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

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: March 07, 2024

SUBJECT: Registration Review Draft Risk Assessment for 3-iodo-2-propynl butyl carbamate (IPBC)

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This document provides the draft human health and ecological risk assessment conducted in support of the antimicrobial pesticide active ingredient (a.i.) 3-iodo-2-propynl butyl carbamate (IPBC).

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EXECUTIVE SUMMARY

The active ingredient (a.i.), 3-iodo-2-propynl butyl carbamate (IPBC), is registered as an antimicrobial and fungicide used as a wood preservative, materials preservatives, surface coatings and dry film mildewcide. No tolerance or exemptions from the requirement of a tolerance have been established for IPBC.

Human Health Risk Summary

Dietary Risk

There is potential for dietary (food) exposure to IPBC as a materials preservative in dish detergents. Drinking water exposure may occur when effluents from industrial uses, such as paper mills and metal working fluids sites, released upstream of drinking water intakes. There are no risks of concern identified from acute dietary (food) or acute drinking water exposure. For acute (food) exposure, the highest exposed population subgroup were females 13-49 years old at 0.0004 % of the Population Adjusted Dose (aPAD). For acute drinking water exposure, the highest population subgroup were children 1-2 years old at 9% of the aPAD. There are no risks of concern identified from chronic dietary or drinking water exposures. The highest exposed population for dish detergent uses were children 1-2 years old at 0.012% of the chronic Population Adjusted Dose (cPAD), while the highest exposed population for drinking water were for all infants <1 year old at 37% of the cPAD.

Co-occurring acute (food and drinking water) dietary exposures are comprised of the aPAD of 9% for females 13-49 years old, 6% for all infants, and 2% for the general population which are not of concern (<100% aPAD). Co-occurring chronic (food and drinking water) dietary exposures are comprised of the cPAD of 37% for all infants <1 year old, 22% for children 1-2 years old, and 14% for the general population and thus are also not of concern (<100% cPAD).

Residential Risk

There is potential for short-term residential handler dermal and inhalation exposures when using paints preserved with IPBC or when using wood preservative stains, caulks, sealants, or adhesives that contain IPBC. The residential paint handler assessment uses paint as a surrogate use for stains, caulks, sealants, coatings, and adhesives. The margin of exposure (MOE) for inhalation exposure to brush/roller paint application is above the LOC of 30 and is not of concern. The MOE for inhalation exposure to airless spray application of paint is 0.21 and is of concern because it is less than the LOC of 30 for short and intermediate term exposures. If the application rate of paint is reduced to 66.13 ppm a.i., the MOE for the airless spray application of IPBC preserved paint would be 30 and would not be of concern. The MOE for aerosol paint primer is 1.2 and is of concern because it is less than the MOE of 30. If the application rate is

reduced to 58.61 ppm a.i., the MOE for aerosol paint increases to 30 and would not be of concern.

The MOE of 6.7 for dermal exposure to airless spray is less than the LOC of 10 and is of concern. If the application rate is reduced from 9,600 ppm to 6,400 ppm, the MOE increases to 10 and is no longer of concern. The MOEs for dermal exposures to brush and roller applications of paint and the dermal exposure to the application of paint primer are not of concern because they are greater than the dermal LOC of 10.

There is also potential for short-term residential handler dermal and inhalation exposures when using soaps and detergents (including dish soaps), laundry detergent, air fresheners, surface cleaners, ready to use wipes, floor care products, bathroom cleaners, window cleaners, fabric care products (including stain removers, and fabric softeners), and automotive care products. The MOEs for dermal and inhalation exposures are not of concern because they are greater than the LOCs of 10 for dermal and 30 for inhalation.

Residential Post-Application Risks

There is potential for short- and intermediate-term dermal and incidental oral exposures to IPBC preserved floor cleaners, household items and clothing manufactured from treated textiles, and when children play on decks and playsets constructed with wood that has been pressure treated with IPBC. The MOEs are not of concern because they are greater than the corresponding LOCs of 10 for dermal exposure and 100 for incidental oral exposure.

There is potential for short- and intermediate-term dermal exposure to IPBC preserved laundry detergent in adults and incidental oral exposures to IPBC preserved laundry detergent in children (1<2 years old). The MOEs are not of concern because they are greater than the LOCs of 10 for dermal exposure to children and adults and 100 for incidental oral exposure.

There is potential for short- and intermediate-term incidental oral and dermal exposures to polyvinyl chloride (PVC) flooring materials and PVC swimming pool liners preserved with IPBC. The transfer percent was assumed to be 100% transfer of available surface residues and 100% for the applied amount leached into the pool water. The MOEs are not of concern because they are greater than the LOCs of 10 for dermal exposure and 100 for incidental oral exposure.

There is potential for short- and intermediate-term incidental oral and dermal exposure to carpet fibers preserved with IPBC during manufacturing. Since transferable residue data are not available for IPBC-treated carpet fibers, the transfer percent was assumed to be 100% transfer. The dermal MOE of 0.20 is of concern because it is less than the LOC of 10. The MOE would be

10 if the percent transfer was 2% transfer. The incidental oral MOE of 0.24 is of concern because it is less than the LOC of 100. The MOE would be 100 if the transfer was 0.24%(w/w).

Aggregate Assessment

Because the toxicity endpoints of the three routes of exposure (oral [including chronic dietary exposure and incidental oral], dermal, and inhalation) are different for the different routes of exposure and there are different toxicological effects across the different routes of exposures, the three routes of exposure were not aggregated in an assessment.

Occupational Handler Risks

There is potential for short- intermediate-, and long-term occupational handler exposures when IPBC is used to preserve materials such as paints, plastics, textiles, cleaning products, and building materials and when using IPBC-treated articles such as paints and cleaning products. The inhalation MOEs for the open pour of liquid and powder materials preservatives are 18 and 0.41, respectively, both less than the LOC of 30 and are of concern. If the application rates are reduced to 293 ppm and 404 ppm, respectively, the MOEs will increase to 30 and are no longer of concern. The inhalation MOE of 0.006 for the airless spray application of paint is of concern because it is less than the LOC of 30. If the application rate is reduced to 6.28 ppm, the MOE will increase to 30 and is no longer of concern. The MOE of 0.062 for the airless spray application of paint is of concern because it is less than the LOC of 30. If the application rate is reduced to 19.83 ppm the MOE increases to 30 and is no longer of concern. The MOE of 0.78 for the application of aerosol paint primer is of concern because it is less than the LOC of 30. If the application rate is reduced to 38.66 ppm the MOE increases to 30 and is no longer of concern. The inhalation MOE of 79 for the brush/roller application of paint is above the LOC of 30 and therefore not of concern.

The dermal MOEs for the materials preservation use regarding the open pour of liquid and powder are 0.043 and 2.1, respectively, and are of concern because they are less than the LOC of 10. If the application rate for the open pour of liquid is reduced to 1,280 ppm, and the open pour of powder is reduced to 6,225 ppm, the MOEs increase to 10 and are no longer of concern. The dermal MOE of 5.5 for the brush and roller application of paint is of concern because it is less than the LOC of 10. If the application rate of the paint is reduced to 5,240 ppm the MOE increases to 10, and it is no longer of concern. The dermal MOE of 2.02 for the application of airless spray paint is of concern because it is less than the LOC of 10. If the application rate of the paint is reduced to 6,400 ppm, the MOE increases to 10, and it is no longer of concern. The dermal MOEs for the application of paint primer are above the LOC of 10 and therefore are not of concern.

The inhalation MOE of 17 for mopping floors is of concern because it is less than the LOC of 30. If the application rate is reduced to 334 ppm, the MOE increases to 30 and would no longer be of concern. The inhalation MOE of 9.1 for spray and wipe application is of concern because it is less than the LOC of 30. If the application rate of the cleaning product is reduced to 182 ppm, the MOE increases to 30 and is no longer of concern. The MOEs regarding mopping floors in non-hospital facilities and ready-to-use wipes (RTU wipes) are greater than the LOC of 30; therefore, there are no risks of concern for inhalation exposures to IPBC preserved cleaning products from both exposure scenarios.

Occupational handler exposures are anticipated to occur during use of IPBC for immersion or spray treatment of wood for sapstain control. These exposures are anticipated to be short-, intermediate-, and long-term in duration, and they can occur via the dermal or inhalation routes. The MOEs for sapstain control of worker inhalation exposures to IPBC were assessed. The MOE of 3.9 for the Dip Tank Operator job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.237%, the MOE will increase to 30 and is no longer of concern for the Dip Tank Operator function. The MOE of 6.6 for the Millwright job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.397%, the MOE will increase to 30 and is no longer of concern for the Millwright job function. The MOE of 4.8 for the Chemical Attendant job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.286%, the MOE will increase to 30 and is no longer of concern for the Chemical Attendant job function. The MOE of 0.19 for Clean-up Crew is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.011%, the MOE will increase to 30 and is no longer of concern for the Clean-up Crew job function.

The MOEs for sapstain control dermal exposures to IPBC were assessed. The dermal MOE of 3.8 for Clean-Up Crew is of concern because it is lower than the LOC of 10. If the application rate is reduced to 0.67% in treatment solution the MOE will increase to 10 and is no longer of concern. The dermal MOEs for Dip Tank Operator, Millwright, and Chemical Attendant range from 81 to 38, and are greater than the LOC of 10, and are not of concern.

The occupational inhalation exposure is anticipated to occur during the use of IPBC-treated preservatives to pressure treat wood. The MOE of 8.7 for the Treatment Operator job function is of concern because it is less than the LOC of 30. If the application rate is reduced to 0.435%, the MOE increases to 30 and is no longer of concern. The MOE for the Wood Handler job function of 21 is of concern because it is less than the LOC of 30. If the application rate is reduced to 0.107% a.i., the MOE increases to 30 and is no longer of concern.

The occupational dermal exposure is anticipated to occur during the use of IPBC-treated preservatives to pressure treat wood. The MOEs are not of concern because they are greater than the LOC of 10 for dermal exposure.

Occupational Post-Application Risks

There is potential for dermal and inhalation exposures when using IPBC-treated metalworking (MWF) fluids. These exposures are anticipated to be short-, intermediate-, and long-term in duration. The MOE of 7 for inhalation exposures to IPBC-treated metalworking fluids is of concern because it is greater than the corresponding LOC of 30 for inhalation exposure. If the application rate is reduced to 1,230 ppm, the MOE increases to 30 and is not of concern. The dermal MOE of 5.7 is of concern because it is less than the LOC of 10. If the application rate is reduced to 3,000 ppm, the LOC will increase to 10 and is no longer of concern.

Environmental Risk Summary

Of the currently registered IPBC uses, pulp and papermill, MWF, exterior paint and coating, and deck and fence uses are expected to result in the highest environmental exposures and, therefore, are expected to be protective of other registered uses. Little to no terrestrial exposure is expected from any of the currently registered uses for IPBC. Rapid degradation (DT_{50} < 3 hours) of IPBC in soil and its high mobility (K_d < 2.46 mL/g) suggests it would move rapidly through soil to water or degrade on the order of hours, resulting in minimal terrestrial exposure. Therefore, only risks to aquatic taxa are quantified and risks to terrestrial taxa are not expected.

IPBC is considered non-persistent and mobile in soil. The dissipation of IPBC in terrestrial and aquatic environments appears to be dependent on alkaline catalyzed hydrolysis, microbial-mediated oxidative mineralization, and leaching. IPBC was rapidly hydrolyzed ($t_{1/2}$ = 0.947 days) in pH 9 buffer solution; however, it was stable ($t_{1/2}$ > 30 days) in pH 5 and 7 buffer solutions (MRID 40947405 & 42329301). IPBC was rapidly degraded ($t_{1/2}$ < 3 hours) in aerobic mineral soil and anaerobic aquatic environments (MRID 40947405). IPBC is expected to be very mobile to mobile (K_d < 2.46 mL/g) in mineral soils (MRID 41975207). Leaching of IPBC from a range of exterior paints was studied over a period of 842 days (28 months) with a total rainfall amount of 52 inches (1348 mm) (MRID 51530601). The maximum amounts of IPBC that leached were 8.3%, 4.1%, and 6.4% for Masonry Paint Application Products, Wood Stain Application Products, and Wood Paint Application Products, respectively. The primary degradate of IPBC was isopropargyl butyl carbamate (PBC). However, based on environmental fate and expected similarity in ecotoxicity between the parent and degradate, the stressor of concern is the parent compound, IPBC (see Section 3.1.2 for more details).

IPBC is found to be slightly toxic to birds on an acute oral basis, and practically non-toxic to slightly toxic on a sub-acute dietary basis. For aquatic species, on an acute basis, IPBC is highly to very highly toxic to freshwater fish; highly toxic to freshwater invertebrates; highly toxic to estuarine/marine fish and highly to very highly toxic to estuarine/marine invertebrates. Algal

toxicity data shows an EC_{50} of 65.8 µg/L based on area under the growth curve. Although acceptable data for aquatic vascular plants are not available, a study with *Lemna gibba* (MRID 51215602) shows that IPBC can cause significant effects in frond number yield, frond number growth rate, final biomass, and biomass growth rate at concentrations around 72 µg/L. However, the study is classified as supplemental qualitative due to numerous deficiencies within the study. Therefore, a new study would be needed to quantify risk to this taxon. Additionally, the chronic daphnid study submitted (MRID 50938202) is classified as supplemental qualitative because of numerous deficiencies including that effects were observed at the lowest concentration tested (3.0 µg/L); thus, a NOAEC could not be defined. A new study would be needed to attain a definitive NOAEC.

Acute and chronic risks of concern from IPBC use in pulp and papermills and MWFs are expected for all aquatic nontarget receptor groups (fish, aquatic invertebrates, and aquatic nonvascular plants) modeled under average-flow and low-flow scenarios for the majority, if not all, of the year. Although, the Agency made the conservative assumption that 0% of IPBC was removed through wastewater treatment due to a lack of data, greater than 99% reduction would be needed to result in no risk to nontarget organisms from pulp and papermill and MWF uses. The Agency therefore expects risk to all aquatic nontarget organisms from the current IPBC registered uses of pulp and papermills and MWF uses.

Risks are also expected for aquatic species from IPBC material preservative uses in exterior paints and coatings and above-ground pressure-treated wood. Based on the current modeling approach, the application rate would need to be reduced to 600 ppm for 30 two-story houses to be painted with IPBC-preserved paint to result in no chronic risk to freshwater fish in an adjacent standard waterbody. The application rate in pressure-treated wood would need to be reduced to 0.51 ppm for 30 decks and fences to be present next to a standard waterbody with IPBC-preserved wood to result in no chronic risk to the most sensitive aquatic receptor groups (chronic freshwater fish).

The model used for pressure-treated wood calculations made the conservative assumption that 100% of applied IPBC leaches from the deck and fence directly into an adjacent waterbody and that no degradation occurs. These assumptions likely overestimate the exposure estimates calculated for pressure-treated wood uses, however, the level of overestimation is unknown and cannot be quantified at this time. The high mobility in soil for IPBC would allow it to reach an adjacent waterbody, but the rapid biodegradation of IPBC in soil would reduce IPBC concentrations. The level of IPBC degradation in soil before it reaches a waterbody cannot currently be quantified, though it is not expected to be 94% or >99%; the reductions that would be needed to result in no risk to nontarget aquatic organisms from 30 houses with IPBC-preserved paint or 30 IPBC pressured-treated fences and decks adjacent to a standard 20,000,000 L waterbody, respectively. The Agency therefore expects risks to all aquatic nontarget organisms

evaluated here (acute and chronic risks to fish and aquatic invertebrates, and nonvascular plants) from the current IPBC registered uses in exterior paints and coatings, to include wood protective stains that can be used on decks, docks, and fences, and in above-ground pressure-treated wood.

It should also be noted that the lowest tested concentration that demonstrated adverse effects for freshwater invertebrates was below the most sensitive endpoint modeled here (chronic NOAEC for freshwater fish = 3.0 µg a.i./L), though was not definitive (NOAEC < 3.0 µg a.i./L). Therefore, the calculated reduction in the maximum application rate needed for modeled uses discussed above to result in no risk to nontarget organisms (*e.g.,* >99% reduction in use rate for pulp and papermill uses), would need to be reduced further to result in no chronic risk to this receptor group. Also, because acceptable ecotoxicity data are not available for vascular plants, risks are assumed for this receptor group. No exposure or ecotoxicity data are available for benthic species, however, IPBC is not expected to accumulate in the benthos or soil given its water solubility, mobility in soil, and its rapid biodegradation expected in sediment.

1.0 INTRODUCTION

1.1 Case Overview

3-iodo-2-propynl butyl carbamate (IPBC), (PC Code 107801) was first registered in 1975 as an antimicrobial disinfectant/fungicide/algicide for multiple industrial processes and residential spaces. Materials preservative uses consist of use in paint/adhesive/emulsion manufacturing, metalworking, cutting, and lubricating fluids, plastics, textile manufacturing, ink manufacturing, paper coating, and canvas manufacturing. IPBC is also used as a wood preservative and a fungicidal protective coating on various surfaces including paint formulations and surfaces of heating and HVAC systems. A reregistration eligibility decision (RED; U.S. EPA 1997) was completed in 1997. A post-RED Generic Data Call In (GDCI 107801-17764) was issued later in 1997. The RED and supporting documents can be found in the EPA Chemical Search database under Regulatory Actions at this website.

The Registration Review docket for IPBC, Case Number 2725, has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2011-0420. A Preliminary Work Plan (PWP) was completed in June 2011 and a Final Work Plan (FWP) was finalized in December 2011 but amended in December 2012 (U.S. EPA 2011a; U.S. EPA, 2012a). A generic data call-in (GDCI-107801-1341) was issued on May 2019 and listed various occupational and residential exposure (ORE), human health toxicity, dietary, ecological toxicity, and environmental fate data needs for the registration review risk assessment. As of May 2023, several studies (*i.e.*, Textile leaching (SS-1221), Leachability from shingles (SS-1223), and Residues from dish detergent (SS-1222) studies) remain outstanding. In the absence of these data, the Agency will model and evaluate risks for the use scenarios using conservative assumptions.

1.2 Recent Regulatory Actions

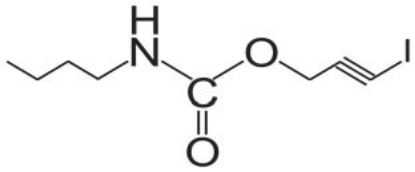
Since the publication of the amended FWP (U.S. EPA, 2012a), no additional regulatory actions have occurred.

1.3 Ingredient Profile

The physical and chemical properties for IPBC relevant to this risk assessment are summarized in Table 1.

Table 1. Physical and Chemical Properties of IPBC

Chemical Name	3-iodo-2-propynl butyl carbamate (IPBC)
IUPAC Name	3-Iodoprop-2-yn-1-yl butylcarbamate or butylcarbamate
Chemical Classification	Carbamate Ester

Chemical Name	3-iodo-2-propynl butyl carbamate (IPBC)
PC Code	107801
CAS No.	55406-53-6
SMILES Code	CCCCNC(=O)OCC#Cl
Molecular Formula	$C_8H_{12}INO_2$
Molecular Weight (g/mol)	281.1
Molecular Structure	
pH	7.01
Melting Point	66°C
Boiling Point	N/A
Density (g/mL)	1.575
UV/Visible Absorption	Maxima at 191 nm and 227 nm
Solubility in water (mg/L)	156 @ 20°C (TOXNET); not very water soluble, but is very soluble in methanol (>1000 g/L) and other organic solvents
Dissociation constant (pK_a)	Not applicable (no ionizable functional groups, MRID 45687203)
Soil-water partition coefficient (L/kg, log K_{oc})	K_{oc} of 62-310 (Log K_{oc} of 1.8-2.5, MRID 41975207)
Octanol-water partition coefficient (K_{ow}) at 25°C	log K_{ow} = 2.4 (EPI-Suite™, v.4.11); 2.81
Vapor pressure (mm·Hg)	<1.8 x 10^{-6} at 20°C and 5 x 10^{-6} at 30°C
Henry's Law Constant ($atm \cdot m^3/mol$) (calculated[1]) at 25°C	8.9 x 10^{-9} $atm \cdot m^3$/mole (EPI-Suite™, v.4.11)

Source: EPISuite (US, EPA, 2012a) and Hazardous Substances Data Bank (HSDB)
[1]Calculated (Vapor Pressure * Molecular Weight) / (760 * Water Solubility)

1.4 Use Pattern Summary

As of May 25, 2023, there are 123 registered antimicrobial use products with IPBC. One hundred sixteen are end-use (EU) products and/or intermediate and seven are manufacturing use products (MUP). IPBC products are registered for use as wood preservatives, industrial preservatives, and as dry film mildewcides. The wood preservative uses include spray, dip and pressure treatment applications for new lumber, millwork and joinery, and brush and spray applications for existing above ground structures such as decks and fences. The industrial preservative uses include metal working fluids, adhesives, caulks, sealants, plastics, textiles, paper coatings, canvas, cordage, and inks. Additional preservative uses include household, consumer, industrial, institutional, and janitorial products such as air fresheners, dish detergents, laundry products, surface cleaners, floor care products and fabric care products. IPBC products are also registered for use as dry film mildewcides in paints and stains. The products are formulated as powders, emulsifiable

concentrates, soluble concentrates, and ready to use solutions. No tolerances or exemptions from tolerances have been established for IPBC. A list of use sites, application methods, maximum application rates along with representative labels are listed in Table 2.

Table 2. Summary of Registered Products for IPBC

Use	Application Method	Maximum[1,2] Application Rate (ppm a.i.)	EPA Reg. No.[3]
Material Preservation			
Ceiling Tiles, Mineral-Based	Open Pour Liquid	4,300 ppm	39967-121
Pigment dispersions, slurries, and gypsum slurries for wallboard (drywall and gypsum board)	Open Pour Liquid	8,000 ppm	5383-170[4]
Paper, wallboard and paperboard products	Open Pour Liquid	6,000 ppm	39967-154
Polyvinyl chloride (PVC) flexible, vinyl flooring, gaskets, tarpaulins, PVC plastisol coated textiles	Open Pour Liquid	1,080 ppm	39967-131
Inks	Open Pour Wettable Powder (WP)	29,000 ppm	6836-466
	Open Pour Liquid	30,000 ppm	6836-415, 6836-416, 6836-467
Metalworking, cutting, cooling and lubricating fluids, aqueous	Open Pour Liquid	5,300 ppm	5383-171, 5383-77, 5383-91
	Open Pour WP	980 ppm	6836-466
Plastics, polymer and coatings – shower curtains, cables, sun umbrella, bathmats, polymer furniture, filter media, PVC, polyurethane	Open Pour Liquid	15,000 ppm	6836-415
	Open Pour WP	9,800 ppm	6836-466
Paint preservative, dry film	Open Pour Liquid	9,000 ppm	5383-171
Paint preservative, dry film - Paints, stains, and latex emulsions	Open Pour WP	7,800 ppm	6836-466
	Open Pour Liquid	8,000 ppm	5383-184
Carpet fibers and backings, canvas and cordage, drapes, shower curtains	Open Pour Liquid	10,000 ppm	6836-467, 6836-469, 464-8124
	Open Pour WP	9,800 ppm	6836-466
Cordage, textiles, fabrics (non-apparel)	Open Pour Liquid	12,000 ppm	5383-171
Textiles: Non-food contact cotton, cotton blend, or canvas for cushions, boat covers, sails, tents, tarpaulins, and awnings. Athletic footwear and outerwear, athletic flooring and mats	Open Pour Liquid	1,100 ppm	6836-443
Textile (non-apparel and apparel use) Fabrics and Fibers – *e.g.* acetate, acrylic, acrylonitrile butadiene styrene Natural Fibers – *e.g.* cotton, paper, wool, *etc*. Textile Coatings & finishes composed of silicone, urethane or vinyl	Open Pour Liquid	500 ppm	39967-129 39967-151 6836-200
Paper coatings -Coatings applied to paper and cardboard (nonfood)	Open Pour WP	7,400 ppm	6836-466
	Open Pour Liquid	9,000 ppm	6836-468
In can preservative - Non-food use agricultural products such as fertilizers and pesticides (inert)	Open Pour Liquid	1,700 ppm	5383-55 5383-118
Wood protective stains	Open Pour Liquid	6,800 ppm	5383-55
Roof coatings, joint cements, and stucco mixtures	Open Pour Liquid	10,400 ppm	5383-114
Joint cements, masonry coatings and stucco mixtures	Open Pour Liquid	900 ppm	5383-55

Use	Application Method	Maximum[1,2] Application Rate (ppm a.i.)	EPA Reg. No.[3]
Paints and Coatings including wood protective stains (includes dry film)	Open Pour Liquid	9,600 ppm	5383-197
Household, Industrial and Institutional Cleaning Products- liquid detergents, soft soaps, room deodorizers and air fresheners.	Open Pour Liquid	600 ppm	5383-91[5]
Household, industrial and institutional cleaning products (bathroom cleaners, window cleaners, fabric care products, laundry products, automotive care products, furniture care products, and liquid and solid air fresheners)	Open Pour Liquid	300 ppm	5383-171, 5383-170, 5383-172, 6836-469, 6836-473
Household, industrial, and institutional dish detergents (indirect dietary)	Open Pour Liquid	300 ppm	5383-171, 5383-170, 6836-469, 6836-473
Pool and pond liners	Open Pour Liquid	1,080 ppm	39967-131
Surface cleaning wipes	Open Pour	320 ppm	67071-83, 67071-66
Adhesive (non-food contact aqueous, solvent and non-solvent-based systems such as natural and synthetic adhesives, caulks, patching compounds, sealants, grouts, latexes such as styrene-butadiene rubber (sbr)/latex used in the manufacture of flooring adhesives or carpet backings and for use in cement-based products)	Open Pour Liquid	6,000 ppm	5383-171, 5383-77, 5838-91
	Open Pour WP	2,500 ppm	6836-466
Residential and Public Access Premises			
Fungicidal protective coating (interior walls, fiberglass and rubber insulation on pipes and other surfaces, concrete and masonry walls, pipe surfaces; and interior metal surfaces; interior surfaces of HVAC duct systems and other HVAC interior surfaces)	Brush, roller, airless spray	1,600 ppm 0.0005 lb. a.i. per sq. Ft.	59682-4, 63836-1
Mold preventing paint primer	Aerosol spray	1,500 ppm	69587-6
Wood Preservation (Note. 10,000 ppm = 1.0%)			
Wood Products – lumber, plywood, particle board (above ground only)	Immersion, Dip, Spray	18,000 ppm in treatment solution	5383-171 5383-91
Wood Composites	Open Pour Liquid, Immersion	5,600 ppm in treatment solution	5383-116
Wood, New (pressure treatment); above ground	Immersion, dipping, brushing, spraying, or pressure/vacuum treatment	15,000 ppm in treatment solution	39967-66
Sapstain Treatment - Millwork	Dip Tank, Immersion, Spray	18,000 ppm in treatment solution	5383-91, 6836-415, 39967-154
Sapstain Treatment - New lumber, plywood, particle board and millwork	Open Pour WP Dipping and brushing	15,000 ppm in treatment solution	6836-466
Sapstain Treatment- New lumber, plywood, particle board and millwork	Open Pour Liquid Immersion	5,100 ppm in treatment solution	5383-55

1: All application rates presented in the table are rounded to two significant figures.
2: The open pour applications used in this table include the % a.i. in product.
3: The listed EPA Reg. No. is a sample registered product that represents the maximum application rate for the listed use pattern.
4: The label states that IPBC can be applied to finished paper and mentions slurries (unspecified). As a result, the Agency assumed that IPBC can be applied to paper slurries (See section 3.3.1 for more details).

5: This label contains a liquid detergent use which is assumed as a detergent use for laundry, not dish detergent uses which may contact food. As a result, the liquid detergent and soft soap uses were not assessed for food contact.

1.5 Label Recommendations

The labels that include materials preservation uses (which are identified in Table 2.) generally list personal protective equipment such as goggles, face shield, or safety glasses and chemical resistant gloves. However, it is recommended for the labels with materials preservation uses to include a PF-10 filtering facepiece or half face elastomeric facepiece respirator requirement to reduce inhalation risks. Additionally, some labels state that IPBC can be applied to finished paper and mentions slurries (unspecified). As a result, the Agency assumed that IPBC can be applied to paper slurries (see footnote 4 in Table 2 and section 3.3.1 for more details). The Agency recommends the labels that mentions slurries to specify the type of slurry IPBC can be applied to. The Agency also recommends that preserved products that are intended for consumer use (*e.g*., liquid detergent, air freshener, bathroom cleaners, *etc*.) to include specific packaging or application details on the label. For perceived dietary uses, label 80285-5 contains a nonfood contact statement for pesticide formulations without labeling all individual uses as nonfood. It is recommended that a nonfood statement be added to all potential dietary uses (*i.e*., adhesives, slurries, pulp and paper, paper coatings, slimicides, polymers, household cleaning products, *etc*.) if uses are intended for nonfood use.

1.6 U.S. Consumption Information

According to the Kline Specialty Biocides 2020 U.S. Consumption Business Marketing Analysis and Opportunities Report (Kline, 2021), IPBC is a major dry film mildewcide/fungicide to preserve adhesives and sealants. The report also lists IPBC as dry film fungicide use in metal working fluid applications. An estimated consumption of 666,600 lb sales annually, 6.3% ranking, for 2.5 % of volume for adhesives and sealants, and 9.6% of for metal working fluid products.

2.0 HUMAN HEALTH RISK ASSESSMENT

2.1 Data Deficiencies

In the FWP, the Agency included the comparative cholinesterase assay (CCA) with thyroid measurements study as well as a dermal sensitization study in the list of anticipated data requirements for IPBC. However, in the generic data call-in (GDCI-107801-1341), the Agency listed the comparative thyroid assay (CTA, SS-1033) instead of the CCA study. The registrant(s) submitted a waiver for the request of the CTA study and the Agency is waiving the need for the CTA study as it is not a required study to finalize the risk assessment for IPBC. The registrant(s)

submitted a Local Lymph Node Assay (LLNA) study to satisfy the dermal sensitization study requirement.

Regarding the CCA study, the acute oral neurotoxicity (MRID 45509401), subchronic dermal (MRID 42168201), and subchronic oral neurotoxicity study (MRID 45509402) showed no treatment related changes in erythrocyte and brain cholinesterase (ChE) activity. Although plasma cholinesterase was inhibited in these studies, this is not considered an adverse effect without concurrent erythrocyte and/or brain cholinesterase inhibition (which were not inhibited in these studies) or other clinical signs (U.S. EPA, 2000; U.S. EPA, 2007). The subchronic inhalation toxicity study (MRID 43530203) is the only study in the IPBC database that shows a significant decrease in brain ChE activity. Since no oral study in the IPBC database shows a decrease in erythrocyte and/or brain ChE activity, it is unlikely a CCA study would provide further refinement to the proposed endpoints and is not needed to conduct this risk assessment.

Regarding the submitted LLNA study (MRID 50938207), the study was required to allow a quantitative risk assessment for dermal sensitization to be conducted. However, an EC3 value was not established in the LLNA study as no tested concentrations exceeded a stimulation index (SI) of 3 at the test concentrations of 0.25, 0.5 and 1 percent. The results were classified as equivocal due to the observation of a dose response in the study up to the highest test concentration of 1 percent. At higher test concentrations, as utilized in the pre-test at 2.5 and 5 percent, irritation signs and body weight loss were observed; therefore, testing at higher concentrations would likely not result in additional refinement of the endpoint. Although skin sensitization can only be definitively ruled out up to 1 percent concentration and some uses of IPBC may exceed this exposure concentration, the endpoints and uncertainty factors established in this assessment based on dermal irritation effects are likely protective of skin sensitization based on the available data. The endpoint is based on a 90-day dermal toxicity study (MRID 42168201) where no irritation was observed at the NOAEL of 50 mg/kg/day and mild irritation was observed at the LOAEL of 200 mg/kg/day which correspond to applied concentrations of 0.83 percent and 3.3 percent, respectively. Based on all of these factors, a quantitative risk assessment for dermal sensitization was not possible and also deemed not necessary for the dermal assessment at this time.

2.2 Anticipated Exposure Pathways

Based on the use sites of the products containing IPBC, exposures to the chemical can occur via the oral, dermal and inhalation pathways. Oral exposure may occur by food contact surfaces when IPBC is used as a materials preservative in dish detergents. Drinking water exposure may occur when effluents from industrial water systems, such as paper mills and metal working fluids sites, are located upstream of drinking water intakes. Incidental oral exposures may occur from treated wood such as decks and children's play sets, treated carpet fibers, treated textiles, and

treated pool liners. Dermal and inhalation exposures may occur during the open pour process of the product in occupational settings. In residential settings, dermal and inhalation exposures may occur during use of treated paint or when using paint primer, wood preservative stains, caulks, sealants, or adhesives that contain IPBC.

2.3 Hazard Characterization and Dose-Response Assessment

2.3.1 Toxicology Studies Available for Analysis

The following toxicology studies are acceptable and considered adequate for characterizing toxicity and conducting human health risk assessments for IPBC:

- Acute neurotoxicity study in rats – MRID 45509401
- 14-day oral toxicity study in rats – MRID 47026402
- 90-day oral toxicity study in rats – MRID 43530202
- 90-day oral toxicity study in rats – MRID 45812301
- 91-day dermal toxicity study in rats – MRID 42168201
- 90-day inhalation toxicity study in rats – MRID 43530203
- 5-day inhalation toxicity study in rats – MRID 43491813
- 2-week repeat dose inhalation toxicity study in rats – MRID 43530213
- 90-day neurotoxicity study in rats – MRID 45509402
- Carcinogenicity study in mice – MRID 42008202
- Combined carcinogenicity/chronic toxicity study in rats – MRID 42008206
- Prenatal developmental toxicity study in rabbits – MRID 43530205
- Prenatal developmental toxicity study in rats – MRID 43530204
- Reproduction and fertility effects study in rats – MRID 44478801
- Reverse mutation assay – MRID 41975206
- Unscheduled DNA synthesis analysis – MRID 40990403
- *In vivo* cytogenetics – MRID 40990404
- Metabolism and pharmacokinetics – MRID 43570701
- Local lymph node assay (LLNA) study in mice – MRID 50938207

2.3.2 Absorption, Distribution, Metabolism, & Elimination (ADME)

The following ADME data is based on a metabolism study performed in rats (MRID 43570701).

Absorption of test chemical at the low single dose of 20 mg of radiolabeled IPBC per kg of body weight of the rat (20 mg/kg) and a high single dose (125 mg/kg) was between 80-90%.

Tissue distribution data demonstrated that after a single high oral dose, the highest concentrations of radioactivity at 2 hours post-dose were in the fat, kidneys, liver, and residual carcass of both sexes of rats. At 4 hours post-dose the radioactivity in these tissues increased in female rats, with the amount doubling in fat tissues compared to the 2-hour time point. At 120 hours post-dose, the carcass, kidneys, liver, and fat contained the highest levels of residual radioactivity. At the single low dose, highest concentrations of radioactivity were observed in the kidneys, liver, and carcass but not in the fat tissues.

