Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2000-02

VigorOx™

The active ingredient peracetic acid VigorOx and associated end-use product Nalco 7650, containing 5.1% peroxyacetic acid and 21.7% hydrogen peroxide for the control of typical paper industry microorganisms, are proposed for full registration under Section 13 of the Pest Control Products Regulations (PCP Regulations).

This proposed regulatory decision document (PRDD) provides a summary of data reviewed and the rationale for the proposed full registration of these products. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address listed below.

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Foreword

The submissions for the registration of VigorOx^{TM} (peroxyacetic acid), manufactured by FMC, and the end-use product Nalco 7650, marketed by Nalco Canada Inc., have been reviewed by the Pest Management Regulatory Agency (PMRA).

VigorOx^{TM} is a solution composed of peracetic acid (~5%) in equilibrium with hydrogen peroxide (~20%). Nalco 7650 has the same formulation as VigorOx^{TM}. VigorOx^{TM} and Nalco 7650 can serve as alternative oxidizing biocides to chlorine based products in pulp and paper facilities. The transformation products are water, oxygen and acetic acid; all have negligible toxicological effects.

The products have been granted a limited term registration by the PMRA to allow users access to this low-risk product, while providing concerned Canadians an opportunity to provide input into the final decision through this Proposed Regulatory Decision Document.

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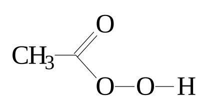
1.0 The active substance, its properties, uses, proposed classification and labelling

1.1 Identity of the active substance and preparation containing it

Common name:	Peracetic acid (VigorOx™)
Function:	Biocide
Chemical name:	Peroxyacetic acid
CAS number:	79-21-0
Molecular formula:	$C_2H_4O_3$
Molecular weight:	76.052
Structure formula:	
Nominal purity of actives:	Peroxyacetic acid . . . . 5.1% Hydrogen peroxide 21.7%
Identity of relevant impurities of toxicological, environmental and other significance:	The technical grade peroxyacetic acid does not form any transformation products that meet the Toxic Substances Management Policy (TSMP) Track-1 criteria

1.2 Physical and chemical properties of active substance and the end-use product

Technical product: VigorOx™ SP Paper System Biocide

Property	Result	PMRA comments
Colour and physical state	Water white colourless liquid	
Odour	Sharp, pungent vinegar-like	
Melting point or range	–25.9EC	
Boiling point or range	99EC, decomposes on boiling	
Density	1.1 g/mL	
Vapour pressure	21.7 mm Hg at 20EC	Volatilizes under field conditions

Property	Result	PMRA comments
UV and visible spectrum	Strong absorbance below 300 nm	Low potential to phototransform in the environment
Water solubility	Miscible	Very soluble in water
Solubility in organic solvents	Miscible in a range of solvents that are not oxidized by the peroxy acid Miscible in ethylacetate, other alkylacetates, chloroform and other halogenated solvents, acetone and hydrocarbons such as isooctane	
n-Octanol–water partition coefficient (K_{ow})	0.3	Very low potential to bioaccumulate in organisms
Dissociation constant (pK_a)	8.2	Predominates as a neutral molecule at pH < 8.2 and as an anion at pH > 8.2 in the environment
Stability	Oxidizer	

End-use product: Nalco 7650

Property	Result
Colour	Water white colourless
Odour	Strong pungent vinegar-like
Physical state	Liquid
Formulation type	Solution
Guarantee	Peracetic acid . . . . 5.1% Hydrogen peroxide 21.7%
Container material and description	Polyethylene containers, stainless steel containers
Specific gravity	1.11 g/mL
pH	Less than 1
Storage stability	Stable for one year when stored at ambient temperature in commercial packaging
Surfactants	None

1.3 Details of uses and further information

VigorOx™ is a mixture of peroxyacetic acid (referred to as peracetic acid throughout this document) in equilibrium with hydrogen peroxide. The guarantee concentrations are 5.1% peracetic acid and 21.7% hydrogen peroxide. Both peracetic acid and hydrogen peroxide have biocidal properties; therefore, they are both considered active ingredients.

The Canadian Bureau of Chemical Safety has issued a "No Objection" letter for the use of VigorOx™ antimicrobial agent in the manufacture of paperboard that may contact foods.

1.4 Classification and labelling

1.4.1 VigorOx™ (technical)

The submitted toxicology data package consists primarily of acute studies, conducted with dilute peracetic acid (17%), 0.15% peracetic acid use dilution or 35% hydrogen peroxide. On the basis of the information on acute toxicity as a whole, the technical active ingredient and end-use product were considered slightly acutely toxic by the oral route, but severely irritating to eyes and skin. Diluted peracetic acid (17%) had an acute dermal median lethal dose (LD_{50}) > 200 mg/kg body weight, the only dose level tested. Hydrogen peroxide (35%) was of low acute dermal toxicity. Dermal sensitization potential was not tested for either 17% peracetic acid or 35% hydrogen peroxide, but 0.15% peracetic acid use dilution was not a dermal sensitizer in guinea pigs.

