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

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: **March 11, 2020**

SUBJECT: **Registration Review Draft Risk Assessment for the Peroxy Compounds**

PC Code: 000595, 063201, 063604, 063607, 063209, 128860	DP Barcode: 455445, 455446
Decision No: 558073, 558074	Docket No: EPA-HQ-OPP-2009-0546
Regulatory Action: Registration Review	Case No: 6059, 4072, 5081
Risk Assessment Type: DRA	CAS No: 7722-84-1, 79-21-0, 33734-57-5, 15630-89-4, 10058-23-8, 70693-62-8

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This document provides the draft human health and ecological risk assessment conducted in support of the antimicrobial use sites of the following peroxy compounds: hydrogen peroxide, peracetic acid, peroxyoctanoic acid, and sodium percarbonate.

Although the peroxymonosulfate compounds were included in the peroxy compounds Final Work Plan (FWP), they will not be included in this risk assessment. The mode of action for the peroxymonosulfate compounds is to create hypochlorous acid rather than to oxidize microbes or degrade into hydrogen peroxide; thus, it is more appropriate to address them with other pesticides which operate via a hypochlorous acid mode of action. The Agency plans to create a hypochlorous acid case which includes the peroxymonosulfate compounds in late 2020.

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EXECUTIVE SUMMARY

This Draft Risk Assessment (DRA) for the peroxy compounds includes the following active ingredients (AIs): hydrogen peroxide, peracetic acid (also known as peroxyacetic acid, ethaneperoxoic acid, or PAA), peroxyoctanoic acid, and sodium percarbonate. These AIs have peroxides as active moieties, which the Agency believes are appropriate to assess together. They will be referred to collectively in this document as peroxy compounds, except for those instances where specific AIs are discussed.

Peroxy compounds are registered as disinfectants, sanitizers, and sterilants. There are approximately 230 end use product registrations, of which approximately 200 are registered by the Antimicrobials Division (AD) and approximately 29 are registered by the Biopesticide and Pollution Prevention Division (BPPD). This DRA focuses solely on the antimicrobial use sites. Uses registered by BPPD will be discussed in a separate memorandum.

Human Health Risk Summary

The anticipated exposure pathway of concern is inhalation. Although dermal exposures can occur, particularly when using concentrate products, these exposures result in acute effects that are mitigated through labeling. In addition, there are no endpoints selected for oral exposure.

The inhalation exposures were assessed using the No Observed Adverse Effect Concentration (NOAEC) of 10 mg/m^3, which was the highest dose tested in a 90-day rat inhalation toxicity study, as the Point of Departure (POD). This POD is supported by a 28-day inhalation toxicity study in rats where necrosis and inflammation of squamous epithelium and anterior nasal cavity were observed at the Lowest Observed Adverse Effect Concentration (LOAEC) of 14.6 mg/m^3. The NOAEC of 10 mg/m^3 was converted to an 8-hour Human Equivalent Concentration (HEC) of 7.5 mg/m^3 and a 24-hour HEC of 2.5 mg/m^3 based upon the rat exposure time of 6 hours per day and a regional gas deposition ratio (RGDR) of 1.0.

Dietary Risk Summary

Peroxy compounds are microbiocides used as sanitizers and disinfectants in a variety of use sites including those with both direct and indirect food contact. There are no oral toxicological endpoints of concern for peroxy compounds. In addition, since peroxy compounds rapidly break down into component degradates upon use, the Agency anticipates negligible residues of peroxy compounds to be available for transfer to food, and when applied directly to food, negligible residues are present for consumption. Therefore, dietary exposures are expected to be negligible, and risks are not of concern.

Residential Handler Risk Summary

There is the potential for residential handler short- and intermediate-term exposure when using peroxy products to clean and disinfect kitchens, bathrooms, floors and carpet. The exposures can be to aerosols released during spray applications and to vapors that are emitted from the spray droplets and treated surfaces. The Margins of Exposure (MOEs) for aerosols are greater than the short- and intermediate- term target MOE of 30 and are not of concern. The MOEs for vapors are of concern because they are less than the target MOE of 30.

Residential Post-Application Risk Summary

There is the potential for residential post application short- and intermediate-term inhalation exposure when products are applied to residential areas by fogging or vaporization. An MOE of 19 was calculated using a ventilation rate of 0.45 air changes. This MOE is of concern because it is less than the short- and intermediate-term target MOE of 30.

Aggregate Risk Summary

Since there are no end points selected for oral and dermal exposures, no aggregate assessment of oral and dermal exposures is needed. There is an end point selected for inhalation exposures, and there are residential handler and post application inhalation exposures that could be aggregated; however, some of these scenarios have risks of concern on their own and would cause the aggregate risk to be of concern. These risks will need to be refined or mitigated before the exposures can be aggregated.

Occupational Handler Surface Treatment Risk Summary

There is the potential for occupational handler inhalation exposure to aerosols and vapors during the application of peroxy products for surface treatments using sprays, mops, or wipes. These exposures are considered to be long term in duration because they occur in facilities, such as hospitals, where surface treatment are conducted on a daily basis.

Most of the MOEs for aerosol exposure are of concern because they are less than the long-term target MOE of 300. All the MOEs for vapor exposure are of concern because they are less than the long-term target MOE of 300.

Occupational Handler Industrial Process Treatment

There is the potential for occupational handler inhalation exposure during the application of peroxy products for the treatment of industrial processes such as paper mills, cooling water systems and oil production. The products contain up to 50 percent hydrogen peroxide and can be open poured into the system or material being treated. Most, but not all, of the labels require respiratory protection when needed and in most cases the correct respirator is specified. Some,

but not all, of the relevant labels also require closed system loading and delivery for specific uses or the implementation of protective engineering solutions.

The MOEs for occupational handler inhalation aerosol exposure during open pouring applications were assessed by assuming that 20 gallons could be handled in one day. This value is based on the largest amount of material (four five-gallon containers) poured from conventional containers in the Antimicrobial Exposure Assessment Task Force (AEATF) liquid pour study (MRID 48917401). It is assumed that larger amounts would be delivered in bulk containers and applied using meter pump closed loading systems. The MOEs are not of concern because they are greater than the short- and intermediate-term target MOE of 30 and the long-term target MOE of 300. There are no data available to assess the occupational handler exposures to peroxy vapors that would occur during the open pouring of peroxy products; therefore, risks cannot be precluded. It is recommended that these applications be made using closed loading and delivery systems. Open pouring should only be done when the process tanks or vessels have local exhaust ventilation.

Occupational Post-Application Risk Summary

Occupational post-application inhalation exposures can occur after fogging applications. The MOEs are not of concern for these exposures because they are all greater than the target MOE of 30. The hospital fogging scenario is of concern for long term exposures because the MOE of 85 is less than the target MOE of 300 for long term exposure.

Environmental Risk Summary

No ecological risks are expected from the registered antimicrobial uses of peroxy compounds. Based on the environmental fate properties of peroxy compounds, aquatic and environmental exposure are not expected from antimicrobial products. In the presence of water, the AIs readily hydrolyze and rapidly break down to hydrogen peroxide (which rapidly degrades into oxygen and water upon contact with organic matter) and respective associated compounds (e.g., acetic acid, octanoic acid, and sodium carbonate), all of which are not of toxicological concern. This degradation is expected to occur rapidly, within the timeframe of the antimicrobial use pattern and/or wastewater treatment plant processes. Therefore, environmental risk from antimicrobial uses of peroxy compounds are assessed qualitatively. No risk to terrestrial or aquatic non-target organisms (including pollinators) is expected from the antimicrobial uses of peroxy compounds.

1. INTRODUCTION

1.1 Case Overview

This Draft Risk Assessment (DRA) for peroxy compounds is comprised of three cases: 4072, 5081, and 6059. Case 4072 contains four active ingredients (AIs): hydrogen peroxide (PC code 000595), peracetic acid (or peroxyacetic acid/PAA, PC code 063201), potassium peroxymonosulfate (PC code 063604), and potassium peroxymonosulfate sulfate (PC code 063607). Case 5081 contains one AI: peroxyoctanoic acid (PC code 063209). Case 6059 contains one AI: sodium percarbonate (PC code 128860). Except for the peroxymonosulfate compounds, the AIs within all three cases are compounds whose active moieties are peroxides, which the Agency believes are appropriate to assess together. They will be referred to collectively in this document as peroxy compounds, except for those instances where specific AIs are discussed.

The mode of action for the peroxymonosulfate compounds is to create hypochlorous acid rather than oxidizing the microbe or degrading into hydrogen peroxide. Due to this mode of action, the Agency has determined that they should be included in the upcoming hypochlorous acid case.

Peroxy compounds are registered as disinfectants, sanitizers, and sterilants. Peroxy compounds are used in antimicrobial use sites such as agricultural premises, food handling and storage establishments, commercial, industrial, and institutional premises, residential, public, and medical premises. The pesticide categories that some of the products fall under include algaecides, bacteriostats, disinfectants, sanitizers, sterilizers and other categories.

Hydrogen Peroxide

Hydrogen peroxide was first registered as a pesticide in 1977. A Reregistration Eligibility Decision (RED) document was issued for peroxy compounds (EPA, 1993). Because other peroxy compounds either break down into or otherwise use hydrogen peroxide as their mode of action, hydrogen peroxide data are often used in lieu of data from other peroxides. The Registration Review docket for peroxy compounds (Case No. 4072) is available at https://www.regulations.gov/ in docket number EPA-HQ-OPP-2009-0546.

Peracetic Acid

Peracetic acid was first registered in 1985. Because peracetic acid breaks down into hydrogen peroxide and acetic acid, it is almost always co-formulated with large quantities of hydrogen peroxide in order to drive the equilibrium towards maintaining the peracetic acid. The mechanics of this process are detailed further in Appendix B. Due to its chemistry and mode of action, it is included as one of the peroxy compounds in Case No. 4072.

Peroxyoctanoic Acid

The first product containing peroxyoctanoic acid as an active ingredient was registered in the United States in 2005. The Agency did not complete a Reregistration Eligibility Decision (RED) for peroxyoctanoic acid. The docket for peroxyoctanoic acid (Case No. 5081) has been established at https://www.regulations.gov/ in docket number EPA-HQ-OPP-2016-0341.

As noted in the 2016 Preliminary Work Plan (PWP) for peroxyoctanoic acid, during the development of the peroxy compounds registration review human health effects scoping document (US EPA, 2009b), the Agency conducted an in-depth review of the similarities between peroxyoctanoic acid and the other peroxy compounds, including hydrogen peroxide and peracetic acid. Based on the physical and chemical properties, toxicity profile, and exposure scenarios for peroxyoctanoic acid, the Agency believes that risks from chronic and subchronic exposures to this pesticide would be similar to the other peroxy compounds. In the PWP, the Agency determined that the data available to support the registrations of the other peroxy compound active ingredients are also applicable to peroxyoctanoic acid.

Sodium Percarbonate

Sodium percarbonate was first registered in 2002. The Agency did not complete a RED for sodium percarbonate. The docket for sodium percarbonate (Case No. 6059) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2017-0354.

In the 2017 PWP for sodium percarbonate, the Agency anticipated calling in the same data as those requested in the peroxy compound risk assessment, given that hydrogen peroxide is a metabolite of sodium percarbonate. Instead, in the 2018 Final Work Plan (FWP), it was noted that, pursuant to 40 CFR Part 155.42(b)(3), the sodium percarbonate case would be combined with the peroxy compounds case for the Draft Risk Assessment, Proposed Interim Decision, and Interim Decision.

Potassium Peroxymonosulfate and Potassium Peroxymonosulfate Sulfate

Potassium peroxymonosulfate commonly refers to both the potassium salt of peroxymonosulfuric acid (CAS No. 10058-23-8, PC Code 063604, $KHSO_5$), and potassium peroxymonosulfate sulfate, the triple salt in which the first salt is the active component (CAS No. 70693-62-8, PC Code 063607, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$). There are three registered uses of potassium peroxymonosulfate, all of which refer to the triple salt. The triple salt is co-formulated with sodium chloride as an active ingredient.

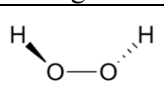
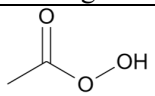
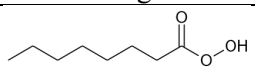
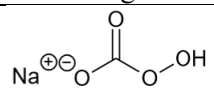
Upon adding the triple salt and sodium chloride to water, the mode of action is for the triple salt and the sodium chloride to dissolve and react together to form molecular chlorine (Cl_2) and potassium bisulfate ($KHSO_4$). The chlorine then rapidly reacts with water to form hypochlorous

acid which acts as an antimicrobial. Because the mode of action for potassium peroxymonosulfate is to create hypochlorous acid rather than oxidizing the microbe or degrading into hydrogen peroxide, the Agency has determined that the chemical will be addressed in the hypochlorous acid case.

1.3 Ingredient Profile

The chemical identity and chemical and physical properties for the peroxy compounds are listed in Table 1.

Table 1: Chemical and Physical Properties of the Peroxy Compounds

Chemical Name	Hydrogen Peroxide	Peracetic Acid	Peroxyoctanoic Acid	Sodium Percarbonate
PC Code	000595	063201	063209	128860
CAS No.	7722-84-1	79-21-0	33734-57-5	15630-89-4
Molecular Formula	H_2O_2	$C_2H_4O_3$	$C_8H_{16}O_3$	$Na_2CO_3 \cdot 1.5H_2O_2$
Smiles Code	OO	CC(=O)OO	CCCCCCCC(=O)OO	[Na+].[O-]C(=O)OO
Molecular Weight	34.01 g/mol	76.05 g/mol	160.11 g/mol	156.98 g/mol
Molecular Structure				
pH at 25°C	0.1-2	0.1 - 2	1.5-2	10.42
Melting point (°C)	-23.5	-0.005	28.5	> 300
Boiling point (°C)	125	108	231.6	N/A, solid at room temperature
Density	1.44	1.226	No Data	900-1,200 g/L
Dissociation constant (pK_a)	11.62	8.20	~8	N/A
Solubility in water (mg/L)	Completely Soluble	13.1	1719	145,000
Octanol/water partition coefficient (log K_{ow})	-1.57	-1.07	1.87	N/A (water soluble)
Vapor pressure (mm Hg)	Varies[1] (~1-5)	14.46	6.34×10^{-3}	2.5×10^{-5}
Henry's law constant (atm-m^3/mol)	7.4×10^{-9}	2.14×10^{-6}	7.59×10^{-6}	N/A

N/A = Not Applicable
1. Value highly dependent on concentration and temperature
References: EPI-Suite (US EPA 2012b); HSDB 2008; CompTox 2020; NIOSH; and PubChem

1.4 Use Pattern

There are approximately 200 antimicrobial end use products that contain some combination of hydrogen peroxide, peracetic acid, peroxyoctanoic acid and sodium percarbonate. There are approximately 195 products that contain hydrogen peroxide, approximately 91 that contain peracetic acid, 5 that contain peroxyoctanoic acid and 5 that contain sodium percarbonate. All

but one of the peracetic acid products also contain hydrogen peroxide and all of the peroxyoctanoic acid products contain some combination of hydrogen peroxide and peracetic acid. The sodium percarbonate products do not contain any other peroxy compound. The active ingredient concentrations in the products range from 0.045-50% for hydrogen peroxide, 0.017-24.5% for peracetic acid, 12-79% for sodium percarbonate, and 0.63-3.1% for peroxyoctanoic acid.

Hydrogen Peroxide and Peracetic acid

The hydrogen peroxide and peracetic acid end-use products are formulated as ready-to-use (RTU) liquids, RTU wipes, and liquid concentrates. A listing of the registered uses of hydrogen peroxide and peracetic acid is included in Table 2.