Urinary and fecal metabolites were identified in animals exposed to a single oral high dose of radiolabeled IPBC (Group A: 125 mg/kg) or a low oral dose of non-radiolabeled IPBC followed by a single radiolabeled dose of 20 mg/kg (Group B), while tissue metabolites were identified in animals exposed to a single oral dose (Group C: 20 mg/kg and Group D: 125 mg/kg) of radiolabeled IPBC. The major fecal metabolite identified in animals exposed to these doses was characterized as a metabolite containing carboxylic acid functional groups as well as hydroxyl groups (FRM-1). In the liver, metabolite URM-4 (propargyl-N-methylcarbamate), URM-11-14 (glucuronide conjugates of URM-2, URM-3, URM-4, and URM-5 metabolites), and URM-15 were identified as major metabolites. After a single high oral dose, the major urinary metabolites identified were the Z- and E-forms of propargyl-N-acetic acid carbamate (URM-9 and URM-10) as well as a mixture of highly polar components, which eluted as the void volume on HPLC (URM-15). At 2 hours post-dose, female rats in Groups C and D were observed with higher percentages of URM-4 in liver than males, while the percentage of glucuronide conjugates in male liver at 2 hours post-dose was higher than female liver. This indicates a possible sex-related difference in velocity of glucuronidation for IPBC metabolites. In the kidney, metabolites identified in the greatest percentage included URM-4, URM 7+8 (mixture of aqueous soluble metabolites), URM 9+10, and URM-15. There were no differences in percentages of kidney metabolites between dose Groups C and D. In blood, parent chemical as well as URM-4 were identified as major components in dose Groups C and D. Increased percentage of parent chemical was observed at the single high dose compared to the single low dose exposure, indicating possible saturation of metabolism at the high dose. Based on the metabolite identification data, a scheme for metabolism of IPBC was proposed. According to this scheme, IPBC undergoes reductive dehalogenation followed by de-alkylation to form URM-9 and URM-10 metabolites. In addition, decarboxylation following reductive dehalogenation yields CO_2. Various other metabolites formed from dehalogenation are glucuronidated and constitute minor metabolites of IPBC.

Most of the dose was eliminated through the urine or exhaled air. Excretion of IPBC radioactivity was mainly via the urine (50-70% administered dose) at 168 hours post-dose. Feces was a minor route of excretion in all dose groups (4-7% administered dose). Radiolabeled CO_2 constituted between 18-24% of the administered dose. Repeated low oral dosing or a single high oral dose appeared to result in a decrease in the percentage of radioactivity excreted as $^{14}CO_2$

compared to a single low dose (38.22%). Urinary and fecal metabolites were identified in animals exposed to 125 mg/kg and tissue metabolites were identified in animals exposed to single oral doses of 20 mg/kg and 125 mg/kg. After a single high oral dose or repeated low oral doses, the major urinary metabolites identified were the Z- and E-forms of propargyl-N-acetic acid carbamate (URM-9 and URM-10) as well as a mixture of highly polar components, which eluted as the void volume on HPLC (URM-15). The major fecal metabolite identified for animals exposed to 125 mg/kg was a compound containing carboxylic acid functional group as well as hydroxyl groups (FRM-1).

In the liver, metabolite URM-4 (propargyl-N-methylcarbamate), URM-11-14 (glucuronide conjugates of metabolites URM-2, URM-3, URM-4, and URM-5), and URM-15 were identified as major metabolites. At 2 hours post-dose, female rats exposed to single oral doses of 20 mg/kg and 125 mg/kg were observed with higher percentages of URM-4 in the liver than males, while the percentage of glucuronide conjugates in the male liver at 2 hours post-dose was higher than the female liver, indicating a possible sex-related difference in velocity of glucuronidation for IPBC metabolites. In the kidney, metabolites identified in the greatest percentage included URM-4, URM 7+8, URM 9+10, and URM-15. There did not appear to be any significant differences in percentages of kidney metabolites between animals exposed to single oral doses of 20 mg/kg and 125 mg/kg. In blood, parent chemical as well as URM-4 were identified as major components in animals exposed to single oral doses of 20 mg/kg and 125 mg/kg. An increased percentage of the parent chemical was observed at the single high dose vs. the single low dose, indicating possible saturation of metabolism at the high dose. Based on the metabolite identification data, a scheme for metabolism of IPBC was proposed. According to this scheme, IPBC undergoes reductive halogenation followed by de-alkylation to form the URM-9 and URM-10 metabolites. In addition, decarboxylation following reductive dehalogenation yields CO_2. Various other metabolites formed from dehalogenation are glucuronidated and constitute minor metabolites of IPBC.

2.3.3 Summary of Toxicological Effects

A complete database of acute toxicity data was available to the Agency at the time of the RED (U.S. EPA, 1997). A summary of the findings is included in Table A1 in Appendix A. IPBC is a severe eye irritant (Toxicity Category I) and is of low to moderate acute toxicity by the other routes of exposure. IPBC is not a dermal sensitizer at concentrations that do not exceed 1 percent (w/w).

In a repeated oral dose range-finding study (MRID 47026402), IPBC (99.3% a.i.) was administered to 5 Sprague Dawley rats/sex/dose at dose level (estimated) of 0, 40, 80, or 120 mg/kg/day (actual estimated dose from food consumption and nominal concentrations were 31, 62, or 91 mg/kg/day in males and 31, 61, or 90 mg/kg/day in females) for 14 days in Phase 1. In

Phase 2, 5 rats/sex/dose were administered 0 or 120 mg/kg/day (actual estimated dose from food consumption and nominal concentration was 156 mg/kg/day in males and 177 mg/kg/day in females) for 14 days. In Phase 3, 5 rats/sex/dose were administered 0 or 120 mg/kg/day (actual estimated dose from food consumption and nominal concentration was 118 mg/kg/day in males and 122 mg/kg/day in females) for 14 days. No unscheduled deaths occurred during all three phases of the study. Few feces (2/5 females) and thin appearance (1/5 female) in the high dose-animals in phase 2 and in phase 3 (all males and females) were the only clinical findings of toxicity observed during the study.

The mean overall body weight gain of high-dose male rats in Phase 1 was 15% lower than the controls with no more than a 7% decrease in body weight during treatment. In Phase 2, high-dose male rats' overall body weight gain was 69% lower than controls with no more than a 14% decrease in body weight throughout treatment. Phase 3 high-dose male rats' overall body weight gain was 59% lower than controls with no more than a 19% decrease in body weight during the 2 weeks of treatment. The mean overall body weight gain of high-dose female rats in Phase 1 was 20% lower than that of the controls corresponding to no more than a 7% decrease in body weight during treatment. In Phase 2, high-dose female rats' overall body weight gain was 103% lower than controls with no more than a 16% decrease in body weight. Phase 3 high-dose female rats' overall body weight gain was 41% lower than controls, and no more than an 18% decrease in body weight occurred.

Food consumption correlated to the decreases in body weights and body weight gains. During the first few days of treatment up to Day 4, high-dose rats of both sexes from all Phases consumed considerably less feed as compared to controls; however, by Day 8, food consumption was at least 84% of the controls. Food consumption generally decreased again at the beginning of week 2 with the introduction of a second batch of formulated diet, but it again recovered to within at least 87% of control values as animals adjusted. The only treatment-related gross necropsy finding was irritation to the non-glandular stomach in 3/5 males and 1/5 females from Phase 3. The lowest-observed adverse effect level (LOAEL) is 120 mg/kg/day based on decreased body weight, body weight gain, and food consumption as well as irritation of the non-glandular stomach. The no-observed adverse effect level (NOAEL) is 80 mg/kg/day.

In a subchronic oral study (MRID 45812301), IPBC was administered by gavage at doses of 0, 10, 20, 35 and 80 mg/kg to rats for 90 days. A Functional Observational Battery (FOB) was performed prior to the first exposure and then weekly. In the last week of the study, assessment of sensory reactivity to visual stimuli (visual placing) and motor activity was added. Food consumption for each rat was determined once a week. Hematology and clinical chemistry examinations were made at week 13, before the terminal sacrifice. Ophthalmoscopic examinations were made on all rats prior to the first administration of the test substance, in rats of the highest dose and on control rats at the termination. A gross necropsy and pathology examination was performed at the end of the study.

There was no test article related findings with respect to food consumption ratio, assessment of hearing, righting reflex, grip strength, visual placing, motor activity, ophthalmoscopy, urinary parameters, or macroscopic and microscopic findings. One male rat dosed at 35 mg/kg/day died on day 87 from a dosing accident. The most frequent clinical finding, observed during the daily post-treatment FOB observations was breathing sounds (slight to moderate in degree) seen in a dose-dependent manner. From Day 19 of the study until the end of the treatment period, the main finding was a dose-related incidence of slight salivation seen 25 minutes after dose administration. The effect may be due to be a local effect of the dosing solutions or to nonpalatability. Clinical observations included statistically significant decreases in body weight gain in males at 35 mg/kg/day (12%) and 80 mg/kg/day (17%). The LOAEL is 35 mg/kg/day based on decreased body weight in males, and salivation and breathing sounds in females. The NOAEL is 20 mg/kg/day.

In a subchronic oral study (MRID 43530202), Omacide (IPBC; 97-98% a.i.) was administered to 15 albino rats/sex/dose by gavage at dose levels of 25, 75, or 200 mg/kg/day for 13 weeks. All treatment groups exhibited excess post-dose salivation; the frequency and severity were concentration-related. Abnormalities in liver function and/or pathology were also observed in all treatment groups. Two males in the 25 mg/kg/day group exhibited dark livers. Increased incidence of abnormal liver shape was observed in male rats at all dose levels, and in female rats at 75 and 200 mg/kg/day. Centrilobular hepatocyte hypertrophy was observed in 1/15 males in the 25 mg/kg/day treatment group; 4/15 males in the 75 mg/kg/day treatment group; and 15/15 males and 3/15 females in the 200 mg/kg/day group. Absolute liver weight in the 75 mg/kg/day females was increased 13% vs. controls, and at 200 mg/kg/day, liver weight was increased 29-32% vs. control in male and female rats, respectively.

Increased relative liver weights were also observed in both sexes at 75 mg/kg/day (12-17% higher) and 200 mg/kg/day (39-41% higher) vs. controls. Also, increased relative kidney weights were noted in the 75 mg/kg/day males and in both sexes from the 200 mg/kg/day groups; no associated macroscopic or microscopic alterations were observed. Hyperkeratosis and squamous epithelial hyperplasia of the nonglandular region of the stomach were observed in all treatment groups, and stomach ulceration and chronic inflammation were observed in the male and female 200 mg/kg/day treatment groups. This effect was most likely due to the irritancy of the test substance. No treatment-related changes were observed in the clinical appearance, body weight, food consumption or ophthalmology parameters for any of the treatment groups. The LOAEL is 25 mg/kg/day for males and females, based on excessive post-dose salivation in both sexes, abnormal liver shapes in males, and hyperkeratosis and squamous epithelial hyperplasia of the nonglandular region of the stomach in males and females. The NOAEL could not be determined.

In a 91-day dermal study (MRID 42168201), 10 rats/dose/sex received 0, 50, 200, and 500 mg/kg/day (0, 8.33, 33.33, and 83.33 mg/ml) of IPBC on the shaved skin for five days a week, six hours per day. Decreased body weight (4-6%) and weight gain (11%) were observed in male rats only at 200 and 500 mg/kg/day, respectively. Dose-dependent dermal irritation was observed in males and females at 200 and 500 mg/kg/day levels. The irritation was mild at the 200 mg/kg/day level and consisted primarily of slight erythema and slight desquamation. At the 500 mg/kg/day level, the irritation was more severe and consisted of slight erythema, slight desquamation, and low incidences of slight edema, moderate erythema, and moderate desquamation. Dermal irritation at the 500 mg/kg/day level progressed to focal and/or pinpoint areas of eschar in a few animals. The LOAEL is 200 mg/kg/day based on incidences of slight erythema and desquamation in females and males. The NOAEL is 50 mg/kg/day.

In a 5-day inhalation toxicity study (MRID 43491813), Omacide (IPBC; 97-98% a.i.) was administered to 5 rats/sex/dose by whole-body exposure at nominal concentrations of 0, 0.4, 1.0, 4.0 mg/m^3 (measured concentrations of 0, 0.3, 1.0 and 3.8 mg/m^3, respectively) for 6 hours per day on 5 consecutive days. Male and female rats in the 4.0 mg/m^3 dose group had histopathologic lesions of the larynx (epithelial hyperplasia in the ventral region and hyperplasia or squamous metaplasia in the ventrolateral regions, with necrosis of the underlying cartilage); in addition, males exhibited a slightly reduced body weight gain. Male and female rats in the 1.0 mg/m^3 dose group had the same larynx lesions reported in the 4.0 mg/m^3 dose rats. No adverse effects were seen in the 0.4 mg/m^3 exposure level rats. The lowest-observed adverse effect concentration (LOAEC) is 1.0 mg/m^3, based on the presence of histopathologic lesions of the larynx. The no-observed adverse effect concentration (NOAEC) is 0.3 mg/m^3. This study wasn't considered for endpoint selection because it's classified as supplemental.

In a 2-week inhalation toxicity study (MRID 43530213), Omacide (IPBC; 97-98% a.i.) was administered to 5 rats/sex/dose by whole-body exposure at nominal concentrations of 0, 4, 12, 40, or 80 mg/m^3 (actual concentrations 0, 4, 10, 38 and 67 mg/m^3, respectively) for 6 hours per day. Rats in the 0, 4, and 12 mg/m^3 treatment groups were exposed 5 days per week for 2 consecutive weeks; exposure of rats in the 40 or 80 mg/m^3 groups was terminated after 3 days because of the severity of the toxic reactions. In the 80 mg/m^3 dose group, mortality occurred (4/10 test subjects), both sexes exhibited clinical signs of toxicity during exposure (agitated grooming of snout, half- or fully closed eyes, licking inside of mouth, gasping and rubbing chin on the grid mesh floor) and after exposure (noisy respiration; sneezing; gasping; brown staining around snout, jaws and forepaws; red ears; red limbs; and discharges from the snout/nostrils). There was marked bodyweight losses, and reduced food and water consumption. Rats that died exhibited high incidences of lung congestion, and all rats in this group had gaseous distention and minimal contents of the gastrointestinal tract.

In the 40 mg/m^3 dose group, mortality occurred (one female), both sexes exhibited clinical signs of toxicity during exposure and after exposure that were similar to those at the higher dose. There was significantly reduced bodyweight gain (21-24%), and reduced food and water consumption in males. For humane reasons, all surviving rats in the 80 and 40 mg/m^3 dose groups were sacrificed after the third exposure. In the group exposed at 12 mg/m^3, agitated grooming, half closed eyes, noisy respiration, and brown staining around the snout and jaws were observed. Weight gain was decreased significantly in both sexes. After 2 weeks of exposure, males had increased liver weights; both sexes exhibited high incidences of gaseous distention and minimal contents of the cecum; and both sexes exhibited histopathologic lesions of the respiratory system (epithelial hyperplasia of the ventral region of the larynx, squamous metaplasia in the ventrolateral region of the larynx accompanied by necrosis of the underlying cartilage). In the group exposed at 4 mg/m^3, both sexes exhibited the same histopathologic lesions described above, but clinical signs were absent. The LOAEC is 4.0 mg/m^3, based on the occurrence of histopathologic lesions of the larynx. A NOAEC was not established. This study wasn't considered for endpoint selection because it's classified as supplemental.

In a 90-day subchronic inhalation toxicity study (MRID 43530203), Omacide (IPBC; 97-98% a.i.) was administered to rats (15 rats/sex/dose) by whole-body exposure at nominal concentrations of 0, 0.25, 1.25, or 6.25 mg/m^3 (measured concentrations of 0, 0.3, 1.16, and 6.7 mg/m^3) for 6 hours per day, 5 days per week, for 13 consecutive weeks. The 0.3 mg/m^3 dose group was repeated based on exposure of the original 0.3 mg/m^3 dose group to twice the concentration during weeks 6-8 of the study. In the 6.7 mg/m^3 treatment group, plasma cholinesterase (ChE) activity was significantly reduced (approximately 20%) in males during weeks 2 and 13, and erythrocyte ChE was decreased in females at study week 2. Brain ChE activity was significantly reduced in males (17%) and females (25%), and hyperplasia or squamous metaplasia with necrosis of the ventral cartilage of the larynx was seen after 13 weeks of treatment. In the 1.16 mg/m^3 treatment group, brain ChE levels were statistically significantly reduced in most of the females (25%; $p<0.05$). No effects were observed in the repeat 0.3 mg/m^3 treatment group. The LOAEC for systemic toxicity is 6.7 mg/m^3 based on epithelial hyperplasia in the ventral region of the larynx and necrosis in the ventral cartilage of the larynx in males and females. The NOAEC was 0.3 mg/m^3.

In an acute neurotoxicity study (MRID 45509401), rats were given a single gavage oral dose of IPBC at doses of 0, 100, 300, or 1000 mg/kg/day and observed twice daily for 15 days. Control and treatment groups were divided into the following 3 sets for neurobehavioral assessment and ChE activity evaluations: Set 1 (12/sex/group) was evaluated for FOB, motor activity (MA), blood, plasma, and brain ChE at pretest on Day 1. Set 2 (12/sex/group) was evaluated for FOB, MA, blood, plasma ChE at pretest Days 1, 8, and 15, and brain ChE on Day 15. Set 3 (6/sex/group) was evaluated for neuropathology on Day 15 at study termination, these animals were euthanized and perfused *in situ* for neuropathological examination.

A statistically significant decreased mean body weight gain was observed for males at 300 and dose level. FOB observations (incidences) included a statistically significant lower number of rears in females treated at 1000 mg/kg/day. This effect was not seen in males. A dose relationship was seen on Day 1 (Sets 1 and 2) and Day 8 (Set 2). Low Locomotor (open field) activity was seen at 1000 mg/kg/day on Day 1 in Sets 1 and 2 in both sexes. This effect was still evident to a lesser degree in both sexes on Day 8. The number of approaches (open field) showed a dose related decrease in Sets 1 and 2 in males which was statistically significant at 1000 mg/kg/day. In females, decreases were noted at 1000 mg/kg/day, but they were not statistically significant.

Rats of both sexes in all treatment groups had an overall lower incidence of motor activity than their control counterparts. For the change in motor activity, the mean, standard deviation, coefficient of variation (CV), and the percent effect were calculated for each treatment group and set. When the sets were broken out for Day 1 for males and females, at 100 mg/kg/day only Set 2 for females had a percent effect greater than 25-30% and at levels greater than the CV of the controls. Dose response is generally followed across all groups with a more robust relationship starting at the 300 mg/kg dose, where all sets had a percent effect greater than the CV in the controls at Day 1. Females treated with 300 and 1000 mg/kg had decreased plasma ChE activity on both Days 8 and 15. No significant changes were observed in erythrocyte and brain ChE activity in either sex. Macroscopic evaluation revealed no evidence of lesion formation due to treatment. Based on the effects seen in this study, the LOAEL was 300 mg/kg/day based on changes in motor activity. The NOAEL was 100 mg/kg/day.

In a subchronic neurotoxicity study (MRID 45509402), IPBC was orally administered to rats via the diet at dose levels of 0, 10, 50, or 120 mg/kg/day for 13 weeks. There were no treatment-related effects on mortality, clinical signs, neurobehavioral activity, or erythrocyte or brain ChE activity. Treatment-related effects included lower mean body weight/body weight gain and decreased food consumption at both 50 and 120 mg/kg/day. Decreased food efficiency at 120 mg/kg/day correlated with the decrease in food consumption, contributing to the lower body weights of treated animals.

Plasma ChE inhibition was observed at 50 and 120 mg/kg/day in females only. Erythrocyte and brain ChE activity was not affected in either sex at any dose or time point. Macroscopic examination indicated that the cervical and lumbar dorsal root ganglion might be potential target tissues of the test article. Microscopic examination by the study pathologist reported neuronal vacuolation, satellite cell hypertrophy/hyperplasia, and neuronal degeneration in these tissues; however, these effects were determined not to be treatment-related after a peer review of the histopathology slides. No other gross, histopathological, or neuropathological effects were observed. All the noted effects in body weight, food consumption, food efficiency, and plasma

ChE activity were reversed during the recovery period, indicating that the effects of the test article were not permanent. No frank neurotoxicity was observed. Based on the effects seen in this study, the LOAEL is 50 mg/kg/day (based on body weight, food consumption, and ChE activity data), with a NOAEL of 10 mg/kg/day.

In a carcinogenicity study (MRID 42008202), mice (50 mice/sex/dose) were administered IPBC in the diet at 0, 20, 50, and 150 mg/kg/day for 78 weeks. In males, a statistically significant trend was observed for hepatocellular adenoma and hepatocellular adenoma/carcinoma combined ($p< 0.01$). A statistically significant pair-wise comparison was also observed for the incidence of hepatocellular adenoma and adenoma/carcinoma combined at 150 mg/kg/day vs. control ($p< 0.05$). At 150 mg/kg/day, the incidence of hepatocellular adenoma (24%) and combined adenoma/carcinoma (33%) exceeded the historical control range for mice provided by the registrant (average benign hepatocellular tumor incidence of 11%, malignant tumor incidence of 7%). There was no increase in hepatocellular tumor incidence in female mice.

There was a significant dose-related positive trend in pulmonary carcinoma for females, but no significant pair-wise comparison at any dose level tested in this study. Since the formation of pulmonary carcinomas in mice is considered part of a continuum from pulmonary adenomas, the positive trend in carcinomas was not considered biologically significant. At the highest dose (150 mg/kg/day), body weight gain in males was decreased to 73% of control for weeks 0-13 of the study, and to 77% of control at study termination. In females, body weight gain for weeks 0-13 at the high dose was decreased to 70% of control, and to 80% of control at study termination. No significant effects on food consumption were observed in this study. In addition, no statistically significant effects on survival were seen in this study. The systemic LOAEL is 20 mg/kg/day, which is the lowest dose tested, and is based on the increased incidence of non-neoplastic pathology of the thyroid in both sexes (atrophic vacuolation, follicular coalescence, and general follicular enlargement). The NOAEL could not be established.

In a chronic toxicity/carcinogenicity study (MRID 42008206), IPBC was administered to Sprague-Dawley rats (50/sex/group) at doses of 0, 20, 40, and 80 mg/kg/day for two years. There were no statistically significant increases in tumor incidences in males. The incidence of mammary gland fibroadenoma and combined fibroadenoma/carcinoma in females was significantly increased at 20 mg/kg/day vs. control by pair wise comparison ($p<0.01$), but there was no dose-related trend. Except at 20 mg/kg/day, the incidence of this tumor type was within historical control range for Sprague-Dawley rats.

Since the mammary tumor incidence at 80 mg/kg/day was almost equal to the control group, the Agency's Office of Pesticide Programs (OPP) Health Effects Division Carcinogenicity Peer Review Committee concluded that the mammary fibroadenomas were not related to treatment with IPBC (U.S. EPA, 2011c). At 80 mg/kg/day, body weight gain decrements of 20% and 15%

were observed in males and females, respectively, during the first 13 weeks of the study. At study termination, body weight gain in males at 80 mg/kg/day was decreased to 71% of the control group, and in females, to 76% of the control group. Significant changes in serum chemistry were observed in males at 80 mg/kg/day, as were significant non-neoplastic changes in the stomach in both sexes. The non-neoplastic changes in the stomach were considered the result of chronic irritation and were not considered indicative of a neoplastic response. The systemic LOAEL is 20 mg/kg/day, which is the lowest dose tested, and it is based on decreased body weight gain in male rats.

In a developmental toxicity study (MRID 43530205), IPBC (>97% a.i.) was administered to 16-18 female New Zealand White rabbits per dose by gavage at dose levels of 0, 10, 20, or 40 mg/kg/day from days 7 through 19 of gestation. Maternal toxicity was evidenced by marked deterioration in condition resulting in the premature sacrifice (days 15-22 of gestation) of one mid-dose and four high-dose females. The prematurely sacrificed animals had exhibited reduced body weight gain and food consumption from the start of dosing. Although food consumption during days 7-19 was decreased similarly at all dose levels (26-30%), food efficiency was not significantly affected during this period. Additionally at the final necropsy, absolute and relative liver weights of the high-dose does were 7-10% greater than the concurrent controls.

In the 40 mg/kg/day dose group, there was a decrease in number of total live fetuses and live fetuses/dam (6.7 compared to 8.5-8.7 for other groups) that was accompanied by a decrease in implantations/dam (7.8 compared to 9.2 for controls). Post-implantation loss was also increased at the 40 mg/kg/day dose level vs. control. The decrease in total implantations may be based partly on the increase in preimplantation loss (which occurs before dosing and is not compound related). There were no effects on pregnancy outcome, gravid uterus weights, nor any teratogenic findings. The maternal LOAEL is 40 mg/kg/day based on clinical signs of toxicity. The maternal NOAEL is 20 mg/kg/day. The developmental LOAEL is 40 mg/kg/day based on decreased total live fetuses, live fetuses/dam, and increased post-implantation loss. The developmental NOAEL is 20 mg/kg/day.

In a developmental toxicity study (MRID 43530204), IPBC (>97% ai) was administered to 24 female Sprague-Dawley rats per dose by gavage at dose levels of 0, 25, 75, or 250 mg/kg/day from days 6 through 15 of gestation. Maternal toxicity as evidenced by aggressive behavior, post-dose salivation, decreased mean body weight gain, and decreased food consumption was observed in the mid-dose (75 mg/kg/day) and high-dose (250 mg/kg/day) rats. During the dosing period (Days 6-15), the mean body weight gain of high- and mid-dose dams were approximately 75 and 83%, respectively of the controls. At the onset of dosing (Days 6-9 of gestation), food consumption by the high-dose group was 71% of the controls ($p < 0.01$) and remained lower (not significant) throughout the dosing period. In the mid-dose group, food consumption was approximately 84% of the controls ($p < 0.01$) from Days 6 to 12 of gestation. Thereafter, mean

food consumption was similar to the controls. The maternal LOAEL is 75 mg/kg/day, based on decreased mean body weight gain and food consumption. The maternal NOAEL is 25 mg/kg/day. No evidence of a treatment-related effect on fetal viability was demonstrated.

At 250 mg/kg/day, mean fetal body weight was reduced to approximately 95-96% of the controls (significant in the females at $p < 0.05$) and developmental delays that included a higher frequency of rib defects and incomplete or non-ossification of bones were noted. The developmental LOAEL is 250 mg/kg/day based on reduced body weight and developmental delays. The developmental NOAEL is 75 mg/kg/day.

In a two-generation reproductive toxicity study (MRID 44478801), Omacide (IPBC; 97-98% a.i.) was administered to groups of 25 male and 25 female rats by gavage at doses of 0, 10, 30, or 100 mg/kg/day for two generations. Clinical signs of toxicity observed in the mid- and high dose levels included salivation, paddling with both forepaws, and hunched posture. No treatment-related gross findings were observed at necropsy of the parental generation (F_0) or first generation (F_1) females. Microscopic examination of the F_0 adults was unremarkable. In the F_1 adults, diffuse acanthosis with hyperkeratosis was observed in the stomach of 10/10 males and 7/10 females from the 30 mg/kg/day groups. Therefore, the LOAEL for systemic toxicity is 30 mg/kg/day based on clinical signs of toxicity in the F_0 and F_1 males and females and on microscopic lesions in the stomach of F_1 males and females. The systemic toxicity NOAEL is 10 mg/kg/day.

Fertility indices for the 100 mg/kg/day F_0 males and females were significantly ($p \leq 0.05$) less than the controls. No treatment-related effects were observed on copulation or fertility of the F_1 rats. The live birth indices for the F_1 litters in the 0, 10, 30, and 100 mg/kg/day groups were 98%, 98%, 90%, and 80% ($p \leq 0.001$). The live birth index was ≥98% for all groups of F_2 litters. For the F_1 pups, the viability indices on lactation Day 4 (precull) were 92%, 96%, 72% ($p \leq 0.01$), and 30% ($p \leq 0.001$), respectively to 0, 10, 30, and 100 mg/kg/day test groups, and the cumulative survival indices were 88%, 94%, 67% ($p \leq 0.01$), and 28% ($p \leq 0.001$), respectively to 0, 10, 30, and 100 mg/kg/day test groups. For the second generation (F_2) pups in the 0, 10, and 30 mg/kg/day groups the viability indices on lactation Day 4 (precull) were 92%, 97%, and 87%, respectively, and the cumulative survival indices were 85%, 93%, and 83%, respectively. Whole litter losses occurred for three mid-dose and six high-dose F_0 females and for two mid-dose F_1 females. Clinical signs of toxicity in the pups associated with whole litter losses were indicative of lack of maternal care.

Body weights of the 100 mg/kg/day F_1 male pups were significantly less than the controls (79 – 86% of controls) beginning on lactation Day 4 (precull) and continuing throughout lactation. Body weights of the 100 mg/kg/day F_1 female pups were significantly less than the controls (81 – 93% of controls) throughout lactation. Body weight gains by the 100 mg/kg/day F_1 male and

female pups were 79% and 82%, respectively, of the control level during lactation days 0-14 and were 93% and 91%, respectively, for lactation days 14-21. Body weights of the 30 mg/kg/day male and female F_1 pups during lactation were slightly but non-significantly lower than the controls. No statistical differences in body weights of the F_2 male pups were observed between the treated and control groups at any time during lactation. F_2 female pups in the 30 mg/kg/day group had significantly lower body weights than the controls on lactation days 14 (93% of controls) and 21 (91% of control). Body weight gains by the 30 mg/kg/day F_2 female pups for lactation days 0-14 and 14-21 were 92% and 87%, respectively, of the control level. Pup body weights in the low-dose group were similar to the controls in both generations. Because dosing of the pups did not begin until after weaning at 25 days of age, the only exposure of the pups to the test article was through the milk.

Treatment with the test article resulted in developmental delays of the offspring including a significantly ($p \leq 0.01$) greater anogenital distance in the 30 mg/kg/day F_2 females as compared to the controls (1.1 mm vs 1.0 mm), delayed eye opening for the 100 mg/kg/day F_1 pups (79% vs 85% of the controls on day 15) and for the 30 mg/kg/day F_2 pups (85% vs 97% of the controls on day 15). Therefore, the LOAEL for reproductive/offspring toxicity is 30 mg/kg/day based on reduced pup survival, lower pup body weights (decrease of 6.1% and based on the litter), and developmental delays during lactation. The reproductive/offspring toxicity NOAEL is 10 mg/kg/day.

In an AMES test (MRID 41975206), IPBC was tested for the ability to cause mutations in *Salmonella typhimurium* strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100. IPBC was found to be non-mutagenic in all five strains with and without metabolic activation at all concentrations tested (1-1000 µg/plate). In a micronucleus assay in mice (MRID 40990404), IPBC at doses of 200, 600, and 2000 mg/kg did not induce any significant increase of the polychromatic erythrocytes (PCE) containing micronuclei from the treated mice when compared to that of the vehicle control mice. In an unscheduled DNA synthesis assay (MRID 40990403), primary rat hepatocytes, eight doses of IPBC ranging from 3.0 to 13.5 µg/mL did not cause an appreciable increase in mean net nuclear grain counts. Doses > 13.5 µg/mL were cytotoxic, supporting the conclusion that IPBC induced cytotoxicity but not genotoxicity in this assay.

In an LLNA study in mice (MRID 50938207), IPBC was administered topically (epidermally) to the dorsal surface of each ear in 16 mice (4 mice per dose) with concentrations of 0, 0.25, 0.5, and 1% (w/w) in acetone: olive oil (4+1v/v). The concentrations were selected based on the results of a pre-test where IPBC was administered topically to the dorsal surface of each ear in 8 mice (1 mice per dose) with concentrations of 0.5, 1, 5, 10, 25, 50, and 75% (w/w) in acetone: olive oil (4+1v/v). In the pre-test, 1% (w/w) was the highest concentration that resulted in avoiding excessive local skin irritation. The application volume, 25 µL/ear/day, was spread over the entire dorsal surface of each ear once daily for three consecutive days. Five days after the

first topical application (Day 6), 250 µL of phosphate-buffered saline (PBS) containing 19.9 µCi of ^{3}H-methyl thymidine (^{3}HTdR) (equivalent to ^{3}HTdR 79.7 µCi/mL) were injected into each test and control mouse via the tail vein. Approximately five hours after treatment with ^{3}HTdR all mice were euthanized by intraperitoneal injection of Sodium Pentobarbital. The draining lymph nodes were rapidly excised and pooled per group (8 nodes per group).

Animals treated with the highest test item concentration showed an erythema of the ear skin (Score 1) from application Day 2 to Day 5, on Day 5, eschar formation was also observed. On Day 6, the animals belonging to this group had ruffled fur. Stimulation Indices (S.I.) of 1.08, 1.31, and 2.50 were determined with the test item at concentrations of 0.25, 0.5, and 1% (w/w) in acetone: olive oil (4+1 v/v), respectively. A clear dose response was observed in the increasing SI values and the 2.50 SI determined for the 1% test item concentration approached the threshold value of 3 in spite of the low-test substance concentration. However, since none of the determined SIs exceeded the threshold value of 3, the result of the LLNA with the test item IPBC was equivocal under the test conditions of this study.

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

A Food Quality Protection Act (FQPA) safety factor of 10x does not have to be retained for risk assessment purposes for IPBC as the toxicological database is complete and does not show offspring susceptibility. Therefore, an FQPA safety factor of 1x will be retained for risk assessment purposes for IPBC.

2.3.4.1 Completeness of the Toxicology Database

The toxicology database for IPBC is complete. The CTA study is being waived and the CCA study is no longer needed to complete the risk assessment. The registrant(s) submitted an LLNA study to satisfy the dermal sensitization study requirement.

2.3.4.2 Evidence of Neurotoxicity

In an acute neurotoxicity study performed in rats (MRID 45509401), changes in motor activity were observed in animals exposed to 300 mg/kg/day IPBC. No neurotoxicity was observed in the subchronic neurotoxicity study (MRID 45509402).

2.3.4.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

The toxicological database for IPBC does not show evidence of sensitivity/susceptibility to the developing or young animal.

2.4 Toxicity Endpoint and Point of Departure Selections

Acute Dietary (Females ages 13-39): The acute dietary (females ages 13-39) endpoint is based on the effects observed in the prenatal developmental toxicity study in rabbits (MRID 43530205). Clinical signs of toxicity such as deterioration resulting in early sacrifice and increased post-implantation loss was observed at the LOAEL of 40 mg/kg/day. None of these effects were observed at the dose of 20 mg/kg/day, therefore, the NOAEL was established at this dose. A 100x uncertainty factor (UF) (10x for interspecies extrapolation, 10x for intraspecies variability) was applied to the POD (see Table 4).

Acute Dietary (General Population): The acute dietary (general population) endpoint is based on the effects observed in the acute neurotoxicity study in rats (MRID 45509401). A change in motor activity was observed at the LOAEL of 300 mg/kg/day. The NOAEL was established at 100 mg/kg/day. A 100x UF (10x for interspecies extrapolation, 10x for intraspecies variability) was applied to the POD.

Chronic Dietary (All Populations): The chronic dietary endpoint is based on the effects observed in the carcinogenicity study in mice (MRID 42008202). An increased incidence of non-neoplastic pathology of the thyroid in both sexes (atrophic vacuolation, follicular coalescence, and general follicular enlargement) was observed at the LOAEL of 20 mg/kg/day. A NOAEL was not established because the lowest dose tested was 20 mg/kg/day. A 1000x UF (10x interspecies extrapolation, 10x for intraspecies variability, 10x use of a LOAEL to extrapolate a NOAEL) was applied to the POD.

