Proposed Registration Decision PRD2012-21

N-Alkyl (40% C12, 50% C14, 10% C16) Dimethyl Benzyl Ammonium Saccharinate and Ethyl Alcohol

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Overview

Proposed Registration Decision for N-Alkyl (40% C12, 50% C14, 10% C16) Dimethyl Benzyl Ammonium Saccharinate and Ethyl Alcohol

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of the technical actives, Onyxide 3300 and SD Alcohol and the end-use product, Lysol Brand III Disinfectant Spray as sanitizers for use on fabric (soft porous surface). Onyxide 3300 and SD Alcohol contain the technical grade active ingredients n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, respectively, while the end-use product, Lysol Brand III Disinfectant Spray contains both n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Onyxide 3300, SD Alcohol and Lysol Brand III Disinfectant Spray.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What are n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol?

N-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate is a quaternary ammonium compound. These compounds are cationic surfactants that disrupt membranes. No products are currently registered under the *Pest Control Products Act* with this active ingredient. Ethyl alcohol, an active ingredient that is found in products currently registered under the *Pest Control Products Act* is known to kill microorganisms by denaturing their proteins and dissolving their lipids. Ethyl alcohol is effective against a wide range of microorganisms.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Onyxide 3300 (n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate) and SD Alcohol (ethyl alcohol) Affect Human Health?

Lysol Brand III Disinfectant Spray, containing Onyxide 3300 and SD Alcohol, is unlikely to affect your health when used according to label directions.

Potential exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol may occur when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

Onyxide 3300 was of moderate acute toxicity via the oral route of exposure. An acute inhalation study conducted with another structurally related chemical, alkyl dimethyl benzyl ammonium chloride (ADBAC), indicated that this chemical was moderately acutely toxic via the inhalation route, and it is expected that Onyxide 3300 would exhibit the same acute inhalation toxicity profile. Onyxide 3300 was of low acute toxicity via the dermal route of exposure. It was extremely irritating to the eyes and moderately irritating to the skin. It did not cause an allergic skin reaction. As a result of the acute toxicity findings, the following signal words and hazard statements are required on the label: “DANGER – CORROSIVE TO EYES. SKIN IRRITANT”, “POISON”.

When assessing the toxicity of Onyxide 3300, it was considered appropriate to use repeat-dose animal studies performed with another structurally related chemical, ADBAC. The health effects following exposure to ADBAC are considered to be representative of Onyxide 3300.

ADBAC did not cause cancer in animals and did not damage genetic material. There was no indication that ADBAC caused damage to the nervous system. ADBAC did not cause birth defects in animals and there were no effects on the ability to reproduce. Following repeated dosing in laboratory animals there was no specific target organ toxicity. Generalized toxicity was observed in rats, mice and dogs as decreases in body weight, body weight gain, and food consumption, which in some cases were accompanied by clinical signs of toxicity. Mortality occurred at higher doses and likely reflected the corrosive nature of the test substance.

When ADBAC was given to pregnant or nursing animals, no effects on the developing fetus or juvenile animal were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to ADBAC than the adult animal.

The risk assessment protects against the effects of Onyxide 3300 by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

The toxicity of ethyl alcohol is extensively documented. Long-term repeated ingestion of ethyl alcohol may result in the development of progressive liver injury or exacerbate liver injury produced from other causes. Repeated ingestion of ethyl alcohol by pregnant mothers has been shown to adversely affect the central nervous system of the fetus, producing a collection of effects which together constitute fetal alcohol syndrome. These effects include mental and physical retardation, disturbances of learning, motor and language deficiencies, behavioural disorders, and small head size.

Considering the history of wide use of ethyl alcohol in consumer and pharmaceutical products and the frequent human exposures to products containing ethyl alcohol, no health concerns are anticipated from the exposure to ethyl alcohol in the Lysol Brand III Disinfectant Spray.

In laboratory animals, the end-use product Lysol Brand III Disinfectant Spray was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and not irritating to the skin. Lysol Brand III disinfectant Spray did not cause an allergic skin reaction.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for non-occupational exposure is not of concern provided that directions for use specified on the label are observed.

Residential exposure to individuals applying Lysol Brand III Disinfectant Spray, containing n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, on fabric (soft porous surface) is not expected to result in unacceptable risk when it is used according to label directions.

A postapplication risk assessment conducted for individuals contacting porous fabric items treated with the Lysol Brand III Disinfectant Spray indicated that risk to adults and children is not of concern when the product is used according to label directions.

Environmental Considerations

Based on the use pattern of the end-use product, an environmental assessment was not required.

Value Considerations

What Is the Value of Lysol Brand III Disinfectant Spray?

Lysol Brand III Disinfectant Spray is used to kill bacteria in fabric (soft porous surfaces) not typically washed.

Lysol Brand III Disinfectant Spray contains two active ingredients n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol. Together they treat fabrics against bacterial proliferation. The value of this product is that it can be used on fabrics that are difficult to wash such as draperies, fabrics covering car seats, rugs, *etc*.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Lysol Brand III Disinfectant Spray to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

No residential risk is expected from using Lysol Brand III Disinfectant Spray on fabric (soft porous surface) according to label directions. Since this is a domestic class product, no personal protective equipment is recommended on the label.

