC = >1000 mg/kg	49300901
Aquatic vascular plants	Duckweed	N/A	7-day EC_{50} = 1.1 mg/L NOAEC = 0.33 mg/L	49327001
Birds	Mallard duck	Acute	LD_{50} = 497 mg/kg	41654801
	Bobwhite quail	Subacute dietary	LC_{50} = >3462 mg/kg	00159307
		Chronic	Not required[1]	--
Nontarget insects	Honeybee	Acute	Not required[1]	--

[1] Not required for this use pattern.

4.3 Ecological Incident Data

There were no reported ecological incidents for polixetonium chloride in the Agency's Incident Data System (IDS) as of 4/20/2020.

4.4 Aquatic Exposure Modeling

Exposure to aquatic species has the potential to occur after polixetonium chloride use in various antimicrobial use sites. This risk assessment focuses on the risks from three uses that would result in highest environmental exposures, which are: 1) pulp and paper processes with use rates of 30-180 ppm a.i, 2) recirculating cooling water towers with use rates of 6-36 ppm a.i., and 3) once-through cooling systems with use rates of 1.2-12 ppm a.i.

4.4.1 Paper Mill Use

4.4.1.1 Pulp and Paper Mill Release Rate Calculations

Retention Rate of the Chemical on the Paper

Depending on where within the paper/paperboard making process a chemical is used, the average retention rate on the paper or within the paper sludge can vary. Based on the label directions, it

was determined that the retention rate of chemicals applied in the wet-end operations was most appropriate. According to the 2009 OECD Paper Scenario's Emissions Table (Table 4.3, OECD 2009), the quantity of chemical from these sources going to an effluent treatment plant is approximately 10% (90% retention on paper and paper sludge).

Environmental Release Calculations

To determine the maximum amount of polixetonium chloride (kg/site/day) that could be used in a paper and paperboard mill, it is necessary to know the maximum amount of paper that can be produced. Based on industry expert opinion, the Agency uses the general assumption that 500 US tons of paper is produced per site per day in pulp and paper mills. This is a conservative assumption and represents production in a moderate sized paper mill. The total a.i used per day (kg/site/day) was calculated based on this assumption and based on 90% absorption of chemical in pulp and paper (see Appendix C for detailed calculations).

Release Sites Information

The General Population and Ecological Exposure from Industrial Releases Module (herein called the Industrial Release module) of the Exposure and Fate Assessment Screening Tool (E-FAST) (US EPA, 2014) was used to perform an upper bound and average screening level estimate of the potential for aquatic organisms located downstream of wastewater treatment plants (WWTPs) to be exposed to polixetonium chloride.

The Agency conducted a high-end (low flow) and an average (average flow) analysis to determine the conditions under which there might be exposure and potential adverse risks to freshwater aquatic organisms. The high-end scenario is based on the 10th percentile of the distribution of the ratio of 7Q10 stream flows to WWTP flows. The average case scenario is based on the median of the distribution of the ratio of 7Q10 stream flows to WWTP flows. The 7Q10 is the lowest 7 consecutive day stream flow over a 10-year period. For the high-end scenario, the ratio of stream flow to plant flow is relatively low since plant flows can contribute considerable volume to the flow of the stream and the resulting surface water concentrations can be relatively high. For the average case scenario, the ratio of stream flow to plant flow is more typical.

In order to run E-FAST, various inputs about the release sites must be determined and are as follows:

- Days per year of release; the assumption is 360 days (USEPA, 1991).
- Standard Industrial Classification (SIC) code analysis or facility analysis; the SIC code “Paper and Paperboard Mills” was chosen because no specific facility was being analyzed.
- The number of use sites. The Agency estimated the exposure downstream from one site, as no data were available to determine how many use sites may be using polixetonium chloride.

Table 14 shows the environmental releases (kg/site/day) for polixetonium chloride in pulp and paper mills based on the uses (Table 3) and labels. Please refer to Appendix C for detailed information for how calculations were performed.

Table 14. Environmental Releases (kg/site/day) of Polixetonium Chloride[1]

ppm Active Ingredient	Environmental Release (kg/site/day)
30	1.36
180	8.16

[1.] Based on Registration Number 83451-20

4.4.1.2 Pulp and Paper Mill Results

Table 15 presents screening-level estimates of numbers of days of exceedance of concentrations of concern (COCs) for freshwater organisms downstream of WWTPs receiving effluent from pulp and paper mills assuming: (1) all releases occur over the course of one year, (2) all water used in pulp and paper mills is discharged to a WWTP, and (3) zero percent of polixetonium chloride that enters WWTPs is removed during wastewater treatment. The environmental release rate (kg a.i./site/day) is based on 30 and 180 ppm active ingredient application rates (Reg No. 83451-20). Surface water concentrations are based on the distribution of plant flows and stream flows. Model results are expressed as days per year of exceedance of concentrations of concerns for aquatic organisms downstream of a pulp and paper mill.

Table 15 shows the average and high-end scenarios for the 30 and 180 ppm polixetonium chloride use rates. Using the high-end scenarios for both rates, acute and chronic risks are of concern for all aquatic receptor groups. The number of exceedances ranged from 4-320 days. There were no exceedances for aquatic vascular plants with 30 ppm application rate or 180 ppm application rate average scenario, however, there was exceedance of 2 day at 180 ppm high-end scenario.

Using the average case scenario and low rate (30 ppm), there were exceedances of 10 days for acute non-listed fish and no exceedance for non-listed invertebrates. For chronic, there were 13 days of exceedances for fish and 17 days for invertebrates. For aquatic plants, COCs exceeded 1 day and there was no exceedance for vascular plants. For high rate (180 ppm) and average case scenario COCs exceeded 56 days for acute fish and 10 days for acute invertebrates. For chronic risk, COCs exceeded 65 days for fish and 75 days for invertebrates. Aquatic plants had 19 days exceedance and there was no exceedance for vascular plants.

Table 15. Number of Days per Year of Exceedance of Concentrations of Concerns for Aquatic Organisms Downstream of Pulp and Paper Mills (30 and 180 ppm Application Rates)

Concentrations of Concern (COC)	30 ppm Application Rate [1]		180 ppm Application Rate [1]	
	High-End	Average	High-End	Average
Acute				

Concentrations of Concern (COC)	30 ppm Application Rate [1]		180 ppm Application Rate [1]	
	High-End	Average	High-End	Average
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[2]	80	10	286	56
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[3]	4	0	81	10
Chronic				
Fish (COC = 19 µg a.i./L)[4]	101	13	303	65
Invertebrate (COC = 15 µg a.i./L)[5]	128	17	320	75
Aquatic Plants				
Non-Listed Aquatic Plant Freshwater diatom (COC = 83 µg a.i./L)[6]	12	1	137	19
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[7]	0	0	2	0

[1]1.36, and 8.16 kg Polixetonium chloride/site/day. Calculated in Appendix C.
[2] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[3]-Based on Daphnia magna study with 48 hr EC_{50}= 280 µg a.i./L. MRID 41352003.
[4] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[5] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[6] Based on freshwater diatom (*Navicula pelliculosa*) with an EC_{50}=83 µg a.i./L. MRID 42013303
[7]Based on Duckweed study EC_{50}=1100 µg a.i./L. MRID 49327001.

Modeling Uncertainties and Limitations

Modeling using E-FAST presents various uncertainties including:

- The model does not account for degradation in surface water or sorption to suspended or bottom sediment.
- The input data (*e.g.,* label, degradation, and sorption rates, water recycling rate) used may not provide the best representation of realistic environmental or use conditions.
- This risk assessment could be further refined with production volume data, additional information on where/when polixetonium chloride is added during the paper making process, information on how much polixetonium chloride is removed during WWT process, and information on how many sites use polixetonium chloride. Additional data would likely result in a more refined risk assessment.

4.4.2 Recirculating Cooling Tower Use

The General population and Ecological Exposure from Industrial Release Module of the Exposure and Fate Assessment Screening Tool (E-FAST) (US EPA, 2014) was used to perform an upper bound and average screening level estimate of the potential for aquatic organisms located downstream of wastewater treatment plants to be exposed to polixetonium chloride. The Office of Pollution Prevention and Toxics (OPPT) Chemical Engineering Branch's (CEB) generic scenario for recirculating cooling towers (USEPA, 1991) was used to estimate daily

releases to surface water from polixetonium chloride in blow-down water in kilograms per site per day. Blow-down, also sometimes referred to as "Draw-off", is the portion of circulating water flow that is removed to reduce Total Dissolved Solids (TDS) and other impurities. Reducing TDS minimizes formation of scale, biological growth, and corrosion, which if, left unchecked, can reduce the efficiency of cooling towers to remove heat from process water to the atmosphere. For complete calculations, see Appendix C.

4.4.2.1 Recirculating tower release rate calculations

Table 16 shows the environmental releases (kg/day/site) for polixetonium chloride in moderate and large size recirculating towers based on registration number 1448-398.

Table 16. Environmental Release Rate (kg/site/day) of Polixetonium Chloride for Use in Recirculating Towers

ppm active ingredient[1]	Environmental Release (kg/site/day)	
	Moderate size cooling tower (2,000 gallons/minute)[2]	Large size cooling tower (100,000 gallons/minute)[2]
6	0.41	20.74
36	2.49	124.42

[1] Reg # 1448-398

[2] The Environmental release (kg polixetonium chloride/site/day) is based on the quantity of polixetonium chloride within the blowdown. Environmental release = (0.6%) (ppm polixetonium chloride) (Recirculation rate) (5,760 x 0.000001 min-kg/day-gal). Where 0.6% is the percentage of cooling tower water that is assumed to be released to surface water via blowdown, 5,760 x 0.000001 min-kg/day-gal is a conversion factor, and the recirculation rate of the cooling water (gal/min) is either 2,000 or 100,000 gal/min.

4.4.2.2 Recirculating Cooling Water Tower Results

Tables 17 and 18 show screening-level estimates of numbers of days of exceedance of COCs for freshwater organisms downstream of cooling water towers assuming:

(1) all releases occur over the course of one year,
(2) all water used in recirculating cooling towers is discharged to WWTPs, and
(3) zero percent of polixetonium chloride that enters WWTPs is removed during wastewater treatment.

The environmental release (kg/site/day) is based on the initial doses of 6 and 36 ppm active ingredient into the system as indicated in Table 3 (Reg # 1448-398). Surface water concentrations are based on the distribution of plant flows and stream flows. Model results are expressed as days per year of exceedance of the COCs for aquatic organisms downstream of recirculating cooling towers.

Table 17 provides the number of days per year COCs are exceeded based on the average and high-end scenarios for moderate and large sized cooling towers for 6.0 ppm use rate of polixetonium chloride. With the exception of aquatic vascular plants in moderate sized cooling towers discharging to average sized streams, risks are of concern for all taxa when polixetonium chloride is used within small and large sized cooling towers, with exceedances of the COCs 3 to 357 days per year when discharged to streams.