On the basis of the above toxicity profile, the proposed signal words and symbols for the VigorOx™ label are considered adequate. The change for the secondary panel is as follows:

> Under *Precaution* add the following statements: "Keep out of reach of children" and "Ensure that acetic acid and hydrogen peroxide air concentrations in the workplace do not exceed the exposure levels established by occupational health and safety authorities in your jurisdiction (e.g., engineering controls, monitoring). If values exceed these levels, wear NIOSH-approved respiratory protection."

1.4.2 Nalco 7650 end-use product

Toxicology data for Nalco 7650 were the same as VigorOx™, since the two formulations are exactly the same. Therefore, the label comments for VigorOx™ apply to Nalco 7650 as well.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

Titration and Fourier transform – infrared methods were used for the determination of the active in the technical product. The titration method has been shown to have satisfactory precision. The method accuracy cannot be determined, since peracetic acid exists only in equilibrium with hydrogen peroxide and is not available as a pure material for spiking.

2.2 Method for formulation analysis

The level of peracetic acid is determined by titration. The end-use product is also the technical material. Please refer to section 2.1 above for further details.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary (Appendix I, Summary table)

The registrant requested waivers for submitting all toxicity studies except the acute studies, which were conducted either with dilute peracetic acid (17%), peracetic acid 0.15% use dilution or 35% hydrogen peroxide. Some published articles were cited. Part of the review of hydrogen peroxide by ECETOC (Joint Assessment of Commodity Chemicals No. 22, Hydrogen Peroxide; European Centre for Ecotoxicology and Toxicology of Chemicals, 1993) was submitted. The evaluation of VigorOx™ /Nalco 7650 was mainly based on the submitted acute studies. Literature articles as well as the assessment of hydrogen peroxide published by ECETOC were also considered.

VigorOx™/Nalco 7650 is a solution composed of peracetic acid (~ 5%) in equilibrium with hydrogen peroxide (~ 20%). Hydrogen peroxide, as well as water and acetic acid, serves as a critical component in maintaining the concentration of peracetic acid in the product. The role of each ingredient in maintaining the labelled levels of peracetic acid and hydrogen peroxide is shown in the following equilibrium reaction:

$$H_2O_2 + CH_3COOH \overset{K_{eq}}{\text{ø}} CH_3COOOH + H_2O$$

where $K_{eq} = \dfrac{[\text{moles } CH_3CO_3H]\,[\text{moles } H_2O]}{[\text{moles } CH_3CO_2H]\,[\text{moles } H_2O_2]}$ • 2.1 for VigorOx™ antimicrobial agent

The technical actives were not tested for subchronic, chronic or oncogenicity or other special toxicity studies in mammalian species owing to the corrosivity of the test material. On the basis of the submitted acute data package, VigorOx™ and Nalco 7650 (5% peracetic acid and 22% H_2O_2) are anticipated to be acutely corrosive to skin, eyes and mucosal membrane. Their oral, dermal and inhalation toxicities are secondary to the corrosivity. Owing to rapid decomposition to water and O_2 upon contact with moisture, the absorption, distribution, metabolism and excretion of peracetic acid and hydrogen peroxide would be negligible.

Literature information indicates that a significant decrease in body weight and bodyweight gain was noted in mice exposed to 70–140 mg/m^3 peracetic acid (concentration unknown) when compared with controls in a subacute inhalation study (one hour per day, three times per week for four weeks). Peracetic acid, 40%, did not show mutagenic potential in the Ames test with or without metabolic activation. It did not induce unscheduled DNA synthesis and repair in vitro. The overall toxicity profile reveals that high concentrations of peracetic acid cause corrosion of the mucous membrane of the mouth, throat and esophagus with immediate pain and dysphagia. Necrosis of the stomach and gastric perforation may eventually lead to death. Subchronic and chronic dermal toxicity studies with different concentrations of peracetic acid in different species resulted in general systemic toxicity but no increase in tumour incidence. Both the International Agency for Research on Cancer (IARC) and the American Conference of Governmental Industrial Hygienists do not consider peracetic acid to pose a carcinogenicity risk in human. On the basis of the limited information available, the conclusion appears valid.

Hydrogen peroxide is a known mutagen in vitro but is not genotoxic in vivo owing to its rapid decomposition to water and oxygen. Chronic exposure of 0.4% hydrogen peroxide in drinking water to mice causes duodenal tumours, but both the IARC and the United States (U.S.) Food and Drug Administration conclude that there is limited or insufficient evidence of carcinogenicity. In the absence of new information, the Health Evaluation Division concurs with this conclusion.

Although no adequate data were available to evaluate the reproductive toxicity, teratogenicity or neurotoxicity of either peracetic acid or hydrogen peroxide, these studies are deemed not necessary in view of the rapid decomposition of the actives to water and oxygen. The actives are unlikely to accumulate in mammalian organs/tissues long enough to exert significant effects on reproduction and development or induce neurotoxicity.