Short-/Intermediate-Term Incidental Oral: The incidental oral short- (1-30 days)/intermediate-term (1-6 months) endpoint is based on effects observed in the reproduction and fertility effects study performed in rats (MRID 44478801). Clinical signs of toxicity in the F_0 and F_1 males and females and microscopic lesions in the stomach of F_1 males and females were observed. Reproductive/offspring effects such as reduced pup survival, reduced pup body weights, and developmental delays during lactation were also observed. These effects were observed at the LOAEL of 30 mg/kg/day. None of these effects were observed at the dose of 10 mg/kg/day, therefore, the NOAEL was established at this dose. A 100x UF (10x for interspecies extrapolation, 10x for intraspecies variability) was applied to the POD.

Short-/Intermediate-/Long-Term Dermal: The dermal short- (1-30 days), intermediate- (1-6 months), and long-term (>6 months) endpoints are based on effects observed in the 91-day dermal toxicity study in rats (MRID 42168201). Incidences of slight erythema and desquamation in females and males were observed at the LOAEL of 200 mg/kg/day. None of these effects were observed at the dose of 50 mg/kg/day; therefore, the NOAEL was established at this dose. The dose was converted to a dermal loading value by dividing the dose applied in µg by 10% of the

surface area of the animal (see Table 3). For male rats, the dermal loading value is 326 µg/cm^2, which was calculated by dividing 12,400 µg by 38.03 cm^2. For female rats, the dermal loading value is 292 µg/cm^2, which was calculated by dividing 8850 µg by 30.34 cm^2. The dermal loading value is the average of the male and female dermal loading value, which is 309 µg/cm^2. A 10x UF (3x for interspecies extrapolation, 3x for intraspecies variability) was applied to the POD for all durations of exposure. The 10x UF was reduced from 100x UF because the dermal effects observed were based on irritation effects and there were no adverse systemic effects observed in the study. The reduction of these values is consistent with the recommendations of the 2001 report from the National Resource Council (NRC, 2001), when evidence supports the finding of direct-acting irritation effects that are not influenced by systemic physiologic processes and the magnitude of response is not expected to differ when compared to systemic effects. Short- and intermediate-term exposures occur during residential and occupational uses and long-term exposures only occur during occupational uses.

Short-/Intermediate-/Long-Term Inhalation: The inhalation short- (1-30 days), intermediate- (1-6 months), and long-term (>6 months) endpoints are based on effects observed in the 90-day inhalation toxicity study in rats (MRID 43530203). An increased incidence of epithelial hyperplasia in the ventral region of the larynx and necrosis in the ventral cartilage of the larynx in males and females was observed at the LOAEC of 6.7 mg/m^3. This effect was not observed at the NOAEC of 0.30 mg/m^3; therefore, the NOAEC was established at this dose. A 30x UF (3x for interspecies extrapolation, 10x for intraspecies variability) was applied to the POD for all durations of exposure. The interspecies extrapolation uncertainty factor was reduced from 10x to 3x based on the use of a human equivalent concentration (HEC). The intraspecies variability uncertainty factor was retained at 10x due to systematic effects observed in the inhalation toxicity study in addition to the irritation effects. Short- and intermediate-term exposures occur during residential and occupational uses and long-term exposures only occur during occupational uses.

The dermal doses in mg/kg/day were converted to dermal loadings in ug/cm^2 using the Meeh's equation for Sprague Dawley rats from Gilpin (1996) as shown in Table 3:

Table 3. Dermal Loading Calculations for MRID 42168201

Sex	Dose Group (mg/kg/day)	Body Weight[A] (gm)	Amount Applied[B] (µg)	Body Surface Area[C] (cm^2)	Dosed Area[D] (cm^2)	Loading[E] (µg/cm^2)
Males	50	248	12,400	380	38.0	326
Females		177	8,850	303	30.3	292
Average						309

A. Measured on Day 1 of the study.
B. Amount Applied = Dose (mg/kg/day) * Body Weight (gm) * 0.001 kg/gm * 1,000 µg/mg
C. Body Surface Area (cm^2) = k x W^0.67, Where k = 9.46 and W = weight in grams (Gilpin, 1996)
D. Dosed Area (cm^2) = Body Surface Area (cm^2) * 10 percent
E. Loading (µg/cm^2) = Amount Applied (µg) / Dosed Area (cm^2)

Table 4. Summary of Toxicological Doses and Endpoints for IPBC

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-49)	NOAEL= 20 mg/kg/day	UF =100x (UF_A = 10x UF_H = 10x) FQPA = 1x	aRfD=aPAD=0.20 mg/kg/day	MRID 43530205 Prenatal developmental toxicity study in rabbits Maternal LOAEL = 40 mg/kg/day based on clinical signs of toxicity Developmental LOAEL = 40 mg/kg/day based on decreased total live fetuses, live fetuses/dam, and increased post-implantation loss.
Acute Dietary (General Population)	NOAEL = 100 mg/kg/day	UF =100x (UF_A = 10x UF_H = 10x) FQPA = 1x	aRfD=aPAD=1.00 mg/kg/day	MRID 45509401 Acute neurotoxicity study in rats LOAEL = 300 mg/kg/day based on changes in motor activity.
Chronic Dietary (All Populations)	NOAEL = Could not be established	UF =1000x (UF_A = 10x UF_H = 10x UF_L=10x) FQPA=1x	cRfD=cPAD = 0.020 mg/kg/day	MRID 42008202 Carcinogenicity study in mice LOAEL = 20 mg/kg/day based on increased incidence of non-neoplastic pathology of the thyroid in both sexes (atrophic vacuolation, follicular coalescence, and general follicular enlargement).
Incidental Oral Short- (1-30 days), Intermediate-Term (1-6 months)	NOAEL = 10 mg/kg/day	UF=100x (UF_A = 10x UF_H = 10x)	Residential LOC for MOE = 100	MRID 44478801 Reproduction and fertility effects in study in rats Parental LOAEL = 30 mg/kg/day based on clinical signs of toxicity in the F_0 and F_1 males and females and on microscopic lesions in the stomach of F_1 males and females. Offspring/Reproductive LOAEL = 30 mg/kg/day based on reduced pup

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
				survival, reduced pup body weights F_1 and F_2 generations (decrease of 6.1% and based on the litter), and developmental delays during lactation.
Dermal Short-Term (1-30 days)/ Intermediate-Term (1-6 months)	NOAEL = 50 mg/kg/day (309 µg/cm^2)	UF=10x (UF_A = 3x UF_H = 3x)	Occupational and Residential LOC for MOE = 10	MRID 42168201 91-day dermal toxicity study in rats LOAEL = 200 mg/kg/day (1236 µg/cm^2) based on incidences of slight erythema and desquamation in females and males.
Dermal Long-Term (>6 months)	NOAEL = 50 mg/kg/day (309 µg/cm^2)	UF=10x (UF_A = 3x UF_H = 3x)	Occupational LOC for MOE = 10	MRID 42168201 91-day dermal toxicity study in rats LOAEL =200 mg/kg/day (1236 µg/cm^2) based on incidences of slight erythema and desquamation in females and males.
Inhalation Short-Term (1-30 days)/ Intermediate-Term (1-6 months)	NOAEC = 0.3 mg/m^3 HEC = 0.037 mg/m^3	UF=30x (UF_A = 3x UF_H = 10x)	Occupational and Residential LOC for MOE = 30	MRID 43530203 90-day inhalation toxicity study in rats LOAEC = 6.7 mg/m^3 based on epithelial hyperplasia in the ventral region of the larynx and necrosis in the ventral cartilage of the larynx in males and females.
Inhalation Long-Term (>6 months)	NOAEC = 0.3 mg/m^3 HEC= 0.037 mg/m^3	UF=30x (UF_A = 3x UF_H = 10x)	Occupational LOC for MOE = 30	MRID 43530203 90-day inhalation toxicity study in rats LOAEC = 6.7 mg/m^3 based on epithelial hyperplasia in the ventral region of the larynx and necrosis in the ventral cartilage of the larynx in males and females.
Cancer (oral, dermal, inhalation)	Classification: IPBC has been classified as “not likely” to be carcinogenic.			

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. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern. cRfD = chronic reference dose.
HEC = NOAEC (0.3 mg/m^3) * (6 hours/8 hours) * RDDR (0.164) = 0.037 mg/m^3

The RRDR was calculated using the RDDR DOS program using the following inputs: MMAD = 3.30, GSD = 2.50, BW = 267 g for males and 204 g for female rats. The body weights used are default body weight values for sub-chronic Sprague-Dawley rats as listed in Table 4-5 of Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (U.S. EPA, 1994).

2.5 Endocrine Disruptor Screening Program

The Federal Food Drug and Cosmetic Act (FFDCA) § 408(p) requires EPA to develop a screening program to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." (21 U.S.C. 346a(p)). In carrying out the Endocrine Disruptor Screening Program (EDSP), FFDCA section 408(p)(3) requires that EPA "provide for the testing of all pesticide chemicals," which includes "any substance that is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), including all active and pesticide inert ingredients of such pesticide." (21 U.S.C. 231(q)(1) and 346a(p)(3)). However, FFDCA section 408(p)(4) authorizes EPA to, by order, exempt a substance from the EDSP if the EPA "determines that the substance is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen." (21 U.S.C. 346a(p)(4)).

The EDSP developed by EPA in 1998 includes human and wildlife testing for estrogen, androgen, and thyroid pathway activity and employs a two-tiered approach. Tier 1 consists of a battery of 11 assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid pathways. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship for any estrogen, androgen, or thyroid effect. If EPA finds, based on that data, that the pesticide has an endocrine effect on humans, FFDCA § 408(p)(6) also requires EPA, "as appropriate, [to] take action under such statutory authority as is available to the Administrator … as is necessary to ensure the protection of public health." (21 U.S.C. 346a(p)(6))[1].

Between October 2009 and February 2010, EPA issued Tier 1 test orders/data call-ins (DCIs) for its first list of chemicals ("List 1 chemicals") for EDSP screening and subsequently required submission of EDSP Tier 1 data for a refined list of these chemicals. EPA received data for 52 List 1 chemicals (50 pesticide active ingredients and 2 inert ingredients). EPA scientists performed weight-of-evidence (WoE) analyses of the submitted EDSP Tier 1 data and other scientifically relevant information (OSRI) for potential interaction with the estrogen, androgen, and/or thyroid signaling pathways for humans and wildlife.[2]

[1] For additional details of the EDSP, please visit https://www.epa.gov/endocrine-disruption.

[2] Summarized in *Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions*; EPA-HQ-OPP-2023-0474-0001; https://www.regulations.gov/document/EPA-HQ-OPP-2023-0474-0001

For FIFRA registration, registration review, and tolerance-related purposes, EPA collects and reviews numerous studies to assess potential adverse outcomes, including potential outcomes to endocrine systems, from exposure to pesticide active ingredients. Although EPA has been collecting and reviewing such data, EPA has not been explicit about how its review of required and submitted data for these purposes also informs EPA's obligations and commitments under FFDCA section 408(p). Consequently, on October 27, 2023, EPA issued a Federal Register Notice (FRN) providing clarity on the applicability of these data to FFDCA section 408(p) requirements and near-term strategies for EPA to further its compliance with FFDCA section 408(p). This FRN, entitled *Endocrine Disruptor Screening Program (EDSP): Near-Term Strategies for Implementation' Notice of Availability and Request for Comment* (88 FR 73841) is referred to here as EPA's EDSP Strategies Notice. EPA also published three documents supporting the strategies described in the Notice:

- *Use of Existing Mammalian Data to Address Data Needs and Decisions for Endocrine Disruptor Screening Program (EDSP) for Humans under FFDCA Section 408(p)*;
- *List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed*; and,
- *Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions* (referred to here as List 1 Screening Conclusions).

The EDSP Strategies Notice and the support documents are available on www.regulations.gov in docket number EPA-HQ-OPP-2023-0474. As explained in these documents, EPA is prioritizing its screening for potential impacts to the estrogen, androgen, and thyroid systems in humans, focusing first on conventional active ingredients. Although EPA voluntarily expanded the scope of the EDSP to screening for potential impacts to the estrogen, androgen, and thyroid systems in wildlife, EPA announced that it is not addressing this discretionary component of the EDSP at this time, taking into account its current focus on its comprehensive, long-term approach to meeting its Endangered Species Act obligations (See EPA's April 2022 ESA Workplan[3] and November 2022 ESA Workplan Update[4]). However, EPA notes that for 35 of the List 1 chemicals (33 active ingredients and 2 inert ingredients), Tier 1 WoE memoranda[5] indicate that available data were sufficient for FFDCA section 408(p) assessment and review for potential effects to the estrogen, androgen, or thyroid pathways for wildlife. For the remaining 17 List 1 chemicals, Tier 1 WoE memoranda made recommendations for additional testing. EPA expects to further address these issues taking into account additional work being done in concert with researchers within the EPA's Office of Research and Development (ORD).

As discussed in EPA's EDSP Strategies Notice and supporting documents, EPA will be using all available data to determine whether or what additional data are needed to meet EPA's obligations and discretionary commitments under FFDCA section 408(p). For some

[3] https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf
[4] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf
[5] https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and

conventional pesticide active ingredients, the toxicological databases may already provide sufficient evaluation of endocrine potential for estrogen, androgen, and/or thyroid pathways and EPA will generally not need to obtain any additional data to evaluate those pathways. For instance, EPA has data for numerous conventional pesticide active ingredients on mammalian estrogen and androgen effects through either an acceptable two-generation reproductive study in accordance with the current guideline (referred to here as the updated two-generation reproduction study; OCSPP 870.3800 - Reproduction and Fertility Effects) or an extended one-generation reproductive toxicity (EOGRT) study (OECD Test Guideline 443 - Extended One-Generation Reproductive Toxicity Study). In these cases, EPA expects to make FFDCA 408(p)(6) decisions for humans without seeking further estrogen or androgen data. However, as also explained in the EPA's EDSP Strategies Notice, where these data do not exist, EPA will assess available data for the conventional active ingredient to determine what additional data, if any, might be needed to assess the potential for impacts to estrogen, androgen, and/or thyroid pathways in humans. For more details on EPA's approach for assessing these endpoints, see EPA's EDSP Strategies Notice and related support documents.

Also described in the EPA's EDSP Strategies Notice is a framework that represents an initial approach by EPA to organize and prioritize the large number of conventional pesticides in registration review. For conventional pesticides that lack an updated two-generation reproduction study or an EOGRT study, EPA has used data from the Estrogen Receptor Pathway and/or Androgen Receptor Pathway Models to identify a group of chemicals with the highest priority for potential data collection (described in EPA's EDSP Strategies Notice as Group 1 active ingredients). For these cases, EPA sought in the Federal Register Notice data and information in response to issuance of EPA's EDSP Strategies Notice to better understand the positive findings in the ToxCast™ data for the Pathway Models and committed to issuing DCIs to require additional EDSP Tier 1 data. For the remaining conventional pesticides (described in EPA's EDSP Strategies Notice as Group 2 and 3 conventional active ingredients), EPA committed to assessing the available data to determine what additional studies, if any, might be needed to assess the potential for impacts to endocrine pathways in humans.

Although EPA has prioritized conventional active ingredients as presented in EPA's EDSP Strategies Notice, EPA is planning to develop similar strategies for biopesticide and antimicrobial pesticide (*i.e.*, nonconventional) active ingredients and will provide public updates on these strategies, when appropriate. At this time, EPA is making no findings associated with the implementation of EDSP screening of IPBC. Such issues will be addressed in future updates by EPA on its strategies for implementing FFDCA section 408(p).

2.6 Dietary Exposure and Risk Assessment

2.6.1 FFDCA Considerations

As of August 1, 2022, the Agency has not established tolerances or exemptions from the requirement of tolerances for IPBC under the Federal Food, Drug and Cosmetic Act (FFDCA) Section 408. Further, the US Food and Drug Administration has not established food contact notifications or food additive approvals for IPBC under FFDCA Section 409.

2.6.2 Food Exposure Profile

There is potential for exposure to food contact surfaces when IPBC is used as a materials preservative in dish detergents.

2.6.3 Drinking Water Exposure Profile

Drinking water exposure has the potential to occur when drinking water intakes are downstream from pulp and paper mills, and when IPBC is used as a materials preservative in metal working fluids applications.

2.6.4 Dietary Risk Assessment

2.6.4.1 Materials Preservative in Dish Detergents Risk Assessment

IPBC may be incorporated as a materials preservative in dish detergents at a maximum labeled application rate of 300 ppm (EPA Reg Nos: 5383-170, 5383-171, 6836-469, 1258-1230). Consequently, there is potential for indirect dietary exposure when the dish detergents are used on food contact surfaces such as dishware. The equations used to assess indirect dietary exposure to IPBC from treated dish detergents are presented below:

$$DDD = \frac{RV * CR}{BW}$$

And:

$$\text{RV} = \frac{AR}{1{,}000{,}000} \times C1 \times Ta \times SA$$

Where:

DDD	=	Daily Dietary Dose (mg a.i./kg-bw/day)
DC	=	Dietary Concentration (mg a.i./g food)
RV	=	Residue Value (mg a.i. in the diet)
AR	=	Application Rate of a.i. in final product (ppm a.i.)
C1	=	Concentration of detergent in dish wash solution (mg/cm^3)
Ta	=	Amount of water left on dishes after rinsing (mL/cm^2).
SA	=	Surface area of dishes in daily contact with food (cm^2).
CR	=	Consumption Ratio (unit-less)
BW	=	Body weight (kg-bw)

Assumptions:

- Application Rate: the maximum application rate of IPBC in dish detergents is 300 ppm a.i.
- Concentration of detergent in dish wash solution (C1) (mg/cm^3): The default is 1 mg rinse aid/cm^3 water based on the 2005 Human and Environmental Risk Assessment (HERA) document for dishwashing.[6]
- Amount of water left on dishes after rinsing (Ta) (mL/cm^2). Default is 5.5×10^{-05} mL/cm^2 dishes washed and is based on the 2005 HERA document for dishwashing. [7]
- Surface area of dishes in daily contact with food (SA) (cm^2). The default is 4000 cm^2 based on the FDA assumption (U.S. FDA, 1993)
- Consumption Ratio (CR) (unitless) for each population subgroup varies and is based on the total food consumed in the National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA) survey (see Appendix D, Table D-1) for exact values and details.
- Body weight (BW) (kg-bw): Average body weight data by population subgroup is from the USDA's NHANES/WWEIA 2003-2008 survey (USDA, 2008).

Acute Assessment

Table 5 summarizes the indirect exposure and risks to IPBC in dish detergents. Estimated risks and exposures for all population subgroups are well below 100% (% aPAD <100%) and were not considered risks of concern. The highest population subgroups are females 13-49 years old at 0.0004% if the aPAD.

[6] Concentration of liquid concentrate in dishwashing solution when hand washing dishes was a maximum of 5 g/5 L wash water. (1g/L= 1 mg/mL = 1 mg/cm^3). (HERA, 2005)

[7] Amount of water left on dishes after rinsing cited from Schmitz, J. (1973) and O.J. France (1990) within the HERA Guidance (HERA, 2005). The table in Appendix G of the HERA document states that for dishwashing residues, 5.5×10^{-04} mL/cm^2 of water is left on non-rinsed dinnerware and that 10% of liquid is left after rinsing.

Table 5. Acute Dietary Risks for IPBC in Dish Detergents (300 ppm)

Population Subgroup[5]	Residue Value (mg a.i.)[1]	Consumption Ratio[2]	Daily Dietary Dose (mg/kg-bw/day)[3]	Acute Risk Estimates % aPAD[4]
General U.S. Population	6.60×10^{-05}	1.000	9×10^{-07}	0.0001
All Infants (<1-year old)		0.196	1.7×10^{-06}	0.0002
Children 1-2 years old		0.453	2.4×10^{-06}	0.0002
Children 3-5 years old		0.496	1.8×10^{-06}	0.0002
Children 6-12 years old		0.629	1.1×10^{-06}	0.0001
Youth 13-19 years old		0.780	8×10^{-07}	0.0001
Adults 20-49 years old		1.051	9×10^{-07}	0.0001
Adults 50-99 years old		0.967	8×10^{-07}	0.0001
Females 13-49 years old		0.941	9×10^{-07}	0.0004

1: Residue Value (mg a.i.) = [Active Ingredient Concentration from the label (ppm) ÷ 1,000,000] x Concentration of rinse aid in dish wash solution (1 mg rinse aid/cm^3 water) x Amount of water left on dishes after rinsing (5.50 E-05 mL rinse aid/cm^2 dishes) x Surface area of dishes in contact with food (4000 cm^2).
2: The FDA assumption that a typical American's diet comes in contact with 4000 cm^2 of treated surface per day is based on habits of the general U.S. population. Because different population subgroup consume various quantities of food, a consumption ratio (CR) is used in the commercial dish washing scenarios to account for this difference. CR (unitless) = Total food consumed by population subgroup (kg) ÷ Total food consumed by the general U.S. Population (kg). For example, Children 1-2 years old's total food consumed is 1.77kg, while the general U.S. population consumes 3.91kg. Therefore, the CR for Children 1-2 = 1.77kg / 3.91kg= 0.45269
3: Daily Dietary Dose (DDD) (mg a.i./kg-bw/day) = Residue Value (mg a.i.) x Consumption Ratio ÷ BW (kg-bw)
4: % aPAD = DDD/PAD. Where the aPAD is 1 mg/kg/day for the general and other population subgroups, and 0.2 mg/kg/day for the female 13-49 group.
All exposures are rounded to 1-3 significant figures.
5: For acute exposure, the WWEIA-FCID consumption data were averaged for the entire U.S. population (*i.e.*, general U.S. population) and within population subgroups (*i.e.*, all infants, children 1-2, children 3-5, children 6-12, *etc*.).

Chronic Assessment

As shown in Table 6, dish detergents with up to 300 ppm IPBC do not present chronic dietary exposure or risks of concern (<100% of the cPAD) for any population subgroups. The highest exposed population subgroup is children 1-2 years old at 0.012% of the cPAD.

Table 6. Chronic Dietary Risks for IPBC in Dish Detergents (300 ppm)

Population Subgroup[5]	Residue Value (mg a.i.)[1]	Consumption Ratio[2]	Daily Dietary Dose (mg/kg-bw/day)[3]	Chronic Risk Estimates % cPAD[4]
General U.S. Population	6.60×10^{-05}	1.000	1×10^{-06}	0.005
All Infants (<1-year old)		0.196	1.7×10^{-06}	0.008
Children 1-2 years old		0.453	2.4×10^{-06}	0.012
Children 3-5 years old		0.496	1.8×10^{-06}	0.009
Children 6-12 years old		0.629	1.1×10^{-06}	0.006
Youth 13-19 years old		0.780	8×10^{-07}	0.004
Adults 20-49 years old		1.051	9×10^{-07}	0.004
Adults 50-99 years old		0.967	8×10^{-07}	0.004
Females 13-49 years old		0.941	9×10^{-07}	0.004

1: Residue Value (mg a.i.) = [Active Ingredient Concentration from the label (ppm) ÷ 1,000,000] x Concentration of rinse aid in dish wash solution (1 mg rinse aid/cm^3 water) x Amount of water left on dishes after rinsing (5.50 E-05 mL rinse aid/cm^2 dishes) x Surface area of dishes in contact with food (4000 cm^2).
2: The FDA assumption that a typical American's diet comes in contact with 4000 cm^2 of treated surface per day is based on habits of the general U.S. population. Because different population subgroup consumes various quantities of food, a consumption ratio (CR) is used in the commercial dish washing scenarios to account for this difference. CR (unitless) = Total food consumed by population subgroup (kg) ÷ Total food consumed by the general U.S. Population (kg). For example, Children 1-2 years old's total food consumed is 1.77kg, while the general U.S. population consumes 3.91kg. Therefore, the CR for Children 1-2 = 1.77kg / 3.91kg= 0.45269
3: Daily Dietary Dose (DDD) (mg a.i./kg-bw/day) = Residue Value (mg a.i.) x Consumption Ratio ÷ BW (kg-bw)
4: % cPAD = DDD/PAD. Where the cPAD is 0.02 mg/kg/day
All exposures are rounded to 1 to 3 significant figures.
5: For chronic exposure, the WWEIA-FCID consumption data were averaged for the entire U.S. population (*i.e.*, general U.S. population) and within population subgroups (*i.e.*, all infants, children 1-2, children 3-5, children 6-12, *etc*.).

2.6.4.2 Drinking Water Risk Assessment

Drinking Water Exposure

To evaluate drinking water exposure from point-source discharges, the Agency uses the Exposure and Fate Assessment Screening Tool (E-FAST) version 2014 (U.S. EPA, 2014b) to estimate the concentration of IPBC available in water downstream of industrial sources (refer to Appendix C for further modeling details and model methodology). Table 7 contains the estimated drinking water concentrations (EDWCs) from 1) pulp and paper mills, and 2) a facility using IPBC in metalworking fluids. All values assume that the effluent goes through a wastewater treatment plant (WWTP) where 0% of IPBC is removed before release into nearby waterbodies. The 30Q5 concentration represents the lowest stream flow for 30 consecutive days over a 5-year period and is used to evaluate potential acute risk to humans from ingestion of drinking water containing IPBC if acute oral toxicity effects are identified. The harmonic mean flow concentration is used to evaluate potential chronic risk to humans from ingestion of drinking water if chronic oral toxicity affects are identified.

It should be noted that EDWC values listed below are likely overestimates of exposure because degradation or removal of IPBC occurring within the environment is not accounted for within the E-FAST (U.S. EPA, 2014b) model. The values selected were based on the median surface water concentrations which represent mid-sized stream flows. The highest acute EDWC is 340.5 µg a.i./L (0.3405 ppm). The highest chronic EDWC from the modeled use patterns is 135.9 µg a.i./L (0.1359 ppm) pulp and paper mills using an application rate of 8,000 ppm IPBC, Reg No. 5383-170. This drinking water concentration is considered protective of other current registered uses of IPBC which may contribute to drinking water exposure.

Table 7. Estimated Drinking Water Concentrations (EDWCs) from IPBC Uses

Use Pattern	Application Rate	30Q5 Concentration (for Acute)[1]	Harmonic Mean Concentration (for Chronic)[1]
Pulp and Paper Mills[2]	8,000 ppm	340.5 µg a.i./L	135.9 µg a.i./L

Metalworking Fluid[3]	5,300 ppm	64.2 µg a.i./L	27.3 µg a.i./L

1: Assumes 0% removal of IPBC within a WWTP for all use patterns.
2: Represents the highest application rate, EPA Reg. No. 5383-170.
3: Represents the highest application rates, EPA Reg. No.s 5383-171, 5383-77, 5383-91.
The application rates are rounded to 3-4 significant figures.

Drinking Water Risks

EDWCs from the 8,000 ppm pulp and paper scenario were used as inputs in the Dietary Exposure Evaluation Model with the Food Commodity Intake Database (DEEM-FCID) Version 3.16 (US EPA, 2014a). The software uses the 2003-2008 food consumption data from the US Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA) (USDA, 2008). The FCID commodity tab within DEEM contains three choices of water available for analysis: 1) Water, direct, tap; 2) water, direct bottled; and 3) water, indirect, all sources. All three sources were considered and evaluated for this assessment, and the definition of each type is available in Appendix D. Table 8 indicates that acute and chronic exposure and drinking water risks from pulp and paper mills are not of concern (<100% of the aPAD and cPAD) for all population subgroups. The highest estimated risks are for females (13-49 years old) at 9.27% of the aPAD. For the chronic scenario, the highest estimated risk is for all infants (<1 year old) at 36.7% of the cPAD.

Table 8. Acute and Chronic Drinking Water Risks for IPBC

Population Subgroup[4]	95th Percentile Exposure (Dose) (mg/kg/day)[1]	Acute Risk Estimates % aPAD[2]	Average Exposure (Dose) (mg/kg/day)[3]	Chronic Risk Estimates % cPAD[2]
General U.S. Population	0.018566	1.86	0.002845	14.2
All Infants (<1 year old)	0.058154	5.82	0.007335	36.7
Children 1-2 years old	0.028630	2.86	0.004103	20.5
Children 3-5 years old	0.023231	2.32	0.003457	17.3
Children 6-12 years old	0.017750	1.78	0.002493	12.5
Youth 13-19 years old	0.015462	1.55	0.002074	10.4
Adults 20-49 years old	0.018271	1.83	0.002838	14.2
Adults 50-99 years old	0.016275	1.63	0.002806	14.0
Females 13-49 years old	0.018531	9.27	0.002828	14.1

1: Acute concentration is based on 30Q5 Stream Flow Distribution (340.5 ppb, or 0.3405 ppm). The 30Q5 is the lowest stream flow for 30 consecutive days over a 5-year period.
2: % PAD = (Exposure Dose / PAD) PAD x 100%. Where the aPAD is 1.0 mg/kg/day, 0.20 mg/kg/day (females 13-49) and the cPAD is 0.02 mg/kg/day from Table 4. % PADs for population subgroups that are of concern are bolded.
3: Chronic Concentration is based on Harmonic Mean Stream Flow Distribution (135.9 ppb, or 0.1359 ppm)
4: WWEIA-FCID consumption data were averaged for the entire U.S. population (*i.e.*, general U.S. population) and within population subgroups (*i.e.*, all infants, children 1-2, children 3-5, children 6-12, *etc*.).

2.6.5 Dietary Co-Occurrence

To obtain the dietary portion of the aggregate risk assessment, the Agency must determine the co-occurrence of dietary sources of chemicals. As discussed and assessed above (Section 2.6.4

Dietary Risk Assessment), dietary and drinking water exposures to IPBC have the potential to occur from the following use sites: 1) materials preservatives in dish detergents evaluated at 300 ppm a.i. and 2) in drinking water exposure from the use of IPBC in industrial water systems with effluent discharged into freshwater waterbodies (acute exposure to 340.5 ppb a.i.; chronic exposure to 135.9 ppb a.i.).

In order for a use pattern to be considered for a dietary aggregate assessment, the use pattern must first pass its individual assessment. Since all the assessed use sites (*i.e.*, dish detergent and drinking water) passed their individual acute and chronic assessments, all were considered within the co-occurrence assessment.

Acute Co-Occurrence

The dietary co-occurrence exposures (acute dietary aggregate) and risks are provided in Table 9. Dietary aggregated risks are shown as 9% of the aPAD for females (13-49 years old), 6% for all infants, 3% for children 1-2 years old which are not a risk of concern (<100% aPAD) for the population subgroups listed the table below.

Table 9. Acute Dietary and Drinking Water Co-Occurrence for IPBC

Dietary Source	All Infants <1 year old[5]		Children 1-2 year[5]		General Population[5]		Females 13-49 years old[5]	
	Daily Dose (mg/kg-bw/day)	% aPAD	Daily Dose (mg/kg-bw/day)	% aPAD	Daily Dose (mg/kg-bw/day)	% aPAD	Daily Dose (mg/kg-bw/day)	% aPAD
Dish Detergent[1]	1.7×10^{-06}	0.0002	2.4×10^{-06}	0.0002	9×10^{-07}	0.0001	9×10^{-07}	0.0004
Drinking Water[2]	0.058	5.82	0.029	2.86	0.019	1.86	0.019	9.27
Dietary Aggregate[3,4]	0.058	6	0.029	3	0.019	2	0.019	9

1: Dish detergents at 300 ppm a.i.
2: Drinking water from intakes downstream of pulp and papermills is expected to be protective of drinking water from intakes downstream of other industrial use sites applying IPBC such as metalworking fluids.
3: Co-Occurrence (mg/kg/day) = Exposure from dish detergents + Exposure from Drinking Water.
4: % aPAD = (Daily Dose / aPAD) * 100%, where the aPAD for IPBC is 1.0 mg/kg/day for general populations, all infants and children 1-2 years old. The aPAD is 0.20 mg/kg/day for females 13-49.
The dietary aggregate has been rounded up for all populations presented.
5: WWEIA-FCID consumption data were averaged for the entire U.S. population (*i.e.*, general U.S. population) and within population subgroups (*i.e.*, all infants, children 1-2, children 3-5, children 6-12, *etc.*).

Chronic co-occurrence

The dietary co-occurrence exposures (chronic dietary aggregate) and risks are provided in Table 10 below and show 37% cPAD for all infants, 22% cPAD for children 1-2 years old, and 14% cPAD for the general population which are not a risk of concern (<100% cPAD) for all

population subgroups. The aggregated dietary risk for the highest exposed population contributes to 37 % of the cPAD for all-infants.

Table 10. Chronic Dietary and Drinking Water Co-Occurrence for IPBC

Dietary Source	All Infants <1 year old[5]		Children 1-2 year[5]		U.S. General Population[5]	
	Daily Dose (mg/kg-bw/day)	% cPAD	Daily Dose (mg/bw-kg/day)	% cPAD	Daily Dose (mg/kg-bw/day)	% cPAD
Dish Detergent[1]	2.4×10^{-06}	0.012	1.7×10^{-06}	0.008	1×10^{-06}	0.005
Drinking Water[2]	0.0073	36.7	0.0041	21.5	0.0028	14.2
Dietary Aggregate[3,4]	0.0073	37	0.0041	22	0.0028	14

1: Dish detergents at 300 ppm a.i.
2: Drinking water from intakes downstream of pulp and papermills is expected to be protective of drinking water from intakes downstream of other industrial use sites using IPBC such as metalworking fluids.
3: Co-Occurrence (mg/kg/day) = Exposure from dish detergents + Exposure from drinking water.
4: % cPAD = (Daily Dose / cPAD) * 100%, where the cPAD for IPBC is 0.02 mg/kg/day.
The dietary aggregate has been rounded up for all populations presented.
5: WWEIA-FCID consumption data were averaged for the entire U.S. population (*i.e.*, general U.S. population) and within population subgroups (*i.e.*, all infants, children 1-2, children 3-5, children 6-12, *etc*.).

2.7 Residential (Non-Occupational) Exposure/Risk Characterization

2.7.1 Residential Handler Exposure

Based on toxicological criteria and potential for exposure, the Agency has conducted inhalation and dermal risk assessments for residential handler exposure. The residential exposure scenarios assessed for IPBC represent the high-end exposure scenarios. The EPA-selected high-end exposure[8] scenarios are assessed at the maximum application rates as stated on the product labels. Exposures from the use of paint, which is a surrogate for stains, caulks, sealants, coatings, and adhesives, and the use of preserved cleaning products are anticipated to be of a short to intermediate term duration. This is because painting is conducted for a few days per year and preserved cleaners are used intermittently.

2.7.2 Residential Paint Exposures from IPBC

There is potential for short-term residential handler dermal and inhalation exposures when using paints preserved with IPBC or when using paint primer, wood preservative stains, caulks,

[8] An estimate of individual exposure or dose for those persons at the upper end of an exposure or dose distribution, conceptually above the 90th percentile, but not higher than the individual in the population who has the highest exposure or dose (U.S. EPA, 2011).

sealants, or adhesives that contain IPBC. The residential paint handler assessment uses paint as a surrogate[9] use for stains, caulks, sealants, coatings, and adhesives.