For moderate sized cooling water towers releasing to low-flow streams (high-end calculations), acute COCs are exceeded 118 days per year for non-listed freshwater fish, and 30 days per year for freshwater invertebrates. For chronic exposures, COCs are exceeded for 133 days for fish and 151 days for invertebrates. For non-listed aquatic plants (freshwater diatom), COCs exceeded 48 days per year and 4 days per year for vascular plants. For moderate sized cooling towers releasing to average sized streams, acute COCs are exceeded 12 days per year for non-listed freshwater fish and 3 days for freshwater invertebrates. For chronic, COCs exceeded, 14 days for chronic fish and 16 days for chronic invertebrates. For aquatic plants COCs exceeded 5 days and there was no exceedance for aquatic vascular plants. For the large sized cooling towers high end scenario, COCs were exceeded 354 days for acute fish and 288 days for acute invertebrates. For chronic and high-end scenario, COCs exceeded 356 days for fish 357 days for invertebrates, COCs exceeded. For large sized cooling towers and high-end scenario, COCs were exceeded 319 days for aquatic plants and 123 days for vascular plants. For the large sized cooling towers and average scenario COCs were exceeded 95 days for acute fish and 42 days for acute invertebrates. For chronic and average case scenario, COCs exceeded 104 days for fish and 116 days for invertebrates. For large sized cooling towers and average case scenario, COCs exceeded 53 days for aquatic plants and 13 days for vascular plants. Exceedances of the COCs for listed species also occurred for all taxa and scenarios, and the results are provided in Appendix C.

For the large sized cooling water towers (Table 18), COCs were exceeded in all taxa categories and were higher than those exceedances for the moderate size cooling towers. Exceedances of the COCs for listed species also occurred for all taxa and scenarios, and the results are provided in Appendix C.

Table 17. Number of Days of Exceedances for Aquatic Risks for Recirculating Towers (6.0 ppm a.i.)

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Freshwater Fish and Invertebrates				
Acute Non-Listed Fish (COC=23.5 µg a.i./L)[3]	118	12	354	95
Acute Non-Listed Invertebrate (COC= 140 µg a,i./L)[4]	30	3	288	42
Chronic				
Chronic Fish (COC = 19 µg a.i./L)[5]	133	14	356	104
Chronic Invertebrate (COC = 15 µg a.i./L)[6]	151	16	357	116
Aquatic Plants				
Non-Listed Aquatic Plant Freshwater diatom (COC = 83 µg a.i./L)[7]	48	5	319	53
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[8]	4	0	123	13

[1] 0.41 kg Polixetonium chloride/site/day. Calculated in Table 16
[2] 20.74 kg Polixetonium chloride/site/day. Calculated in Table 16
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on freshwater diatom (*Navicula pelliculosa*) with an EC_{50}=83 µg a.i./L. MRID 42013303
[8]Based on Duckweed study EC_{50}=1100 µg a.i./L. MRID 49327001.

Table 18. Number of Days of Exceedances for Aquatic Risks for Recirculating Cooling Towers (36.0 ppm ai)

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Freshwater Fish and Invertebrates				
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[3]	263	35	360	191
Acute Non-Listed Invertebrate (COC= 140 µg a.i./L)[4]	119	12	354	95
Chronic				
Chronic Fish (COC = 19 µg a.i./L)[5]	279	39	360	202
Chronic Invertebrate (COC =15 µg a.i./L)[6]	295	44	360	215
Aquatic Plants				
Non-Listed Aquatic Plant Freshwater diatom (COC = 83 µg a.i./L)[7]	158	17	358	120
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[8]	23	2	268	36

[1] 2.49 kg polixetonium chloride/site/day. Calculated in Table 16
[2] 124.42 kg polixetonium chloride/site/day. Calculated in Table 16
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on freshwater diatom (*Navicula pelliculosa*) with an EC_{50}=83 µg a.i./L. MRID 42013303
[8]Based on Duckweed study EC_{50}=1100 µg a.i./L. MRID 49327001.

4.4.2.3 Recirculating Cooling Towers Modeling Uncertainties and Limitations

It should be noted that the cooling tower assessment presented above is a conservative, high-end, screening-level approach that uses many assumptions which may not be representative of realistic conditions in the environment. The major assumptions are:

- The model does not account for degradation in surface water or sorption to suspended or bottom sediment; and
- The model assumes 0% removal of polixetonium chloride during wastewater treatment.

4.4.3 Use in Once-Through Cooling Systems

To control mollusks such as corbicula species, the label (EPA Reg. No. 1448-42) recommends use of polixetonium chloride in recirculating or once-through cooling water and industrial systems. The screening level ecological assessment of polixetonium chloride used in once-through-cooling systems was performed using the Exposure and Fate Assessment Screening Tool (E-FAST).

Table 19 shows the environmental release (kg/site/day) for polixetonium chloride in a moderate size once-through cooling system with a 2 MGD (Million Gallons per Day) capacity per day.

Table 19. Environmental Release Rate (kg/site/day) of Polixetonium Chloride for Use in Once-Through Cooling Towers

ppm Active Ingredient[1]	Environmental Release (kg/site/day)[2]
1.2	9.0
12.0	90.0

[1]Reg. No. 1448-42
[2] See Appendix C for calculations

4.4.3.1 Once-Through Cooling Tower Results

Table 20 presents screening-level estimates of numbers of days of exceedance of COCs for freshwater organisms downstream of once-through cooling tower assuming:

(1) all releases occur over the course of one year,
(2) all water used in once-through cooling towers is discharged to WWTPs, and
(3) zero percent of polixetonium chloride that enters WWTPs is removed during wastewater treatment.

The environmental release (kg/site/day) is based on the initial doses of 1.2 and 12 ppm active ingredient into the system (registration number 1448-42). Surface water concentrations are based on the distribution of plant flows and stream flows. Model results are expressed as days per year of exceedance of the COCs for aquatic organisms downstream of once-through cooling towers.

Table 20 presents the screening level estimates of number of days of exceedance of COCs for freshwater organisms downstream of once-through cooling system with dose of 1.2 ppm polixetonium chloride. Risks are of concern for all taxa for both high-end and average scenarios when polixetonium chloride is used in once-through cooling towers with exceedances of COCs 7-348 days per year. The exceedances were higher for the high-end scenario.

Table 20. Number of Days of Exceedances for Aquatic Risks for Use of Polixetonium Chloride in Once-Through Cooling Systems (1.2 ppm)

Concentrations of Concern (COC)	2 MGD[1] Once-Through Cooling Systems	
	High-End	Average
Acute Non-Listed Fish (COC=23.5 µg a.i./L)[3]	336	65

Concentrations of Concern (COC)	2 MGD[1] Once-Through Cooling Systems	
	High-End	Average
Acute Non-Listed Invertebrate (COC= 140 µg a.i./L)[4]	223	27
Chronic Fish (COC= 19 µg a.i./L)[5]	342	72
Chronic Invertebrate (COC=15 µg a.i./L)[6]	348	80
Non-Listed Aquatic Plant Freshwater diatom (COC=83 µg a.i./L)[7]	266	36
Non-Listed Aquatic Vascular plant Duckweed (COC =1100 µg a.i./L)[8]	72	7

[1] 2 Million Gallons per Day
[2] 9.0 kg Polixetonium chloride/site/day. Calculated in Table 19
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on freshwater diatom (*Navicula pelliculosa*) with an EC_{50}=83 µg a.i./L. MRID 42013303
[8]Based on Duckweed study EC_{50}=1100 µg a.i./L. MRID 49327001.

Table 21 presents the screening level estimates of number of days of exceedance of COCs for freshwater organisms downstream of once-through cooling system with dose of 12 ppm polixetonium chloride. Risks are of concern for all taxa for both high-end and average scenarios when polixetonium chloride is used in once-through cooling towers with exceedances of COCs 31-360 days per year. The exceedances were higher for the high-end scenario.

Table 21. Number of Days of Exceedances for Aquatic Risks for Use of Polixetonium Chloride in Once-Through Cooling Systems (12 ppm)

Concentrations of Concern (COC)	2 MGD[1] Once-Through Cooling Systems	
	High-End	Average
Acute Non-Listed Fish (COC=23.5 µg a.i./L)[3]	360	172
Acute Non-Listed Invertebrate (COC= 140 µg a.i./L)[4]	349	82
Chronic Fish (COC= 19 µg a.i./L)[5]	360	184
Chronic Invertebrate (COC=15 µg a.i./L)[6]	360	198
Non-Listed Aquatic Plant Freshwater diatom (COC=83 µg a.i./L)[7]	356	104
Non-Listed Aquatic Vascular plant Duckweed (COC =1100 µg a.i./L)[8]	242	31

[1]Million Gallons per Day
[2] 90.0 kg polixetonium chloride/site/day. Calculated in Table 19
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.

[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on freshwater diatom (*Navicula pelliculosa*) with an EC_{50}=83 µg a.i./L. MRID 42013303
[8]Based on Duckweed study EC_{50}=1100 µg a.i./L. MRID 49327001.

4.4.4 Ecological Risk Estimation

There are exceedances for all aquatic taxa modeled for the pulp and paper mill use except for non-listed aquatic vascular plants for the lower application rate modeled (30 ppm) in both high-end and average scenarios, and non-listed invertebrate with average scenario using the screening level E-FAST model. For the highest label rate (180 ppm) using the high-end case exposure scenario, the COCs are exceeded for 286, 81, 137, and 2 days for non-listed fish, non-listed freshwater invertebrates, non-listed aquatic plants, and non-listed aquatic vascular plants, respectively. Using the average case scenario with the same application rate (180 ppm) the COCs are exceeded for all aquatic taxa except aquatic vascular plants and were 56, 10, and 19 respectively. There were exceedances for fish and invertebrate from chronic exposure for both application rates and both scenarios and the COCs ranged from 13 to 320 days.

There were exceedances for all taxa for the use of polixetonium chloride in recirculating cooling towers except for aquatic vascular plants in moderate size cooling towers and the average scenario at the lower application rate (6 ppm). The exceedances for a moderate sized cooling tower (2,000 gallons per minute[7]) ranged from 23 to 295 days for the highest rate (36 ppm) and high-end scenario. There were exceedances for all taxa for use of polixetonium chloride in large sized cooling towers (100,000 gallons per minute[7]). Using the high-end scenario and high use rate (36 ppm), there were exceedances for all taxa and COCs ranged from 268 to 360 days. There were exceedances for the average case scenario for both use rates, but the number of days of exceedances were less.

The screening level evaluation of polixetonium chloride used in once-through cooling systems for a moderate size (2MGD, Table 21), and high use rate (12 ppm) indicated exceedances for all COCs for both the high end and average scenarios and the COCs ranged from 31 to 360 days. There were exceedances for the lower rate (1.2 ppm) for both high-end and average scenarios but generally the number of days of exceedances were lower than the high rate (12 ppm).

Although acute and chronic endpoints for polixetonium chloride are available for organisms that represent estuarine/marine invertebrates, the E-FAST model is appropriate only for estimating magnitude of exposure in streams and cannot be used to estimate potential exposure to aquatic organisms in estuarine/marine environments. However, based on ecotoxicity endpoints, the Agency assumes the magnitude of risk to estuarine/marine organisms is comparable to freshwater organisms if polixetonium chloride is used in cooling towers/paper mills and releasing blowdown and effluent into estuarine/marine environment of similar volume.

[7] Determination of recirculation rates require information on evaporation rate, heat absorption through sensible heat, and temperature difference across cooling tower (https://www.awt.org/pub/019E3A00-DF82-84B1-E8A9-3599FC74D720). Currently the Agency uses recirculation rates based on the standard scenario developed by OPPT CEB (US EPA, 1991).

