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Evaluation Report

# Ammonium Bromide

# Fuzzicide

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# Overview

## Registration Decision for Ammonium Bromide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of Fuzzicide (Ammonium Bromide) and the end-use product Fuzzicide Solution (35% solution of ammonium bromide), both containing the active ingredient ammonium bromide.

Current scientific data from the applicant and relevant scientific reports were evaluated to determine if, under the proposed conditions of use, ammonium bromide has value and does not present an unacceptable risk to human health or the environment.

This report summarizes the information evaluated and provides the results of the evaluation as well as the reasons for the conditional registration, with an outline of the additional scientific information required from the applicant. It also describes the conditions of registration that the applicant must meet to ensure that the health and environmental risks as well as the value of these pest control products are acceptable for their intended use.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of Fuzzicide (Ammonium Bromide) and the end-use product Fuzzicide Solution.

## What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks[1] to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable 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 conditions or 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.

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 (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects

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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".

observed and the uncertainties present 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 PMRA's website at www.pmra-arla.gc.ca.

## What Is Fuzzicide?

The technical product Fuzzicide consists of 99% ammonium bromide, while the end-use product Fuzzicide Solution is a 35% solution of ammonium bromide. The end-use product is used as a slimicide[3] in pulp and paper mill whitewater systems and starch slurries. Fuzzicide Solution is used with sodium hypochlorite to produce the active biocide[4] (Fuzzicide biocide).

## Health Considerations

### Can Approved Uses of Ammonium Bromide Affect Human Health?

**Ammonium bromide is unlikely to affect your health when used according to the label directions**.

When assessing health risks, the PMRA considers two key factors: 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 (e.g. children and nursing mothers). The risk assessment is conducted to ensure that the level of human exposure is well below the lowest dose at which effects occurred in animal tests. 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 at which no effects are observed. All of the toxicology studies routinely required to register a pesticide were not available for ammonium bromide. However, because exposure was determined to be negligible for the proposed use on pulp and paper, no further studies were requested. For any future use expansions, however, the PMRA will reconsider the need to address data gaps.

The technical grade active ingredient ammonium bromide caused mild eye irritation in animals and showed the potential to cause acute health effects in animals when it was inhaled. Consequently, the statements "Caution—Eye Irritant" and "Warning—Poison" are required on the label as well as the skull and crossbones symbol. Health effects in animals given daily doses of ammonium bromide over short periods (4 weeks to 3 months) included clinical signs of toxicity, decreased body- and organ-weights as well as effects on blood and urine. Although ammonium bromide was not tested to see if it

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[3] Chemical added to the pulp and paper process to inhibit the growth of undesirable microorganisms that cause slime.

[4] This active biocide prevents the presence of undesirable organisms.

causes cancer, it was not found to be genotoxic[5]. Ammonia on its own, however, has been found to cause some forms of genotoxicity. Some effects were noted on the nervous system, including clinical signs of toxicity, behavioural effects and some indications of effects on nervous tissue. When ammonium bromide was given to pregnant animals, effects on the developing fetus and on offspring were observed at doses that were not toxic to the mother, indicating that the fetus or young animal was more sensitive to ammonium bromide than the adult animal. Effects on reproduction were also seen, but at doses that were toxic to adult animals.

Studies conducted with sodium bromide were also provided to supplement the ammonium bromide toxicology database. When given to pregnant animals, sodium bromide caused effects on offspring at doses that were also toxic to the mother. Effects on reproduction were seen at doses that were toxic to adult animals. Other effects on adult animals included decreased thyroid-hormone levels, decreased body weights and organ weights as well as effects on blood at very high doses.

**Occupational Risks From Handling Ammonium Bromide**

**Occupational risks are not of concern when ammonium bromide is used according to the label directions, which include protective measures.**

Due to the requirement for closed loading and transfer of Fuzzicide Solution, workers mixing and loading the product are not expected to have direct contact with ammonium bromide. In addition, the label will specify that anyone mixing or loading Fuzzicide Solution must wear face protection, a long-sleeved shirt and long pants, chemical-resistant gloves and chemical-resistant footwear. Taking into consideration these label requirements, risk to workers handling Fuzzicide Solution is not of concern.

Postapplication exposure of workers to treated process water in pulp and paper mills is considered negligible when the recommended personal protective equipment is worn and is, therefore, not of concern.

**Risks in Non-Occupational Environments**

**Estimated risk for non-occupational exposure is not of concern when directions specified on the label are observed.**

Exposure to individuals contacting treated paper is not expected to result in unacceptable risk when Fuzzicide Solution is used according to the label directions.

For bystanders, exposure is expected to be much less than that of workers and is considered negligible.

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[5] Genotoxic chemicals are those capable of causing damage to DNA. Such damage can potentially lead to the formation of a malignant tumour, but DNA damage does not lead inevitably to the creation of cancerous cells.

## Environmental Considerations

### What Happens When Fuzzicide Biocide is Introduced Into the Environment?

**Fuzzicide biocide is toxic to freshwater alga and vascular plants and to both freshwater and marine invertebrates and fish; therefore, label instructions are required to protect these organisms and to minimize exposure to the aquatic environment.**

Fuzzicide Solution has to be reacted with a 12.5% aqueous solution of sodium hypochlorite to form the active biocide, Fuzzicide biocide or bromide-activated chloramine (BAC). Fuzzicide biocide has the potential to enter into the environment when used as a slimicide in pulp and paper mills. This active biocide is not persistent in the aquatic system and is rapidly degraded to substances such as ammonia/ammonium, nitrate, chloride, bromide, bromoform and chloroform which are already found in natural and effluent waters. With the exception of ammonium, the transformation products of BAC are not expected to adsorb to sediment. Under actual use conditions in an operational pulp and paper mill, Fuzzicide biocide concentrations were below the detection limit (0.05 mg $Cl_2$/L) at the point of discharge into the watercourse. Soil is not expected to be exposed to Fuzzicide residues; therefore, these residues are not expected to be found in the terrestrial environment.

Based on the specific use pattern for Fuzzicide Solution in pulp and paper mills, Fuzzicide biocide presents a negligible risk to aquatic organisms. Specific statements regarding its toxicity to aquatic organisms and statements to minimize exposure to the aquatic environment are provided on the product label.

## Value Considerations

### What Is the Value of Fuzzicide Solution?

Fuzzicide Solution is a slimicide for use in pulp and paper mill whitewater systems and starch slurries. Fuzzicide Solution is used with sodium hypochlorite (12.5%) via the Fuzzicide feeder/delivery system to produce Fuzzicide biocide. This product is a new alternative slimicide that can be used to prevent the fouling of whitewater systems and starch slurries caused by bacterial, fungal and algal contamination that have been known to result in loss of productivity in pulp and paper mills.

## 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 PMRA is requiring key risk-reduction measures on the label of Fuzzicide Solution.

**Human Health**

- To avoid direct contact with ammonium bromide on the skin, only closed loading and transfer is permitted for Fuzzicide Solution. In addition, anyone handling Fuzzicide Solution or contacting treated process fluids must wear face protection, a long-sleeved shirt and long pants, chemical-resistant gloves and chemical-resistant footwear.