Inhalation MOEs for Residential Painters

The MOEs for residential handler inhalation exposures to IPBC from the paint use were assessed as outlined in Table 11. An MOE greater than or equal to 30 is considered adequately protective for the inhalation route of exposure. Inhalation exposures from the paint uses were assessed as 8-hour time weighted averages (TWA) as outlined in Table 11. The MOEs for brush/roller paint application is above the LOC of 30 and are not of concern. The MOE for airless spray application of paint is 0.21 and is of concern because it is less than the LOC of 30 for short- and intermediate-term exposures. If the application rate of paint is reduced to 66.13 ppm a.i., the MOE for the airless spray application of IPBC preserved paint would be 30 and would not be of concern. The MOE for aerosol paint primer is 1.2 and is of concern because it is less than the MOE of 30. If the application rate is reduced to 58.61 ppm a.i., the MOE for aerosol paint increases to 30 and would not be of concern.

Table 11. Short-Term Residential Handler Painter Inhalation MOEs

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Product Density (lb/gal)	Amount a.i. Handled (lb)[C]	8-Hour Inhalation Unit Exposure (UE)[D] (mg/m^3/lb a.i.)	Inhalation Exposure (mg/m^3)[H]	Inhalation MOE (LOC= 30)[I]
Airless Spray Paint Application	9,600	15	10	1.4	0.124 [E]	0.18	**0.21**
Brush/Roller Paint Application	9,600	2	10	0.19	0.00097 [F]	0.00019	200
Aerosol paint primer	1,500	0.31	9.05	0.0042	7.5 [G]	0.032	**1.2**

A. The application rates are the maximum rates from the labels: 5383-197, 69587-6.
B. Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c).
C. Amount of a.i. Handled (per day) (AaiH in lb ai) = Application Rate (ppm a.i./1,000,000) x product density x number of gallons applied. Assumption for paint density is 10 lb/gal. Aerosol paint primer density (69587-6) is 9.05 lb/gal.
D. Inhalation unit exposures are based on AEATF II.
E. 8-hour TWA from the AEATF II Airless Sprayer Study (MRID 50879401).
F. 8-hour TWA from the AEATF II Brush/Roller Study (MRID 50521701).
G. 8-hour TWA from the AEATF II Aerosol Study (MRID 48659001).
H. 8-hour TWA Inhalation Exposure (mg/m^3) = Amount a.i. Handled (lb) x UE (mg/m^3/lb a.i.).
I. Inhalation MOE = HEC (0.037 mg/m^3) / Daily inhalation exposure (mg/m^3). *MOEs are rounded to two significant figures.

Dermal MOEs for Residential Painters

[9] Standard exposure scenarios have been conservatively developed to represent the high-end of exposures and these scenarios are used to represent other exposures from uses that are believed to be somewhat similar. Using high-end exposure scenarios to represent other uses is analogous to batching (*e.g.*, the exposure to paint represents exposure to stains, inks, adhesives, caulks, coatings) (U.S. EPA, 2012)

The MOEs for residential handler dermal exposures to IPBC were assessed as outlined in Table 12. An MOE greater than or equal to 10 is considered adequately protective for the dermal route of exposure. The MOE of 6.7 for airless spray is less than the LOC of 10 and is of concern. If the application rate of the paint is reduced from 9,600 ppm to 6,400 ppm, the MOE increases to 10 and is no longer of concern. The MOEs for brush roller applications of paint and the application of paint primer are of not of concern because they are greater than the LOC of 10.

Table 12. Short-Term Residential Handler Painter Dermal MOEs

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Product Density (lb/gal)	Amount AI Handled (lb)[C]	Dermal Unit Exposure (UE) (mg/lb a.i.)[D]	Dermal Exposure (mg/day)[H]	Dermal Loading (µg/cm^2)[I]	MOE Dermal (LOC = 10)[J]
Airless Spray Paint Application	9,600	15	10	1.4	105[E]	150	46	**6.7**
Brush/Roller Paint Application	9,600	2	10	0.19	144[F]	27	25	12
Aerosol paint primer	1,500	0.31	9.05	0.0042	43.6[G]	0.18	0.049	6,300

A. The application rates are the maximum rates from the labels: 5383-197, 69587-6.
B. Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c).
C. Amount of AI Handled (per day) (lb a.i.) = Application Rate (ppm a.i./1,000,000) x product density x number of gallons applied. Assumption for paint density is 10 lb/gal. Aerosol paint primer density (69587-6) is 9.05 lb/gal.
D. Dermal (short pants/short sleeved shirts, no gloves) unit exposures are based on AEATF II.
E. AEATF II Airless Sprayer Study (MRID 50879401). Hand Exposure = 25%
F. AEATF II Brush/Roller Study (MRID 50521701). Hand Exposure = 76%
G. AEATF II Aerosol Study (MRID 48659001). Hand Exposure = 22%
H. Dermal Exposure = Amount AI Handled (lb) x UE (mg/lb a.i.).
I. Dermal Loading = [Dermal Exposure (mg/day) * Hand Exposure (%/100) * 1000 µg/mg]/Hand Area (820 cm^2)
J. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm^2). MOEs in **bold** are below the LOC and of concern.*MOEs are rounded to two significant figures.

2.7.3 Residential Handler Exposures from IPBC Preserved Cleaning Products

There is potential for short-term inhalation and dermal exposure to homeowners applying IPBC preserved products including detergents (*e.g.,* dish soaps), laundry detergent, air fresheners, surface cleaners, ready to use wipes, floor care products, bathroom cleaners, window cleaners, fabric care products (including stain removers and fabric softeners), and automotive care products. Many of the products mentioned applied to surfaces such as countertops, fabrics, and floors using trigger pump sprays, wipes, and mops and represent the high-end of exposures. These scenarios are used to represent other exposures from uses that are believed to be somewhat

similar (the use of air fresheners, dish soap, and laundry detergent). There is also the potential for post-application exposure to treated surfaces (*e.g.*, floors).

Inhalation MOEs for Residential Cleaning Products

For inhalation exposures, the LOC for identifying inhalation risks of concern for short- and intermediate-term durations is 30. Inhalation exposures from the cleaning uses were assessed as 8-hour TWA as outlined in Table 10. The inhalation MOEs for mopping, spray and wipe, and ready-to-use wipes (RTU wipes) are all greater than 30; therefore, there are no risks of concern for inhalation exposures.

Table 13. Residential Handler Inhalation Cleaning MOEs for IPBC

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Amount AI Handled (lb)[C]	8-Hour TWA Inhalation Unit Exposure (UE)[D] (mg/m^3/lb AI)	Inhalation Exposure (mg/m^3)[H]	Inhalation MOE (LOC= 30)[I]
Mopping floors	600	1	0.005	0.0098 [E]	0.000049	750
Trigger Spray & wipe		0.06	0.0003	3.12 [F]	0.00094	39
Ready-to-use (RTU) Wipes				0.079 [G]	0.000024	1,600

A. Maximum application rate on label 5383-91.
B. Antimicrobial Exposure Joint Venture (AEJV) (MRIDs 46799302 and 46730501).
C. Amount of a.i. Handled (lb/day) = Application Rate (ppm a.i./1,000,000) x Amount Applied x Cleaner Density (8.35 lb/gallon)
D. Inhalation unit exposures are based on AEATF II.
E. 8-hour TWA from the AEATF II Studies for Mopping (MRIDs 48210201, 48231201, 48231901).
F. 8-hour TWA from the AEATF II Study for Trigger Spray and Wipe (MRID 48375601).
G. 8-hour TWA from the AEATF II Study for RTU wipes (MRID 48375601).
H. 8-hour TWA Inhalation Exposure (mg/m^3) = Amount AI Handled (lb) x UE (mg/m^3/lb ai).
I. Inhalation MOE = HEC (0.037 mg/m^3) / Daily inhalation exposure (mg/m^3). *MOEs are rounded to two significant figures.

Dermal MOEs for Residential Cleaning Products

For dermal exposures, the LOC for identifying risks of concern for short- and intermediate-term durations is 10. The dermal MOEs for mopping, spray, and wipe, and RTU wipes are all greater than 10; therefore, there are no risks of concern for dermal exposures.

Table 14. Residential Dermal Cleaning MOEs for IPBC

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Amount AI Handled (lb)[C]	Dermal Unit Exposure (mg/lb AI)[D]	Dermal Exposure (mg/day)[H]	Dermal Loading (µg/cm^2)[I]	Dermal MOE (LOC = 10)[J]
Mopping floors	600	1	0.005	82 [E]	0.41	0.19	1,600
Trigger Spray & wipe		0.06	0.0003	1,740 [F]	0.52	0.33	950
Ready-to-use (RTU) Wipes				2,740 [G]	0.82	0.82	380

A. Maximum application rate on the proposed label 5383-91.
B. Antimicrobial Exposure Joint Venture (AEJV) (MRIDs 46799302 and 46730501).
C. Amount of a.i. Handled (lb/day) = Application Rate (ppm a.i./1,000,000) x Amount Applied x Cleaner Density (8.35 lb/gallon)
D. Dermal unit exposures are based on AEATF II.
E. AEATF Studies for Mopping (MRIDs 48210201, 48231201, 48231901). Hand Exposure = 38%
F. AEATF Study for Trigger Spray and Wipe (MRID 48375601). Hand Exposure = 51%
G. AEATF II Study for RTU wipes (MRID 48375601). Hand Exposure = 82%
H. Dermal Exposure: Amount AI Handled (lb) x UE (mg/lb ai).
I. Dermal Loading = [Dermal Exposure (mg/day) * Hand Exposure (%/100) * 1000 µg/mg]/Hand Area (820 cm^2)
J. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm2) *MOEs are rounded to two significant figures.

2.8 Residential (Non-Occupational) Post-Application Exposure

There is the potential for residential post-application exposures to materials that are preserved with IPBC. These materials include wood structures such as decks and children's play sets, PVC flooring, IPBC preserved carpet fibers, IPBC preserved textiles, textiles laundered in IPBC preserved detergent, floors cleaned with IPBC preserved cleaners, and IPBC preserved pool liners. The exposures can occur via the dermal and incidental oral exposure routes.

2.8.1 Post-Application Exposure to Treated Wood

Use of the SHEDS Wood Model to Assess Post-Application Exposures to Treated Wood

There is a potential for toddler exposure to biocide residues when playing on treated wood structures such as decks and children's play sets. Both dermal and incidental oral exposures are anticipated. The frequency of exposure is believed to be best represented by the short-term

duration; *i.e.*, 1 to 30 days of continuous exposure. Intermediate-term exposures are also possible; *i.e.*, a small portion of the population of children may play continuously on treated structures up to 6 months at a time.

AD's initial post-application exposure scenario for pressure treated wood was developed collaboratively between EPA's Office of Research and Development (ORD) and AD. ORD led this effort and developed the Stochastic Human Exposure and Dose Simulation (SHEDS) wood model. The SHEDS report along with the Agency's response to the Science Advisory Panel's (SAP) review comments are included in the EPA/600/X-05/009 report (Zartarian et al., 2005).

SHEDS is a probabilistic exposure model and assesses children contacting chromate copper arsenate (CCA) treated structures (*i.e.*, decks and play sets). It was reviewed at the Agency's SAP for use in the CCA assessment. The SHEDS model can be modified for chemicals that are applied to wood as preservatives. However, using SHEDS is a resource intensive effort. Therefore, a deterministic approach using knowledge obtained from the SHEDS assessment is presented herein. The high-end screening-level estimate presented herein is appropriate to determine "reasonable certainty of no harm" (Zartarian et al., 2005).

Input parameters, such as the transferable residue, as well as algorithms have been slightly modified from those presented in the SHEDS documents, based on assumptions that have been selected by the Agency. Specific assumptions have been outlined regarding the dermal and incidental oral exposure MOE calculations to IPBC in pressure treated wood.

The SHEDS model includes the following exposure scenarios for children playing on treated structures:

- Dermal exposure to wood transferable residues;
- Incidental ingestion from hand-to-mouth activities (wood residues);
- Incidental ingestion from soil; and
- Dermal exposure to soil.

Based on the results of the CCA assessment, direct contact with the treated wood exhibits the highest potential for exposure. It is expected for wood preservative to leach into the soil, and for the leached wood preservative in the soil to result in dermal exposure to children. However, the leached wood preservative in the soil and subsequent exposure to children is anticipated to be much less than that attributed to direct contact with the preservative on treated wood itself by more than a factor of ten (Zartarian et al., 2005). Therefore, the exposure from soil is expected to be a minimal additional contribution compared to the exposure from contact with the treated wood; and therefore, only contact to treated wood is quantified in this assessment.

Assumptions:

SR: The surface residue, also referred to as dislodgeable residue (DLR), is used to determine the available residue transfer to an individual contacting the treated wood (*i.e.*, transferable residue). In lieu of chemical-specific wipe data, the Agency uses a generic residue estimate of 1 µg/cm^2. The transferable residue estimate of 1 µg/cm^2 accounts for the skin reduction factor, or "transfer efficiency" from a cloth wipe (*i.e.*, cloth wipe surface residues are higher than that available to the skin) and represents a bounding estimate of the steady state amount of residue on a hand wiping the surface of treated wood (U.S. EPA, 2006). The 1 µg/cm^2 value is based on an analysis of wood transfer data from decks from geographic regions including DC, PA, GA, and FL for arsenic and chromium (Zartarian et al., 2005). For more information the reader is referred to the Zartarian et al, 2005 report and the studies from the American Chemistry Council (ACC) (ACC, 2003) and US Consumer Product Safety Commission (CPSC) (CSPC, 2003a; 2003b; 2003c).

MOEs for Dermal Exposure to IPBC in Pressure Treated Wood

The MOEs were calculated for dermal exposures (ages 1<2 years old) to IPBC using the DLR data and the dermal NOAEL as outlined in Table 15. The MOE is 309 for short- and intermediate-term exposure and is not of concern because it is above the LOC of 10.

Table 15. Dermal MOEs for IPBC Treated Wood

Dislodgeable Residue (µg/cm^2)	Short and Intermediate Term Dermal MOE[B] (LOC = 10)
1.0[A]	309
A. The 1 µg/cm^2 value is the highest estimate of residue transfer from the data available. B. MOE = NOAEL (309 µg/cm2) / Dislodgeable Residue (µg/cm^2). *MOEs are rounded to two significant figures.	

Calculation of the Incidental Oral Exposure

To assess incidental oral exposures for hand to mouth contact with treated wood, the dislodgeable surface residue (DLR) values along with exposure algorithms and parameters from the probabilistic SHEDS model (U.S. EPA, 2008) is used. Since the incidental oral toxicological endpoint of concern for IPBC is not based on long-term effects such as cancer, the lifetime averaging of exposure over time that is provided in the SHEDS model for CCA is not appropriate for this assessment. The frequency of exposure for IPBC is believed to be best represented by the short to intermediate-term duration (*i.e.*, 1 to 180 days of continuous exposure).

The potential daily incidental oral dose is estimated using the following modified equation from the SHEDS report (*i.e.*, U.S. EPA, 2008 Appendix 2, pages A2-A8):

$$D = (SR \times SA \times FQ \times ET \times SE \times CF) / BW$$

Where:

D = Dose (mg/kg/day);
SR = Wood surface residue adjusted for dermal transfer or "transfer efficiency" (μg/cm^2);
SA = Surface area of the hands that contact the treated area and subsequently the child's mouth (cm^2/event);
FQ = Frequency of hand-to-mouth events (events/hour);
SE = Saliva extraction efficiency (unitless fraction);
ET = Exposure Time (hours/day);
BW = Body weight (kg);
CF = Unit conversion factor (0.001 mg/μg)

Assumptions:

- SR: see surface residue discussion above (same residues assumed from the dermal exposure route);

- SA: Surface area of the hands that contact the treated area and subsequently the child's mouth (20 cm^2/event) from the Exposure SAC Policy No. 12, Revised 2/22/01 (U.S. EPA, 2001b). This is the product of the amount of the hand mouthed and the size of a hand. The amount mouthed is the arithmetic average fraction of a hand mounted per event observed in Leckie et al 2000 and calculated in Zartarian et al, 2005 of 0.127 rounded to 0.13. The size of the hand of a 1<2-year-old is 150 cm^2. HED uses these assumptions, however in their SOP they have the two terms separated out (U.S. EPA, 2012c).

- FQ: Frequency of hand-to-mouth events (20 events/hour) as recommended by the Exposure Factors Handbook: 2011 Edition (citing 2007 Xue, et al. meta-analysis).

- SE: Saliva extraction efficiency is 50%. (Zartarian et al., 2005).

- ET: Exposure Time (mean 1.5 hour/day) from the HED Residential SOP for outdoor exposure time for turf (U.S. EPA, 2012c). This value is 0.5 hours higher than the assumption from the SHEDS final wood report; the value of 1.5 hours (rounded to 2 hours) was used instead because the 2012 residential SOP is more recent;

MOEs for Incidental Oral Exposure to Treated Wood

The incidental oral MOEs were calculated for IPBC as outlined in Table 16. The MOE of 270 is greater than the LOC of 100 and is not of concern.

Table 16. Incidental Oral MOEs for IPBC Treated Wood

Dislodgeable Residue (µg/cm^2)	Hand Area Mouthed (cm^2/event)	Frequency of Hand to Mouth Events per Hour	Exposure Time (hours/day)	Exposure[B] (mg/day)	Dose[C] (mg/kg/day)	MOE[D] (LOC = 100)
1.0[A]	20	20	2	0.4	0.036	270

A. The 1 µg/cm^2 value is the highest estimate of residue transfer from the data available.
B. Exposure (mg/day) = DLR (µg/cm2) * Hand Area Mouthed (cm^2/event) * Exposure Frequency (events/hr) * Exposure Time (hrs/day) * Saliva Extraction Factor (50%/100) * 0.001 mg/µg
C. Dose (mg/kg/day) = Exposure (mg/day) / BW (11 kg for 1 <2-year-old children)
D. MOE = NOAEL / Dose where the NOAEL is 10 mg/kg/day for IPBC. *MOEs are rounded to two significant figures.

2.8.2 Post-Application Exposures from IPBC Preserved Carpets

EPA Reg. No. 6836-467 indicates that carpet fibers can be treated with IPBC as a material preservative during the manufacturing process. Therefore, post-application dermal and incidental oral exposures to IPBC residues may occur from playing on carpet fibers. Since the carpet fibers are impregnated with the antimicrobial and the carpeting can be used in a residential setting, there is potential for exposure to occur every day, assuming the antimicrobial has a relatively long half-life in indoor environments. Therefore, both short- and intermediate-term exposures durations are assessed.

Dermal MOE for Irritation Effects from Preserved Carpet Fibers

To calculate the potential for dermal exposures when the toxicological endpoint is based on dermal irritation the following equation was used:

DL = SR x TF

Where:

DL = Dermal Loading (µg/cm^2)
SR = Surface residue (µg/cm^2)
TF = Transfer factor from carpet to skin (%/100)

The surface residue (SR) on cleaned carpets is calculated with the following equation:

SR = CD x WF x CF

Where:

SR = Surface residue (ug/cm^2)
CD = Carpet density (mg/cm^2)
WF = Weight fraction a.i. in carpet (% a.i./100)
CF = Unit conversion factor (1,000 µg/mg)

Dermal exposures were assessed as shown in Table 17. Since transferable residue data are not available for IPBC-treated carpet, the transfer factor was assumed to be 100% transfer. The MOE of 0.20 is of concern because it is less than the LOC of 10. The MOE would be 10 if the transfer was 2%[10].

Table 17. Dermal MOE for Exposure to IPBC Preserved Carpets

Application Rate[A] (ppm a.i.)	Carpet Density[B] (mg/cm^2)	Surface Residue[C] (mg/cm^2)	Dermal Loading[F] (µg/cm^2)	Dermal MOE[G] (LOC = 10)
10,000	153	1.53	1,530	**0.20**

A. Based on the product application rate of 2.5% for fabric and fibers listed in EPA Reg. No. 6836-467 which contains 40% a.i.
B. Average face-weight of 45 ounces (153 mg/cm^2) reported for residential carpet (Fletcher, 2022).
C. Surface Residues (mg/cm^2) = Application Rate (ppm/1,000,000) * Carpet Density (mg/cm^2)
F. Dermal Loading (µg/cm2) = Surface Residues (mg/cm2) * Transfer Factor (100%) * 1000 ug/mg
G. MOE = NOAEL (309 µg/cm2) / Dermal Loading (µg/cm2) MOEs of concern are **bold**. *MOEs are rounded to two significant figures.

Incidental Oral Exposure from Preserved Carpet Fibers

There is potential for incidental oral exposures when children exhibiting hand-to-mouth behavior come into contact with preserved carpet. These exposures are assessed using the Post-application Hand-to-Mouth Exposure Algorithm from Section 7.2.3 of the Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c). This algorithm is as follows:

$$Exp = HR * (F_M * SA_H) * (ET * NR) * [1 - (1\text{-}SE)^{FHtM / NR}]$$

Where:

Exp = Exposure (mg/day)
HR = Hand Residue (mg/cm^2)
F_M = Fraction of hand surface area mouthed / event (fraction/event)
ET = Exposure time (hours/day)
SA_H = Surface area of one hand (cm^2)
NR = Number of replenishment intervals per hour (U.S. EPA, 2012c)
SE = Saliva extraction factor (*i.e.* mouthing removal efficiency)
FHtM = Number of hand to mouth contacts per hour (U.S. EPA, 2012c)

The exposure was calculated using the surface residue value of 1.53 mg/cm^2 that was used for dermal exposures to carpets (Table 17) as the hand residue and the following assumptions from

[10] If the application rate were reduced to 201.96 ppm a.i., the LOC increases to 10 and is not of concern.

Table 7-13 of U.S. EPA, 2012c.

- F_M: The fraction of the hand mouthed per event is 0.13.
- SA_H: The surface area of one hand is 150 cm^2.
- ET: The exposure time is 4 hours/day for carpet.
- NR: The number of replenishment intervals per hour is 4.
- SE: The saliva extraction fraction is 0.48.
- FHtM: The number of hand-to-mouth contacts per hour is 20 for indoor environments.

The SHEDs Exponent term, $1 – (1\text{-SE})^{FHtM / NR}$, is simplified to 0.962 based on the standard assumptions of 0.48 for saliva extraction efficiency (SE), 20 per hour for Frequency of Hand to Mouth Events (FHtM) and 4 per hour for Number of Hand Replenishments (NR) (U.S. EPA, 2012c)).

The incidental oral MOE for exposure to carpet fibers preserved with IPBC was calculated using the above formulas and assumptions as outlined in Table 18. The MOE of 0.24 is of concern because it is less than the LOC of 100. If the transfer factor is reduced to 0.0024 for a 0.24% transfer, the incidental oral MOE for IPBC preserved carpet fibers would increase to 100 and is not of concern. Data can be submitted to determine that the transfer percentage from preserved carpet fibers is 0.24% or below.[11]

Table 18. Incidental Oral MOE for IPBC Preserved Carpet

Application[A] Rate (ppm a.i.)	Carpet Density[B] (mg/cm^2)	Surface Residue[C] (mg/cm^2)	Hand Residue[D] (mg/cm^2)	SHEDs Exponent Term[E]	Exposure[F] (mg/day)	Dose[G] (mg/kg/day)	Incidental Oral MOE[H] (LOC = 100)
10,000	153	1.53	1.53	0.962	460	42	**0.24**

A. Based on the product application rate of 2.5% for fabric and fibers listed in EPA Reg. No. 6836-467 which contains 40% a.i.
B. Average face-weight of 45 ounces (153 mg/cm^2) reported for residential carpet (Fletcher, 2022).
C. Surface Residue (SR) = Density (153 mg/cm^3) * Application Rate/1,000,000.
D. Hand Residue (HR) = SR (mg/cm^2) * Transfer Factor (1.0).
E. SHEDs Exponent Term = $[1 – (1\text{-SE})^{FHtM/NR}]$, where SE = 0.48, FHtM = 20/hr and NR = 4/hr.
F. Exposure (mg/day) = HR (mg/cm^2) * F_M (0.13) * SA_H (150 cm^2) * ET (4 hrs) * NR (4/hr) * SHEDS Exponent Term.
G. Dose (mg/kg/day) = Exposure (mg/day) / BW (11 kg child).
H. MOE = NOAEL (10 mg/kg/day) / Dose (mg/kg/day). MOEs of concern are **bold**. *MOEs are rounded to two significant figures.

2.8.3 Post-Application Exposures from IPBC in PVC Flooring

There is potential for residential post-application incidental oral and dermal exposure to polyvinyl chloride (PVC) flooring materials preserved with IPBC. The maximum application rate for the preservation of PVC flooring, is 1,080 ppm; thus, this rate was used to assess post-

[11] If the application rate is reduced to 23.95 the LOC increases to 100 and is not of concern.

application exposures.

Dermal MOEs for IPBC in PVC Flooring

Dermal exposures are shown in Table 19. The transfer factor was assumed to be 100% transfer. The MOE of 150 is not of concern because it is greater than the LOC of 10. The registrant (Troy Chemical Corporation) submitted MRID 50918901 "Leaching of IPBC from Swimming Pool Liner Roof Membrane, and Flooring/Wallpaper." However, because there are no risks of concern with an assumed dermal absorption factor (DAF) of 100%, an alternative transfer factor does not need to be assessed.

Table 19. Dermal MOE for Exposure to IPBC Treated PVC Flooring

Application Rate[A] (ppm a.i.)	PVC Density (mg/cm^3)	PVC Thickness (cm)	Availability Factor[B]	Surface Residue[C] (mg/cm^2)	Dermal Loading[F] ($\mu g/cm^2$)	Dermal MOE[G] (LOC = 10)
1,080	1,300	0.3	0.5%	0.0021	2.1	150

A. The application rate is 1,080 ppm a.i. based on EPA Reg. No. 39967-133.
B. Percent of residue that is at the surface and available for transfer based on the AMEM Model.
C. Surface Residue (SR) = Application Rate(ppm)/1,000,000 * Density (mg/cm^3) * Thickness (cm) * (Availability Factor/100)
F. Dermal Loading ($\mu g/cm^2$) = Surface Residue (mg/cm^2) * DAF (100%) * 1000 µg/mg
G. MOE = NOAEL (309 $\mu g/cm^2$) / Dermal Loading ($\mu g/cm^2$). *MOEs are rounded to two significant figures.

Post-Application Incidental Oral Exposure from IPBC in PVC Flooring

Incidental oral exposures are assessed using the Post-application Hand-to-Mouth Exposure Algorithm from Section 7.2.3 of the Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c). This algorithm is as follows:

$$Exp = HR * (F_M * SA_H) * (ET * NR) * [1 - (1\text{-}SE)^{FHtM / NR}]$$

Where:

- Exp = Exposure (mg/day)
- HR = Hand Residue (mg/cm^2)
- F_M = Fraction of hand surface area mouthed / event (fraction/event)
- ET = Exposure time (hours/day)
- SA_H = Surface area of one hand (cm^2)
- NR = Number of replenishment intervals per hour (N_Replen in U.S. EPA, 2012c)
- SE = Saliva extraction factor (*i.e.*, mouthing removal efficiency)
- FHtM = Number of hand to mouth contacts per hour (Freq_HTM in U.S. EPA, 2012c)

The exposure was calculated using the surface residue value of 0.0021 mg/cm^2 that was used for dermal exposure (Table 14) as the hand residue and the following assumptions from Table 7-13

of U.S. EPA, 2012c:

- F_M: The fraction of the hand mouthed per event is 0.13.
- SA_H: The surface area of one hand is 150 cm^2.
- ET: The exposure time is 2 hours/day for hard surfaces.
- NR: The Number of replenishment intervals per hour is 4.
- SE: The saliva extraction fraction is 0.48.
- FHtM: The number of hand-to-mouth events per hour is 20 for children 1 to <2 years old.

The SHEDs Exponent term: $1 – (1\text{-SE})^{FHtM / NR}$ is simplified to 0.962 based on the standard assumptions of 0.48 for saliva extraction efficiency (SE), 20 per hour for Frequency of Hand to Mouth Events (FHtM), and 4 per hour for Number of Hand Replenishments (NR) (U.S. EPA, 2012c).

The incidental oral MOE for hand to mouth exposures from IPBC in PVC was calculated from the above formulas and assumptions as shown in Table 20. The resulting MOE of 350 is not of concern because it is greater than the LOC of 100.

Table 20. Incidental Oral MOE for IPBC in PVC Flooring

Surface Residue[A] (mg/cm^2)	Hand Residue[B] (mg/cm^2)	Fraction of Hand Mouthed (F_M)	Surface Area of Hand (SA_H)	Exposure Time (hours/day)	SHEDs Exponent Term[C]	Exposure[D] (mg/day)	Dose[E] (mg/kg/day)	Incidental Oral MOE[F] (LOC = 100)
0.0021	0.0021	0.13	150 cm^2	2.0	0.962	0.32	0.029	350

A. Based on the application rate of 1,080 ppm from EPA Reg. No. 39967-133 (see Table 17 above)
B. Hand Residue = Surface Residue (mg/cm^2) * Transfer Factor (1.0)
C. SHEDs Exponent Term = $[1 – (1\text{-SE})^{FHtM/NR}]$, where SE = 0.48, FHtM = 20/hr and NR = 4/hr.
D. Exposure (mg/day) = HR (mg/cm^2) * F_M (0.13) * SA_H (150 cm^2) * ET (2 hrs) * NR (4/hr) * SHEDS Exponent Term
E. Dose (mg/kg/day) = Exposure (mg/day) / BW (11 kg child)
F. MOE = NOAEL (10 mg/kg/day) / Dose (mg/kg/day). *MOEs are rounded to two significant figures.

2.8.4 Post-Application Exposures from IPBC in Floor Cleaners

Post-Application Dermal Exposure from IPBC in Floor Cleaners

Dermal exposures were assessed as shown in Table 21. Children (1 <2 years old) were used to represent the most highly exposed population sub-group. The surface area contacting the flooring is 5300 cm^2/day, which is the average of the male and female surface areas provided in the EPA Exposure Factors Handbook 2011 Edition. The dermal MOE of 350 is not of concern because it is greater than the target MOE of 10.

Table 21. Dermal MOE for IPBC in Floor Cleaners

Application Rate (ppm a.i.)	Application Rate[A] (g/gallon)	Cleaner Coverage (ft^2/gallon)	Surface Residue[B] (mg/cm^2)	Transfer Factor (percent)	Dermal Loading[C] ($\mu g/cm^2$)	Dermal MOE[D] (LOC = 10)
600	2.3	1000	0.0025	100	2.5	120

A. Application rate (g/gallon) = Application rate (ppm ai)/1,000,000 * Cleaning Solution Density (8.35 lb/gallon) * 454 g/lb. Application rate is based on label EPA Reg. No. 5383-91.
B. Surface Residue (SR) = Application Rate (g/gallon) * Coverage (1 gallon/1000 ft^2)* (1 ft^2/929 cm^2) * 1000 mg/g
C. Dermal Loading ($\mu g/cm^2$) = Surface Residue (mg/cm^2) * Transfer Factor (100%) * 1000 µg/mg
D. MOE = NOAEL (309 $\mu g/cm^2$) / Dermal Loading (ug/cm^2) *MOEs are rounded to two significant figures.

Post-Application Incidental Oral Exposure from IPBC in Floor Cleaners

Incidental oral exposures were assessed using the Post-application Hand-to-Mouth Exposure Algorithm from Section 7.2.3 of the Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c). This Algorithm includes the SHEDs Exponent term: $1 – (1\text{-SE})^{FHtM/NR}$, which is simplified to 0.962 by inputing the standard assumptions of 0.48 for saliva extraction efficiency (SE), 20 per hour for Frequency of Hand to Mouth Events (FHtM) and 4 per hour for Number of Hand Replenishments (NR). Because transferable residue data are not available for IPBC, the transfer factor was assumed to be 1.0 for 100% residue transfer.

The exposure was calculated using the surface residue value of 0.0025 mg/cm^2 for dermal exposures (Table 198) as the hand residue. The resulting incidental oral MOE of 830 (for children 1 < 2) is not of concern because it is greater than the LOC of 100. Results are presented in Table 22 below.

Table 22. Incidental Oral MOE for IPBC in Floor Cleaners

Surface Residue[A] (mg/cm^2)	Hand Residue[B] (mg/cm^2)	Fraction of Hand Mouthed (F_M)	Surface Area of Hand (SAH)	Exposure Time (hours/day)	SHEDs Exponent Term[c]	Exposure[D] (mg/day)	Dose[E] (mg/kg/day)	Incidental Oral MOE[F] (LOC = 100)
0.00088	0.00088	0.13	150 cm^2	2.0	0.962	0.13	0.012	830

A. Based on the application rate of 600 ppm (see Table 198 above)
B. Hand Residue = Surface Residue (mg/cm^2) * Transfer Factor (1.0)
C. SHEDs Exponent Term = $[1 – (1\text{-SE})^{FHtM/NR}]$, where SE = 0.48, FHtM = 20/hr and NR = 4/hr.
D. Exposure (mg/day) = HR (mg/cm^2) * F_M (0.13) * SA_H (150 cm^2) * ET (2 hrs) * NR (4/hr) * SHEDS Exponent Term
E. Dose (mg/kg/day) = Exposure (mg/day) / BW (11 kg child)
F. MOE = NOAEL (10 mg/kg/day) / Dose (mg/kg/day). MOEs in **bold** are of concern. *MOEs are rounded to two significant figures.

2.8.5 Post-Application Exposure from IPBC Preserved Textiles

There is potential for residential post-application incidental oral and dermal exposure to household items and clothing manufactured from textiles preserved with IPBC from EPA Reg. Nos. 39967-129, 39967-151, 6836-200, and 6836-443. The exposure duration is anticipated to be short- to intermediate-term.

Incidental Oral MOE for IPBC Applied to Textiles

The MOE for incidental oral exposure to IPBC in textiles is summarized in Table 23. The MOE is 230 and is not of concern because it is greater than the LOC of 100.

Table 23. Incidental Oral MOE for Textiles Treated with IPBC

Application Rate (ppm)	Cloth Density[B] (mg/cm^2)	Surface Residue[C] (mg/cm^2)	Area Mouthed[D] (cm^2/day)	Saliva Extraction Efficiency[E]	Exposure[F] (mg/day)	Dose[G] (mg/kg/day)	MOE[H] (LOC = 100)
500[A]	20	0.010	100	48%	0.48	0.044	230

A. The application rate is 500 ppm a.i. based on EPA Reg. No. 39967-129, 39967-151, 6836-200.
B. The cloth density is 20 mg/cm^2 based on the density of cotton as listed in U.S. EPA (2012c).
C. IPBC Surface Residue = Application Rate (ppm/1,000,000) x Cloth Density (mg/cm^2)
D. Represents the area of blanket or shirt sleeve that a toddler would mouth.
E. The saliva extraction efficiency is assumed to be 48%.
F. Exposure = Surface Residue × Surface Area Mouthed × Saliva Extraction Efficiency
G. Dose = Exposure (mg/day) / Body Weight (11 kg)
H. MOE = NOAEL (10 mg/kg/day) / Daily Dose (mg/kg/day). *MOEs are rounded to two significant figures.