4.4.5 Ecological Risk Characterization

Risks to terrestrial taxa (including pollinators) are not expected from the currently registered uses of polixetonium chloride due to low exposure potential. There is a potential for aquatic exposures to polixetonium chloride from several use patterns, with the highest exposures expected from the following uses: pulp and paper mill, recirculating cooling towers, and once through cooling systems.

E-FAST is a conservative, screening-level model, and it does not account for several chemical/fate properties of the chemical being modeled. The fate data indicate that polixetonium chloride is miscible in water and is not expected to degrade by biotic and abiotic processes. However, polixetonium chloride does sorb to sediment and will be removed from the water column in a stream or lake. As a result, any polixetonium chloride that enters surface water is not anticipated to be present in water for an extended time period, but the extent of sorption to sludge is unknown at this time. Additionally, because of the lack of data, a 0% percent removal was assumed in the model for recirculating cooling tower use.

E-FAST does consider several scenarios that can reduce its conservativeness by: (1) accounting for both low-flow and average-flow streams, (2) using a range of application rates including the maximum and minimum application rates, (3) evaluating two sizes of cooling towers, (4) evaluating a paper mill that is moderately sized, and (5) assuming polixetonium chloride is used within a part of the wet-end paper making process where it is added with the intent of preserving the paper, and thus 90% is removed during the paper making process.

Taken together, the calculations indicate there are risks to all aquatic taxa except aquatic vascular plants even at a lower use rate (30 ppm), and acute invertebrates with average scenario and lower rate for polixetonium chloride in pulp and paper mills. For both application rates and for high-end and average scenarios the exceedances ranged from 2 to 320 days. Although there is a potential for sorption of the chemical to sediment in a wastewater treatment plant, there is no apparent route of chemical or microbial degradation for this chemical in the environment. Therefore, based on the available data, the use of polixetonium chloride is expected to result in risks to freshwater aquatic taxa (*i.e.*, aquatic plants, fish, and aquatic invertebrates) from the cooling water and paper mill uses.

No risk assessment was performed for estuarine/marine organisms or benthic invertebrates. Polixetonium chloride is expected to partition from water to soil and sediment. However, based on ecotoxicity endpoints, the Agency assumes the magnitude of risk to estuarine/marine organisms is comparable to freshwater organisms if polixetonium chloride is used in cooling tower/paper mills and releasing blowdown and effluent into estuarine/marine environment of similar volume.

Therefore, based on the available data, the use of polixetonium chloride is expected to result in risks to aquatic taxa (*i.e.*, aquatic plants, fish, and aquatic invertebrates) from the cooling water and paper mill uses. Risks to terrestrial taxa (including pollinators) are not expected due to the limited exposure potential to terrestrial habitats from the current uses of polixetonium chloride.

5 REFERENCES

Cinalli, 1992. A Laboratory Method to Determine the Retention of Liquids on the Surface of Hands, EPA 747-R-92-003.

Itoh, 2018. Measurements of body surface area and volume in laboratory rabbits (New Zealand White rabbits) using a computed tomography scanner. Itoh, T., Kawabe, M., Nagase,T., Koike, T., Miyoshi, M., and Miyahara, K., Exp Anin. 67 (4) pp 527-534, 2018.

Kline, 2017. Specialty Biocides 2016: United States Market Analysis, Kline & Company, Inc., February 16, 2017

McAneny, 1995. Volatilization of Mineral Oil Mist Collected on Sampling Filters, McAneny, J., Leith, D. and Boundy, M., Applied Occupational and Environmental Hygiene, Volume 10, Issue 9, September,1995

MRID 00151205. McCarroll, N. (1985). *Polixetonium chloride- Drosophila* Sex-Linked Recessive Lethal Assay: Laboratory ID: 197-183. Prepared by Hazleton Biotechnologies Corporation. 7 p.

MRID 00159307 Beaver, J.B. 1985. Polixetonium chloride - A Dietary LC50 Study with the Bobwhite. Project No. 210-104. Study performed by Wildlife International, Ltd. for Buckman Laboratories, Inc., Memphis, TN.

MRID 00157906. Cargile, N. (1986) Soil Column Leaching of [Carbon-14]- WSCP: Final Report: Project No. 84E-303L. Unpublished study prepared by Biospherics Inc. 13 p.

MRID 00157907. Cargile, N. (1986) Leaching Characteristics of Aged [Carbon-14]-WSCP: Final Report: Project No. 84E-303AL. Unpublished study prepared by Biospherics Inc. 9 p.

MRID 40025001. Tisdel, M. (1986) Polixetonium chloride--Thirteen-week Subchronic Toxicity Study in Rats: Project ID: Study No. 6176-106. Unpublished study prepared by Hazleton Laboratories of America, Inc. 285 p.

MRID 40139201. Bosch, A. (1987) Dermal Absorption of [Carbon 14]-Polixetonium chloride (WSCP) in Male Rats: HLA Study No. 6176-117: Final Report. Unpublished study prepared by Hazleton Laboratories America, Inc. 52 p.

MRID 40139202 Surprenant, D.C. 1987a. Acute Toxicity of Polixetonium chloride to Sheepshead Minnow (Cyprinodon variegates). Report No. BW-87-2-2294. Study performed by Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 40139203 Surprenant, D.C. 1987b. Acute Toxicity of Polixetonium chloride to Mysid Shrimp (Mysidopsis bahia). Report No. BW-87-3-2346. Study performed by Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 40165201. Obrist, J. (1987) Anaerobic Aquatic Metabolism of Polixetonium chloride: Final Report: Laboratory Project Identification: HLA 6015-250. Unpublished study prepared by Hazleton Laboratories America, Inc. 50 p.

MRID 40165202. Das, Y. (1987) Aerobic Soil Metabolism of WSCP: Biospheric No. 84E-301A. Unpublished study prepared by Biospheric Inc. 50 p.

MRID 40170601. Spindler, M. (1987) 13-Week Dermal Toxicity Study with Polixetonium chloride in Rabbits: Laboratory Project ID: HLA 6176-118. Unpublished study prepared by Hazleton Laboratories America, Inc. 290 p.

MRID 40334101. Obrist, J. (1987) Aerobic Aquatic Metabolism of Polixetonium chloride: Laboratory Project ID: HLA 6015-251: Final Report. Unpublished study prepared by Hazleton Laboratories America, Inc. 69 p.

MRID 40334201. Surprenant, D.C. 1987c. Acute Toxicity of Polixetonium chloride to Embryos-Larvae of the Quahog Clam (Mercenaria mercenaria). Report No. BW-87-8-2459. Study performed by
Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 40578201. MacKenzie, K. (1988) Two-Generation Reproduction Study with Polixetonium chloride in
Rats (One Litter per Generation): Project ID: HLA 6176-104. Unpublished study prepared by Hazleton Laboratories America, Inc. 952 p.

MRID 40978701. Cifone, M. (1989) Mutagenicity Test on Polixetonium chloride in the in vivo/in vitro Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay: Project ID: HLA Study No. 10280-0-494. Unpublished study pre- pared by Hazleton Laboratories America, Inc. 26 p.

MRID 41234501. Kehoe, D. (1989) One-Year Chronic Toxicity Study with Polixetonium chloride in Dogs: Laboratory Project ID HLA 6176-111. Unpublished study prepared by Hazleton Laboratories America, Inc. 301 p.

MRID 41248001. Rodwell, D. (1989) Teratology Study in rabbits with Busan 77: SLS Study No. 3138.29. Unpublished study prepared by Springborn Life Sciences, Inc. 229 p.

MRID 41561409. Lee, K. (1989) R-25788--Hydrolysis Study at 25 Degrees Centigrade: Lab Project Number: WRC 89-03. Unpublished study prepared by ICI Americas Inc., Western Research Ctr. 15 p.

MRID 41352001 LeLievre, M.K. et al. 1990c. (Polixetonium chloride) - Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Static Conditions. Report No. 89-12-3182. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41352003 LeLievre, M.K. et al. 1990b. (Polixetonium chloride) - Acute Toxicity to Daphnids (Daphnia magna) Under Static Conditions. Report No. 89-11-3181. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41407401. Smith, A. (1990) Determination of Aqueous Hydrolysis Rate Constant and Half-life of Polixetonium chloride: Final Report: Lab Project Number: 995-1089-6116-715: Lab Report Number 90-2-3216. Unpublished study prepared by Springborn Laboratories, Inc. 32 p.

MRID 41420901. Smith, A. (1990) Determination of Aqueous Photolysis Rate Constant and Half-life of Polixetonium chloride: Lab Project Number: 995-1089-6117-720; 90-3-3251. Unpublished study prepared by Springborn Laboratories, Inc. 37p.

MRID 41561301. Kehoe, D. (1990) Combined Chronic Toxicity and Carcinogenicity Study with Polixetonium chloride in Rats: Draft Report: Lab Project Number: HLA 6176-107. Unpublished study prepared by Hazleton Laboratories America, Inc. 1511 p.

MRID 41561409. Lee, K. (1989) R-25788--Hydrolysis Study at 25 Degrees Centigrade: Lab Project Number: WRC 89-03. Unpublished study prepared by ICI Americas Inc., Western Research Ctr. 15 p.

MRID 41561411. Ericson,J. (1989) R-25788--Photolysis on a Soil Surface: Lab Project

Number: ENV-014: RR 89-009B. Unpublished study prepared Americas Inc., Western Research Ctr. 36 p.

MRID 41561412. Dohn, D. (1990) Aerobic Soil Metabolism of R-25788: Lab Project m Number: PMS 293: RR 90-014B. Unpublished study prepared by ICI Americas Inc., Western Research Ctr. 78 p.

MRID 41573701. Lawler, T.L. and DaCosta, K. (1990). Mutagenicity Test on Polixetonium chloride in the *Salmonella* Mammalian—Microsome Reverse Mutation Assay with Confirmatory Assay. Buckman Laboratories, Inc. Study #: 12144-0-401R.

MRID 41654801 Campbell, S. et al. 1990. Polixetonium chloride: An Acute Oral Toxicity Study with the Mallard. Project No. 210-114A. Study performed by Wildlife International, Ltd. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41809101. Kehoe, D. (1991) Combined Chronic Toxicity and Carcinogenicity Study with Polixetonium chloride in Rats: Final Report (Supplement to MRID 41561301): Lab Project Number 6176-107. Unpublished study pre- pared by Hazleton Labs America, Inc. 1511 p.

MRID 42038101 Hoberg, J.R. 1991a. Polixetonium chloride - Determination of Effects on Seed Germination, Seedling Emergence, and Vegetative Vigor of Ten Plant Species. Report No. 91-3-3695. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN

MRID 42372401. Bowles, D. (1991) Product Chemistry for WSCP: Lab Project Number: NA 909218/1. Unpublished study prepared by Twin City Testing Corp. and NATEC Institut fur Naturwissenschaftlich-technische Dienste GmbH. 88 p.

MRID 46276202. Watson, C.; Eickhoff, J. (2004) Bubond 60 Tolerance Exemption. Petition: Data Evaluation Records (DERs) for Ecotoxicology, Environmental Fate and Plant Protection Studies Submitted in Support of Polixetonium chloride and WSCP. Project Number: BUBOND/2004/3. Unpublished study prepared by Toxcel LLC. 253 p.

MRID 47120304. Tillman, A. (2007) Waiver Request for Certain Data Requirements for WSCP MUP. Project Number: KT/200704. Unpublished study prepared by Kerley Trading, Inc. 7 p.

