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Proposed Re-evaluation Decision

PRVD2022-16

# Dodecylguanidine Hydrochloride and Its Associated End-use Products

*Consultation Document*

*(publié aussi en français)*

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Publications  
Pest Management Regulatory Agency  
Health Canada  
2720 Riverside Drive  
A.L. 6607 D  
Ottawa, Ontario K1A 0K9

Internet: [canada.ca/pesticides](https://canada.ca/pesticides)  
[pmra.publications-arla@hc-sc.gc.ca](mailto:pmra.publications-arla@hc-sc.gc.ca)  
Facsimile: 613-736-3758  
Information Service:  
1-800-267-6315 or 613-736-3799  
[pmra.info-arla@hc-sc.gc.ca](mailto:pmra.info-arla@hc-sc.gc.ca)

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## Table of Contents

Proposed re-evaluation decision for dodecylguanidine hydrochloride and associated end use products .....	1
Proposed re-evaluation decision for dodecylguanidine hydrochloride.....	1
Risk mitigation measures .....	2
Other information .....	3
Additional scientific information .....	3
Science evaluation .....	4
1.0 Introduction.....	4
2.0 Technical grade active ingredient .....	4
2.1 Identity.....	4
2.2 Physical and chemical properties .....	5
3.0 Human health assessment .....	5
3.1 Toxicology summary .....	5
3.2 Dietary exposure and risk assessment .....	8
3.3 Occupational and non-occupational exposure and risk assessment .....	8
3.3.1 Toxicology reference values .....	9
3.3.2 Dermal absorption .....	10
3.3.3 Occupational exposure and risk assessment .....	10
3.3.4 Dietary, residential and aggregate exposure .....	11
3.4 Cumulative assessment .....	12
3.5 Health incident reports .....	12
4.0 Environmental assessment.....	12
4.1 Fate and behaviour in the environment .....	13
4.2 Environmental risk characterization.....	13
4.2.1 Environmental incident reports .....	13
4.3 Toxic substances management policy considerations .....	14
4.3.1 Formulants and contaminants of health or environmental concern.....	14
5.0 Value assessment .....	15
List of abbreviations.....	16
Appendix I Registered products containing dodecylguanidine hydrochloride in Canada <sup>1</sup> .....	18
Table 1 Products containing dodecylguanidine hydrochloride subject to proposed label amendments.....	18
Appendix II Registered uses of dodecylguanidine hydrochloride in Canada <sup>1</sup> .....	19
Table 1 Registered commercial uses of dodecylguanidine hydrochloride in Canada .....	19
Appendix III Toxicology information .....	20
Table 1 Toxicology reference values for use in health risk assessment for dodecylguanidine hydrochloride .....	20
Table 2 Toxicity profile of dodecylguanidine hydrochloride (Supplemented with dodine toxicity studies) .....	20
Table 3 Identification of Select Metabolites .....	27

Appendix IV Occupational exposure and risk assessment .....	28
Table 1 Use rate summary of dodecylguanidine hydrochloride .....	28
Table 2 Dodecylguanidine hydrochloride long-term occupational exposure and risk assessment .....	29
Appendix V Toxic Substances Management Policy Considerations -Comparison to TSMP Track 1 Criteria.....	30
Appendix VI Proposed label amendment for products containing dodecylguanidine hydrochloride .....	31
References .....	33

## **Proposed re-evaluation decision for dodecylguanidine hydrochloride and associated end use products**

Under the authority of the *Pest Control Products Act*, all registered pesticides must be re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

Dodecylguanidine hydrochloride is registered in Canada to control slime-forming bacteria and other microorganisms that form problematic biofilms on the surfaces of equipment in contact with process waters in pulp and paper mills, cooling towers, and air washers. Dodecylguanidine hydrochloride is a non-oxidizing alternative in biofilm control and acts as a surfactant to break up biofilm then kills isolated bacteria via membrane disruption. Dodecylguanidine hydrochloride is found in co-formulation with *n-alkyl* dimethyl benzyl ammonium chloride or methylene bithiocyanate in currently registered products. Currently registered products containing dodecylguanidine hydrochloride can be found in the [Pesticide Product Information Database](#) and in Appendix I. Appendix II lists all uses for which dodecylguanidine hydrochloride is presently registered.

This document presents the proposed re-evaluation decision for dodecylguanidine hydrochloride, including the proposed amendments (risk mitigation measures) to protect human health and the environment, as well as the science evaluation on which the proposed decision is based. All products containing dodecylguanidine hydrochloride that are registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period,<sup>1</sup> during which the public (including the pesticide manufacturers and stakeholders) may submit written comments and additional information to [PMRA Publications](#). The final re-evaluation decision will be published after taking into consideration the comments and information received during the consultation period.

### **Proposed re-evaluation decision for dodecylguanidine hydrochloride**

Under the authority of the *Pest Control Products Act* and based on an evaluation of available scientific information, Health Canada is proposing continued registration of dodecylguanidine hydrochloride and associated end-use products registered for sale and use in Canada.

Dodecylguanidine hydrochloride has value as a slimicide for pulp and paper mills, cooling towers, and air washers. With respect to human health and the environment, risks were shown to be acceptable when dodecylguanidine hydrochloride is used according to proposed conditions of registration, which includes new mitigation measures, as identified below.

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<sup>1</sup> "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

## **Risk mitigation measures**

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. The proposed label amendments, including any revised/updated label statements and/or mitigation measures as a result of the re-evaluation of dodecylguanidine hydrochloride, are summarized below. Refer to Appendix VI for details.

### **Human health**

As a result of the re-evaluation of dodecylguanidine hydrochloride, the PMRA is proposing further risk-reduction measures in addition to those already present on dodecylguanidine hydrochloride product labels. Additional revisions to the dodecylguanidine hydrochloride labels are also proposed to meet the current labelling standards.

To reduce potential exposure to occupational workers using dodecylguanidine hydrochloride in industrial or manufacturing settings and for label improvement, the following revisions to the product labels are proposed:

- When an open liquid pour application method is used, the maximum amount of active ingredient handled per day is limited to 16.74 kg a.i./day. When applying more than this amount per day, a closed loading and transfer system is required.
- Definition of a closed transfer system is required on all end-use product labels.
- A standard label statement for single layer personal protective equipment (PPE) is proposed for all products, unless more protective statements are already present.

### **Environment**

To minimize the exposure to the environment, the following label updates are proposed:

- An update to label statements for the protection of aquatic habitats.

### **International context**

Dodecylguanidine hydrochloride is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including the United States and Mexico. As of 3 March 2022, no decision by an OECD member country to prohibit all uses of dodecylguanidine hydrochloride for health or environmental reasons has been identified.

### **Next steps**

Upon publication of this proposed re-evaluation decision the public, including the registrants and stakeholders, are encouraged to submit additional information that could be used to refine risk assessments during the 90-day public consultation period.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of the re-evaluation decision document,<sup>2</sup> which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Refer to Appendix I for details on specific products impacted by this proposed decision.

## **Other information**

The relevant confidential test data on which the proposed decision is based are available for public inspection, upon application, in Health Canada's Reading Room. For more information, please contact Health Canada's [Pest Management Information Service](#).

## **Additional scientific information**

No additional scientific data are required at this time.

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<sup>2</sup> "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

# Science evaluation

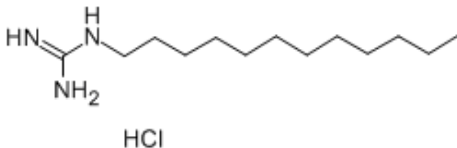
## 1.0 Introduction

Dodecylguanidine hydrochloride is a broad spectrum antimicrobial registered to control a wide range of microorganisms for use in industrial processes (Use-site Category) #17), fluids of pulp and paper mills, recirculating cooling water towers and air washers. Dodecylguanidine hydrochloride is also registered as a material preservative (Use-site Category #18) for pulp and paper products. Dodecylguanidine hydrochloride is an important alternative for use in process fluid treatments to combat microbial resistance.

Appendix I lists all dodecylguanidine hydrochloride products that are registered under the authority of the *Pest Control Products Act*. Appendix II lists all uses for which dodecylguanidine hydrochloride is presently registered.