Table 2: Registered Uses of Hydrogen Peroxide and Peracetic Acid

Use	Application Method	Application Rate[A]	
		Hydrogen Peroxide	Peracetic Acid
Agricultural Premises and Equipment			
Greenhouse premises and equipment	Sponge, Mop, Spray	0.18 to 0.25%	0.041 to 0.060%
Cattle, Swine and Poultry Farms Hatching facilities and incubators	Sponge, Mop, Wipe RTU Spray	0.0855 to 0.5% 6.14%	0.020 to 0.066% 0.6%
Trucks and other vehicles	Fogging	5.5 ppm (in air)	1.0 ppm (in air)
Commercial/Institutional/Industrial (CII) Premises and Equipment			
Laundry Sanitizer and Disinfectant (Commercial, Industrial and Institutional Laundries)	60 gallons Laundry Machine	45 to 396	30 to 292
Nonporous, nonfood contact surfaces	Sponge/Mop/Spray RTU Spray	209 to 2140 ppm 0.5 to 6.14%	44 to 460 ppm 0.6%
Enclosures	Fogging	3,800 to 360,000 ppm (in air)	N/A
Animal Housing Facility	RTU Spray	6.0%	N/A
Post-Harvest Fruit Treatment and Wash			
Post-harvest fruit and vegetable wash	Immersion, Spray	130 to 350 ppm	83 to 84 ppm
Food Handling Premises and Equipment			
Food contact surfaces Bottle Rinse, Final Sanitizing Entryway Sanitization (Boot Wash) Aseptic Food Packaging Non-Food contact surfaces	Spray, Sponge, Mop Immersion, Spray Immersion Closed System Fogging	131 to 2140 ppm 131 to 209 ppm 209 to 1790 ppm 35 to 50% 18 ppm (in air)	38 to 456 ppm 4 ppm 44 to 420 ppm N/A 3 ppm (in air)
Industrial Processes			
Industrial Water Systems (Cooling, paper mill)	Open Pour	13 to 500 ppm	8 to 104 ppm
Oil Drilling Muds, worker over and completion fluids	Open Pour	1,530 ppm	990 ppm
Packaging and Storage Vessel Cleaning	Spray, Wipe, Flood	10%	N/A
Materials Preservative			
Coatings, pigments for paper and paint	Open Pour	111 to 130 ppm	72 to 84 ppm

Use	Application Method	Application Rate[A]	
		Hydrogen Peroxide	Peracetic Acid
Medical Premises and Equipment			
Hard Surface Disinfection	Spray, Wipe	0.5 to 6.1%	0.14 to 0.60%
Hard Surface Disinfection	Fogging	140 to 14,000 ppm (in air)	N/A
Residential and Public Access Premises			
Laundry Sanitizer (EPA Reg No. 3573-73)	Open Pour	1.61%	N/A
Kitchen and bathroom disinfectant cleaner	RTU Spray	0.5 to 6.0%	0.13 to 0.6%
Floors and Carpeting	RTU Spray	0.5%	N/A

A. Except as indicated, the application rates are in percent AI by weight or ppm AI by weight
N/A = Not Applicable

Peroxyoctanoic Acid

The five peroxyoctanoic acid end-use products are formulated as liquid concentrates. All five products contain hydrogen peroxide and one product also contains peracetic acid. A listing of the registered uses for products that contain peroxyoctanoic acid is included in Table 3. This listing also includes the application rates for hydrogen peroxide when it is co-formulated with peroxyoctanoic acid. These co-formulation application rates are lower than the rates for hydrogen peroxide only.

Table 3: Summary of Peroxyoctanoic Acid Registered Uses

Use	Application Method	Application Rate (ppm AI)	
		Peroxyoctanoic acid	Hydrogen peroxide
Agricultural Premises and Equipment			
Animal Housing Facilities	Mop, sponge, spray, foam	73 to 126	588 to 2140
Hard surface cleaning	Mop, sponge, spray	126 to 211	1586
Poultry and swine premises, trucks, coops and crates	Mop, sponge, spray, foam	126	2140
Poultry hatchery disinfection	Mop, sponge, spray, foam	73 to 126	588 to 2140
Poultry premises, trucks, coops and crates	Mop, sponge, spray, foam	73 to 78	588
Commercial/Institutional/Industrial (CII) Premises and Equipment			
Industrial facility Hard surface disinfection	Mop, sponge, spray, foam	73 to 126	588 to 2140
Food Handling Premises and Equipment			
Beverage containers, new or pre-cleaned	Spray, immersion	126	2140
Bottle rinse	Immersion	12	98 to 209
Conveyor Equipment	Spray	12 to 16	98 to 209
Dairy, food and beverage processing plant equipment	Immersion, spray, foam, CIP	12 to 33	98 to 201
Eating, drinking and food prep utensils	Immersion	33	201
Entryway floor treatment, shoe bath treatment	Foam, immersion	12 to 78	209 to 588
Food contact surfaces and gloved hands	Immersion, spray, foam, CIP	12	209
Hard surface disinfection	Mop, sponge, spray	49 to 78	588 to 836
Non-Food contact surfaces and equipment[A]	Spray, foam, immersion	12 to 56	209 to 452
Outside surfaces of airtight sealed packages	Spray, immersion	12 to 16	131 to 209

Use	Application Method	Application Rate (ppm AI)	
		Peroxyoctanoic acid	Hydrogen peroxide
Veterinary Premises and Equipment			
Hard surface disinfection	Mop, sponge, spray, foam	73 to 126	588 to 2140
Residential and Public Access Premises			
Hard surface disinfection	Mop, sponge, spray	126	2140
Shower room floors and bathmats	Mop, sponge, spray	12	209

A. Includes floors, walls, tables, benches, trough and drip pans

Sodium Percarbonate

There are five sodium percarbonate end-use products, and the products are formulated as powders, granules or tablets. In the presence of water, sodium percarbonate dissolves and transforms into hydrogen peroxide and sodium carbonate. Its products are registered as disinfectants and sanitizers for a variety of use sites as listed in Table 4.

Table 4: Summary of Sodium Percarbonate Registered Uses

Use	Application Method	Application Rate (ppm AI)
Agricultural Premises and Equipment		
Animal and Poultry Housing and Equipment	Mop, Sponge, Spray, Soak	2072
Disinfecting Animal Drinking Lines	Circulate in Place	2072
Commercial/Institutional/Industrial (CII) Premises and Equipment		
Laundry Disinfectant (Industrial and Institutional)	Laundry Machine (24 gallon)	40 to 60
Hair and Nail Salon Instruments and Tools	Soak	1,674
Food Handling Premises and Equipment		
Entryway Sanitization Systems (Footbaths)	Soak	498 to 1519
Floor Sanitizer (Powder Application to Wet Floor)	Open Pour Powder	230 to 1843[A]
Sanitizing Non-Food Contact Surfaces	Mop, Sponge, Spray	498 to 1519
Medical and Dental Premises and Equipment		
Dental Unit Water Lines	Circulate in Place	17
Hard Surface Disinfectant (General)	Mop, Wipe, Spray	6655
Hard Surface Disinfectant (PED Virus)	Mop, Wipe, Spray	8448
Hard Surface Disinfectant and Cleaner	Mop, Wipe, Spray	2072
Residential and Public Access Premises		
Whirlpool Bath, Spa and Jacuzzi Surface Disinfection	Circulate in Place	2072 to 6655
NF Surfaces in Offices, schools and homes	Mop, Wipe, Spray	2072

A. These application rates are based on the application of 3.7 to 7.4 ounces by weight of EPA Reg No. 63761-5 per 100 square feet to a wet floor containing 1.3 to 5.1 fluid ounces of water per square foot.

2.0 HUMAN HEALTH RISK ASSESSMENT

2.1 Data Deficiencies

The toxicology database for peroxy compounds is considered adequate for risk assessment.

2.2 Label Recommendations

Some highly concentrated products do not have correct personal protective equipment (PPE) required on the labels. It is recommended that all labels for occupational handler use be checked for appropriate PPE (i.e., protective eyewear (goggles or face shield), rubber gloves, coveralls over long-sleeved shirt, long pants, and chemical resistant footwear including socks) and first aid statements.

2.3 Anticipated Exposure Pathways

The anticipated exposure pathway to be assessed in this DRA for peroxy compounds is inhalation. Although dermal exposures can occur, particularly when using concentrated products, these exposures result in acute effects that are managed through labeling with appropriate PPE.

While dietary exposure may be expected from peroxy compounds, they decompose rapidly to hydrogen peroxide, and (in the case of sodium percarbonate), sodium carbonate, both of which are considered Generally Recognized as Safe (GRAS) for use in food by the Food and Drug Administration (FDA).

Drinking water exposure is not expected from peroxy compounds as they rapidly dissociate on contact with water into hydrogen peroxide which then further decomposes into oxygen and water.

2.4 Hazard Characterization and Dose-Response Assessment

2.4.1 Toxicology Studies Available for Analysis

The peroxy compounds database is considered adequate for hazard characterization and toxicity endpoint selection and contains the following acceptable studies:

- Developmental toxicity study in mice (MRID 46833610)
- Drinking water study on peroxide metabolizing enzymes (MRID 46833618)
- 28-day inhalation toxicity study in rats (CEFIC Peroxygen Sector Group, 2002)
- 90-day inhalation study in rats (MRID 49469301)

The toxicity studies were reviewed for the purposes of establishing points of departure (PODs) and endpoints used to inform the risk from exposures to peroxy compounds.

2.4.2 Summary of Toxicological Effects

The FDA designated hydrogen peroxide as GRAS. Hydrogen peroxide is also found in the human body and naturally breaks down as a result of detoxifying enzymes found in cells (e.g., catalase, glutathione peroxidase). The primary active ingredient for all peroxy compounds is hydrogen peroxide, which rapidly dissociates into oxygen and water, thus mitigating concern for oral exposures. Inhalation exposures are of concern because the dissociation process produces reactive oxygen species (ROS) which are highly reactive and may cause oxidative damage to biological systems (in fact, this is the pesticidal mode of action).

Inhalation is the primary route of exposure. High concentrations of peroxy compounds are corrosive and can be acutely toxic and/or extremely irritating to the lungs and skin. Hydrogen peroxide is volatile, with a vapor pressure of 1-5 mm Hg. The average half-life of hydrogen peroxide in air is about 1 day.

In a non-guideline developmental toxicity study (MRID 46833610), a mixture of 40% peracetic acid, 27% acetic acid, 14% hydrogen peroxide, and stabilizers was administered to presumed pregnant ICR mice via whole-body inhalation exposure at concentrations of 0 (distilled water), 1%, or 5% commercial formulation (equivalent to 0, 20, or 100 mg/m^3 peracetic acid vapor) twice daily for 10 min/day from post-conception until the 19th day of pregnancy. At 100 mg/m^3 peracetic acid, significant ($p<0.10$) decreases in fetal body weight (13-18%) and fetal body length (6-8%) were observed compared to controls. At 20 mg/m^3 peracetic acid, fetal body weights and length were comparable to controls. The developmental LOAEL is 100 mg/m^3 peracetic acid based on decreased fetal body weight and body length. The developmental NOAEL is 20 mg/m^3.

A non-guideline study (MRID 46833618) was performed to establish whether the levels of peroxide metabolizing enzymes in rat tissues were affected by repeated daily oral intake of reagent hydrogen peroxide. One-month old CFY inbred rats were exposed to 0.5% hydrogen peroxide in their drinking water for two months; rats given untreated water served as controls. At three months of age, the rats were killed and tissues and hemolysate were collected. The activities of superoxide dismutase, peroxidase, and catalase were determined in homogenates of the tissues. Young rats exposed to 0.5% aqueous hydrogen peroxide in drinking water for two months displayed increased activity of the peroxide metabolizing enzymes in various tissues.

There are two inhalation studies available: a 28-day rat study and a 90-day rat study.

1. 28-day inhalation toxicity study in rats (CEFIC Peroxygen Sector Group 2002):

In this study cited in the European Union (EU (2003) report, groups of five male and female Alpk:APrSD (Wistar-derived) rats were exposed whole-body for 6 hours per day to 0 (control), 2.9, 14.6, or 33 mg/m^3 hydrogen peroxide vapor for 5 days per week, for a period of 28 days. Clinical signs demonstrated respiratory tract irritation at the exposure levels of 14.6 and 33

mg/m^3, but not at 2.9 mg/m^3. Regarding histopathology (Table 5), necrosis and inflammation of the epithelium in the anterior regions of the nasal cavity were found at the two higher concentration levels. In the larynx, mononuclear cell infiltration was seen in two females at the highest exposure concentration. Moreover, one male rat in each exposure group and two female rats in the high concentration group exhibited perivascular neutrophil infiltration in the lungs, and hemorrhage was found in some animals at the two lower concentration levels.

The Agency does not have access to the complete study report; only a summary of the study cited in the EU risk assessment report for hydrogen peroxide is available for review (see US EPA, 2019). The Agency concluded the effects in the 28-day inhalation study should not be excluded because in the study, in addition to hemorrhage, lung inflammation was noted in at least one animal in each treated group, along with other effects in the nasal cavity and larynx.

Table 5: Microscopic Findings of the Respiratory Tract in the 28-day Rat Inhalation Study

Target organ	0 mg/m^3	2.9 mg/m^3	14.6 mg/m^3	33 mg/m^3
Nasal cavity	No findings	No findings	Necrosis[A] and inflammation (squamous epithelium, anterior regions of the nasal cavity) 3/5 M, 2/5F	Rhinitis 1/5 M Necrosis[A] and inflammation (squamous epithelium, anterior regions of the nasal cavity) 4/5 M, 4/5 F
Larynx	No findings	Inflammation 1/5F		Mononuclear cell infiltration, 2/5F Epithelial erosion, 1/5M
Lung	No findings	↑Perivascular neutrophil infiltration 1/5M Hemorrhage 2/5M, 1/5F	↑ Perivascular neutrophil infiltration 1/5M Hemorrhage 2/5M	↑ Perivascular neutrophil infiltration 1/5M, 2/5F

Source: US EPA, 2019
A. Necrosis in the context of this report refers to the more common type of cell death following external stimuli (cf. apoptosis), manifested by severe cell swelling or rupture, denaturation and coagulation of cytoplasmic proteins, and breakdown of cell organelles.
F - female; M - male

2. 90-day inhalation toxicity study in rats (MRID 49469301):

Hydrogen peroxide was administered by nose only to 10 rats/sex/group at 0, 1.43, 3.49 or 9.95 mg/m^3 six hours per day, five days per week. Rats were sacrificed under pentobarbital anesthesia followed by exsanguination from the abdominal aorta. The NOAEC from the 90-day study is 9.95 mg/m^3 (LOAEC not established in this study). The microscopic observations of lungs are summarized in Table 6.

Table 6: Microscopic Observations of Lungs in the 90-day Inhalation Study

	Male				Female			
Group	**Control**	**Low**	**Mid**	**High**	**Control**	**Low**	**Mid**	**High**
Hydrogen Peroxide (mg/m^3)	0	1.43	3.49	9.95	0	1.43	3.49	9.95
Lung Examined	10	10	10	10	10	10	10	10

	Male				Female			
Group	**Control**	**Low**	**Mid**	**High**	**Control**	**Low**	**Mid**	**High**
Hydrogen Peroxide (mg/m^3)	0	1.43	3.49	9.95	0	1.43	3.49	9.95
Accumulation:								
macrophage, focal	**1**	0	0	**2**	**1**	**1**	**4**	**1**
…. minimal	0	0	0	0	0	0	**4**	**1**
…. mild	**1**	0	0	**2**	**1**	**1**	0	0
Hemorrhage(s): alveolar,								
focal	0	**2**	**3**	0	0	0	0	0
…. minimal	0	**1**	0	0	0	0	0	0
…. mild	0	**1**	**3**	0	0	0	0	0
Infiltration, neutrophil;								
focal	0	**1**	0	0	0	**1**	**1**	0
…. minimal	0	**1**	0	0	0	**1**	**1**	0
Inflammation:								
mixed, focal	0	0	**1**	0	0	0	**1**	0
…. minimal	0	0	**1**	0	0	0	**1**	0
Ossification; focal	0	0	0	0	0	0	0	**1**
…. marked	0	0	0	0	0	0	0	**1**
Accumulation, pigment,								
brown; focal	0	**1**	0	0	0	0	0	0
…. minimal	0	**1**	0	0	0	0	0	0

NB: Ten animals per treatment group.
Data obtained from Table 12; Appendix 10 of the study report (MRID 49469301).

2.4.3 Safety Factor for Infants and Children (FQPA Safety Factor)

The Food Quality Protection Act (FQPA) safety factor does not apply to the peroxy compounds as there are no expected dietary exposures to peroxy compounds. PODs and endpoints were not established for dietary exposures for this chemical.

2.5 Toxicity Endpoint and Point of Departure Selections

PODs and endpoint selection for oral (any duration, dietary or incidental) exposures are not necessarily based on the rapid decomposition of hydrogen peroxide into water and oxygen, adequate worker protection, use of highly diluted end-use products, and the FDA GRAS status of peroxy compounds. This determination applies to hydrogen peroxide, peracetic acid, and peroxyoctanoic acid.

The Agency granted data waivers for subchronic toxicity studies (90-day oral, 90-day dermal) for sodium percarbonate for both antimicrobial and biopesticidal uses. The subchronic studies were waived based on (1) the lack of systemic effect from hydrogen peroxide exposure in 90-day oral studies performed in rats and in sensitive catalase-deficient mice (HERA, 2002); (2) significant or prolonged dermal exposure to hydrogen peroxide from use of sodium percarbonate is not anticipated based on the label use instructions; and (3) the product is a granular formulation that is too large to be inhaled (350-550 μm) (HERA, 2002).

Available acute toxicity information indicates that sodium percarbonate is of low oral and dermal toxicity (Toxicity Category III & IV, respectively, see Appendix Table A3). Sodium percarbonate dermal irritation and skin sensitization studies revealed slight dermal irritation in rabbits (Toxicity Category IV); however, no dermal sensitization was identified in guinea pigs (Toxicity Category IV). Eye irritation studies demonstrated severe irritation to the eyes of rabbits (Toxicity Category I).

Data waivers for the acute and 90-day inhalation studies were originally granted by the Agency on the basis that the sodium percarbonate product was formulated as a non-inhalable granule. Since that time, other product formulations such as powders that are inhalable have been registered. Data waivers are no longer appropriate for the newer inhalable powder product formulations as there is now potential for exposure.

For inhalation risk assessment for all peroxy compounds, the Agency concluded that both the 28-day rat inhalation study (CEFIC Peroxygen Sector Group, 2002) and 90-day rat inhalation study (MRID 49469301) are co-critical studies to use as endpoints and PODs for the inhalation risk assessment. The high dose of 10 mg/m^3 (rounded from 9.95 mg/m^3) from the 90-day rat inhalation study is the NOAEC, and 14.6 mg/m^3 (the mid-dose from the 28-day inhalation study) is the LOAEC based on the necrosis and inflammation of squamous epithelium and anterior of the nasal cavity (3/5 M and 2/5F).

