Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note

REG2003-07

BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment containing Hydrogen Peroxide

The technical active ingredient hydrogen peroxide and the associated end-use product BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment (containing 27% hydrogen peroxide) for the control of Fusarium tuber rot, bacteria soft rot and silver scurf on potatoes before and during storage, have been granted temporary registration under Section 17 of the Pest Control Products (PCP) Regulations.

This Regulatory Note provides a summary of data reviewed and the rationale for the regulatory decision for these products.

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Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has issued temporary registrations for technical hydrogen peroxide and the associated end-use product (EP), BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment, manufactured by BioSafe Systems Inc., for the control of Fusarium tuber rot, bacteria soft rot and silver scurf on potatoes before and during storage. Hydrogen peroxide has previously been registered by the PMRA for non-food uses; however, this end-use product represents the first food use for this active ingredient (a.i.).

Hydrogen peroxide is an oxidizing agent that is rapidly transformed to water and oxygen.

Because the residues in or on stored potatoes are expected to be negligible, no maximum residue level (MRL) is recommended.

BioSafe Systems Inc. will be carrying out additional efficacy trials as a condition of temporary registration. Following the review of the resulting information, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

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1.0 The active substance, its properties and uses

1.1 Identity of the active substance and impurities

Table 1.1.1 Product identity: BioSafe M-70 Hydrogen Peroxide Technical

Trade name	M-70 Hydrogen Peroxide Technical
Other names	Hydrogen dioxide Hydrogen superoxide Hydrogen peroxide Peroxide
Common name	Hydrogen peroxide
IUPAC chemical name	Hydrogen dioxide
CAS number	7722-84-1
Structural formula	H-O-O-H
Molecular formula	H_2O_2
Molecular weight	34.01
Identity of relevant impurities of toxicological, environmental and other significance	None of the known impurities has been identified as being of toxicological significance. The technical grade hydrogen peroxide does not form any transformation product that meets the Toxic Substances Management Policy (TSMP) Track-1 criteria.

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

Table 1.2.1 Technical product: BioSafe M-70 Hydrogen Peroxide Technical

Property	Result	PMRA Comments
Colour	Colourless	
Physical state	Liquid	
Odour	Mildly pungent	
Melting point/range	Liquid	

Property	Result	PMRA Comments
Boiling point/range	% conc. Boiling point °C 10 102 45 108 50 114 70 125 90 141	
Density or specific gravity at 20°C	% conc. Density 10 1.034 45 1.113 50 1.195 70 1.228 90 1.367	
Water solubility	Miscible	
Solvent solubility	Miscible with many solvents	
Vapour pressure at 25°C	% Vapour pressure, mm Hg 20 1.07 35 1.13 50 1.19 60 1.24	High volatility, will volatilize in the environment
Dissociation constant (pK_a)	8.2	Molecule is neutral at pH<8.2 and anion at pH>8.2, in the environment
Octanol/water partition coefficient (K_{ow})	0.3	Low potential for bioaccumulation
UV/visible absorption spectrum (indicate conditions, if any)	Mixtures of H_2O_2 and peracetic acid absorb below 300 nm	Low potential for phototransformation

Property	Result	PMRA Comments
Stability (temperature, metals, sunlight)	Stable in high purity aluminum and 304/316 series stainless steel. A pure solution is at pH 3.5–4.5. Decomposition is highly exothermic and catalyzed by: transition metal ion, solid metals or metal oxides, pH 7 or greater, heat, sunlight. H_2O_2 is miscible with many low molecular weight alcohols, glycols and ketones, and concentrated aqueous solutions may become explosive with these solvents.	
Storage stability	Relatively stable in the dark in a clean inert container. Concentrated solutions are more stable. Stabilizers are added.	

Table 1.2.2 End-use product: BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment

Property	Result
Colour	Colourless
Physical state	Liquid
Odour	Similar to acetic acid
Formulation type	Liquid
Container material and description	10 L holding unit made of high density polyethylene
Density or specific gravity	1.091
pH	1.05
Oxidizing or reducing action	Strong oxidizer
Storage stability data	Relatively stable in the dark in a clean inert container. Concentrated solutions are more stable. Stabilizers are added.

Property	Result
Miscibility	This product is not to be diluted with petroleum solvents.

1.3 Details of uses

BioSafe OxiDate is a hydrogen peroxide based product (27% guarantee) that is currently registered in the United States (U.S.) for control of fungal and bacterial diseases on field and stored potatoes, as well as other vegetables. It is proposed for use in Canada on potato tubers to control fungal and bacterial diseases during storage. Disease claims include silver scurf, *Fusarium* tuber rot (dry rot) and bacterial soft rot. Applications are to be made at the rate of 1:100 (OxiDate:water), applied in two stages. In the first stage, tubers are treated as they enter the storage facility from the bin pilers. Secondly, OxiDate is applied to the tubers as a fine mist or atomized fog, delivered through the waters of humidification. Tubers are to be sprayed daily during the storage period.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

An analytical method based on titration was provided for the determination of the active substance. The method was assessed to be specific, precise, and accurate for use as an enforcement analytical method.