**Environment**

- Fuzzicide biocide is toxic to freshwater alga, vascular plants, freshwater and marine invertebrates as well as to fish; therefore, specific statements to minimize exposure to the aquatic environment are provided on the product label.

## What Additional Scientific Information Is Required?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information within the time frames indicated.

- **Environment**

  A hydrolysis study conducted with the Fuzzicide biocide, the bromide-activated chloramine, in sterile water at 3 different pHs (e.g. pH 4.0, pH 7.0 and pH 9.0) is required. This study is to be submitted to the PMRA by 1 September 2009.

## Other Information

As these conditional registrations relate to a decision on which the public must be consulted[6], the PMRA will publish a consultation document when there is a proposed decision on the applications to convert the conditional registrations to full registrations or on the applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

[6] As per subsection 28(1) of the *Pest Control Products Act*.

# Science Evaluation

**Fuzzicide (Ammonium Bromide)**

## 1.0 The Technical Grade Active Ingredient, its Properties and Uses

### 1.1 Identity of the Technical Grade Active Ingredient

| | |
|---|---|
| **Active substance** | ammonium bromide |
| **Function** | antimicrobial |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | ammonium bromide |
| **2. Chemical Abstracts Service (CAS)** | ammonium bromide |
| **CAS number** | 12124-97-9 |
| **Molecular formula** | $BrH_4N$ |
| **Molecular weight** | 97.94 |
| **Structural formula** | $NH_4^+ Br^-$ |
| **Purity of the active ingredient** | 99% nominal |

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

**Technical Product—Fuzzicide (Ammonium Bromide) Technical**

| Property | Result |
|---|---|
| Colour and physical state | White powder |
| Odour | Odourless |
| Melting point | >370°C |
| Boiling point | N/A |
| Density | 2.4550 g/mL |
| Vapour pressure at 25°C | $1.3 \times 10^{-4}$ Pa |

| Property | Result | |
|---|---|---|
| Henry's law constant at 20°C | $1.3 \times 10^{-10}$ atm·m$^3$/mol | |
| Ultraviolet (UV)—visible spectrum | Not expected to absorb at $\lambda > 300$ nm | |
| Solubility in water at 25°C | 97 g/100 mL | |
| Solubility in organic solvents | **Solvent**<br>alcohol<br>acetone<br>ether<br>ammonia | **Solubility**<br>10 g/100 cm$^3$ at 78°C<br>soluble<br>soluble<br>soluble |
| *n*-Octanol–water partition coefficient ($K_{ow}$) | N/A | |
| Dissociation constant (p$K_a$) | N/A | |
| Stability (temperature, metal) | Stable to sunlight and elevated temperature; stable to metals when pure substances are used, but may corrode metals after exposure to moisture | |

**End-Use Product—Fuzzicide Solution (35% Ammonium Bromide)**

| Property | Result |
|---|---|
| Colour | Colourless |
| Odour | Weak ammonia |
| Physical state | Liquid |
| Formulation type | Solution |
| Guarantee | 35% nominal |
| Container material and description | HDPE intermediate bulk containers (1000 L) and drums (210 L) |
| Specific gravity at 20°C | 1.22–1.24 |
| pH | 6.5–6.8 |
| Oxidizing or reducing action | No significant oxidizing or reducing action |
| Storage stability | Stable over 24 months at ambient conditions |
| Explodability | Not known to be explosive |

### 1.3 Directions for Use

Fuzzicide Solution is used in conjunction with sodium hypochlorite (12.5%) in the Fuzzicide feeder/delivery system to produce the active biocide. Mixing is carried out at a ratio of 2.2 litres of sodium hypochlorite (12.5%) with 1.0 L of Fuzzicide Solution in the feeder, to control algal, bacterial and fungal slimes in pulp and paper mill whitewater systems and starch slurries. The relevant parameters for treatment (Table 1.3.1) are supported by data.

**Table 1.3.1 Microbial Slime Control Claims for Fuzzicide Solution in Pulp and Paper Mills**

| Site | Residual biocide to be maintained, expressed as total chlorine |
|---|---|
| Whitewater Systems | 0.5–5.0 ppm |
| Starch Slurries | up to 10.0 ppm |

### 1.4 Mode of Action

The Fuzzicide biocide resulting from the reaction between chlorine and ammonium bromide, affects protein-associated processes in bacteria by reacting with multiple targets including amino acids, particularly tryptophan and those with sulfur groups. In addition the biocide inhibits nucleic acid (DNA and RNA) and protein synthesis and inhibits bacterial growth.

Furthermore, the Fuzzicide biocide is an oxidizing biocide that is less reactive than chlorine (hypochlorous acid). Therefore, it is not consumed as rapidly by organic compounds in the pulp and paper process and is available to react with strong reducing groups present on the cell membrane or within the cytoplasm of microorganisms.

## 2.0 Methods of Analysis

### 2.1 Methods for Analysis of the Technical Grade of Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Fuzzicide (ammonium bromide) have been assessed to be acceptable.

### 2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in Fuzzicide Solution has been assessed to be acceptable for use as an enforcement analytical method.

### 2.3 Methods for Residue Analysis

Spectrophotometric, colourimetric, potentiometric titration and ion chromatographic methods were provided for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision for use in environmental media.

# 3.0 Impact on Human and Animal Health

## 3.1 Toxicology Summary

The PMRA has conducted a detailed review of the toxicological database for ammonium bromide. The toxicology database was reduced in comparison to the current toxicology data requirements and consisted of acute toxicity studies, 4-week and 90-day dietary studies in rats, developmental and range-finding reproductive toxicity studies in rats and genotoxicity studies conducted with ammonium bromide. The 90-day dietary study included assessments of neurotoxic potential. Literature references were provided to address the toxicokinetics of ammonia and bromide. Studies conducted with sodium bromide were also submitted to supplement the ammonium bromide database, including a published article on reproductive effects and an in vitro chromosomal aberration assay. Although the toxicology database was reduced, further hazard characterization of ammonium bromide was not undertaken since exposure was determined to be negligible for the proposed use pattern in pulp and paper mills. For any future use expansions, the need to address several areas in the toxicology database including neurotoxicity, chronic/carcinogenicity, developmental toxicity in a second species, as well as reproductive toxicity will be reconsidered.

Ammonium bromide is of low acute toxicity by the oral and dermal routes and is considered to be moderately toxic via the inhalation route in rats. Ammonium bromide was mildly irritating to the rabbit eye, non-irritating to rabbit skin and is not considered to be a dermal sensitizer based on results from a Guinea Pig Maximization test.

Fuzzicide Solution is of low acute toxicity via the oral, dermal and inhalation routes in rats. It was non-irritating when applied to the skin of rabbits and minimally irritating to the rabbit eye. Fuzzicide Solution is not considered to be a dermal sensitizer (on the basis of the Guinea Pig Maximization test conducted with ammonium bromide technical).

According to the submitted literature, ammonium is readily absorbed following oral ingestion and is widely distributed once in systemic circulation. Ammonium is mainly metabolized in the liver, where it is primarily converted to urea and glutamine; however, conversion to glutamine can also occur in the brain and other tissues. Excretion of ammonia, which is relatively slow (60–72% excreted within 3 days of dosing), occurs primarily as urinary urea, with minimal excretion via the feces, expired air and sweat.