Environmental

Not applicable

Next Steps

Before making a final registration decision on n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

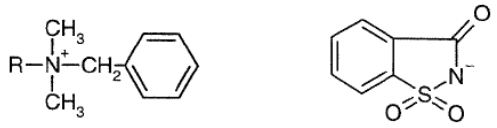
When the PMRA makes its registration decision, it will publish a Registration Decision on n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

N-Alkyl (40% C12, 50% C14, 10% C16) Dimethyl Benzyl Ammonium Saccharinate (Onyxide 3300) and Ethyl Alcohol (SD Alcohol)

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Onyxide 3300	SD Alcohol
Function	Fabric Sanitizer (soft porous surfaces)	
Chemical name **1. International Union of Pure and Applied Chemistry (IUPAC)** **2. Chemical Abstracts Service (CAS)**	n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate quaternary ammonium compounds, benzyl-C12-18-alkyldimethyl, salts with 1,2-benzisothiazol-3-(2H)-one, 1,1-dioxide (1:1)	ethanol ethyl alcohol
CAS number	68989-01-5	64-17-5
Molecular formula	$C_{16}H_{17}O_3N_2SR$ where R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$	C_2H_6O
Molecular weight	Avg. = 506.4 g/mol	46.06
Structural formula	 Where R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{33}$	CH_3 - CH_2 - OH
Purity of the active ingredient	99.0%	92.7%

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Onyxide 3300

Property	Result
Colour and physical state	white brittle solid
Odour	amine / ammonia-like
Melting range	74.5–79°C
Boiling point or range	decomposes at 190°C before boiling
Density	1.10 g/cm^3
Vapour pressure at 20°C	1.5×10^{-4} Pa
Ultraviolet (UV)-visible spectrum	no observed absorption maxima at $\lambda > 300$ nm

Property	Result
Solubility in water at 20°C	pH Solubility (mg/L) 5 269, 83.8, 25.0 for R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$ respectively 7 254, 19.7, 2.7 for R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$ respectively 9 248, 22.1, 3.0 for R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$ respectively
Solubility in organic solvents at 20°C (g/ L)	Solvent Solubility ethanol >1000 1,2-dichloroethane >1000
n-Octanol–water partition coefficient (K_{ow})	pH log K_{ow} 5 4.4 , 5.6, >6.2 for R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$ respectively 7 5.9, >6.2, >6.2 for R = $C_{12}H_{25}$, $C_{14}H_{29}$, or $C_{16}H_{37}$ respectively 9 >6.2 for all alkyl chains
Bioaccumulation Potential	ADBAC substances, including N-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate are not expected to be bioaccumulative. The maximum bioconcentration factor reported for ADBAC substances in freshwater fish was 33 fold for edible tissues, 160 fold for non-edible tissues and 79 fold for whole fish tissues (PRVD2008-23).
Dissociation constant (pK_a)	Not applicable - the quaternary ammonium moiety is ionized
Stability (temperature, metal)	Stable at room temperature in air and nitrogen. Stable for over 30 days in sunlight at 25°C and pH 7.

Technical Product—SD Alcohol

Property	Result
Colour and physical state	clear colourless liquid
Odour	characteristic odour – pleasant, sweet, fragrant
Melting range	-114°C
Boiling point or range	78°C
Specific gravity at 15.6°C	0.7943
Vapour pressure at 20°C	6.0×10^3 Pa
Ultraviolet (UV)-visible spectrum	not expected to absorb at λ >300 nm
Solubility in water at 20°C	completely miscible
Solubility in organic solvents at 20°C (g/100 mL)	Soluble in most organic solvents
n-Octanol–water partition coefficient (K_{ow})	Not applicable
Dissociation constant (pK_a)	estimated pK_a of 15.5 in water
Stability (temperature, metal)	Stable under normal conditions

End-use Product—Lysol Brand III Disinfectant Spray

Property	Result
Colour	Clear, Colourless
Odour	Various fragrances
Physical state	Liquid
Formulation type	Pressurized Product (PP)
Guarantee	58.00% Ethanol 0.10% n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate
Container material and description	Steel cans with aerosol valve and actuator
Density	0.8708 g/cm^3
pH of 1% dispersion in water	10.51
Oxidizing or reducing action	No strong oxidizing or reducing action
Storage stability	Stable on storage for 12 months at 25°C
Corrosion characteristics	Not corrosive to packaging material
Explodability	Pressurized product – container can explode if heated

1.3 Directions for Use

Lysol Brand III Disinfectant Spray is for use on fabrics that are not typically or frequently washed: backpacks and sports bags, fabric covering upholstered furniture, rugs, draperies and fabric shower curtains. This product is not intended to treat and penetrate thick material such as foam and is not for use on human clothing.

The product is sprayed on fabric until wet then air dried.

1.4 Mode of Action

N-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate is a quaternary ammonium compound. These compounds are strong surfactants. Ethyl alcohol is known to kill microorganisms by denaturing their proteins and dissolving their lipids. It is effective against a wide range of microorganisms.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Onyxide 3300 and SD Alcohol have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredients in the formulation have been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

Residue methods are not applicable for these products.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Onyxide 3300 contains a quaternary ammonium compound (n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate) as the active ingredient. Although acute toxicity data and a single genotoxicity study were submitted for Onyxide 3300, a bridging rationale was provided to use the metabolism and repeat-dose toxicity studies conducted with a cluster of quaternary ammonium compounds, alkyl dimethyl benzyl ammonium chlorides (ADBAC), in support of Onyxide 3300. These studies were performed using 80-81% formulations of ADBAC. The ADBAC compounds are all structurally similar quaternary ammonium compounds that are characterized by having a positively charged nitrogen covalently bonded to three alkyl group substituents and a benzyl substituent. In finished form they are salts with the positively charged nitrogen (cation) balanced by a negatively charged molecule (anion). Onyxide 3300 and ADBAC have identical active moieties (cations), and only differ in the weakly attached counter ion. PMRA considers the rationale to bridge to the ADBAC cluster acceptable.

A detailed review of the toxicological database in support of Onyxide 3300 was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The majority of the studies were conducted using formulations of ADBAC. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to Onyxide 3300.

Toxicokinetic studies with ADBAC demonstrate that after oral administration (single or repeated dose) of radiolabelled doses approximately 87-99% of the recovered radioactivity is observed in the feces, with 5-8% noted in the urine. However, after intravenous (i.v.) administration, 45-55% of the radioactivity was recovered in the feces, with 20-30% in the urine and therefore it is difficult to quantify absorption via the oral route. Tissue residues were <1% of the administered dose 7 days following oral administration, however 33-36% of the administered radioactivity was observed in tissues 7 days after i.v. administration. Of the 90% recovered radioactivity in the feces after oral administration, the majority (54-72%) was associated with the parent compound. In addition, four oxidative metabolites were identified (hydroxy and hydroxy keto derivatives of the dodecyl and tetradecyl analogs of the ADBAC mixture). There were no differences in the metabolism, distribution or excretion patterns between sexes or dose groups, or following single or repeated dosing.