3.2 Acceptable daily intake

Since there is no food use proposed, an acceptable daily intake (ADI) was not determined.

3.3 Acute reference dose

Since no food use is proposed, it was not necessary to propose an acute reference dose (ARfD).

3.4 Toxicology end-point selection

An acute toxicology end point is considered most appropriate for health risk assessment because:

- both peracetic acid and hydrogen peroxide are highly reactive, subject to rapid decomposition to water and oxygen upon contact with moisture;
- the occupational exposure is expected to be brief; and
- the most salient feature of this compound is its corrosivity.

The Health Evaluation Division concurs with the U.S. Environmental Protection Agency's (EPA) assessment that peroxy compounds are corrosive and pose acute risk of severe eye and skin irritation to handlers (EPA R.E.D. FACTS, Peroxy Compounds, December 1993). The corrosive nature of these compounds will in itself preclude significant dermal exposure.

A qualitative risk assessment is deemed appropriate.

3.5 Impact on human and animal health arising from exposure to VigorOx™ /Nalco 7650

3.5.1 Operator exposure assessment

Workers may be exposed to hydrogen peroxide and peroxyacetic acid (and the decomposition product acetic acid) when these chemicals are added to the pulp and paper system. Nalco 7650 would not be diluted prior to application. The product may be applied to the system as a slug or continuously depending on the facility needs. Transfer would likely occur using a closed transfer system, but could occur through open transfer systems. Typically, transfer occurs intermittently (e.g., two to three times per week) and potential exposure would be brief (e.g., several minutes). There is a potential for dermal and inhalation exposure. The label specifies that workers wear goggles and a face shield, protective coveralls, boots and chemical-resistant gloves while transferring or handling the product.

It is the conclusion of the Health Evaluation Division that mitigation against acute exposures through labelling is the most appropriate regulatory approach for these active ingredients. Specifically, the label should be modified to specify the following additional precautionary measures: "Ensure that acetic acid and hydrogen peroxide air concentrations in the workplace do not exceed the exposure levels established by occupational health and safety authorities in your jurisdiction (e.g., engineering controls, monitoring). If values exceed these levels, wear NIOSH-approved respiratory protection."

Together with the exposure reduction statements on the draft label (e.g., personal protective equipment and clothing), these measures are considered adequate to protect workers against acute hazards.

3.5.2 Bystanders

Given the proposed use, bystander exposure is not anticipated.

3.5.3 Workers

Given the proposed use, worker exposure is expected to be negligible.

4.0 Fate and behaviour in the environment

Most of the data for hydrogen peroxide were obtained from the published literature and were previously reviewed. Data were submitted on peracetic acid.

4.1 Fate and behaviour in soil

Studies were either not required for this use site category or were waived because there is limited potential for exposure to soil.

4.2 Fate and behaviour in aquatic systems

Neither hydrogen peroxide nor peracetic acid is persistent. Several studies (phototransformation in water, aquatic aerobic and aquatic anaerobic transformation, aquatic field dissipation and accumulation) were waived for peracetic acid because of its use pattern, lack of persistence in aquatic systems and non-toxic transformation products.

Peracetic acid is miscible in water. The vapour pressure of 1426 Pa at 20EC (2893 Pa at 20EC for VigorOx^{TM}) indicates that peracetic acid has a potential to volatilize under field conditions, but when placed in water it is expected to remain in solution. Peracetic acid has a low potential to phototransform in the environment (strong absorbance < 300 nm) and to bioaccumulate in organisms (log K_{ow} = 0.3). The dissociation constant value (VigorOx^{TM} pK_a = 8.2) indicates that peracetic acid exists in the environment as a neutral molecule at pH < 8.2 and as an anion at pH > 8.2.

Hydrogen peroxide is miscible in water. The vapour pressure of 1.7 Pa (35%) at 20EC and the Henry's Law Constant of 1×10^{-3} Pa m^3/mol (ECETOC, 1993) indicate that hydrogen peroxide has a potential to volatilize, but when placed in water it is expected to remain in solution. Hydrogen peroxide has a low potential to bioaccumulate in organisms (log K_{ow} = 0.4).

4.2.1 Hydrolysis

For peracetic acid, hydrolysis, spontaneous decomposition and metal-catalysed decomposition are the three decomposition pathways that occur simultaneously in water at various pHs.

Hydrolysis	($CH_3CO_3H + H_2O \rightarrow CH_3CO_2H + H_2O_2$)
Spontaneous decomposition	($2CH_3CO_3H \rightarrow 2CH_3CO_2H + O_2$)
Metal-catalysed decomposition	($CH_3CO_3H + \{M\} \rightarrow CH_3CO_2H + O_2 + \{M\}$)

The half-lives of peracetic acid at pH 6, 7, 8 and 9 were calculated using rate constants obtained from Yuan et al. (1997*b*). Hydrolysis followed first-order kinetics with respect to the total peracetic acid concentration. Hydrolysis was dependent on pH (half-lives at pH 6, 7, 8 and 9 were nine months and 28, 4, and 2 days, respectively) and on temperature (half-lives at 25, 50 and 70°C were 28, 6 and 2 days, respectively at pH 7). These results indicate that hydrolysis of peracetic acid is a major route of transformation in the environment under neutral and alkaline conditions.