Bromide is rapidly and completely absorbed following oral ingestion and is distributed almost exclusively to the extracellular fluid, with some accumulation also occurring in red blood cells, cerebrospinal fluid, thyroid gland, blood vessel walls, cartilage, tendons, dentine, kidneys, urinary bladder, stomach and the eye. Elimination of bromide is slow (half-lives of approximately 12 days in humans and 3 days in rats), with excretion occurring primarily in the urine and, to a lesser extent, in the feces. Absorption, distribution and elimination of bromide appear to be linear processes, with saturation of reabsorption only occurring at extremely high

dose levels. Information in the submitted literature indicates that cross-placental transfer of bromide occurs with accumulation occurring in fetal cartilage and kidneys and that fetal elimination of bromide may be slower in comparison to elimination from the plasma and brain of maternal animals.

In subchronic toxicity studies conducted with ammonium bromide, clinical signs of toxicity (including rolling gait, hunched posture, piloerection, subdued behaviour, partially closed eyes, limpness, long claws and splayed hind limbs), decreased body weight and body weight gain and decreased organ weights were observed in both 4-week and 90-day studies. Organ weight changes were recorded in several tissues, including the epididymis, heart, prostate, salivary glands, adrenal, lung, testes, kidneys, thyroid, pituitary, liver, spleen, thymus and uterus. Gross necropsy and histopathological findings were noted in the 90-day study at the high dose (500 and 750 mg/kg bw/day in males and females, respectively); affected tissues included the lung (both sexes) as well as isolated findings in the adrenal, testes, epididymis and prostate in males and in the harderian gland in females. Blood effects (increased white blood cell parameters), alterations in clinical chemistry (decreased cholesterol and bilirubin and increased phosphate levels) and decreased urine pH were also observed in the 90-day study. A 4-week recovery period was included in the 90-day study. Following the recovery period, treatment-related effects included clinical signs of toxicity, decreased body weight and effects on haematological and clinical chemistry parameters, as well as on organ weights.

No chronic toxicity and/or carcinogenicity studies were provided for ammonium bromide.

Three genotoxicity studies were conducted with ammonium bromide, including an Ames bacterial mutation test, a mammalian gene mutation assay (conducted with mouse lymphoma cells) and an in vivo micronucleus assay. Under the conditions of the in vitro Ames and mouse lymphoma assays, there was no indication of mutagenic potential. In the in vivo mouse micronucleus assay, ammonium bromide was not observed to induce micronuclei. An in vitro chromosome aberration study conducted with sodium bromide was submitted in fulfilment of the clastogenicity data requirement. Sodium bromide was not found to induce chromosomal aberrations in human lymphocytes. However, the study was considered to be supplemental due to the test substance used and due to a lack of detail regarding the methods used in the study. No studies were provided to address the clastogenic potential of ammonia. However, information from the literature indicates that ammonia may have the potential to induce chromosomal aberrations, based on a study with workers exposed occupationally to ammonia and the results from an in vitro study conducted with chick fibroblasts.

There was evidence of increased susceptibility of the young in the rat teratology study; a second study in a non-rodent species was not provided. Maternal toxicity was evident at the highest dose tested (1000 mg/kg bw/day) and included clinical signs of toxicity and decreased body weight gain, effects that are consistent with the general toxicity observed in the subchronic studies. At this dose, one dam was also sacrificed due to severe clinical signs. Developmental toxicity was observed at all doses tested (100–1000 mg/kg bw/day). Undescended/displaced testes and skeletal variations were observed at all doses. At the high dose, decreased body weight and an increased incidence of malformations (of the kidney, spleen, uterus, ovary and thyroid) and visceral variations, as well as additional skeletal variations were noted. As fetal effects

(undescended/displaced testes and skeletal variations) were observed in the absence of signs of maternal toxicity, it suggests that young animals may be more susceptible to the effects of ammonium bromide than adult animals.

Evidence of increased susceptibility of the young was also observed in a range-finding (one-generation) reproductive toxicity study conducted with ammonium bromide; a multi-generation study was not provided. Parental toxicity, observed at the mid and high doses (3200 and 6400 ppm), included clinical signs of toxicity (similar to those observed in the other studies) and decreased body weight gain and food consumption. In offspring, increased incidence of pup mortality and decreased litter and pup weights were observed, beginning at the lowest dose tested (1600 ppm). An increased incidence of total litter loss and decreased fertility were observed (at $\geq$3200 ppm), which are indicative of reproductive toxicity. As this was a range-finding study, it was considered to be supplemental. In addition, it should be noted that this study consisted of only one generation, the pre-mating dosing period and group sizes were insufficient and microscopic examinations were not performed.

A journal article summarizing a special 3-generation reproductive toxicity study conducted with sodium bromide, in which thyroid hormones were also measured in $F_0$ adult animals, was submitted by the applicant. This information was considered to be supplemental to the ammonium bromide toxicity database due to the test substance used and a general lack of information regarding the details of the study methods. However, based on the available information, exposure to sodium bromide was noted to cause a reduction in fertility and offspring viability at higher dose levels ($\geq$4800 ppm) and also caused decreases in thyroid hormone (thyroxine) levels at lower levels ($\geq$75 ppm). The study results suggested that the effects on fertility may be mediated by males and/or females and also provided evidence that bromide crosses the placental barrier. Other effects noted in this study included decreased body weight, adrenal and uterine weights and altered white blood cell parameters in adult animals.

Potential neurotoxicity was assessed in the 90-day dietary study. Findings indicative of neurotoxicity included decreased grip strength, delayed tail flick response and increased landing foot splay. Many of the clinical signs of toxicity noted in this study were also indicative of potential neurotoxicity, including the gait and posture abnormalities, piloerection and subdued behaviour. In addition, there was a slight increase in the number of animals with histopathological nerve findings at $\geq$225 mg/kg bw/day. Some of the findings (decreased grip strength, increased landing foot splay and posture/gait abnormalities) were observed at all doses tested (100 to 750 mg/kg bw/day), indicating that neurotoxic effects occurred at the lowest dose tested. However, NOAELs and LOAELs were not established for neurotoxicity in this study, as the study was considered to be supplemental due to limitations identified with the motor activity and neuropathology data.

Breakdown products resulting from the use of ammonium bromide and determined to appear in treated paper, include chloride, bromide, ammonia and nitrate. Information was provided to address potential health concerns for these breakdown products in relation to handling treated paper. Ammonium bromide was not found to be a dermal sensitizer in the submitted sensitization study, which alleviates sensitization concerns for ammonia and bromide residues in treated paper. Chloride is used in many pulp and paper mill products, as well as in the treatment

of drinking water and swimming pool water and is not known to be associated with any dermal sensitization potential. Although no information was provided regarding the sensitization potential of nitrate, the amount of nitrate in treated paper is reportedly less than the Canadian drinking water limit for nitrate (45 mg/L; Health Canada, 2007) and is therefore not expected to be of toxicological concern with the proposed use.

A summary of the results are provided in Appendix I, Tables 1, 2 and 3.

## 3.2 Determination of Acceptable Daily Intake

An acceptable daily intake is not required since the proposed uses of Fuzzicide Solution do not involve direct food uses.