For hydrogen peroxide, which is highly water-soluble, the effects of concern are limited to the extra-thoracic region including necrosis and inflammation of squamous epithelium in the anterior nasal cavity. No other systemic effects were noted. In accordance with the EPA guidance document "Advances in Inhalation Gas Dosimetry for Derivation of a Reference Concentration (RfC) and Use in Risk Assessment" (EPA, 2012a), the Agency concluded that the peroxy compounds should be classified as Category 1 gas (highly water-soluble, highly reactive). In calculating the human equivalent concentration (HEC), the regional gas deposition ratio (RGDR) should be set as 1.

Based on the HEC, a total uncertainty factor (UF) of 30x is applied for short- and intermediate-term inhalation exposures. This UF includes an UF_A of 3x for interspecies variation and a UF_H of 10x for intraspecies variation.

For long-term inhalation exposure, utilizing the HEC, a total UF of 300x is applied. This UF includes an UF_A of 3x for interspecies variation, an UF_H of 10x for intraspecies variation, and a UF_{DB} of 10x to extrapolate from intermediate-term to long-term exposure due to the lack of a long-term inhalation toxicity study.

Table 7: Summary of Toxicological Doses and Endpoints for the Peroxy Compounds

Exposure Scenario	POD for Risk Assessment	Target MOE[B]	Studies and Observed Effects (Both studies are co-critical)
Short-term (0 to 30 Days) and Intermediate-term (30 Days to 6 Months)	NOAEC = 10 mg/m^3 8 Hour HEC[A] = 7.5 mg/m^3	UF_{A-3} = 3 UF_H = 10 Total UF = 30 (Target MOE)	28-day rat inhalation study (CEFIC Peroxygen Sector Group, 2002) 90-day rat inhalation study (MRID 49469301) NOAEC = 10 mg/m^3 (highest dose tested from the 90-day study).
Long-term Exposure (Greater than 6 months)	24 Hour HEC[A] = 2.5 mg/m^3	UF_{A-3} = 3 UF_H = 10 UF_S= 10 Total UF = 300 (Target MOE)	LOAEC = 14.6 mg/m^3 (mid-dose from the 28-day study) based on the necrosis and inflammation of squamous epithelium and anterior of the nasal cavity (3/5 M and 2/5 F).

Source: US EPA, 2019
A. HEC = NOAEC (mg/m^3) * Animal Exposure *(6 hrs/day) / Human Exposure * (8 or 24 hrs/day) * RGDR (1.0)
B. These target MOEs apply to both occupational and residential exposures
Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEC = no observed adverse effect concentration. LOAEC = lowest observed adverse effect concentration. UF = uncertainty factor. 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. LOC = level of concern. N/A = not applicable.

The toxicological endpoints for peroxyoctanoic acid are the same as those used for hydrogen peroxide.

2.6 Dietary Exposure and Risk Assessment

2.6.1 Tolerance and Clearance Considerations

2.6.1.1 FFDCA Clearances

The Food and Drug Administration (FDA) considers hydrogen peroxide as Generally Recognized as Safe (GRAS) for use in foods under 21 CFR 184.1366. According to the FDA website[1], "Hydrogen peroxide is GRAS when used as a bleaching agent in foods and in cotton and cotton fabrics for dry food packaging. It is considered GRAS by the Department of the Treasury in the treatment of wines. It is used as an antimicrobial agent in cheese manufacturing under standards of identity and also in whey processing."

[1] http://wayback.archive-it.org/7993/20171031063925/https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260427.htm

According to Federal Register Vol. 65, No. 232, the FDA put hydrogen peroxide on the GRAS list when used on food processing equipment, utensils, and food contact articles (21 CFR part 178). In addition, hydrogen peroxide presently has the following additional FDA clearances:

Table 8: FFDCA Clearances for Peroxy Compounds

21 CFR	Use	Compound	Maximum use rate
133.113	Cheddar cheese	Hydrogen peroxide	The weight of the hydrogen peroxide shall not exceed 0.05 percent of the weight of the milk.
113.118	Colby cheese	Hydrogen peroxide	The weight of the hydrogen peroxide shall not exceed 0.05 percent of the weight of the milk.
133.144	Granular and stirred cheese	Hydrogen peroxide	The weight of the hydrogen peroxide shall not exceed 0.05 percent of the weight of the milk.
160.105	Egg	Hydrogen peroxide	The hydrogen peroxide solution used shall comply with the specifications of the United States Pharmacopeia, except that it may exceed the concentration specified therein and it does not contain a preservative.
160.185	Dried egg yolks	Hydrogen peroxide	The hydrogen peroxide solution used shall comply with the specification of the United States Pharmacopeia, except that it may exceed the concentration specified therein and it does not contain a preservative.
172.892	Food starch modified for human consumption	Hydrogen peroxide, peracetic acid	Active oxygen obtained from hydrogen peroxide and/or peracetic acid, not to exceed 0.45 percent of active oxygen.
173.315(a)(5)	To assist in peeling of fruits and vegetables that are not raw agricultural commodities	Hydrogen peroxide	Used in combination with acetic acid to form peracetic acid. Not to exceed 59 ppm in wash water.
173.315(a)(5)	To assist in peeling of fruits and vegetables that are not raw agricultural commodities	Peracetic acid	Prepared by reacting acetic acid with hydrogen peroxide. Not to exceed 80 ppm in wash water.
178.1005	To sterilize specified polymeric food-contact surfaces	Hydrogen peroxide	No use of hydrogen peroxide solution in the sterilization of food packaging material shall be considered to be in compliance if more than 0.5 part per million of hydrogen peroxide can be determined in distilled water packaged under production conditions (assay to be performed immediately after packaging).
178.1010(b)(30), 178.1010(c)(25)	Food-processing equipment, utensils, other food-contact articles,	An aqueous solution containing hydrogen peroxide, peracetic acid, acetic acid, and 1-	550 ppm – 1,100 ppm hydrogen peroxide, 100 ppm – 200 ppm peracetic acid, 150 ppm – 330 ppm acetic acid.

21 CFR	Use	Compound	Maximum use rate
		hydroxyethylidene-1,1-diphosphonic acid.	
178.1010(b)(38), 178.1010(c)(33)	Food-processing equipment, utensils, other food-contact articles, dairy-processing equipment	An aqueous solution containing hydrogen peroxide, peracetic acid, and acetic acid, sulfuric acid, and 2,6-pyridinedicarboxylic acid.	300 ppm – 465 ppm hydrogen peroxide, 200 ppm – 315 ppm peracetic acid, 200 ppm – 340 ppm acetic acid.
178.1010(b)(45), 178.1010(c)(39)(i)	Food-processing equipment, utensils, including dairy and beverage-processing equipment, excluding food-contact surfaces in public eating places and dairy and beverage containers	An aqueous solution of hydrogen peroxide, peracetic acid, acetic acid, peroxyoctanoic acid, octanoic acid, sodium 1-octanesulfonate, and 1-hydroxyethylidene-1,1-diphosphonic acid.	72 ppm – 216 ppm hydrogen peroxide; 46 ppm – 138 ppm peracetic acid; 281 ppm – 686 ppm acetic acid; 40 ppm – 122 ppm octanoic acid (including peroxyoctanoic acid).
178.1010(b)(45), 178.1010(c)(39)(ii)	Food-processing equipment, utensils, food-contact equipment and utensils in warewashing machines, including warewashing machines in public eating places, at temperatures no less than 120 deg. F (49 deg. C)	An aqueous solution of hydrogen peroxide, peracetic acid, acetic acid, peroxyoctanoic acid octanoic acid, sodium 1-octanesulfonate, and 1-hydroxyethylidene-1,1-diphosphonic acid.	30 ppm – 91 ppm hydrogen peroxide; 19 ppm – 58 ppm peracetic acid; 119 ppm – 290 ppm acetic acid; 17 ppm – 52 ppm octanoic acid (including peroxyoctanoic acid).
178.1010(b)(45), 178.1010(c)(39)(iii)	Food-processing equipment, utensils, food-contact surfaces in public eating places, dairy or beverage containers	An aqueous solution of hydrogen peroxide, peracetic acid, acetic acid, peroxyoctanoic acid octanoic acid, sodium 1-octanesulfonate, and 1-hydroxyethylidene-1,1-diphosphonic acid.	36 ppm – 108 ppm hydrogen peroxide; 23 ppm – 69 ppm peracetic acid; 140 ppm – 343 ppm acetic acid; 20 ppm – 61 ppm octanoic acid (including peroxyoctanoic acid).

2.6.1.2 Tolerances

While tolerances and exemptions from tolerance exist for hydrogen peroxide, they do not specify use on either raw agricultural commodities or processed commodities. Upon review of the labeled uses and applied concentrations, and considering the chemistry of hydrogen peroxide, the current uses are not expected to result in residues of concern. As such, there is no need for either a tolerance or exemption for hydrogen peroxide for antimicrobial direct or indirect dietary uses.

The following tolerances have been established for peroxy compounds:

Table 9: Tolerances Established for Peroxy Compounds.

40 CFR Section	Compounds	Maximum Residue Value
173.370	An aqueous solution of hydrogen peroxide, acetic acid, peracetic acid, octanoic acid, peroxyoctanoic acid, sodium 1-octanesulfonate, and 1-hydroxyethylidene-1,1-diphosphonic acid. In addition to use on food-processing equipment and utensils, this solution may be used on food-contact surfaces in public eating places	**Food processing equipment and utensils, including dairy and beverage-processing equipment but excluding food-contact surfaces in public eating places and dairy and beverage containers** At least 72 parts per million and not more than 216 parts per million of hydrogen peroxide; at least 46 parts per million and not more than 138 parts per million of peracetic acid; at least 40 parts per million and not more than 122 parts per million of octanoic acid (including peroxyoctanoic acid); at least 281 parts per million and not more than 686 parts per million of acetic acid; at least 7 parts per million and not more than 34 parts per million of 1-hydroxyethylidene-1,1-diphosphonic acid; and at least 36 parts per million and not more than 109 parts per million of sodium 1- octanesulfonate. **Food-contact equipment and utensils in warewashing machines, including warewashing machines in public eating places, at temperatures no less than 120 deg. F (49 deg. C)** At least 30 parts per million and not more than 91 parts per million of hydrogen peroxide; at least 19 parts per million and not more than 58 parts per million of peracetic acid; at least 17 parts per million and not more than 52 parts per million of octanoic acid (including peroxyoctanoic acid); at least 119 parts per million and not more than 290 parts per million of acetic acid; at least 3 parts per million and not more than 14 parts per million of 1-hydroxyethylidene-1,1-diphosphonic acid; and at least 15 parts per million and not more than 46 parts per million of sodium 1-octanesulfonate. **Dairy or beverage containers** At least 36 parts per million and not more than 108 parts per million of hydrogen peroxide; at least 23 parts per million and not more than 69 parts per million of peracetic acid; at least 20 parts per million and not more than 61 parts per million of octanoic acid (including peroxyoctanoic acid); at least 140 parts per million and not more than 343 parts per million of acetic acid; at least 3 parts per million and not more than 17 parts per million of 1-hydroxyethylidene-1,1-diphosphonic acid; and at least 18 parts per million and not more than 55 parts per million of sodium 1-octanesulfonate.
173.370	The additive is used as an antimicrobial agent on meat carcasses, parts, trim, and organs in accordance with current industry practice.	The additive is a mixture of peracetic acid, octanoic acid, acetic acid, hydrogen peroxide, peroxyoctanoic acid, and 1-hydroxyethylidene-1,1-diphosphonic acid, where the maximum concentration of peroxyacids is 220 ppm as peracetic acid, and the maximum concentration of hydrogen peroxide is 75 ppm.
173.370	The additive is used as an antimicrobial agent on poultry carcasses, poultry parts, and organs in accordance with current industry standards of good manufacturing practice	The additive is a mixture of peracetic acid, octanoic acid, acetic acid, hydrogen peroxide, peroxyoctanoic acid, and 1-hydroxyethylidene-1,1-diphosphonic acid, where the maximum concentration of peroxyacids is 220 parts per million (ppm) as peracetic acid, the maximum concentration of hydrogen peroxide is 110 ppm, and the maximum concentration of 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP) is 13 ppm.

40 CFR Section	Compounds	Maximum Residue Value
	(unless precluded by the U.S. Department of Agriculture's standards of identity in 9 CFR part 381, subpart P).	

As of November 2019, there are 76 Food Contact Substance Notifications (FCSNs) which include hydrogen peroxide and 76 FCSNs which include peracetic acid. There are no FCSNs which include peroxyoctanoic acid or sodium percarbonate.

21 CFR 178.1010 notes peroxy compounds which may be used as indirect food additives.

2.6.1.3 Exemptions

As of November 2019, the EPA has established the following exemptions from the requirement of a tolerance for peroxy compounds:

Table 10: Exemptions from Requirements for Tolerance for Peroxy Compounds.

40 CFR Section	Exemption	Use	Chemical	Maximum Residue Level
180.1196 (a)	In or on all food commodities when used as an antimicrobial treatment, per application on fruits, vegetables, tree nuts, cereal grains, herbs, and spices.	Fruit/Veg wash	Peracetic acid	100 ppm
180.1196 (b)	In or on all food commodities when used in sanitizing solutions and applied to tableware, utensils, dishes, pipelines, tanks, vats, fillers, evaporators, pasteurizers, aseptic equipment, milking equipment, and other food processing equipment in food handling establishments including, but not limited to dairies, dairy barns, restaurants, food service operations, breweries, wineries, and beverage and food processing plants.	Food contact hard surface cleaners	Peracetic acid	500 ppm
180.1196 (c)	Residues of the biochemical pesticide peracetic acid and its metabolites and degradates, including hydrogen peroxide and acetic acid, in or on all food commodities, when used in accordance with good agricultural practices.	Biopesticide	Peracetic acid and its degradates: hydrogen peroxide and acetic acid	No limits given.
180.1197	Residues of hydrogen peroxide in or on all food commodities at the rate of ≤1%	Biopesticide	Hydrogen peroxide	≤ 1%

40 CFR Section	Exemption	Use	Chemical	Maximum Residue Level
	hydrogen peroxide per application on growing and postharvest crops.			
180.940 (a)	When ready for use, the end-use concentration is not to exceed 58 ppm	Food-contact surfaces in public eating places, dairy-processing equipment, and food-processing equipment and utensils	Peracetic acid	58 ppm
180.940 (a)	When ready for use, the end-use concentration is not to exceed 52 ppm	Food-contact surfaces in public eating places, dairy-processing equipment, and food-processing equipment and utensils	Peroxyoctanoic acid	52 ppm
180.940 (a)	When ready for use, the end-use concentration is not to exceed 91 ppm	Food-contact surfaces in public eating places, dairy-processing equipment, and food-processing equipment and utensils	Hydrogen peroxide	91 ppm
180.940 (b)	When ready for use, the end-use concentration is not to exceed 315 ppm	Dairy processing equipment, and food-processing equipment and utensils.	Peracetic acid	315 ppm
180.940 (b)	When ready for use, the end-use concentration is not to exceed 122 ppm	Dairy processing equipment, and food-processing equipment and utensils.	Peroxyoctanoic acid	122 ppm
180.940 (b)	When ready for use, the end-use concentration is not to exceed 465 ppm	Dairy processing equipment, and food-processing equipment and utensils.	Hydrogen peroxide	465 ppm
180.940 (c)	When ready for use, the end-use concentration is not to exceed 315 ppm	Food-processing equipment and utensils.	Peracetic acid	315 ppm

40 CFR Section	Exemption	Use	Chemical	Maximum Residue Level
180.940 (c)	When ready for use, the end-use concentration is not to exceed 122 ppm	Food-processing equipment and utensils.	Peroxyoctanoic acid	122 ppm
180.940 (c)	When ready for use, the end-use concentration is not to exceed 1100 ppm	Food-processing equipment and utensils.	Hydrogen peroxide	1100 ppm
180.1234	An exemption from the requirement of a tolerance is established for residues of sodium carbonate.	N/A	Sodium Percarbonate	N/A

An exemption from the requirement of a tolerance is established for residues of sodium carbonate. [70 FR 33363, June 8, 2005]

An exemption from the requirement of a tolerance is established for residues of hydrogen peroxide in or on all food commodities at the rate of ≤ 1% hydrogen peroxide per application on growing and postharvest crops. [67 FR 41844, June 20, 2002]

2.6.2 Food Exposure Profile

Hydrogen Peroxide

Many registered labels include use as an antibacterial cleaner on countertops and other surfaces which could result in indirect dietary exposure. However, based on the chemistry of peroxy compounds, it is expected that the parent compounds will degrade rapidly on application to form mainly water and oxygen. Therefore, the Agency anticipates negligible residues to be available for transfer to food, and therefore, a quantitative dietary exposure and risk assessment was not conducted. The Agency also recognizes that commercially available 3% hydrogen peroxide solutions have been used for many years for personal and medicinal uses. The use directions for some of these products state that these 3% solutions can be used as a sanitizing mouthwash. Other food contact and medicinal uses for hydrogen peroxide include applications for wines and liquors, sanitary lotions, and pharmaceutical preparations (Federal Register Vol. 65, No. 232).

Peracetic acid

A dietary exposure risk assessment has not been performed for peroxy compounds. Dietary (food and drinking water) exposures of concern are not anticipated for peroxy compounds. The Agency previously assessed dietary exposure uses for peracetic acid and found that, due to the chemistry of peracetic acid, there was no expectation of a residue of concern.