Dermal Irritation Effects to Textiles

To calculate the potential for dermal exposures when the toxicological endpoint is based on dermal irritation the following equation was used:

DL = SR x TF

Where:

DL = Dermal Loading ($\mu g/cm^2$)
SR = Surface residue ($\mu g/cm^2$)
TF = Transfer factor from clothing to skin (%/100)

The surface residue (SR) on treated textiles is calculated with the following equation:

SR = FD x WF x CF

Where:

SR = Surface residue ($\mu g/cm^2$)
FD = Fabric density (mg/cm^2)
WF = Weight fraction of a.i. in treated textile (% a.i./100)
CF = Unit Conversion Factor (1,000 µg/mg)

Assumptions:

D: The fabric density is 20 mg/cm^2 based on the density of cotton (U.S. EPA, 2012c).
WF1: The weight fraction (%/100) of a.i. in the fabric is based on the product label.
SA (adults): The median surface area is 18,250 cm^2 which is the total body surface area of 19,500 cm^2 times a factor of 0.064 and minus 1,250 cm^2 to account for the exclusion of the head (U.S. EPA, 2011d). The EPA Exposure Factors Handbook 2011 Edition provides a mean value for percent of total surface area for male and female adult heads of 6.4%.

$$SR = FD \times WF \times CF$$

Dermal MOEs for IPBC Applied to Textiles

Dermal exposures were assessed as shown in Table 24. The MOEs of 31 for children and 15 for adults are both greater than the LOC of 10 and are not of concern. The registrant (Troy Chemical Corporation) submitted MRID 50914601 "Leachability of P-100 from Treated Textile Matrices". However, the transfer factor in Table 21 was assumed to be 100% and an additional dermal assessment using the results of the leachability study for refinement is not needed at this time.

Table 24. Dermal MOE for Exposure to IPBC-Treated Textiles

Population	Application Rate (ppm a.i.)	Cloth Density (mg/cm^2)	Surface Residue[C] (mg/cm^2)	Dermal Loading[D] (µg/cm^2)	Dermal MOE[E] (LOC = 10)
Children	500[A]	20	0.010	10	31
Adults	1,100[B]		0.022	22	14

A. The application rate is 500 ppm a.i. based on EPA Reg. No. 39967-129, 39967-151, 6836-200.
B. The application rate is 1,100 ppm a.i. based on the athletic outer wear use from EPA Reg. No. 6836-443.
C. Surface Residues (mg/cm^2) = Application Rate (ppm/1,000,000) * Cloth Density (mg/cm2).
D. Dermal Loading (µg/cm^2) = Surface Residue (mg/cm^2) * Transfer Factor (100%) * 1000 µg/mg.
E. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm^2). *MOEs are rounded to two significant figures.

2.8.6 Post Application Exposures from IPBC Preserved Laundry Detergent

There is the potential for residential post-application incidental oral exposure for children 1-2 years old and dermal exposures for children and adults to clothing laundered with IPBC preserved laundry detergents. The residential post-application exposure duration is anticipated to be short-term to intermediate-term.

Post-Application Dermal Exposure to IPBC from Laundry Detergent

To calculate the potential for dermal exposures when the toxicological endpoint is based on dermal irritation, the following equation that is based on guidance provided in Human and Environmental Risk Assessment Guidance Document (HERA, 2005) is used:

$$DL = \frac{M \times F1 \times DF \times F'}{WI} \times F2 \times F3 \times CF$$

Where:

DL = Dermal Loading (µg/cm^2)
M = Amount of undiluted product used (mg)
F1 = Weight fraction of a.i. in product (% a.i./100)
DF = Density of fabric (mg/cm^2)
F' = Weight fraction of detergent deposited on fabric (%/100)
WI = Total weight of fabric (mg)
F2 = Weight fraction transferred from clothing to skin (%/100)
F3 = Weight fraction remaining on skin (%/100)
CF = Conversion factor (1000 µg/mg)

Dermal exposures were assessed as shown in Table 25 by comparing the calculated dermal loading to the dermal NOAEL of 309 µg/cm^2. Since transferable residue data are not available for IPBC treated textiles, the transfer factor was assumed to be one for 100% transfer.

The resulting dermal MOE of 2,200 for children (1 to < 2 years-old) and adults is not of concern because it is greater than the LOC of 10.

Table 25. Dermal MOE for IPBC in Laundered Clothing

WF in Detergent (F1)[A]	Amount Detergent Used (M)	Fabric Density	WF of Detergent Deposited on Fabric (F')	Laundry Weight (mg)	Residues on Clothing after Laundering[B]	Dermal Loading[C] (µg/cm^2)	Short/ Intermediate Term MOE[D] (LOC =10)
0.00060	230,000 mg	20 mg/cm^2	5%	1,000,000	0.00014 mg/cm^2	0.14	2,200

A. Based on the application rate of 600 ppm a.i. from EPA Reg. No. 5383-91 for detergent preservation. WF = 600 ppm/1,000,000 ppm.
B. Residues = F1 (0.00060) x M (mg) x Fabric Density (mg/cm^2) x F' (0.05) / Laundry Weight (1,000,000 mg)
C. Dermal Loading (µg/cm^2) = Residues (mg/cm2) x F2 (100%) x F3(100%) x Transfer Factor (100%) x 1000 µg/mg
D. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm^2). *MOEs are rounded to two significant figures.

Post Application Incidental Oral: Laundry Detergent

There is the potential for residential post-application incidental oral exposure to clothing laundered with IPBC preserved laundry detergents. The residential post-application exposure duration is anticipated to be short-term to intermediate term. The sub-population of concern is for children 1 < 2 years old. These exposures were assessed using the following equation that is based on guidance provided in Human and Environmental Risk Assessment (HERA) Guidance Document (2005):

$$PDD = \frac{\frac{M \times F1 \times D \times F'}{WI} \times SA \times SE}{BW}$$

Where:

PDD	=	Potential daily dose (mg/kg/day)
M	=	Amount of undiluted product used (mg)
F1	=	Weight fraction of AI in product (% AI /100)
D	=	Fabric density (mg/cm^2)
F'	=	Weight fraction of detergent deposited on fabric (%/100)
WI	=	Total weight of fabric (mg)
SA	=	Surface area of fabric mouthed or worn (cm^2/day)
SE	=	Saliva extraction efficiency (%/100)
BW	=	Body weight (kg)

To simplify the calculation process, the term SR for IPBC Surface Residues on Clothing After Laundering is substituted for the term "M x F1 x D x F' / WI" in the above equation. The resulting equations are as follows:

$$PDD = \frac{SR \times SA \times SE}{BW}$$

And

$$SR = \frac{M \times F1 \times D \times F'}{WI}$$

Where:

PDD	=	Potential daily dose (mg/kg/day)
SR	=	IPBC Surface Residues on Clothing after Laundering (µg/cm^2)
M	=	Amount of undiluted product used (mg)
F1	=	Weight fraction of AI in product (% AI /100)
D	=	Fabric density (mg/cm^2)
F'	=	Weight fraction of detergent deposited on fabric (%/100)
WI	=	Total weight of fabric (mg)
SA	=	Surface area of fabric mouthed or worn (cm^2/day)

SE = Saliva extraction efficiency (%/100)
BW = Body weight (kg)

The following assumptions were used to calculate the surface residue and potential daily dose:
M: To determine the amount of laundry preservative on treated articles of clothing, industry data indicate that the amount of detergent used per load ranges from 55,000 milligrams to 290,000 milligrams (International Association for soap, detergents, and maintenance products [AISE], HERA, 2002). The standard assumptions for the amount of laundry detergent used per load for machine washing are 290,000 milligrams for powder and 230,000 milligrams for liquid.

F1: The weight fraction (%) of IPBC in laundry detergent is 0.00060 based on the application rate of 600 ppm for detergent preservation.
D: The density of the fabric is 20 mg/cm^2 based on the density of pure cotton (U.S. EPA, 2012c; HERA 2005).
F': The weight fraction of the detergent deposited on the clothing (5%) is based on a HERA assumption.
WI: The total weight of fabric laundered of 1E+6 mg is based on HERA (2005) assumption.
SA: The surface area of textiles mouthed by children is 100 cm^2/day (standard EPA assumption based on the area of a shirt sleeve or corner of a blanket or towel).
SE: The saliva extraction efficiency is 100%.
BW: The body weight inputs used for this calculation were taken from the EPA Exposure Factors Handbook 2011 Edition. The average child's (1 < 2 years-old) bodyweight is 11 kg.

As shown in Table 26, the incidental oral MOE from IPBC in laundered clothing is 17,000 and is not of concern because it is greater than the LOC of 100.

Table 26. Incidental Oral MOE for IPBC in Laundered Clothing

WF in Detergent[A]	Amount Detergent Used (M)	Fabric Density	WF of Detergent Deposited on Fabric (F')	Laundry Weight (mg)	Residues on Clothing after Laundering[B]	Dose[C] (mg/kg/day)	Short/ Intermediate Term MOE[D] (LOC =100)
0.00060	230,000 mg	20 mg/cm^2	0.05	1,000,000	0.00014 mg/cm^2	0.00060	17,000

A. Based on the application rate of 600 ppm ai for detergent preservation. WF = 600 ppm/1,000,000 ppm
B. Residues = WF (0.00060) x M (mg) x Fabric Density (mg/cm^2) x F' (0.05) / Laundry Weight (1,000,000 mg)
C. Dose (mg/kg/day) = [Residue (mg/cm^2) x Surface Area Mouthed (100 cm^2) x Saliva Extraction (0.48)] / BW (11 kg)
D. MOE = NOAEL (10 mg/kg/day) / Dose (mg/kg/day). *MOEs are rounded to two significant figures.

2.8.7 Post-Application Exposures from IPBC Preserved Pool Liners

There is potential for recreational swimmer dermal and incidental oral exposures to IPBC that leaches out of swimming pool liners in residential settings. Adults and children ages 11 to <16 and 6 to <11 years are the relevant age groups for this exposure scenario. The exposures are assumed to be short- and intermediate-term in duration.

Assumptions Used to Calculate the IPBC Concentration in the Pool Water

For the purposes of a screening assessment, it was assumed that 100% of the IPBC in the pool liner would leach into the pool water. The following assumptions were used to calculate the IPBC water concentration:

- The IPBC concentration in the pool liner is 1,080 ppm based on EPA Reg. No. 39967-131.
- The volume of the pool is 89,900 liters based on a side height of 4 feet and a diameter of 30 feet. The surface area of the liner is 101 m^2 based on the above dimensions.
- The total weight of the liner is 108 kg based on the above surface area, a thickness of 0.066 cm for a 30-gauge liner and a density of 1.35 g/cm^3. The amount of IPBC in the liner is 120 grams (120,000 mg) based on the liner weight times the application rate of 1,080 ppm.
- The IPBC concentration in the pool water is 1.3 mg/L based on the amount of IPBC in the pool liner (120,000 mg) divided by the pool water volume of 89,900 liters.

Calculation of Dermal Exposures for Comparison to Systemic Effects

Dermal exposures for pool water uses are assessed differently than dermal exposures for the other treated article uses because the whole body is immersed in the pool water which contains a very low concentration (1.3 mg/L) of active ingredient. The surface area exposed (100% of the body) also is much larger than what was tested in the dermal toxicity study (10% of the body) and the concentration is much lower. This means that a greater percentage and total amount of active ingredient could be absorbed which would lead to the systemic effects that were seen in the oral toxicity studies. Dermal exposures are therefore assessed using the SWIMODEL 3.0 (U.S. EPA, 2003). This model was developed by EPA as a screening tool to conduct exposure assessments of pesticides found in swimming pools and spas (U.S. EPA, 2003). The inputs and parameters have been updated for this risk assessment based on information provided in the 2011 edition of the EPA Exposure Factors Handbook (U.S. EPA, 2011d).

The equation below taken from SWIMODEL 3.0 (U.S. EPA, 2003) is used to calculate dermal exposures for comparison to the systemic effects seen in the oral toxicity studies:

$$PDD = \frac{CW \times Kp \times SA \times ET \times CF}{BW}$$

Where:

PDD = Potential daily dose (mg/kg/day),
CW = Chemical concentration in pool water (mg/L),
Kp = Permeability constant (see equation below),

SA = Surface area (cm^2),
ET = Exposure time (hrs/day),
CF = Conversion factor (0.001 L/cm^3),
BW = Body weight (kg).

$$Kp = 10^{[-2.72 + (0.71 \times \log K_{ow}) - (0.0061 \times MW)]}$$

Where:
Kp = Permeability Constant (cm/hr)
Log K_{ow} = Log of the Octanol-Water Partition Coefficient
MW = Molecular Weight (g/mol)

Assumptions for Calculating Pool Water Dermal Exposures

- Kp: The Kp is 0.0068 cm/hr based on a log K_{ow} of 3.72 and a molecular weight of 342 g/mol.
- ET: The exposure times for non-competitive and/or recreational swimmers is one hour per day based on National Human Activity Pattern Survey (NHAPS) data (U.S. EPA, 1996b).
- SA (Adult): The body surface area exposed to pool water is 19,500 cm^2 which represents the entire body including the head. This value is the recommended average provided by the 2011 EPA Exposure Factors Handbook (EFH).
- SA (Child): The body surface areas exposed to pool water is 10,800 cm^2 for children age 6 to <11 years and 15,900 cm^2 for children age 11 to <16 years, the recommended values from the 2011 EFH.
- BW (Adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights from the 2011 EFH.
- BW (Child): The body weight is 57 kg for children age 11 to < 16 years, and 32 kg for children age 6 to < 11 the recommended values from the 2011 EFH.

Dermal Exposures to IPBC in Pool Liners

It was assumed that 100% of the applied amount leached into the pool water. The MOEs are not of concern because they are greater than the corresponding LOCs of 100 for dermal exposure and 100 for incidental oral exposure. The dermal MOEs were calculated as shown in Table 27. The MOEs range from 4,500 to 3,300 and are not of concern because they are greater than the LOC of 100. The registrant (Troy Chemical Corporation) submitted MRID 50918901 "Leaching of IPBC from Swimming Pool Liner Roof Membrane, and Flooring/Wallpaper." However, because there are no risks of concern with an assumed transfer factor of 100%, the results of the leaching study are not needed for any refinements.

The calculation of dermal exposures for comparison to the irritation effects is not needed in this assessment because the concentration of IPBC in water (1.3 mg/L) is much lower than the dose concentration of 8.3 mg/L (83.33 mg/ml) which corresponds to the dermal loading NOAEL of 50 mg/kg/day (309 µg/cm^2) (Section 2.3.3).

Table 27. Dermal MOEs for Swimmer Exposures to IPBC in Pool Liners

IPBC Water Concentration[A]	Age Group (years)	Body Surface Area (cm^2)	Exposure[B] (mg/day)	Body Weight (kg)	Dose[C] (mg/kg/day)	Dermal MOE[D] (LOC = 100)
1.3 mg/L	Adult	19,500	0.18	80	0.0022	4,500
	Child (11 to <16)	15,900	0.14	57	0.0025	3,900
	Child (6 to <11)	10,800	0.095	32	0.0030	3,300

A. Based on 100% leaching from a 30-gauge PVC pool liner containing 1,080 ppm IPBC (EPA Reg. No. 39967-131). Water Concentration (mg/L) = IPBC in Pool Liner (120,000 mg)/Pool Water Volume (89,900 L) from Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c).
B. Exposure = Water Concentration (mg/L) * Kp (0.0068 cm/hr) * Body Surface Area (cm^2) * Exposure Time (1 hr/day) * 0.001 L/cm^3
C. Dose = Exposure (mg/day) / Body weight (kg).
D. MOE = Incidental Oral NOAEL (10 mg/kg/day) / Dose (mg/kg/day). *MOEs are rounded to two significant figures.

Calculation Methods for Incidental Oral Exposures

Incidental oral exposures are also assessed using the formulas from SWIMODEL 3.0. The inputs and parameters have been updated for this risk assessment based on information provided in the 2011 edition of the EPA Exposure Factors Handbook (U.S. EPA, 2011d).

Assumptions Used to Calculate Swimmer Exposures

The following assumptions were used for the assessment of incidental oral exposures. Many of these assumptions were taken from the Residential SOPs and are also used in the SWIMODEL. The exposure time for noncompetitive and/or recreational swimmers is one hour per day based on National Human Activity Pattern (NHAP) data (U.S. EPA, 1996b). The adult body weight is 80 kg which is the average of the median male and female body weights from U.S. EPA (2011d).

- The adult body weight is 80 kg which is the average of the median male and female body weights from the U.S. EPA (2011d).
- The body weight for children is 57 kg for age 11 to < 16 years, and 32 kg for age 6 to < 11 from the recommended values from the U.S. EPA (2011d).
- The ingestion rate is 0.05 liters/hour for adult, 11 to <16-year-old and 6 to <11-year-old swimmers, respectively. This value is from the Superfund Exposure Assessment Manual (U.S. EPA, 1988).

Incidental Oral MOEs

The incidental oral exposures and MOEs were calculated as shown in Table 28. The MOEs range from 12,000 to 4,800 and are all greater than the LOC of 100 which means that the risks are not of concern.

Table 28. Incidental Oral MOEs for Swimmer Exposure to IPBC in Pool Liners

IPBC Water Concentration[A]	Age Group (years)	Exposure[B] (mg/day)	Body Weight (kg)	Dose[C] (mg/kg/day)	Incidental Oral MOE[D] (LOC = 100)
1.3 mg/L	Adult	0.067	80	0.00083	12,000
	Child (11 to <16)	0.067	57	0.0012	8,500
	Child (6 to <11)	0.067	32	0.0021	4,800

A. Based on 100% leaching from a 30-gauge PVC pool liner containing 1,080 ppm IPBC. (EPA Reg. No. 39967-131). Water Concentration (mg/L) = IPBC in Pool Liner (120,000 mg)/Pool Water Volume (89,900 L) from Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012c).
B. Exposure = Water Concentration (mg/L) * Ingestion Rate (0.050 L/hour) * Exposure Time (1 hour)
C. Dose = Exposure (mg/day) / Body weight (kg)
D. MOE = NOAEL (10 mg/kg/day) / Dose (mg/kg/day)

2.9 Aggregate Exposure/Risk Characterization

There is potential indirect dietary exposure when IPBC is used as a material preservative in dish detergent. There is the potential for drinking water exposure as a result of IPBC uses in pulp/paper mill water systems and metalworking fluid as discussed in Section 2.6.4 above. There is also the potential for incidental oral, dermal, and inhalation exposure from the use of IPBC as a material preservative in the residential market. Residential exposure scenarios considered in the overall aggregate exposure are a result of inhalation exposure to IPBC as a material preservative in paints and cleaners, and dermal and oral exposure (for children ages 1<2) to pressure treated wood, impregnated flooring, carpet fibers, laundry detergent, textiles, floor cleaners, and chronic dietary exposure to dish detergent and drinking water (oral only) as described in Sections 2.6 and 2.7 above. However, if the toxicological effects through different routes of exposure are not the same, then those exposure scenarios should not be combined (U.S. EPA, 2001a). Because the toxicity endpoints of the three routes of exposure (oral [which includes incidental oral and chronic dietary exposure], dermal, and inhalation) are different, and there are different toxicological effects across the different routes of exposure (identified in Table 4) the three routes of exposure cannot be combined in an aggregate assessment. The inhalation route of exposure for IPBC treated paint, and the incidental oral and dermal route of exposures for carpet fiber, have risk concerns on their own. These routes of exposure (oral, dermal, and inhalation) will not be aggregated separately since they trigger risks of concern alone.

2.10 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 IPBC and any other substances. For the purposes of this action, therefore, EPA has assumed that IPBC does not 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)[12] and conducting cumulative risk assessments (CRA)[13].

2.11 Occupational Exposure/Risk Characterization

2.11.1 Occupational Handler Exposures from IPBC

IPBC is registered for use in paints, cleaners, and building materials, therefore there is the potential for handlers to be exposed when applying IPBC to these materials and when using the treated materials. The occupational handler assessment regarding the open pour of materials preservatives in inks is a surrogate use for the preservation of the following uses: paints, adhesives, caulks, sealants, plastics, textiles, paper coatings, canvas, and cordage. Additional preservative uses, which are also included in the surrogacy use for the open pour of materials preservatives, include household, consumer, industrial, institutional, and janitorial products such as air fresheners, dish detergents, laundry products, surface cleaners, floor care products and fabric care products.

The occupational paint handler assessment is a surrogate use for stains, coatings including building materials (interior walls, fiberglass and rubber insulation on pipes and other surfaces, concrete and masonry walls, pipe surfaces; and interior metal surfaces; interior surfaces of HVAC duct systems and other HVAC interior surfaces), caulks, sealants, and adhesives. Exposures are expected to be of short-, intermediate-, and long-term duration.

Occupational Handler Inhalation Exposures

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

The MOEs for occupational handler inhalation exposures to IPBC were assessed as outlined in Table 29. Inhalation exposures from the occupational handler uses were assessed as 8-hour TWA as outlined in Table 29. The MOE of 0.29 for the materials preservation use regarding the open pour of liquids, is of concern when assessed at an application rate of 29,000 ppm because it is less than the LOC of 30. If the application rate is reduced to 293 ppm the MOE increases to 30 and it is no longer of concern.

The MOE of 0.006 for the materials preservation use involving the open pour of powders is of concern because it is less than the LOC of 30.

If the application rate for the open pour of powders is reduced to 6.28 ppm, the MOE increases to 30 and it is no longer of concern. The requirement of a PF-10 filtering facepiece or half face elastomeric facepiece respirator, would increase the MOE by a factor of 10 and is not of concern if the application rate is reduced to 62.8ppm.

The MOE of 0.062 for the airless spray application of paint is of concern because it is less than the LOC of 30. If the application rate of the paint is reduced to 19.83 ppm the MOE increases to 30 and it is no longer of concern.

The MOE of 0.78 for the application of paint primer is of concern because it is less than the LOC of 30. If the application rate is reduced to 38.66 ppm the MOE increases to 30 and it is no longer of concern.
The MOEs for brush/roller application of paint is above the LOC of 30 and therefore are not of concern.

Table 29. Occupational Handler Inhalation Exposures to IPBC

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied or Material Treated per Day[B]	Amount a.i. Handled (lb/day)[C]	8-Hour TWA Unit Exposure (mg/m^3/lb a.i.)[D]	Inhalation Exposure[J] (mg/m^3)	MOE[K] (LOC = 30)
Open pour of liquid for Materials Preservation	30,000 (inks)	2,000 gal. of material treated	600	0.00021[E]	0.13	**0.29**
Open pour of powder for Materials Preservation	29,000 (inks)	2,000 gal. of material treated	580	0.0098[F]	5.7	**0.0065**
Airless Spray Application of Paint	9,600	50 gal. of paint	4.8	0.124[G]	0.60	**0.062**
Brush/Roller Paint Application	9,600	5 gal. of paint	0.48	0.00097[H]	0.00047	79
Aerosol paint primer	1,500	60 fl. oz.	0.00070	7.5[I]	0.0053	**0.78**

A. The application rates are the maximum rates from the labels: EPA Reg. No. 6836-415, 6836-416, 6836-467, 6836-466, 5383-55, 5383-197, 69587-6.
B. Standard assumptions used for occupational exposure assessments of AD chemicals.
C. Amount of a.i. Handled (lb/day) = [Application Rate (ppm a.i./1,000,000) x Product Density x Amount Treated (gal/day)]. Assumed that the product density of paint is 10 lb/gal. Aerosol paint primer density (69587-6) is 9.05 lb/gal.
D. Inhalation unit exposures are based on AEATF II.
E. Conventional pour unit exposure from AEATF II human exposure liquid pour study (MRID 48917401).
F. 8-hour TWA AEATF II from the Solid Pour (Powder & Granule) Human Exposure Monitoring Study MRID 49905201
G. 8-hour TWA AEATF II from the airless sprayer study (MRID 50879401).
H. 8-hour TWA AEATF II from the brush/roller study (MRID 50521701).
I. 8-hour TWA AEATF II from the Aerosol Study (MRID 48659001).
J. Inhalation Exposure (mg/m3) = Amount a.i. Handled (lb/day) * Unit Exposure (mg/m3/lb a.i.)
K. MOE = HEC (0.037 mg/m^3) / Inhalation Exposure (mg/m^3). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

Occupational Handler Dermal Exposures

The MOEs for occupational handler dermal exposures to IPBC were assessed as outlined in Table 30.

The MOE of 0.043 for the materials preservation use involving the open pour of liquid is of concern because it is less than the LOC of 10. If the application rate for the open pour of liquid is reduced to 1,280 ppm the MOE increases to 10 and it is no longer of concern.

The MOE of 2.1 for the materials preservation uses regarding the open pour of powder is of concern because it is less than the LOC of 10. If the application rate is reduced to 6,225 ppm the MOE increases to 10 and it is no longer of concern.

The MOEs for the application of airless spray paint is of concern because it is less than the LOC of 10. If the application rate is reduced to 1,940 ppm the MOE increases to 10 it is no longer of concern.

The MOEs for the brush and roller application of paint is of concern because it is less than the LOC of 10. If the application rate is reduced to 5,240 ppm the MOE increases to 10 and it is no longer of concern.

The MOEs for the application of paint primer at a use rate of 280 ppm is above the LOC of 10 and therefore are not of concern.

Table 30. Occupational Handler Dermal Exposures

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied or	Amount a.i. Handled (lb/day)[C]	Unit Exposure (mg/lb a.i.)[D]	Dermal Exposure (mg/day)[J]	Dermal Loading (µg/cm^2)[K]	MOE[L](LOC = 10)

		Material Treated per Day[B]					
Open pour of liquid for Materials Preservation	30,000 (inks)	2,000 gal. of material treated	600	10[E]	6,000	7,200	**0.043**
Open pour of powder for Materials Preservation	29,000 (inks)	2,000 gal. of material treated	580	0.226[F]	130	140	**2.1**
Airless Spray Application of Paint	9,600	50 gal. of paint	4.8	43.6[G]	210	150	**2.02**
Brush/Roller Paint Application	9,600	5 gal. of paint	0.48	115[H]	55	57	**5.5**
Aerosol paint primer	1,500	60 fl. oz.	0.0064	248[I]	1.6	1.1	280

A. The application rates are the maximum rates from the labels: EPA Reg. No. 6836-415, 6836-416, 6836-467, 6836-466, 5383-55, 5383-197, 69587-6.
B. Standard assumptions used for occupational exposure assessments of AD chemicals
C. Amount of a.i. Handled (lb/day) = [Application Rate (ppm a.i./1,000,000) x Product Density x Amount Treated (gal/day)]. Assumed that the product density of paint is 10 lbs/gal. The product density for aerosol paint primer (EPA Reg. No. 69587-6) is 9.05 lbs/gal.
D. Dermal unit exposures are based on AEATF II.
E: Open pour value from the AEATF II human exposure liquid pour study (MRID 48917401); gloves were worn. Hand Exposure = 99%
F. Solid Pour (Powder & Granule) Study MRID 49905201; gloves worn. Hands = 90% (Powder);.
G Long sleeves, long pants, no gloves value from the Airless Sprayer Study (MRID 50879401). Hand Exposure = 60%
H. Long sleeves, long pants, no gloves value from the Brush/Roller Study (MRID 50521701). Hand Exposure = 84%
I. Long sleeves, long pants, no gloves value from the Aerosol Study (MRID 48659001). Hand Exposure = 57%
J. Dermal Exposure (mg/day) = [Amount a.i. Handled (lb/day) * Unit Exposure (mg/lb a.i.)].
K. Dermal Loading = [Dermal Exposure (mg/day) * Hand Exposure (%/100) * 1000 µg/mg]/Hand Area (820 cm^2)
L. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm^2). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

2.11.2 Occupational Exposures from IPBC Preserved Cleaning Products

Occupational Inhalation MOEs from Cleaning Products

The MOEs for occupational inhalation exposures to IPBC preserved cleaning products were assessed as outlined in Table 31. The inhalation MOE of 17 for mopping floors in hospital settings is of concern because it is less than the LOC of 30. If the application rate is reduced to 334 ppm, the MOE increases to 30 and would no longer be of concern.

The inhalation MOE of 9.1 for spray and wipe application is of concern because it is less than the LOC of 30. If the application rate is reduced to 182 ppm, the MOE increases to 30 and is no longer of concern.

The MOEs regarding mopping floors in non-hospital facilities and ready-to-use wipes (RTU wipes) are greater than the LOC of 30; therefore, there are no risks of concern for inhalation exposures to IPBC preserved cleaning products.

Table 31. Occupational Inhalation Cleaning MOEs for IPBC

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Amount AI Handled (lb)[C]	8-Hour TWA Inhalation Unit Exposure (UE)[D] (mg/m^3/lb AI)	Inhalation Exposure (mg/m^3)[H]	Inhalation MOE (LOC= 30)[I]
Mopping floors (hospital setting)	600	45	0.23	0.0098 [E]	0.0022	**17**
Mopping floors (non-hospital setting)		2	0.010		0.000098	380
Trigger Spray & wipe		0.26	0.0013	3.12 [F]	0.0041	**9.1**
Ready-to-use (RTU) Wipes				0.079 [G]	0.00010	360

A. Maximum application rate on the proposed label 5383-91.
B. Antimicrobial Exposure Joint Venture (AEJV) (MRIDs 46799302 and 46730501).
C. Amount of a.i. Handled (lb/day) = Application Rate (ppm a.i./1,000,000) x Amount Applied x Cleaner Density (8.35 lb/gallon)
D. Inhalation unit exposures are based on AEATF II.
E. 8-hour TWA from the AEATF II Studies for Mopping (MRIDs 48210201, 48231201, 48231901).
F. 8-hour TWA from the AEATF II Study for Trigger Spray and Wipe (MRID 48375601).
G. 8-hour TWA from the AEATF II Study for RTU wipes (MRID 48375601).
H. 8-hour TWA Inhalation Exposure (mg/m^3) = Amount AI Handled (lb) x UE (mg/m^3/lb a.i.).
I. Inhalation MOE = HEC (0.037 mg/m^3) / Daily inhalation exposure (mg/m^3). *MOEs are round to two significant figures.

Occupational Dermal MOEs from Cleaning Products

The MOEs for occupational dermal exposures to IPBC preserved cleaning products were assessed as outlined in Table 32. The MOEs for spray and wipe and mopping floors are greater than the LOC of 10; therefore, there are no risks of concern for dermal exposures to IPBC preserved cleaning products.

Table 32. Occupational Dermal Cleaning MOEs for IPBC

Scenario	Application Rate (ppm a.i.)[A]	Amount of Product Applied (gal/day)[B]	Amount AI Handled (lb)[C]	Dermal Unit Exposure (mg/lb AI)	Dermal Exposure (mg/kg)[H]	Dermal Loading (µg/cm²)[I]	Dermal MOE (LOC = 10)[J]
Mopping floors (hospital setting)	600	45	0.23	23.2 [E]	5.2	5.9	52
Mopping floors (non-hospital setting)		2	0.010		0.23	0.26	1200
Trigger Spray & wipe		0.26	0.0013	1,050 [F]	1.4	1.5	200
Ready-to-use (RTU) Wipes				2,380 [G]	3.1	3.7	83

A. Maximum application rate on the proposed label 5383-91.
B. Antimicrobial Exposure Joint Venture (AEJV) (MRIDs 46799302 and 46730501).
C. Amount of a.i. Handled (lb/day) =Application Rate (ppm/1,000,000) x Amount Applied x Cleaner Density (8.35 lb/gallon)
D. Inhalation and Dermal unit exposures are based on AEATF II.
E. AEATF Studies for Mopping (MRIDs 48210201, 48231201, 48231901). Hand Exposure = 93%.
F. AEATF Studies for Trigger Spray and Wipe (MRID 48375601). Hand Exposure = 92%.
G. AEATF II Study for RTU wipes (MRID 48375601). Hand Exposure = 98%.
H. Dermal Exposure: Amount AI Handled (lb) x UE (mg/lb ai).
I. Dermal Loading = [Dermal Exposure (mg/day) * Hand Exposure (%/100) * 1000 µg/mg]/Hand Area (820 cm^2)
J. MOE = NOAEL (309 µg/cm2) / Dermal Loading (µg/cm^2). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

2.11.3 Occupational Exposure Assessment for Sapstain Treatment Applications

Occupational handler exposures are anticipated to occur during use of IPBC for immersion or spray treatment of wood for sapstain control. These exposures are anticipated to be short- to intermediate- to long-term in duration, and they can occur via the dermal or inhalation routes. The sapstain treatment solutions are applied at a maximum concentration of 1.8%, which is the same concentration that is used for pressure treatment.

Sapstain Control Worker Unit Exposure Data Unit exposure assumptions were retrieved from MRID 455243-04 "*Measurement and Assessment of Dermal and Inhalation Exposures to Didecyl Dimethyl Ammonium Chloride (DDAC) Used in the Protection of Cut Lumber (Phase III)".* The DDAC sapstain control study measured worker exposure to DDAC at 11 sawmills/planar mills in Canada where DDAC formulations were applied to cut wood using either automated elevator diptanks (5 mills), spray boxes (5 mills) or both (1 mill). Eighty-six

workers and 18 job functions were monitored. The job functions were divided into four "strata" which include diptank operations (9 diptank operators), maintenance operations (3 millwrights, 11 chemical operators, 6 cleanup crew), wet operations (13 graders, 3 end stackers, 2 bin patrols, 2 pilers, 1 sorter, 1 stenciller, 2 trimmers, 1 tray attendant and 2 tallymen) and dry operations (6 forklift drivers, 1 strapper operator, 2 painter, 2 hula saw operators, 3 packagers, 2 tallymen, 1 end stacker, 1 papercapper and 1 stickman). In general, each worker was monitored for one workday except for the 7 of 9 diptank operators which were monitored for two days each.

The measured DDAC exposure values were normalized by the treatment solution concentration to extrapolate the measured exposures in the DDAC study to unit exposure values in terms mg or ug of exposure per % ai in the treatment solution. This normalization was done for each of the 11 facilities reviewed in the study, and the treatment solution contained 4192 to 27490 ug ai/ml. Mill #5 had both a diptank process with a DDAC concentration of 4338 ug/ml and a spray process with a DDAC concentration of 22,776 ug/ml and it was not possible to tell which process the workers were associated with. In this case, the lower concentration was used which would overestimate the unit exposure.

Sapstain Worker Inhalation MOEs for IPBC

The MOEs for sapstain control worker inhalation exposures to IPBC were assessed as outlined in Table 33. The MOE of 3.9 for the Dip Tank Operator job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.237%, the MOE will increase to 30 and is no longer of concern for the Dip Tank Operator function.

The MOE of 6.6 for the Millwright job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.397%, the MOE will increase to 30 and is no longer of concern for the Millwright job function.

The MOE of 4.8 for the Chemical Attendant job function is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.286%, the MOE will increase to 30 and is no longer of concern from the Chemical Attendant job function.

The MOE of 0.19 for Clean-up Crew is less than the LOC of 30 and is of concern. If the application rate is reduced to 0.011%, the MOE will increase to 30 and is no longer of concern for the Clean-up Crew job function.

Table 33. Sapstain Control Worker Inhalation MOEs for IPBC

Application Rate[A]	Job Function	Unit Exposure[B] (mg/m^3/% a.i.)	Exposure[C] (mg/m^3)	Inhalation MOE[D] (LOC = 30)
	Dip Tank Operator	0.0052	0.0094	**3.9**

1.8 % IPBC in treatment solution	Millwright	0.0031	0.0056	**6.6**
	Chemical Attendant	0.0043	0.0077	**4.8**
	Clean-up Crew	0.11	0.20	**0.19**

A: EPA Reg. No. 5383-91, 6836-415, and 39967-154 is representative of the maximum application rate for sapstain treatment uses of IPBC.
B: Unit exposures are from the Sapstain Phase III study (MRID 45524301).
C: Exposure (mg/m^3) = [Application Rate (% a.i.) * Unit Exposure (mg/m^3/% a.i.)]
D: Inhalation MOE = [HEC (0.037 mg/m^3) / Exposure (mg/m^3)]. *MOEs are rounded to two significant figures.