## 3.3 Determination of Acute Reference Dose

An acute reference dose is not required since the proposed uses of Fuzzicide Solution do not involve direct food uses.

## 3.4 Occupational and Bystander Risk Assessment

### 3.4.1 Toxicological Endpoints

Occupational exposure to ammonium bromide is characterized as intermittent long-term in duration and is predominately by the dermal route. Toxicological endpoints were not required because occupational exposure (handler and postapplication) was determined to be negligible.

### 3.4.2 Occupational Exposure and Risk

#### 3.4.2.1 Handler Exposure and Risk

There is potential for exposure to workers mixing/loading and applying the Fuzzicide Solution. To mitigate exposure to handlers mixing, loading and applying Fuzzicide Solution, a statement limiting the use of Fuzzicide Solution to closed loading and transfer systems (i.e. dry coupling) is required to appear on the principal display panel of the Fuzzicide Solution label and the applicant is required to design their delivery system to satisfy the criteria of this definition. This requirement is expected to result in negligible exposure to occupational handlers.

#### 3.4.2.2 Postapplication Exposure and Risk

Based on the information provided by the applicant to characterize postapplication exposure to workers exposed to treated process water in the pulp and paper mill, exposure to these workers is expected to be negligible when wearing face protection, long-sleeved shirt and long pants, chemical-resistant gloves and chemical-resistant footwear.

### 3.4.3 Residential Exposure and Risk

#### 3.4.3.1 Handler Exposure and Risk

As there are no domestic class products, a residential handler assessment was not required.

#### 3.4.3.2 Postapplication Exposure and Risk

There is potential for consumer exposure to Fuzzicide Solution and its breakdown products from contacting treated paper and paper products. Ammonia, bromide, chloride and nitrate have been identified as quantifiable in paper and paperboard treated with Fuzzicide Solution. However, there are several products currently registered for use in pulp and paper mills that are expected to have similar by-products in treated paper. Based on the low quantities of breakdown products measured in treated paper and the lack of sensitization triggers for the breakdown products identified, exposure to treated paper and paperboard products is not of concern.

### 3.4.4 Bystander Exposure and Risk Assessment

For bystanders, exposure is expected to be much less than that of workers and is considered negligible.

## 4.0 Impact on the Environment

### 4.1 Fate and Behaviour in the Environment

The active Fuzzicide biocide, the bromide-activated chloramine (BAC), is generated *in situ* by reacting Fuzzicide Solution, a 35% aqueous solution of ammonium bromide, with a 12.5% aqueous solution of commercially available sodium hypochlorite. BAC is, therefore, the compound that is of concern to the environment.

BAC is not persistent in the aquatic system. The half-lives of BAC were almost the same in 0.5 and 5.0 mg $Cl_2$/L solutions: 50.6 and 45.6 hours, respectively, at 25°C and 26.6 and 22.6 hours, respectively, at 35°C. BAC degradation products were ammonia/ammonium, nitrate, chloride, bromide, bromoform and chloroform. With the exception of ammonium, the transformation products of BAC are not expected to adsorb to sediment. Phototransformation and volatilization in water is not expected to be important routes of transformation of BAC. The presence of secondary treatment facilities minimizing effluent load from pulp and paper mills is expected to result in minimal BAC entering the environment. BAC did not adversely affect aerobic microbial activity in the treatment facilities of pulp and paper mills. Thus, these aerobic microbes will be very efficient in reducing residual BAC levels in pulp and paper mill effluents and BAC is, therefore, not expected to be found in the effluent of pulp and paper mills when Fuzzicide Solution is used at the label recommended rate.

BAC is not expected to enter the soil during its use as a slimicide in pulp and paper mills. BAC residues are, therefore, not expected to be found in the terrestrial environment.

BAC is expected to be slightly volatile due to the presence of ammonium salts, but as BAC is readily dissociable in aqueous environments and is not persistent, BAC residues are not expected in the atmosphere. Long-range transportation of BAC will not be a concern under relevant environmental conditions.

Data on the fate and behaviour of Fuzzicide Solution and BAC in the environment are summarized in Appendix I, Table 5.

## 4.2 Effects on Non-Target Species

To estimate risk of potential adverse effects on non-target species, a quotient method is used. The risk quotient (RQ) is calculated by dividing the exposure estimate by a value representing the most sensitive toxic endpoint. A screening-level risk assessment is initially performed using the expected environmental concentrations (EECs) for a worst-case scenario (e.g. direct overspray of a body of water) and the most sensitive toxicity endpoint. Low risk is predicted if the risk quotient is less than the trigger value of one. In these cases, no further assessment is done. For those groups of organisms for which the RQ is greater than one, a refined assessment is undertaken. A refined assessment takes into consideration more realistic exposure scenarios (e.g. drift to non-target habitats and runoff to water bodies) and may consider different toxicity endpoints.

### 4.2.1 Effects on Terrestrial Organisms

Fuzzicide (Ammonium Bromide) caused mortality to one bird at a concentration of 2000 mg a.i./kg when administered orally in a gelatine capsule. Clinical signs were limited to the observation of white vomit from two birds. No other clinical or sublethal effects were observed in orally treated birds. Dietary short-term exposure of birds to Fuzzicide (Ammonium Bromide) did not result in any mortality or toxicity and no treatment-related effects were observed for body weight or feed consumption in all surviving birds. Based on the use pattern, the exposure of terrestrial organisms to Fuzzicide (Ammonium Bromide) or BAC is not expected to occur. The risk assessment towards these organisms was, thus, not conducted (Appendix I, Table 6).

### 4.2.2 Effects on Aquatic Organisms

Risk of BAC to aquatic organisms was based upon the evaluation of toxicity data for five freshwater species (one invertebrate, two fish, one alga and one vascular plant) and three estuarine/marine species (two invertebrate and one fish) (Appendix I, Table 6).

In dose response studies, BAC caused sublethal effects at various concentrations on daphnids, mysid shrimp, all fish species and eastern oyster (NOEC values between 0.0026 mg $Cl_2$/L to 0.33 mg $Cl_2$/L). BAC was toxic to vascular plants at concentrations greater than 0.16 mg $Cl_2$/L. On an acute basis, BAC negatively affected biomass of the freshwater green alga at concentrations greater than 0.0075 mg $Cl_2$/L.

It is anticipated, however, that BAC will pose a negligible risk to aquatic organisms as the use of BAC in pulp and paper mills is not expected to result in any measurable BAC residues discharged into the aquatic environment. Label statements indicating the toxicity of this pesticide to aquatic organisms and statements to minimize exposure to the aquatic environment have been added to the product label.

# 5.0 Value

## 5.1 Effectiveness Against Pests

Data from one laboratory trial and three paper mill operational trials were submitted. Each of these studies was found to have appropriate experimental design.

Data in support of pulp and paper mill Whitewater Systems:

- The laboratory trial, a biofilm test, was conducted as a simulation of paper machine process water. Fuzzicide Solution was able to prevent the formation of slime on the stainless steel coupons at residual biocide concentrations of 2.5 and 5 ppm expressed as total chlorine. (Table 1.3.1)

- The first operational trial involved the comparison of the efficacy of Fuzzicide Solution to a HOBr-based biocidal program used within two paper machines. Fuzzicide Solution was effective in reducing planktonic bacteria within the process waters of the paper machines at residual biocide concentrations ranging between 0.5–5 ppm expressed as total chlorine.