MRID 49300901 Picard, C.R. (2014). 10-day toxicity test exposing estuarine amphipods (*Leptocheirus plumulosus*) to WSCP applied to sediment under static conditions following OCSPP draft guideline 850.1740. Smithers Viscient, Wareham, Massachusetts. Project ID No.: 995.6191. Submitted by Buckman laboratories, Inc., Memphis, TN.

MRID 49327001 Softcheck, K.A. (2014). [^{14}C] WSCP – 7 day toxicity test with duckweed (*Lemna gibba*) following OCSPP guideline 850.4400. Smithers Viscient. Study No. 995.6189. Submitted by Buckman Laboratories, Inc., Memphis, TN.

MRID 49362401 Schwader, A.L. 2014. WSCP; Early life-stage toxicity test with fathead minnow (Pimephales promelas), following OECD guideline #210 and OSCPP guideline 850.1400. Smithers Viscient, Wareham, MA. Study No. 995.6187. Submitted by Buckman Laboratories, Inc., Memphis, TN.

MRID 49453501 Softcheck, K.A. 2014. [14C]WSCP – 96-hour toxicity test with the freshwater green algae, Pseudokirchneriella subcapitata, following OCSPP guideline 850.4500. Smithers Viscient, Study No. 995.6190. Sponsored by Buckman Laboratories, Inc., Memphis, TN.

MRID 49606601 Fournier, A.E. 2014. Full Life-Cycle Toxicity Test with Water Flea, Daphnia magna, under static renewal conditions, following OSCPP draft guidelines 850.1300. Performed by Smithers Viscient, Wareham, MA, Submitted by Buckman USA, Memphis, TN, USA.

MRID 50510601. Boeri, R.L and T.J. Ward. July 14, 1998. Activated Sludge Respiration Inhibition Test with WSCP. T.R. Wilbury Study Number 1591-BU Unpublished study conducted by T.R. Wilbury Laboratories, and Submitted by Buckman Laboratories.

MRID 50510602. Boeri, R.L and T.J. Ward. October 16, 2002. WSCP: Determination of the Ready Biodegradability (Biotic Degradation) Using the CO_2 Evolution Test (Modified Sturm). T.R. Wilbury Study Number 2333-BU. Unpublished study conducted by T.R. Wilbury Laboratories, and Submitted by Buckman Laboratories.

OECD, 2009, (Organisation for Economic Co-operation and Development). OECD Series on Emission Scenario Documents Number 23: Emission Scenario Document on Pulp, paper, and Board Industry. ENV/JM/MOMO (2009)25, Dated July 2009

Park, 2003. Loss of Straight Metalworking Fluid Samples from Evaporation during Sampling and Desiccation. Park, D., Kim, S., Yoon, C., American Industrial Hygiene Association Journal, Volume 64, November/December 2003, pp 837-841.

US EPA, 1988. Superfund Exposure Assessment Manual, EPA/540/1-881001, U.S. Environmental Protection Agency, Office of Remedial Response, April 1988.

US EPA, 1991.Chemical Engineering Branch Manual for the preparation of Engineering Assessments. February 28, 1991. https://nepis.epa.gov/Exe/ZyPDF.cgi/P10000VS, PDF/Docky=P10000.PDF

US EPA, 1996. Occupational and Residential Exposure Test Guidelines OPPTS 875.1200 Dermal Exposure – Indoor, US EPA Office of Prevention, Pesticides, and Toxic Substances (OPPTS), February 1996. (Available in Regulations.Gov in Docket # EPA-HQ-OPPT-2009-0157)

US EPA, 1996a. US EPA, Office of Research and Development, Descriptive Statistics Tables from a Detailed Analysis of the National Human Activity Pattern (NHAPS) Data; EPA/600/R-96/148, July 1996. Data Collection Period October 1992 - September 1994.

US EPA, 2003. User's Manual - Swimmer Exposure Assessment Model (SWIMODEL) Version 3.0, U.S. EPA/OPP/AD November 2003.

US EPA, 2011. Exposure factors handbook: 2011 edition. National Center for Environmental Assessment, Washington, DC; EPA/600/R-09/052F

US EPA, 2012. Standard Operating Procedure for Residential Pesticide Exposure Assessment. Health Effects Division, Office of Pesticide Programs, October 2012.

U. S. EPA Office of Prevention, Pesticides and Toxic Substances. 1994. RfD/Peer Review Report of Polixetonium chloride [Poly (oxyethylene(dimethyliminio) ethylene (dimethyliminio) ethylene dichloride]. Memorandum from George Z. Ghali to Ruth Douglas. TXR #0055528.

U. S. EPA Office of Chemical Safety and Pollution Prevention. 2018. Polixetonium chloride (Poly (oxy-1,2-ethanediyl(dimethyliminio)-1,2-ethandiyl (dimethyliminio-1,2-ethanediyl dichloride)): Summary of Hazard and Science Policy Council (HASPOC) Meeting on April 19, 2018: Recommendations on the need for 90-day inhalation toxicity, neurotoxicity, *in vitro* mammalian cell gene mutation, *in vitro* mammalian chromosome aberration, and immunotoxicity studies. Memorandum from Melinda Wilson to Jorge G. Muñiz Ortiz. TXR #0057760.

U.S. EPA. February 24, 2020. 50510601_50510602_D444814_D444820_D445546_D445547_D455158_DER waiver request for Polixetonium chloride final for signout (MP).

Wright, 2006. Development of Factors for Estimating Swimmers' Exposures to Chemicals in Swimming Pools, Richard Reiss, Gerald P. Schoenig & Gary A. Wright, Human and Ecological Risk Assessment, 12:1, 139-156.

6 APPENDIX A: Toxicology Profile

Table A1 below summarizes the acute toxicity profile for polixetonium chloride.

Table A1. Acute Toxicity Profile for polixetonium chloride

Guideline No./Study Type	MRID No.	Results	Toxicity Category
870.1100/Acute oral toxicity Rat 61.6%	41373401	LD_{50} = 1951 (1727-2203) mg/kg (M); LD_{50} = 2587 (2059-3250) mg/kg (F)	III
870.1200/Acute dermal Rabbit 61.6%	41327101	LD_{50} > 2000 mg/kg	III
870.1300/Acute inhalation Rabbit 60%	41877501	LC_{50} = 4.0 (2.3-7.1) mg/L (M) LC_{50} = 2.4 (1.7-3.3) mg/L (F) LC_{50} = 2.9 (2.3-3.7) mg/L (combined)	III
870.2400/Primary eye irritation Rabbit 61.6%	41361701	Redness cleared on day 3	III
870.2500/Primary dermal irritation Rabbit 61.6%	41298601	Slight irritant	IV
870.2600/Dermal sensitization Guinea pig 60.1%	40750301	Not a sensitizer	N/A

Table A2 below summarizes the subchronic, chronic, developmental and mutagenic toxicity and metabolism and dermal penetration profile of polixetonium chloride. All doses have been adjusted to account for 60% a.i.

Table A2. Subchronic and Chronic Toxicity Values for polixetonium chloride

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
870.3100 90-day oral Rat Purity: 60% a.i.	MRID 40025001 Tisdel, Merrill (1986). Thirteen Week Subchronic Toxicity Study with Polixetonium chloride in Rats. Buckman Labs, Inc. Memphis, TN. Study #: 6176-106.	NOAEL = 3000 ppm (79.2 mg/kg/day) LOAEL = 10,000 ppm (270 mg/kg/day) based on mineralization of renal tubules.

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	0, 3000, 10,000, 30,000, 40,000 ppm (0, 79.2, 270, 811, 1326 mg/kg/day) Core-Minimum Acceptable	
870.3250 90-day dermal Rabbit 60% a.i.	MRID 40170601 Spindler, M. (1987). 13-week dermal toxicity study with Polixetonium chloride in Rabbits. Buckman Laboratories, Inc. Memphis, TN. Study #6176-118 Core Acceptable 0, 6, 60, 600 mg/kg	Systemic Toxicity NOAEL > 600 mg/kg/day LOAEL: Not Established Dermal Toxicity NOAEL = 6 mg/kg/day LOAEL = 60 mg/kg/day based on treatment related dermatological changes consistent with chronic irritation/inflammation. The skin lesions consisted of one or more combinations of ulceration of the epidermis, chronic inflammation of the dermis, acanthosis, hyperkeratosis, parakeratosis, folliculitis, and epidermititis.
Chronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
870.4100 Chronic oral toxicity Dog 60% a.i.	MRID 41234501 Kehoe, Daniel F. (1989). One-Year Chronic Toxicity Study with Polixetonium chloride in Dogs. Buckman Laboratories, Inc. Memphis, TN. Study #: HLA 6176-111. 0, 10,000, 20,000, 40,000 ppm (0, 150, 300, 600 mg/kg/day) Supplementary Acceptable	NOAEL = 150 mg/kg/day (M) 300 mg/kg/day (F) LOAEL = 300 mg/kg/day (M), based on testicular hypoplasia, atrophy/degeneration, aspermia, dysplasia and cellular debris of testicular origin in epididymis. LOAEL = 600 mg/kg/day (F), based on G-I disturbances, weight loss and nervous symptoms (bloody stools, emaciation and ataxia, respectively).
870.4200 Carcinogenicity Mouse 60.8% a.i.	MRID 41494301 Kehoe, Daniel F. (1989). One-Year Chronic Toxicity Study with Polixetonium chloride in Dogs.	NOAEL= not established LOAEL < 364 mg/kg/day, based on enlarged kidney pelvis, diffuse rough kidney in females; dose-

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	Buckman Laboratories, Inc. Memphis, TN. Study #: HLA 6176-111 0, 4000, 8000, 16,000 ppm (0, 364, 720, 1459 mg/kg/day) Core-Minimum Acceptable/Guideline	related increase in proteinaceous casts in males and females, and pelvic and tubular dilation in males.
870.4300 Combined chronic toxicity/carcinogenicity Rat 60% a.i.	MRID 41809101 Kehoe, Daniel F. (1991). Combined Chronic Toxicity Study and Carcinogenicity Study with Polixetonium chloride. Buckman Laboratories, Inc. Memphis, TN. Study #: HLA 6176-107. 0, 2000, 6000, 18,000 ppm (0, 60, 180, 540 mg/kg/day) Core-Minimum Acceptable	Chronic: NOAEL = 60 mg/kg/day LOAEL = 180 mg/kg/day, based on reduced body weight (M), body weight gain (M), and a dose related increase in blood crusts in males. Carcinogenicity: In females, possible increased incidence of thyroid C-cell adenoma at 180 and 540 mg/kg/day, and positive trend for this tumor in both sexes.
Developmental Toxicity and Reproduction		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
870.3700 Prenatal developmental Rat Gavage 61.21% a.i.	MRID 41423001 Nemac, Marc D. (1987). A Teratology Study in Rats with Polixetonium chloride. Buckman Laboratories, Inc. Study #: WIL-94020. Control I study: 0, 42, 214, 428 mg/kg/day Control II study: 0, 306 mg/kg/day Core-Minimum Acceptable/Guideline	Maternal Toxicity NOAEL = 214 mg/kg/day LOAEL = 306 mg/kg/day based on increase in early resorptions and increase in post implantation loss. Developmental Toxicity NOAEL = 306 mg/kg/day LOAEL: Not established
870.3700 Prenatal developmental Rabbit Gavage 60.8% a.i.	MRID 41248001 Rodwell, Dean E. (1989). Teratology Study in Rabbits with Polixetonium chloride. Buckman Laboratories, Inc. Study #: 3138.29	Maternal Toxicity NOAEL = 27 mg/kg/day LOAEL = 75 mg/kg/day, based on increased incidence of abortions, clinical signs including