Peracetic acid decomposes spontaneously in aqueous solution to yield acetic acid and oxygen (Yuan et al. 1997*a*). The decomposition reaction follows second-order kinetics with the maximum rate at pH 8.2, which is the pK_a of peracetic acid. According to Yuan et al. (1997*a*), spontaneous decomposition is dominant at pH 5.2–8.2, and both hydrolysis and spontaneous decomposition take place at pH 8.2–9.0. Decomposition, catalysed by metal ion, is more pronounced at a higher pH.

Hydrogen peroxide is unstable in water and decomposes to oxygen and water (ECETOC, 1993; Moffett and Zafiriou, 1990). Petasne and Zika (1987), as cited in ECETOC (1993), reported a half-life of 60 hours for H_2O_2 in seawater samples from the Bay of Biscay. Cooper and Lean (1989) studied the degradation of natural H_2O_2 in Northern (Jacks) Lake, Ontario and reported a half-life of 7.8 hours in unfiltered water. The half-lives were 8.6, 31 and greater than 24 hours in 5, 1 and 0.45 µm filtered water, respectively. Algae can produce and decompose H_2O_2 (Zepp et al. 1987). Hydrogen peroxide was decomposed in the dark in the supernatant of an algal culture with a first-order half-life of 1.5 hours.

4.2.2 Phototransformation in water

A waiver was granted for peracetic acid because it has a short half-life and because the transformation products, water, oxygen and acetic acid, have no toxicological effects. Further, the UV and visible absorption maximum (<300 nm) indicated that peracetic acid has a low potential to phototransform in the environment.

Moffett and Zafiriou (1993), citing results from Mopper and Zhou (1990), reported a half-life of 10 days for H_2O_2 decomposition by photolysis. Hydrogen peroxide at various concentrations (up to 51.6 mg/L) was added to seawater samples and irradiated by sunlight. This study indicated that phototransformation of hydrogen peroxide may be a route of transformation in the marine environment. Draper and Crosby (1983) reported a first-order half-life of approximately one hour after the exposure of an eutrophic water sample to sunlight for three hours.

4.2.3 Aquatic aerobic biotransformation

A waiver was granted on the basis of the rapid breakdown of peracetic acid into water, oxygen and acetic acid. Acetic acid, in turn, is mineralized into CO_2.

Biotransformation of H_2O_2 is not a major route of transformation in seawater. No information was available on biotransformation in freshwater.

4.3 Expected environmental concentration in water

The end-use product Nalco 7650 is intended for use in a closed system. Environmental exposure would only be likely to occur during the clean-up operation, accidental discharge or spills.

4.4 Fate and behaviour in air

The vapour pressures of peracetic acid and VigorOx^{TM} were 1426 and 2933 Pa at 20EC, respectively, which indicates that they have a potential to volatilize. As Nalco 7650 is injected into the pulp and paper fluid system and VigorOx^{TM} is miscible in water, there is limited potential for volatilization into the atmosphere.

5.0 Effects on non-target species

5.1 Effects on terrestrial non-target species

Waivers were granted for wild birds and mammals because of the use pattern, lack of persistence under alkaline conditions of pulp and paper processing and limited potential for exposure. In addition, the use pattern of this product will result in reduction of VigorOx^{TM} concentration during treatment, considerable dilution during waste treatment of effluents and further dilution (in the range of parts per billion) when discharged into the receiving waters.

5.2 Effects on aquatic non-target species

5.2.1 Bioconcentration or depuration (bivalve or crustacean)

A waiver was granted on the basis of the low exposure to marine and estuarine organisms and because the log K_{ow} of 0.3 indicates that peracetic acid has a very low potential to bioaccumulate in organisms. Similarly, with a log K_{ow} of 0.4, hydrogen peroxide is unlikely to bioaccumulate.

5.2.2 Fish

Peracetic acid is moderately toxic to fish. The most susceptible fish species is bluegill sunfish (*Lepomis macrochirus*) with median lethal concentration (LC_{50}) and no observed effect concentration (NOEC) values of 1.1 and <0.23 mg active ingredient (a.i.)/L, respectively (Gardner, C. and J.D. Bucksath, 1996*a*). This LC_{50} value indicates that peracetic acid is moderately toxic to bluegill sunfish on an acute basis, according to the EPA classification scheme. These NOEC and LC_{50} values correspond to <4.6 and 21.6 mg VigorOx™/L, respectively.