- In a second operational trial, the time lost due to slime formation in the paper mill was recorded for a number of different biocide treatment programs over a period of nearly two years. The Fuzzicide Solution regime resulted in less slime-related downtime compared to other biocides used at the mill.

Data in support of Starch Slurries:

- The operational trial examined the use of Fuzzicide Solution in starch preservation by sampling starch from the size press circulation tanks over a period of 14 months. Fuzzicide Solution was successful in maintaining or lowering viable counts when total chlorine residuals were maintained between 1–10 ppm in the starch slurries, over the 14 month test period.

### 5.1.1 Acceptable Efficacy Claims

The submitted data demonstrated that Fuzzicide Solution, when used in conjunction with 12.5% sodium hypochlorite via the Fuzzicide feeder/delivery system, effectively prevented fouling caused by algae, bacteria and fungi when used at rates ranging from 0.5 to 5.0 ppm residual biocide (expressed as total chlorine) in whitewater systems and up to 10.0 ppm residual biocide (expressed as total chlorine) in starch slurries.

### 5.2 Sustainability

#### 5.2.1 Survey of Alternatives

Fuzzicide Solution is an alternative slimicide for the prevention of fouling caused by bacterial, fungal and algal slimes which results in the formation of biofilms. These biofilms are formed by diverse microorganisms under a wide range of conditions. Furthermore, some biocides may be chemically incompatible with certain industrial processes or other chemicals. For this reason, it is important to have a variety of biocides available. There are numerous slimicide products currently registered in Canada for use in pulp and paper mills. These are generally broad-spectrum biocides based on a number of different active ingredients with modes of action ranging from oxidizing compounds to membrane-disrupting surfactants.

The options available for microbial slime control for use in pulp and paper mills are summarized in Table 7 of Appendix I.

#### 5.2.2 Compatibility with Current Management Practices Including Integrated Pest Management

Fuzzicide Solution is not expected to have an impact on current microbial control practices.

#### 5.2.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

The bromide-activated chloramine, formed during the reaction between the chlorine (sodium hypochlorite) and the ammonium bromide in the Fuzzicide Solution, is a broad-spectrum biocide that affects protein-associated processes. Long-term resistance is not expected to develop due to the mode of action and to the industry's current practice of regularly alternating slimicide products.

## 6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track-1 substances.

During the review process, Fuzzicide (Ammonium Bromide) was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of Fuzzicide (Ammonium Bromide) were also considered, including major transformation

products formed in the environment, microcontaminants in the technical product and formulants in the end-use product Fuzzicide Solution. The PMRA has reached the following conclusions:

- Ammonium bromide is an inorganic salt and does not meet the criteria for persistence, bioaccumulation and toxicity. Fuzzicide biocide, bromide-activated chloramine (BAC), does not meet the criteria for persistence. Its value for half-life in water (50 hours) is below the TSMP Track-1 cut-off criteria for water ($\geq$182 days). BAC is an inorganic compound and is not expected to be bioaccumulative. It is readily dissociable, is highly soluble in water and of low solubility in organic solvents, therefore, its octanol–water partition coefficient (log $K_{ow}$) will be below the TSMP Track-1 cut-off criterion of $\geq$5.0. Fuzzicide biocide meets the criteria for toxicity. Fuzzicide biocide does not form any major transformation products that meet the TSMP Track-1 criteria. As BAC does not meet all Track-1 criteria, it is not classified as a Track-1 substance.

- Fuzzicide (Ammonium Bromide) does not contain any by-products or microcontaminants that meet the TSMP Track-1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

- Fuzzicide (Ammonium Bromide) does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

- The end-use product Fuzzicide Solution does not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

Therefore, the use of Fuzzicide Solution is not expected to result in the entry of Track-1 substances into the environment.

# 7.0 Summary

## 7.1 Human Health and Safety

The toxicology database was reduced in comparison to current standard toxicology data requirements. Further hazard characterization of ammonium bromide was not undertaken, however, since exposure was determined to be negligible for the proposed scenario on pulp and paper. For any further use expansions, the need to address deficiencies in several areas including neurotoxicity, chronic/carcinogenicity, developmental toxicity in a second species, as well as reproductive toxicity will be reconsidered.

Mixer, loader, applicators and workers exposed to treated process water are not expected to be exposed to levels of ammonium bromide that will result in unacceptable risk when Fuzzicide Solution is used according to label directions. The label specifies the personal protective equipment required to protect workers mixing and loading Fuzzicide Solution and handling treated process water.

Exposure to individuals contacting treated paper is not expected to result in unacceptable risk when Fuzzicide Solution is used according to label directions.

### 7.2 Environmental Risk

Based on the use pattern for Fuzzicide Solution in pulp and paper mills, Fuzzicide biocide presents a negligible risk to aquatic organisms. Specific statements regarding its toxicity to aquatic organisms and statements to minimize exposure to the aquatic environment are provided on the product label.

### 7.3 Value

The submitted data indicated that Fuzzicide Solution used in conjunction with sodium hypochlorite via the Fuzzicide feeder/delivery system effectively prevented the fouling of pulp and paper mill whitewater systems and starch slurries caused by bacterial, fungal and algal contamination.

## 8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of technical grade active ingredient Fuzzicide (Ammonium Bromide) and the end-use product Fuzzicide Solution. An evaluation of current scientific data from the registrant, scientific reports and information from other regulatory agencies has resulted in the determination that, under the approved conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been determined to be acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the registrant as a result of this evaluation (see below).

- **Environment**

  A hydrolysis study conducted with the Fuzzicide biocide, bromide-activated chloramine, in sterile water at three different pH's (e.g. pH 4.0, pH 7.0 and pH 9.0) is required. This study is to be submitted to the PMRA by 1 September 2009.

**NOTE:** The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

# List of Abbreviations

| | |
|---|---|
| µg | micrograms |
| a.i. | active ingredient |
| atm | atmospheres |
| BAC | bromide activated chloramine |
| bw | body weight |
| CAS | chemical abstracts service |
| cm | centimetres |
| DACO | data code |
| DNA | deoxyribonucleic acid |
| $EC_{10}$ | effective concentration on 10% of the population |
| $EC_{25}$ | effective concentration on 25% of the population |
| g | gram |
| HOBr | hypobromous acid |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram |
| $K_{oc}$ | organic-carbon partition coefficient |
| $K_{ow}$ | *n*–octanol–water partition coefficient |
| L | litre |
| $LC_{50}$ | lethal concentration 50% |
| $LD_{50}$ | lethal dose 50% |
| LOAEL | lowest observed adverse effect level |
| LOEC | low observed effect concentration |
| LOQ | limit of quantitation |
| $LR_{50}$ | lethal rate 50% |
| mg | milligram |
| mL | millilitre |
| MAS | maximum average score |
| MOE | margin of exposure |
| m/z | mass to charge ratio |
| N/A | not applicable |
| NOAEL | no observed adverse effect level |
| NOEC | no observed effect concentration |
| NOEL | no observed effect level |
| N/R | not required |
| PMRA | Pest Management Regulatory Agency |
| ppm | parts per million |
| $t_{1/2}$ | half-life |
| TSMP | Toxic Substances Management Policy |
| USEPA | United States Environmental Protection Agency |