Onyxide 3300 was of moderate acute toxicity via the oral route in rats, and of low acute toxicity via the dermal route in rabbits. An acute inhalation study was not provided; however, the USEPA Reregistration Eligibility Decision for Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) (USEPA RED, 2006) cited the results of an acute inhalation toxicity study in rats conducted with ADBAC. The results of the study indicated that ADBAC was moderately acutely toxic via the inhalation route. Onyxide 3300 was extremely irritating to the eyes and moderately irritating to the skin of rabbits. It was not a dermal sensitizer when tested in guinea pigs using the Buehler method.

Results from short- and long-term toxicology studies in laboratory animals indicate that ADBAC did not elicit any specific target organ toxicity. Generalized toxicity was observed in rats, mice and dogs following oral exposure as decreases in body weight, body weight gain, and food consumption, which in some cases were accompanied by clinical signs of toxicity (including audible respiration, perioral wetness and loose feces). Mortality occurred at higher doses ($\geq$4000 ppm in the diet) in the 90-day dietary studies in mice and rats, as well as in the range-finding gavage developmental toxicity studies in rats (at $\geq$200 mg/kg bw/day) and rabbits (at $\geq$30 mg/kg bw/day). These mortalities likely reflected the corrosive nature of the test substance. Long term studies in both rats and mice provided no evidence of treatment-induced oncogenicity at any dose level tested. No treatment-related systemic effects or signs of dermal irritation were noted in rats following 90 days exposure to ADBAC via the dermal route. The highest dose tested in the study was 20 mg/kg bw/day, and was limited by the volume of test chemical which could be applied to the animals without run-off.

No evidence of mutagenic potential of ADBAC was observed in vitro in Chinese hamster ovary cells, or in two studies investigating unscheduled DNA synthesis in primary rat hepatocyte cultures. In addition, ADBAC was negative in an in vivo mouse micronucleus assay. Based on the data presented, ADBAC was not considered to be genotoxic. In addition, Onyxide 3300 was not mutagenic when tested in bacterial cultures in vitro.

A series of developmental toxicity studies (both range-finding and main studies) were conducted with ADBAC in both rats and rabbits. There were no treatment-related effects on measured gestational parameters and no evidence of developmental toxicity in any of the studies. Clinical signs of maternal toxicity were similar throughout all of the studies and included hypoactivity, laboured/audible respiration and perioral wetness. There were no effects on measured reproductive parameters in a two-generation reproductive toxicity study conducted with ADBAC in rats. Decreases in body weight were observed in the pups at the same dose level that resulted in decreases in body weight, body weight gain and food consumption in the parental animals, indicating that the young were not more susceptible to the effects of ADBAC than the parental animals.

Results of the toxicology studies conducted on laboratory animals with Onyxide 3300 and its associated end-use product are summarized in Tables 1 and 2 of Appendix I. The toxicology endpoints for use in the human health risk assessment are summarized in Table 3 of Appendix I.

The toxicity of ethyl alcohol is extensively documented. Available information notes that in humans, long-term repeated exposure to ethanol may result in the development of progressive liver injury with fibrosis or exacerbate liver injury produced from other causes. Repeated ingestion of ethanol by pregnant mothers has been shown to adversely affect the central nervous system of the fetus, producing a collection of effects which together constitute the fetal alcohol syndrome. These effects include mental and physical retardation, disturbances of learning, motor and language deficiencies, behavioural disorders, and small head size.

Considering the history of wide use of ethyl alcohol in consumer and pharmaceutical products and the frequent human exposures to products containing ethyl alcohol, no health concerns are anticipated from the exposure to ethyl alcohol in the Lysol Brand III Disinfectant Spray (refer to Section 3.4.3 for more details).

Lysol Brand III Disinfectant Spray was of low acute toxicity in rats via the oral and inhalation routes and of low acute toxicity via the dermal route in rabbits. It was minimally irritating to the eyes and not irritating to the skin of rabbits. Lysol Brand III Disinfectant Spray was not a dermal sensitizer when tested in mice using the local lymph node assay.

Incident Reports

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found at the PMRA website. Incidents from Canada and the United States were searched and reviewed for the ADBAC cluster of compounds, as well as for ethyl alcohol.

As of April, 2012, the PMRA had received six human incident reports involving one or more of the active ingredients in the ADBAC cluster of chemicals. There were five Canadian human incidents (four minor, one moderate). One human major incident occurred in the United States and also involved the active ingredient ethyl alcohol. Five of the human incidents involved products that had guarantees of ADBAC that were higher than that of the Lysol Brand III Disinfectant Spray product.

Eye symptoms were most frequently reported (a trend also observed by the USEPA), followed by respiratory symptoms. In all cases, the symptoms were considered to be related to exposure to the pesticide product. All reported effects that related to the use of products containing ADBAC were minor and resolved rapidly. Serious effects were only reported in one incident where the product was accidentally ingested. In that case, the product contained ADBAC and ethyl alcohol.

The PMRA concluded that the information from the incident reports is consistent with the effects noted in the toxicology database; therefore, it did not impact the risk assessment. Detailed information for the incidents can be found on the PMRA Public Registry.

3.1.1 Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, extensive data were available in support of Onyxide 3300. The database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased susceptibility of fetuses or offspring compared to parental animals in the reproductive and prenatal developmental toxicity studies with ADBAC. Decreases in pup weights during the latter part of lactation were observed in the rat reproductive toxicity study; however, this occurred in the presence of maternal toxicity (decreased body weight, body weight gain and food consumption). In addition, the effects on pup weight gain occurred during the latter stages of lactation, a stage during which the pups are also beginning to consume the adult diet, and as such are likely consuming a higher dose of the test substance on a mg/kg bw basis. Overall, endpoints in the young were well-characterized and not considered serious in nature. On the basis of this information, the *Pest Control Products Act* factor was reduced to 1-fold.