Sapstain Control Worker Dermal Exposures for IPBC Exposures

The MOEs for sapstain control worker dermal exposures were assessed as outlined in Table 34.

The MOE of 3.7 for clean-up crew is of concern because it is lower than the LOC of 10. If the application rate is reduced to 0.67% in treatment solution the MOE will increase to 10 and is no longer of concern.

The MOEs for Dip Tank Operator, Millwright, and Chemical Attendant range from 12 to 52 are greater than the LOC of 10 and are therefore not of concern.

Table 34. Sapstain Control Worker Dermal MOEs for IPBC

Application Rate	Job Function	Unit Exposure[B] (mg/day/% a.i.)	Dermal Exposure[C] (mg/day)	Percent Hand Exposure[D]	Dermal Loading (µg/cm²)[E]	Dermal MOE[F] (LOC = 10)
1.8 % IPBC in treatment solution[A]	Dip Tank Operator	2.99	5.4	91	6.0	52
	Millwright	7.1	13	51	7.9	39
	Chemical Attendant	17.1	31	71	27	12
	Clean-up Crew	72.4	130	52	83	**3.7**

A: EPA Reg. No. 5383-91, 6836-415, and 39967-154 is representative of the maximum application rate for sapstain treatment uses of IPBC.
B: Unit exposures are from the Sapstain Phase III study (MRID 45524301). Glove use was assumed.
C: Dermal Exposure (mg/day) = [Application Rate (% a.i.) * Unit Exposure (mg/day/% a.i.)].
D: Percent hand exposures from the Sapstain Phase III study (MRID 45524301). Glove use was assumed.
E: Dermal Loading = [Dermal Exposure (mg/day) * Hand Exposure (%/100) * 1000 µg/mg]/Hand Area (820 cm^2)
F: MOE = NOAEL (309 $\mu g/cm^2$) / Dermal Loading ($\mu g/cm^2$). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

2.11.4 Occupational Exposure Assessment for Pressure Treatment Applications

Occupational handler exposures are anticipated to occur during use of IPBC to pressure treat wood. These exposures are anticipated to be short-, intermediate-, and long-term in duration, and they can occur via the dermal or inhalation routes.

Pressure Treatment Worker Inhalation MOEs

A summary of the MOEs for IPBC for pressure treatment workers is included in Table 35. The MOE of 8.7 for the Treatment Operator job function is of concern because it is less than the LOC of 30. If the application rate is reduced to 0.435%, the MOE increases to 30 and is no longer of concern. The MOE for the Wood Handler job function of 21 is of concern because it is less than the LOC of 30. If the application rate is reduced to 0.107% a.i., the MOE increases to 30 and is no longer of concern.

Table 35. Pressure Treatment Workers MOEs for IPBC

Job Function	Application Rate[A] (% a.i.)	Inhalation Unit Exposure[B] (µg/m^3/percent a.i.)	Inhalation Exposure[C] (mg/m^3)	Inhalation MOE[E] (LOC = 30)
Treatment Operator	1.5	2.83	0.0042	**8.7**
Wood Handler		11.5	0.0017	**21**

A. Application rate is for pressure treatment listed on EPA Reg. No. 39967-66.
B. Estimated Arithmetic Average (AMm) for the 8-hour Time Weighted Average (TWA) total inhalable fraction unit exposures from the AEATF II Pressure Treatment Exposure Study (MRID 49434501) for sites ABDE as listed in Table 15 of Cohen (2018).
C. Inhalation Exposure (mg/m3) = Fraction a.i. * Unit Exposure (µg/m3/fraction a.i.) * 0.001 mg/µg
D. Inhalation MOE = HEC (0.037 mg/m3) / Exposure (mg/m3)

Pressure Treatment Worker Dermal MOEs for IPBC

A summary of the dermal MOEs for IPBC for pressure treatment workers is included in Table 36. The MOEs of 190 and 33 for Treatment Operator and Wood Handler are not of concern because they are greater than the LOC of 10.

Table 36. Pressure Treatment Workers Dermal MOEs for IPBC

Job Function	Application Rate[A] (% a.i.)	Dermal Unit Exposure[B] (mg/% a.i.)	Dermal Exposure[C] (mg/day)	Dermal Loading[D] (µg/cm^2)	Dermal MOE[E] (LOC = 10)
Treatment Operator	1.5	0.87	1.3	1.6	190
Wood Handler		5.05	7.6	9.2	33

A. Based on EPA Reg. No. 39967-66
B. Estimated Arithmetic Average (AMm) from the AEATF II Pressure Treatment Exposure Study (MRID 49434501) for sites ABDE as listed in Tables 15 and 23 of Cohen (2018).
C. Dermal Exposure (mg/day) = Application Rate (% a.i.) * Unit Exposure (mg/% a.i.)
D. Dermal Dose (µg/cm^2) =[Dermal Exposure (mg/day) * Hand Exposure (%/100) x 1000 µg/mg]/ Hand Area (820 cm^2)
E. MOE = NOAEL (309 µg/cm^2) / Dermal Loading (µg/cm^2). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

2.11.5 Occupational Post Application Exposures to Metal Working Fluids (MWF)

The inhalation exposure of machinists to MWFs treated with IPBC is assessed by multiplying an estimated MWF aerosol concentration times the amount of biocide that is added to the MWF as follows:

$$\text{Inhalation Exposure } (mg/m^3) = WF * \text{MWF aerosol concentration } (mg/cm^3)$$

The following assumptions are used in this assessment:

- WF: The weight fraction (WF) is based on the application rate from the product labels. If the application rate is given in ppm; for example, the WF = application rate (ppm)/1000000.
- The MWF aerosol concentration is 1.0 mg/m^3 based on 544 OSHA personal breathing zone (PBZ) air samples that were collected for the period 2000 to 2009. This value is based on the arithmetic mean of 0.80 mg/m^3 and is corrected by a factor of 25%. To account for oil mist volatilization losses of 10 of 30 percent have been observed in literature studies during chamber testing of new and used straight oils, respectively (McAneny et al., 1995 and Park et al., 2003). This value is supported by the 359 straight oil results for total particulate (geometric mean [GM] = 0.52 mg/m^3, geometric standard deviation [GSD] = 2.09) (Piacitelli 2001) which is comparable to the GM of 0.50 mg/m^3 and GSD of 2.61 for the OSHA samples.

Inhalation Risk Summary

The inhalation risks are calculated as a MOE as shown in Table 37. The MOE is the ratio of the Human Equivalent Concentration (HEC) over the biocide air concentration. As an example, the MOE is calculated for IPBC, which is applied at 5,300 ppm and has an HEC of 0.037 mg/m^3. IPBC is registered for use in MWFs; therefore, there is the potential for machinists to be exposed when using treated MWFs. Short-, intermediate-, and long-term dermal and inhalation exposures are anticipated.

Machinist Inhalation MOEs

The inhalation MOE of 7 is was calculated as outlined in Table 37. This MOE is of concern because it is less than the LOC of 30 for long-term exposure. If the application rate is reduced to 1,230 ppm, the MOE increases to 30 and is not of concern.

Table 37. Inhalation MOE for Machinists Using MWF Treated with IPBC

Application Rate (ppm a.i.)[A]	MWF	IPBC Air Concentration	HEC (mg/m^3)	Inhalation MOE[F]

	Aerosol Concentration (mg/m^3)	(mg/m^3)		(LOC = 30)
5,300	1.0[B]	0.0053[C]	0.037	**7**

A. Maximum application rate for cutting fluids listed on EPA Reg No. 5383-171, 5383-77, 5383-91.
B. Average 8 hr TWA for oil mist air (n=544 samples) measured by OSHA (2000 to 2009) corrected for 25% volatilization loss based on McAneny (1995) and Park (2003).
D. IPBC Air Concentration = Application Rate (ppm) / 1,000,000 ppm * MWF Air Concentration (1.0 mg/m^3).
E. MOE = HEC/ IPBC Air Concentration where the HEC is 0.037 mg/m3 for IPBC. *MOEs are round to two significant figures.

Machinist Dermal Exposure and MOE

The dermal exposure of machinists to MWFs treated with IPBC as shown in Table 38 was assessed by using the thin film approach for comparison to the POD which is expressed as the amount of a.i. per given area of skin. This approach uses the following equation:

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

The following assumptions were used in this assessment:

- WF: The weight fraction is based on the application rate of 5,300 ppm.
- Qu: The quantity remaining on the skin is 10.3 mg/cm^2 based on the hand immersion with no wiping results for mineral oil reported in Cinalli (1992). This value is used to evaluate dermal irritation effects because these effects can be localized.
    - It is not feasible for machinists to wear chemical resistant gloves because they interfere with the fine motor skills needed to operate the metalworking machines and measure the materials being machined.

The dermal MOE of 5.7 is of concern because it is less than the LOC of 10. If the application rate is reduced to 3,000 ppm, the LOC will increase to 10 and is no longer of concern.

Table 38. Dermal MOE for Machinists Using MWF Treated with IPBC

Application Rate (ppm a.i.) [A]	Quantity of MWF Remaining on Skin (Qu)[B]	Dermal Loading ($\mu g/cm^2$)[C]	Dermal MOE[D] (LOC = 10)
5,300	10.3 mg/cm^2	55	**5.7**

A. Maximum application rate for metalworking fluids (MWF) listed on EPA Reg. No. 5383-171, 5383-77, 5383-91.
B. Qu = 10.3 mg/cm^2 based on mineral oil hand immersion with wiping results reported in Cinalli (1992).
C. Dermal Loading = Application Rate/1,000,000 x MWF Thin Film Retention (Qu) x 1000 µg/mg.
D. MOE = NOAEL (309 $\mu g/cm^2$) / Dermal Loading ($\mu g/cm^2$). *MOEs are round to two significant figures. *MOEs in **bold** are of concern.

2.12 Human Health Incidents

A search of the Agency's Incident Data System (IDS) on February 7th, 2024, did not identify any severe (*i.e.*, deaths or incidents classified as 'major') in the last five years (February 2019-February 2024) that involved IPBC.

3.0 ENVIRONMENTAL RISK ASSESSMENT

Currently registered IPBC uses in pulp and papermills, MWFs, and those uses expected to go down-the-drain, are expected to result in little to no terrestrial exposure because IPBC would be released to the aquatic environment through effluent into a waterbody. Exterior uses of IPBC preserved materials (*e.g.,* preserved exterior paints and coating) have the potential to result in terrestrial exposure during a rain event from runoff of IPBC leachate. However, the rapid degradation ($t_{1/2}$ < 3 hours) of IPBC in soil and its high mobility (K_{ads} < 2.64 mL/g) in this media, suggests it would move rapidly through soil to water or degrade on the order of hours, resulting in minimal terrestrial exposure from current registered IPBC uses. Additionally, low potential for aquatic exposure is expected from material preservative uses in air fresheners, surface cleaners, and wipes. Therefore, risk to terrestrial and aquatic animals from these uses are not of concern. There is, however, potential for aquatic exposure from all other uses. This risk assessment focuses on metal working fluids, pulp and papermills, wood preservative, and exterior paint uses because these uses have the highest environmental exposure potential and thus, would be protective of the other material preservative and industrial uses.

3.1 Environmental Fate

IPBC is non-persistent and mobile in soil. The dissipation of IPBC in terrestrial and aquatic environments appears to be dependent on alkaline catalyzed hydrolysis, microbial-mediated oxidative mineralization, and leaching. IPBC was rapidly hydrolyzed ($t_{1/2}$ = 0.947 days) in pH 9 buffer solution; however, it was stable ($t_{1/2}$ > 30 days) in pH 5 and 7 buffer solutions (MRID 40947405 & 42329301). IPBC was rapidly degraded ($t_{1/2}$ < 3 hours) in aerobic mineral soil and anaerobic aquatic environments (MRID 40947405) but is expected to be very mobile to mobile (K_{ad} < 2.64 mL/g) in mineral soils (MRID 41975207). The primary degradate of IPBC is isopropargyl butyl carbamate (Propargyl butyl carbamate (PBC), parent compound minus an iodine, the carrier molecule). This degradate was detected in hydrolysis, aerobic soil, and anaerobic aquatic metabolism studies (MRIDs 42329301, 42329302, 42481601). The half-lives of PBC are < 13 days in aerobic soil and anaerobic aquatic environments (MRID 42481601). Degradates of PBC in anaerobic aquatic environments were identified as 2-propenylbutylcarbamate (2-PBC, PBC with a propenyl group added) and minor unidentified degradates (MRID 40947405). No mobility data are available for the degradates of IPBC or parent compound (*e.g.,* data from OCSPP guideline numbers 835.1110, 835.3110, 835.3220, 835.3240, and 835.3280).

3.1.1 Available Data

An environmental fate summary for IPBC is provided in Table 36. IPBC is moderately soluble in water at 156 mg/L (ppm), semi-volatile (vapor pressure <1.8 x 10^{-6} mm·Hg at 20°C and 5 x 10^{-6} mm·Hg at 30°C) but is unlikely to volatilize from water based on the Henry's Law Coefficient of 8.9 x 10^{-9} atm·m^3/mole. It has some potential to bioconcentrate in fish based on the log K_{ow} of 2.45 but is not expected to be significant because the log K_{ow} (log P) is <3 (Table 1).

Abiotic degradation is only expected to be a significant route of dissipation of IPBC at pH 9. IPBC was stable at pH 5, degraded slowly at pH 7 with a half-life of 139 days, and degraded rapidly at pH 9 with a half-life of 0.947 days (23 hours). Propargyl butyl carbamate (PBC, parent compound minus the iodine) was identified as the only hydrolysis degradate (MRID 42329301). IPBC was essentially stable in an indirect photodegradation in water study with a direct photolytic half-life (DT_{50}) of 172 days in in natural summer sunlight at latitudes 30° to 50°N (standard latitude is 40° N). Six minor (<10 % of applied)[14] radioactive fractions were observed during the study, and one minor transformation product, PBC, was identified in the irradiated sterilized natural pond water and dark control (MRID 50938201).

Metabolic degradation of IPBC is a significant route of dissipation. The half-lives of IPBC in non-sterile Blackoar loam soil under aerobic conditions were 2.13 hours at 22 ºC and 8.6 hours at 5 ºC. The primary degradate of IPBC was identified as PBC, which degraded slowly under sterile conditions at 22 ºC, consistent with the results of the hydrolysis study (MRID 42329301). Under non-sterile conditions in the Blackoar loam soil, applied PBC degraded with DT_{50} of 4.31 days at 22 ºC, and as expected, the mineralization rate was slower at 5 ºC because reaction rates decline by a factor of 2 for every 10 ºC decrease in temperature. Applied PBC degrades to form CO_2, bound soil residues, and an unidentified metabolite (MRID 42329302).

Under anaerobic conditions representing bottom sediment (MRID 42481601), the DT_{50} of parent IPBC was 1.5 hours in a nonsterile, static, anaerobic (pe[15] + pH< 7) sediment water test system at 22°C. Under sterile conditions, the DT_{50} of IPBC was 13.3 hours. Radiolabeled residues were predominantly detected (80% of applied IPBC) in the water phase of sediment-water systems, and the primary degradate of IPBC was PBC. The half-life of applied PBC as parent compound was 11.5 days in the nonsterile, static, anaerobic aquatic system. Secondary degradates of IPBC were 2-propenyl-butylcarbamate (2-PBC) and two unidentified compounds. Volatile degradates were identified as PBC, 2-PBC, CO_2 and possibly CH_4.

[14] Environmental fate studies (835 guidelines) define a major residue as ≥10 % of applied compound, and a minor residue is <10 % of applied compound.
[15] PE is a measure of the redox potential (*i.e.*, a measure of the tendency of a chemical species to acquire electrons from or lose electrons to an electrode and thereby be reduced or oxidized, respectively). It varies indirectly with the pH.

Leaching-adsorption-desorption data (MRID 41975207) were submitted for both IPBC and PBC for sandy loam, sand, silty clay, and sandy soils. For IPBC, Freundlich adsorption coefficients (K_{fads}) ranged from 0.67 to 2.46 mL/g and organic carbon-water partition coefficients (K_{focs}) ranged from 61–309 mL/g. IPBC adsorption was not correlated to organic matter content, clay content, and cation exchange capacity of soil. IPBC is mobile in soil and aquatic environments based on K_{oc} values and the Food & Agriculture Organization of the United Nations (FAO, 2000) soil mobility classification system. The primary degradate of IPBC was PBC with K_{oc} values ranging from 62-310 mL/g. PBC is mobile to moderately mobile based on K_{oc} and FAO Soil mobility classification system. PBC adsorption was not correlated to organic matter content, clay content, and cation exchange capacity of soil.

The 3-hour IC_{50}[16] value for IPBC (test substance) was 39.3 mg/L (>20 mg/L), and the 3-hour IC_{50} for the reference compound 3,5-dichlorophenol (3,5-DCP) was 14.9 mg/L, which was within the guideline acceptable range of 5 to 30 mg/L. Based on the 3,5-DCP results, the activated sludge was confirmed to be suitable (MRID 50938205).

The leaching of IPBC from a range of exterior paints was studied over a period of 842 days (28 months) with a total rainfall amount of 52 inches (1348 mm) using the NT-509 guideline in Taastrup, Denmark (MRID 51530601). All panels were facing south per the guideline requirement (either south or southwest) to account for prevailing winds with rainfall which affect biocide leaching because of either paint thinning (ablation) or increased diffusion. A total of 14 products were tested, including six Masonry Paint Application Products, five Wood Stain Application Products, and three Wood Paint Application Products.

After a study period of 842 days and total rainfall of 1348.0 mm, total leached IPBC values were 6.8%-19% for Masonry Paint Application Products, were 4.18% -12.52% for Wood Stain Application Products, and 5.38% - 24.49% for Wood Paint Application Products. The maximum one major rainfall percent leached values were 1.9%-8.3% for Masonry Paint Application Products, were 1.2% -4.1% for Wood Stain Application Products, and 1.9% - 6.4% for Wood Paint Application Products. Overall, the maximum one major rainfall event resulted in 25.8-50.1% of total leaching with an average of 34.4% (U.S. EPA, 2022). The Agency chose to use the 6.4% maximum one major rainfall event leaching value for the water based acrylic paint (product 14B) because it is the most representative of the paints used on houses (refer to Section 3.3.3 for further discussion about paint modeling).

[16] A concentration of a chemical that is needed to inhibit a given biological process to half (50%) of the maximum.

Table 39. Environmental Fate Summary of 3-Iodoprop-2-yn-1-yl butylcarbamate (IPBC)

Test guideline (OCSPP No.)	Guideline Results	Half-life	Degradates	MRID/Study Status (Acceptable, Unacceptable, Supplemental)/ Comments
835.1110 Activated Sludge Sorption Isotherm	Not Required			
835.2120 Hydrolysis	pH 5 pH 7 pH 9	>30 days (Stable), 139 days (Stable), <1 day (0.947 d)	None None Propargyl butyl carbamate (PBC) [Parent IPBC minus iodine atom]	40947405 & 42329301 Supplemental
835.2240 Photodegradation in water	DT_{50} of 172.1 days in natural summer sunlight at latitudes 30° to 50°N. One minor transformation product was identified (PBC), 5 others formed, not identified.	DT_{50} of 172.1 days (DT_{90} 575 days)	PBC (propynyl butyl carbamate)	50938201 Acceptable
835.2410 Photodegradation on Soil	Not required because the paper use is for stored paper as a paper coating and not for use in a paper slurry (EPA Reg. No. 5383-170)			
835.3110 Ready Biodegradability				
835.3220 Porous Pot Test				
835.3240 Simulation Test- Aerobic Sewage Treatment A. Activated Sludge Units				
835.3280 Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater				
835.4100 Aerobic Soil Metabolism	***IPBC-Non-Sterile Conditions:*** Blackoar Loam Soil at 22°C Blackoar Loam Soil at 5°C ***Sterile Conditions:***	 2.13 hours 8.6 hours	***IPBC-Non-Sterile Conditions & Sterile Conditions:*** PBC PBC	 42329302 Acceptable

Test guideline (OCSPP No.)	Guideline Results	Half-life	Degradates	MRID/Study Status (Acceptable, Unacceptable, Supplemental)/ Comments
	Blackoar Loam Soil at 22°C ***PBC-Non-Sterile Conditions:*** Blackoar Loam Soil at 22°C Blackoar Loam Soil at 5°C	Slow degradation of IPBC was observed in sterile soil. 4.30 days PBC was more resistant to degradation at 5°C. Mineralization rates were significantly lower at 5°C.	***PBC-Non-Sterile Conditions:*** Mineralized to Carbon dioxide (CO_2)	
835.4200 Anaerobic Soil Metabolism	No data submitted, but anaerobic aquatic data were submitted (42481601)			
835.4300 Aerobic Aquatic Metabolism	Not Required			
835.4400 Anaerobic Aquatic Metabolism	***IPBC-Non-Sterile Conditions:*** Static Sediment water at 22°C ***Sterile Conditions:*** Static Sediment water at 22°C ***PBC-Non-Sterile Conditions:*** Static Sediment water at 22°C	1.5 hours 13.3 hours 11.5 days	***IPBC-Non-Sterile Conditions & Sterile Conditions:*** PBC PBC ***PBC-Non-Sterile Conditions:*** 2-propenylbutylcarbamate (2-PBC) Mineralized to CO_2 & Me IPBC and its major degradate PBC are not expected to	42481601 Acceptable

Test guideline (OCSPP No.)	Guideline Results	Half-life	Degradates	MRID/Study Status (Acceptable, Unacceptable, Supplemental)/ Comments
			persist in anaerobic aquatic or anaerobic soils.	
835.1230 Adsorption/Desorption	Freundlich adsorption coefficients of (K_{ads}) of 0.67 to 2.46 mL/g K_{oc} (organic carbon-water partition coefficient) of 61 – 309.	None	PBC K_{oc} values ranging from 62-310.	41975207 Supplemental Sandy loam, sand, loam, silty clay soils IPBC is mobile in soil and aquatic environments based on K_{oc} and FAO soil mobility classification system PBC is mobile to moderately mobile based on K_{oc} and FAO Soil mobility classification system
835.1240 Leaching Studies	Total rainfall (major + potentially minor rainfall events) was 1348.0 mm (*ca*. 52 inches) over 842 days (28 months; study termination). Total leached IPBC values were 6.47% - 19.00%, for Masonry Paint Application Products, 4.18% - 12.52% for Wood Stain Application Products, and 5.38% - 24.49% for Wood Paint Application	None	None identified	51530601 Supplemental 6.4 % used in Section 3.3.3 because this value represents wood-applied acrylic paint and is most representative of all paints studied for modeled uses on houses (Product 14B in study).

Test guideline (OCSPP No.)	Guideline Results	Half-life	Degradates	MRID/Study Status (Acceptable, Unacceptable, Supplemental)/ Comments
	Products. Overall, the maximum one major rainfall event resulted in 25.8-50.1% of total leaching with an average of 34.4%			
850.3300 Modified activated sludge, respiration inhibition test	3-hour IC_{50} value for IPBC (test substance) was 39.3 mg/L, 3-hour IC_{50} for the reference item 3,5-dichlorophenol was 14.9 mg/L ((within acceptable range of 5 to 30 mg/L per guideline),	None	None	50938205 Acceptable

3.1.2 Residues of Potential Concern

Based on the submitted environmental fate studies, the degradate PBC was the primary residue formed from both abiotic and biotic degradation. While PBC is the primary degradate of IPBC, it accounts for less than 10% of applied radioactivity; therefore, it is considered a minor degradate. Additionally, the removal of those components (*i.e.*, iodine and the organoiodine) to form the degradate PBC will not have a significant impact on the reactivity of that chemical. Furthermore, based upon the physical and chemical properties of iodine and the organoiodine bond attached to IPBC, the low reactivity of iodine and the weakness of the organoiodine bond demonstrates that they are not major contributing factors to the chemical reactivity nor the chemical bond strength of the chemical (Zhdankin & Stang, 2008). Therefore, the toxicity of PBC and parent IPBC are expected to be similar. Based on environmental fate and expected similarity in ecotoxicity between the parent and degradate, the stressor of concern is the parent compound, IPBC.

3.1.3 Water Quality – Total Maximum Daily Load

Based on a search of the Assessment and, Total Maximum Daily Load (TMDL) Tracking and Implementation System (ATTAINS)[17] database on June 8, 2023, IPBC and its major degradate PBC are not identified as causes of impairment for any water bodies listed as impaired under Section 303(d) of the Clean Water Act. In addition, no TMDLs have been developed for IPBC

[17] https://www.epa.gov/waterdata/get-data-access-public-attains-data

and PBC.[18] More information on impaired water bodies and TMDLs can be found at the Agency's website.[19]

3.1.4 Monitoring Data

The Water Quality Portal[20] was searched on February 9, 2024, and water monitoring data were not found for IPBC and PBC.

3.2 Ecological Effects

Ecological effects data are used to estimate the toxicity of IPBC to surrogate species. The ecotoxicity data currently available for IPBC include endpoints from acute and chronic freshwater fish, acute and chronic freshwater invertebrates, acute estuarine/marine fish, acute estuarine/marine invertebrates, aquatic vascular and non-vascular plants, and avian species (acute oral and dietary), and pollinator studies (acute contact).

3.2.1 Selected Ecotoxicity Endpoints

The most sensitive endpoints are selected for each tested taxon and are used for the risk assessment (Table 37). Based on available acute ecotoxicity data, IPBC is found to be slightly toxic to birds, very highly toxic to freshwater fish, highly toxic to freshwater invertebrates, very highly toxic to estuarine/marine fish, and very highly toxic to estuarine/marine invertebrates. IPBC has an EC_{50} of 3.56 µg/L for aquatic non-vascular plants based on area under the growth curve. The study for vascular plants was classified as supplemental qualitative. However, qualitatively, results indicated significant effects in frond number yield at concentrations around 72 µg/L for aquatic vascular plants.

Chronic ecotoxicity data for rainbow trout (most acutely sensitive species) is not available. Therefore, an acute-to-chronic ratio (ACR) was used to estimate the NOAEC (3.0 µg/L) for that species. For freshwater invertebrates, although the chronic daphnid study submitted (MRID 50938202) was classified as supplemental qualitative, ecotoxicity data indicate that IPBC can elicit chronic effects (time to first brood) at concentrations at or below 3.0 µg/L.

[18] https://www.epa.gov/sites/default/files/2019-05/services_retrieve.xlsx
[19] Impaired Waters and TMDLs Program in your EPA Region, State or Tribal Land | US EPA
[20] https://www.waterqualitydata.us/

Table 40. Ecological Effects Endpoints Selected for IPBC

Receptor Group	Surrogate Species	Exposure Scenario	Exposure Scenario	Toxicity Endpoint (µg a.i./L, unless specified)	Reference
Birds	Bobwhite quail *(Colinus virginianus)*		Acute	LD_{50}: 749 mg/kg bw Slightly toxic	42430901 42623605 Acceptable
			Dietary	LC_{50}: >3881 mg a.i./kg diet Slightly toxic	42430902 Acceptable
Freshwater Fish	Rainbow trout *(Oncorhynchus mykiss)*		Acute	LC_{50}: 67 Very highly toxic	41627107 Acceptable
			Chronic	NOAEC: 3.0	ACR[1]
Freshwater Invertebrates	Water flea *(Daphnia magna)*		Acute	EC_{50}: 160 Highly toxic	43530210 Acceptable
			Chronic	NOAEC: <3.0 LOAEC: 3.0 Time to first brood	50938202 Supplemental qualitative
Estuarine/Marine Fish	Sheepshead minnow *(Cyprinodon variegatus)*		Acute	LC_{50}: 418 Highly toxic	42168203 Acceptable
			Chronic	No data	NA
Estuarine/Marine Invertebrates	Eastern oyster (*Crassostrea virginica*)		Acute (Shell deposition)	EC_{50}: 23.4 Very highly toxic	42168202 Acceptable
			Chronic	No data	NA
Aquatic Non-Vascular Plants	Freshwater diatom (*Navicula pelliculosa)*		All	EC_{50}: 3.56 NOAEC: 2.55 Area under the curve	51215601 Acceptable
Aquatic Vascular Plants	Duckweed *(Lemna gibba)*		All	EC_{50}: 72.3 NOAEC: < 4.2 Frond number yield	51215602 Supplemental qualitative
Nontarget Terrestrial Insects	Honeybee (*Apis mellifera*)		Acute	LD_{50}: >100 µg a.i./bee Practically non-toxic	50915401 Supplemental quantitative

LD_{50} = 50% lethal dose, EC_{50} = 50% effect concentration, NOAEC = no observed adverse effect concentration, LOAEC = lowest observed adverse effect concentration

[1]An acute-to-chronic ratio (ACR) was used to estimate the chronic endpoint for the most sensitive freshwater fish species, Rainbow trout (*Oncorhynchus mykiss*). An ACR of 22.3 is derived from the acute and chronic studies (MRIDs 43530208, 42389801, respectively) for Fathead minnow (*Pimephales promelas*). ACR = Acute fathead minnow/chronic fathead minnow; ACR= 200/8.97; ACR=22.3; The NOAEC for rainbow trout was estimated using the following equation: NOAEC = Acute rainbow trout/ACR; 67/22.3; NOAEC = 3.0 µg/L.

3.2.2 Ecotoxicity Data Gaps and Uncertainties

There are no acceptable chronic ecotoxicity endpoints available for IPBC on freshwater invertebrates. In the daphnid life-cycle study (MRID 50938202, supplemental qualitative), numerous deviations were noted to include that the test substance was unstable under the test conditions, and measurements both before and immediately after renewal were not reported. Furthermore, sublethal effects (time to first brood) were observed at the lowest concentration tested (3.0 µg a.i./L), thus a definitive NOAEC could not be determined from the study.

Additionally, there are no acceptable endpoints available for IPBC and vascular plants. Although the study submitted (MRID 51215602) demonstrates significant effects (frond number yield, frond number growth rate, final biomass, and biomass growth rate), it lacks analytical information on the renewal solutions. Given that IPBC was unstable under the test conditions, the lack of analysis brings into question the calculated concentrations, thus the study is classified as supplemental qualitative. The reported endpoints could not be used quantitatively in this risk assessment.

To quantitively assess the chronic risks to freshwater invertebrates, and risks to aquatic vascular plants, new freshwater invertebrate life cycle and aquatic vascular plant studies would be needed.

3.3 Aquatic Exposure

3.3.1 Pulp and Papermill Exposure Modeling

IPBC is used in the production of paper products such as drywall, gypsum wallboard, and other paperboard products. It is applied in the wet-end of the paper making process (including in the wet-slurry) at up to 8,000 ppm (EPA Reg. No. 5383-170; Table 2). The label states that IPBC can be applied to finished paper and mentions slurries (unspecified). As a result, the Agency assumed that IPBC can be applied to paper slurries. Aquatic exposure has the potential to occur when IPBC is applied to the wet-end process of pulp and paper manufacturing. During the wet-end process, 90% of IPBC is expected to adhere to paper and sludge pulp/slurry material while the remaining 10% is expected to be then discharged in wastewater either directly to surface waters or after treatment in a wastewater treatment plant (WWTP). Currently, no information is available on the amount of IPBC degradation that occurs during the wastewater treatment process. Therefore, the following screening-level assessment assumes no removal of IPBC from pulp and papermill discharge waters during the wastewater treatment process. The General Population and Ecological Exposure from Industrial Releases Module (herein called the Industrial Release module) of the E-FAST (U.S. EPA, 2014b) was used to perform an upper bound and average screening level estimate of exposure for aquatic organisms located downstream of pulp and paper mills. Additionally, although the Industrial Release module is

appropriate only for estimating exposures in flowing water bodies (*e.g.*, streams) and cannot be used to estimate potential exposures to aquatic organisms in estuarine/marine environments, the most sensitive acute endpoint for the aquatic invertebrate receptor group is an estuarine/marine invertebrate. The Agency, therefore, used this endpoint to represent the most sensitive acute endpoint for the aquatic invertebrate receptor group, including freshwater invertebrates. Similarly, the most sensitive fish endpoint was for a freshwater fish species but is expected to be representative of the most sensitive endpoint for the entire fish receptor group, including estuarine/marine fish.

To determine the maximum amount of IPBC (kg/site/day) that could be released within effluent from a pulp and papermill, it is necessary to know the maximum amount of paper that can be produced. The Agency uses the general assumption that 500 US tons of paper are produced per site per day in pulp and papermills. This assumption represents production in a moderate sized papermill. Using the maximum application rate of 8,000 ppm a.i. (0.8% a.i.; Table 2), the Agency estimates the total kg of a.i. used by a pulp and papermill per day with the following equation:

Total a.i. used/site/day = $0.8\%\ a.i.\ \ x\ \frac{500\ US\ ton\ paper}{site{\cdot}day}\ x\ \frac{1\ kg\ a.i.}{0.00110231\ US\ ton\ a.i..} =$

3,629 kg a.i./site/day

The amount of a.i. released from pulp and papermills to wastewater treatment is then estimated using the assumption that 90% of the a.i. is retained in the paper, leaving 10% to be released in wastewater (Organisation for Economic Co-operation and Development, OECD 2009).

3,629 kg a.i./site/day x 10% = 362.9 kg a.i. released in wastewater/site/day

Concentrations of concern (COCs) for nontarget organisms were calculated for non-listed[21] species in the following way and are expressed in µg a.i./L (see Table 38 for COCs calculated for IPBC):

- Acute COCs for non-listed vertebrates and invertebrates: LC_{50} or EC_{50} values from acute toxicity tests multiplied by the acute LOC: 0.5.
- Chronic COCs for non-listed vertebrates and invertebrates: NOAEC values from chronic toxicity tests multiplied by the chronic LOC: 1.0.
- COCs for non-listed vascular plants and algae: EC_{50} values from toxicity tests multiplied by the aquatic plant LOC: 1.0.

[21] A non-listed species is a species that has not been designated as endangered or threatened by the U.S. Fish and Wildlife Service or the U.S. National Marine Fisheries Service.

Table 41. Summary of COCs Calculated for IPBC

Species	Exposure Scenario	Concentration of Concern (COC; µg a.i./L unless specified)
Rainbow trout *(Oncorhynchus mykiss)*	Acute	33.5
	Chronic	3.0[1]
Water flea *(Daphnia magna)*	Acute	80
Water flea *(Daphnia magna)*	Chronic	< 3.0[2]
Freshwater diatom (*Navicula pelliculosa)*	All	3.56
Estuarine/marine sheepshead minnow (*Cyprinodon variegatus)*	Acute	209
Estuarine/marine Eastern oyster (*Crassostrea virginica*)	Acute	11.7

a.i. = active ingredient

[1] An acute-to-chronic ratio is used to calculate the chronic endpoint for freshwater fish, Rainbow trout (*Oncorhynchus mykiss*) because it is the more acutely sensitive species but there are no chronic data available. The ACR of 22.3 is derived from the acute and chronic studies (MRIDs 43530208, 42389801, respectively) for Fathead minnow (*Pimephales promelas*). See Table 37 for details on ACR calculations.

[2] The NOAEC was non-definitive, with adverse effects being observed at all test concentrations in this study. Here this value was used for risk characterization. See Table 37 for details.