Hydrogen peroxide is slightly toxic to fish. The most susceptible species is the fathead minnow (*Pimephales promelas*) with NOEC and LC_{50} values of 5 and 16.4 mg a.i./L, respectively (Shurtleff, 1989, as cited in ECETOC, 1993). This LC_{50} value indicates that hydrogen peroxide is slightly toxic to fish on an acute basis, according to the EPA classification scheme.

5.2.3 Aquatic invertebrates

Peracetic acid is highly toxic to aquatic invertebrates. The most susceptible species is *Daphnia magna*. On the basis of the immobility of daphnids, the NOEC and median effective concentration (EC_{50}) values for peracetic acid were 0.56 and 0.73 mg a.i./L, respectively (Gardner, C. and J.D. Bucksath, 1996*b*). These values indicate that peracetic acid is highly toxic to daphnids on an acute basis, according to the EPA classification scheme. The NOEC and EC_{50} values correspond to 11.0 and 14.3 mg VigorOx™/L, respectively.

Hydrogen peroxide is moderately toxic to aquatic invertebrates. The most susceptible species is *Daphnia pulex* with 48-hour NOEC and LC_{50} values of 1.0 and 2.4 mg a.i./L, respectively (Kay et al. 1982, as cited in ECETOC, 1993). The LC_{50} value indicates that hydrogen peroxide is moderately toxic to aquatic invertebrates on an acute basis, according to the EPA classification scheme.

5.2.4 Algae

Peracetic acid significantly affects algal growth. The 120-hour EC_{50} and NOEC values, on the basis of growth inhibition, were 0.18 and 0.12 mg a.i./L, respectively (Hicks, S.L., T.A. Ziegler and J.D. Bucksath, 1996). These NOEC and EC_{50} values correspond to 2.4 and 3.5 mg VigorOx™/L, respectively.

Hydrogen peroxide is toxic to algae and will adversely affect algal growth. Kay et al. (1982) reported that hydrogen peroxide at 1.7, 6.8, 9.9 and 17 mg a.i./L reduced the chlorophyll content to approximately 5% in *Mycrocystis*, *Raphidiopsis*, *Ankistrodesmus* and *Anabaena*, respectively (as cited in ECETOC, 1993). In the case of marine diatom, *Nitzchia closterium*, hydrogen peroxide at a concentration of 0.85 mg a.i./L reduced the growth (percent count) by 50% (Florence and Stauber, 1986). The results of these studies indicate that hydrogen peroxide will adversely affect algal growth at concentrations greater than approximately 1.0 mg a.i./L. Hydrogen peroxide at a concentration of 34 mg a.i./L caused 80 and 30% necrosis in coontail (*Ceratophyllum demersum*) and *Hydrilla verticillata*, respectively (Quimbay, 1981 as cited in ECETOC, 1993).

5.2.5 Aquatic plants

A waiver was granted on the basis of the use pattern and lack of persistence under alkaline conditions of pulp and processing. Further, the use pattern of this product will result in the reduction of peracetic acid concentration during treatment, considerable dilution during waste treatment of effluents and further dilution (in the range of parts per billion) when discharged into receiving waters.

5.3 Environmental risk assessment

5.3.1 Terrestrial organisms

No data were submitted on toxicity of peracetic acid and hydrogen peroxide to wild birds and mammals. Under the proposed use in a closed system, the exposure of birds and mammals to VigorOx^{TM} or the end-use product Nalco 7650 will be very limited and, therefore, the risks to these organisms was not assessed.

5.3.2 Aquatic organisms

The risk assessment to aquatic organisms was done using the most sensitive invertebrate, fish and algal species (Table 1).

Nalco 7650 (VigorOx^{TM})
As Nalco 7650 is intended for use in a closed system, environmental exposure would only be likely to occur during the clean-up operation, accidental discharge or spills. In addition, both peracetic acid and hydrogen peroxide decompose so readily that any aquatic release is not expected to be of concern.

The proposed maximum application rate is 2.7 kg Nalco 7650 per 1000 kg of paper. As the paper content is approximately 0.5% of the total slurry, there would be 200 000 L of water in a slurry containing 1000 kg of paper. The addition of 2.7 kg of Nalco 7650 to 200 000 L of water would result in a concentration of 13.5 mg VigorOx^{TM}/L. Even in a worst case scenario of accidental release of paper mill effluent and no loss by hydrolysis and decomposition, the concentration of VigorOx^{TM} would be 13.5 mg/L. Assuming a conservative estimate of 100-fold dilution when the effluent is released into the aquatic systems, the expected environmental concentration (EEC) of VigorOx^{TM} in water would be 0.135 mg a.i./L.

On the basis of immobility, the NOEC and EC_{50} values for *Daphnia magna* are 11.0 and 14.3 mg VigorOx^{TM}/L, respectively. The values of the risk factor (0.01) and the margin of safety (81.5) calculated with the NOEC indicate that VigorOx^{TM} will not pose a risk to *Daphnia* on an acute basis under the proposed maximum application rates.