## 2.0 Technical grade active ingredient

### 2.1 Identity

<b>Common name</b>	Dodecylguanidine Hydrochloride
<b>Function</b>	Slimicide, material preservative
<b>Chemical Family</b>	Guanidine
<b>Chemical name</b>	
<b>1 International Union of Pure and Applied Chemistry (IUPAC)</b>	1-dodecylguanidine hydrochloride (1:1)
<b>2 Chemical Abstracts Service (CAS)</b>	Guanidine, N-dodecyl-, hydrochloride (1:1)
<b>CAS Registry Number</b>	13590-97-1
<b>Molecular Formula</b>	$C_{13}H_{29}N_3.HCl$
<b>Structural Formula</b>	
<b>Molecular Weight</b>	263.85
<b>Purity of the Technical Grade Active Ingredient</b>	35%
<b>Registration Number</b>	23787

## 2.2 Physical and chemical properties

Property	Result
Vapour pressure at 25°C	6000 Pa
Ultraviolet (UV) / visible spectrum	$\lambda_{\text{max}}$ about 300 nm. Absorbs between 300–400 nm.
Solubility in water	347.46 g/L
n-Octanol/water partition coefficient at 23°C	Log $P_{\text{ow}}$ -0.86
Dissociation constant	Not required

## 3.0 Human health assessment

### 3.1 Toxicology summary

Dodecylguanidine hydrochloride is a salt of dodecylguanidine that belongs to the guanidine class of chemicals. Dodecylguanidine acetate, also known as dodine, is also a salt of dodecylguanidine. Both chemicals dissociate in a similar manner. As such, detailed reviews of the toxicological database for both dodecylguanidine hydrochloride and dodine were conducted in support of the dodecylguanidine hydrochloride review. Toxicology studies for dodecylguanidine hydrochloride were conducted with test material containing 35% of the active ingredient dodecylguanidine hydrochloride; for the purpose of this review, the administered dose levels in the repeat-dose studies were expressed in terms of the active ingredient content in the test material. The test material was considered representative of the registered technical grade active ingredient in Canada. Toxicology studies with dodine had purities that ranged from 94-99.8%, although purities were not reported for a small number of studies. The range of purities with dodine was not considered to have an impact on the observed results. Observed effects were consistent among studies from the two salts, thus, dodecylguanidine hydrochloride and dodine were considered toxicologically equivalent. When the data for dodecylguanidine hydrochloride and dodine are considered collectively, the toxicology database is considered complete as it consists of the full array of studies currently required for hazard assessment purposes. Studies were conducted in accordance with international testing protocols and Good Laboratory Practices. The scientific quality of the data is considered sufficient to characterize the potential health hazards associated with dodecylguanidine hydrochloride.

In the rat, radiolabelled dodine was rapidly absorbed following either a repeated or a single gavage dose. Most of the administered dose (AD) was recovered in excreta 48 and 96 hours post-dose in low and high doses, respectively; the extent of absorption was estimated to be 41–46% of the AD based on urinary elimination data. Dodine was widely distributed with the highest amounts recovered from fat, liver, skin, muscle, bone and the gastrointestinal tract at 120 hours post-dosing. Tissue concentrations were all less than 4% AD indicating a lack of tissue retention. Elimination of radioactivity was largely complete by five days post-dosing, with slightly more radioactivity present in feces compared to urine. A preliminary study showed trace amounts of

radioactivity expired as volatiles or carbon dioxide. Metabolism occurred via beta-oxidation. Radioactivity in urine consisted primarily of hydroxydodecylguanidine (M2); other urinary metabolites consisted of a mixture of acidic products of beta-oxidation (M4), an unidentified metabolite (M3) and urea (M5). Feces contained mostly unchanged dodine. There were no significant differences in the kinetics or metabolism of dodine associated with dose level, dose regimen or sex.

Dodecylguanidine hydrochloride and dodine have similar acute toxicity profiles. Both compounds exhibited slight acute toxicity via the oral route in rats. Clinical signs observed following acute oral dosing with dodecylguanidine hydrochloride included oral discharge, dyspnea, wet rales, soft stools, fecal staining, decreased food consumption, abdominal gripping and hypoactivity. Dodecylguanidine hydrochloride and dodine had low acute dermal toxicity in rabbits. In acute inhalation studies in rats, dodecylguanidine hydrochloride was of moderate toxicity following a 4-hour exposure whereas dodine was of slight toxicity following a 1-hour exposure. Clinical signs noted in the dodecylguanidine hydrochloride inhalation study included facial wetness/encrustation, labored breathing, ataxia, prostration, reduced reflexes and unkempt appearance. Both compounds were severely irritating or corrosive to the eyes and skin of rabbits. No dermal sensitization potential was noted with dodecylguanidine hydrochloride in a Buehler assay performed in guinea pigs or with dodine in a study conducted in humans.

The repeat-dose dermal toxicity studies in rats for both dodecylguanidine hydrochloride and dodine were consistent in their identification of irritative properties. Erythema, desquamation, fissuring, edema, eschar and other signs of irritation were observed in both sexes in both studies, consistent with the irritation observed in the acute dermal toxicity and irritation studies. Histopathological changes to the skin were similar following repeated exposure to dodecylguanidine hydrochloride and dodine and included inflammatory cell accumulation, hyperkeratosis, parakeratosis, squamous cell hyperplasia, ulcers/erosion and inflammation. Systemic effects were minimal and only evident at dose levels above those that produced significant irritation responses.

In repeat-dose oral toxicity studies in dogs, animals in both the 90-day (dodecylguanidine hydrochloride) and 52-week (dodine) studies exhibited clinical signs including excessive salivation, emesis, or diarrhea. In the 90-day dodecylguanidine hydrochloride study, body weight was decreased at the high dose level in both sexes and animals were observed as being thin/emaciated. In the 52-week dodine study, there were individual dogs that had marked weight loss, requiring supplementary feeding, in both the mid- and high-dose groups. In a 90-day dietary toxicity study in mice conducted with dodine, adverse effects were observed at the high-dose level and included decreased body weight and body weight gain in both sexes, as well as increased mortality and tail stiffening in females. Repeat-dose oral toxicity studies indicated an increase in toxicity associated with an increased duration of exposure.

There were two long-term dietary studies conducted with dodine. In a 78-week mouse study, decreases in body weight and body weight gain in females occurred at the lowest dose level. At higher dose levels, effects included decreases in body weight, body weight gain, food consumption and food efficiency in both sexes and organ weight changes in females. There was an increased incidence of hepatocellular adenomas in female mice at the high dose level. The

increased incidence did not achieve statistical significance but did exceed the historical control range for this tumour type. No increased incidence of hepatocellular carcinomas was noted in female mice and there was no evidence of other treatment-related tumours. Consequently, the increased incidence of hepatocellular adenomas in female mice was considered equivocal. In a 104-week rat study, there was a decrease in body weight in females at the mid-dose level and above. At the high-dose level, an increase in the incidence of clinical signs was observed consisting of hunched posture, dehydration or absent reflex responses. There was no evidence of treatment-related tumours in rats.

Collectively a standard battery of genotoxicity studies was available for dodecylguanidine hydrochloride and dodine. The results of these studies did not suggest that dodecylguanidine hydrochloride or dodine were genotoxic.

There were three developmental toxicity studies conducted via gavage administration in the dodecylguanidine hydrochloride/dodine database; one study was conducted in rats with dodecylguanidine hydrochloride and one study each was conducted in rats and rabbits with dodine. The maternal effects in the dodecylguanidine hydrochloride rat study consisted of decreases in body weight gain and food consumption as well as increases in salivation at the mid-dose level and above. An increased incidence in moist rales was present at the high-dose level. Maternal effects in the dodine rat study were similar to those in the dodecylguanidine hydrochloride study, with decreases in body weight, body weight gain and food consumption at a similar dose level. In rabbits administered dodine, maternal body weight loss and decreased food consumption were observed, with some animals struggling during dose administration. No developmental toxicity was observed in any study in either species.

Dietary administration of dodine in a 2-generation reproductive toxicity study in rats resulted in decreases in body weight, body weight gain and food consumption in parental animals. The decreases were noted in both sexes during pre-mating, as well as in females during gestation. In pups, decreased body weight was observed in both generations but occurred at a lower dose level than in parental animals. There were no effects on reproductive parameters.

No neurotoxicity studies were available. Although some clinical signs (salivation, stiffening of the tail, hunched posture, and absent reflexes for righting, grasping and traction) were present in repeat-dose oral studies, they were most likely associated with an agonal or irritant response. There was no evidence of selective neurotoxicity.

The toxicology reference values for use in the human health risk assessment are summarized in Appendix III, Table 1. Results of the toxicology studies conducted on laboratory animals in support of dodecylguanidine hydrochloride are summarized in Appendix III, Table 2. Chemical names of dodecylguanidine hydrochloride metabolites can be found in Appendix III, Table 3.

### ***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. This factor should take into account the completeness of the data with respect

to the exposure of, and toxicity to, infants and children, as well as potential pre- and post-natal 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, the collective data for dodecylguanidine hydrochloride and dodine contain the full complement of required studies including gavage developmental toxicity studies in rats (dodecylguanidine hydrochloride, dodine) and rabbits (dodine) and a dietary 2-generation reproductive toxicity study in rats (dodine).

With respect to potential prenatal and postnatal toxicity, there was some indication of increased sensitivity of offspring compared to parental animals in the reproductive toxicity study. In the absence of maternal toxicity, there was a decrease in pup body weight, which was not considered a serious effect. There were no treatment-related developmental effects in the rat or the rabbit.

Overall, endpoints in the young were well-characterized and the toxicology reference values selected for risk assessment provided adequate margins to the effects noted above. On the basis of this information, the PCPA factor (*Pest Control Products Act*) was reduced to onefold.

### **3.2 Dietary exposure and risk assessment**

There are no food uses associated with the preservative uses of dodecylguanidine hydrochloride. In addition, current dodecylguanidine hydrochloride product labels specify that “This product is not to be used in the production of paper or paperboard that comes in contact with food.” Residues of dodecylguanidine hydrochloride in potential drinking water sources are not anticipated as a result of the preservative uses. Therefore, no dietary exposure is anticipated.

#### **Determination of the acute reference dose (ARfD)**

The establishment of an ARfD is not required, as no exposure via the diet or drinking water is expected.

#### **Determination of the acceptable daily intake (ADI)**

The establishment of an ADI is not required, as no exposure via the diet or drinking water is expected.