It should be noted that there were no toxicological endpoints established in the peroxy compound RED (which includes active ingredients such as hydrogen peroxide and peracetic acid), and risks

were not expected based on rapid decomposition of hydrogen peroxide to non-toxic breakdown products, use of highly diluted products, and designation of hydrogen peroxide as GRAS by FDA. As a result, the Agency has determined that a quantitative dietary assessment is not required for this registration review.

Peroxyoctanoic Acid

A dietary exposure risk assessment has not been performed for peroxyoctanoic acid. Dietary (food and drinking water) exposures of concern are not anticipated for peroxyoctanoic acid, due to (1) its rapid decomposition to non-toxic substances, including water and oxygen; (2) tolerance exemption; and (3) use of highly diluted products.

The degradate octanoic acid is a naturally occurring fatty acid and is a registered food and nonfood grade inert; therefore, it is not expected to be toxic to humans via the oral route of exposure for its currently registered pesticide uses.

Sodium Percarbonate

A dietary exposure risk assessment has not been conducted for sodium percarbonate for the following reasons: (1) residues of sodium percarbonate in drinking water are anticipated to be negligible; (2) sodium percarbonate readily transforms into sodium carbonate and hydrogen peroxide (which is broken down into water and oxygen upon contact with organic matter); and (3) there is negligible risk that food, municipal drinking water and runoff to surface or groundwater will be affected because of the instability of the sodium percarbonate molecule in the presence of water (U.S. EPA, 2002). Based on the above-mentioned reasons, dietary exposure from the pesticidal use of sodium percarbonate is expected to be minimal.

2.6.3 Water Exposure Profile

Hydrogen Peroxide

According to the "Hydrogen Peroxide; Exemption from the Requirement of a Tolerance" (*63 Federal Register 87* [6 May, 1998], pp 24955-24963), "Although the proposed food contact uses for hydrogen peroxide acid may result in transfer of minor amounts of residues to potential drinking water sources, no risk assessment is warranted because of: (i) the rapid degradation of hydrogen peroxide into oxygen, and water, and (ii) these degradates are not of toxicological concern. Information from the EPA Office of Water also indicates that when used for potable water disinfection, no residues of hydrogen peroxide acid are present by the time the water is pumped through a distribution system." Therefore, the Agency has determined that a quantitative drinking water risk assessment will not be needed in this registration review.

Peracetic acid

Certain registered outdoor use sites (or those directly discharged) are likely to result in dietary exposure via drinking water. Such sites include human water systems (bottled water containers, water filters, drinking water coolers, ice making machines, chemigation systems connected to public water systems and dental unit water lines) and industrial processes and water systems (air washer water systems, evaporative condenser water systems, commercial/industrial cooling water [recirculating], commercial/industrial cooling water, etc.).

According to the Federal Register: May 6, 1998 (Volume 63, Number 87, pages 24955-24963), "Although the proposed food contact uses for peracetic acid may result in transfer of peracetic acid to potential drinking water sources, no risk assessment is applicable because of: (a) the rapid degradation of peracetic acid into acetic acid, oxygen, and water, and (b) there are not expected to be any residues of toxicological concern. Information from the EPA Office of Water also indicates that when used for potable water disinfection, no measurable residues of peracetic acid were present by the time the water is pumped through the distribution system and arrived at the tap."

Therefore, the Agency has determined that a quantitative drinking water risk assessment will not be needed in this registration review.

Peroxyoctanoic Acid

No drinking water assessment is required for peroxyoctanoic acid or its degradation products: hydrogen peroxide and octanoic acid. No exposure to peroxyoctanoic acid is expected due to its rapid degradation rate. The Agency has determined that a quantitative drinking water risk assessment for the degradate hydrogen peroxide is not needed. The degradate octanoic acid is a registered food and nonfood grade inert and is a naturally occurring fatty acid; therefore, a drinking water assessment is not needed for its registered uses.[2]

Sodium Percarbonate

Sodium percarbonate consists of an adduct of sodium carbonate and hydrogen peroxide. In the presence of water, the granules or crystals of sodium percarbonate dissolve into hydrogen peroxide and sodium carbonate. Upon contact, the hydrogen peroxide oxidizes its target while breaking down into water and oxygen, neither of which is of toxicological concern.

2.7 Residential Exposure/Risk Characterization

[2] EPA's Office of Pesticides InertFinder database may be found at: https://www.epa.gov/pesticide-registration/inert-ingredients-overview-and-guidance#inertfinder and search for octanoic acid.

2.7.1 Residential Handler Exposure/Risk Characterization

There is the potential for residential handler exposure when using kitchen and bathroom disinfectant cleaners and floor and carpet cleaners that contain one or more of the peroxy compounds. These products are packaged in ready-to-use trigger sprayers, aerosol cans, wipes and liquid concentrates. The exposures are anticipated to be of a short- to intermediate-term duration because household cleaning is done intermittently. The exposures can be to aerosols released during spray applications and to vapors that are emitted from the spray droplets and treated surfaces. Data from the Antimicrobial Exposure Assessment Task Force II (AEATF II) were used to assess the aerosol portion of the exposures; however, these data were only designed for low vapor pressure chemicals. Therefore, the AEATF II data were supplemented with the EFAST model to account for the vapor-phase of the exposure.

2.7.1.1 Residential Handler Inhalation Exposure to Peroxy Aerosols

The MOEs for residential handler inhalation exposures to peroxy aerosols were assessed using unit exposure data from the AEATF II and application rates of 0.5 and 6.0 percent as outlined in Table 11. The MOEs are greater than the target MOE of 30 at both application rates and are not of concern.

Table 11: **Residential Handler Inhalation MOEs for the Peroxy Compounds**

Scenario	Application Rate[A] (percent AI)	Amount Product Applied per Day	Amount AI Handled[C] (lb/day)	Unit Exposure (mg/m^3/lb AI)	Inhalation Exposure[E] (mg/m^3)	MOE[F] (LOC = 30)
Trigger Spray and Wipe RTU Disinfectant Cleaner	0.5	0.06 gallons[B]	0.0025	3.12[D]	0.0078	960
	6.0		0.030	3.12[D]	0.094	80

A. The rate of 0.5% AI is from EPA Reg. No. 70627-78 and the rate of 6.0% AI is from EPA Reg. No. 85837-1
B. Antimicrobial Exposure Joint Venture (AEJV) Survey Data (MRID 46799302).
C. Amount AI Handled (lb/day) = Application Rate (% AI/100) * Amount Product Applied (gal) * Density (8.35 lb/gal)
D. 8 Hour TWA Value from the AEATF II Trigger Spray and Wipe Exposure Study (MRID 48375601).
E. Inhalation Exposure (mg/m^3) = Amount AI Handled (lb/day) * Unit Exposure (mg/m^3/lb AI)
F. MOE = HEC (7.5 mg/m^3) / Inhalation Exposure (mg/m^3)

2.7.1.2 Residential Handler Inhalation Exposure to Peroxy Vapors

The Agency has not received any data regarding peroxy compound exposure during the residential use of peroxy compounds; therefore, inhalation exposure to peroxy compound vapors was assessed using the General Purpose Cleaner Scenario in the EPA's Consumer Exposure Module (CEM) of E-FAST (EPA, 2014).

The following chemical-specific inputs were used in the model:

- The molecular weight of hydrogen peroxide is 34 grams/mol.

- The vapor pressure is 2.25 mm Hg, which is within the range of vapor pressures listed in Table 1, or 0.225 mm Hg, which is an assumed value selected to illustrate the sensitivity of the CEM model. These values were chosen as inputs because the vapor pressure of pure hydrogen peroxide cannot be measured due to its reactivity. The reported vapor pressures for pure hydrogen peroxide are based on extrapolation from vapor pressures measured for hydrogen peroxide in solution.
- The weight fraction of hydrogen peroxide is 0.005 based on the low application rate products, such as EPA Reg. No. 70627-78, that contain 0.5% AI or 0.06 for the high rate products, such as EPA Reg. No. 85837-1, that contain 6% AI.
- The mass of product used is 227 grams (0.06 gal) based on Antimicrobial Exposure Joint Venture (AEJV) Survey Data (MRID 46799302).
- The air exchange rate of 0.45 air changes per hour (ACH) which is the default value for CEM.
- The product use occurs in the kitchen.
- For residential activity, the patterns were set to typical CEM assumptions.
- The average size of a home is 523 m^3 (or 2,340 ft^2 with an 8-foot ceiling).
- The room in which the product is applied is the kitchen and is 36 m^3.

Because the CEM calculates either peak concentrations for comparison to an acute endpoint or Lifetime Average Daily Concentrations for comparison to chronic or cancer endpoints, the following inputs were used to allow the model to calculate a one-day average concentration for comparison to the short/intermediate-term endpoint:

- The frequency of use was set to 365 days per year.
- The duration was set to 78 years.
- The central tendency and high-end weight fractions were both set to 0.005 or 0.06.
- The central tendency and high-end mass of product used were both set to 227 grams.
- The central tendency and high-end event duration were both set to 1.42 hours.

The results of the CEM model runs and the MOEs are summarized in Table 12. It should be noted that CEM calculates daily exposures as 24-hour time-weighted averages (TWAs); therefore, the MOEs were calculated using the 24-hour HEC of 2.5 mg/m^3 instead of the 8-hour HEC of 7.5 mg/m^3. When the measured vapor pressure of 2.25 mm Hg is used as an input, the MOEs are 6.8 for the low application rate and 0.6 for the high application rate. These MOEs are of concern because they are less than the target MOE of 30. When the vapor pressure is reduced by 10x to 0.225 mm Hg (to test the sensitivity of the model to the vapor pressure), the resulting MOEs are increased only by a factor of approximately 2x. This indicates that the model is not proportionately sensitive to changes in vapor pressure.

Table 12: Residential Handler Inhalation MOEs (Vapor Exposures)

Scenario	Vapor Pressure (mm Hg)	Application Rate[C]	Amount of Cleaner Applied (g/day)	Air Exchange Rate (per hour)	Inhalation Exposure (24 Hour TWA)[F] (mg/m^3)	MOE[G] (Target MOE = 30)
Residential General-Purpose Cleaner	2.25[A]	0.5%	227[D] (0.06 gallons)	0.45[E]	0.37	**6.8**
		6.0%			4.5	**0.6**
	0.225[B]	0.5%			0.21	**12**
		6.0%			2.5	**1.0**

A. Measured vapor pressure listed in Table 1.
B. Assumed vapor pressure to test the sensitivity of CEM to vapor pressure.
C. Based on EPA Reg. No. 70627-78, which contains 0.5% AI, and EPA Reg. No. 85837-1, which contains 6% AI.
D. Is an AD standard assumption used for residential risk assessments. Density is assumed to be 8.34 lb/gal.
E. The air exchange rate is the default value for the CEM model
F. The CEM calculates daily exposures as 24-hour time-weighted averages (TWAs).
G. MOE = 24 hour HEC (2.5 mg/m^3)/ Exposure (mg/m^3)

***MOEs highlighted in bold font are of concern because they are less than the target MOE of 30.**

2.7.2 Residential Post-Application Exposure

Products such as EPA Reg. Nos. 93324-1, which are liquid concentrates, can be applied to residential areas such as day care centers, cruise ships, homes, hotels, multifamily housing, and schools by fogging or vaporization. These products typically require the use of a brand specific fogging machine, and detailed instructions regarding the operation of these machines are included in the product label.

The target hydrogen peroxide air concentration is >139 ppm for EPA Reg. No. 93324-1. The contact times range from 15 to 90 minutes. Once the treatment has been completed, an aeration cycle is initiated which removes the hydrogen peroxide using mechanisms such as ventilation, dehumidification or scrubbing. The aeration is continued until the Occupational Safety and Health Administration Permissible Exposure Limit (OSHA PEL) of 1.0 ppm (1.4 mg/m^3) is reached at which point the treated area can be released for occupancy.

Calculation Methods

The air concentrations after occupancy are calculated using the following single chamber ventilation formula that is included in the EPA Multi-Chamber Concentration and Exposure Model (MCCEM):

$$C_T = C_0 \, x \, 0.5 \left(\frac{T}{0.693} x \frac{Q}{V} \right)$$

Where:

C_T = Air concentration at time T
C_0 = Air concentration at time zero
Q = Ventilation rate in cubic feet per minute (CFM)

T = Elapsed time in minutes
V = Volume of room in cubic feet

Assumptions Used

The following assumptions were used in assessing the exposures to hydrogen peroxide:

- The initial air concentration at occupancy is 1.0 ppm.
- The air exchange rate is 0.45 air changes per hour (ACH) which is the average ventilation rate for residential housing as listed in the Exposure Factors Handbook (EPA, 2011).
- The daily exposure duration is 24 hours per day.

MOEs for Hydrogen Peroxide

The MOE for residential exposures to hydrogen peroxide was calculated by comparing the POD of 2.5 mg/m^3 to the 24-hour TWA. As shown in Table 13, the MOE is 19 is of concern because it is less than the target MOE of 30.

Table 13: Residential Fogging Post-Application Inhalation MOEs

Hydrogen Peroxide Air Concentration at Occupancy[A]	Air Exchange Rate at Occupancy[B]	24 Hour TWA	MOE for 24 Hour TWA[C] (Target MOE = 30)
1.4 mg/m^3	0.45	0.13 mg/m^3	**19**

A. The label indicates that the room can be released for occupancy at 1.0 ppm (1.4 mg/m^3).
B. Average ventilation rate for residential housing as listed in the 2011 Exposure Factors Handbook (EPA, 2011)
C. MOE = 24 Hour HEC (2.5 mg/m^3) / 24 Hour TWA (mg/m^3)
***MOEs highlighted in bold font are of concern because they are less than the target MOE**

2.8 Aggregate Exposure/Risk Characterization

Since there are no endpoints selected for oral and dermal exposures, no aggregate assessment of oral and dermal exposures is needed. There is an endpoint selected for inhalation exposures, and there are residential handler and post application inhalation exposures that could be aggregated; however, some of these scenarios have risks of concern on their own and would cause the aggregate risk to be of concern. These risks will need to be refined or mitigated before the exposures can be aggregated.

2.9 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 the peroxy compounds and any other substances and the peroxy compounds do not appear to produce a toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that the peroxy compounds have 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)[3] and conducting cumulative risk assessments (CRA)[4]. During Registration Review, the Agency will utilize this framework to determine if the available toxicological data for the peroxy compounds suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

2.10 Occupational Handler Exposure/Risk Characterization

2.10.1 Occupational Handler Hard Surface Disinfection Uses

There is the potential for occupational handler inhalation exposure during the application of peroxy products for surface treatments using sprays, mops, or wipes. Exposures can be to peroxy aerosols or peroxy vapors. The exposure duration is assumed to be primarily intermediate- to long-term because these uses occur in medical and commercial facilities that operate all year.

2.10.1.1 Occupational Handler Hard Surface Disinfection Uses Aerosol Exposures

The MOEs for occupational handler inhalation aerosol exposure during hard surface treatment were assessed as outlined in Table 14. One MOE is of concern for short/intermediate-term exposures because it is less than the short/intermediate-term target MOE of 30. Three MOEs are of concern for long-term exposures because they are less than the long-term target MOE of 300.

Table 14: MOEs for Occupational Handler Hard Surface Treatment Aerosol Exposures

Scenario	Application Rate (percent AI)	Amount Solution Applied per Day[D]	Amount AI Handled[E] (lb/day)	Unit Exposure (mg/m^3/lb AI)	Inhalation Exposure[I] (mg/m^3)	MOE[J, K] (Target MOE = 30ST or 300LT)
Trigger Spray and Wipe Diluted Disinfectant	0.73[A]	0.26 gallons (1 liter)	0.016	3.12[F]	0.050	**150**
Trigger Spray and Wipe RTU Disinfectant Cleaner	6.0[B]	0.26 gallons (1 liter)	0.13	3.12[F]	0.41	**18**
Low Pressure Handwand	0.25[C]	5 gallons	0.10	0.017[G]	0.0017	4,400
High Pressure Handwand	0.25[C]	100 gallons	2.09	0.019[H]	0.039	**190**

A. Medical hard surface disinfection rate based on the OxyCide product used in the NIOSH studies.
B. Hard surface cleaner and disinfection rate based on EPA Reg No. 85837-1
C. Greenhouse hard surface application rate based on EPA Reg No. 65402-7
D. Standard assumptions used in AD risk assessments.

[3] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (EPA, 1999)
[4] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (EPA, 2002)

E. Amount AI Handled (lb/day) = Application Rate (% AI/100) * Amount Solution Applied (gal) * Density (8.35 lb/gal)
F. AEATF II Trigger Spray and Wipe Exposure Study (MRID 48375601).
G. Arithmetic average from the AHETF MLAP Greenhouse Backpack Sprayer study converted to an 8 hr. TWA.
H. Arithmetic average from PHED Scenario #35 High Pressure Handwand, MLAP Liquids converted to an 8 hr. TWA.
I. Inhalation Exposure (mg/m^3) = Amount AI Handled (lb/day) * Unit Exposure (mg/m^3/lb AI)
J. MOE = 8 Hour HEC (7.5 mg/m^3) / Inhalation Exposure (mg/m^3)
K. The target MOE is 30 for short/intermediate-term exposures and 300 for long-term exposures.