The fish species most sensitive to VigorOx^{TM} is the bluegill sunfish with NOEC and LC_{50} values of <4.6 and 21.6 mg VigorOx^{TM}/L, respectively. The values of the risk factor (0.03) and the margin of safety (34.1) calculated with the NOEC indicate that VigorOx^{TM} will not pose a risk to fish on an acute basis under the proposed maximum application rates.

The NOEC and EC_{50} values for algae on the basis of growth inhibition are 2.4 and 3.5 mg VigorOx^{TM}/L, respectively. The values of the risk factor (0.05) and the margin of safety (18) calculated with the NOEC indicate that VigorOx^{TM} will not pose a risk to algae under the proposed maximum application rates.

Table 1. Summary of risk assessment of VigorOx^{TM} to aquatic organisms

Species	NOEC (mg a.i./L)	EEC (mg a.i./L)	Risk factor	Margin of safety	Effect
Invertebrates (*Daphnia magna*)	11	0.135	0.01	81.5	No risk
Fish (bluegill sunfish) (*Lepomis macrochirus*)	4.6	0.135	0.03	34.1	No risk
Algae (*Selenastrum capricornutum*)	2.4	0.135	0.05	18	No risk

5.4 Precautionary label statement

The following statement should be included in the label to ensure a margin of safety in the use of Nalco 7650:

> "This product is toxic to fish, aquatic invertebrates and other wildlife. Do not apply directly into lakes, streams, ponds, rivers, estuaries, oceans or other water bodies. Do not discharge effluent containing this product into these waters."

6.0 Efficacy data and information

6.1 Effectiveness

Peracetic acid formulations are equilibrium mixtures of peracetic acid, hydrogen peroxide, acetic acid, water and stabilizer. Although hydrogen peroxide has some biocidal activity, it has poor activity at low temperatures and concentrations and is quickly decomposed by catalase and peroxidase (Coughlin, 1997).

Peracetic acid has been demonstrated under laboratory conditions to be biocidal at low concentrations against a broad spectrum of microorganisms, including gram-positive and gram-negative bacteria, yeasts, molds and algae under a wide variety of conditions. It is also effective against anaerobic and spore forming bacteria. Peracetic acid is effective at killing biofilm microorganisms at low concentrations and short contact times. The biocidal activity of peracetic acid is not affected by pH or water hardness and biocidal activity is retained even in the presence of organic matter. For these reasons, peracetic acid is suited as a biocide in industrial cooling water and papermaking systems. Peracetic acid is compatible with additives commonly used in these systems.

Peracetic acid has been demonstrated under operational conditions, in a pulp mill, to be biocidal at low concentrations against aerobic bacteria producing a three log reduction in the total bacteria population in three different areas of the paper machine. By extension, it can be surmised that peracetic acid, by controlling the bacterial population, would prevent the formation of slime. In addition, Nalco Canada has provided the summaries of various case studies confirming the above.

6.1.1 Intended use

Nalco 7650 is being proposed as an oxidizer for use in the production of paper (Use Site 17) for the control of slime and biofilm forming microorganisms.

Nalco 7650 should be added to the system at a point of uniform mixing such as the beater, hydropulper, fan pump and broke pump at the following rates.

Apply 0.1–2.7 kg Nalco 7650 per tonne (dry basis) of pulp or paper produced. This will provide 7–138 parts per million (ppm) of peroxyacetic acid and 29–586 ppm of hydrogen peroxide. Additions may be continuous or intermittent, depending on the type of system and the severity of contamination.

6.1.2 Mode of action

Nalco 7650 (peracetic acid 5.1%, hydrogen peroxide 21.7%) is an oxidizing chemical being proposed as a viable alternative to traditional oxidizers such as chlorine dioxide and sodium hypochlorite. Nalco 7650 would be a benefit to the environment in that the adsorbable organic halide contribution is reduced, contrary to current oxidizing materials. In addition, owing to a high synergy between Nalco 7650 and some organic biocides, the amount of such biocides used in a given system can be reduced, thus reducing the environmental impact as well as the cost.

An oxidant such as Nalco 7650 works by breaking sulfhydril bonds in components of cell walls and membranes. Thus, the integrity of the microorganisms is compromised, causing lysis and subsequently death. The organic tail of the peracetic molecule also penetrates the cell, allowing for internal oxidizing action against interior structures containing sulfhydril bonds. As there was a reference in the literature (Hugo, 1992) that hydrogen peroxide interferes with DNA synthesis, the FMC Corporation was questioned on this topic. The FMC Corporation supplied the Agency with recent (1997) animal data that indicates that hydrogen peroxide does not damage DNA.

6.2 Information on the occurrence or possible occurrence of the development of resistance

None reported.

6.3 Observation on undesirable or unintended side effects

None reported.