### **3.3 Occupational and non-occupational exposure and risk assessment**

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

### **3.3.1 Toxicology reference values**

#### **Long-term dermal**

For long-term exposure via the dermal route, the NOAEL of 2 mg/kg bw/day from the 52-week oral toxicity study in dogs with dodine was selected for risk assessment. Marked weight loss in females was observed at 10 mg/kg bw/day and above, along with salivation in both sexes and increased testes weights in males. Although short-term dermal toxicity studies were available, these studies were of insufficient duration given that there was some evidence of increased toxicity associated with increased duration of exposure in the oral repeat-dose studies. Since it was necessary to extrapolate from an oral toxicity study to the dermal route of exposure, a 50% correction factor was applied to the NOAEL to account for the low oral absorption, resulting in a point of departure (POD) of 1 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied resulting in a target MOE of 100. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

#### **Long-term inhalation**

For long-term exposure via the inhalation route, no route-specific repeat-exposure studies were available. The NOAEL of 2 mg/kg bw/day from the 52-week oral toxicity study in dogs with dodine was selected for risk assessment. Marked weight loss in females was observed at 10 mg/kg bw/day and above, along with salivation in both sexes and increased testes weights in males. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied along with a 10-fold database uncertainty factor, resulting in a target MOE of 1000. The database uncertainty factor was applied due to the absence of repeat-dose inhalation toxicity data and the presumed increased toxicity from inhalation exposure given the corrosive properties of the compound, which are likely to exacerbate portal of entry effects in the respiratory tract. The magnitude of the database uncertainty factor was supported by the occurrence of greater acute inhalation toxicity (for example,  $LC_{50} = 0.14$  mg/L, equivalent to a systemic dose of approximately 24 mg/kg bw when considering such factors as respiratory volume and body weight of rats) compared to acute oral toxicity ( $LD_{50} = 1400$  mg/kg bw) of a formulation containing 35% of dodecylguanidine hydrochloride. The considerations regarding low oral absorption were also relevant when extrapolating from an oral toxicity study to the inhalation route of exposure. However, due to the application of the additional 10-fold database uncertainty factor, it was not considered necessary to apply an additional correction factor to account for low oral absorption. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

#### **Combined exposure**

Decreased body weight was a common systemic toxicological effect across the database, and therefore, it was appropriate to combine dermal and inhalation exposure for the occupational risk assessment based on this endpoint. For the long-term combined dermal and inhalation exposure risk assessment, the NOAEL of 2 mg/kg bw/day from the 52-week oral dog toxicity study was

selected based on marked body weight loss observed in females at 10 mg/kg bw/day. A correction factor of 50% was applied to the NOAEL when extrapolating from an oral toxicity study to other routes of exposure to account for the low oral absorption, resulting in a POD of 1 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied resulting in a target MOE of 100. Since the endpoints for common systemic toxicity are more relevant than potential portal of entry effects for the combined exposure assessment, it was not considered necessary to apply the additional 10-fold database uncertainty factor to account for presumed increased toxicity due to the corrosive nature of dodecylguanidine hydrochloride.

### **Cancer assessment**

There was no evidence of carcinogenicity in rats or male mice administered dodine. As previously discussed, the increase in hepatocellular adenomas in female mice following long-term dietary administration of dodine was considered equivocal based on the weight of evidence, which included the lack of statistical significance or progression to carcinoma, and a negative genotoxicity battery. Overall, the toxicology reference values selected for the non-cancer risk assessment are protective of any residual concerns regarding the carcinogenic potential of dodecylguanidine hydrochloride.

#### **3.3.2 Dermal absorption**

One rat in vivo dermal absorption study for dodine was on file and an additional in vivo dermal absorption study and an in vitro percutaneous absorption study for dodine from the EFSA review (2009) were examined to determine the dermal absorption value for dodecylguanidine hydrochloride. A dermal absorption value of 2% was selected based on a weight of evidence approach including the observation that absorbed dodine residues were all below 2% (0.76–1.67%) in both rat in vivo studies.

#### **3.3.3 Occupational exposure and risk assessment**

There is potential for exposure to workers handling dodecylguanidine hydrochloride commercial-class products when treating fluids used in pulp and paper mill systems, air washers and recirculating cooling water systems, as well as the treatment of solutions used in the manufacture of paper (material preservative use). Exposure to dodecylguanidine hydrochloride is expected to be intermittent (a few minutes daily or once a week) over an intermediate- to long-term duration (in other words, >30 days to several months) as work in the industrial or manufacturing facilities could occur year-round.

Current product labels do not specify when a closed transfer system is required, therefore all types of systems were considered in the risk assessment:

- Closed transfer of liquids
- Manual mixing/transfer of liquids using conventional containers (liquid pour)

Based on the use information provided by the registrants, most applications utilize pumps and

automated feed (closed) systems resulting in little to no direct worker contact. When a closed system is used, exposure was considered to be minimal and risk acceptable based on a qualitative assessment.

An open liquid pour scenario was conducted for small scale industrial and manufacturing scenarios. No appropriate chemical-specific handler exposure data were available for dodecylguanidine hydrochloride. Therefore, dermal and inhalation exposures for occupational applicators were estimated using the unit exposures obtained from the liquid pour exposure study submitted by the Antimicrobial Exposure Assessment Task Force II (AEATF II). While there are limitations in the use of generic data, these exposure data represent the most reliable information currently available. Inhalation exposures were based on light inhalation rates (17 L/min). Dermal and inhalation unit exposure values from this study were combined with the standard amounts of biocide applied per day by workers in industrial or manufacturing facilities to estimate exposures. The amount of biocide handled per day (38 L end-use product/day) was based on the amount a worker conducting industrial processes and non-potable water systems (including cooling and process water systems) would handle from in the USEPA Antimicrobial Division Draft Summary of Amounts Handled or Treated for Occupational Handler Scenarios. Calculated worker dermal and inhalation exposure MOEs, as well as the combined MOEs for this liquid open pour scenario were greater than the target MOEs at single layer PPE (long pants, long-sleeved shirt, chemical resistant gloves) and risks were determined to be acceptable (Appendix IV, Table 2).

Considering that there is a wide range of sizes of industrial and manufacturing facilities, the amount of active ingredient that can be handled per day with acceptable risks was calculated. Target MOEs are met for workers handling 16.74 kg a.i./day (equivalent to 140 L end-use products containing 10.6% dodecylguanidine hydrochloride or 340 L end-use products containing 5% dodecylguanidine hydrochloride) or less while wearing single layer (long pants, a long-sleeved shirt, shoes (plus socks) and chemical-resistant gloves). In excess of this amount, a closed system for mixing/loading will be required.

Downstream workers in industrial settings are subject to provincial or territorial occupational health and safety standards, including wearing PPE and complying with established exposure limits, if applicable. As such, risks are considered to be acceptable for downstream workers.

### **3.3.4 Dietary, residential and aggregate exposure**

Current dodecylguanidine hydrochloride product labels specify that “This product is not to be used in the production of paper or paperboard that comes in contact with food.” Therefore, potential food dietary exposure to dodecylguanidine hydrochloride is not expected. Contamination of drinking water is not expected according to the use conditions; therefore, potential drinking water dietary exposure to dodecylguanidine hydrochloride is not anticipated.

There are no domestic-class products containing dodecylguanidine hydrochloride registered in Canada, therefore, residential handler exposure is not expected. The only potential residential exposure is contact with paper products when dodecylguanidine hydrochloride is used in industrial process fluids of pulp and paper mills. Although limited, data are available showing very low concentrations of dodecylguanidine hydrochloride in paper products. Therefore,

considering the low concentration of dodecylguanidine hydrochloride residues in the paper products and the generally short half-life of this antimicrobial, it can be concluded that, under normal exposure circumstances, incidental oral and dermal exposure to dodecylguanidine hydrochloride would be minimal and not of concern. Therefore, the residential and aggregate exposure and risks were considered to be acceptable based on a qualitative assessment.

### **3.4 Cumulative assessment**

The *Pest Control Products Act* requires that Health Canada consider the cumulative effects of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for dodecylguanidine hydrochloride. Health Canada has determined that dodecylguanidine hydrochloride shares a common mechanism of toxicity with dodine. These active ingredients are considered to be toxicologically equivalent, and the collective toxicology data for both dodecylguanidine hydrochloride and dodine were considered when establishing the toxicology reference values for dodecylguanidine hydrochloride. Dodine is registered for agricultural use on pome and stone fruits in Canada, and there are Canadian MRLs established for pome and stone fruits, strawberries and bananas. Therefore, cumulative risks were considered for potential dietary and residential exposure of dodine and potential residential exposure resulting from the antimicrobial use of dodecylguanidine hydrochloride. However, the contribution of dodecylguanidine hydrochloride to the cumulative assessment is minimal since dietary exposure is not expected and residential exposure is minimal and not of concern. Therefore, cumulative risks are acceptable at this time. Since the toxicology reference values for dodine have been updated during the current re-evaluation of dodecylguanidine hydrochloride, these will be considered in the upcoming re-evaluation of dodine. The conclusions of the cumulative assessment for dodecylguanidine hydrochloride and dodine will also be confirmed at that time.

### **3.5 Health incident reports**

As of 24 March 2022, one minor human incident involving dodecylguanidine hydrochloride had been submitted to the PMRA. This incident occurred as a result of an accidental spill in an occupational setting and involved minor skin effects. Based on accidental nature of the incident and the presence of appropriate hazard and precautionary statements, as well as personal protective equipment on dodecylguanidine hydrochloride end-use product labels, no additional mitigation is recommended based on the incident report review.