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	0, 9, 27, 76 mg/kg/day Core-Guideline Acceptable/Guideline	reduced defecation and emaciation. Developmental Toxicity NOAEL = 75 mg/kg/day LOAEL: Not established
870.3800 Reproductive effects toxicity study Rat Dietary 60% a.i.	MRID 40578201 MacKenizie, K.M., 1988. Two-generation reproduction study with Polixetonium chloride in rats (one litter per generation). Hazleton Laboratories America, Inc. HLA 6176-104. 0, 6000, 12,000, 18,000 ppm (0, 180, 360, 540 mg/kg/day) Core-Minimum Acceptable/Guideline	Parental NOAEL = 180 mg/kg/day LOAEL = 360 mg/kg/day based on significantly decreased body weights in F1 males and females, and in F1 generation females during gestation, absolute and relative liver and kidney weight of male and female rats of both generations as well as increased incidence of mineralization of the kidneys. Reproductive NOAEL = 540 mg/kg/day LOAEL: Not established
Mutagenicity		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
870.5100 Reverse mutation assay – *Salmonella typhimurium* 60% a.i.	MRID 41573701 Lawler, T.L. and DaCosta, K. (1990). Mutagenicity Test on Polixetonium chloride in the *Salmonella* Mammalian—Microsome Reverse Mutation Assay with Confirmatory Assay. Buckman Laboratories, Inc. Study #: 12144-0-401R. Polixetonium chloride doses of 66.7, 100, 333, 667, 1000 and 3330 µg/plate Strains: salmonella (TA1535, TA1537, TA1538, TA98 and TA100) Acceptable/Guideline	Negative In the initial mutagenic assay, using strains TA1535, TA1537, TA1538, TA100 and TA98 in the presence and absence of S9 activating system, at doses of 66.7, 100, 333, 667, 1,000 and 3,330 mg/plate, did not increase the number of histidine revertants. The experiment was repeated, and all data were acceptable except for strain TA98 for which the means were outside the acceptable range both in the presence and absence of S9. The TA98 strain was retested both in the presence/absence of activation system and the results

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
		were acceptable. Revertant frequencies for all doses of Polixetonium chloride in all strains approximated or were less than those observed in the concurrent negative controls. All positive controls produced positive responses expected of the chemicals. Based on the results of the *Salmonella* Reverse Mutation Assay the test article Polixetonium chloride did not cause a positive increase in the number of histidine revertants per plate.
870.5275 Sex-linked recessive lethal test 100% a.i.	MRID 00151205 McCarroll, N. (1985). *Drosophila* Sex-linked Recessive Lethal Assay [with WSCP (Polixetonium chloride)]: Hazelton Laboratories, Inc. Project #: 197-183. Unpublished Polixetonium chloride administered at 0.08, 0.3 and 0.8 mg/ml Test strain: Flies Acceptable	Negative A dose-related increase in sterility was observed in the mated P1 males to increasing concentration of the test material when compared to the solvent control.
870.5550 Unscheduled DNA synthesis in mammalian cells in culture Rat 60% a.i.	MRID 40978701 Cifone, M. (1989) Mutagenicity Test on Polixetonium chloride in the in vivo/in vitro Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay: Project ID: HLA Study No. 10280-0-494. Unpublished study pre- pared by Hazleton Laboratories America, Inc. 26 p. Polixetonium chloride administered at 188, 375, 750 and 1500 mg/kg 3 rats/group	Negative Hepatocyte viability/attachment efficiency ranged from 85.4 to 95.2%/66.2 to 81.5%. Polixetonium chloride at a concentration of 188, 375, 750 and 1500 mg/kg resulted in hepatocyte viability (attached cells) of 93.9, 93.2, 94.9 and 93.3%, respectively; *i.e.*., no toxicity. None of the treatments with Busan resulted in a significant increase in nuclear labeling, when compared to the

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	Acceptable/Guideline	controls and did not meet the minimum criteria for UDS assay for mean net nuclear grain count exceeding 6, or at least 10% of the nuclei containing 6 or more grains, or at least 2% of the nuclei containing 20 or more grains, to conclude a positive response. Furthermore, there was no dose-related trend observed. Positive control treated cultures exceeded all three criteria used to indicate UDS.
Special		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
870.7485 Metabolism and pharmacokinetics Rat 60% a.i.	MRID 40268601 Puhl, R. (1987) Metabolism Study with Polixetonium chloride (WSCP) in Rats: Final Report: Laboratory Project ID: HLA 6176-115. Unpublished study prepared by Hazleton Laboratories America, Inc. 98 p. Acceptable	Intravenous excretion at 10 mg/kg; urine, 38-44% feces, 11-14%. Tissue contained 43-55% of the dose. Single and repeated oral dose excretion: urine, 3% of dose, feces 85-105% of dose. Tissue levels low in these groups (0.14% highest levels in any tissue) Oral 1000 mg/kg dose: urine, 14-17%; feces 68-71% of dose. Expired CO2 was not detected. In the intravenous dose group, the major routes of excretion of radioactivity were via urine and feces. Over a 7-day period, approximately 52-55% of the test material administered was excreted in the urine (38—44%) and feces (11—14%); 43—55% was, found in the tissues. In a single repeated oral dosed groups 88-106% of the test compound administered was excreted in the urine (3%) and feces (85—105%); kidneys, liver, and spleen

Toxicity Profile for polixetonium chloride		
Subchronic		
Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
		had a highest residue level. In these groups, tissue residue levels were low in all tissues, except kidneys. Not more than 0.14% of the administered dose was recovered in tissues. Potential for bioaccumulation at the single, or repeated oral is minimal. At the highest oral dose, 85% of the administered dose was recovered in urine (14—17%) and feces (68—71%). The information provided by the sponsor explains that almost all of the administered dose was excreted in the feces unchanged and remaining 40% of the composition of the technical or radiolabeled material was water.
870.7600 Dermal penetration Rat 60% a.i.	MRID 40139201 Bosch, A. (1987) Dermal Absorption of [Carbon 14]-Polixetonium chloride (WSCP) in Male Rats: HLA Study No. 6176-117: Final Report. Unpublished study prepared by Hazleton Laboratories America, Inc. 52 p. 1.2, 12, 120 mg/rat (0.09, 0.97, 9.73) mg/cm^2) Acceptable/Guideline	The total amount of Polixetonium chloride absorbed (expressed as percent of '4C-dose) from rats at various times following dermal administration of '4C-Polixetonium chloride at 2, 20 or 200 mg/animal is negligible (less than 0.2% of the dose). Also, no radioactivity was found in carcass and blood of all treated animals indicating no dermal absorption of Polixetonium chloride. Only less than 0.2% of the Polixetonium chloride was absorbed. Mean % recovery of radioactive dose ranged from 74.5 - 92.7%. Majority of the dose was recovered in the skin rinse (65.5% - 88.6%) and at the skin site (0.4% — 13.7%).

MRID Study Citation

40750301 Glaza, S. (1987) Dermal Sensitization Study in Guinea Pigs with WSCP: Proj. ID 70303995. Unpublished study prepared by Hazleton Laboratories America, Inc. 30 p.

41298601 Rush, R. (1989) Primary Skin Irritation Study in Rabbits with Polixetonium chloride: SLS Study No. 3138.49. Unpublished study prepared by Springborn Laboratories, Inc. 19 p.

41327101 Rush, R. (1989) Acute Dermal Toxicity Study in Rabbits with Polixetonium chloride: Lab Project Number: 3138.50. Unpublished study prepared by Springborn Laboratories, Inc. 26 p.

41361701 Rush, R. (1989) Primary Eye Irritation Study in Rabbits with Polixetonium chloride (EPA-FIFRA): Lab Project Number: 3138/52. Unpublished study prepared by Springborn Laboratories, Inc. 25 p.

41373401 Rush, R. (1990) Acute Oral Toxicity Study in Rats with Polixetonium chloride: SLS Study No. 3138.51. Unpublished study prepared by Springborn Laboratories, Inc. 65 p.

41877501 Hoffman, G. (1991) An Acute Inhalation Toxicity Study of Polixetonium chloride in the Rat: Lab Project Number: 90-8305. Unpublished study prepared by Bio/dynamics, Inc. 105 p.

7 APPENDIX B: Ecotoxicity Profile

Toxicity to Terrestrial Receptors

Birds, Acute:

In order to establish the toxicity of polixetonium chloride to avian species, the Agency requires an acute oral toxicity study using the technical grade active ingredient (TGAI). The preferred test species is either mallard duck (a waterfowl) or bobwhite quail (an upland game bird). The results of two acute oral toxicity studies, submitted for polixetonium chloride are provided in the following table (Table B1).

Table B1. Acute Oral Toxicity of Polixetonium chloride to Birds

Species	Chemical, % Active Ingredient Tested	Endpoint (mg/kg a.i.)	Toxicity Category	Satisfies Guidelines (850.2100)/ Comments	Reference (MRID No. unless specified)
Mallard duck (*Anas platyrhynchos*)	Polixetonium chloride 61.7%	LD_{50} = 497 NOAEL = 51	Slightly toxic	Yes (acceptable) - 14-day test duration - 36 weeks of age	41654801
Bobwhite quail (*Colinus virginianus*)	Polixetonium chloride % purity unknown	LD_{50} = 690 NOAEL = <172 (Based on the assumption of 60% a.i.)	Slightly toxic	No (supplemental) - cannot be used in a qualitative assessment based on unknown test concentration - 21-day test duration - young adult - study conducted before adoption of GLP principles	ID 0522-010-20

There is one acceptable acute oral toxicity studies that indicates that polixetonium chloride is slightly toxic to slightly toxic to birds on an acute oral basis. A second study was supplemental but could not be used in a risk assessment based on an unknown test concentration.

Birds, Subacute:

A subacute dietary study using the TGAI may be required on a case-by-case basis depending on the results of lower-tier ecological studies and pertinent environmental fate characteristics in order to establish the toxicity of a chemical to avian species. This testing was required for polixetonium chloride. The preferred-test species is either the mallard duck or bobwhite quail. The results of two subacute dietary toxicity studies, submitted for polixetonium chloride, are provided in the following table (Table B2).

Table B2. Subacute Oral Toxicity of Polixetonium chloride to Birds

Species	Chemical, % Active Ingredient Tested	Endpoint (ppm a.i.)	Toxicity Category	Satisfies Guidelines (850.2200)/ Comments	Reference (MRID No.)
Mallard duck (*Anas platyrhynchos*)	Polixetonium chloride 60.3%	LC_{50} (diet) = >12,000 NOAEC = 3,000	Relatively nontoxic	No (supplemental) - but can use in a qualitative assessment - 8-day test duration - 10 days of age - study conducted before adoption of GLP principles	41411501
Bobwhite quail (*Colinus virginianus)*	Polixetonium chloride 61.6%	LC_{50} (diet) = >3,462 NOAEC = 3,462	Slightly toxic	Yes (acceptable) - 8-day test duration - 11 days of age	00159307

There is one acceptable study that indicates that polixetonium chloride is slightly toxic to avian species through subacute dietary exposure. A second supplemental study indicated that polixetonium chloride is relatively nontoxic to avian species through subacute dietary exposure.