3.2 Determination of Acute Reference Dose and Acceptable Daily Intake

An acute reference dose (ARfD) and an acceptable daily intake (ADI) value were not established as there are no proposed food uses, and contamination of drinking water is not expected.

3.3 Cancer Assessment

There was no evidence of carcinogenicity and, therefore, no cancer risk assessment is necessary.

3.4 Occupational and Residential Risk Assessment

Residential handler and postapplication exposure to Lysol Brand III Disinfectant Spray is characterized as long-term/intermittent and is predominantly by the dermal/inhalation route.

3.4.1 Toxicological Endpoints

N-Alkyl (40% C12, 50% C14, 10% C16) Dimethyl Benzyl Ammonium Saccharinate

Short- to long-term dermal
The most appropriate toxicology endpoint for all dermal exposure scenarios (short- to long-term) was the no observed adverse effects level (NOAEL) of 20 mg/kg bw/day from the rat dermal 90-day study (highest dose tested). The target Margin of Exposure (MOE) is 100, which includes ten-fold factors each for interspecies extrapolation and intraspecies variability. The *Pest Control Products Act* factor was reduced to 1-fold as outlined in the *Pest Control Products Act* Hazard Characterization section. This MOE is considered to be protective of all individuals including the unborn children of exposed women.

Short- to long-term inhalation
The most appropriate toxicology endpoint for all inhalation exposure scenarios (short- to long-term) was the NOAEL of 3 mg/kg bw/day for maternal toxicity from the rabbit developmental toxicity study (based on clinical signs of toxicity at the next dose of 9 mg/kg bw/day). The target MOE is 100, which includes ten-fold factors each for interspecies extrapolation and intraspecies variability. The *Pest Control Products Act* factor was reduced to 1-fold as outlined in the *Pest Control Products Act* Hazard Characterization section. This MOE is considered to be protective of all individuals including the unborn children of exposed women.

Short-term incidental oral
The most appropriate toxicology endpoint for the oral exposure scenario (short-term) was the NOAEL of 3 mg/kg bw/day for maternal toxicity from the rabbit developmental toxicity study (based on clinical signs of toxicity at the next dose of 9 mg/kg bw/day). The target MOE is 100, which includes ten-fold factors each for interspecies extrapolation and intraspecies variability. The *Pest Control Products Act* factor was reduced to 1-fold as outlined in the *Pest Control Products Act* Hazard Characterization section. This MOE is considered to be protective of all children who may receive incidental oral exposure.

Ethyl Alcohol
A quantitative risk assessment was not conducted for ethyl alcohol; therefore, no toxicological endpoints were necessary.

3.4.1.1 Dermal Absorption

No in vivo dermal absorption studies for both active ingredients, n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, were submitted. As a dermal end point was chosen for the dermal risk assessment, a dermal absorption factor was not required. However, for the incidental oral ingestion for toddlers, 100% dermal absorption value was used.

3.4.2 Occupational Exposure and Risk

Lysol Brand III Disinfectant Spray is a domestic product; therefore, no occupational exposure was conducted.

3.4.3 Residential Exposure and Risk Assessment

A quantitative risk assessment was only conducted for n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate for the current use pattern as no health concerns are anticipated from the exposure to ethyl alcohol in Lysol Brand III Disinfectant Spray.

Ethyl Alcohol
Ethyl alcohol is currently present as a formulant in several insecticide and antimicrobial products such as insect repellents (up to 67% w/w of the product), sanitizers and swimming pool products. Ethyl alcohol also has a history of wide use in consumer and pharmaceutical products such as household cleaning products, hand sanitizers, cough syrups, cosmetics and beverages. Considering the frequent human exposures to the products listed above, the label instructions which include the requirement to allow the product to dry before use, and that ethyl alcohol is highly volatile, a determination of reasonable certainty of no harm for homeowners, as well as subgroups including infants and children, was made.

N-Alkyl (40% C12, 50% C14, 10% C16) Dimethyl Benzyl Ammonium Saccharinate
Details of the risk assessment from exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate are presented below.

3.4.3.1 Handler Exposure and Risk

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. No other information was submitted by the applicant for estimating exposure of individuals spraying the product on fabric (soft porous surface).

The end-use product is a ready-to-use spray; therefore no mixing/loading is required. A quantitative risk assessment was conducted for applicator exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate. A homeowner was assumed to apply a maximum of one aerosol can (680 g) per day to porous fabrics, as per the USEPA Residential SOP (2001). The unit of exposure chosen from a generic database, Pesticide Handlers Exposure Database (PHED), in estimating the exposure was the aerosol application scenario with short pants, short sleeves, no gloves.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using a 70 kg adult body weight.

Exposure estimates were compared to the toxicological end point (NOAEL) to obtain the margin of exposure (MOE). Estimates are presented in Table 3.4.1.

Table 3.4.1 Applicator Dermal and Inhalation Exposure estimates and MOE

Application Method	Exposure Scenario	Unit of Exposure µg ai/kg ai handled[1]	kg product handled/day	Guarantee	kg ai handled/day[2]	Exposure µg/kg bw/day[3]	MOE[4,5]
Aerosol	dermal	482077.69	0.68	0.1%	0.00068	4.68	4264
Aerosol	inhalation	1646	0.68	0.1%	0.00068	0.016	188679

1. From PHED scenarios, short pants, short sleeves with no gloves
2. One can per day, 680 g product per can, guarantee of 0.1 % n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate
3. Unit of Exposure × Amount ai handled per day/70 kg bw
4. Long-term dermal NOAEL of 20 mg/kg bw/day from the rat dermal 90-day study (highest dose tested). The target Margin of Exposure (MOE) is 100 for both occupational and residential scenarios.
5. For inhalation a NOAEL of 3 mg/kg bw/day from the rabbit developmental toxicity study (based on clinical signs of toxicity at the next dose of 9 mg/kg bw/day). The target Margin of Exposure (MOE) is 100 for both occupational and residential scenarios.

Dermal and inhalation MOEs were within the target MOE of 100. Therefore, the risk to a homeowner applying the product on porous fabric is not expected to be of concern.