## **4.0 Environmental assessment**

Dodecylguanidine hydrochloride is registered in Canada in industrial process fluids of pulp and paper mills, recirculating cooling water towers and air washers and can potentially enter the environment when it is present in discharged effluent.

## 4.1 Fate and behaviour in the environment

This review considers environmental fate data for dodecylguanidine hydrochloride and (dodine) as these compounds share the same cationic form (dodecylguanidine) under typical environmental conditions in water and moist soil.

Dodecylguanidine hydrochloride is very soluble in water and is not expected to volatilize from moist soil. Dodecylguanidine hydrochloride is persistent in the aquatic environment (aerobic aquatic metabolism half-life of 38.9 to 227 days at 25°C), but is not persistent in the terrestrial environment (aerobic soil metabolism half-life of 17.5 to 22.3 days). Lab studies indicated that dodecylguanidine hydrochloride is strongly adsorbed to soil ( $K_{oc}$  values of  $1.29 \times 10^7$ ,  $5.51 \times 10^5$ ,  $2.77 \times 10^6$  and  $7.25 \times 10^5$  for sand, sandy loam, clay loam and silt loam soils, respectively) and is therefore expected to be immobile in soil. Guanidine was identified as the major transformation product (USEPA, 2015). Dodecylguanidine hydrochloride is not expected to bioaccumulate.

## 4.2 Environmental risk characterization

On an acute exposure basis, dodecylguanidine hydrochloride is very highly toxic to the freshwater aquatic invertebrate *Daphnia magna* (48-hour  $EC_{50}$  of 0.088 mg a.i./L) and moderately toxic to freshwater fish (bluegill sunfish: 96-hour  $EC_{50}$  of 2.0 mg a.i./L and rainbow trout: 96-hour  $EC_{50}$  of 4.2 mg a.i./L). With respect to estuarine/marine species, dodecylguanidine hydrochloride is moderately toxic to estuarine/marine fish (sheepshead minnow 96-hour  $EC_{50}$  of 5.4 mg a.i./L) and highly toxic to estuarine/marine invertebrates (mysid shrimp 96-hour  $EC_{50}$  of 0.18 mg a.i./L) and estuarine/marine mollusk (Eastern oyster 96-hour  $EC_{50}$  of 0.21 mg a.i./L) on an acute basis. Dodecylguanidine hydrochloride is very highly toxic to algae (*Pseudokirchneriella subcapitata*:  $EC_{50}$  = 0.082 µg a.i./L 96-hr test). In addition, a 7-day toxicity study with the freshwater vascular plant, *Lemna gibba*, resulted in an  $EC_{50}$  value of 30 µg a.i./L.

Dodecylguanidine hydrochloride was determined to be slightly toxic to birds on an acute oral exposure basis (bobwhite quail  $LC_{50}$  of 1100 mg a.i./kg bw) and practically non-toxic to birds on a sub-acute dietary exposure basis (mallard duck 8-day  $LC_{50}$  > 5000 mg a.i./kg diet).

Updates to label statements are presented in Appendix VI. These updates include label statements to inform users of the toxicity to fish and aquatic invertebrates and restrictions on the discharge or release of effluents containing dodecylguanidine hydrochloride into aquatic systems. Based on the registered use pattern, the potential for environmental exposure to dodecylguanidine hydrochloride is considered to be low and the risk is considered to be acceptable.

### 4.2.1 Environmental incident reports

As of 24 March 2022, there have been no environment incidents involving dodecylguanidine hydrochloride reported to the PMRA.

### 4.3 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, in other words, those that meet all four criteria outlined in the policy: 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 *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, dodecylguanidine hydrochloride and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03<sup>3</sup> and evaluated against the Track 1 criteria.

In accordance with the PMRA Regulatory Directive DIR99-03, the assessment of dodecylguanidine hydrochloride against Track 1 criteria of Toxic Substances Management Policy (TSMP) under *Canadian Environmental Protection Act* was conducted. It determined that:

- Dodecylguanidine hydrochloride does not meet all Track 1 criteria, and is not considered a Track 1 substance (refer to Appendix V)
- Dodecylguanidine hydrochloride does not form any transformation products that meet all Track 1 criteria.

#### 4.3.1 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.<sup>4</sup> The list is used as described in the PMRA Notice of Intent NOI2005-01<sup>5</sup> and is based on existing policies and regulations, including the Toxic Substances Management Policy and Formulants Policy,<sup>6</sup> and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol).

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<sup>3</sup> DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

<sup>4</sup> SI/2005-114, last amended on June 25, 2008. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

<sup>5</sup> PMRA's 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*

<sup>6</sup> DIR2006-02, *Formulants Policy and Implementation Guidance Document*

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

## **5.0 Value assessment**

As a slimicide for paper mills, cooling towers and air washers, dodecylguanidine hydrochloride is an important biocide. The nature of biofilms and microbial slime is that they tend to be resistant to biocides. It is often necessary for operations using process fluids susceptible to biofilms to change the biocide regime from time to time in order to maintain effective control and prevent the build-up of biofilm resistance to any one biocide chemistry. As a powerful non-oxidizing biocide, dodecylguanidine hydrochloride is an important alternative for effective control of microbial slime.

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**List of abbreviations**

♂	males
♀	females
↑	increased
↓	decreased
µg	microgram
AD	administered dose
ADI	acceptable daily intake
AEATF	Antimicrobial Exposure Assessment Task Force
AHPD	amount handled per day
a.i.	active ingredient
ARfD	acute reference dose
bw	bodyweight
bwg	body weight gain
C	Celsius
DNA	Deoxyribonucleic acid
EC <sub>50</sub>	effective concentration on 50% of the population
EFSA	European Food Safety Authority
fc	food consumption
fe	food efficiency
F0	parental generation
F1	first filial generation
g	gram(s)
GD	gestation day
HC	historical control
hr(s)	hour(s)
HGPRT	Hypoxanthine-guanine phosphoribosyl transferase
kg	kilogram
K <sub>oc</sub>	organic-carbon partition coefficient
L	litre
LC <sub>50</sub>	median lethal concentration
LD <sub>50</sub>	median lethal dose
mg	milligram
mL	millilitre(s)
MOE	Margin of Exposure
NOAEL	No Observed Adverse Effect Level
PCPA	<i>Pest Control Products Act</i>
pH	measure of the acidity or basicity of an aqueous solution
PMRA	Pest Management Regulatory Agency
PND	post-natal day
PPE	personal protection equipment
ppm	parts per million
TSMP	Toxic Substances Management Policy

USEPA	United States Environmental Protection Agency
WBC	white blood cell
wk(s)	week(s)
wt	weight

## Appendix I Registered products containing dodecylguanidine hydrochloride in Canada<sup>1</sup>

**Table 1 Products containing dodecylguanidine hydrochloride subject to proposed label amendments**

Marketing class	Registrant	Registration number	Product name	Formulation type	Active ingredient (% , g/L)
Technical	Lanxess Corporation	23787	Dodecylguanidine Hydrochloride (Microbiocide-Technical)	Solution	35% (DUW)
Commercial	Solenis Canada ULC	23804	Spectrum RX4700 Microbiocide Agent	Solution	5% (DUW) 8% (QAC)
		24506	Spectrum RX3100 Microbiocide Agent	Solution	10.6% (DUW) 5% (MBC)
		32050	Biosperse CN8059 Microbiocide	Solution	5% (DUW) 8% (QAC)
		32109	Biosperse CN8109 Microbiocide	Solution	10.6% (DUW) 5% (MBC)
	Suez Water Technologies & Solutions Canada	23805	Spectrus NX1104	Solution	5% (DUW) 8% (QAC)
		24507	Spectrus NX1103	Solution	10.6% (DUW) 5% (MBC)

DUW = Dodecylguanidine Hydrochloride

QAC = N-Alkyl (40% C12, 50% C14, 10% C16) Dimethylbenzylammonium Chloride

MBC = Methylene Bis(Thiocyanate)

<sup>1</sup> as of 26 May 2022, excluding discontinued products or products with a submission for discontinuation

## Appendix II Registered uses of dodecylguanidine hydrochloride in Canada<sup>1</sup>

**Table 1 Registered commercial uses of dodecylguanidine hydrochloride in Canada**

Use-site Category	Active	Materials preserved	Application method and equipment
17-Industrial Process Fluids	Dodecylguanidine hydrochloride	<b>Air washers</b> (for use in industrial air washer systems that maintain effective mist eliminating components)	Directly incorporate in to the system when needed
		<b>Pulp and paper mill systems</b> (emulsions, adhesives, defoamers, alum, paper mill coatings and pigment slurries)	
		<b>Recirculating cooling water systems</b> (commercial and industrial cooling water towers, flow-through filters, lagoons, brewery pasteurizers, industrial water scrubbing systems, evaporative condensers, heat exchange water systems)	

Uses from discontinued products or products with a submission for discontinuation are excluded.

## Appendix III Toxicology information

**Table 1 Toxicology reference values for use in health risk assessment for dodecylguanidine hydrochloride**

Exposure scenario	Study	Point of departure and endpoint	MOE <sup>1</sup>
Long-term dermal <sup>2</sup>	52-week Oral Toxicity in Dogs (Dodine)	NOAEL = 1 mg/kg bw/day (corrected for 50% oral absorption) Marked body weight loss, clinical signs of toxicity, increased testes weight	100
Long-term inhalation <sup>3</sup>	52-week Oral Toxicity in Dogs (Dodine)	NOAEL = 2 mg/kg bw/day Marked weight loss, clinical signs of toxicity, increased testes weight	1000
Cancer	Equivocal increase in hepatocellular adenomas in female mice. Toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential.		