# Appendix I Tables and Figures

## Table 1 Acute Toxicity of Ammonium Bromide Technical and Its Associated End-use Product (Fuzzicide Solution)

| Study Type | Species | Result | Comment | Reference |
|---|---|---|---|---|
| **Acute Toxicity of Ammonium Bromide Technical** | | | | |
| Oral | Rat (Sprague-Dawley) | $LD_{50}$ (M) = 2868 mg/kg bw<br>$LD_{50}$ (F) = 2566 mg/kg bw<br>$LD_{50}$ (M/F) = 2714 mg/kg bw | Low toxicity | 665852 |
| Dermal | Rat (Sprague-Dawley) | $LD_{50}$ > 2000 mg/kg bw | Low toxicity | 665853 |
| Inhalation | Rat (Sprague-Dawley) | $LC_{50}$ > 0.10 mg/L | Moderate toxicity | 665854 |
| Skin irritation | Rabbit (New Zealand White) | MAS[a] = 0 | Non-irritating | 665856 |
| Eye irritation | Rabbit (New Zealand White) | MAS = 5.4 | Mildly irritating | 665855 |
| Skin sensitization (Maximization) | Guinea pig | Negative | Not a dermal sensitizer | 665857 |
| **Acute Toxicity of End-Use Product: Fuzzicide Solution** | | | | |
| Oral | Rat (Sprague-Dawley) | $LD_{50}$ > 5000 mg/kg bw | Low toxicity | 665948 |
| Dermal | Rat (Sprague-Dawley) | $LD_{50}$ > 5000 mg/kg bw | Low toxicity | 665949 |
| Inhalation | Rat (Sprague-Dawley) | $LC_{50}$ > 4.21 mg/L | Low toxicity | 665950 |
| Skin irritation | Rabbit (New Zealand White) | MAS = 0 | Non-irritating | 665952 |
| Eye irritation | Rabbit | MAS = 2 | Minimally irritating | 665951 |
| Skin sensitization (not provided) | N/A | Negative (based on study conducted with ammonium bromide technical) | Not a dermal sensitizer | 665857 |

[a] MAS = maximum average score for 24, 28 and 72 hours

## Table 2 Toxicity Profile of Ammonium Bromide Technical

| Study Type | Species | Results[a] (mg/kg/day) | Reference |
|---|---|---|---|
| 28-day dietary | Rat (Sprague-Dawley) | A NOAEL and LOAEL were not established since the study is considered to be supplemental.<br><br>Decreased absolute testes weights were noted at 100 mg/kg bw/day. Effects noted at the next highest dose (500 mg/kg bw/day) included clinical signs of toxicity, decreased body weight and body weight gain and decreased absolute epididymis, heart, kidneys, testes, lung and liver weights. | 665858 |
| 90-day dietary<br><br>Complete functional operational battery, motor activity and neurohistopathology assessments also performed | Rat (Sprague-Dawley) | NOAEL: not established<br>LOAEL: 100 mg/kg bw/day; clinical signs of toxicity (long claws), decreased cholesterol and increased phosphate levels (F), decreased absolute brain, thyroid, kidney, liver, testes and epididymis weights (M) and increased haemoglobin levels (M).<br><br>A NOAEL and LOAEL for neurotoxicity were not established since the neurotoxicity component of the study was considered to be supplemental.<br><br>Effects indicative of neurotoxicity were observed at 100 mg/kg bw/day (the lowest dose tested), including decreased hindlimb grip strength (M/F) and increased landing foot splay, posture/gait abnormalities and limpness (M). | 665859<br>930894<br>930896 |
| One-generation reproduction | Rat (Sprague-Dawley) | NOAELs and LOAELs were not established since the study is considered to be supplemental.<br><br>**Parental:** No effects were noted at 151/176 mg/kg bw/day (M/F). Effects noted at the next highest dose (277/347 mg/kg bw/day [M/F]) included clinical signs of toxicity (F) and decreased body weight gain and food consumption (M).<br><br>**Offspring:** At 151/176 mg/kg bw/day (M/F; the lowest dose tested), one pup was sacrificed in extremis (signs of toxicity included cold to touch, subdued behaviour and abnormal breathing).<br><br>**Reproductive:** No effects were noted at 151/176 mg/kg bw/day (M/F). At the next highest dose (277/347 mg/kg bw/day [M/F]), decreased pup viability was observed (one litter with all pups born dead). | 1093412 |
| Developmental toxicity | Rat (Sprague-Dawley) | **Maternal NOAEL:** 300 mg/kg bw/day<br>**Maternal LOAEL:** 1000; clinical signs of toxicity, decreased body weight gain and one dam sacrificed due to severe clinical signs.<br>**Developmental NOAEL:** not established<br>**Developmental LOAEL:** 100; increased incidence of undescended/displaced testes and skeletal variations. | 665862 |

| Study Type | Species | Results[a] (mg/kg/day) | Reference |
|---|---|---|---|
| Reverse gene mutation assay | *Salmonella typhimurium/ E.coli* | Negative | 665849 |
| In vitro mammalian gene mutation assay | Mouse Lymphoma L5178Y cells | Negative | 665850 |
| In vivo mammalian cytogenetics | Mouse micro nucleus assay | Negative | 665851 |

[a] Effects observed in males as well as females unless otherwise reported

## Table 3 Toxicity Studies Conducted with Sodium Bromide

| Study Type | Species | Results[a] (mg/kg/day) | Reference |
|---|---|---|---|
| Special Reproduction Investigations (3-Generations; 2 litters/generation) | Rat (strain not specified) | NOAELs and LOAELs were not established since the study is considered to be supplemental.<br><br>**Parental:** Effects were noted for males at 75 ppm (3.7 mg/kg bw/day), including decreased thyroid hormone (thyroxine) levels and decreased body weight ($F_2$).<br><br>For females, no effects were noted at 300 ppm (15 mg/kg bw/day). Effects noted at the next highest dose (1200 ppm; 60 mg/kg bw/day) included decreased body weight ($F_2$) and decreased adrenal ($F_0$) and uterine weights ($F_1$).<br><br>**Offspring:** No effects were noted at 1200 ppm (15 mg/kg bw/day). Decreased offspring viability was noted at the next highest dose (4800 ppm; 240 mg/kg bw/day).<br><br>**Reproductive:** No effects were noted at 1200 ppm (15 mg/kg bw/day). Decreased fertility was noted at the next highest dose (4800 ppm; 240 mg/kg bw/day). | 665861 |
| In vitro chromosome aberrations | Human lymphocyte cells | Negative<br><br>Supplemental: Lack of detail regarding study methods. | 1093414 |

| Study Type | Species | Results[a] (mg/kg/day) | Reference |
|---|---|---|---|
| Metabolism:<br>Various literature references | | **Absorption**<br>Bromide is rapidly and completely absorbed following oral ingestion.<br>**Distribution**<br>Bromide is distributed almost exclusively to the extracellular fluid, with some accumulation also occurring in red blood cells, cerebrospinal fluid, thyroid gland, blood vessel walls, cartilage, tendons, dentine, kidneys, urinary bladder, stomach and the eye.<br>**Excretion**<br>Elimination of bromide is slow (half-lives of approximately 12 days in humans and 3 days in rats); excretion primarily in the urine and to a lesser extent in the feces.<br><br>Absorption, distribution and elimination of bromide appear to be linear processes, with saturation of reabsorption only occurring at extremely high dose levels. Information in the literature indicates that cross-placental transfer of bromide occurs, with accumulation occurring in fetal cartilage and kidneys and that fetal elimination of bromide may be slower in comparison to elimination from the plasma and brain of maternal animals. | 665863<br>665864<br>934180<br>1424675 |