3.4.3.2 Postapplication Exposure and Risk

Lysol Brand III Disinfectant Spray is not permitted for use on human clothing. The product is to be used as a sanitizer on porous fabrics that are not typically washed: backpacks and sports bags, fabric covering upholstered furniture, rugs, draperies and fabric shower curtains. There is potential for exposure for adults, children and infants if they come into contact with household items treated with Lysol Brand III Disinfectant Spray.

Postapplication exposures to treated backpacks, sports bags, fabric-covered upholstered furniture, draperies, and fabric shower curtains are not expected to be greater than the exposure to treated rugs as long as sprays have dried before contact. Therefore, postapplication exposure was conducted only for the use on rugs. A quantitative risk assessment conducted for rugs as the high end exposure scenario will ensure that there are no human health concerns from postapplication exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate from Lysol Brand III Disinfectant Spray.

Exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate during postapplication activities is expected to occur primarily via the dermal route. There is also a potential for incidental oral exposure for toddlers via hand to mouth exposure. Inhalation exposure is not expected to be of concern since it is recommended on the label to allow the residues to dry.

3.4.2.2.1 Re-entry Exposure

The USEPA Residential SOP (2001) provides guidance to estimate postapplication dermal exposure immediately after application of the sanitizer to carpets. Exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate was estimated based on the following formula:

Exposure (mg/ kg bw/day) = TR × TC × ET/BW

Where:

TR indoor surface transferable residue µg ai/cm^2 = Deposited residue (µg ai/cm^2) × F fraction for transfer from treated surface

TC = Highest transfer coefficient (cm^2/hr)
ET = Exposure time (hr/day)
BW = Body weight

Detail of the exposure and risk assessment is presented in Table 3.4.2.

Table 3.4.2 Postapplication Dermal Exposure estimates and MOE based on Residential USEPA SOP (2001)

Deposited residue	Application rate[1] µg ai/cm^2	F[2]	TC[3] cm^2/hr	ET[4] hr/day	Exposure µg/kg bw/day[5]	MOE[6]
Postapplication for Adults	3	5%	16700	8	286	70
Postapplication for children 1 – 6 yr	3	5%	6000	8	480	42

1. Amount used per day (0.00068)/carpet area (conservative size of 22 m^2)
2. Fraction of residues deposited on indoor surface that may be available for transfer
3. Default transfer coefficient for adults and children for indoor surface
4. Default hours of contact for adults and children (1-6 yr) on carpet per day
5. Body weight: 70 kg for adults; 15 kg for children age 1-6 yr
6. Long-term dermal NOAEL of 20 mg/kg bw/day from the rat dermal 90-day study (highest dose tested). The target Margin of Exposure (MOE) is 100 for both occupational and residential scenarios

Using the default values from the USEPA Residential SOP, estimated dermal exposure to adults and children contacting treated porous fabrics resulted in dermal MOEs that were below the target MOE. However, when considering the revised defaults from the 2012 USEPA Residential SOP (which PMRA has been made aware of) the MOEs for both adults and children were considered acceptable based on the following:

- TCs for adults and children in the 2012 SOP were considerably lower than those from the 2001 SOP (6800 cm^2/hr vs. 16700 cm^2/hr for adults and 1800 cm^2/hr vs. 6000 cm^2/hr for children).
- The exposure duration from the 2001 SOP was revised from 8 hours to 4 hours.

3.4.2.2.2 Toddler hand-to-mouth exposure

Toddler hand-to-mouth transfer from indoor soft surfaces after spray treatment is estimated based on the USEPA Residential SOP (2001) as follows:

Exposure (mg/kg bw/day) = (DR × TR × SA × FQ × ET × SE × CF1)/BW

Where:

DR = deposited residue; (3 µg ai/cm^2, Amount used per day (0.00068)/carpet area (conservative size of 22 m^2))
TR = transferable residue available (5% for carpet)
SA = surface area of the hands (20 cm^2/event)
FQ = frequency of hand-to-mouth activity (20 events/hr)
ET = exposure time (8 hr/day)
SE = extraction by saliva (50%)
CF1= weight unit conversion factor to convert µg units to mg for the daily exposure (1 mg/1000 µg)
BW = body weight (15 kg)

Table 3.4.3 Toddler hand-to-mouth Oral Exposure estimates and MOE

Scenario	Application rate (µg ai/cm^2)	Transferable Residue (as proportion)	Exposure Time (hr/day)	Surface Area of hand (cm^2)	Frequency of mouthing events	Estimated exposure (µg/kg bw/day)	Intermediate-term MOE[1] (target = 100)
Carpet/ textiles	3	0.05	8	20	20	16	188

1. A NOAEL of 3 mg/kg bw/day from the rabbit developmental toxicity study (based on clinical signs of toxicity at the next dose of 9 mg/kg bw/day). The target Margin of Exposure (MOE) is 100 for both occupational and residential scenarios.

The exposure to n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate from hand-to-mouth activity of a child contacting treated porous fabrics is acceptable.

3.4.3.3 Bystander Exposure and Risk

No bystander scenario is considered for residential sanitizer.

3.5 Aggregate Exposure and Risk

N-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate

Dermal aggregate exposure for applicator and postapplication is as follows:

0.286 + 0.00468 = 0.290 mg/kg bw/day; MOE = 69

Although the dermal aggregate MOE was slightly below the target MOE, the risk is considered acceptable based on the conservatisms mentioned above.

Dermal and oral exposures for toddlers are not aggregated since oral and dermal NOAELs did not result in the same toxicological effect.

4.0 Impact on the Environment

Based on the use pattern of the end-use product, an environmental assessment was not required.

5.0 Value

5.1 Effectiveness Against Pests

Data from two laboratory trials were provided. Studies were carried out with two different blends of fabrics containing cotton, polyester and acrylic. Fabric carriers of 1 inch by 1 inch were inoculated with two bacterial strains, dried and treated with the Lysol Brand III Disinfectant Spray with a 30 seconds contact time. These studies demonstrated the capacity of Lysol Brand III Disinfectant Spray to kill 99.9% of the two bacterial strains representing both Gram positive and Gram negative bacteria.