<sup>1</sup> MOE (margin of exposure) refers to a target margin of exposure for occupational assessments.

<sup>2</sup> Since an oral NOAEL was selected, a dermal absorption factor of 2% was used in route-to-route extrapolation.

<sup>3</sup> Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

**Table 2 Toxicity profile of dodecylguanidine hydrochloride (Supplemented with dodine toxicity studies)**

NOTE: Effects in both sexes are presented first followed by sex-specific effects in males, then in females, each separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to bodyweight) weight unless otherwise noted.

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
<b>Toxicokinetic studies</b>		
<b>Dodine</b>		
Sprague-Dawley Rats Single oral (gavage) dose of 40 or 400 mg/kg bw <sup>14</sup> C-labeled dodine Multiple oral (gavage) doses of 40 mg/kg bw/day non-labelled dodine for 14 days followed by single dose of 40 mg/kg bw <sup>14</sup> C-labeled dodine PMRA# 2793824		
<b>Absorption:</b> Rapid absorption at low single and repeat doses (based on total urinary/fecal excretion within 48 hrs being >90% AD respectively). Absorption at a high dose (based on total urinary/fecal excretion within 96 hrs being >90%) was slightly slower. Absorption rate was similar regardless of sex. Extent of absorption was estimated at 41–46% AD (based on urinary elimination data).		
<b>Distribution/Retention:</b>		

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
<p>The recovery from all tissues ranged from 0.62% to 3.34% AD at 120 hrs with highest amounts in fat, liver, gastrointestinal tract, bone, muscle and skin. Distribution was similar regardless of sex, dose level or dose regimen.</p> <p><b>Metabolism:</b>            Urinary metabolites consisted of hydroxydodecylguanidine (M2, 11–23% AD major metabolite), a mixture of acidic products of beta-oxidation (M4, 8–13% AD), an unidentified metabolite (M3, 7–11% AD) and urea (M5, 3–5% AD). Unchanged dodine was not detected in urine. Feces contained mostly unchanged dodine. Metabolism occurs via <math>\beta</math>-oxidation. Metabolism was similar regardless of sex, dose level or dose regimen.</p> <p><b>Elimination:</b>            At 120 hrs (5 days) post-exposure, 41 to 46% AD was excreted in the urine and 48 to 60 % was excreted in the feces in all dose groups. Total recovery at 120 hrs ranged from 94 to 102% AD. A preliminary study showed trace amounts of radioactivity expired as volatiles or carbon dioxide. Elimination was similar regardless of sex, dose level or dose regimen.</p>		
<b>Acute toxicity studies</b>		
<b>Dodecylguanidine hydrochloride (35% technical a.i.)</b>		
Acute Oral		<b>Slight acute toxicity</b>
Sprague Dawley Rat		LD <sub>50</sub> ♂ = 1450 mg/kg bw LD <sub>50</sub> ♀ = 1300 mg/kg bw LD <sub>50</sub> combined sexes = 1400 mg/kg bw
PMRA# 2725575		Clinical signs included oral discharge, dyspnea, wet rales, soft stools, fecal staining, ↓fc, abdominal gripping and hypoactivity
Acute Oral		<b>Slight acute toxicity</b>
Rat		LD <sub>50</sub> ♂ = 1600 mg/kg bw LD <sub>50</sub> ♀ = 1150 mg/kg bw LD <sub>50</sub> combined sexes = 1450 mg/kg bw
PMRA# 2934247		
Acute Dermal		<b>Low acute toxicity</b>
New Zealand White Rabbit		LD <sub>50</sub> >2000 mg/kg bw
PMRA# 2725576		Observations included bw loss, ↓fc, fecal staining, soft stools and severe dermal effects (necrosis, eschar and exfoliation)
Acute Inhalation (4-hr, whole body)		<b>Moderate acute toxicity</b>
Sprague Dawley Rat		LC <sub>50</sub> ♂ = 0.13 mg/L LC <sub>50</sub> ♀ = 0.17 mg/L LC <sub>50</sub> combined sexes = 0.14 mg/L
PMRA# 2725577		Clinical signs during exposure included facial wetness/encrustation and labored breathing. Decedents exhibited ataxia, prostration, reduced reflexes, unkempt appearance
Primary Skin Irritation		<b>Severely irritating</b>
New Zealand White Rabbit		Maximum Irritation Score: 6.5 (at 24 hrs) Maximum Average Score: 6.1
PMRA# 2725579		

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
Acute Oral  Sprague Dawley Rat  PMRA# 2725575	<b>Slight acute toxicity</b>  LD <sub>50</sub> ♂ = 1450 mg/kg bw LD <sub>50</sub> ♀ = 1300 mg/kg bw LD <sub>50</sub> combined sexes = 1400 mg/kg bw  Clinical signs included oral discharge, dyspnea, wet rales, soft stools, fecal staining, ↓fc, abdominal gripping and hypoactivity	
Acute Oral  Rat  PMRA# 2934247	<b>Slight acute toxicity</b>  LD <sub>50</sub> ♂ = 1600 mg/kg bw LD <sub>50</sub> ♀ = 1150 mg/kg bw LD <sub>50</sub> combined sexes = 1450 mg/kg bw	
Acute Dermal  New Zealand White Rabbit  PMRA# 2725576	<b>Low acute toxicity</b>  LD <sub>50</sub> >2000 mg/kg bw  Observations included bw loss, ↓fc, fecal staining, soft stools and severe dermal effects (necrosis, eschar and exfoliation)	
Acute Inhalation (4-hr, whole body)  Sprague Dawley Rat  PMRA# 2725577	<b>Moderate acute toxicity</b>  LC <sub>50</sub> ♂ = 0.13 mg/L LC <sub>50</sub> ♀ = 0.17 mg/L LC <sub>50</sub> combined sexes = 0.14 mg/L  Clinical signs during exposure included facial wetness/encrustation and labored breathing. Decedents exhibited ataxia, prostration, reduced reflexes, unkempt appearance	
Primary Skin Irritation  New Zealand White Rabbit  PMRA# 2725579	<b>Severely irritating</b>  Maximum Irritation Score: 6.5 (at 24 hrs) Maximum Average Score: 6.1	
Primary Eye Irritation  New Zealand White Rabbit  PMRA# 2725578	<b>Extremely corrosive</b>  Due to the severity of the response, all animals were sacrificed after the 24 hr observation and the effects were deemed irreversible.  Maximum Irritation Score: 55 (at 1 hr)	
Primary Eye Irritation  New Zealand White Rabbit  PMRA# 2725578	<b>Extremely corrosive</b>  Due to the severity of the response, all animals were sacrificed after the 24 hr observation and the effects were deemed irreversible.  Maximum Irritation Score: 55 (at 1 hr)	
Skin Sensitization (Buehler)  Hartley Guinea Pig  PMRA# 2725580	<b>Negative</b>	

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
Skin Sensitization (Buehler)  Hartley Guinea Pig  PMRA# 1237968	<b>Negative</b>	
<b>Dodine</b>		
Acute Oral  Rat  PMRA# 2934247	<b>Slight acute toxicity</b>  LD <sub>50</sub> ♂ =1931 mg/kg bw LD <sub>50</sub> ♀ =1171 mg/kg bw LD <sub>50</sub> combined sexes =1456 mg/kg bw	
Acute Dermal  Rabbit  PMRA #2934247	<b>Low acute toxicity</b>  LD50 >2000 mg/kg bw	
Acute Inhalation (1-hr) Rat  PMRA 2934247	<b>Slight acute toxicity</b>  LC <sub>50</sub> = 1.05 mg/L	
Primary Skin Irritation  Rabbit  PMRA #2934247	<b>Corrosive</b>  Primary Dermal Irritation Index, PDII - 7.5	
Primary Eye Irritation  Rabbit  PMRA #2934247	<b>Severely irritating</b>	
Skin Sensitization  Human  PMRA #2934247	<b>Negative</b>	
<b>Short-term toxicity studies</b>		
<b>Dodecylguanidine hydrochloride</b>		
21-Day Dermal Toxicity  Sprague Dawley Rat  PMRA #2793853	<b>Systemic NOAEL &gt; 18 mg/kg bw/day (a.i.)</b>  ≥ 4.4 mg/kg bw/day (a.i.): erythema (slight), desquamation (slight) (♂/♀) ≥ 8.8 mg/kg bw/day (a.i.): erythema (moderate), desquamation (marked), fissuring (slight) (♂/♀); ↑WBC (♀) 18 mg/kg bw/day (a.i.): bwg, ↓(non-adverse), edema (slight), necrosis, atonia (marked), eschar, exfoliation, fissuring (marked), skin lesions (inflammatory cell accumulation, hyperkeratosis, parakeratosis, squamous cell hyperplasia, ulcers/erosion, chronic inflammation) (♂/♀); ↑WBC (♂) (non-adverse); ↑ liver wt (♀) (non-adverse).  Note: histopathology conducted on controls and 17.5 mg/kg bw/day group only	