***The MOEs highlighted in bold font are of concern because they are less than the target MOE.**

2.10.1.2 Occupational Handler Hard Surface Disinfection Uses Vapor Exposure

Inhalation exposure to peroxy vapors was assessed using two health hazard evaluations (HHE) of hospital employee exposures that were conducted by NIOSH. Both these HHEs were conducted at hospitals where a peroxy product (OxyCide, EPA Reg. No. 1677-237) was diluted at the rate of 3 ounces per gallon and applied via wipes to disinfect hard surfaces in patient care areas.

In HHE 2015-0053-3269 (NIOSH, 2018), 49 full shift personal air samples were taken on workers disinfecting thirteen different areas of the hospital including the operating rooms, the birth center rooms, intensive care rooms, oncology and the outpatient clinic. The highest average exposure 186 ppb (n = 10, SD = 132) was measured in the birth center. The next highest average exposure of 175 ppb (n = 3, SD = 59) was measured in the birth center operating room. The average exposures in the other 11 areas ranged from 6 on the floors (n = 1) to 133 ppb in the neonatal intensive care unit (n = 5, SD = 168).

In HHE 2017-0114-3357 (NIOSH, 2019), 56 full shift personal air samples were taken on or near environmental service staff workers cleaning and disinfecting nine different areas of the hospital. These areas included the emergency department, intensive care unit, labor and delivery, pediatrics and patient rooms following discharge. The highest average exposure (reported as a Minimum Variance Unbiased Estimate, or MVUE) of 168 ppb (n = 6, SD = 150) was measured during discharge room cleaning. The next highest average (MVUE) exposure of 90.5 ppb (n = 4, SD = 30.5) was measured in the labor and delivery area. The average (MVUE) exposures in the other 7 areas ranged from 29.5 ppb in the emergency department (n = 6, SD = 19.2) to 89.3 ppb (n = 5, SD = 89.3) in pediatrics.

An overall average was calculated from the HHEs by weighting the averages for each area sampled. The overall average for HHE 2015-0053-3269 is 99 ppb (n = 49, SD = 104 ppb), and the overall average for HHE 2017-0114-3357 is 70 ppb (n = 56, SD = 78 ppb). The overall average for both HHEs combined is 83 ppb (n = 105, SD = 92 ppb).

The occupational handler MOEs during wipe application were calculated using the overall average of 83 ppb and application rates that range from 0.5 to 5.44 percent AI as outlined in Table 15. The MOEs range from 8.4 to 91 depending upon the application rate. The MOE of 8.4, which is for the application rate of 5.44 percent, is of concern for short- and intermediate-term

exposures because it is less than the target MOE of 30. The remaining MOEs which range from 33 to 91 are not of concern for short- and intermediate-term exposure. All the MOEs are of concern for long-term exposure because they are less than the target MOE of 300.

Table 15: Occupational Handler Inhalation MOEs for Peroxy Vapor Exposures

Scenario	Product Reg. No.	Application Rate (Percent H_2O_2)	Inhalation Exposure 8 hr TWA (mg/m^3)	Short/Intermediate-Term MOE[E] (Target MOE = 30)	Long-term MOE[E] (Target MOE = 300)
Wipe Application Hospital	1677-237	0.73[A]	0.12[C]	63	**63**
	70627-60	0.5[B]	0.082[D]	91	**91**
	67619-25	1.4[B]	0.23[D]	33	**33**
	67619-34	5.44[B]	0.89[D]	**8.4**	**8.4**

A. Concentrate product that contains 27.5% H_2O_2 and 5.8% peracetic acid diluted at the rate of 3 liquid ounces per gallon.
B. Ready-To-Use wipe product that is applied undiluted
C. Average breathing zone air concentration (83 ppb, n = 105) from NIOSH (2018) and NIOSH (2019) converted to mg/m^3. 1 ppm = 1.4 mg/m^3
D. NIOSH value adjusted for the application rate (i.e., (0.5% H_2O_2 / 0.73% H_2O_2) / 100% x (0.12 mg/m^3 @ 0.73% H_2O_2) = 0.082 mg/m^3 @ 0.5% H_2O_2).
E. MOE = 8 Hour HEC (7.5 mg/m^3) / Inhalation Exposure (mg/m^3)

***The MOEs highlighted in bold font are of concern because they are less than the target MOE**

2.10.2 Occupational Handler Industrial Process and Material Treatment Uses

There is the potential for occupational handler inhalation exposure during the application of peroxy products for the treatment of industrial processes such as paper mills, cooling water systems and oil production. Exposures can be to peroxy aerosols or peroxy vapors. The exposure duration is assumed to be primarily intermediate- to long-term because these uses occur in industrial facilities that operate on a year-round basis.

The products contain up to 50 percent hydrogen peroxide and can be open poured into the process or material being treated. Most of the labels require respirator protection which varies from half air purifying respirators with organic vapor cartridges (for EPA Reg. No. 68660-1, which contains 18.5% hydrogen peroxide and 12% peracetic acid) to full face air supplied respirators when the OSHA PEL of 1 ppm could be exceeded (for EPA Reg. No. 72372-1, which contains 35% H_2O_2).

Some of the labels also require closed system loading and delivery for specific uses. For example, EPA Reg. No. 68660-1 requires a closed mixing/loading and delivery transfer system for the oil and gas uses.

Some products, such as EPA Reg. No. 72372-1, require the implementation of protective engineering solutions, such as ventilation, to maintain hydrogen peroxide levels below the OSHA PEL of 1 ppm.

2.10.2.1 Occupational Handler Process and Material Treatment Uses Aerosol Exposures

The MOEs for occupational handler inhalation aerosol exposure during open pouring applications for industrial processes and material preservation treatments were assessed as outlined in Table 16. It is assumed that 20 gallons could be handled in one day. This value is based on the largest amount of material (four five-gallon containers) poured from conventional containers in the AEATF liquid pour study (MRID 48917401). It is assumed that larger amounts would be delivered in bulk containers and applied using meter pump closed loading systems. The MOEs of 360 and 770 are not of concern because they are greater than the target MOE of 30 for short- and intermediate- term exposures and 300 for long- term exposures.

Table 16: Occupational Handler Process and Material Treatment Aerosol Exposures

Scenario	Percent AI in Product[A]	Amount Product Handled (gallons)	Product Density (lb/gal)	Amount AI Handled[C] (lb/day)	Unit Exposure (mg/m^3/lb AI)	Inhalation Exposure[E] (mg/m^3)	MOE[F] (Target MOE = 30 or 300)
Open pour for process and material treatment	50	20[B]	10	100	0.00021[D]	0.021	360
	25		9.2	46		0.0097	770

A. Based on current registered end-use products.
B. Based on the largest amount (four five-gallon containers) poured from conventional containers in the AEATF liquid pour study (MRID 48917401).
C. Amount of AI Handled (lb/day) = (Percent AI in Product /100) x Amount Product Applied (gal) * Density (lb/gal)
D. Conventional pour unit exposure from AEATF II human exposure liquid pour study (MRID 48917401).
E. Inhalation Exposure (mg/m^3) = Amount of AI Handled (lb/day) * Unit Exposure (mg/m^3/lb AI)
F. MOE = HEC (7.5 mg/m^3) / Inhalation Exposure (mg/m^3)

2.10.2.2 Occupational Handler Process and Material Treatment Uses Vapor Exposures

There are no data available to assess the occupational handler exposures to peroxy vapors that would occur during the open pouring of peroxy products into process tanks or vessels during industrial process and material preservation treatments. In the absence of occupational handler exposure data to peroxy vapors, risks cannot be precluded. If these applications could be made using closed loading and delivery systems that are designed to prevent the release of peroxy vapors, it could be assumed that exposures would be minimal, and the risks would not be of concern. Open pouring should only be done when the process tanks or vessels have local exhaust ventilation to capture the vapors.

2.11 Occupational Post-Application Exposure/Risk Characterization

Occupational post-application inhalation exposures can occur after fogging applications are made in hospitals, food processing plants, pharmaceutical and medical device sterile processing enclosures and poultry premises. These exposures are primarily short- to intermediate-term in

duration because fogging applications are made on an intermittent basis; however, long term exposures may occur in areas such as hospitals, when applications are made on a daily basis.

2.11.1 Occupational Post-Application Exposure from Hospital Fogging Applications

Products such as EPA Reg. Nos. 58779-4, 84526-6, 90150-2, 90607-3, and 93324-1 can be applied to hospital areas such as patient rooms by fogging or vaporization. These products typically require the use of a brand specific fogging machine and detailed instructions regarding the operation of these machines is included in the product label.

The target hydrogen peroxide air concentrations are >139 ppm for EPA Reg. No. 93324-1, 150 ppm for EPA Reg. No. 90150-2, 410 ppm for EPA Reg. No. 84526-6, 250 and 400 ppm for EPA Reg. No. 58779-4 and 14,000 ppm for EPA Reg. No. 90607-3. The contact times range from 15 to 90 minutes. Once the treatment has been completed, an aeration cycle is initiated which removes the hydrogen peroxide using mechanisms such as ventilation, dehumidification or scrubbing. The aeration is continued until a specific air concentration is reached at which point the room can be released for occupancy. Some labels list the Occupational Safety and Health Administration Permissible Exposure Limit (OSHA PEL) of 1.0 ppm (1.4 mg/m^3) as the specific air concentration while other labels list 0.2 ppm as the specified level.

Calculation Methods

The air concentrations after occupancy were calculated using the following single chamber ventilation formula that is included in the EPA Multi-Chamber Concentration and Exposure Model (MCCEM):

$$C_T = C_0 \, x \, 0.5 \left(\frac{T}{0.693} x \frac{Q}{V} \right)$$

Where:

C_T = Air concentration at time T
C_0 = Air concentration at time zero
Q = Ventilation rate in cubic feet per minute (CFM)
T = Elapsed time in minutes
V = Volume of room in cubic feet

Assumptions Used

The following assumptions were used in assessing the exposures to hydrogen peroxide:

- The initial air concentration at occupancy is either 1.0 ppm or 0.2 ppm depending upon the product label.
- The air exchange rate for patient rooms is 2.0 air changes per hour (ACH). This rate is specified in design guidelines from the American Institute of Architects (AIA) and the American Society of Heating, Refrigeration and Air Conditioning Engineers (ASHRAE)

as discussed in (Begg, 2008). This is the air exchange rate for outdoor air and does not include the recirculated air that is included in the recommended total air exchange rate of 6.0 ACH.

- The daily exposure duration is 8 hours for hospital staff.

MOEs for Hydrogen Peroxide

The MOEs for worker exposures to hydrogen peroxide were calculated by comparing the POD of 7.5 mg/m^3 to the 8-hour time weighted average (TWA) air concentrations. As shown in Table 17, the MOE is 85 when the initial air concentration is 1.0 ppm and the MOE is 420 when the initial air concentration is 0.2 ppm. Both MOEs are greater than the target MOE of 30 for short/intermediate-term exposures and are not of concern. The MOE of 85 is less than the target MOE of 300 for long-term exposures and is of concern.

Table 17: Hospital Fogging Post-Application Inhalation MOEs

Hydrogen Peroxide Air Concentration at Occupancy (mg/m^3)	Ventilation Rate in Air Changes per Hour	8 Hour TWA (mg/m^3)	MOE [C, D] (Target MOE = 30 or 300)
1.4[A]	2.0	0.0881	**85**
0.28[B]	2.0	0.018	420

A. Some labels indicate that the room can be released for occupancy at 1.0 ppm (1.4 mg/m^3).
B. Other labels indicate that the room can be released for occupancy at 0.2 ppm (0.28 mg/m^3).
C. MOE for 8 Hour TWA = 8 Hour HEC (7.5 mg/m^3) / 8 Hour TWA (mg/m^3)
D. The target MOE is 30 for short/intermediate-term exposures and 300 for long-term exposures.
***The MOEs highlighted in bold font are of concern because they are less than the target MOE**

2.11.2 Occupational Post-Application Exposure from Food Processing Plant Fogging

Products such as EPA Reg. No. 1677-129 can be applied to food processing areas such as dairies, beverage plants, food processing plants, and meat and poultry processing facilities. These products typically do not require the use of a brand specific fogging machines and detailed instructions regarding the operation of these machines are not included in the product label.

Calculation Methods

The air concentrations after occupancy were calculated using the single chamber ventilation formula that is included in MCCEM with the following assumptions:

- The initial air concentration is 25 mg/m^3. This is based on the application of one quart of fogging solution that contains 1.4 fluid ounces of EPA Reg. No. 1677-129 per four gallons. This product contains 27.5% hydrogen peroxide and 5.8% peracetic acid.
- The air exchange rate for food processing areas is 4.0 air changes per hour (ACH) and the room is ventilated for two hours.
- The daily exposure duration is 8 hours for food processing workers.

MOEs for Hydrogen Peroxide

The MOEs for worker exposures to hydrogen peroxide were calculated by comparing the POD of 7.5 mg/m^3 to the 8-hour time weighted average (TWA) air concentrations. As shown in Table 18, the MOE for workers is 28,000 which is not of concern because it is greater than the target MOE of 30.

Table 18: Food Processing Fogging Post-Application Inhalation MOEs

Amount Hydrogen Peroxide in Fogging Solution[A]	Hydrogen Peroxide in Air at Application[B]	Hydrogen Peroxide in Air After Aeration[C]	Hydrogen Peroxide 8 Hour TWA	MOE[D] (Target MOE = 30)
0.075 percent	25 mg/m^3	0.0084 mg/m^3	0.00027 mg/m^3	28,000

A. Based on 1.4 fluid ounces of EPA Reg. No. 1677-129 per 4 gallons of water. This product contains 27.5% H_2O_2.
B. Based on the application of 32 ounces of fogging solution per 1,000 ft^3 of room area.
C. The label requires 2 hours of aeration (or 8 air exchanges) after fogging is completed.
D. MOE for 8 Hour TWA = 8 Hour HEC (7.5 mg/m^3) / 8 Hour TWA (mg/m^3)

2.11.3 Occupational Post-Application Exposure from Enclosure Fogging

Products such as EPA Reg No. 72372-1 are used as a sterilant in treated enclosures up to 3,500 ft^3 (validated for efficacy) or greater (non-validated for efficacy). These enclosures include production operations in pharmaceutical manufacturing, manufacturing clean rooms, and medical device manufacturing. The application rate for enclosures up to 35 ft^3 is 170.5 grams of product which yields 60,000 mg/m^3 (43,000 ppm) hydrogen peroxide at 35 ft^3. The application rate for enclosures 36 to 3,500 ft^3 is 1,500 grams of product which yields 500,000 mg/m^3 (360,000 ppm) hydrogen peroxide at 36 ft^3 and 5,300 mg/m^3 (3,800 ppm) hydrogen peroxide at 3,500 ft^3.

After the hydrogen peroxide vapor is allowed to remain in the enclosure for the required time, which ranges from 10 minutes to 3 hours depending upon the chamber size, the chamber is aerated until the hydrogen peroxide air concentration is at or below 1.0 ppm.

Calculation Methods

The air concentrations after occupancy were calculated using the MCCEM single chamber ventilation formula with following assumptions:

- The initial air concentration at occupancy is 1.0 ppm.
- The air exchange rate ranges from 1.0 to 8.0.
- The daily exposure duration is 8 hours for workers entering the enclosure after it has been fogged and aerated.

MOEs for Hydrogen Peroxide

The MOEs for worker exposures to hydrogen peroxide following enclosure fogging were calculated by comparing the POD of 7.5 mg/m^3 to the 8-hour time weighted average (TWA) air concentrations. As shown in Table 19, the MOEs range from 43 to 320 depending upon the ventilation rate and are not of concern because they are greater than the target MOE of 30.

Table 19: Enclosure Fogging Post-Application Inhalation MOEs

Hydrogen Peroxide Air Concentration at Occupancy[A]	Ventilation Rate[B] (Air Changes per Hour)	8 Hour TWA (mg/m^3)	MOE for 8 Hour TWA[C] (Target MOE = 30)
1.4 mg/m^3	1	0.175	43
	2	0.0881	85
	4	0.045	170
	8	0.023	320

A. The labels indicate that the enclosure should be aerated until H_2O_2 levels are 1.0 ppm (1.4 mg/m^3).
B. Ventilation rates vary based on the enclosure size and purpose.
C. MOE for 8 Hour TWA = 8 Hour HEC (7.5 mg/m^3) / 8 Hour TWA (mg/m^3)

2.11.4 Occupational Post-Application Exposure from Poultry Premise Fogging

Products such as EPA Reg No. 70299-1 can be applied as a fog as an adjunct to acceptable manual cleaning and disinfecting to treat hard, non-porous surfaces in poultry premises, trucks, coops and crates. The areas are ventilated for a minimum of one hour after fogging.

Calculation Methods

The air concentrations after occupancy were calculated using the MCCEM single chamber ventilation formula with following assumptions:

- The initial air concentration is based on the application rate.
- The air exchange rate is 4.0 air changes per hour-based on Jacobson, Larry. 2005. Professor and Extension Engineer at University of Minnesota.
- The daily exposure duration is 8 hours for workers entering the poultry house after it has been fogged and aerated.

MOEs for Hydrogen Peroxide

The MOEs for worker exposures to hydrogen peroxide following poultry premise fogging were calculated by comparing the POD of 7.5 mg/m^3 to the 8-hour time weighted average (TWA) air concentrations. As shown in Table 20, the MOE is 1,700 which is not of concern.