Terrestrial Plants

One study that evaluates the toxicity of polixetonium chloride to several species of terrestrial plants (seedling emergence-tier I and vegetative vigor-tier I and tier II) has been submitted to the Agency. Results of the terrestrial plant study are presented in Tables B3-B5.

Table B3. Seedling Emergence (Tier I) Toxicity of Polixetonium chloride to Terrestrial Plants

Species	Chemical, % Active Ingredient Tested	Endpoint (ppm a.i.)*	Satisfies Guidelines (850.4100)/ Comments	Reference (MRID No.)
Monocot Oat (*Avena sativa*)	Polixetonium chloride 60.3%	$EC_{25} \geq 73$ NOAEC = 73	Yes (acceptable) - 14-day test duration - most sensitive parameter: shoot length (14% reduction)	42038101
Dicot Lettuce (*Lactuca sativa*)	Polixetonium chloride 60.3%	$EC_{25} \geq 73$ NOAEC = 73	Yes (acceptable) - 14-day test duration - most sensitive parameter: shoot length (17% reduction)	42038101

Table B4. Vegetative Vigor (Tier I) Toxicity of Polixetonium chloride to Terrestrial Plants

Species	Chemical, % Active Ingredient Tested	Endpoint** (ppm a.i.)	Satisfies Guidelines (850.4150)/ Comments	Reference (MRID No.)
Monocot Corn (*Zea mays*)	Polixetonium chloride 60.3%	EC_{25} = >74 NOAEC = 74	Yes (acceptable) -14-day test duration -most sensitive parameter: shoot weight (39% reduction)	42038101
Dicot Cucumber (*Cucumis sativus*)	Polixetonium chloride 60.3%	EC_{25} = >74 NOAEC = 74	Yes (acceptable) - 14-day test duration - most sensitive parameter: root weight (31% reduction)	42038101

Table B5. Vegetative Vigor (Tier II) To Toxicity of Polixetonium chloride to Terrestrial Plants

Species	Chemical, % Active Ingredient Tested	Endpoint* (ppm a.i.)	Satisfies Guidelines (850.4150)/ Comments	Reference (MRID No.)
Monocot Ryegrass (*Lolium perenne*)	Polixetonium chloride 60.3%	EC_{25} = >74 NOAEC = 74	No (supplemental) - but can use in a qualitative assessment - 14-day test duration - most sensitive parameter: root weight (0% reduction)	42038101
Dicot Tomato (*Lycopersicon esculentum*)	Polixetonium chloride 60.3%	EC_{25} = >74 NOAEC = 74	No (supplemental) - but can use in a qualitative assessment - 14-day test duration - most sensitive parameter: shoot weight (15% reduction)	42038101

Toxicity to Aquatic Receptors

Freshwater Fish:

In order to establish the acute toxicity of polixetonium chloride to freshwater fish, the Agency requires freshwater fish toxicity studies using the TGAI. The preferred test species are rainbow trout (a coldwater fish) and bluegill sunfish (a warm water fish). Chronic toxicity testing (fish early life stage and aquatic invertebrate life cycle) is required for pesticides when certain conditions of use and environmental fate apply. The preferred freshwater fish test species is the fathead minnow. The results of 3 freshwater fish acute studies and one chronic study submitted for polixetomium chloride are presented in Table B6.

B6. Toxicity of Polixetonium chloride to Freshwater Fish

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Acute (850.1075)					
Rainbow Trout (*Oncorhynchus mykiss)*	Polixetonium chloride 61.9%	LC_{50} = 0.047 NOAEC = 0.037	Very highly toxic	Yes (acceptable) - 96-hr test duration - static test system	41352001
Bluegill sunfish (*Lepomis macrochirus)*	Polixetonium chloride 61.9%	LC50 = 0.21 NOAEC = 0.13	Highly toxic	Yes (acceptable) - 96-hr test duration - static test system	41352002
Rainbow Trout (*Oncorhynchus mykiss)*	Polixetonium chloride 60%	LC_{50} = 0.26 NOAEC = 0.11	Highly toxic	No (supplemental) - but can use in a qualitative assessment - 96-hr test duration - static test system - study lacks important information - study conducted before adoption of GLP principles	00107207
Chronic (850.1400)					
Fathead minnow (*Pimephales promelas*)	Polixetonium chloride (59.8% ai)	NOAEC = 0.019 LOAEC = 0.033	N/A	Yes (Acceptable) -flow-through	49362401

Freshwater acute toxicity tests indicate that Polixetonium chloride is very highly toxic to highly toxic to fish on an acute basis. A chronic toxicity test indicated that Polixetonium chloride is very highly toxic to the fathead minnow.

Freshwater Invertebrates:

The Agency requires a freshwater aquatic invertebrate study using the TGAI to establish the acute toxicity to freshwater invertebrates. The preferred test species is *Daphnia magna*. Chronic invertebrate testing is required for the polixetonium chloride because of its once-through cooling water uses. The preferred freshwater invertebrate is *Daphnia magna*. The results of an acute toxicity study, two chronic studies and a whole sediment study submitted for polixetonium chloride are provided in the following table (Table B7).

Table B7. Toxicity of Polixetonium chloride to Freshwater Invertebrates

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Acute (850.1010)					
Waterflea (*Daphnia magna)*	Polixetonium chloride 61.9%	EC_{50} = 0.280 NOAEC = 0.130	Highly toxic	Yes (acceptable) - 48-hr test duration - static test system	41352003
Chronic (850.1300)					
Water flea (*Daphnia magna*)	Polixetonium chloride 60.3%	LOAEC = 0.020 NOAEC = 0.012	N/A	No (supplemental) - but can use in a qualitative assessment - 21-day test duration - static renewal test system - organisms not distributed or fed properly - excess mortality	42479601
Water flea (*Daphnia magna*)	Polixetonium chloride >98%	NOAEC = 0.015 LOAEC = 0.025	N/A	Yes (acceptable) -21-day duration Semi-static test system	49606601
Whole Sediment Toxicity Study (850.1735)					

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Chironomus riparius	Polixetonium chloride 99.8%	LC_{50} = 3.56 in overlying water LC_{50} = >966 in sediment	Moderately toxic in water Practically nontoxic in sediment	Yes (supplemental) -28-day test duration -insufficient number of replications	48715801

The results of the aquatic invertebrate study indicate that polixetonium chloride is highly toxic to freshwater invertebrates on an acute basis. The acceptable chronic study indicates that polixetonium chloride is very highly toxic to daphnids. The sediment study indicated that polixetonium chloride is moderately toxic to freshwater invertebrates in the overlying water and practically nontoxic in the sediment.

Estuarine/Marine Fish and Invertebrates:

Acute toxicity testing with estuarine and marine organisms using the TGAI is required when the end-use product is intended for direct application to the marine/estuarine environment or effluent containing the active ingredient is expected to reach this environment. The preferred fish test species is the sheepshead minnow. The preferred invertebrate test species are mysid shrimp and eastern oysters. This testing is required for polixetonium chloride based on the chemical's potential to reach estuarine and marine environments. The results of four toxicity studies submitted for polixetonium chloride are presented in Table B8.

Table B8. Acute Toxicity of Polixetonium chloride to Estuarine and Marine Organisms

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Sheepshead minnow (*Cyprinodon variegates*) (850.1075)	Polixetonium chloride 60.0%	LC_{50} > 360 NOAEC = 360	Practically nontoxic	Yes (acceptable) - 96-hr test duration - static test system	40139202
Mysid shrimp (*Mysidopsis bahia*) (850.1035)	Polixetonium chloride 60.0%	LC_{50} = 7.8 NOAEC <7.8	Moderately toxic	Yes (acceptable) - 96-hr test duration - static test system	40139203
Quahog clam (*Mercenaria mercenaria*) (850.1025)	Polixetonium chloride 60.0%	EC_{50} = 0.21 NOAEC = 0.14	Highly toxic	Yes (acceptable) - 48-hr test duration - static test system - embryo/larval stage	40334201

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Whole Sediment Toxicity Testing (850.1740)					
Whole sediment acute/ marine invertebrate (*Leptocheirus plumulosus*)	Polixetonium chloride >98%	LC_{50} = >1000 NOAEC = >1000 LOAEC = >1000 (survival)	Practically nontoxic	Yes (acceptable) -10-day test duration -static test system	49300901

The results of these four acceptable studies indicate that polixetonium chloride is highly toxic to moderately toxic to estuarine/marine invertebrates on an acute basis and practically nontoxic to estuarine/marine fish on an acute basis.

Aquatic Plants:

Non-target plant phytotoxicity testing is required for pesticides when certain conditions of use and environmental fate apply. This testing is required for the once-through cooling water uses of polixetonium chloride. Testing has been conducted with polixetonium chloride on several aquatic plant species. Testing is normally conducted with one species of aquatic vascular plant (*Lemna gibba*) and four species of algae: (1) freshwater green alga, *Selenastrum capricornutum,* (2) marine diatom, *Skeletonema costatum,* (3) freshwater diatom, *Navicula pelliculosa,* and (4) bluegreen cyanobacteria, *Anabaena flos-aquae.*

Table B9. Toxicity of Polixetonium chloride to Aquatic Plants

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
Nonvascular				
Marine diatom (*Skeletonema costatum*) (850.4500)	Polixetonium chloride 60.3%	EC_{50} = 0.090 NOEC < 0.024	No (supplemental) - but can use in a qualitative assessment - 120-hour test duration - static test system	42013302
Freshwater diatom (*Navicula pelliculosa*) (850.4500)	Polixetonium chloride 60.3%	EC_{50} = 0.083 NOEC = 0.044	Yes (acceptable) - 96-hour test duration - static test system	42013303
Bluegreen cyanobacteria	Polixetonium chloride 60.3%	EC_{50} = 0.11 NOEC = 0.05	Yes (acceptable) - 120-hour test duration - static test system	42013304

Species	Chemical, % Active Ingredient Tested	Endpoint (mg a.i./L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
(*Anabaena flos-aquae*) (850.4550)				
Green algae (*Selenastrum capricornutum*) (850.4500)	Polixetonium chloride 60.3%	EC_{50} = 0.0088 NOEC < 0.001	No (supplemental) - but can use in a qualitative assessment - 120-hour test duration - static test system	42013305
Green alga (*Pseudokirchneriella subcapitata*) (850.4500)	Polixetonium chloride 59.8%	EC_{50} = 0.003 NOAEC = 0.0012	No (supplemental) -96-hour test duration -test material sorbing to test vessel glass	49453501
Vascular (850.4400)				
Duckweed (*Lemna gibba)*	Polixetonium chloride >98%	EC_{50} = 1.1 NOAEC = 0.33 LOAEC = 1.1 (biomass)	Yes (Acceptable) -7-day test duration	49327001
Duckweed (*Lemna gibba*)	Polixetonium chloride 60.3%	EC_{50} > 0.65 NOEC = 0.043	No (supplemental) - but can use in a qualitative assessment -14-day test duration -static renewal test system - maximum concentration tested produced only 30% growth inhibition	42013301

Ecotoxicity References

MRID 00107207 Knott, W.B. 1970. Polixetonium chloride (WSCP) - Evaluation of Acute LC50 for Rainbow Trout. Study performed by Woodward Research Corporation for Buckman Laboratories, Inc., Memphis, TN.