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
90-Day Oral Toxicity (Capsule)  Beagle Dog  PMRA# 1237974	<b>NOAEL = 8.8 mg/kg bw/day (a.i.)</b>  35 mg/kg bw/day (a.i.): ↓bw (♂ weeks 3–13; ♀ from wks 7–13), clinical signs (thin/emaciated, excessive salivation, emesis) (♂/♀)  Note: The study report indicated that because of concerns for one high-dose female’s survival, the standard laboratory ration was supplemented with commercial canned dog food for the final three wks of the study.	
<b>Dodine</b>		
28-Day Dermal Toxicity  Sprague Dawley Rat  PMRA# 2793823	<b>Systemic NOAEL = 125 mg/kg bw/day (♂); ≥ 200 mg/kg bw/day (♀)</b>  ≥ 50 mg/kg bw/day: erythema, edema, desquamation, blanching, eschar (♂/♀)  ≥ 125 mg/kg bw/day: exfoliation, encrustation, skin lesions (ulcer, exudate, parakeratosis, epidermal hyperplasia, hyperkeratosis subacute inflammation) (♂/♀)  200 mg/kg bw/day: ↓bw, ↓bwg (♂)	
90-Day Oral Toxicity (Dietary)  CD-1 Mouse  PMRA# 2934247	<b>NOAEL = 181/223 mg/kg bw/day</b>  ≥ 181/223 mg/kg bw/day: ↓ fc (♂/♀) (non-adverse)  350/305 mg/kg bw/day: ↓ bw, ↓ bwg (♂/♀); ↑mortality, ↑clinical signs (stiffening of the tail) (♀)	
52-week Oral Toxicity (Capsule)  Beagle Dog  PMRA# 2793860	<b>NOAEL = 2 mg/kg bw/day</b>  ≥ 10 mg/kg bw/day: salivation (♂/♀); ↑ testes wt (♂); marked weight loss in one animal in first few weeks requiring supplementary feeding until wk 15 (♀)  20 mg/kg bw/day: diarrhea, 1/sex with marked weight loss in first few weeks requiring supplementary feeding until wk 8 (♂) or 52 (♀); ↑ ovary wt (♀)	
<b>Chronic toxicity/Carcinogenicity studies</b>		
<b>Dodine</b>		
78-Week Oncogenicity (Dietary)  CD-1 Mouse  PMRA# 2793863	<b>NOAEL = 30 mg/kg bw/day (♂); not established (♀)</b>  ≥ 30 mg/kg bw/day: ↓bw (from wk 58 onward at low dose), ↓bwg (♀)  ≥ 113 mg/kg bw/day: ↓fc (♂/♀); ↓bw (significant from wk 9-62) (♂); ↓adrenal wt (♀)  225 mg/kg bw/day: ↓fe, ↑ liver wt (♂/♀); ↓bwg (♂); ↑kidney wt, equivocal ↑ hepatocellular adenomas (0%, 1.7%, 1.7%, 6.7% at respective dose levels of 0, 30, 113 and 225 mg/kg bw/day; HC mean of 0.8%; HC range of 0 to 3%) (♀)  <b>Equivocal evidence of tumourigenicity in ♀ (adenomas)</b>	

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
104-Week Chronic Toxicity/ Carcinogenicity (Dietary)  Sprague Dawley Rat  PMRA #2793825		<b>NOAEL = 20/13 mg/kg bw/day</b>  $\geq 26$ mg/kg bw/day: $\downarrow$ bw, $\uparrow$ dehydration ( $\text{♀}$ )  42/53 mg/kg bw/day: $\downarrow$ bw, clinical signs ( $\uparrow$ absent righting reflex, $\uparrow$ hunched posture, grasping absent, traction absent), $\downarrow$ WBC, $\downarrow$ lymphocytes ( $\text{♂}$ ); $\downarrow$ bwg, $\downarrow$ fc ( $\text{♀}$ )  No evidence of tumourigenicity
<b>Developmental/Reproductive toxicity studies</b>		
<b>Dodecylguanidine hydrochloride</b>		
Developmental Toxicity (Gavage)  Sprague Dawley Rat  PMRA# 1237980		<b>Maternal NOAEL = 16 mg/kg bw/day (a.i.)</b>  $\geq 32$ mg/kg bw/day (a.i.): $\uparrow$ salivation, $\downarrow$ bwg GD 6-9/GD 6-15, $\downarrow$ fc GD 6-11  63 mg/kg bw/day (a.i.): $\uparrow$ moist rales, $\downarrow$ fc GD 6-16.  <b>Developmental NOAEL <math>\geq 63</math> mg/kg bw/day (a.i.)</b>  No evidence of treatment-related malformations or sensitivity of the young.
<b>Dodine</b>		
Developmental Toxicity (Gavage) Sprague Dawley Rat  PMRA# 2793857		<b>Maternal NOAEL = 10 mg/kg bw/day</b>  $\geq 45$ mg/kg bw/day: $\downarrow$ bw (GD 9), $\downarrow$ bwg (GD 6-9), $\downarrow$ fc (GD 6-10/GD 6-16)  <b>Developmental NOAEL <math>\geq 90</math> mg/kg bw/day</b>  No evidence of treatment-related malformations or sensitivity of the young
Developmental Toxicity (Gavage)  New Zealand White Rabbit  PMRA# 2793856		<b>Maternal NOAEL = 40 mg/kg bw/day</b>  80 mg/kg bw/day: animals struggled during dosing, bw loss GD 6-9, $\downarrow$ fc  <b>Developmental NOAEL <math>\geq 80</math> mg/kg bw/day</b>  No evidence of treatment-related malformations or sensitivity of the young
2-Generation Reproductive Toxicity (Dietary)  Sprague Dawley Rat  PMRA# 2793859		<b>Parental:</b> <b>NOAEL = 28 mg/kg bw/day</b>  57 mg/kg bw/day: $\downarrow$ bw pre-mating ( $F_0/F_1$ ), $\downarrow$ bwg pre-mating ( $F_0/F_1$ ), $\downarrow$ bwg gestation ( $F_1$ ) $\downarrow$ fc ( $F_0/F_1$ )  <b>Reproductive:</b> <b>NOAEL = 57 mg/kg bw/day</b>  <b>Offspring:</b> <b>NOAEL = 17 mg/kg bw/day</b>  $\geq 28/33$ mg/kg bw/day: $\downarrow$ pup bw ( $F_1$ – PND 4, 7, 14, 21; $F_2$ – PND 14, 21)  Evidence of sensitivity of the young

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
<b>Genotoxicity studies</b>		
<b>Dodecylguanidine hydrochloride</b>		
In Vitro Bacterial Reverse Mutation Assay  S. typhimurium (TA 1535, TA 1537, TA 98, TA 100, E.coli WP2 uvrA)  PMRA 2725581		Negative with and without metabolic activation
In Vitro – Unscheduled DNA Synthesis  Rat Hepatocytes  PMRA 1237984		Negative
In Vivo Mouse Micronucleus Assay (Gavage)  ICR Mouse  PMRA 2725582		Negative
<b>Dodine</b>		
In Vitro Bacterial Reverse Mutation Assay  S. typhimurium (TA 1535, TA 1537, TA 1538, TA 98, TA 100)  PMRA 2793852		Negative with and without metabolic activation
In Vitro Mammalian Gene Mutation Assay  Chinese Hamster Ovary Cells (HGPRT locus)  PMRA# 2793855		Negative with and without metabolic activation
In Vitro Mammalian Chromosome Aberration Test  Human Lymphocytes  PMRA# 2793854		Negative with and without metabolic activation

Study/ Animal/PMRA#	Purity/Group Size/Exposure	Study results
In Vivo Mouse Micronucleus Assay (Gavage)  ICR Mouse  PMRA# 2793858	Negative	
In Vivo Mouse Micronucleus Assay (Gavage)  Swiss Albino Mouse PMRA# 1246591	Negative	

**Table 3 Identification of Select Metabolites**

<b>M2</b>	Hydroxydodecylguanidine
<b>M3</b>	Undefined
<b>M4</b>	10-Guanidinodecanoic acid 10-Guanidino-2-decenoic acid 10-Guanidino-3-oxodecanoic acid 8-Guanidino-2-octenoic acid 8-Guanidino-3-oxooctanoic acid 12-Aminododecanoic acid
<b>M5</b>	Urea

## Appendix IV Occupational exposure and risk assessment

**Table 1 Use rate summary of dodecylguanidine hydrochloride**

Sites	Registration number	Product density (kg/L)	Concentration of active ingredient (% w/w) (+ Co-formulated pesticide, % w/w)	AI rate range (ppm = mg/L)			
				Slug dose		Continuous	
				Initial	Subsequent	Initial	Subsequent
Pulp and Paper Mill Systems	23804	0.99	5.0 (+ alkyldimethyl ammonium chloride - 8.0)	0.6–12	0.6–9	0.6–6	0.6–9
	24506	1.1	10.6 (+ methylene bis(thiocyanate) - 5.0)	6–51	3.2–25	6–51	1.3–19
Recirculating Cooling Water Systems	23804	0.99	5.0 (+alkyldimethyl ammonium chloride - 8.0)	1.5–12	0.9–9	1.8–12	0.3–3
	23805	0.99					
	32050	0.99					
	24506	1.1	10.6 (+ methylene bis(thiocyanate) - 5.0)	2.5–13	1.3–9.5	2.5–13	1.3–9.5
	24507	1.1					
	32109	1.1					
Air Washers	24506	1.1	10.6 (+ methylene bis(thiocyanate) - 5.0)	2.5–13	1.3–9.5	2.5–13	1.3–9.5
	24507	1.1					
	32109	1.1					
Sites	Registration number		Concentration of active ingredient (% w/w)	AI rate (ppm)			
				Typical conditions (up to 2 weeks storage)	Extreme conditions (up to 2 weeks storage)	Greater than 2 weeks storage	
Materials used in the manufacture of paper (material preservative use)	23804	0.99	5.0 (+ alkyldimethyl ammonium chloride - 8.0)	21–32	26–85	106	
	24506	1.1	10.6 (+ methylene bis(thiocyanate) - 5.0)				

AI = active ingredient; ppm = parts per million.