Table 20: Poultry Premise Fogging Post-Application Inhalation MOEs

Amount Hydrogen Peroxide in Fogging Solution[A]	Hydrogen Peroxide in Air at Application[B]	Hydrogen Peroxide in Air After Aeration[C]	Hydrogen Peroxide 8 Hour TWA	MOE[D] (Target MOE = 30)
0.18 percent	7.7 mg/m^3	0.14 mg/m^3	0.0045 mg/m^3	1,700

A. Based on 1.0 fluid ounces of EPA Reg. No. 70299-11 per gallon of water. This product contains 23% H_2O_2.
B. Based on the application of 32 ounces of fogging solution per 1,000 ft^2 of room area with an 8-foot ceiling (8,000 ft^3).
C. The label requires 1 hour of aeration after fogging is completed.
D. MOE = 8 Hour HEC (7.5 mg/m^3) / 8 Hour TWA (mg/m^3)

2.12 Human Health Incident Report

Based on a search of the Incident Data System (IDS) for all peroxy compound incidents from February 2014 to October 2019, there were 91 discrete reports. Of these, there were no reported deaths and 13 incidents which were reported as "major." Major incidents included chemical burns and respiratory symptoms.

Hospital employee complaints of respiratory irritation were investigated by the National Institute for Occupational Safety and Health (NIOSH) in two Health Hazard Evaluations (HHEs). Both these HHEs were conducted at hospitals where a peroxy product (OxyCide, EPA Reg. No. 1677-237) was applied via wipes to clean and disinfect hard surfaces. In HHE 2015-0053-3259 (NIOSH, 2018), NIOSH found that increased exposure to hydrogen peroxide, peracetic acid and acetic acid vapors were associated with increases in acute work-related nasal and eye symptoms and increased shortness of breath on level ground reported by cleaning staff. In HHE 2017-0114-3357 (NIOSH, 2019), NIOSH reported similar findings regarding increased exposure to hydrogen peroxide, peracetic acid or acetic acid and symptoms reported by hospital staff. In both HHEs, NIOSH provided recommendation to reduce exposure. These recommendations included calibrating the product dispensers to properly dilute the product to maintain a pH of 2.7 to 4.0 and minimizing the use of the product in non-patient care areas.

3 ENVIRONMENTAL RISK ASSESSMENT

3.1 Environmental Fate

3.1.1 Available Data

Hydrogen Peroxide

In the FWP of the peroxy compounds case, the Agency required a modified activated sludge respiration inhibition (ASRI, originally 850.6800, now renamed to 850.3300), an activated sludge sorption isotherm (ASSI, 835.1110) and a ready biodegradability study (835.3110) to be performed with either hydrogen peroxide or peracetic acid. Since then, waiver requests have been accepted for the ready biodegradability study (EPA, 2014), the ASSI (EPA, 2016), and the ASRI study (EPA, 2016).

Hydrogen peroxide is an extremely powerful oxidizer and will react readily with organic material. According to the European Union Risk Assessment Report on hydrogen peroxide (2003), hydrogen peroxide had a half-life of 2-minutes in wastewater treatment plants (WWTPs) with an estimated removal of over 99% during wastewater treatment, biodegrading to water and oxygen prior to discharge from WWTPs. Hydrogen peroxide is not expected to volatilize or bioaccumulate based on its low Henry's law constant of 7.4×10^{-9} and its estimated log K_{ow} of -1.57 (Table 1). Therefore, little to no environmental exposure to hydrogen peroxide is expected.

Further information can be found in Appendix B.

Peracetic acid

Peracetic acid is not manufactured as a pure compound but instead in equilibrium as a mixture with water, hydrogen peroxide, and acetic acid. In the pH range of 5.5 to 9.0, there are several mechanisms by which it may be consumed: transition metal catalytic decomposition, spontaneous decomposition, and hydrolysis.

As detailed in Appendix B, both peracetic acid and hydrogen peroxide have short half-lives under currently registered use conditions. While under controlled conditions, the kinetics slightly favor the formation of peracetic acid. However, under use conditions, the thermodynamic properties become dominant, favoring the breakdown of peracetic acid and hydrogen peroxide. It is expected that when these compounds are used according to the labeled antimicrobial uses, peracetic acid and hydrogen peroxide will completely break down within hours. Further information is provided in Appendix B.

Peroxyoctanoic Acid

Due to the highly reactive nature of peracetic acid with metals and organics, peroxyoctanoic acid is expected to degrade rapidly into its degradation products, hydrogen peroxide and octanoic acid. Based on the use patterns of peroxyoctanoic acid, the Agency does not expect environmental exposure to peroxyoctanoic acid. All labeled uses result in down-the-drain exposure to WWTPs where peroxyoctanoic acid is not expected to be released into the environment, given its half-life of <20 minutes.

Octanoic acid is a naturally occurring fatty acid and will be readily utilized by animals, plants, and microbial organisms as a source of carbon and energy (Ecolab, 2000). The Agency has previously issued a registration review Final Decision for octanoic acid (US EPA, 2008a). No risk assessment was considered necessary based on octanoic acid being of low toxicity, highly biodegradable, and found extensively in nature. The docket for octanoic acid (case 5028) is available at http://www.regulations.gov in docket number EPA-HQ-OPP-2008-0477. Aquatic

organisms in surface waters downstream of both direct and indirect sources of peroxyoctanoic acid would be expected to be exposed primarily to octanoic acid.

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

Further information can be found in Appendix B.

Sodium Percarbonate

Sodium percarbonate consists of a hydrogen peroxide loosely held in place with the carbonate and sodium counterions. Upon exposure to moisture, these counterions immediately release the hydrogen peroxide. Therefore, exposure to sodium percarbonate is considered the same as that of hydrogen peroxide. The antimicrobial uses of sodium percarbonate are not anticipated to result in significant exposure to non-target organisms due to the rapid breakdown into hydrogen peroxide and sodium carbonate. Further information is provided in Appendix B.

3.1.2 Degradates of Potential Concern

There are no degradates of potential concern for any of the peroxy compounds.

3.1.3 Water Quality – Total Maximum Daily Load (TMDL)

Hydrogen peroxide, peracetic acid, peroxyoctanoic acid, and sodium percarbonate are not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[5]. In addition, no Total Maximum Daily Loads (TMDL) have been developed for peroxyoctanoic acid.[6] More information on impaired water bodies and TMDLs can be found at the Agency's website[7].

The National Water Quality Monitoring Council's Water Quality Portal[8] was queried on January 23rd, 2020 and water monitoring data were not found for the peroxy compounds.

3.2 Aquatic Exposure

Products containing peroxy compounds are registered as antimicrobials for use on hard, non-porous surfaces (*i.e.,* floors, drains, toilet bowls, spas, food processing lines), in laundries, and in dental water lines. The use of these products could result in down-the-drain (DtD) exposure

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

when the products are rinsed off surfaces or when the laundries are drained. The water containing these products would then proceed to a municipal wastewater treatment plant (WWTP). Likewise, recirculating cooling tower and pulp and paper mills utilize products containing peroxy compounds, and the blowdown or effluent water would proceed to an industrial or municipal WWTP before environmental release. Finally, some peroxy products have antimicrobial use sites, such as once-through cooling water towers, that could result in direct discharge to aquatic areas without wastewater treatment.

Based on the environmental fate properties of peroxy compounds, aquatic and environmental exposure are not expected from these antimicrobial products. In the presence of water, the AIs readily hydrolyze and rapidly break down to hydrogen peroxide (which rapidly degrades into oxygen and water upon contact with organic matter) and respective associated compounds (e.g., acetic acid, octanoic acid, and sodium carbonate), all of which are not of toxicological concern. This degradation is expected to occur rapidly, within the time-frame of the use pattern and/or WWTP processes. Therefore, environmental risk from antimicrobial uses of peroxy compounds are assessed qualitatively.

3.3 Ecological Effects

3.3.1 Ecotoxicity Data

Various guideline studies have been submitted to the Agency for review. These include studies performed on technical grade active ingredients (TGAIs) as well as end-use products (EPs) and utilized the following active ingredients: sodium percarbonate, hydrogen peroxide, products containing peracetic acid and hydrogen peroxide in equilibrium, potassium peroxymonosulfate, and potassium peroxymonosulfate sulfate. The studies are summarized in Table 21. Individual studies are detailed within Appendix C.

Peroxyoctanoic Acid (PC Code 063209)

The Agency has various products registered containing peroxyoctanoic acid. No ecotoxicity data are available to the Agency under this PC code.

Sodium Percarbonate (PC Code 128860)

Sodium percarbonate was found to be practically non-toxic to freshwater fish and slightly toxic to freshwater invertebrates. Additionally, a product containing 44% sodium percarbonate was found to be practically non-toxic to bees.

Hydrogen Peroxide (PC Code 000595)

Products containing 18-35% hydrogen peroxide as an active ingredient were found to be slightly toxic to birds, freshwater fish, and freshwater invertebrates. Information on chronic toxicity to freshwater fish and invertebrates is available in Appendix C.

Peroxy Compound Mixes (PC Codes 063201 and 000595)

The majority of studies submitted in support of the peroxy compounds case were performed on end-use products (EPs) containing peracetic acid and hydrogen peroxide in equilibrium. Since these chemicals are in equilibrium, the Agency is unable to determine which chemical is causing the toxic effect to tested species. Therefore, the Agency evaluated the studies from the product level. Some studies presented endpoints based on the nominal or measured product while others presented endpoints based on nominal or measured concentrations of peracetic acid. Therefore, Appendix C contains two endpoint tables for these mixtures.

Endpoints from the product-specific studies found the products to be practically non-toxic to bees; slightly toxic to birds and freshwater fish; moderately toxic to freshwater invertebrates, estuarine/marine invertebrates, and bivalves; and showed toxicity to aquatic vascular plants at levels above 1 ppm and to aquatic non-vascular plants at levels below 1 ppm. Information on chronic toxicity to estuarine/marine fish and effects on seedling emergence in terrestrial plants is available in Appendix C.

The studies that presented endpoints based on peracetic acid found the products to be moderately toxic to estuarine/marine fish; highly toxic to freshwater fish, freshwater invertebrates, estuarine/marine invertebrates, and bivalves; and showed toxicity to aquatic non-vascular plants at levels below 1 ppm. Information on chronic toxicity to freshwater fish and both estuarine/marine fish and invertebrates is available in Appendix C.

Potassium Peroxymonosulfate (PC 063604) and Potassium Peroxymonosulfate Sulfate (PC 063607)

For potassium peroxymonosulfate, one chronic study for estuarine/marine fish has been submitted to the Agency and is summarized in Appendix C.

Potassium peroxymonosulfate sulfate was found to be moderately toxic to freshwater invertebrates, slightly toxic to freshwater fish, and toxic to aquatic non-vascular plants at 1.0 ppm (Appendix C). No products are currently registered for potassium peroxymonosulfate sulfate under PC 063607.

Because the modes of action for potassium peroxymonosulfate and potassium peroxymonosulfate sulfate are to react with the sodium chloride to create hypochlorous acid, potential environmental risks to potassium peroxymonosulfate and potassium peroxymonosulfate sulfate will be addressed in the hypochlorous acid case.

Table 21: Ecotoxicity Classifications by Peroxy Compounds[1]

Receptor Group	Sodium Percarbonate (PC Code 128860)	Hydrogen Peroxide (PC Code 000595)	Products with Peroxy Compounds in Equilibrium (PC Codes 063201 and 000595)		Potassium Peroxy-monosulfate Sulfate (PC Code 067607)[2]
	Classification for AI	Classification for Product	Classification for Product	Classification for peracetic acid	Classification for AI
Birds	--	Slightly Toxic	Slightly Toxic	--	--
Bees	Practically Non-toxic (product)	--	Practically Non-toxic	--	--
Freshwater Fish	Practically Non-toxic	Slightly Toxic	Slightly Toxic	Highly Toxic	Slightly Toxic
Estuarine/ Marine Fish	--	--	--	Moderately Toxic	--
Freshwater Invertebrates	Slightly Toxic	Slightly Toxic	Moderately Toxic	Highly Toxic	Moderately Toxic
Estuarine/ Marine Invertebrates	--	--	Moderately Toxic	Highly Toxic	--
Bivalves	--	--	Moderately Toxic	Highly Toxic	--
Aquatic Vascular Plants	--	--	> 1 mg/L	--	--
Aquatic Non-Vascular Plants	--	--	< 1 mg/L	< 1 mg/L	1.0 mg/L

1. Individual studies are detailed within Appendix C
2. Active ingredient reacts with the sodium chloride to create hypochlorous acid, not peroxy compounds

3.4 Ecological Risk Characterization and Conclusions

No ecological risks are expected from the registered antimicrobial uses of peroxy compounds (peroxyoctanoic acid, sodium percarbonate, hydrogen peroxide, and peracetic acid) due to minimal environmental exposure expected for terrestrial and aquatic non-target organisms.

3.5 Major Uncertainties and Ecotoxicity Data Gaps

There are no ecological data gaps for peroxy compounds.

3.6 Ecological Incident Data

The Incident Data System (IDS) was searched on November 22, 2019. One ecological incident was reported involving plant damage from a registered use of hydrogen peroxide on potato seedlings in 2001.

4. LISTED SPECIES OF CONCERN

Due to the nature of the antimicrobial use patterns and environmental fate properties of peroxy compounds, environmental exposure to peroxy compounds is expected to be negligible. No reasonable expectation of direct or indirect adverse effects to threatened or endangered species nor adverse modification of any designated critical habitat for such species is expected from the antimicrobial uses of peroxy compounds. Therefore, for the antimicrobial uses, the Agency is making a "no effect" determination under the Endangered Species Act (ESA) based on low expected of exposure from the antimicrobial uses.

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APPENDIX A: Toxicology Profile

The acute toxicity studies for hydrogen peroxide, peracetic acid, and sodium percarbonate are summarized in Tables A1-A3, respectively. The technical form of the peroxy compounds are corrosive to the skin at high concentrations and irritating to the skin (Toxicity Category I), except for sodium percarbonate which is slightly irritating (Category IV). All the peroxy compounds are strong eye irritants (Toxicity Category I). Acute oral toxicity is Toxicity Category III and appears to be less of a concern for peroxy compounds than other exposure routes for pesticidal use. Exposure via the inhalation route is moderately irritating to the lungs for hydrogen peroxide (Toxicity Category II). Dermal sensitization studies for technical products were waived for hydrogen peroxide and peracetic acid due to the strong irritant properties at high concentrations US EPA, 1993). Sodium percarbonate does not appear to be a dermal sensitizer.

In the 2016 Peroxyoctanoic Acid PWP, the Agency decided that because of the similarity of peroxyoctanoic acid to other peroxy compounds, acute toxicity testing was not required and that acute toxicity data supporting the registration of the other peroxy compound active ingredients, particularly hydrogen peroxide, are also applicable to peroxyoctanoic acid.

Table A1: Acute Toxicity Studies for Hydrogen Peroxide[1]

Guideline No./ Study Type	Results	Toxicity Category
870.1100 Acute oral toxicity (mouse)	LD_{50} = 2000 mg/kg	III
870.1200 Acute dermal toxicity (rat)	LD_{50} = 4060 mg/kg	III
870.1300 Acute inhalation toxicity (mouse)	LC_{50} = 227 µl/L	II
870.2400 Acute eye irritation (rabbit)	Severe irritation	I
870.2500 Acute dermal irritation (rabbit)	Corrosive	I
870.2600 Skin sensitization	Waived	

1. Sax, *et al* (1989) cited in 1993 RED

Table A2: Acute Toxicity Studies for Peracetic Acid[1]

Guideline No./ Study Type	Results	Toxicity Category
870.1100 Acute oral toxicity (rat)	LD_{50} = 1540 mg/kg	III
870.1200 Acute dermal toxicity (rabbit)	LD_{50} = 1410 mg/kg	II
870.1300 Acute inhalation toxicity (rat)	LC_{50} = 0.450 mg/L	II
870.2400 Acute eye irritation (rabbit)	Severe irritation	I

Guideline No./ Study Type	Results	Toxicity Category
870.2500 Acute dermal irritation (rabbit)	Corrosive	I
870.2600 Skin sensitization	Waived	

1. Sax *et al* (1989) cited in 1993 RED

Table A3: Acute Toxicity Studies for Sodium Percarbonate[1]

Guideline No./ Study Type	Results	Toxicity Category
870.1100 Acute oral toxicity (rat)	LD50 > 1526 mg/kg	III
870.1200 Acute dermal toxicity (rat)	LD50 > 5,000 mg/kg	IV
870.1300 Acute inhalation toxicity (rat)	Waived for the biochemical products based on non-respirable large particle size (350- 550 µm) in granular formulation. Previously granted waiver is no longer appropriate for antimicrobial use patterns where people are potentially exposed to hydrogen peroxide. **Antimicrobial Data Gap[2]**	
870.2400 Primary eye irritation (rabbit)	Severely irritating	I
870.2500 Primary dermal irritation (rabbit)	Slightly irritating	IV
870.2600 Dermal sensitization (guinea pig)	Not a skin sensitizer	

1. Sodium Percarbonate PWP, 2017
2. The acute inhalation toxicity study is identified as a data gap but is not needed for the registration review risk assessment.