[a] Effects observed in males as well as females unless otherwise reported

## Table 4 Toxicity Studies Conducted with Ammonia

| Study Type | Species | Results[a] (mg/kg/day) | Reference |
|---|---|---|---|
| In vitro chromosome aberrations (literature information | **Positive:** Information from the literature indicates that ammonia may have the potential to induce chromosomal aberrations, based on a study with workers exposed occupationally to ammonia and the results from an in vitro study conducted with chick fibroblasts. | | 1093415 |
| Metabolism:<br>Various literature references | | **Absorption**<br>Ammonium is readily absorbed following oral ingestion.<br>**Distribution**<br>Ammonium is widely distributed once it reaches circulation.<br>**Excretion**<br>Excretion is relatively slow (60-72% excreted within 3 days of dosing) and occurs primarily as urinary urea, with minimal excretion via the feces, expired air and sweat.<br>**Metabolism**<br>Ammonium is mainly metabolized in the liver, where it is primarily converted to urea and glutamine. Conversion to glutamine can also occur in brain and other tissues. | 1093415 |

[a] Effects observed in males as well as females unless otherwise reported

## Table 5 Fate and Behaviour in the Environment

| Property | Test substance | Value | Comments | Reference (PMRA #) |
|---|---|---|---|---|
| **Soil** | | | | |
| Hydrolysis | BAC | NA | Study required | |
| Phototransformation on soil | BAC | No data required. | Low potential for phototransformation under environmentally relevant conditions | |
| Phototransformation in air | BAC | No data required. | Low volatilization potential under environmentally relevant conditions | |
| Biotransformation in aerobic soil | BAC | No data required. | Exposure to soil is not expected. | |
| Biotransformation in anaerobic soil | BAC | No data required. | Exposure to soil is not expected. | |
| Adsorption/desorption in soil | BAC | Waiver accepted. | Exposure to soil is not expected. | 930988 |
| Soil leaching | BAC | Data not required. | Exposure to soil is not expected. | |
| Volatilization | BAC | No data required. | Volatilization is not expected to be a concern. | |
| Field dissipation | BAC | Data not required. | Exposure to soil is not expected. | |
| Field leaching | BAC | Data not required. | Exposure to soil is not expected. | |
| **Aquatic systems** | | | | |
| Hydrolysis | BAC | N/A | Study required. | |
| Phototransformation in water | BAC | Waiver accepted. | Low potential for phototransformation under environmentally relevant conditions | 665879 |

| Property | Test substance | Value | Comments | Reference (PMRA #) |
|---|---|---|---|---|
| Biotransformation in aerobic water systems | BAC | Half-life at 5.0 mg $Cl_2$:<br>25°C: 50.6 hours<br>35°C: 26.6 hours<br>Half-life at 0.5 mg $Cl_2$:<br>25°C: 45.6 hours<br>35°C: 22.6 hours | | 665867 |
| Biotransformation in anaerobic water systems | BAC | | Not expected to be an issue. | |
| Adsorption/desorption in sediment | BAC | Waiver accepted. | Not expected to be an issue | 930988 |
| Field dissipation:<br>Pulp and paper mill | BAC | Not detected at outlet | BAC was not detected in the effluent that was discharged into the environment. | 1093417 |

## Table 6 Effects on Terrestrial and Aquatic Organisms

| Organism | Species | Study Type | Test substance | Endpoint value | Reference (PMRA #) |
|---|---|---|---|---|---|
| **Terrestrial organisms** | | | | | |
| Bird | Mallard duck | Acute single oral dose | Fuzzicide (ammonium bromide) | NOEL: 1600 mg a.i./kg bw<br>$LD_{50}$: > 2000 mg a.i./kg bw | 665869 |
| | | Dietary 5-day exposure | Fuzzicide (ammonium bromide) | NOEC: 5000 mg a.i./kg diet<br>$LC_{50}$: > 5000 mg a.i./kg diet | 665878 |
| | | Reproduction | Fuzzicide (ammonium bromide) | Not required | |
| | Bobwhite quail | Acute | Fuzzicide (ammonium bromide) | Waiver accepted | 931039 |
| Vascular plant | | Seedling emergence | Fuzzicide (ammonium bromide) | Not required | |
| | | Vegetative vigour | Fuzzicide (ammonium bromide) | Not required | |

| Organism | Species | Study Type | Test substance | Endpoint value | Reference (PMRA #) |
|---|---|---|---|---|---|
| **Freshwater species** | | | | | |
| Invertebrates | *Daphnia magna* | Acute | BAC | 48-h NOEC: 17 µg $Cl_2$/L (based on sublethal effects)<br>48-h $EC_{50}$: 23.3 µg $Cl_2$/L | 665870 |
| | | Chronic | BAC | Waiver accepted | 931006 |
| Fish | Rainbow trout | Acute | BAC | 96-h NOEC: 14 µg $Cl_2$/L (based on sublethal effects)<br>96-h $LC_{50}$: 57.33 µg $Cl_2$/L | 665873 |
| | | Chronic | BAC | Not required | |
| | Bluegill sunfish | Acute | BAC | 96-h NOEC: 0.072 mg $Cl_2$/L<br>96-h $LC_{50}$: 0.33 mg $Cl_2$/L | 665875 |
| | | Chronic | BAC | Not required | |
| Algae | Green alga | Acute | BAC | 72-hr $EC_{10}$: 0.0075mg $Cl_2$/L (based on biomass inhibition)<br>72-hr $EC_{50}$: 0.017 mg $Cl_2$/L | 665879 |
| Plant | *Lemna gibba* | Dissolved | BAC | 7-day NOEC: 0.16 mg $Cl_2$/L<br>7-day $LC_{50}$: 0.61mg $Cl_2$/L | 665880 |
| **Marine species** | | | | | |
| Invertebrates | Mysid shrimp | Acute | BAC | 96-h NOEC: 17 µg $Cl_2$/L<br>96-h $LC_{50}$: 35.4 µg $Cl_2$/L | 665871 |
| | | Chronic | BAC | Not required | |
| | Mollusk | Acute | BAC | 96-h NOEC: 2.6 µg $Cl_2$/L<br>96-h $EC_{50}$: 18 µg $Cl_2$/L (based on reduction in shell deposition) | 665872 |
| | | Chronic | BAC | Not required | |

| Organism | Species | Study Type | Test substance | Endpoint value | Reference (PMRA #) |
|---|---|---|---|---|---|
| Fish | Sheepshead minnow | | | 96-h NOEC: 0.24 mg $Cl_2$/L<br>96-hour $LC_{50}$: 0.36 mg $Cl_2$/L | 665877 |
| | Salmonid | Acute | BAC | Waiver accepted. | 931033 |
| | | Salinity challenge | BAC | Waiver accepted. | 931033 |