6.4 Consideration of benefits

6.4.1 Description of the pest problem

The pulp and paper industry presents a scenario where microbial growth is offered prime conditions to flourish. Nutrient rich warm water is fundamental to papermaking, also making it ideal for a substantial microbial population to develop and accumulate if left unchecked. Essentially, two main areas can be targeted when searching to control and eliminate microbial growth. Incoming fresh water constantly supplies new microbes to a system that is trying to eliminate them. Process water recirculates through the paper machine, therefore, constantly resupplying any given area with the possibility for new growth. Carryover from one contaminated area on a machine to a previously uncontaminated one is common. This accumulation of microbial growth often develops as a slime, coating machine surfaces and tanks as well as showing up in the finished product itself. Microbial growth can contribute to a significant portion of the downtime of a paper system. If slime breaks free from the machine and lands on the sheet being made, it can cause a break, meaning costly downtime. Slime buildup in and on machine surfaces can cause deterioration and corrosion of the mechanics and structural integrity.

6.4.2 Assessment of submitted efficacy trials data

To effectively control microbial contamination in industrial water systems, a biocide must have the following features: fast acting, broad spectrum of activity, effective at low concentrations, effective against biofilms and compatible with other additives. Peracetic acid has demonstrated in laboratory studies all of these features. In comparative efficacy testing, peracetic acid was superior to two organic biocides that are commonly used in industrial water systems. Synergy studies found very strong synergistic activity between the organic peroxides and many non-oxidizing biocides.

Peracetic acid has been demonstrated under operational conditions, in a pulp mill, to be biocidal at low concentrations against aerobic bacteria, producing a three log reduction in the total bacteria population in three different areas of the paper machine. By extension, it can be surmised that Nalco 7650, by controlling the bacterial population, would prevent the formation of slime.

In addition, Nalco Canada has provided the summaries of various case studies confirming the above.

6.5 Economics

A major problem in operating pulp and paper machine systems is the production losses that occur when bacterial slime buildup causes the paper machines to be shut down to perform boilouts. The boilouts are done to clean the bacterial slime buildup on the paper machines and can last up to 14 hours, resulting in 14 hours of lost production time. Each hour lost costs the paper manufacturer substantial amounts of money. The amounts were not specified in this particular trial and will vary from mill to mill, depending on the size of the mill, its production, the type of paper produced and other similar parameters.

The following is an example of how Nalco 7650 helped a Nalco customer achieve some financial gains during their production process.

Prior to Nalco 7650, treatment of the bacterial slime with non-oxidizing biocides was the only option open to a pulp and paper manufacturer located in the northeastern United States. Along with high doses of biocides, boilouts were performed weekly, losing up to 14 hours of production time with each cleaning. In spite of these measures, slime problems at the mill were to the point that 20% of the molded paper plates were unsatisfactory for sale and had to be re-pulped. As much as 80% of the system's broke was due to slime. Production losses were so great that the mill was on the verge of telling its customers it could not meet their orders.

In October of 1996, Nalco introduced Nalco 7650 with the following results:

- Nalco 7650 application prevented slime formation on the paper machines and reduced slime related broke from 70–80% to 0.1–0.2%.

- The application reduced the frequency of boilouts. Immediately prior to Nalco 7650 trial, boilouts were being performed weekly. After initiating the Nalco 7650 program, a boilout was not performed until 11 weeks into the trial, during the New Year's shutdown, although no slime had formed in the previously troublesome areas.

- By achieving high enough toxicities for a long enough period of time, some of the old slime deposits from inaccessible areas were slowly sloughed from the machine, providing an overall cleanup to the system.

- Oxidation of the system was achieved, showing peroxide residuals and high ORPs through all 32 machines.

- Good correlation was seen between cleanliness and product performance.

By reducing the frequency of boilouts, Nalco 7650 can reduce the amount of lost production that the paper mills normally incur and financial gains were possible.

6.6 Survey of alternatives (chemical and non-chemical)

Nalco 7650 has demonstrated improved biocidal effectiveness against typical paper industry microorganisms compared with other oxidizing chemicals. This serves to reduce machine deposits, improving system performance and decreasing the amount of slime related downtime. Nalco 7650 is effective over a wide range of pH, allowing for its effective use in a wide variety of industrial process water. Typical oxidizers used such as gaseous chlorine or sodium hypochlorite result in HOCL, which has reduced efficacy at low pH.

Nalco 7650 reacts more slowly than other oxidizing chemicals, resulting in greater persistence in systems processes and reduced impact on dyes, brighteners and sizing compared with the halogenated oxidizers.

Unlike typical oxidizing biocides, Nalco 7650 is not aggressive to machine fabrics or mill equipment. It may help mills to extend fabric life and reduce equipment corrosion by reducing the use of halogenated oxidizers. Comparison runs on machine felt samples between Nalco 7650, chlorine, hypochlorite, chlorine dioxide and activated bromine have shown that the Nalco 7650 will not adversely affect machine fabric. These tests showed the chlorine dioxide and activated bromine to be the most damaging, followed closely by chlorine and sodium hypochlorite. Nalco 7650 showed no felt damage even at 100 ppm.