**Table 2 Dodecylguanidine hydrochloride long-term occupational exposure and risk assessment**

Use	Product density (kg/L)	AHPD <sup>a</sup>	Amount active ingredient handled per day (kg a.i./day) <sup>b</sup>	Unit exposure value <sup>c</sup> (mg/kg a.i.)		Daily exposure <sup>d</sup>		Margin of exposure (MOE) <sup>e</sup>		Combined MOE' <sup>h</sup>
						(mg/kg bw/day)				
				Dermal	Inhalation	Dermal	Inhalation	Dermal <sup>f</sup>	Inhalation <sup>g</sup>	
Personal Protection Equipment: Single layer (long pants, a long-sleeved shirt, and shoes (plus socks) and chemical-resistant gloves)										
All uses (open pour) <sup>i</sup>	1.1 (products containing 10.6% dodecylguanidine hydrochloride)	38 L end- use product/day	4.4138	2.13538	0.00508	0.00236	0.00028	420	7100	380

MOE = margin of exposure; AHPD = amount handled per day

<sup>a</sup> For this assessment, the worker would handle 38 L end-use product/day, based on the USEPA Antimicrobial Division Draft Summary of Amounts Handled or Treated for Occupational Handler Scenarios.

<sup>b</sup> Amount active ingredient handled per day (kg a.i./day) = Amount of biocide product handled per day (38 L) × product density (kg/L) × maximum concentration of active ingredient in the treated fluid. The maximum concentration of active ingredient in the treated fluid (in other words, the maximum application rate as stated on product labels) was used in the risk assessment.

<sup>c</sup> Unit exposure values were obtained from an AEATF II liquid, open pour study.

<sup>d</sup> Dermal or inhalation daily exposure = (Amount active ingredient handled per day × Unit exposure value × Dermal or inhalation absorption value) / 80 kg bw. A dermal absorption value of 2% is applied for dermal exposure; an inhalation absorption value of 100% is applied for inhalation exposure.

<sup>e</sup> MOE = NOAEL/Dermal or Inhalation daily exposure. Combined MOE = NOAEL/(Dermal daily exposure + Inhalation daily exposure).

<sup>f</sup> Based on a NOAEL of 1 mg/kg bw/day from a 52-week dog oral toxicity study. Target MOE = 100.

<sup>g</sup> Based on a NOAEL of 2 mg/kg bw/day from a 52-week dog oral toxicity study. Target MOE = 1000.

<sup>h</sup> Combined long-term dermal and inhalation NOAEL of 1 mg/kg bw/day from a 52-week dog oral toxicity study. Target MOE = 100.

<sup>i</sup> All uses include all registered use of dodecylguanidine hydrochloride in industrial processes/fluids of pulp and paper mills, recirculating cooling water towers and air washers, as well as materials used in the manufacture of paper (material preservative use). This table represents the facilities that do not have closed mixing and loading systems in place.

## Appendix V Toxic Substances Management Policy Considerations - Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Dodecylguanidine hydrochloride Endpoints*
CEPA toxic or CEPA toxic equivalent <sup>1</sup>	Yes		Yes
Predominantly anthropogenic <sup>2</sup>	Yes		Yes
Persistence <sup>3</sup> :	Soil	Half-life ≥ 182 days	No: 17.5–22.3 days
	Water	Half-life ≥ 182 days	Yes: 38.9–227 days
	Sediment	Half-life ≥ 365 days	Yes: 2492 days (anaerobic sediment)
	Air	Half-life ≥ 2 days or evidence of long range transport	No information
Bioaccumulation <sup>4</sup>	Log $K_{ow} \geq 5$		No: approximately 1.0
	BCF ≥ 5000		Not available
	BAF ≥ 5000		Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet all TSMP Track 1 criteria.

\* End-points for persistence (soil and water) are based on data from both dodecylguanidine acetate (dodine) and dodecylguanidine hydrochloride as they behave the same under environmental conditions and the fate data can be used as a combined data set because these compounds share the same cationic form (dodecylguanidine). Similarly, the end-point for bioaccumulation is based on information for dodecylguanidine hydrobromide and dodecylguanidine acetate (dodine).

<sup>1</sup> All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).

<sup>2</sup> The policy considers a substance “predominantly anthropogenic” if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

<sup>3</sup> If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

<sup>4</sup> Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log  $K_{ow}$ ).

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## **Appendix VI Proposed label amendment for products containing dodecylguanidine hydrochloride**

Information on labels of currently registered products should not be removed unless it contradicts the following label statements.

### **1.0 Label amendments for dodecylguanidine hydrochloride technical products**

#### **HEALTH**

- i. On the primary display panel, include the following poison symbol: Skull and crossbones in a diamond.
- ii. In the PRECAUTIONS section on the secondary display panel, add the following statement:  
  
“May be fatal if inhaled. DO NOT inhale/breathe sprays, fumes or vapours.”
- iii. In the FIRST AID section, include the following text:  
  
“If Inhaled: Move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible.”

#### **ENVIRONMENTAL PRECAUTIONS**

- i. Replace the term: “ENVIRONMENTAL HAZARDS”  
  
with the term: “ENVIRONMENTAL PRECAUTIONS”.
- ii. Replace: “This pesticide is toxic to fish and other aquatic organisms.”  
  
With: “Toxic to aquatic organisms.”
- iii. Include: “DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.”

### **2.0 Label amendments for dodecylguanidine hydrochloride commercial end-use products (solutions)**

#### **GENERAL LABEL IMPROVEMENTS**

- i. Under PRECAUTIONS,  
  
When mixing, loading, and applying end-use product formulations, the following statement is proposed, unless more protective statements are already present:

“Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes when handling the concentrated product or treated process fluids and during clean-up and repair. Remove and wash contaminated clothing before re-use.”

- ii. Under the DIRECTIONS FOR USE, add:

“DO NOT handle more than 16.74 kg active ingredient per person per day when using liquid pour application. [16.74 kg active ingredient to be reported as a product equivalent value on product label]. If handling more than 16.74 kg active ingredient per person per day, a closed loading and transfer system is required.”

“A closed transfer system is defined as a procedure for removing a pesticide from its original container, rinsing the emptied container and transferring the pesticide and rinse solution through connecting hoses pipes, and coupling that are sufficiently tight to prevent exposure of any person to the pesticide or rinse solution. Furthermore, the closed transfer system must be equipped with a dry coupling system that is designed to drip less than 2 mL per coupling.”

## ENVIRONMENTAL PRECAUTIONS

- i. Replace the term: “ENVIRONMENTAL HAZARDS”  
with the term: “ENVIRONMENTAL PRECAUTIONS”.
- ii. Replace: “This pesticide is toxic to fish and other aquatic organisms.”  
With: “Toxic to aquatic organisms.”
- iii. Add the following statements to the section titled DIRECTIONS FOR USE:
- “This registration is granted under the *Pest Control Products Act* and does not exempt the user from any other legislative requirements.
- Use of this product and management of any resulting discharge or release of effluents containing this product must also be in accordance with the *Fisheries Act* and with any other applicable federal or provincial legislation.
- Consult with provincial regulatory authorities on any authorizations or other requirements for use of this product and management of any resulting discharge or release of effluents containing this product.”

## References

### A. Information considered in the updated chemistry assessment

List of studies/information submitted by registrant

PMRA document number	Title
2930719	2018, Batch Analysis of Dodecylguanidine Monohydrochloride (DGH) Formulation N-2001 Antimicrobial, Source 1, DACO: 2.13.2,2.13.3,2.13.4
2930720	2018, Batch Analysis of Dodecylguanidine Monohydrochloride (DGH) Formulation N-2001 Antimicrobial, Source 2, DACO: 2.13.2,2.13.3,2.13.4
2930721	2018, Method Validation for Product Ingredients of Dodecylguanidine Monohydrochloride (DGH) Technical Concentrates, DACO: 2.13.1,2.13.2,2.13.4
2930722	2016, Analytical Test Method - Determination of DGH, DACO: 2.13.1
2930723	2017, Dodecylguanidine Hydrochloride (PCP No. 23787) Production Process, DACO: 2.11.1,2.11.2,2.11.3
2944467	2018, Chemical Equivalency Notice for, DACO: 2.11.2
3001095	2019, Dodecylguanidine Hydrochloride - Discussion of Formation of Impurities, DACO: 2.11.4
3001096	1988, Five Month Stability Data for DGH, DACO: 2.14.14
3001097	2019, Clarification Response Submission Number 2018-5640 Re-evaluation 2015-1555, DACO: 2.14.14
3009629	2003, Determination Of The Partition Coefficient (N-Octanol / Water) of Dodecylguanidine-hydrochloride (DGH), DACO: 2.14.11
3009630	2012, CYTOX, 2014 Industrial Microbiocide: Vapour Pressure, DACO: 2.14.9
3009631	2012, Physical and Chemical Characteristics: Color, Physical State, Odor, pH, Boiling Point, Density/Relative Density, Partition Coefficient and Solubility, DACO: 2.14.1, 2.14.11, 2.14.15, 2.14.2, 2.14.3, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 830.7000
3009632	2019, Dodecylguanidine Hydrochloride (Microbiocide-Technical) PMRA Reg. No. 23787, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1
1145901	Laboratory Studies- Vapour Pressure (Dodecylguanidine Hydrochloride), DACO: 8.2.1
1145902	Final Report Hydrolysis of Dodecylguanidine HCl as a Function of pH at 25°C (38680), DACO: 8.2.1
1145903	Final report: determination of the photolysis of 14c-dodecylguanidine hydrochloride in pH 5 buffered solution at 25°C (38681), DACO: 8.2.1
1145904	Solubility in water (dodecylguanidine hydrochloride), DACO: 8.2.1
1145905	N-octanol/water partitioning coefficient (kow) (dodecylguanidine hydrochloride), DACO: 8.2.1
2998752	2012, Cytox 2014 Industrial Microbiocide Accelerated Storage Stability and Corrosion Characteristics, DACO: 2.14.14
1800329	Confirming address letter, response to comments for analytical methodology, analysis of water,, storage stability, batch analyses, DACO: 2.13,2.14.14,2.15,2.2
2994249	2015, N-2014 MU (EPA Reg. No. 39967-125) -Updated Description of Production Process, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1