## Table 7 Alternative Slimicides for Pulp and Paper Mill Use

| Active | Example of End-Use Product | Claims | Mode of Action |
|---|---|---|---|
| 1,2-DIBROMO-2,4-DICYANOBUTANE | Tektamer 2200 | bacteria; fungi; yeasts | cellular oxidation |
| 1-BROMO-3-CHLORO-5,5-DIMETHYLHYDANTOIN<br>1,3-DICHLORO-5,5-DIMETHYLHYDANTOIN<br>1,3-DICHLORO-5-ETHYL-5 METHYLHYDANTOIN | B.I.O. Blast 650 | microbial slimes | cellular oxidation |
| 1-ALKYL (C8-C18)-1,3-PROPANEDIAMINE ACETATE | Rasio 936 | bacterial & fungal slimes | unknown |
| 1-BROMO-3-CHLORO-5,5-DIMETHYLHYDANTOIN | Aquate | slime-forming bacteria; fungi; algae | cellular oxidation |
| 2,2-DIBROMO-3-NITRILOPROPIONAMIDE | Fennosan 150-C | bacteria; fungi; yeast | cellular oxidation |
| 2-METHYL-4-ISOTHIAZOLIN-3-ONE<br>5-CHLORO-2-METHYL-4-ISOTHIAZOLIN-3-ONE | Irgacide PT 286X | slime-forming bacteria; fungi | inhibition of membrane-bound enzymes |
| BRONOPOL | Rasio 937 | slimicide | cellular oxidation |
| DAZOMET | Amerstat 223 | slime-forming bacteria; fungi | unknown |
| DECYL ISONONYL DIMETHYL AMMONIUM CHLORIDE | Bardac CW-50 | bacteria; fungi; algae | membrane disruption |
| GLUTARALDEHYDE<br>N-ALKYL (40% C12, 50% C14, 10% C16) DIMETHYL BENZYL AMMONIUM CHLORIDE | Nalcon 7637 | slime-forming bacteria; sulfate-reducing bacteria; fungi; yeast | protein cross-linking; membrane disruption |

| Active | Example of End-Use Product | Claims | Mode of Action |
|---|---|---|---|
| GLUTARALDEHYDE | Prior 285 | slime-forming bacteria; sulfate-reducing bacteria; fungi; yeast | protein cross-linking |
| METHYLENE BIS(THIOCYANATE) | Process B-2008 | slime-forming and spoilage bacteria | protein alteration |
| NABAM;<br>SODIUM DIMETHYLDITHIOCARBAMATE | X-Cell 419 | papermill slimes | unknown |
| N-ALKYL (40% C12, 50% C14, 10% C16) DIMETHYL BENZYL AMMONIUM CHLORIDE | Process B-1001 | slime-forming bacteria | membrane disruption |
| SODIUM BROMIDE (+ HYDROCHLORIC ACID) | Basabrom 40 | slime-forming bacteria; fungi; algae | cellular oxidation |

## Table 8 Unsupported Proposed Use (label) Claims

| Applicant-proposed Label Claims | Accepted Label Claims | Unsupported Label Claims and Comment |
|---|---|---|
| RECIRCULATING COOLING SYSTEMS<br>Used effectively at recommended dosage to achieve measured concentration of 0.3–5.0 ppm residual biocide expressed as total chlorine, or as needed to maintain control of algal, bacterial, and fungal slimes in industrial cooling towers, heat exchange water towers, industrial water scrubbing systems, brewery and canning pasteurizers and industrial air washing systems equipped with mist eliminator, influent systems such as flow through filters and lagoons, etc.<br><br>Dosage Rates<br>Initial dose: When noticeably fouled, add sufficient biocide produced by the feeder to achieve a measured concentration of 0.3–5.0 ppm residual biocide, expressed as total chlorine. The recommended dosage is typically achieved by mixing 2.03 litres of Sodium Hypochlorite (12.5%) with 1.0 kg (0.83 litres) of FUZZICIDE SOLUTION in the feeder.<br><br>Subsequent Dose: Once microbial control is evident, add sufficient biocide produced by the feeder to maintain the measured residual biocide concentration at 0.3–5.0 ppm in process waters, expressed as total chlorine. Continue as in initial dose. | PULP AND PAPER MILLS: Used for the prevention of algal, bacterial and fungal slimes, in pulp and paper mill whitewater systems and starch slurries. Badly fouled process systems must be cleaned before initial treatment. Total chlorine residuals can be monitored using a DPD standard chlorine test kit.<br><br>Whitewater Systems: Add sufficient biocide produced by the feeder to achieve and maintain a measured concentration of 0.5–5.0 ppm residual biocide, expressed as total chlorine.<br><br>Starch Slurries: Add sufficient biocide produced by the feeder to achieve and maintain a measured residual biocide concentration of up to 10.0 ppm in process waters, expressed as total chlorine. | RECIRCULATING COOLING SYSTEMS: Used effectively at recommended dosage to achieve measured concentration of 0.3–5.0 ppm residual biocide expressed as total chlorine, or as needed to maintain control of algal, bacterial and fungal slimes in industrial cooling towers, heat exchange water towers, industrial water scrubbing systems, brewery and canning pasteurizers and industrial air washing systems equipped with mist eliminator, influent systems such as flow through filters and lagoons, etc.<br><br>Dosage Rates<br>Initial dose: When noticeably fouled, add sufficient biocide produced by the feeder to achieve a measured concentration of 0.3–5.0 ppm residual biocide, expressed as total chlorine. The recommended dosage is typically achieved by mixing 2.03 litres of Sodium Hypochlorite (12.5%) with 1.0 kg (0.83 litres) of FUZZICIDE SOLUTION in the feeder.<br><br>Subsequent Dose: Once microbial control is evident, add sufficient biocide produced by the feeder to maintain the measured residual biocide concentration at 0.3–5.0 ppm in process waters, expressed as total chlorine. Continue as in initial dose. |

| Applicant-proposed Label Claims | Accepted Label Claims | Unsupported Label Claims and Comment |
|---|---|---|
| PULP AND PAPER MILLS<br>Used for the control of algal, bacterial and fungal slimes, in pulp and paper mill fresh water influent systems, cooling water systems, wastewater treatment systems, pulp, paper and paper board mills systems, non potable water systems, starch slurries and other process water. Apply biocide as directed.<br><br>Dosage Rates<br>Initial dose: When noticeably fouled, add sufficient biocide produced by the feeder to achieve a measured concentration of 0.3–10.0 ppm residual biocide, expressed as total chlorine. The recommended dosage is typically achieved by mixing 2.03 litres of Sodium Hypochlorite (12.5%) with 1.0 kg (0.83 litre) of FUZZICIDE SOLUTION in the feeder.<br><br>Subsequent Dose: Once microbial control is evident, add sufficient biocide produced by the feeder to maintain the measured residual biocide concentration at 0.3–10.0 ppm in process waters, expressed as total chlorine. | | |

# List of References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

## 1.0 Chemistry Assessment


| PMRA Document Number | Reference |
|---|---|
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