5.1.1 Acceptable Efficacy Claims

The acceptable claim of Lysol Brand III Disinfectant Spray is to sanitize fabrics.

5.2 Economics

No information provided.

5.3 Sustainability

5.3.1 Survey of Alternatives

Other types of quaternary ammonium compounds are registered as laundry sanitizers and one as a sanitizing spray for fabrics that cannot be washed easily. See Table 4, Appendix I for an example of some of the registered fabric sanitizers.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

The active ingredients do not meet Track 1 criteria as they are unlikely to be bioaccumulative.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette.*[5] The list is used as described in the PMRA Notice of Intent NOI2005-01[6] and is based on existing policies and regulations including: DIR99-03;[7] and DIR2006-02[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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5 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-11-30) pages 2641-2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613: *Part I Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

6 Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*

7 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

8 Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*

The technical actives, Onyxide 3300 and SD Alcohol and the end-use product, Lysol Brand III Disinfectant Spray do not contain any formulants or contaminants of health or environmental concern identified in the Canada Gazette.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The toxicology database supporting Onyxide 3300 is adequate to define the majority of toxic effects that may result from exposure. Long term studies in rats and mice provided no evidence of carcinogenicity, and results from genotoxicity studies were negative. There was no evidence of increased susceptibility of the young in reproduction or developmental toxicity studies. In short and long-term toxicology studies with laboratory animals there was no specific target organ toxicity. Generalized toxicity was observed in rats, mice and dogs as decreases in body weight, body weight gain, and food consumption, which in some cases were accompanied by clinical signs of toxicity. Mortality occurred at higher doses in mice, rats and rabbits, which likely reflected the corrosive nature of the test substance. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

The quantitative risk assessment for n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate was conducted for the sanitizer use on porous fabrics. The dermal and inhalation risk assessment for adults was conducted and the MOE was considered acceptable. Postapplication risk assessment (dermal) for both adults and toddler contacting treated soft surfaces was conducted and the MOEs were considered acceptable in light of the conservatisms used in the assessment. Toddler non-dietary ingestion risk assessment for hand-to-mouth, was conducted and the MOE was considered acceptable.

The toxicity of ethyl alcohol is extensively documented. In humans, long-term repeated ingestion of ethanol may result in the development of progressive liver injury with fibrosis or exacerbate liver injury produced from other causes. Repeated ingestion of ethanol by pregnant mothers has been shown to adversely affect the central nervous system of the fetus, producing a collection of effects which together constitute the fetal alcohol syndrome. These effects include mental and physical retardation, disturbances of learning, motor and language deficiencies, behavioural disorders, and small head size.

Considering the history of wide use of ethyl alcohol in consumer and pharmaceutical products, the frequent human exposures to products containing ethyl alcohol and the label direction to allow residues to dry, no health concerns are anticipated from the exposure to ethyl alcohol in the Lysol Brand III Disinfectant Spray.

7.2 Value

The data submitted in support of Lysol Brand III Disinfectant Spray were adequate to demonstrate its efficacy and value for use as a fabric sanitizer. The availability of this product will provide a new sanitation tool for fabrics that cannot be easily washed such as fabrics covering mattresses, fabrics covering car seats, rugs, etc.

7.3 Unsupported Uses

Certain uses originally proposed with this application are not supported as their value has not been adequately demonstrated. Unsupported uses are outlined in Table 5 (Appendix I).

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of the technical actives, Onyxide 3300 and SD Alcohol and the end-use product, Lysol Brand III Disinfectant Spray for use as sanitizers for fabric (soft porous surface). Onyxide 3300 and SD Alcohol contain the technical grade active ingredients n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol, respectively, while the end-use product, Lysol Brand III Disinfectant Spray contains both n-alkyl (40% C12, 50% C14, 10% C16) dimethyl benzyl ammonium saccharinate and ethyl alcohol.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

°C	Degree Celsius
µg	micrograms
♀	female
♂	male
ADBAC	alkyl dimethyl benzyl ammonium chloride
ADI	acceptable daily intake
ai	active ingredient
ARfD	acute reference dose
bw	body weight
bwg	bodyweight gain
CAS	Chemical Abstracts Service
cm^2	Centimetre Square
cm^3	Centimetre Cube
F_0	Parental generation
F_1	first generation
F_2	second generation
fc	food consumption
g	gram
GD	gestation day
HDT	highest dose tested
hr	hour(s)
i.v.	intravenous
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD	lactation day
LD_{50}	lethal dose to 50%
LLNA	Local Lymph Node Assay
LOAEL	lowest observed adverse effect level
MAS	maximum average score for 24, 48 and 72 hours
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre
MOE	margin of exposure
nm	nanometre
NOAEL	no observed adverse effect level
NZW	New Zealand white
Pa	Pascal
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million

SOP	Standard Operating Procedure
TGAI	technical grade active ingredient
USEPA	United States Environmental Protection Agency
UV	ultraviolet
wk	week(s)
wt	weight(s)

Appendix I Tables and Figures

Table 1 Toxicity Profile of Lysol Brand III Disinfectant Spray (Containing Onyxide 3300 and SD Alcohol)

Study Type/Animal	Study Results	Reference/ PMRA#
Acute oral toxicity Sprague Dawley rats	LD_{50} > 5050 mg/kg bw Low toxicity	1723775
Acute dermal toxicity New Zealand White rabbits	LD_{50} > 5050 mg/kg bw Low toxicity	1723776
Acute inhalation toxicity (nose-only) Sprague Dawley rats	LC_{50} > 2.75 mg/L Low toxicity	1723777
Eye irritation New Zealand White rabbits	MAS = 2.8, MIS = 15.3 at 1 hr Minimally irritating	1723780
Dermal irritation New Zealand White rabbits	MAS = 0, MIS = 0.33 at 1 hr Non irritating	1723781
Dermal sensitization (LLNA test) CBA/J mice	Stimulation index < 3 Non-sensitizer	1723782

Table 2 Toxicity Profile of Technical Onyxide 3300

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted)

NOTE: Five acute toxicity studies and one genotoxicity study were conducted using Onyxide 3300. A bridging rationale was provided (and determined to be acceptable) to use the toxicology data conducted with alkyl dimethyl benzyl ammonium chloride (ADBAC), previously submitted to the PMRA, in support of the remainder of data requirements for Onyxide 3300.