MRID 00159307 Beaver, J.B. 1985. Polixetonium chloride - A Dietary LC50 Study with the Bobwhite. Project No. 210-104. Study performed by Wildlife International, Ltd. for Buckman Laboratories, Inc., Memphis, TN.

MRID 052201020 WARF Institute, Inc. 1971. Report on Acute Oral LD50 in Bobwhite Quail. Prepared for Buckman Laboratories, Inc., Memphis, TN.

MRID 40139202 Surprenant, D.C. 1987a. Acute Toxicity of Polixetonium chloride to Sheepshead Minnow (Cyprinodon variegates). Report No. BW-87-2-2294. Study performed by Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 40139203 Surprenant, D.C. 1987b. Acute Toxicity of Polixetonium chloride to Mysid Shrimp (Mysidopsis bahia). Report No. BW-87-3-2346. Study performed by Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 40334201 Surprenant, D.C. 1987c. Acute Toxicity of Polixetonium chloride to Embryos-Larvae of the Quahog Clam (Mercenaria mercenaria). Report No. BW-87-8-2459. Study performed by Springborn Bionomics, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41352001 LeLievre, M.K. et al. 1990c. (Polixetonium chloride) - Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Static Conditions. Report No. 89-12-3182. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41352002 LeLievre, M.K. et al. 1990a. "(Polixetonium chloride) - Acute Toxicity to Bluegill (Lepomis macrochirus) Under Static Conditions. Report No. 89-12-3176. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41352003 LeLievre, M.K. et al. 1990b. (Polixetonium chloride) - Acute Toxicity to Daphnids (Daphnia magna) Under Static Conditions. Report No. 89-11-3181. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41411501 Bodden, R.M. 1974. Polixetonium chloride - Acute Avian Dietary Toxicity Study in Mallard Ducks. Report No. 4043621. Study performed by the WARF Institute, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 41654801 Campbell, S. et al. 1990. Polixetonium chloride: An Acute Oral Toxicity Study with the Mallard. Project No. 210-114A. Study performed by Wildlife International, Ltd. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42013301 Hoberg, J.R. 1991b. Polixetonium chloride - Toxicity to the Duckweed Lemna gibba G3. Report No. 91-5-3749. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42013302 Hoberg, J.R. 1991c. Polixetonium chloride - Toxicity to the Marine Diatom Skeletonema costatum. Report No. 91-9-3864. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42013303 Hoberg, J.R. 1991d. Polixetonium chloride - Toxicity to the Freshwater Diatom Navicula pelliculosa. Report No. 91-4-3728. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42013304 Hoberg, J.R. et al. 1991e. Polixetonium chloride - Toxicity to the Freshwater Bluegreen Algae Anabaena flos-aquae. Report No. 91-4-3726. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42013305 Hoberg, J.R. 1991f. Polixetonium chloride - Toxicity to the Freshwater Green Algae Selenastrum capricornutum. Report No. 91-4-3732. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42038101 Hoberg, J.R. 1991a. Polixetonium chloride - Determination of Effects on Seed Germination, Seedling Emergence, and Vegetative Vigor of Ten Plant Species. Report No. 91-3-3695. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 42479601 Putt, A.E. et al. 1992. Polixetonium chloride – Chronic Toxicity to Daphnids (Daphnia magna) Under Static Renewal Conditions. Report No. 92-7-4343. Study performed by Springborn Laboratories, Inc. for Buckman Laboratories, Inc., Memphis, TN.

MRID 48715801 Kranzfelder, J.A., L. Stuerman, and D. Malorin. 1998. Sediment bioassay procedure for determining the toxicity of WSCP to Chironomus sp. Report No. 44908. Study performed by ABC Laboratories for Buckman Laboratories International, Memphis, TN.

MRID 49300901 Picard, C.R. (2014). 10-day toxicity test exposing estuarine amphipods (*Leptocheirus plumulosus*) to WSCP applied to sediment under static conditions following OCSPP draft guideline 850.1740. Smithers Viscient, Wareham, Massachusetts. Project ID No.: 995.6191. Submitted by Buckman laboratories, Inc., Memphis, TN.

MRID 49327001 Softcheck, K.A. (2014). [^{14}C] WSCP – 7 day toxicity test with duckweed (*Lemna gibba*) following OCSPP guideline 850.4400. Smithers Viscient. Study No. 995.6189. Submitted by Buckman Laboratories, Inc., Memphis, TN.

MRID 49362401 Schwader, A.L. 2014. WSCP; Early life-stage toxicity test with fathead minnow (Pimephales promelas), following OECD guideline #210 and OSCPP guideline 850.1400. Smithers Viscient, Wareham, MA. Study No. 995.6187. Submitted by Buckman Laboratories, Inc., Memphis, TN.

MRID 49453501 Softcheck, K.A. 2014. [14C]WSCP – 96-hour toxicity test with the freshwater green algae, Pseudokirchneriella subcapitata, following OCSPP guideline 850.4500. Smithers Viscient, Study No. 995.6190. Sponsored by Buckman Laboratories, Inc., Memphis, TN.

MRID 49606601 Fournier, A.E. 2014. Full Life-Cycle Toxicity Test with Water Flea, Daphnia magna, under static renewal conditions, following OSCPP draft guidelines 850.1300. Performed by Smithers Viscient, Wareham, MA, Submitted by Buckman USA, Memphis, TN, USA.

8 APPENDIX C: Risk Estimation Methods

Risk estimation integrates the results of the exposure and ecotoxicity data to evaluate the potential for the active ingredient and its transformation products to cause adverse effects to nontarget organisms. Depending on the uses being assessed, risk estimates are determined from calculations of acute and chronic risk quotients (RQs) or, for down-the-drain (DtD) assessments, from concentrations of concern (COCs).

Risk Quotient Methodology

The RQ method used by OPP compares the estimates of acute and chronic exposure (EECs) to the acute and chronic ecotoxicity endpoint values for each receptor group being assessed. EECs are developed through the use of various exposure models for the uses being assessed (e.g., antifoulant paint, pressure-treated wood). If available, relevant aquatic monitoring concentrations may be used as well. The acute and chronic ecotoxicity endpoints are obtained mainly from guideline ecotoxicity studies (850 harmonized series) submitted to support registration or, in some cases, from the open literature.
For animals (fish[8], aquatic invertebrates, birds[9], mammals), acute and chronic RQs are calculated as follows:

Acute RQ = acute EEC/LC50 (or EC50 or LD50)
Chronic RQ = chronic EEC/NOAEC

For aquatic or semi-aquatic plants, because of the short life cycles, there is no distinction between acute and chronic exposure. The RQs for plants are determined as follows:

RQ for non-listed species = EEC/EC50
RQ for listed species = EEC/NOAEC (or EC05 if NOAEC not available)

The RQs are compared to OPP's levels of concern (LOCs) to identify potential acute and chronic risks to each receptor group. Exceedance of an LOC indicates a need to consider regulatory action to reduce these potential risks. The development of the LOCs are discussed in detail in the Agency's Overview Document[10]. OPP's LOCs are tabulated below for listed and non-listed species. A listed species is a species that has been designated as endangered or threatened by the U.S. Fish and Wildlife Service or the U.S. National Marine Fisheries Service.

Table C1. Risk Presumptions and LOCs

Aquatic and Terrestrial Animals	LOC
Acute presumption of risk to listed aquatic species	RQ $\geq$ 0.05

[8] Freshwater fish also may be used as a surrogate for aquatic-phase amphibians
[9] Birds also may be used as surrogate for terrestrial-phase amphibians and reptiles
[10] http://www.epa.gov/espp/consultation/ecorisk-overview.pdf

Aquatic and Terrestrial Animals	LOC
Acute presumption of risk to listed terrestrial species	RQ ≥ 0.1
Acute presumption of risk to non-listed aquatic and terrestrial species	RQ ≥ 0.5
Chronic presumption of risk to listed and non-listed aquatic and terrestrial species	RQ ≥ 1.0
Risk Presumption for Aquatic/Semi-aquatic Plants	**LOC**
Presumption of risk to listed species	RQ ≥1
Presumption of risk to non-listed species	RQ ≥1

Down-the-Drain Methodology

The DtD module of E-FAST[11] (Exposure and Fate Assessment Screening Tool) is used when discharge into the aquatic environment is from municipal (*i.e.*, domestic) wastewater treatment plants (WWTPs) or from industrial sources of discharge (*e.g.*, cooling towers). The ecotoxicity data used in the model are the same as those used for RQ calculations. The levels of concern for listed and non-listed aquatic organisms also are factored into the calculations for estimating the COCs.

For antimicrobials disposed to municipal WWTPs, the DtD module is used with the Probabilistic Dilution Model (PDM) option (SIC code: steam electric power plants). This option estimates the number of days per year that the COC is exceeded for listed and non-listed freshwater fish, freshwater invertebrates, and aquatic plants. Key input data include: (1) percent removal of active ingredient during wastewater treatment; (2) acute and chronic ecotoxicity endpoints for each receptor group; and (3) WWTP influent volume derived from such sources as production volume data, marketing data, and/or data on fraction of antimicrobial leached/removed from an end-use product.

For antimicrobials disposed to industrial WWTPs, the General Population and Ecological Exposure from Industrial Releases Module of E-FAST is used. This option estimates the number of days per year COCs are exceeded for listed and non-listed fish, aquatic invertebrates, and aquatic plants. In addition to the input data required to run the DtD module, the Industrial Release module also requires an estimate of environmental release to surface water in kilograms per site per day, the number of release sites, and the number of days of release to surface water.

I. Estimating Environmental Releases to Surface Water from Recirculating Cooling Towers Blowdown Water (B) in kilograms per site per day

A generic scenario developed by OPPT/CEB (Office of Pollution Prevention and Toxics/Chemical Engineering Branch) for recirculating cooling towers (USEPA, 1991) was used

[11] Additional information on E-FAST is available on the EPA website http://www.epa.gov/oppt/exposure/pubs/efast.htm

to estimate daily releases to surface water of polixetonium chloride in blowdown water in kilograms per site per day.

The following equation is used to estimate releases of antimicrobial pesticide to surface water from blowdown:

$$B = (0.6\%)\ (X_R)\ (R)\ (5{,}760 \times 10^{-6}\ \text{min-kg/day-gal})$$

where:

B = release of antimicrobial pesticide via blowdown water to surface water (kg/site/day);
X_R = concentration of antimicrobial pesticide in recirculating water (ppm); and
R = recirculation rate of cooling water (gallons per minute).

The conversion factor, 5760 x 10^{-6} min-kg/day-gal is derived from :

(1,440 min/day) (4 kg/gal) (10^{-6} ppm) in which the blowdown water is assumed to have a specific gravity of 1.0; thus, 1 liter weighs 1 kilogram, and the conversion of 3.78 liters per gallon is expressed in kilograms per gallon and rounded up to the nearest significant figure. The value 0.6% is the percentage of cooling tower water that is assumed to be released to surface water via blowdown.

Recirculating Tower Exposure Results

The results of the recirculating tower exposure modeling are shown in Tables C2, and C3. For all taxa and both use rates, concentrations of concerns were exceeded for some to all of the year.