## B. Information considered for the updated toxicological assessment

Studies/information submitted by registrant

PMRA document number	Title
1237968	CT-334-87 Dermal Sensitization Study in the Guinea Pig (51-522), DACO: 4.2.6
1237974	A Subchronic (3-Month) Oral Toxicity Study in the Dog with CT-334-87 Via Capsule Administration. Final Report (88-3311), DACO: 4.3.1
1237980	A Teratogenicity Study in Rats with CT-334-87. Final Report (88-3309), DACO: 4.5.2
1237984	Mutagenicity Test on CT-334-87 in the In Vitro Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay. Final Report (11071-0-447), DACO: 4.5.4
1246591	Examination of Dodine in the Micronucleus Test, DACO: 4.5.4
2725575	1988, Acute Oral Toxicity Study in Rats with CT-335-87, DACO: 4.2.1
2725576	1988, Acute Dermal Toxicity Study in Rabbits with CT-335-87, DACO: 4.2.2
2725577	1988, CT-335-87: Acute Aerosol Inhalation Toxicity Test in Rats, DACO: 4.2.3
2725578	1988, Eye Irritation Study in Rabbits with with CT-335-87, DACO: 4.2.4
2725579	1988, Primary Dermal Irritation Study in Rabbits with with CT-335-87, DACO: 4.2.5
2725580	1988, Closed-Patch Repeated Insult Dermal Sensitization Study in Guinea Pigs with CT-335-87, DACO: 4.2.6
2725581	1995, Salmonella/Escherichia coli Plate Incorporation Mutagenicity Assay, DACO: 4.5.4
2725582	1990, Mutagenicity Test on CT-334-87 in vivo Mouse Micronucleus Assay, DACO: 4.5.6
2793823	1999, A 28-Day Dermal Toxicity Study of Dodine Technical Material in Rats, DACO: 4.3.5
2793824	1992, Disposition and Metabolism of carbon 14 -labeled Dodine in Rats (Preliminary and Definitive Study): Final Report, DACO: 4.5.9
2793825	1998, Chronic Toxicity and Carcinogenicity Study of Dodecylguanidine Acetate (Dodine) in the Sprague-Dawley Rat by Dietary Administration, DACO: 4.4.4
2793852	1981, Evaluation of Dodine Tech. 95% for Mutagenic Activity in the Ames Test, DACO: 4.5.4
2793853	1989, A 21-Day Dermal Toxicity Study in Rats with CT-334-87, DACO: 4.3.5
2793854	1985, Chromosome Analysis of Cultured Human Lymphocytes Treated in vitro with Dodine, DACO: 4.5.5
2793855	1985, An Investigation into the Possible Induction of Point Mutation at the HGPRT Locus of Chinese Hamster Ovary Cells by Dodine, DACO: 4.5.6
2793856	1989, Dodine: Teratogenicity Study in Rabbits., DACO: 4.5.3
2793857	1989, Dodine: Teratogenicity Study in Rats, DACO: 4.5.2
2793858	1992, Mutagenicity Test on Dodecylguanidine Acetate Technical: in vivo Micronucleus Assay, DACO: 4.5.7
2793859	1996, Two-generation Reproduction Study with Dodine in Rats, DACO: 4.5.2
2793860	1996, 52-Week Toxicity Study in Dogs with Dodine: Final Report, DACO: 4.3.2
2793863	1998, 78-Week Dietary Oncogenicity Study with Dodine in mice: Final Report, DACO: 4.4.3

## Additional information considered

### Published information

PMRA document number	Title
2934247	United States Environmental Protection Agency, 2016, Dodine: Human Health Draft Risk Assessment and Scoping Document in Support of Registration Review, DACO: 12.5.4

## C. Information considered in the updated occupational and non-occupational assessment

Studies/information submitted by registrant

PMRA document number	Title
1237986	Dodecylguanidine hydrochloride – Exposure data waiver. Date not specified.
1422807	Dodecylguanidine hydrochloride – Exposure, Product Use Description. Submitted under Submission Number 1999-2214.
2758519	2017, Applicator Exposure - Product Use Information Dodecylguanidine Hydrochloride for Antimicrobial Uses.
2793826	1995, Dodine formulation: Absorption study in the male rat after topical application Bounds

Studies/information submitted by AEATF II task force

PMRA Document Number	Title
2296582	A Study for Measurement of Potential Dermal and Inhalation Exposure during Manual Pouring of a Liquid Containing an Antimicrobial. American Chemistry Council, Antimicrobial Exposure Assessment Task Force II, Washington, DC. (AEATF II) Project ID: AEA05.
2296584	A Study for Measurement of Potential Dermal and Inhalation Exposure during Manual Pouring of a Liquid Containing an Antimicrobial. Supplement Report, American Chemistry Council, Antimicrobial Exposure Assessment Task Force II, Washington, DC. (AEATF II) Project ID: AEA05.
3325049	American Chemistry Council Biocides Panel Presentation, October 2014; Understanding Pesticide Use Scenarios: Information on Pulp and Paper Industry, , AEATF presentation, 2014.

## Additional information considered

### Published information

PMRA document number	Title
3341912	EFSA, 2009. Additional Report to the Draft Assessment Report (DAR) - Public Version - Initial Risk Assessment Provided by the Rapporteur Member State Portugal for the Existing Active

	Substance Dodine. Volume 3, Annex B6, August 2009.
3341946	USEPA, 2009. Addendum to the 2005 Dodine Reregistration Eligibility Decision (RED): Antimicrobial Uses of Dodecylguanidine Hydrochloride (DGH).

### Unpublished information

PMRA document number	Title
3084493	Summary of Amounts Handled or Treated for Occupational Handler Scenarios, USEPA draft of 11/28/2018.

### D. Information considered in the updated environmental assessment

Studies/information submitted by registrant

PMRA document number	Title
1145897	Leaching (Dodecylguanidine Hydrochloride). DACO 8.2.4.1.
1145898	Final Report and Raw Data: Aerobic Aquatic Metabolism of Metasol DGH (Dodecylguanidine Hydrochloride). DACO 8.2.3.1.
1145908	(cont'd from roll#1075) Final Report and Raw Data: Aerobic Aquatic Metabolism of Metasol DGH (Dodecylguanidine Hydrochloride). DACO 8.2.3.1.
1145901	Laboratory Studies- Vapour Pressure (Dodecylguanidine Hydrochloride). DACO 8.2.1.
1145902	Final Report: Hydrolysis Of Dodecylguanidine HCl as a Function of pH at 25°C . DACO 8.2.1.
1145903	Final Report: Determination of the Photolysis of <sup>14</sup> C-Dodecylguanidine Hydrochloride in pH 5 Buffered Solution at 25°C DACO 8.2.1
1145904	Solubility in Water (Dodecylguanidine Hydrochloride). DACO 8.2.1.
1145905	n-Octanol/Water Partitioning Coefficient (K <sub>ow</sub> ) (Dodecylguanidine Hydrochloride). DACO 8.2.1.
1145906	Final Report: Soil/Sediment Adsorption-Desorption of DGH (CALTES 900026) Dodecylguanidine Hydrochloride). DACO 8.2.4.1.
1237990	Metabolism: Aquatic-Anaerobic & Aerobic. Testing of Dodecylguanidine Hydrochloride (DGH) for its Biodegradability (1721/1). DACO 8.2.3.1.
1237991	Material Safety Data Sheet-CYTOX 2014 Industrial Microbiocide (0357-02). DACO 8.4.1.
1237994	Acute Toxicity of CT-334-87 to <i>Daphnia Magna</i> . DACO 9.3.1.
1237995	Acute Toxicity of CT-334-87 to Bluegill Sunfish DACO 9.5.2.1.
1237996	Acute Toxicity of CT-334-87 to Rainbow Trout. DACO 9.5.2.1.

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**Additional information considered****Published information**

<b>PMRA document number</b>	<b>Title</b>
3020119	US EPA 2015. United States Environmental Protection Agency. November 18, 2015. Registration Review: Draft Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments for Dodine/DGH. Docket No. EPA-HQ-OPP-2015-0477-0003.