Mills using chlorinated products can develop elevated levels of chloride ions in the machine system, which results in a more corrosive environment. Nalco 7650 does not contribute chloride ions to the system and therefore helps to minimize the corrosivity of the system.

Improved felt performance and reduced system corrosivity decrease the amount of maintenance downtime necessary, leading to increased productivity.

6.7 Conclusions and recommendations

The data submitted in support of the value of Nalco 7650 are adequate to allow the Agency to grant registration under the *Pest Control Products Act* to Nalco 7650 for use in the pulp and paper industry at the rates indicated on the label. Apply 0.1–2.7 kg (135–2700 g) of Nalco 7650 solution per tonne (dry basis) of pulp or paper produced. This will provide an application rate of 7–138 ppm of peroxyacetic acid and 29–586 ppm of hydrogen peroxide. Addition can be continuous or intermittent, depending upon the type of system and severity of the contamination. Treat to a residue level of 10 ppm peroxyacetic acid.

7.0 Toxic Substance Management Policy considerations

During the review of VigorOx™/Nalco 7650, the PMRA has taken into account the federal TSMP and has followed its Regulatory Directive Dir99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. It has been determined that VigorOx™/Nalco 7650 does not meet TSMP Track-1 criteria nor does it contain any by-products or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concern are not present in the raw materials nor are they generated during the manufacturing process.

8.0 Overall conclusion

The toxicology profiles of peracetic acid and hydrogen peroxide are considered. Both active ingredients are highly reactive, subject to rapid decomposition to water and oxygen upon contact with moisture; therefore, absorption, distribution, metabolism and excretion of peracetic acid and hydrogen peroxide would be negligible.

The occupational exposure to hydrogen peroxide and peracetic acid is expected to be intermittent and brief. The submitted acute data package as a whole indicates that VigorOx™/Nalco 7650 is corrosive and poses acute risk of eye damage and severe skin irritation to handlers. Mitigation against acute exposures through labelling is the most appropriate regulatory approach for these active ingredients. Specifically, the precautions proposed on the label, together with the recommended statement regarding measures to reduce exposure by the inhalation route, are considered adequate to protect workers against acute hazards.

Neither an ADI or an ARfD was determined, since no food use is proposed.

Under the proposed closed system use, the risks from exposure of terrestrial organisms to VigorOx™/Nalco 7650 would be minimal. As Nalco 7650 is intended for use in a closed system, environmental exposure would only be likely to occur during the clean-up operation, accidental discharge or spills. In addition, both peracetic acid and hydrogen peroxide decompose so readily that any such short term aquatic release is not expected to be of concern.

9.0 Proposed Regulatory Decision

The active ingredient peracetic acid, VigorOx™ and associated end-use product Nalco 7650, containing 5.1% peroxyacetic acid and 21.7% hydrogen peroxide for the control of typical paper industry microorganisms, have been given limited term registration for use in pulp and paper facilities for the control of slime and biofilm forming microorganisms and are proposed for full registration under Section 13 of the Pest Control Products Regulations. This proposed decision for full registration is open for comments.

List of Abbreviations

ADI	allowable daily intake
a.i.	active ingredient
ARfD	acute reference dose
DNA	deoxyribonucleic acid
EC_{50}	median effective concentration
EEC	expected environmental concentration
EPA	Environmental Protection Agency
IARC	International Agency for Research on Cancer
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
NIOSH	National Institute for Occupational Safety and Health
NOEC	no observed effect concentration
PCP	Pest Control Products
pH	$-\log_{10}$ hydrogen ion concentration
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
TSMP	Toxic Substances Management Policy
U.S.	United States

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Appendix I Summary of submitted acute toxicity studies for VigorOx™

Test	Toxicity			Label comments
	Dilute peracetic acid (17% peracetic acid)	Peracetic acid (0.15% use dilution)	35% hydrogen peroxide	
Acute oral toxicity	LD_{50} > 1000 mg/kg LD_{50} for females not determined (rat)	LD_{50} > 5000 mg/kg (rat)	LD_{50} = 1193 mg/kg (males) and 1270 mg/kg (females) Slightly toxic (rat)	Existing signal words of “Danger Poison” and symbol of octagon and skull and cross-bones are adequate
Acute dermal toxicity	LD_{50} > 200 mg/kg (rabbit)	LD_{50} > 2000 mg/kg (rat)	LD_{50} > 2000 mg/kg (rabbit)	
Acute inhalation toxicity	—	LC_{50} > 7.660 mg/L (equivalent total formulation) Low toxicity (rat)	—	
Primary dermal irritation	Corrosive (rabbit)	Non-irritating (rabbit)	Moderately irritating (rabbit)	Existing signal words of “Danger — Corrosive to Eyes and Skin” are adequate
Primary eye irritation	Severely irritating or corrosive (rabbit)	Mildly irritating (rabbit)	Severely irritating corrosive	
Dermal sensitization	Non-sensitizing (Guinea pig)			