The number of days per year that COCs would be exceeded for nontarget organisms downstream of a WWTP receiving effluent from a pulp and papermill are calculated assuming (1) pulp and papermill facilities operate 360 days per year, (2) all releases occur over the course of one year, (3) the facility is applying the maximum application rate of 8,000 ppm IPBC (4) all water used in pulp and papermills are discharged to WWTPs, (5) only one pulp and papermill with IPBC effluent is received by a WWTP or stream, (6) no IPBC is removed from effluent during wastewater treatment because no data on removal were available (*e.g.,* data from OCSPP guideline numbers 835.1110, 835.3110, 835.3220, 835.3240, and 835.3280), and (7) WWTP effluent is released into either a low-flow or average-flow receiving stream.

Estimated exposure concentrations (EECs) using this screening-level approach are 500 µg a.i./L for average-flow scenarios (50th percentile of the 7Q10) and 7,558.2 µg a.i./L for low-flow scenarios (10th percentile of the 7Q10). If pulp and papermill effluent is released into streams with low flow (high-end estimate), acute and chronic COCs are exceeded for 360 days per year for all aquatic nontarget receptor groups examined (Table 39). If pulp and papermill effluent is released to streams with average flow, COCs for aquatic nontarget organisms are exceeded for 298 to 338 days per year (Table 41).

In summary, modeling indicates that risks of concern are expected from IPBC use in pulp and papermills for all aquatic nontarget receptor groups examined under average-flow and low-flow scenarios for the majority, if not all, of the year.

Table 42. Days Per Year of Exceedance of COCs for IPBC and Nontarget Organisms Based on the Maximum Application Rate (8,000 ppm a.i.)

Concentrations of Concern (COC)	360 Days[1]	
	High-End[2]	Average[3]
Acute		
Fish (COC = 33.5 µg a.i./L)[4]	360	243
Aquatic Invertebrate (COC = 11.7 µg a.i./L)[4, 5]	360	298
Chronic		
Freshwater Fish (COC = 3.0 µg a.i./L)[4]	360	338
Plant		
Aquatic Non-vascular Plant (COC = 3.56 µg a.i./L)[4]	360	335

[1] 36,287 kg IPBC released to surface waters/site/day for 360 days per year.
[2] High-end (*i.e.*, low-flow) is based on the 10th percentile of the distribution of the ratio of 7Q10 stream flow to WWTP flow
[3] Average is based on the median of the distribution of the ratio of 7Q10 stream flow to WWTP flows
[4] See Table 38 for calculated concentrations of concern (COC)
[5] The most sensitive acute endpoint for the aquatic invertebrate receptor group, which includes freshwater invertebrates, was an estuarine/marine species(see Table 37).

Given the estimated risks from IPBC use in pulp and papermills using the maximum application rate (8,000 ppm a.i.) and the assumption that no removal occurs during WWTP processing, the Agency determined the reduction in IPBC needed for environmental concentrations to be below the COC for the most sensitive receptor group. The maximum application rate (or reduction through treatment) would need to be reduced to 0.30 ppm (>99% reduction from the current max of 8,000 ppm) for there to be no exceedance of COCs to the most sensitive receptor group (chronic exposure to freshwater fish). However, it should be noted that the lowest tested concentration that showed adverse effects for freshwater invertebrates (NOAEC < 3.0 µg a.i./L) is not definitive, meaning that effects were observed at the lowest concentration tested. These results suggest that the chronic endpoint for freshwater invertebrates is lower than 3.0 µg a.i./L and thus the application rate would need to be lowered further to have no risks to this receptor group.

As the pulp and papermill modeling results presented above are conservative screening-level estimates (Table 39), they may not be representative of all environmental conditions. These results likely overestimate exposure to IPBC in some locations.

3.3.2 Metalworking Fluid Exposure Modeling

Aquatic exposure has the potential to occur when IPBC is used in fluids treated for metal-working applications and subsequently discharged in wastewater either directly to surface waters or after treatment in a wastewater treatment plant (WWTP). The Agency therefore modeled the potential risk to nontarget organisms from aquatic exposure to IPBC released from MWF uses. The assumptions and data used to estimate environmental releases of IPBC to surface water are based on OECD (2011), which is the latest revised draft of the "Emission Scenario Document on the Use of Metalworking Fluids." This document, initially prepared by U.S. EPA, is one of the documents in the OECD Environmental Health and Safety Publications Series on Emission Scenario Documents (ESDs). This ESD provides a generic scenario for industrial use of MWFs and is intended to provide upper bound, screening-level environmental release estimates of chemicals used in metalworking operations.

To estimate the release rate of IPBC to WWTPs from MWF facilities, the Agency uses the Industrial Release module within E-FAST. The Industrial Release module is used to estimate the upper bound and average screening-level exposure concentrations of IPBC to aquatic organisms located downstream of WWTPs receiving IPBC effluent. Several inputs and assumptions are made in the use of this model. These assumptions and inputs include:

- The number of operating days per year is 360 days. Although OECD (2011) recommends a default number of 247 days, there may be manufacturing plants that operate more than 247 days; therefore, the 360-day scenario is used for this assessment.
- The typical dilution of MWFs in water is 5% for machining operations and 3% for grinding operations, the two most common MWF operations (OECD, 2011). To be protective, the Agency uses 5% dilution.
- The default annual use volume of neat (undiluted) MWF is 12,000 gallons of neat MWF (end-use product) per site per year. This is the 90th percentile use volume of MWFs from a National Institute for Occupational Safety and Health (NIOSH) study of 79 metalworking sites (OECD, 2011).
- The default number of MWFs containing IPBC used per site is 1 (OECD, 2011).
- The default number of different MWFs used per site is 1 (OECD, 2011).
- All water used in MWFs are discharged to WWTPs.
- The number of MWF facilities with IPBC effluent being received by a WWTP is 1.
- Standard Industrial Classification (SIC) code analysis or facility analysis; the SIC code "Primary Metal Forming Manuf. (major users of metal working fluids)" was chosen because no specific facility was being analyzed.
- Because no data are available on the removal of IPBC in wastewater treatment, the Agency assumes 0% removal during treatment (*e.g.,* data not submitted from OCSPP guidelines 835.1110, 835.3110, 835.3220, 835.3240, and 835.3280).

- The Agency assumed that the most sensitive acute endpoint for aquatic invertebrates, an estuarine/marine species, was representative of all invertebrates.
- The Agency assumed that the most sensitive acute endpoint for fish, a freshwater species, was representative of all fish.

The annual use rate of neat MWFs used per site is calculated as follows:

12,000 gal neat MWF/site/year *x* 3.785 L/gal *x* 1 kg/L (default density of neat MWF)

= 45,420 kg neat MWF/site/year

Based on the 5% dilution of MWF in water (OECD, 2011) and the product label stated maximum end-use fluid concentration of 5,250 ppm IPBC (see Table 2; Registration No.s 5383-171, 5383-77, 5383-91) when diluted for use, the concentration of IPBC in the concentrate prior to dilution with water is 105,000 ppm a.i., or 10.5% a.i. Therefore, for the purpose of estimating the annual use rate per site, the percentage of IPBC in neat MWF is assumed to be 10.5%.

The daily use rate of a.i. used per site can then be calculated as:

(45,420 kg neat MWF/site/year *x* 10.5%/100% *x* 1 MWF containing IPBC/site) / 1 MWF used/site

= 4769.1 (kg IPBC/site/year) / 360 (days/year)

= 13.25 kg IPBC/site/day

Aquatic Risk Estimates from MWF Uses:

The number of days per year that COC would be exceeded for nontarget organisms downstream of a WWTP receiving effluent from a MWF facility is calculated using the described model inputs (Table 40) for the Industrial Release module in E-FAST. The Agency estimates risks to nontarget organisms from the industrial release of IPBC from a MWF facility using two scenarios, effluent releases to low-flow rate streams (high-end estimate) and average-flow rate streams (Table 41).

Table 43. Input Data for IPBC for General Population and Ecological Exposure from Industrial Releases Module

Model Input Parameter (Units)	Value
BCF in Fish (L/kg)	No data
WWTP Removal Percentage (%)	No data (assumed to be 0%)

Model Input Parameter (Units)	Value
Drinking Water Treatment Removal Percentage (%)	No data (assumed to be 0%)
Daily Use Rate by MWF Facility (kg/site/day)	13.25 kg IPBC/site/day (based on the maximum application rate of 5,250 ppm a.i.)
Number of MWF facilities releasing IPBC to WWTPs	1
Acute COC – Freshwater fish (µg/L)[1]	33.5
Chronic COC – Freshwater fish (µg/L)[1]	3.0
Acute COC –Invertebrate (µg/L)[1]	11.7
Aquatic Plant COC – Non-Vascular (µg/L)[1]	3.56

[1] See Table 38 for COC calculations.

a.i. = active ingredient; COC = concentration of concern

Based on the maximum end use application rate (5,250 ppm a.i., Table 2), EECs using this screening-level approach are 99.9 µg a.i./L for average-flow scenarios (50th percentile of the 7Q10) and 1,472,2 µg a.i./L for low-flow scenarios (10th percentile of the 7Q10). In the high-end (low-flow streams) scenario for acute risks, COCs are exceeded for 338 days for fish and 357 days for invertebrates (Table 41). Under this scenario, the COC for chronic sublethal adverse effects to freshwater fish are exceeded for all MWF operation days of the year (360 days per year). For aquatic non-vascular plants, 360 days of COC exceedance are estimated. For the average-case (average-flow streams) scenario for acute risks, COCs are exceeded for 111 days for fish and 170 days for aquatic invertebrates. COC for chronic sublethal adverse effects on freshwater fish are exceeded 241 days under the average-flow scenario and 233 days for non-vascular plants (Table 41).

Table 44. Number of Days per Year of COC Exceedance for IPBC to Nontarget Organisms Downstream of Metalworking Fluid Sites

Concentrations of Concern (COCs)	Application Rate (5,250 ppm a.i. or 13.25 kg a.i./site/day)	
	High-End[1]	Average[2]
Acute		
Fish (COC = 33.5 µg a.i./L)[3]	338	111
Aquatic Invertebrate (COC = 11.7 µg a.i./L)[3]	357	170
Chronic		
Freshwater Fish (COC = 3.0 µg a.i./L)[3]	360	241
Aquatic Plants		
Aquatic Non-Vascular Plant (COC = 3.56 µg a.i./L)[3]	360	233

[1] High-end (*i.e.*, low-flow) is based on the 10th percentile of the distribution of the ratio of 7Q10 stream flow to WWTP flow

[2] Average-case (*i.e.*, average-flow) is based on the median of the distribution of the ratio of 7Q10 stream flow to WWTP flow

[3] see Table 38 above for calculations of concentrations of concern (COC) for each nontarget receptor group.

a.i. = active ingredient

Given the estimated risks from IPBC use in MWFs when using the maximum application rate (5,250 ppm a.i.) and the assumption of no removal during WWTP processing, the Agency determined the reduction in IPBC needed for environmental concentrations to be below the COC for the most sensitive receptor group. Based on the current modeling approach, the max application rate would need to be reduced to 0.15 ppm (>99% reduction) for there to be no exceedance of COCs to the most sensitive receptor groups (chronic exposure to freshwater fish and invertebrates). However, it should be noted that the lowest tested concentration that showed adverse effects for freshwater invertebrates (NOAEC < 3.0 µg a.i./L) is not definitive, meaning that adverse effects were observed at the lowest tested concentration of 3.0 µg a.i./L. These results suggest that the chronic endpoint for freshwater invertebrates is lower than 3.0 µg a.i./L and thus the application rate would need to be lowered further to have no risk to this receptor group.

The MWF modeling results presented above are conservative screening-level estimates and therefore may not be representative of all environments. Consequently, these results likely overestimate exposure to IPBC in some locations.

3.3.3 Exterior Paints and Coatings Exposure Modeling

IPBC is used as a material preservative in the preservation of paints, coatings, and stains. If paints are used indoors, aquatic exposure would be unlikely. If paints or coatings are used on exterior surfaces such as siding, fencing, or decking, then aquatic exposure could occur when IPBC leaches from painted surfaces during rain events and subsequent run off into aquatic habitats. Here the Agency modeled exposure to nontarget organisms from IPBC use in paint applied to a house adjacent to a standard-sized waterbody (20,000,000 L) at a maximum application rate of 9,600 ppm a.i. (EPA Reg. No. 5383-197, Table 2). This use pattern is assumed to be protective of IPBC uses in paints and coatings applied to decks and fences adjacent to a standard waterbody despite the higher labeled maximum use rate for wood coatings (18,000 ppm a.i., EPA Reg. No.s 5383-171 and 5383-91, Table 2). This conclusion is based on a preliminary examination of model results supporting that using IPBC preserved paint with 9,600 ppm a.i. on the larger surface area of a house (2750 ft^2 for a one-story and 3250 ft^2 for a two-story house[22]) resulted in higher risk to aquatic organisms than applying 18,000 ppm IPBC preserved wood coatings to the smaller surface area of a deck and fence (assumed to total 77 m^2 per house, with 55 m^2 for a fence and 22.2 m^2 for a deck, OECD 2013).

Exterior paint release rate calculations:

[22] 2015 Characteristics of New Housing. US Department of Commerce and US Department of Housing and Urban Development. https://www.census.gov/construction/chars/pdf/c25ann2015.pdf

IPBC in paints and coatings are estimated to leach at a rate of 6.4% (MRID 51530601). The maximum application rate used in paint is 9,600 ppm a.i. (Table 2). Additionally, since there is no standard number of houses on a standard waterbody, the paint/coating assessment calculates the maximum surface area at which the LOC is exceeded for the receptor group species. To do the calculation, the minimum EEC to result in risk is determined by taking an endpoint and multiplying it by the respective LOC for the receptor group. This value is then substituted into the below equation to obtain the maximum surface area to trigger risk.

The Agency calculates the amount of surface area needed to result in risk using the following equation:

$$SA = \frac{EEC \cdot V}{AR \cdot PA \cdot D \cdot CF1 \cdot CF2 \cdot LR \cdot T}$$

Where:

SA= Maximum Surface Area of painted surface that results in no risk (ft^2)
EEC= Minimum Estimated Environmental Concentration (µg a.i./L) that results in risk[23]
AR= Application Rate (0.003 gallons paint per square feet)[24]
PA = Percent Active ingredient in final paint (0.96% a.i.)[25]
D = Density of formulation (1.38 g/mL)[26]
CF1= Conversion Factor one (1,000,000 µg/g)
CF2= Conversion Factor two (3,785.4 mL/gallon)
LR = Leach Rate (6.4 % a.i./day)[27]
T = Time (1 day)
V = Volume of water in a waterbody (20,000,000 L)[28]

Risks to nontarget organisms from use of exterior paints/coatings:

Due to the variability in the sizes, number, and distribution of houses in the United States, the maximum quantity of treated surface area adjacent to a waterbody that results in risk to non-listed, nontarget organisms was derived (Table 42). Based on the most sensitive receptor group (chronic sublethal effects on freshwater fish) and a 6.4% leaching rate (MRID 51530601), the Agency estimated that painting 6,231.4 ft^2 or more would result in estimated concentrations in adjacent waterbodies exceeding a LOC. Because the Agency assumed that the most sensitive acute endpoint for fish and invertebrates was the most sensitive endpoint from each group,

[23] Endpoint * level of concern (LOC). *E.g.,* the endpoint for freshwater fish is 67 µg a.i./L (MRID 41627107) and the acute LOC of 0.5. Thus, the minimum EEC that results in risk is 67 µg/L * 0.5 = 33.5 µg/L

[24] According to paint manufacturers a gallon of paint may cover 250-400 ft^2 of wall in a single coat. Therefore, the average gallon covers 325 ft^2 which is equivalent to 0.003 gal paint/ft^2

[25] The maximum active ingredient use is 9600 ppm in the final paint according to use Table 2 in this document.

[26] A gallon of paint weighs approximately 11.5 pounds, which converts to a density of 1.38 g/mL. https://bhs.econ.census.gov/bhs/cfs/weightConversion.html

[27] Estimated IPBC leach rate = 6.4% (MRID 51530601)

[28] The Agency's standard waterbody for pesticide ecological assessments is 20,000,000 liters. This waterbody is used as a proxy for all non-flowing aquatic habitats.

regardless of whether they were freshwater or estuarine/marine, the least sensitive of the fish and invertebrate receptor groups was the acute freshwater fish endpoint, representing all fish. Based on this least sensitive nontarget receptor group (acute LOC for freshwater fish), 69,584.2 ft^2 or more painted surface area would result in an exceedance of the LOC for the fish receptor group in an adjacent waterbody (Table 42).

Table 45. Maximum IPBC Painted Surface Area Next to a Waterbody That Results in No Risk

Nontarget Receptor Group	Minimum EEC that Results in Risk[1] (µg a.i./L unless specified)	Minimum Surface Area to Result in Risk[2] (ft^2)
Acute		
Fish	33.5[3]	69,584.2
Aquatic Invertebrate	11.7[4]	24,302.5
Chronic		
Freshwater Fish	3[5]	6,231.4
Aquatic Plants		
Aquatic Non-Vascular Plant	3.56[6]	7,394.6

[1] Minimum EEC that Results in Risk is calculated by multiplying the endpoint with the LOC
[2] See Equation above for details
[3] Based on rainbow trout *(Oncorhynchus mykiss)* study with 96-hr LC_{50} = 67 µg a.i./L (MRID 41627107) and the acute LOC of 0.5; 67*0.5 = 33.5 µg a.i./L.
[4] Based on Eastern oyster (*Crassostrea virginica*) shell deposition study with EC_{50} = 23.4 µg a.i./L (MRID 42168202) and the acute LOC of 0.5; 23.4*0.5 = 11.7 µg a.i./L.
[5]Based on rainbow trout *(Oncorhynchus mykiss)* study with NOAEC = 3 µg a.i./L (ACR; see Table 37) and the chronic LOC of 1.0; 3*1.0 = 3 µg a.i./L.
[6] Based on freshwater diatom *(Navicula pelliculosa)* with 96-h EC_{50} = 3.56 µg a.i./L (MRID 51215601) and the aquatic plant LOC of 1; 3.56*1 = 3.56 µg a.i./L.
a.i. = active ingredient

The Agency calculated the number of median-sized houses that result in the maximum surface area calculated that exceeds nontarget LOCs (Table 42). These calculations are based on statistics within the 2015 Characteristics of New Housing document from the US Department of Commerce[29] which states that single-family houses built in the United States in 2015 contained a median square footage of 2,467 ft^2.

Based on this median-sized single-family house estimate[21], the Agency determined that a one-story house would have approximately 2,750 ft^2 of siding and a two-story house would have approximately 3,250 ft^2 of siding. Therefore, risk to the most sensitive nontarget receptor group (chronic sublethal effects on freshwater fish) could occur if two one-story houses or one two-story house is located next to a standard-sized waterbody (20,000,000 L) and painted with IPBC-preserved paint leaching at 6.4% (MRID 51530601; Table 47). It should be noted that the lowest

[29] 2015 Characteristics of New Housing. US Department of Commerce and US Department of Housing and Urban Development. https://www.census.gov/construction/chars/pdf/c25ann2015.pdf

tested concentration that showed adverse effects for freshwater invertebrates is lower than 3.0 µg a.i./L and thus less than two one-story houses or one two-story house located next to a waterbody painted with IPBC-preserved paint leaching at 6.4% would be expected to result in risk to this receptor group. For the least sensitive receptor group (acute LOC for fish), less than 25 one-story houses and 21 two-story houses could be painted with IPBC-preserved paint leaching at 6.4% next to a waterbody and result in no risk (Table 47).

Table 46. Maximum Number of Houses Next to a Waterbody that Result in No Risk from IPBC in Paints/Coatings

Number of Stories[1]	Floor Plans With 2500 ft^2 of Space	Square Feet of Siding on the House[2]	# Houses Represented by 6,231.4 ft^2 of Siding[3] (Most Sensitive Species)	# Houses Represented by 69,584.2ft^2 of Siding[3] (Least Sensitive Species)
1 Story	25ft x 100ft	2,750 ft^2	2	25
2 Stories	25ft x 50ft	3,250 ft^2	1	21

1: The Agency has assumed that each story is 10 feet tall. Therefore, the exterior wall height is either 10 feet (one story) or 20 feet (two story) and the gable has a height of 10 ft.
2: Square Feet of Siding = The surface area of the exterior walls including the gable. (Length*Height) *2 + (Width*Height)*2 + (0.5*Base*10 ft)*2; where Base = 25ft and represents the base of the triangle that makes-up the gable.
3: Square footage of painted siding expected to result in risk to the most sensitive and least sensitive nontarget species (see Table 40)

Exterior paint calculation uncertainties and limitations:

The exterior paint modeling presented above is a conservative, high-end, screening-level approach that uses many assumptions which may not be representative of wide-spread conditions in the environment. The major assumptions are:

- All painted surfaces are impacted by rain equally, and eaves and gutters do not protect the house's siding from rainfall.
- Houses are newly painted.
- Every house next to a waterbody is painted with paint/coating preserved with IPBC
- The application rate assumes that a gallon of paint covers 325 ft^2 (*i.e.,* 0.003 gallons paint per ft^2 /gal), whereas many paint manufacturers state that one gallon of paint may cover 250-400 ft^2 of wall in a single coat.
- All leachate goes directly into a waterbody with a volume of 20,000,000 L via run-off, and no degradation, sorption, or removal of the leachate occurs before entering the waterbody.
- Instantaneous mixing of IPBC occurs throughout the modeled waterbody.
- The amount of chemical leached within a day is lost in the same day, resulting in no long-term accumulation of the leached chemical or its degradates over time.
- The Agency assumed that the most sensitive acute endpoint for aquatic invertebrates, an estuarine/marine species, was representative of all invertebrates.

- The Agency assumed that the most sensitive acute endpoint for fish, a freshwater species, was representative of all fish.

3.3.4 Wood Preservative (Pressure-Treated) Exposure Modeling

IPBC used as a wood preservative has the potential to result in direct environmental exposure when leachate from pressure-treated wood runs-off or leaches into the environment. Wood preservatives used in docks result in direct leaching into aquatic areas; however, labeled uses here specify 'above-ground' use only. Consequently, IPBC exposure from outdoor uses of pressure-treated wood for fences and decks adjacent to aquatic ecosystems is expected to result in the highest aquatic exposures for all currently registered IPBC pressure-treated wood preservative uses. Thus, the following modeling is protective of the other pressure-treated wood preservative uses for the aquatic environment. Exposure to IPBC from treated decks and fences was estimated using the maximum labeled application rate of 15,000 ppm IPBC (EPA Reg. No. 39967-66).

Leachable Wood Volume of a Standard Deck and Fence

Due to the variability in deck/fence size, number, and distribution, the Agency characterizes the number of decks/fences required to make up the maximum surface area using the dimensions of the deck/fence within the Emissions Scenario Document for Wood Preservatives (OECD, 2013). The document defines a medium-sized deck with dimensions of 6 m by 3.7 m per house (22.2 m^2) and a fence with dimensions of 30.5 m by 1.8 m per house (54.9 m^2). Therefore, the total deck and fence per house is 77.1 m^2 (830 ft^2). Using the assumed width of wood used for docks in the OECD guidelines for decks and fences (0.05 m), the Agency calculates the volume of pressure-treated wood in a deck and fence per house as:

(Total deck and fence surface area) x (assumed average width of the wood used for the deck and fence) = 77.1 m^2 x 0.05 m = 3.855 m^3

Amount of Active Ingredient (a.i.) in Pressure-Treated Wood in a Deck and Fence

Using the maximum labeled application rate of 15,000 ppm IPBC (15 kg/m^3; EPA Reg. No. 39967-66) for pressure-treated wood preservation, the assumption that 100% of IPBC applied is retained in wood of a standard size deck and fence for a house, the Agency calculated the following amount of IPBC.

Amount of a.i. within a deck and fence = 3.855 m^3 x 15 kg/m^3 IPBC x 1,000,000,000 µg/kg= 57,825,000,000 µg IPBC

Calculating EECs for Wood

Because no data are available on the leach rate of IPBC from pressure-treated wood products, the Agency conservatively assumes that 100% of the IPBC applied to pressure-treated wood products could leach into the environment. The Agency also assumes that the deck/fence is adjacent to a waterbody that contains 20,000,000 L of water, and that the leached chemical instantaneously mixes with the entire waterbody. Therefore, the EEC of IPBC within the waterbody from use in wood preservatives is calculated in the following equation:

$$EEC\ per\ deck/fence = \frac{mg\ a.i.\ in\ the\ deck/fence\ x\ Leach\ Rate}{L\ Water\ in\ a\ Water\ Body}$$

$$= \frac{57{,}825{,}000{,}000\ \mu g\ IPBC\ x\ 100\%}{20{,}000{,}000\ L}$$

$$= 2{,}891.3\ \mu g\ IPBC/L$$

Determining Risk from Wood Preservative Use

Acute and chronic COCs for non-listed aquatic species are exceeded when a single medium-sized (3.855 m^3 volume) IPBC pressure-treated wood deck and fence are next to an aquatic ecosystem of 20,000,000 L (Table 44). These results are consistent for all fish, aquatic invertebrate, and nonvascular plant receptor groups.

Table 47. IPBC Risk Quotients and Number of Decks and Fences needed to exceed a LOC for Pressure-Treated Wood Preservatives

Representative Species	EEC[1] (µg a.i./L)	Minimum EEC that Results in Risk[2] (µg a.i./L unless specified)	Number of Modeled Decks and Fences Needed to Exceed COC[2]
Acute Fish[3]	2891.3	33.5	<<1
Acute Aquatic Invertebrate[4]	2891.3	11.7	<<1
Chronic Freshwater Fish[5]	2891.3	3.0	<<1
Non-vascular Aquatic Plant[6]	2891.3	3.56	<<1

[1] Estimated environmental concentration (EEC) based on one deck and fence next to a waterbody. See equations above.

[2] Concentrations of concern (COC) for nontarget receptor groups (see Table 40)

[3] Based on rainbow trout *(Oncorhynchus mykiss)* study with 96-hr LC_{50} = 67 µg a.i./L (MRID 41627107) and the acute LOC of 0.5; 67*0.5 = 33.5 µg a.i./L.

[4] Based on Eastern oyster (*Crassostrea virginica*) shell deposition study with EC_{50} = 23.4 µg a.i./L (MRID 42168202) and the acute LOC of 0.5; 23.4*0.5 = 11.7 µg a.i./L.

[5] Based on rainbow trout *(Oncorhynchus mykiss)* study with NOAEC = 3.0 µg a.i./L (ACR; see Table 37) and the chronic LOC of 1.0; 3.0*1.0 = 3 µg a.i./L.

[6] Based on freshwater diatom *(Navicula pelliculosa)* with 96-h EC_{50} = 3.56 µg a.i./L (MRID 51215601) and the aquatic plant LOC of 1; 3.56*1 = 3.56 µg a.i./L.

a.i. = active ingredient

Wood Preservative Calculations, Assumptions, Uncertainties, and Limitations

The wood preservative modeling presented above is a conservative screening-level approach that uses many assumptions which may not be a good representation of all possible environments. The major assumptions are:

- The size (surface area of 77.1 m^2) and other specifications of the deck and fence used for these calculations may not be representative of all decks and fences built next to waterbodies.
- The deck and fence are newly treated with 15,000 ppm IPBC
- The retention rate is assumed to be 100%
- The leach rate is assumed to be 100%
- All leachate goes into a water body with a volume of 20,000,000 L
- Instantaneous mixing of IPBC occurs throughout the modeled waterbody. The amount of chemical leached within a day is lost in the same day, resulting in no long-term accumulation of the leached chemical or its degradates.
- The Agency assumed that the most sensitive acute endpoint for aquatic invertebrates, an estuarine/marine species, was representative of all invertebrates.
- The Agency assumed that the most sensitive acute endpoint for fish, a freshwater species, was representative of all fish.

3.3.5 Ecological Incidents

A search in the Agency's Incident Data System (IDS) on March 14, 2023, showed that a single ecological incident (Incident Package No. I011634) was reported involving a registered wood preservative use of IPBC. The incident occurred in 2001 when the registered product (Thompson's Wood Protector Clear Preservative; EPA Reg. No. 577-557) was sprayed on a wood deck that overhung the surface of a small pond. Some of the product was deposited into the water. Two days later, two swans were found dead. The investigation concluded that although the autopsy did not determine the cause of death, circumstances strongly suggested that the product (EPA Reg. No. 577-557) was responsible for the incident. However, upon further investigation, it is clear that restrictive language on the label prohibits direct application to water or contamination of water. This determines that the incident was a misuse and not a registered use of the product. Furthermore, IPBC is slightly toxic to birds (LD_{50} 749 mg/kg bw; Table 39). Given that the product contains 0.5% IPBC, there is some uncertainty that the chemical was responsible for the death of the swans.

3.4 Ecological Risk Characterization

Currently registered IPBC uses in industrial water systems (*e.g.,* pulp and papermills, MWF) and those uses expected to go down-the-drain (*e.g.,* adhesives, caulks, sealants, plastics, textiles, paper coatings, canvas, cordage, ink, and as a preservative in household, consumer, industrial, institutional, and janitorial products such as dish detergents, laundry products, floor care products and fabric care products) are expected to result in minimal terrestrial exposure because IPBC from these uses would be released to the aquatic environment through effluent into a waterbody. Conversely, outdoor uses of IPBC preserved materials (*e.g.,* preserved paints and coating used through spray and other methods, pressure-treated wood preservation used for decks and fences) have the potential to result in terrestrial exposure from IPBC leachate runoff during a rain event. However, the rapid degradation ($t_{1/2}$ < 3 hours) of IPBC in soil and its high mobility in this media, suggest it would move rapidly through soil to water or degrade on the order of hours, leaving a low potential for terrestrial exposure from registered antimicrobial uses of IPBC. Nevertheless, because there is the potential for exposure, risks to terrestrial organisms cannot be precluded from these material preservative uses, though is expected to be minimal.

IPBC is stable in water at pH levels found in the environmental (pH 5 and 7). Thus, there is potential for aquatic exposure from IPBC-preserved materials used adjacent to a waterbody (*e.g.,* paints and stains), or that result in direct discharge to a waterbody (*i.e.*, MWF, wood preservative uses and pulp and papermills). Additionally, releases in effluent are expected to result in continuous exposure near discharge sites. Consequently, of the currently registered IPBC uses, pulp and papermill, MWF, exterior paint, and deck and fence uses were modeled because they are expected to have the most direct route of aquatic environmental exposures and, thus, would be protective of other uses expected to go down-the-drain. Therefore, environmental uses modeled here are assumed to be protective of other registered uses.

Based on modeling results, risk from IPBC use in pulp and papermills, at the maximum application rate of 8,000 ppm, is expected for all aquatic nontarget receptor groups modeled under average-flow and low-flow scenarios for the majority, if not all, of the year. Acute and chronic risks to nontarget receptor groups assessed from IPBC uses in MWFs at a maximum application rate of 5,250 ppm are also expected under average-flow and low-flow scenarios for the majority, if not all, of the year. Based on the current modeling approaches, the maximum label application rates for pulp and papermill and MWF uses would need to be reduced to 0.3 ppm and 0.15 ppm respectively, for there to be no exceedance of COCs to the most sensitive receptor groups (chronic exposure to freshwater fish). However, it should be noted that the lowest tested concentration for freshwater invertebrates was the same as the chronic endpoint for freshwater fish and showed adverse effects, making the NOAEC non-definitive (NOAEC < 3.0 µg a.i./L). This result suggests that the COC for this receptor group is below the one used here to calculate the needed reduction in the use rate to result in no risk to nontarget organisms. Therefore, the application rates for pulp and papermill and MWF uses would need to be lowered even further to result in no chronic risk estimates to the aquatic invertebrate receptor group.

Additionally, the Agency assumed that 0% of IPBC was removed through wastewater treatment. However, based on an estimate using the Estimation Program Interface Suite (EPISuite)[30], approximately 77% of IPBC could be removed through biodegradation during the treatment process. Nevertheless, the reduction in the maximum application rate (or reduction through treatment) that would be needed to result in no risk to nontarget organisms from pulp and papermill and MWF uses is >99%. The Agency therefore expects risk to all aquatic nontarget organisms from the current IPBC registered uses of pulp and papermill and MWF uses.

Risks are also expected for aquatic species from IPBC material preservative uses in exterior paint and pressure-treated wood based on modeling. LOCs for the most sensitive aquatic species (chronic risks to freshwater fish) are exceeded if two one-story houses or one two-story house, adjacent to a standard-sized waterbody (20,000,000 L), are painted with IPBC-preserved paint using a maximum application of 9,600 ppm IPBC and leach rate of 6.4%. Less than 30 houses painted with IPBC-preserved paint were seen to result in acute and chronic LOC exceedances for fish, aquatic invertebrates, and nonvascular plants. Based on the current modeling approach, the application rate would need to be reduced to 600 ppm (94% reduction) for 30 two-story houses to be painted with IPBC-preserved paint to result in no chronic risk to freshwater fish. The lowest tested concentration that showed adverse effects for freshwater invertebrates was below the NOAEC for freshwater fish (NOAEC < 3.0 µg a.i./L), suggesting less than two one-story houses or one two-story house located next to a waterbody painted with IPBC-preserved paint leaching at 6.4% would be expected to result in risk to this receptor group. Fate characteristics for IPBC suggest that if leachate from paint reached soil first, it would be mobile, likely reaching an adjacent waterbody. However, fate data also suggested that rapid degradation in soil would likely reduce IPBC concentrations prior to reaching the water. The level of IPBC degradation in soil cannot currently be quantified, though is expected to be less than the 94% reduction needed for 30 two-story houses to be painted with IPBC-preserved paint adjacent to a waterbody and result in no risks of concern for nontarget organisms. The Agency therefore expects acute and chronic risks to fish and aquatic invertebrates, and to nonvascular plants from the current IPBC registered uses in exterior paints and coatings, to include wood protective stains that can be used on decks, docks, and fences.

Based on modeled results, acute and chronic LOCs for all nontarget organisms examined (fish, aquatic invertebrates, and nonvascular plants) are exceeded when a single deck and fence is built with IPBC pressure-treated wood using a maximum application rate of 15,000 ppm IPBC next to a standard-sized waterbody (20,000,000 L). Based on the current modeling approach, the application rate in pressure-treated wood would need to be reduced to 0.51 ppm (>99% reduction) for 30 decks and fences to be present next to a waterbody with IPBC-preserved wood to result in no chronic risk to the most sensitive aquatic receptor group (chronic freshwater fish)

[30] U.S. EPA. 2012. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA.

assuming a 100% leaching rate. Additionally, the lowest tested concentration that showed chronic adverse effect for freshwater invertebrates (NOAEC < 3.0 µg/L) was below those of freshwater fish, suggesting an even greater reduction in the maximum application rate for wood preservative uses would be required to result in no chronic risks to this receptor group. The model used for these calculations made the conservative assumption that 100% of applied IPBC would leach from the deck and fence directly into an adjacent waterbody and that no degradation would occur to the leachate before it reached the waterbody. The latter assumption stands if the deck or fence overhangs or is directly adjacent to a waterbody as runoff would not be expected to contact soil in those circumstances. If soil is present between the deck and fence and the waterbody, the high mobility of IPBC in soil would allow it to reach an adjacent waterbody, but the concentration would be reduced as some would biodegrade in soil. The level of IPBC degradation in soil before it reaches a waterbody cannot currently be quantified, though it is not expected to be >99%; the reduction that would be needed to result in no risks of concern to nontarget aquatic organisms. The Agency therefore expects acute risks to all nontarget organisms evaluated here (acute and chronic risks to fish and aquatic invertebrates, and nonvascular plants) from the current IPBC registered uses in above-ground wood preservative uses.