Table C2.-Number of days of exceedances for 6.0 ppm Use Rate of Polixetonium Chloride in Recirculating Cooling Towers

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Acute				
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[3]	118	12	354	95
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[4]	30	3	288	42
Chronic				
Chronic Fish (COC = 19 µg a.i./L)[5]	133	14	356	104
Chronic Invertebrate (COC = 15 µg a.i./L)[6]	151	16	357	116
Aquatic Plants				

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Non-Listed Aquatic Plant Green Algae (COC = 83 µg a.i./L)[7]	48	5	319	53
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[8]	4	0	123	13
Listed Species				
Acute Listed Fish (COC = 2.35 µg a.i./L)[3]	298	45	360	218
Acute Listed Invertebrate (COC = 14 µg a.i./L)[4]	157	17	358	119
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)[8]	13	1	220	27

[1]0.41 kg Polixetonium chloride/site/day. Calculated in Table 15
[2] 20.74 kg Polixetonium chloride/site/day. Calculated in Table 15
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on freshwater diatom study an EC_{50}=83 µg a.i./L. MRID 42013303.
[8]Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L. MRID 49327001.

Table C3. Number of Days of Exceedances for 36.0 ppm Use Rate of Polixetonium Chloride in Recirculating Cooling Towers- Aquatic Risks for Recirculating Cooling Towers

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Freshwater Fish and Invertebrates				
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[3]	263	35	360	191
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[4]	119	12	354	95
Chronic				
Chronic Fish (COC = 19 µg a.i./L)[5]	279	39	360	202
Chronic Invertebrate (COC=15 µg a.i./L)[6]	295	44	360	215
Aquatic Plants				
Non-Listed Aquatic Plant Green Algae (COC = 83 µg a.i./L)[7]	158	17	358	120
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[8]	23	2	268	36
Listed Species				
Acute Listed Fish (COC= 2.35 µg a.i./L)[3]	355	103	360	295

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]		Large Sized Cooling Tower (100,000 gal/min)[2]	
	High-End	Average	High-End	Average
Acute Listed Invertebrate (COC = 14 µg a.i./L)[4]	300	45	360	218
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)[8]	68	7	335	64

[1]2.49 kg Polixetonium chloride/site/day. Calculated in Table 15
[2] 124.42 kg Polixetonium chloride/site/day. Calculated in Table 15
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 33 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7] Based on green algae study with an EC_{50}=83 µg a.i./L. MRID 50981803.
[8]Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L . MRID 49327001.

Estimating Exposure to Aquatic Organisms from Release of Polixetonium chloride from once-through cooling Systems (Sic Code: Steam electric power plant)

I. Convert once-through cooling tower throughput in million gallons per day (MGD) to liters per day

II. Convert maintenance concentration of a.i. in ppm to µg/L

III. Use throughput in liters per day and concentration of a.i. in ug/L to derive kilograms of ai per site per day

For example, to convert 2 MGD of throughput with 2.0 ppm of product at 60% active ingredient to kilograms per site per day of active ingredient released to surface water:

Convert 2 MGD to liters per day:

2,000,000 gal/day x 3.785 L/gallon = 7,570,000 L/day

Calculate ppm a.i.:

2.0 ppm product x 60% a.i. = 1.2 ppm ai

Use liters of throughput per day and concentration of a.i. in µg/L to determine kg/site/day

1.2 mg/L x 7,570,000 L/day x (1 kg/10^6 mg) = 9.084 kg/site/day

Once-Through Cooling Systems

The results of the once through cooling systems are outlined in Tables C4 and C5. For all taxa and both listed and non-listed, concentrations of concerns were exceeded for some to all of the year.

Table C4. Number of Days of Exceedances for Aquatic Risks for Use of Polixetonium Chloride in Once-Through Cooling Systems (1.2 ppm)

Concentrations of Concern (COC)	2 MGD[1] Once-Through Cooling Systems	
	High-End	Average
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[3]	336	65
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[4]	223	27
Chronic Fish (COC= 19 µg a.i./L)[5]	342	72
Chronic Invertebrate (COC = 15 µg a.i./L)[6]	348	80
Non-Listed Aquatic Plant Freshwater diatom (COC = 83 µg a.i./L)[7]	266	36
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[7]	72	7
Listed Species		
Acute Listed Fish (COC = 2.35 µg a.i./L)[3]	360	173
Acute Listed Invertebrate (COC = 14 µg a.i./L)[4]	349	83
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)[7]	152	16

[1] Million Gallons per Day
[2] 9.0 kg Polixetonium chloride/site/day. Calculated in Table 18
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC=19 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7]Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L . MRID 49327001.

Table C5. Number of Days of Exceedances for Aquatic Risks for Use of Polixetonium Chloride in Once-Through Cooling Systems (12 ppm)

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]	
	High-End	Average
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[3]	360	172
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[4]	349	82
Chronic Fish (COC = 19 µg a.i./L)[5]	360	184

Concentrations of Concern (COC)	Moderate Sized Cooling Tower (2,000 gal/min)[1]	
	High-End	Average
Chronic Invertebrate (COC = 15 µg a.i./L)[6]	360	198
Non-Listed Aquatic Plant Freshwater diatom (COC =83 µg a.i./L)[7]	356	104
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a,i./L)[7]	242	31
Listed Species		
Acute Listed Fish (COC = 2.35 µg a.i./L)[3]	360	283
Acute Listed Invertebrate (COC = 14 µg a.i./L)[4]	360	201
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)[7]	323	56

[1]Million Gallon Per Day
[2] 90.0 kg polixetonium chloride/site/day. Calculated in Table 18
[3] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[4]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[5] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 33 µg a.i./L. MRID 49362401.
[6] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[7]Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L. MRID 49327001.

II. Assessment for Pulp and Paper Mill Use Site:

Estimated Environmental Releases Calculations:

In order to determine the amount of AI released from the paper mill, the amount of AI used per day needed to be calculated. The calculation includes the assumptions that polixetonium chloride is being used in a moderately sized paper mill, and therefore, 500 US tons of paper is produced per site per day.

Total AI used at the maximum labeled rate per site per day (180 ppm):

$$\frac{3\ lbs\ product}{1\ US\ ton\ paper} x \frac{0.12\ lbs\ a.i.}{1\ lbs\ product} x \frac{500\ US\ tons\ paper}{site/day} x \frac{1\ kg\ a.i.}{2.204\ lbs\ a.i.}$$

= 81.6 kg a.i./site/day

In order to estimate the total environmental release to surface water after use within the mill and wastewater treatment plants (WWTPs), the amount of a.i. I retained within/on the paper and the amount of a.i. removed during WWT must be taken into account. The following calculation includes two base assumptions: (1) polixetonium chloride is applied during wet-end operations

and its retention rate in paper is 90% (10% of polixetonium chloride applied ends up in the effluent water) (OECD, 2009) and (2) no degradation or removal occurs within the WWTP.

AI Released to Surface Water:

$$Total\ a.i.\ Used\ x\ (1 - X\%\ retention\ in\ paper)\ x\ (1 - X\%\ removed\ in\ WWT)$$

For the maximum labeled rate (180 ppm):

a.i. Released to Surface Water = 81.6 kg/site/day x (1-0.90) x (1 - 0.00) = 8.16 kg a.i./site/day

Release Sites Information:

In order to run EFAST, various inputs about the release sites must be determined and are as follows:

- Days per year of release; the default assumption is 360 days[12].
- Standard Industrial Classification (SIC) code analysis or facility analysis; the SIC code "Paper and Paperboard Mills" was chosen because no specific facility was being analyzed.
- The number of use sites. The Agency estimated the exposure downstream from one site, as no data were available to determine how many use sites may be using polixetonium chloride.

III. Pulp and Paper Mill Exposure Results

The results of the pulp and paper exposure modeling are outlined in table C6.

Table C6. Aquatic Risks for Pulp and Paper Mill Use of Polixetonium Chloride (30 ppm)

Concentrations of Concern (COC)	High-End Case Estimate of Number of Days per Year of Exceedance of COC	Average Case Estimate of Number of Days per Year of Exceedance of COC
Freshwater Fish and Invertebrates		
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[2]	80	10
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[3]	4	0
Chronic		
Chronic Fish (COC = 19 µg a.i./L)[4]	101	13
Chronic Invertebrate (COC = 15 µg a.i./L)[5]	128	17
Aquatic Plants		

[12] Based on CEB Manual for preparation of Engineering Assessments. https://nepis.epa.gov/Exe/ZyPDF.cgi/P10000VS.PDF?Dockey=P10000VS.PDF

Concentrations of Concern (COC)	High-End Case Estimate of Number of Days per Year of Exceedance of COC	Average Case Estimate of Number of Days per Year of Exceedance of COC
Non-Listed Aquatic Plant freshwater diatom (COC = 83 µg a.i./L)[6]	12	1
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[7]	0	0
Listed Species		
Acute Listed Fish (COC = 2.35 µg a.i./L)[2]	323	77
Acute Listed Invertebrate (COC = 14 µg a.i./L)[3]	136	19
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)6	1	0

[1]1.36 kg Busan/site/day, Table 13
[2] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[3]-Based on Daphnia magna study with 48 hr EC_{50}= 280µg a.i./L. MRID 41352003.
[4] Based on Fathead minnow fish (*pimephales promelas*) study with a 30-day NOAEC= 19 µg a.i.. MRID 49362401.
[5] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[6]Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L . MRID 49327001.

Table C7. Aquatic Risks for Pulp and Paper Mill Use of Polixetonium Chloride (180 ppm)

Concentrations of Concern (COC)	High-End Case Estimate of Number of Days per Year of Exceedance of COC	Average Case Estimate of Number of Days per Year of Exceedance of COC
Freshwater Fish and Invertebrates		
Acute Non-Listed Fish (COC = 23.5 µg a.i./L)[2]	286	56
Acute Non-Listed Invertebrate (COC = 140 µg a.i./L)[3]	81	10
Chronic		
Chronic Fish (COC = 19 µg a.i./L)[4]	303	65
Chronic Invertebrate (COC = 15 µg a.i./L)[5]	320	75
Aquatic Plants		
Non-Listed Aquatic Plant Freshwater diatom (COC = 83 µg a.i./L)[6]	137	19
Non-Listed Aquatic Vascular plant Duckweed (COC = 1100 µg a.i./L)[7]	2	0
Listed Species		
Acute Listed Fish (COC = 2.35 µg a.i./L)[2]	359	174
Acute Listed Invertebrate (COC = 14 µg a.i./L)[3]	324	78

Concentrations of Concern (COC)	High-End Case Estimate of Number of Days per Year of Exceedance of COC	Average Case Estimate of Number of Days per Year of Exceedance of COC
Listed Aquatic Vascular Plants Duckweed (COC = 330 µg a.i./L)[6]	25	3

[1] 8.6 kg Busan/site/day. Table 13
[2] Based on rainbow trout study with a 96 hr LC_{50}= 47 µg a.i./L. MRID 41352001.
[3]-Based on Daphnia magna study with 48 hr EC_{50}= 280 µg a.i./L. MRID 41352003.
[4] Based on Fathead minnow fish (*pimephales promelas*) study NOAEC= 19 µg a.i./L. MRID 49362401.
[5] Based on Water Flea (*Daphnia magna*) study NOAEC=15 µg a.i./L. MRID 49606601.
[6] Based on Duckweed study EC_{50}=1100 µg AI/L and NOAEC=330 µg a.i./L . MRID 49327001.