Study Type/Animal/	Study Results	Reference/ PMRA #
Acute Oral (Onyxide 3300) Sprague Dawley Rat	500 mg/kg bw < LD_{50} <5000 mg/kg bw Moderate toxicity	1844692

Study Type/Animal/	Study Results	Reference/ PMRA #
Acute Dermal (Onyxide 3300) NZW Rabbit	LD_{50} > 5000 mg/kg bw Low toxicity	1844693
Acute Inhalation (ADBAC) Rat	0.054< LC_{50}<0.51 mg/L Moderate toxicity	Cited in USEPA RED (2006)
Eye Irritation (Onyxide 3300) NZW Rabbit	MIS = 110/110, observed at 48 and 72 hours Extremely irritating	1844694
Dermal Irritation (Onyxide 3300) NZW Rabbit	MAS = 3.55 MIS = 4.0, at 24 hours Moderately irritating	1844695
Dermal Sensitization (Onyxide 3300) Buehler method Hartley Guinea Pig	Negative	1844696
Range-finding 90-day oral toxicity (Diet) (ADBAC) CD-1 Mice	NOAEL not established since range-finding study. **1000 ppm (≈174/210 mg/kg bw/day):** ↓bw and bwg in ♀ ≥ **4000 ppm:** general ill health and malnutrition (emaciation, unkempt appearance, hunched posture), ↑ mortality. *Study considered supplemental since hematology/clinical chemistry parameters not evaluated	1155905
90-day oral toxicity (Diet) (ADBAC) Sprague-Dawley Rat	NOAEL = 62/77 mg/kg bw/day **≥4000 ppm:** ↑mortality (animals at 8000 ppm between days 4-8 of study; animals at 4000 ppm between days 7-19), ↓bw, bwg and fc, emaciation, body swelling, abdominal distention, unkept appearance, loose feces, red cutis, fecal staining of perineal skin, colour changes in various organs, distended fluid-and gas-filled viscera extending from stomach to the cecum, microscopic lesions of various organs/tissues (primarily intestinal tract), hepatocellular atrophy.	1155906
90-day dermal toxicity (ADBAC) Sprague Dawley Rat	NOAEL = 20 mg/kg bw/day (HDT) No treatment-related effects observed. <u>Note:</u> Largest volume of aqueous test solution which could be applied without run-off was 2.0 mL/kg bw.	1155907

Study Type/Animal/	Study Results	Reference/ PMRA #
12-month oral toxicity (Diet) (ADBAC) Beagle Dog	NOAEL = 13.1/14.6 mg/kg bw/day **33.8/38.6 mg/kg bw/day:** ↓bw, bwg and fc, ↓cholesterol	1155920
78-week oral toxicity (Diet) (ADBAC) CD-1 Mice	NOAEL = 73.4/92.1 mg/kg bw/day **229.3/288.6 mg/kg bw/day:** ↓ bwg No evidence of carcinogenicity.	1155925
2-year oral toxicity (Diet) (ADBAC) Sprague Dawley Rat	NOAEL = 44/57 mg/kg bw/day **88/116 mg/kg bw/day:** ↓ bw, bwg and fc (↓bwg observed only in the first half of the study) No evidence of carcinogenicity.	1155918, 1155919
Two generation Reproductive toxicity (Diet) (ADBAC) Sprague Dawley Rat	**Parental Toxicity:** NOAEL = 52.9/68.1 mg/kg bw/day **106.8/138.7 mg/kg bw/day:** ↓bw (F_0♀) & bwg (F_0♂/♀ F_1♂), ↓ fc during premating [F_0♂ (wk 1 only) /F_0♀(1^{st} 4 wk); F_1♂ (2 of 10 treatment wk)], and gestation (F_1) **Offspring Toxicity:** NOAEL = 52.9/68.1 mg/kg bw/day **106.8/138.7 mg/kg bw/day:** ↓pup wt (F_1 and F_2♂/♀) occurring at LD 21 & LD 28. **Reproductive Toxicity:** NOAEL = 106.8/138.7 mg/kg bw/day (HDT) No effects on reproductive parameters. No evidence of sensitivity of the young.	1155922
Range-finding Developmental Toxicity (gavage) (ADBAC) CD Rat	NOAEL not established since range-finding study. **≥25 mg/kg bw/day:** audible respiration **≥100 mg/kg bw/day:** perioral wetness **≥200 mg/kg bw/day:** mortality of all animals after receiving 2-4 doses of test substance, clinical signs of toxicity preceding death (perioral wetness and/or perioral encrustation, ataxia, hypoactivity, urogenital area wetness, audible respiration, and loose feces) No evidence of malformations. No evidence of sensitivity of the young.	1155924

Study Type/Animal/	Study Results	Reference/ PMRA #
Developmental Toxicity (gavage) (ADBAC) CD Rat	**Maternal toxicity:** NOAEL = 10 mg/kg bw/day **30 mg/kg bw/day:** audible respiration in 2 animals, one of which also exhibited urine stains, gasping, perinasal encrustation, loose feces and perioral wetness. **100 mg/kg bw/day:** perioral wetness, audible respiration in 3 animals, one of which also exhibited dehydration, unkempt appearance, loose feces, urine stains, and perioral wetness. **Developmental toxicity:** NOAEL = 100 mg/kg bw/day (HDT) No evidence of malformations. No evidence of sensitivity of the young.	1155936
Range-finding Developmental Toxicity (gavage) (ADBAC) NZW Rabbit	NOAELs not established since range-finding study. **≥10 mg/kg bw/day:** audible respiration, bw loss, ↓food consumption **≥30 mg/kg bw/day:** mortality/animals sacrificed moribund [2/5animals at 30 mg/kg bw/day (one found dead on GD 12 and the other sacrificed moribund on GD 9) and 5/5 animals at 60 mg/kg bw/day (4 animals died between GD 9-12 and one sacrificed moribund on GD 12)] -clinical signs of toxicity in animals that died (audible respiration, loose feces, hypoactivity, perioral wetness), and full food hoppers No evidence of malformations. No evidence of sensitivity to the young.	1155939
Developmental Toxicity (gavage) (ADBAC) NZW Rabbit	**Maternal toxicity:** NOAEL = 3 mg/kg bw/day **9 mg/kg bw/day**: clinical signs of toxicity (hypoactivity and laboured respiration in one animal and audible respiration in another). **Developmental toxicity:** NOAEL = 9 mg/kg bw/day (HDT) No evidence of malformations. No evidence of sensitivity of the young.	1155941