Table A4. Existing Toxicological Points of Departure and Endpoints for Hydrogen Peroxide[1]

Exposure Scenario	POD for Risk Assessment	Target MOE[B]	Studies and Observed Effects (Both studies are co-critical)
Short-term (0 to 30 Days) and Intermediate-term (30 Days to 6 Months)	NOAEC = 10 mg/m^3 8 Hour HEC[A] = 7.5 mg/m^3	UF_A = 3 UF_H = 10 Total UF = 30 (Target MOE)	28-day rat inhalation study (CEFIC Peroxygen Sector Group, 2002) 90-day rat inhalation study (MRID 49469301) NOAEC = 10 mg/m^3 (highest dose tested from the 90-day study). LOAEC = 14.6 mg/m^3 (mid-dose from the 28-day study) based on the necrosis and inflammation of squamous epithelium and anterior of the nasal cavity (3/5 M and 2/5 F).
Long-term Exposure (Greater than 6 months)	24 Hour HEC[A] = 2.5 mg/m^3	UF_A = 3 UF_H = 10 UF_D = 10 Total UF = 300 (Target MOE)	

Source: US EPA, 2019
A. HEC = NOAEC (mg/m^3) * Animal Exposure (6 hours/day) / Human Exposure (8 or 24 hours/day) * RGDR (1.0)
B. These target MOEs apply to both occupational and residential exposures.
Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEC = no observed adverse effect concentration. LOAEC = lowest observed adverse effect concentration. UF = uncertainty factor. UFA = extrapolation from animal to human (interspecies). UFH = potential variation in sensitivity among members of the human population (intraspecies). UFD = use of a short-term study for long-term risk assessment. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table A6. Summary of Human Health Assessment Data for Sodium Percarbonate[1]

Harmonized Guideline Number	Data Requirement	Results (and Toxicity Category)	MRID No. or Other Source
870.3550	Immunotoxicity	Waived based on the lack of systemic effect of hydrogen peroxide in 90-day oral studies performed in rats and in sensitive catalase-deficient mice.	47499502 HERA, 2002
870.3100	90-Day Oral (one species)	Waived based on the lack of systemic effect of hydrogen peroxide in 90-day oral studies performed in rats and in sensitive catalase-deficient mice.	47499502 HERA, 2002
870.3250	90-Day Dermal – Rat	Waived as significant or prolonged human exposure to sodium carbonate by the dermal route is not anticipated based on the label use instructions.	47499502
870.3465	90-Day Inhalation – Rat	Originally waived due to the fact that the parent AI is a granular formulation too large (350-550 μm) to be inhaled and no repeated inhalation exposures are expected for biopesticide/agricultural uses. This previously granted waiver on parent AI is no longer appropriate for antimicrobial use patterns where people are potentially exposed to hydrogen peroxide.[2]	47499502
870.3700	Prenatal Developmental – Rat Preferably	Waived because hydrogen peroxide (active metabolite formed on contact with moisture) is degraded enzymatically upon absorption and is not systemically available.	47499502
870.4100	Chronic Toxicity	N/A – 90-day studies waived & chronic toxicity of hydrogen peroxide (active metabolite of AI) known in public literature[3]	

Harmonized Guideline Number	Data Requirement	Results (and Toxicity Category)	MRID No. or Other Source
870.4200	Carcinogenicity	N/A – Potential for carcinogenicity of hydrogen peroxide (active metabolite of AI) known in public literature[4]	
870.5100	Bacterial Reverse Mutation Assay	Waived as hydrogen peroxide (active metabolite) is not genotoxic *in vivo* based on studies evaluated by the EU and the known rapid metabolism of hydrogen peroxide in the body.	47499502 EU, 2002
870.5300 870.5375	*In vitro* Mammalian Cell Assay	Waived because hydrogen peroxide (active metabolite of sodium percarbonate) is genotoxic *in vitro*, but not *in vivo* based on studies evaluated by the EU and the known rapid metabolism of hydrogen peroxide in the body	47499502

1. Sodium Percarbonate PWP, 2017
2. This identified data gap was addressed in US EPA, 2019
3. The MAK Collection for Occupational Health and Safety, 2012.
4. IARC, 1999.

APPENDIX B: Environmental Fate Profile

Hydrogen Peroxide

Hydrogen peroxide is a strong, short-lived oxidizer that is not expected to volatilize in the presence of water based on its low Henry's law constant of 7.4×10^{-9}. The chemical is also not expected to bioaccumulate due to its estimated log K_{ow} of -1.57. It is estimated that 99.3% of hydrogen peroxide is removed during wastewater treatment and rapidly degrades in sediment (EU Assessment Report, 2003). Hydrogen peroxide is not expected to photodegrade in the aquatic environment as it is not decomposed by infrared light (EU Assessment Report, 2003). Hydrogen peroxide has a half-life of a few minutes to hours in municipal wastewater and only a few seconds in sludge (EU Assessment Report, 2003). Hydrogen peroxide is expected to biodegrade to water and oxygen prior to discharge from WWTPs. Therefore, little to no exposure to hydrogen peroxide is expected.

Peracetic acid

Peracetic acid is not manufactured as a pure compound but instead in equilibrium as a mixture with water, hydrogen peroxide, and acetic acid. In the pH range of 5.5 to 9.0, peracetic acid may be consumed by the following mechanisms: spontaneous decomposition, metal ion decomposition, and hydrolysis. Peracetic acid is expected to have a hydrolytic half-life of 46.7 hours, 31.7 hours, and 3.6 hours at pH 5, 7, and 9, respectively (EU Assessment Report, 2015).

There is limited data available in the open literature regarding the specific kinetics of the degradation of peracetic acid on a surface. Much of what is available is calculated based on sealed containers or under very specific circumstances unrelated to hard surfaces, or highly dependent on the particular ratio of components in the formulation. As such, it is not possible to provide quantitative justification for the degradation based upon the reaction kinetics at this time.

Decomposition of peracetic acid is spontaneous (Figure B1) and is influenced primarily by temperature and pH. At room temperature and an expected solution pH of ~ 3-3.5, literature data indicates that the peracetic acid solution would be expected to degrade slowly over the course of several weeks. However, that assumes the peracetic acid is in a sealed, stable environment. Peracetic acid is a very strong oxidizing agent and will react with almost any commercial or residential surface it is exposed to and even leach metal ions from stainless steel. Once equilibrium is disturbed, decomposition will begin. Even in sealed, stable form, the compound begins to degrade within days to weeks.

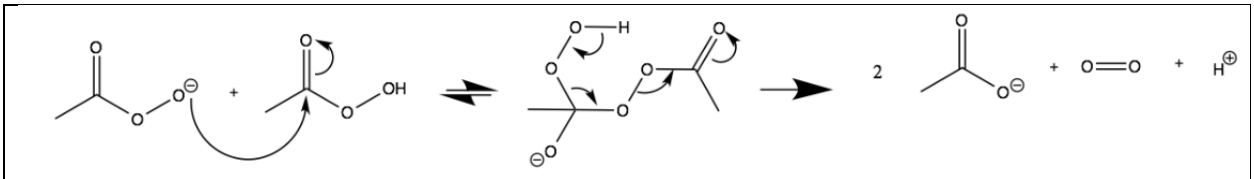

Figure B1: Mechanism of spontaneous decomposition of peracetic acid with peracetic ion

At high concentrations, this decomposition may be self-sustaining. At typical use concentrations, it is not anticipated that the reaction will be self-sustaining. Instead, the peracetic acid will react with nearly everything it comes into contact with: microbes, the surface, and the air. The strength of this oxidizing agent (E^0 = 1.762 V vs Ag/AgCl) means that the localized concentration will decrease rapidly in real world use. This is particularly visible in the vapor phase. Airborne peracetic acid vapors have a half-life of about 20 minutes at ambient temperature.

The temperature of application is often 40-60°C. While specific numbers are indeterminate from the literature, there is a consensus that increased temperatures such as these would lead to more rapid decomposition.

Peracetic acid also degrades from hydrolysis (Figure B2). Peracetic acid exists in a quasi-stable equilibrium with hydrogen peroxide and acetic acid. Hydrolysis is accelerated by increasing temperature and more so by increasing pH. From a kinetics standpoint, adding increased amount of one of the reagents (in this case, water from the potable water rinse) drives the reaction forward towards the products of acetic acid and hydrogen peroxide. The peroxide similarly degrades rapidly, and acetic acid is degraded by aerobic microbes and is of concentrations not of toxicological concern.

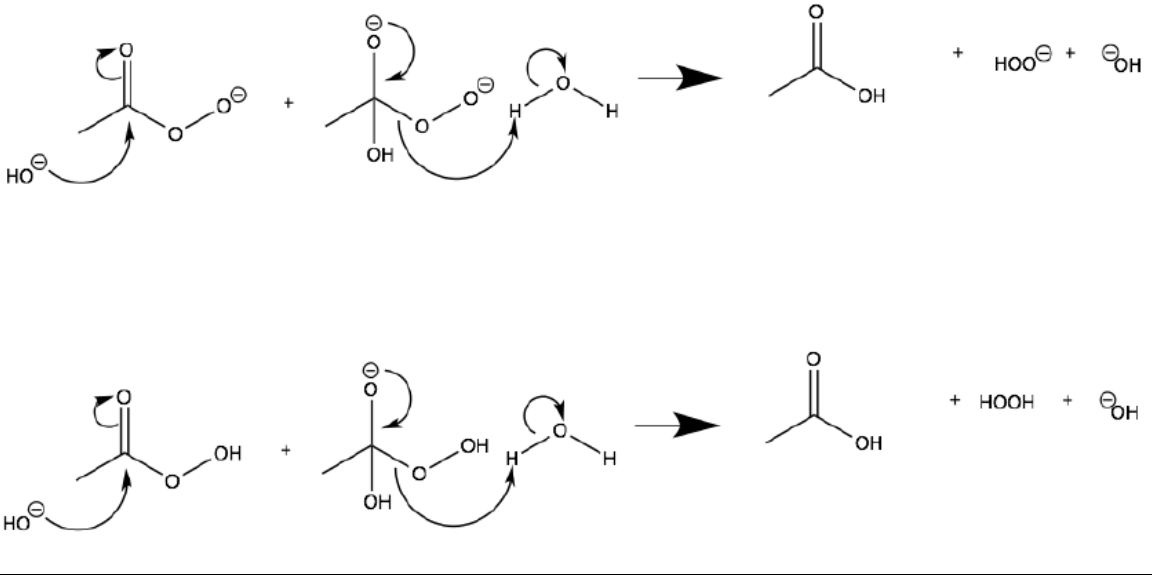

Figure B2. Hydrolysis mechanism of peracetic acid and peracetic ion

As with the decomposition reaction, while no specific numbers are available for this use, increased temperature promotes hydrolysis of peracetic acid.

Commercially produced peracetic acid, particularly in diluted forms, contains stabilizers designed to act as chelating agents to prevent the peracetic acid from undergoing transition metal-catalyzed decomposition. The stabilizers help preserve the peracetic acid from decomposing in the container before use and are not in sufficient concentrations to preserve the

peracetic acid once the container is breeched and the peracetic acid is exposed to the surface. Upon container breech, the peracetic acid will degrade primarily via decomposition and hydrolysis. After use it is expected that peracetic acid will come in contact with metal ions in the environment, which will catalytically degrade the peracetic acid into its degradates.

Peroxyoctanoic Acid

Much of the Agency's database on peroxyoctanoic acid, octanoic acid, and hydrogen peroxide has been drawn from open literature. Peroxyoctanoic acid reacts rapidly with metals and organics to form octanoic acid and hydrogen peroxide as degradates.

Peroxyoctanoic acid is expected to have the same half-life of peracetic acid because hydrolysis is associated with the functional group and not the carbon chain. Octanoic acid has no hydrolysable functional groups; therefore, hydrolysis is not expected to be an important environmental fate process (Lyman, 1990).

Peroxyoctanoic acid is used in products that would be expected to be released down-the-drain to WWTPs. Chemicals that are released down-the-drain can typically take several hours to reach wastewater treatment plant intakes following their discharge and from several hours to roughly a day following their discharge down-the-drain to subsequently be discharged from wastewater treatment plants to surface water. Peracetic acid has a half-life of 3 minutes in sewage sludge (E.U. Assessment Report, 2015).

Based on the similar molecular structures of peracetic acid and peroxyoctanoic acid, peroxyoctanoic acid is expected to have a half-life of <20 minutes in WWTPs. Chemicals that are released down-the-drain can typically take from a few to several hours to reach wastewater treatment plant intakes and from several hours to roughly a day following their discharge down-the-drain to subsequently be discharged from wastewater treatment plants to surface water; therefore, no acute or chronic exposure is expected from peroxyoctanoic acid.

Aquatic organisms in surface water downstream of both direct and indirect sources of peroxyoctanoic acid would be expected to be exposed primarily to octanoic acid. A final registration review decision was made for Octanoic Acid (Case 5028) and it was determined that octanoic acid posed no toxicological or ecological risks from its uses and no further data or risk assessments would be needed (docket EPA-HQ-OPP-2008-0477). Octanoic acid is classified as a saturated fatty acid, a group of substances which is completely biodegradable and found extensively in nature. Specifically, octanoic acid occurs in a number of plants, and animal sources such as animal oils, fats, butter, coconut oil, *etc*. It is a food-grade substance, non-volatile and relatively inert to aqueous hydrolysis. It is a minimal risk and low concern inert, a normal constituent in animal diet and is readily metabolized by all forms of life. Microorganisms rapidly degrade fatty acids in soil. The breakdown products of fatty acids are expected to be carbon dioxide and water. No risk assessment was considered necessary because octanoic acid has low toxicity, is highly biodegradable, and is found extensively in nature.

Sodium Percarbonate

Sodium percarbonate is a non-complex chemical and its physical and chemical characteristics are well understood (U.S. EPA, 2002). In the presence of water, the granules or crystals of sodium percarbonate are dissolved and transformed into hydrogen peroxide and sodium carbonate. Upon contact, the hydrogen peroxide oxidizes its target while breaking down into water and oxygen, neither of which is of toxicological concern.

An environmental risk assessment is not needed for antimicrobial uses. The end-use products are mainly used to control bacteria, algae, moss, and slime molds and are sold for indoor and outdoor horticultural, agricultural, residential, and commercial use sites, in addition to use in and around water bodies. When applied in accordance with label directions, the unstable nature of the chemical accounts for the use of the product without expected harm to birds and other terrestrial animal species. In the presence of water, the active ingredient rapidly breaks down to hydrogen peroxide and sodium carbonate, and hydrogen peroxide rapidly breaks down, on contact, to water and oxygen, neither of which presents toxicological concern. When considering the uses for associated with sodium percarbonate, harm to aquatic species, freshwater fish and freshwater aquatic invertebrates is not foreseen. For non-target plants, submitted data from the open literature allowed EPA to grant waivers for required studies as specified in OPP Guideline 154.10, provided the label directs that any treated turf grasses be tested for phytotoxicity prior to application, and that repeated applications may cause the possible elevation of the pH of the soil that may adversely affect plant growth. A waiver for studies testing non-target insects and honey bee acute contact toxicities was also granted, provided that precautionary statements or mitigating language is present on the labels.

APPENDIX C: Ecotoxicity Profile

Peroxyoctanoic Acid (PC Code 063209)

The Agency has various products registered containing peroxyoctanoic acid (POOA, PC Code 063209). No ecotoxicity data are available to the Agency under this PC code.

Sodium Percarbonate (PC Code 128860)

For sodium percarbonate (PC Code 128860), various studies have been submitted to the Agency and are summarized in Table C1. These studies indicated sodium percarbonate was practically non-toxic to freshwater fish and slightly toxic to freshwater invertebrates; a product containing 44% sodium percarbonate was found to be practically non-toxic to bees.

Table C1: Ecological Effects Endpoints for Sodium Percarbonate (PC 128860) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint	Toxicity Category	Reference
Freshwater fish (850.1075)	Rainbow trout (*Oncorhynchus mykiss*)	96-h NOEC >120 mg AI/L (measured[1])	Practically Non-toxic	46667311 (Acceptable) Static 46806402 (Supplemental Information)
	Rainbow trout (*Oncorhynchus mykiss*)	96-h EC_{50} = 150 mg/L product (nominal)[2] NOEC = 110 mg/L product	Practically Non-toxic	MRID 45554901 (Acceptable) Static
Freshwater invertebrates (850.1010)	Daphnid (*Daphnia magna*)	48-h EC_{50} = 12 mg AI/L (measured) NOEC = 6.9 mg AI/L	Slightly Toxic	46667312 (Acceptable) Static
	Daphnid (*Daphnia magna*)	48-h EC_{50} = 14 mg AI/L (nominal) NOEC = 7.2 mg AI/L	Slightly Toxic	MRID 45771601 (Acceptable) Static
Non-target terrestrial insects (850.3020)	Honey bee (*Apis mellifera*)	LC_{50} >125 µg product[3] per bee	Practically Non-toxic	49184701 (Acceptable)

LC_{50} = Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/L, mg/kg or ppm.
EC_{50} = Median Effective Concentration. A statistically derived concentration of a substance that can be expected to cause a 50% reduction in either algae growth, algae growth rate, or daphnid immobilization.
NOEC = No Observed Effect Concentration

1. MRID 46667311 had no analytics available. MRID 46806402 provided information from the daphnid study that showed the AI became more stable as doses increased (95% recovery at the 60 mg/L nominal dose). The fish study was done at levels greater than the daphnid study and therefore was expected to be stable.
2. Product contained sodium percarbonate (CAS No. 15630-89-4) and sodium carbonate (CAS No. 497-19-8), but the concentrations of each were not provided. The study tested the whole product and presented the nominal values.