Because acceptable ecotoxicity data are not available for vascular plants, risks are also assumed for this receptor group. No exposure or toxicity data are available for benthic species, however, IPBC is not expected to accumulate in the benthos or soil given its water solubility, mobility in soil (K_{ad} < 2.64 mL/g), and its rapid biodegradation expected in sediment.

4.0 LISTED SPECIES OF CONCERN

Consistent with EPA's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to federally listed threatened and endangered (listed) species from registered uses of pesticides in accordance with the Joint Interim Approaches developed to implement the recommendations of the April 2013 National Academy of Sciences (NAS) report, *Assessing Risks to Endangered and Threatened Species from Pesticides.* The NAS report[31] outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA. EPA will address concerns specific to IPBC in connection with the development of its final registration review decision for IPBC.

In November 2013, EPA, the U.S. Fish and Wildlife Service, National Marine Fisheries (the Services), and USDA released a white paper containing a summary of their joint Interim Approaches for assessing risks to listed species from pesticides. These Interim Approaches were developed jointly by the agencies in response to the NAS recommendations and reflect a

[31] Assessing Risks to Endangered and Threatened Species from Pesticides. Available at http://www.nap.edu/catalog.php?record_id=18344

common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. Details of the joint Interim Approaches are contained in the November 1, 2013 white paper[32], *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report.*

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, this ecological risk assessment supporting the registration review of IPBC does not describe the specific ESA analysis, including effects determinations for specific listed species or designated critical habitat, to be conducted during registration review. While the agencies continue to develop a common method for ESA analysis, the risk assessment for the registration review of IPBC describes only the level of ESA analysis completed at this time. This assessment allows EPA to focus its future evaluations on the types of species where the potential for effects exists, once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methods necessary to complete risk assessments for listed species and their designated critical habitats, these methods will be applied to subsequent analyses as part of completing this registration review.

[32] Available at: Assessing Pesticides under the Endangered Species Act | US EPA

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APPENDIX A: Toxicology Profile

Table A1. Acute Toxicity Profile

Acute Toxicity Profile for IPBC			
Test (species)	MRID	Result	Toxicity Category
Oral Toxicity (rat)	00148277 (99% a.i.)	LD_{50}=1,100 mg/kg (F) LD_{50}=1,500 mg/kg (M&F)	III
Dermal Toxicity (rabbit)	42135501 (98% a.i.)	LD_{50}>2,000 mg/kg	III
Inhalation Toxicity (rat)	45919201 (98.7% a.i.)	LC_{50}=0 .68 mg/L	III
Eye Irritation (rabbit)	41627109 (97% a.i.)	Severely irritating	I
Dermal Irritation (rabbit)	41627110	Slightly irritating	IV
Dermal Sensitization (guinea pig)	43005701	Non-sensitizer at 0.32% (w/w)	N/A
Dermal Sensitization (mice)	50938207	Equivocal	N/A

Table A2. Toxicity Profile for IPBC

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
OCSPP 870.6200 Acute neurotoxicity study in rats Purity: 99.97-100.35% a.i.	MRID 45509401 Weiler, M. (2001). Acute oral neurotoxicity study with 3-Iodopropynylbutyl Carbamate (IPBC) administered by gavage in CD® rats. Covance Laboratories Inc. (Madison, Wisconsin). Laboratory Study ID 7071-101, August 31, 2001. Unpublished. Acceptable/Non-guideline 0, 100, 300, 1000 mg/kg	NOAEL = 100 mg/kg/day LOAEL = 300 mg/kg based on changes in motor activity.
Subchronic		
14-Day oral toxicity study in rats Purity: 99.3% a.i.	MRID 47026402 Weiler, M. (2002) 2-Week Dietary Range-finding and Palatability Study with 3-Iodopropynylbutyl Carbamate (IPBC) in CD® rats. Covance Laboratories, Wisconsin. Laboratory Study Identification Covance 7071-102, April 25, 2002. Unpublished. Acceptable/Non-guideline 0, 40, 80, 120 mg/kg/day	NOAEL = 80 mg/kg/day LOAEL = 120 mg/kg/day based on body weight, body weight gain, and food consumption; irritation of the non-glandular stomach.

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
OCSPP 870.3100 90-Day oral toxicity study in rats Purity: 97-98% a.i.	MRID 43530202 Twomey, K. (1994) Omacide (IPBC) 13 week oral (gavage) toxicity study in the rat. Toxicol Laboratories Limited, Herefordshire, England. Laboratory Project ID OLA/24/C. August 16, 1994. Unpublished. Acceptable/Guideline 0, 25, 75, 200 mg/kg/day	NOAEL = Could not be established LOAEL = 25 mg/kg/day based on hyperkeratosis and squamous epithelial hyperplasia of the non-glandular region of the stomach in males and females.
OCSPP 870.3100 90-Day oral toxicity study in rats Purity: 98% a.i.	MRID 45812301 Bien, E. (2002). Repeated Dose, Toxicity 90-Day Oral Toxicity Study in Rats with IPBC Technical (Protram™ 98). Harlan Bioservice for Science, Südkampen 31, 29644, Walsrode, Germany. Final Report Harlan Bioservice Project No. 20-4-0132-01. Unpublished. Acceptable/Guideline 0, 10, 20, 35, 80 mg/kg/day	NOAEL = 20 mg/kg/day LOAEL = 35 mg/kg/day based on decreased body weight in the male and salivation and breathing sounds in the female.
OCSPP 870.3250 91-Day dermal toxicity study in rats Purity: 97.5% a.i.	MRID 42168201 Siglin, J.C. 1991. 91-day dermal toxicity study in rats with Troysan Polyphase P-100. Study No.: SLS study #3228.14. Troy Chemical Corp. East Hanover, NJ 07936-0366. Springborn Labs., Inc., Life Sciences Division, Spencerville, OH 45887. December 6, 1991. Unpublished. Acceptable/Guideline 0, 50, 200, 500 mg/kg/day	NOAEL = 50 mg/kg/day LOAEL = 200 mg/kg/day based on incidences of slight erythema and desquamation in females and males.
OCSPP 870.3465 90-Day inhalation toxicity study in rats Purity: >97% a.i.	MRID 43530203 Kenny, T.J. (1994) Omacide IPBC. 13-Week Inhalation Toxicity Study in Rats. Huntingdon Research Center Ltd., Huntingdon, Cambridgeshire, PE18 6ES, England. Laboratory Project Number TXC 7/942772. November 3, 1994. Unpublished. Acceptable/Guideline	NOAEC = 0.3 mg/m^3 (0.0003 mg/L) LOAEC = 6.7 mg/m^3 (0.0067 mg/L) based on epithelial hyperplasia in the ventral region of the larynx and necrosis in the ventral cartilage of the larynx in males and females.

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	Measured concentrations: 0, 0.3, 1.16, 6.7 mg/m^3 (0, 0.0003, 0.00116, 0.0067 mg/L)	
Five-day inhalation toxicity study in rats Purity: 97-98% a.i.	MRID 43491813 Kenny, T.J. 1994. Omacide IPBC. 5-Day Repeat Dose Inhalation Toxicity Study in Rats. Huntingdon Research Centre Ltd., Huntingdon PE18 6ES, England. Laboratory Project Number TXC 8/942212. November 9, 1994. Unpublished. Supplemental (may be used for a pilot range finding study) Measured concentrations: 0, 0.3, 1.0, 3.8 mg/m^3 (0, 0.0003, 0.001, 0.0038 mg/L)	NOAEC = 0.3 mg/m^3 (0.0003 mg/L) LOAEC = 1.0 mg/m^3 (0.001 mg/L) based on the presence of histopathologic lesions such as epithelial hyperplasia in the ventral region and hyperplasia or squamous metaplasia in the ventrolateral regions of the larynx, with necrosis of the underlying cartilage.
Two-week repeat dose inhalation toxicity study in rats Purity: 97-98% a.i.	MRID 43530213 Kenny, T.J. (1994) Omacide IPBC. 2-Week repeat dose inhalation toxicity study in rats. Huntingdon Research Center Ltd., Huntingdon, Cambridgeshire, PE18 6ES, England. Laboratory Project Number TXC 6/932373. December 8, 1994. Unpublished. Supplemental (may be used for a pilot range finding study) 0, 4, 10, 38, 67 mg/m^3 (0, 0.004, 0.01, .038, 0.067 mg/L)	NOAEC = Could not be established LOAEC = 4.0 mg/m^3 (0.004 mg/L) based on histopathologic lesions of the larynx.
OCSPP 870.6200 90-Day neurotoxicity study in rats Purity: 100% a.i.	MRID 45509402 Weiler, M. (2001). 13-Week dietary neurotoxicity study with 3-Iodopropynylbutyl Carbamate (IPBC) in CD® rats. Covance Laboratories Inc. (Madison, Wisconsin). Laboratory Study ID: 7071-103, September 20, 2001. Unpublished. Acceptable/Guideline 0, 10, 50, 120 mg/kg/day	NOAEL = 50 mg/kg/day LOAEL = 120 mg/kg/day based on decreased body weight and body weight gain.
Chronic		

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
OCSPP 870.4200 Carcinogenicity in mice Purity: 98.68% a.i.	MRID 42008202 Mulhern, M., Finn, J.P., Everett, D.J., and Perry, C.J. 1989. IPBC: 78-week dietary carcinogenicity study in mice. Inveresk Research International, Tranent EH 22 2NE, Scotland. Study Number 436165. June 16, 1989. Unpublished Acceptable/Non-guideline 0, 20, 50, 150 mg/kg/day	NOAEL = Could not be established LOAEL = 20 mg/kg/day based on increased incidence of non-neoplastic thyroid histopathology (mild and moderate atrophic follicular vacuolation) in males and females.
OCSPP 870.4200 Combined carcinogenicity chronic toxicity in rats Purity: 98.68% a.i.	MRID 42008206 Mulhern, M., Everett, D.J., Perry, C.J., Finn, J.P., and Hudson, P. 1989. 3-Iodo-2-Propynyl Butyl Carbamate (IPBC): 104 Week Dietary Carcinogenicity Study in Rats. Inveresk Research International, Tranent EH 22 2NE, Scotland. Study Number 435580. March 21, 1989. Unpublished Acceptable/Guideline 0, 20, 40, 80 mg/kg/day	NOAEL = 20 mg/kg/day LOAEL = 40 mg/kg/day based on decreased mean body weights in males and body weight gain.
Developmental and Reproductive		
OCSPP 870.3700 Prenatal developmental toxicity study in rabbits Purity: 97-98% a.i.	MRID 43530205 Twomey, K. (1994) Omacide (IPBC): Oral (gavage) rabbit developmental toxicity study. Toxicol Laboratories Limited, Ledbury, Herefordshire, England. Study Nos. OLA/20/R (range-finding) and OLA/26/R. August 1994. Unpublished. Acceptable/Guideline 0, 10, 20, 40 mg/kg/day MRID 43491804 (dose-range finding study) 0, 10, 25, 75, 100 mg/kg/day	Maternal NOAEL= 20 mg/kg/day Maternal LOAEL = 40 mg/kg/day based on clinical signs of toxicity. Developmental NOAEL = 20 mg/kg/day Developmental LOAEL = 40 mg/kg/day based on decreased total live fetuses, live fetuses/dam, and increased post-implantation loss.
OCSPP 870.3700 Prenatal developmental toxicity study in rats Purity: 97-98% a.i.	MRID 43530204 Twomey, K. (1994) Omacide (IPBC): Oral (gavage) rat developmental toxicity (teratogenicity) study. Toxicol	Maternal and Developmental: NOAEL = 75 mg/kg/day LOAEL = 250 mg/kg/day based on reduced fetal body weight.

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
	Laboratories Limited, Ledbury, Herefordshire, England. Study Nos. OLA/18/R (range-finding) and OLA/19/R. August 1994. Unpublished. Acceptable/Guideline 0, 25, 75, 250 mg/kg/day MRID 43491803 0, 50, 150, 200, 300 mg/kg/day	
OCSPP 870.3800 Reproduction and fertility effects study in rats Purity: >97% a.i.	MRID 44478801 Twomey, K. (1996) Omacide® IPBC oral (gavage) rat one-generation reproductive toxicity study (expanded to two generation). Quintiles England Limited, Bromyard Road, Ledbury, Herefordshire, HR8 1LH, England. Report No. OLA/28/95. July 1996. Unpublished. Acceptable/Guideline 0, 10, 30, 100 mg/kg/day	Parental: NOAEL = 10 mg/kg/day LOAEL = 30 mg/kg/day based on clinical signs of toxicity in the F_0 and F_1 males and females and on microscopic lesions in the stomach of F_1 males and females. Reproductive/offspring: NOAEL = 10 mg/kg/day LOAEL = 30 mg/kg/day based on reduced pup survival, reduced pup body weights in F_1 and F_2 generations (decrease of 6.1%), and developmental delays during lactation.
Mutagenicity		
OCSPP 870.5100 Reverse mutation assay Purity: 98.6% a.i.	MRID 41975206 Cattanach, P.; Riach, C. 1989. Troysan Polyphase PlOO-IPBC 97%: Testing for Mutagenic Activity with *Salmonella typhimurium* TA 1535, TA 1537, TA 1538, TA 98, TA 100: Lab Project No: 740140: 4896. Unpublished. Acceptable/Guideline With and without S9: 1, 3, 10, 33, 100, 333 µg/plate Strains: TA1535, TA1537, TA1538, TA98, TA100	IPBC was found to be non-mutagenic in all five strains with and without metabolic activation at all concentrations tested (1-1000 µg/plate).

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
OCSPP 870.5550 Unscheduled DNA Synthesis Assay	MRID 40990403 McBride, D.; Riach. C. (1988) Troysan Polyphase (IPBC): Assessment of Genotoxicity in an Unscheduled DNA Synthesis Assay Using Adult Rat Hepatocyte Primary Cultures: Laboratory Project ID 737447. Unpublished. Acceptable/Guideline 3, 4.5, 6, 7.5, 9, 10.5, 12, 13.5 µg/mL	In primary rat hepatocytes, IPBC did not cause an appreciable increase in mean net nuclear grain counts. IPBC induced cytotoxicity but not genotoxicity in this assay.
OCSPP 870.5395 *In vivo* cytogenetics Purity: 99% a.i.	MRID 40990404 McCarroll, N. (1984) Troysan Polyphase (IPBC): *In vivo* Micronucleus Assay in Mice: Final Report: Laboratory Project· ID 2277-103.Unpublished. Acceptable/Guideline 0, 200, 660, 2000 mg/kg/day	IPBC did not induce any significant increase of the PCE containing micronuclei from the treated mice when compared to that of the vehicle control mice.
Special		
OCSPP 870.7485 Metabolism and pharmacokinetics Purity: Labeled 99.4% a.i. Purity: Non labelled 98.3%	MRID 43570701 (submitted to address deficiencies in MRIDs 40947404) Ampofo, S. 1995. Metabolism of ^{14}C-IPBC in Rats. Hazleton Wisconsin, Inc. Laboratory Project ID: HWI 6491-100 Acceptable/Guideline Single oral high dose of radiolabeled IPBC 125 mg/kg Repeated low oral dose of non-radiolabeled IPBC followed by a single radiolabeled dose: 20 mg/kg	Absorption of test chemical at the low and high dose was between 80-90% for all dose groups, as suggested by excretion data showing the majority of a dose eliminated through urine or exhaled air. Tissue distribution data showed that after a single high oral dose, the highest concentrations of radioactivity at 2 hours post-dose were in the fat, kidneys, liver, and residual carcass of male and female rats. Radioactivity in these tissues at 4 hours post-dose was increased in female rats over the 2 hour post-dose time point, with the amount in fat more than doubled from the 2 hour value. At 120 hours post-dose, the carcass, kidneys, liver, and fat again contained the highest levels of residual radioactivity. At the single low dose, highest

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
		concentrations of radioactivity were observed in the kidneys, liver, and carcass, while the fat did not play as prominent a role at the low dose. Excretion of IPBC-derived radioactivity was mainly via the urine, with between 50-70% of an administered dose excreted by this route at 168 hours post-dose. Feces was a minor route of excretion in all dose groups (4-7% of the administered dose), while radiolabeled CO_2 constituted between 18-24% of the administered dose. Repeated low oral dosing or a single high oral dose appeared to result in a decrease in the percentage of radioactivity excreted as $^{14}CO_2$ compared to a single low dose (38.22% in MRID 40947404). Urinary and fecal metabolites were identified in dose groups A and B, while tissue metabolites were identified in dose groups C and D. After a single high oral dose or repeated low oral dose, the major urinary metabolites identified were the Z- and E-forms of propargyl-N-acetic acid carbamate (URM-9 and URM-10) as well as a mixture of highly polar components which eluted as the void volume on HPLC (URM-15). The major fecal metabolite identified in dose groups A and B was characterized as a metabolite containing carboxylic acid functions as well as hydroxyl groups (FRM-1). In the liver, metabolite URM-4 (propargyl-

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
		N-methylcarbamate), URM-11-14 (glucuronide conjugates of metabolites URM-2, URM-3, URM-4, and URM-5), and URM-15 were identified as major metabolites. At 2 hours post-dose, female rats in groups C and D were observed with higher percentages of URM-4 in liver than males, while the percentage of glucuronide conjugates in male liver at 2 hours post-dose was higher than female liver, indicating a possible sex-related difference in velocity of glucuronidation for IPBC metabolites. In the kidney, metabolites identified in the greatest percentage included URM-4, URM 7+8 (mixture of aqueous soluble metabolites), URM 9+10, and URM-15. There did not appear to be any significant differences in percentages of kidney metabolites between dose groups C and D. In blood, parent chemical as well as URM-4 were identified as major components in dose groups C and D. Increased percentage of parent chemical was observed at the single high dose vs the single low dose, indicating possible saturation of metabolism at the high dose. Based on the metabolite identification data, a scheme for metabolism of IPBC was proposed. According to this scheme, IPBC undergoes reductive dehalogenation followed by de-alkylation to form the URM-9 and URM-10 metabolites. In addition, de-

Guideline number/Study Type/Test Substance (% a.i.)	MRID number (Year)/Citation/Classification/Doses	Results
		carboxylation following reductive dehalogenation yields carbon dioxide. Various other metabolites formed from dehalogenation are glucuronidated and constitute minor metabolites of IPBC.

APPENDIX B: Ecotoxicity Profile

Table B1. Ecotoxicity Profile

Receptor Group	Surrogate Species	Exposure Scenario	Toxicity Endpoint (µg a.i./L, unless specified)	Reference
Birds	Bobwhite quail *(Colinus virginianus)*	Acute	LD_{50}: 749 mg/kg bw Slightly toxic	42430901 42623605 Acceptable
		Dietary	LC_{50} : >3881 mg a.i./kg diet Slightly toxic	42430902 Acceptable
Freshwater Fish	Rainbow trout *(Oncorhynchus mykiss)*	Acute	LC_{50}:67 Very highly toxic	41627107 Acceptable
		Acute	LC_{50}: 72 Very highly toxic	43530209 Supplemental Weights of test organisms were below guideline recommendations
		Chronic	NOAEC: 3.0	ACR[1]
	Fathead minnow (*Pimephales promelas)*	Acute	LC_{50}: 200 Highly toxic	43530208 Supplemental quantitative Weights of test organisms were below guideline recommendations
		Chronic	NOAEC: 8.97 LOAEC: 17.28 Larval fish growth	42389801 Supplemental quantitative Test material was unstable under test conditions
		Chronic	NOAEC: 14 LOAEC: 38 Growth (length)	50938204 Acceptable
	Bluegill sunfish (*Lepomis macrochirus*)	Acute	LC_{50}: 226 Highly toxic	41627106 Acceptable
Freshwater Invertebrates	Water flea *(Daphnia magna)*	Acute	EC_{50}: 160 Highly toxic	43530210 Acceptable
		Acute	EC_{50}: 956 Highly toxic	41627108 Acceptable
		Acute	EC_{50}: 387 Highly toxic	50938203 Acceptable
		Chronic	NOAEC: <.3.0 LOAEC: 3.0 Time to first brood	50938202 Supplemental qualitative Test material was unstable under the test conditions; NOAEC for the most

Receptor Group	Surrogate Species	Exposure Scenario	Toxicity Endpoint (µg a.i./L, unless specified)	Reference
				sensitive endpoint is undefined
Estuarine/Marine Fish	Sheepshead minnow *(Cyprinodon variegatus)*	Acute	LC_{50}: 418 Highly toxic	42168203 Acceptable
		Chronic	No data	NA
Estuarine/Marine Invertebrates	Mysid *(Americamysis bahia)*	Acute	EC_{50}: 88 Very highly toxic	42168204 Acceptable
		Chronic	No data	NA
	Eastern oyster (*Crassostrea virginica*)	Acute (shell deposition)	EC_{50}: 23.4 Very highly toxic	42168202 Acceptable
Aquatic Non-Vascular Plants	Freshwater diatom (*Navicula pelliculosa)*	All	EC_{50}: 3.56 NOAEC: 2.55 Area under the curve	51215601 Acceptable
	Freshwater Green Algae (*Pseudokirchneriella subcapitata*)	All	EC_{50}: 97.83 NOAEC: 20.29 Area under the curve	50938206 Supplemental qualitative Test substance was unstable under test conditions; Starting density was below guideline recommendations; EC_{50} values could not be determined for yield and growth, despite maximum inhibitions of 100%
		All	EC_{50}: 65.8 NOAEC: 22.9 Area under the curve	51215603 Acceptable
	Green algae (*Selenastrum capricornutum*)	All	EC_{50}: 100 NOAEC: <89 Cell density	43530211 Acceptable
	Cyanobacteria (*Anabaena flos-aquae*)	All	EC_{50}: >102 NOAEC: 102 No effects observed	51215604 Supplemental quantitative Test substance was unstable under test conditions; an EC_{50} could not be defined
Aquatic Vascular Plants	Duckweed *(Lemna gibba)*	All	EC_{50}: 72.3 NOAEC: < 4.2 Frond number yield	51215602 Supplemental qualitative Test substance was unstable under test conditions; Lack of analytical measurements on the new renewal solution on Days 3 and 5

Receptor Group	Surrogate Species	Exposure Scenario	Toxicity Endpoint (µg a.i./L, unless specified)	Reference
Nontarget Terrestrial Insects	Honeybee (*Apis mellifera*)	Acute	LD_{50} : >100 µg a.i./bee Practically non-toxic	50915401 Supplemental quantitative Details on the control solution composition and application procedures were not provided

LD_{50} = 50% lethal dose, EC_{50} = 50% effect concentration, NOAEC = no observed adverse effect concentration, LOAEC = lowest observed adverse effect concentration

[1]An acute-to-chronic ratio was used to calculate the chronic endpoint for freshwater fish, Rainbow trout (*Oncorhynchus mykiss*) because it is the more acutely sensitive species but there are no chronic data available. The ACR of 22.3 was derived from the acute and chronic studies (MRIDs 43530208, 42389801, respectively) for Fathead minnow (*Pimephales promelas*). ACR = Acute fathead minnow/chronic fathead minnow; ACR= 200/8.97; ACR=22.3; The NOAEC for rainbow trout was estimated using the following equation: NOAEC = Acute rainbow trout/ACR; 67/22.3; NOAEC = 3.0 µg/L.

APPENDIX C: Ecological Risk Estimation Methods

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

Risk Quotient Methodology

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

For animals (fish[33], aquatic invertebrates, birds[34], mammals), acute and chronic RQs are calculated as follows:

Acute RQ = acute EEC/LC_{50} (or EC_{50} or LD_{50})
Chronic RQ = chronic EEC/NOAEC

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

RQ for non-listed species = EEC/EC_{50}
RQ for listed species = EEC/NOAEC (or EC_{05} if NOAEC not available)

The RQs are compared to OPP's levels of concern (LOCs) to identify potential acute and chronic risks to each receptor group. Exceedance of a LOC indicates a need to consider regulatory action to reduce these potential risks. The development of the LOCs are discussed in detail in the Agency's Overview Document[35]. OPP's LOCs are tabulated below for listed and nonlisted species. A listed species is a species that has been designated as endangered or threatened by the U.S. Fish and Wildlife Service or the U.S. National Marine Fisheries Service.

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

Table C1: Risk Presumptions and LOCs

Aquatic and Terrestrial Animals	**LOC**
Acute presumption of risk to listed aquatic species	RQ $\geq$ 0.05
Acute presumption of risk to listed terrestrial species	RQ $\geq$ 0.1
Acute presumption of risk to nonlisted aquatic and terrestrial species	RQ $\geq$ 0.5
Chronic presumption of risk to listed and nonlisted aquatic and terrestrial species	RQ $\geq$ 1.0
Risk Presumption for Aquatic/Semi-aquatic Plants	**LOC**
Presumption of risk to listed species	RQ $\geq$1
Presumption of risk to nonlisted species	RQ $\geq$1

Down-the-Drain Methodology

The Industrial Release module of E-FAST[36] (Exposure and Fate Assessment Screening Tool) is used when discharge into the aquatic environment is from municipal (*i.e.*, domestic) wastewater treatment plants (WWTPs) or from industrial sources of discharge (e. g., cooling towers). The ecotoxicity data used in the model are the same as those used for RQ calculations. The levels of concern for listed and nonlisted aquatic organisms also are factored into the calculations for estimating the COCs.

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

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

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

APPENDIX D: Dietary Consumption Ratio and DEEM Drinking Water Exposure Results

Consumption Ratio Calculations

The FDA assumption that a typical American's diet comes in contact with 4000 cm^2 of treated surface per day is based on habits of the general U.S. population (U.S. FDA, 1993). Because different population subgroups consume various quantities of food, a consumption ratio (CR), based on the population subgroup-specific food consumptions found within the 2003-2008 USDA's NHANES/WWEIA survey, is used in the wood preservative crate scenario to account for this difference and is calculated as follows:

$$CR\ (unitless) = \frac{\text{Total solid food consumed by population subgroup (g)}}{\text{Total solid food consumed by the general US Population (g)}}$$

For example, Children 1-2 years old's total food consumed is 1150 g, while the general US population consumes 1510 kg. Therefore, the CR for Children 1-2 years old:

$$CR\ (unitless) = \frac{1150\ \text{g}}{1510\ \text{g}} = 0.761$$

Table D1. Food Consumption and Consumption Ratios by Population Subgroup

Population Group	Total Food Consumed (g)[1]	Consumption Ratio (unitless)	Total Solid Food Consumed (g)[1]	Solid Food Consumption Ratio (unitless)
General U.S. Population	3910	1.000	1510	1.000
All Infants (<1 year old)	766	0.196	302	0.201
Children 1-2 years old	1770	0.453	1150	0.761
Children 3-5 years old	1940	0.496	1140	0.757
Children 6-12 years old	2460	0.629	1280	0.851
Youth 13-19 years old	3050	0.780	1220	0.807
Adults 20-49 years old	4110	1.051	1250	0.828
Adults 50-99 years old	3780	0.967	1160	0.770
Females 13-49 years old	3680	0.941	1090	0.724

1: Food consumption data is from the US Department of Agriculture's (USDA) NHANES/WWEIA 2003-2008 survey (USDA, 2008)

DEEM Drinking Water Exposure Details

In order to run a drinking water assessment, the Dietary Exposure Evaluation Model with the Food Commodity Intake Database (DEEM-FCID) Version 3.16 (3.18) was run. The following are various inputs used to run the model, as well as, the full results for the acute and chronic evaluations. The acute assessment determines the risk from a single exposure to drinking water

by a member of the 95th percentile of the population subgroup, while the chronic assessment determines the long-term or life-time risk from consumption of drinking water by the average individual.

DEEM Residue File for Drinking Water

The following definitions regarding drinking water food codes are from the FCID-WWEIA frequently asked questions (FAQs, no date) and help to explain the food codes selected within this assessment. It should be noted that each DEEM run considered both direct and indirect drinking water sources.

> The FCID Commodity tab contains three choices of water available for analysis: Water, direct, tap; water, direct bottled; and water, indirect, all sources.
>
> **Direct water** is water consumed from a tap or faucet ("water, direct, tap") or from bottled water ("water, direct, bottled"). For example, drinking fountain water, tap water from restaurants, and your kitchen sink (including filtered water like Brita) are all direct water sources. Bottled water includes those bought in stores (*e.g.*, Evian) as well as water from a water cooler (*e.g.*, Poland Spring in your office).
>
> **Indirect water** is water added by a food preparer (individual or restaurant) to make beverages or foods. For example, water added to re-constitute frozen orange juice concentrate or to make tea, coffee, infant formula, soups, and pasta, would be considered in calculation of consumption of indirect water. For example, when (dry) pasta such as spaghetti is boiled, it absorbs a certain amount water, and this water is considered indirect water when consumed, with the amount based on the difference in water content between dry (uncooked) and cooked spaghetti.

IPBC Drinking water inputs and Results 8,000 ppm Paper Mills (340.5 ppb) IPBC

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US EPA                                                    Ver. 3.18, 03-08-d
DEEM-FCID Acute analysis for IPBC
Residue file name: C:\Program Files\DEEM 3.18\CalendexWWEIAFCID\deeminstall\IPBC DW. acute.
female 13-49 endpoint. 1.19.24.r08
Analysis Date 01-19-2024            Residue file dated: 01-19-2024/08:56:45
Reference dose (aRfD) = 0.2 mg/kg bw/day
Comment: DW run for pulp and paper at 0.3405 ppm; female 13-49 aPAD
--------------------------------------------------------------------------------
  EPA      Crop                                    Def Res     Adj.Factors   Comment
  Code      Grp  Food Name                          (ppm)       #1    #2
---------- ---- ------------------------------  ----------  ------ ------  -------
8602000000 86B  Water, indirect, all sources       0.340500   1.000  1.000
8601100000 86A  Water, direct, tap                 0.340500   1.000  1.000
8601200000 86A  Water, direct, bottled             0.340500   1.000  1.000


US EPA                                                      Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for IPBC                        NHANES 2003-2008 2-Day
Residue file: IPBC DW. new acute 1.19.24.r08      Adjustment factor #2 NOT used.
```

Analysis Date: 01-19-2024/08:52:16 Residue file dated: 01-19-2024/08:50:15
RAC/FF intake summed over 24 hours
Run Comment: "DW run for pulp and paper at 0.03405ppm"

Summary calculations--per capita:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9th Percentile Exposure	% aRfD
Total US Population:						
	0.018566	1.86	0.030616	3.06	0.058160	5.82
All Infants:						
	0.058154	5.82	0.078769	7.88	0.115445	11.54
Children 1-2:						
	0.028630	2.86	0.043111	4.31	0.106171	10.62
Children 3-5:						
	0.023231	2.32	0.035579	3.56	0.057109	5.71
Children 6-12:						
	0.017750	1.78	0.029131	2.91	0.044899	4.49
Youth 13-19:						
	0.015462	1.55	0.025467	2.55	0.038450	3.85
Adults 20-49:						
	0.018271	1.83	0.027190	2.72	0.039556	3.96
Adults 50-99:						
	0.016275	1.63	0.024678	2.47	0.038899	3.89
Female 13-49:						
	0.018531	1.85	0.027250	2.72	0.038216	3.82

US EPA Ver. 3.18, 03-08-d
DEEM-FCID Acute analysis for IPBC
Residue file name: C:\Program Files\DEEM 3.18\CalendexWWEIAFCID\deeminstall\IPBC DW. acute. female 13-49 endpoint. 1.19.24.r08
Analysis Date 01-19-2024 Residue file dated: 01-19-2024/08:56:45
Reference dose (aRfD) = 0.2 mg/kg bw/day
Comment: DW run for pulp and paper at 0.3405 ppm; female 13-49 aPAD

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
8602000000	86B	Water, indirect, all sources	0.340500	1.000	1.000	
8601100000	86A	Water, direct, tap	0.340500	1.000	1.000	
8601200000	86A	Water, direct, bottled	0.340500	1.000	1.000	

Summary calculations--per capita:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9th Percentile Exposure	% aRfD
Female 13-49:						
	0.018531	9.27	0.027250	13.62	0.038216	19.11

IPBC Drinking water inputs and Results 8,000 ppm Paper Mills (Harmonic Mean 135.9 ppb) IPBC

```
US EPA                                                          Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for IPBC
Residue file: C:\Models\Deem3\InstallDEEM_CALENDEX_FCID\IPBC.Chronic. DW papermills. med
stream flow.r08
                                                        Adjust. #2 NOT used
Analysis Date 03-14-2023            Residue file dated: 03-08-2023/16:55:24
Reference dose (RfD) = 0.02 mg/kg bw/day
Comment:Paper mills, DW 0.13585 ppm, median surface water conc; midsize stream flow
-------------------------------------------------------------------------------
 Food      Crop                                    Residue       Adj.Factors
EPA Code    Grp  Food Name                         (ppm)        #1         #2
---------- ---- ------------------------------   ---------- ------     ------
8602000000 86B  Water, indirect, all sources       0.135850   1.000      1.000
8601100000 86A  Water, direct, tap                 0.135850   1.000      1.000
8601200000 86A  Water, direct, bottled             0.135850   1.000      1.000

US EPA                                                          Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for IPBC                        NHANES 2003-2008 2-day
Residue file name: C:\Models\Deem3\InstallDEEM_CALENDEX_FCID\IPBC.Chronic. DW papermills.
med stream flow.r08
                                                  Adjustment factor #2 NOT used.
Analysis Date 03-08-2023/16:55:55     Residue file dated: 03-08-2023/16:55:24
Reference dose (RfD, Chronic) = .02 mg/kg bw/day
COMMENT 1: Paper mills, DW 0.13585 ppm, median surface water conc; midsize stream flow
===============================================================================
                    Total exposure by population subgroup
-------------------------------------------------------------------------------

                                          Total Exposure
                                    ---------------------------------
          Population                      mg/kg              Percent of
           Subgroup                     body wt/day            Rfd
-------------------------------------  -------------       ----------------
Total US Population                       0.002845               14.2%
Hispanic                                  0.002716               13.6%
Non-Hisp-White                            0.002926               14.6%
Non-Hisp-Black                            0.002347               11.7%
Non-Hisp-Other                            0.003279               16.4%
Nursing Infants                           0.002574               12.9%
Non-Nursing Infants                       0.009461               47.3%
Female 13+ PREG                           0.002678               13.4%
Children 1-6                              0.003643               18.2%
Children 7-12                             0.002372               11.9%
Male 13-19                                0.001955                9.8%
Female 13-19/NP                           0.002191               11.0%
Male 20+                                  0.002650               13.3%
Female 20+/NP                             0.002988               14.9%
Seniors 55+                               0.002750               13.8%
All Infants                               0.007335               36.7%
Female 13-50                              0.002831               14.2%
Children 1-2                              0.004103               20.5%
Children 3-5                              0.003457               17.3%
Children 6-12                             0.002493               12.5%
Youth 13-19                               0.002074               10.4%
Adults 20-49                              0.002838               14.2%
Adults 50-99                              0.002806               14.0%
Female 13-49                              0.002828               14.1%
```

References

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