Study Type/Animal/	Study Results	Reference/ PMRA #
Reverse mutation assay in bacteria (Onyxide 3300) *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100, *Escherichia coli* strain WP2uvrA	Negative	1844698
Gene mutations in mammalian cells *in vitro* (ADBAC) Chinese hamster ovary cells (HGPRT locus)	Negative Cells dosed at 24 μg/mL and above were terminated due to excessive cytotoxicity.	1155943
Unscheduled DNA synthesis (*in vitro)* (ADBAC) Primary rat hepatocytes (male SD rat)	Negative	1155944, 1155945
Unscheduled DNA synthesis *(in vitro)* (ADBAC) Primary rat hepatocytes (female SD rat)	Negative	1155946
Micronucleus assay (*in vivo*) (ADBAC) NMRI SPF (Bom:NMRI) mice	Negative One male from 72 hr treatment group found dead on Day 3. Signs of toxicity not reported.	1155942

Study Type/Animal/	Study Results	Reference/ PMRA #
Toxicokinetics (ADBAC) Sprague Dawley Rat	**Rate and extent of absorption and excretion:** A negligible amount of radioactivity was excreted as $^{14}C\ CO_2$ following oral administration of ^{14}C ADBAC. A preliminary blood level experiment showed that while very little radioactivity was absorbed; detectable levels of radioactivity were present in the blood within 15 minutes. Peak blood levels occurred between 3 and 8 hours for both sexes. At 24 hours blood levels were approximately one-quarter peak values in both sexes. In all groups involving oral administration, approximately 87-99% of recovered radioactivity was observed in the feces, with minor amounts excreted in the urine (5-8). Biliary excretion was not assessed in the study. The pattern of excretion was similar in all groups, and there was no difference between males and females. After i.v. administration, 45-55% of the radioactivity was recovered in the feces and 20-30% was observed in the urine. No differences were noted between males and females. **Distribution / target organ(s):** Tissue residues were less than 1% of the administered dose in all groups involving oral administration of the test substance. There were no significant differences noted in the distribution patterns between sexes, or among dose groups. However, after single i.v. administration, 33% and 36% of the administered radioactivity was observed in the tissues of males and females, respectively. The majority of the radioactivity was noted in the heart, kidneys, GI tract and its contents, liver, pancreas, muscle, and carcass. **Toxicologically significant compound(s):** Of the 87-99% recovered radioactivity in feces after oral administration, 54-72% was associated with the unchanged compound. Four oxidative metabolites were identified, which were the hydroxy and hydroxy keto derivatives of the dodecyl (A1 and A2) and tetradecyl (B1 and B2) analogs of the ADBAC mixture. Metabolites A1 and A2 represented 6.6 - 12.4% and metabolites B1 and B2 represented 8.0 - 16.4% of the total extracted radioactivity. The ratio of metabolite A1:A2 could not be determined, however the B1:B2 ratio was approximately 2:1. No significant differences in the metabolic profile were observed between male or female rats or among animals administered ADBAC at either a single low oral dose, repeated low oral dose, or a single high oral dose.	1155927, 1155928

Table 3 Toxicology Endpoints for Use in the Health Risk Assessment for Onyxide 3300

Exposure Scenario	Study	Point of Departure and Endpoint	Target MOE
Short- to long-term dermal	90-day dermal study in rats	NOAEL = 20 mg/kg bw/day Highest dose tested in the study.	100
Short- to long-term inhalation[1]	Rabbit developmental toxicity study	NOAEL = 3 mg/kg bw/day Based on clinical signs of toxicity in dams (hypoactivity, laboured/audible respiration)	100
Non-dietary oral ingestion (short-term)	Rabbit developmental toxicity study	NOAEL = 3 mg/kg bw/day Based on clinical signs of toxicity in dams (hypoactivity, laboured/audible respiration)	100

[1] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 4 Alternative - Registered Laundry Sanitizers

PCP Registration No.	Product name	Active ingredient
23612	ENDEW	Didecyl dimethyl ammonium chloride
28789	INHIBIT	
29724	POWER STAT	
30284	LYSOL FABRIC MIST	

Table 5 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed uses	Proposed rates
DEODORIZES soft surfaces	N/A
Sanitizer for mattresses, pet beds, pillows, etc. (implies that the sanitizing effect penetrates thick porous material)	N/A

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA #	Reference
1723229	2008, Product Chemistry Data ONYXIDE 3300, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1,2.13.1 CBI
1993909	2008, [CBI removed] Information, DACO: 2.11.2
1993908	2010, [CBI removed], DACO: 2.11.3 CBI
1993911	2010, Discussion of Formulation of Impurities, DACO: 2.11.4 CBI
1723230	2009, Product Chemistry Testing for 5 Lot Preliminary Analysis - ONYXIDE 3300, DACO: 2.13.2,2.13.3 CBI
1993912	2010, Discussion Response - 2.13.1 Methodology-Validation, DACO: 2.13.1 CBI
1993913	2008, Appendix 1 - Storage Stability Study, DACO: 2.13.1 CBI
1993914	2009, Appendix 2 - [CBI removed] Determination, DACO: 2.13.1 CBI
1993915	2009, Appendix 3 - [CBI removed] Determination, DACO: 2.13.1 CBI
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