3. The product (Ato Cide II) consists of 44% sodium percarbonate, 20.8% tetraacetylethylenediamine (TAED), 9.93% sodium, potassium silicates.

Hydrogen Peroxide (PC Code 000595)

For hydrogen peroxide (PC Code 000595) as an active ingredient, various studies have been submitted to the Agency, most of which have undergone full Agency review and classification.[9] These studies are summarized in Table C2. Products containing 18-35% hydrogen peroxide as an active ingredient were found to be slightly toxic to birds, freshwater fish, and freshwater invertebrates. Chronic endpoints for both freshwater fish and invertebrates are likewise available.

[9] Full Agency review and classification involved a determination is the study is "Core", "Acceptable", "Supplemental", or "Invalid" and whether the study may be used for quantitative assessments. For the peroxy compounds not all studies have undergone full review and classification because the studies are being utilized qualitatively.

Table C2: Ecological Effects Endpoints for Products Containing Only Hydrogen Peroxide as the Active Ingredient (PC Code 000595) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Toxicity Category of the Product	Reference
Avian Acute Oral (850.2100)	Mallard Duck (*Anas platyrhynchos*)	LD_{50} = 1,049 mg Product/kg-bw	35% H_2O_2	Slightly Toxic	MRID 00153758 (Core)
Avian Dietary (850.2200)	Mallard Duck (*Anas platyrhynchos*)	LC_{50} > 5,000 ppm Product	35% H_2O_2	Practically Non-toxic	MRID 00153757 (Core)
	Bobwhite quail (*Colinus virginianus*)	LC_{50} > 5,000 ppm Product	35% H_2O_2	Practically Non-toxic	MRID 00153756 (Supplemental)
Freshwater fish acute (850.1075)	Rainbow trout *(Salmo gairdneri*)	96-Hr LC_{50} = 93 mg/L Product	35% H_2O_2	Slightly toxic	MRID 00153761 (Core) Static
	Fathead minnow (*Pimephales promelas)*	48-hr LC_{50} = 785 mg/L Product	18% H_2O_2	Practically Non-toxic	MRID 46671934 Static
	Bluegill sunfish (*Lepomis macrochirus*)	96-Hr LC_{50} = 150 mg/L Product	35% H_2O_2	Practically Non-toxic	MRID 00153760 (Core) Static
Freshwater fish chronic (850.1400)	Fathead minnow (*Pimephales promelas)*	7-day NOEC (survival) > 500 mg/L Product 7-day NOEC (growth) > 250 mg/L Product	18% H_2O_2	NA	MRID 46671935 Static Renewal
Freshwater Invertebrates Acute (850.1010)	Daphnid (*Daphnia magna*)	48-Hr LC_{50} = 24 mg/L Product	35% H_2O_2	Slightly toxic	MRID 00153759 (Supplemental) Static
	Water Flea (*Ceriodaphnia dubia*)	48-hr LC_{50} = 139 mg/L Product	18% H_2O_2	Practically Non-toxic	MRID 46671932 Static
Freshwater Invertebrates Chronic (850.1300)	Water Flea (*Ceriodaphnia dubia*)	7-day NOEC (survival) > 200 mg/L Product 7-day NOEC (reproduction) > 200 mg/L Product	18% H_2O_2	NA	MRID 46671933 Static Renewal

NA: Not applicable. Chronic studies do not have a toxicity category.

Peroxy Compound Mixes

Various studies performed using products containing peroxy compounds in equilibrium (peracetic acid and hydrogen peroxide), have been submitted to the Agency. Most of these studies are cited under PC Codes 063201 and 000595, and all have undergone a full Agency review and classification.

Since the chemistries contained within these products are in equilibrium, the Agency is unable to determine which chemical is causing the toxic effect to tested species. Therefore, the Agency evaluated the studies from the product level. However, certain studies presented endpoints based on the product while others presented endpoints based on peracetic acid. Therefore, two tables have been constructed and each table indicates the % AI concentration within the product (if available).

Table C3 contains studies that tested nominal and/or measured concentrations of products. The endpoints indicate the products were practically non-toxic to bees; slightly toxic to birds and freshwater fish; moderately toxic to freshwater invertebrates, estuarine/marine invertebrates, and bivalves; showed toxicity to aquatic vascular plants and marine diatoms at levels above 1 ppm; and showed toxicity to cyanobacteria and freshwater diatoms at levels below 1 ppm. A chronic endpoint for both estuarine/marine fish is likewise available.

Table C4 contains studies that tested products but presented nominal and/or measured concentrations of peracetic acid. The endpoints indicated peracetic acid was moderately toxic to estuarine/marine fish; highly toxic to freshwater fish, freshwater invertebrates, estuarine/marine invertebrates, and bivalves; and showed toxicity to marine diatoms and freshwater algae at levels below 1 ppm. Chronic endpoints for freshwater invertebrates and both estuarine/marine fish and invertebrates, and seedling emergence endpoints for terrestrial plants are likewise available.

Table C3: Ecological Effects Endpoints for Studies Performed on Products with Peracetic acid and Hydrogen Peroxide in Equilibrium. Endpoints Determined on the Whole Product (PC Codes 063201 and 000595) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Toxicity Category of the Product	Reference
Avian Acute Oral (850.2100)	Mallard Duck (*Anas platyrhynchos*)	LD_{50} = 619 mg Product/kg-bw	% AI not given.	Slightly Toxic	MRID 47477201 (Acceptable) Gavage
Freshwater Fish Acute (850.1075)	Rainbow trout *(Salmo gairdneri)*	96-Hr LC_{50} = 13.4 mg/L Product	15% peracetic acid 14% H_2O_2 28% acetic acid	Slightly Toxic	MRID 46833606 (Acceptable) Static Renewal
Estuarine/Marine Fish Chronic (850.1400)	Inland Silverside *(Menidia beryllina)*	7-day LC_{50} = 35.6 mg/L Product	15% peracetic acid, 14.3% H_2O_2	NA	MRID 46833604 (Acceptable) Static Renewal
Freshwater Invertebrates Acute (850.1010)	Daphnid (*Daphnia magna*)	48-Hr LC_{50} = 3.3 mg/L Product	15% peracetic acid, 14% H_2O_2 28% acetic acid	Moderately Toxic	MRID 46833603 (Acceptable) Static
Estuarine/Marine Invertebrates Acute (850.1035)	Mysid (*Americamysis bahia)*	96-Hr LC_{50} > 3.0 mg/L Product	% AI not given.	Moderately Toxic	MRID 47477203 (Acceptable) Static
Bivalve acute toxicity test (embryo larval) (850.1055)	Mediterranean Blue mussel *(Mytilus galloprovincialis)*	48-Hr EC_{50} = 3.7 mg/L Product	15% peracetic acid 24% H_2O_2	Moderately Toxic	MRID 46833604 (Acceptable) Static
	Blue mussel *(Mytilus galloprovincialis)*	48-Hr EC_{50} = 3.68 mg/L product	15% peracetic acid 14% H_2O_2 26.5% acetic acid	Moderately Toxic	MRID 46833605 (Acceptable) Static
Aquatic plant toxicity test using Lemna spp. (850.4400)	Duckweed (*Lemna gibba*)	7-day EC_{50} = 230 mg/L Product (nominal) (biomass)	12.08% peracetic acid 19.44% H_2O_2	NA	MRID 46966604 (Core) Static
	Duckweed (*Lemna gibba*)	7-day EC_{50} = 81 mg/L Product (nominal) (frond density) 7-day EC_{50} = >200 mg/L Product (nominal) (growth rate) 7-day EC_{50}= 67 mg/L Product (nominal) (biomass)	% AI not given.	NA	MRID 47477202 (Acceptable) Static Renewal

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Toxicity Category of the Product	Reference
Alga toxicity (850.4500)	Marine Diatom (*Skeletonema costatum*, strain CCMP 1332)	Cell Density 96-Hr EC_{50}= 27 mg/L Product	12.12% peracetic acid 18.95% H_2O_2	NA	MRID 46966607 (Core) Static
	Marine Diatom (*Skeletonema costatum*)	Cell Density 96-Hr EC_{50}= 19 mg/L Product	% AI not given.	NA	MRID 47477204 (Supplemental) Static
	Freshwater Diatom (*Navicula pelliculosa,* strain 664)	Cell Density 96-Hr EC_{50}= 0.56 mg/L Product	12.12% peracetic acid 18.95% H_2O_2	NA	MRID 46966605 (Core) Static
	Freshwater Diatom (*Navicula pelliculosa*)	Cell Density 96-Hr EC_{50}= 2.3 mg/L Product	% AI not given.	NA	MRID 47477205 (Supplemental) Static
Cyanobacteria Toxicity (850.4550)	Cyanobacteria (*Anabaena flos- aquae*, strain 1444)	Cell Density 96-Hr EC_{50}= 1.5 mg/L Product	12.12% peracetic acid 18.95% H_2O_2	NA	MRID 46966606 (Core) Static
	Cyanobacteria (*Anabaena flos- aquae*)	Cell Density 96-Hr EC_{50}= 0.21 mg/L Product	% AI not given.	NA	MRID 47477206 (Supplemental) Static
Terrestrial Seedling Emergence 850.4100 and 850.4225	Rice (*Oryza sativa* of the Japonica variety)	Percent emergence: EC_{50}= 4700 mg/kg Product Shoot length: EC_{50}> 6000 mg/kg Product Shoot dry weight (mg) EC_{50}= 6200 mg/kg Product	12.08% peracetic acid 19.44% H_2O_2	NA	MRID 46966608 (Core) Static
	Red Rice (*Oryza sativa*)	NOEC= 60 mg/L Product (% emergence, shoot length, and shoot dry weight (mg))	15% peracetic acid 22% H_2O_2	NA	46696003 (Acceptable) Static
Terrestrial Invertebrate-Honeybee Toxicity (850.3020)	Honey Bee (*Apis mellifera*)	96-hr LD_{50} > 25 µg product/bee or	Product was 2.05% peracetic acid 26.93% H_2O_2	Practically Non-Toxic	MRID 49801001 (Acceptable)

NA: Not applicable. Aquatic plants and chronic studies do not have a toxicity category.

Table C4: Ecological Effects Endpoints for Studies Performed on Products with Peracetic acid and Hydrogen Peroxide in Equilibrium. Endpoints Determined Based on Peracetic acid (PC Codes 063201 and 000595) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Toxicity Category of the Product	Reference
Freshwater Fish Acute (850.1075)	Rainbow trout (*Oncorhynchus mykiss)*	96-Hr LC_{50} = 0.72 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696001 (Acceptable) Flow-through
	Fathead minnow (*Pimephales promelas)*	96-Hr LC_{50} = 0.99 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696001 (Acceptable) Flow-through
	Bluegill sunfish (*Lepomis macrochirus*)	96-Hr LC_{50} = 1.21 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Moderately Toxic	MRID 46696001 (Acceptable) Flow-through
Estuarine/Marine Fish Acute (850.1075)	Inland Silverside *(Menidia beryllina)*	96-Hr LC_{50}= 2.17 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Moderately Toxic	MRID 46696002 (Supplemental) Flow-through
Estuarine/Marine Fish Chronic (850.1400)	Inland Silverside *(Menidia beryllina*)	7-day LC_{50} = 0.48 mg/L peracetic acid (Survival) 7-day LC_{50} = 0.36 mg/L peracetic acid (Growth)	15% peracetic acid 22% H_2O_2	NA	MRID 46696002 (Supplemental) Flow-through
Freshwater Invertebrates Acute (850.1010)	Daphnid (*Daphnia magna*)	48-Hr LC_{50}= 0.67 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696001 (Acceptable) Flow-through
	Water Flea (*Ceriodaphnia dubia*)	48-Hr LC_{50}= 0.27 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696001 Flow-through
Freshwater Invertebrates Chronic (850.1300)	Water Flea (*Ceriodaphnia dubia*)	6-day LC_{50} = 0.86 mg/L peracetic acid (Survival) 6-day IC_{50} = 1.03 mg/L peracetic acid (Reproduction)	15% peracetic acid 22% H_2O_2	NA	MRID 46696001 Flow-through
Estuarine/Marine Invertebrates Acute (850.1035)	Mysid (*Mysidopsis bahia)*	96-Hr LC_{50} = 0.65 mg/L peracetic acid (Survival)	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696002 (Supplemental) Flow-through
Estuarine/Marine Invertebrates Chronic (850.1300)	Mysid (*Mysidopsis bahia)*	7-day LC_{50} = 0.34 mg/L peracetic acid NOEC = 0.14 mg/L peracetic acid (Survival and growth)	15% peracetic acid 22% H_2O_2	NA	MRID 46696002 (Supplemental) Flow-through
	Bay Mussel (*Mytilus edulis*)	48-Hr IC_{50} = 0.36 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	Highly Toxic	MRID 46696002 (Supplemental)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Toxicity Category of the Product	Reference
Bivalve Acute Toxicity (embryo larval) (850.1055)		48-Hr IC_{25} = 0.33 mg/L peracetic acid			Static
	Blue mussel *(Mytilus galloprovincialis)*	72-Hr EC_{50} = 0.69 mg/L peracetic acid	Product is a mixture of (>10% - <20%) peracetic acid. (>10% - <20%) H_2O_2, and (>25%-<90%) acetic acid in equilibrium. Tested as if 15% peracetic acid	Highly Toxic	MRID 46833609 (Acceptable) Static
Alga Toxicity (850.4500)	Marine Diatom (*Skeletonema costatum*)	96-Hr IC_{50} = 0.63 mg/L peracetic acid (Growth)	15% peracetic acid 22% H_2O_2	NA	MRID 46696002 (Supplemental) Static
	Freshwater green alga (*Selenastrum capricornutum*)	Cell Density 120-Hr EC_{50} = 0.18 mg/L peracetic acid	5.22% peracetic acid (measured)	NA	MRID 46966609 (Core) Static
	Freshwater green alga (*Selenastrum capricornutum*)	Growth 96-Hr IC_{50} = 0.44 mg/L peracetic acid	15% peracetic acid 22% H_2O_2	NA	MRID 46696001 (Acceptable) Static

NA: Not applicable. Aquatic plants and chronic studies do not have a toxicity category.

Since the modes of action for potassium peroxymonosulfate and potassium peroxymonosulfate sulfate are to react with the sodium chloride to create hypochlorous acid risks to potassium peroxymonosulfate and potassium peroxymonosulfate sulfate will be addressed in the hypochlorous acid case. However, their ecotoxicity endpoints are outlined below.

Potassium Peroxymonosulfate (PC Code 063604)

For potassium peroxymonosulfate (PC Code 063604; CAS No. 10058-23-8. Molecular formula: $K(H_2O_5S)$) one chronic study has been submitted to the Agency and is summarized in Table C5.

Table C5: Ecological Effects Endpoints for Potassium Peroxymonosulfate (PC 063604) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)	AI Mixture in Product	Reference
Estuarine/Marine Fish Chronic Toxicity (850.1400)	Sheepshead minnow (*Cyprinodon variegatus*)	Post-Hatching Survival: NOEC = 444 µg product/L MATC = 628 µg product/L Growth: NOEC = 222 µg product/L MATC = 314 µg product/L	45% AI[A]	MRID 47143401 (Acceptable) Flow-Through

A. The product contains 45% potassium monopersulfate $KHSO_5$, which is another name for potassium peroxymonosulfate.
MATC: Maximum Acceptable Toxicant Concentration, which is calculated as the geometric mean of the NOEC and LOEC values.

Potassium Peroxymonosulfate Sulfate (PC Code 063607)

There are no active registrations for potassium peroxymonosulfate sulfate (PC 063607. CAS No. 70693-62-8, Molecular formula: $K_5H_3(SO_3(O_2))_2(SO_4)_2)$). However, the Agency has various guideline studies for in support of this PC code, all of which have received an Agency classification of "core" (Table C6). These studies indicated potassium peroxymonosulfate sulfate was moderately toxic to freshwater invertebrates, slightly toxic to freshwater fish, and a toxicity to aquatic plants at 1.0 ppm.

Table C6: Ecological Effects Endpoints for Potassium Peroxymonosulfate Sulfate (PC 063607) (Summarized)

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)[1]	Toxicity Category of the Product	Reference
Freshwater Fish Acute (850.1075)	Rainbow trout *(Salmo gairdneri*)	96-Hr LC_{50} = 53 mg/L Product (measured)	Slightly Toxic	MRID 46119001 (Core) Static-renewal
Freshwater Invertebrates Acute (850.1010)	Daphnid (*Daphnia magna*)	48-Hr LC_{50} = 3.5 mg/L Product (nominal)[2]	Moderately Toxic	MRID 46119002 (Core) Static-renewal

Receptor Group	Surrogate Species	Toxicity Endpoint (Product)[1]	Toxicity Category of the Product	Reference
Alga Toxicity (850.4500)	Freshwater green alga (*Selenastrum capricornutum*)	96-Hr LC_{50} = 1.0 mg/L Product (nominal)	NA	MRID 46119003 (Core) Static

1. Product had a purity of 99.665%. Active ingredients: 44.5% potassium monopersulfate, 26.1% potassium sulfate, and 25.1% potassium bisulfate.
2. Tested as nominal because analytical method was insufficiently sensitive to analyze most test concentrations (limit of quantification 10 mg/L and limit of detection 2.0 mg/L). Stock solution was 82-102% of nominal.
NA: Not applicable. Aquatic plants do not have a toxicity category

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