2.2 Method for formulation analysis

The same method was used as for the analysis of the active substance (Section 2.1).

2.3 Methods for residue analysis

Crop residue data were not required to support the use of BioSafe OxiDate Bactericide/Fungicide, containing hydrogen peroxide, for use on newly harvested potatoes before storage or as a direct injection into humidification water for post-harvest potatoes in storage, as residues of H_2O_2 are expected to be negligible. Therefore, methods for residue analysis of plants, plant products and food of animal origin (DACO 7.2) were not required. However, the U.S. Environmental Protection Agency (USEPA) has indicated that they have a method available (not validated) for access by interested parties.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

The registrant submitted waiver requests for all requested toxicity data. The Proposed Regulatory Decision Document (PRDD) 2000-02 and a review of hydrogen peroxide by ECETOC (Joint Assessment of Commodity Chemicals No. 22, Hydrogen Peroxide; European Centre for Ecotoxicology and Toxicology of Chemicals, 1993) were submitted. The Re-registration Eligibility Decision (RED) of Peroxy Compounds was provided, as well as exemptions from requirement of a tolerance for hydrogen peroxide from the Federal Register of the USEPA from 1998 and 1999 final rules.

The rapid degradation to water and oxygen upon contact with moisture makes absorption, distribution, metabolism and excretion of hydrogen peroxide negligible (PRDD2000-02).

At high doses, hydrogen peroxide is corrosive to the eyes and irritating to the skin and mucous membranes; however, residues are not expected to remain on crops after application of this product. Hydrogen peroxide is highly reactive and short-lived due to instability of the peroxide bond, which leads to rapid degradation and low residues of hydrogen peroxide expected after application.

The available literature indicates that hydrogen peroxide (35%) has slight toxicity by the acute oral route in rats (LD_{50} males 1193 mg/kg), has low dermal acute toxicity in rabbits (LD_{50}>2000 mg/kg), is moderately irritating to the skin and severely irritating or corrosive to the eyes (PRDD2000-02). Hydrogen peroxide is moderately toxic by the inhalation route in mice (LC_{LO} 227 μL/L) (RED on Peroxy Compounds by the USEPA).

ECETOC (1993) reported clinical signs from acute oral exposure to hydrogen peroxide included: tremors; decreased motility; prostration; oral, ocular and nasal discharge; reddened lungs; haemorrhagic and white stomachs; and blood-filled intestines. Symptoms after dermal exposure included lacrimation and nasal discharge, while exposure via inhalation resulted in severe pulmonary congestion and emphysema. Mild erythema and moderate to slight edema were observed at 24 hours and severe to moderate erythema and slight to very slight edema were seen at 48 hours after the dermal application of 35% hydrogen peroxide. In preliminary studies at concentrations of 15 and 30% hydrogen peroxide, epidermal necrosis was seen 24 hours after application, with marked epidermal hyperplasia and leukocytic infiltration seen within 6 days of application and the epidermis returning to normal by day 10.

Available literature on human exposure indicates that ingestion will cause irritation of the upper gastrointestinal tract. Decomposition of H_2O_2 results in rapid liberation of oxygen, leading to distension of the esophagus or stomach, and possibly severe damage and internal bleeding. Human exposure by inhalation may result in extreme irritation

and inflammation of nose, throat and respiratory tract; pulmonary edema, headache, dizziness, nausea, vomiting, diarrhea, irritability, insomnia, hyper-reflexia; or tremors, numbness of extremities, convulsions, unconsciousness and shock. Skin contact with hydrogen peroxide liquid will result in temporary whitening of the skin; if the contamination is not removed, erythema and vesicle formation may occur. Exposure to mist or spray may cause stinging and tearing of the eyes. Hydrogen peroxide contact with the eye can cause severe damage such as ulceration of the cornea; sometimes, though rarely, this may appear as long as a week after exposure (International Labour Office 1998).

Hydrogen peroxide is a known mutagen in vitro but is not genotoxic in vivo due to its rapid decomposition to water and oxygen (PRDD2000-02). Although the in vitro genotoxicity data would indicate that a genotoxic mechanism for tumour induction is feasible for hydrogen peroxide, the in vivo data suggests a non-genotoxic mechanism. Because only hydroxyl radicals and singlet oxygen are capable of damaging DNA directly, the genotoxic potential depends on the accessibility of the extremely reactive hydroxyl radical to its target DNA. Since the hydroxyl radical and singlet oxygen are short-lived, damage would be local to the area exposed. In vitro, the bacteria or other cells come into direct contact with hydrogen peroxide and genotoxic effects can be induced; in general, the addition of an exogenous metabolic agent or catalase reduces or abolishes the mutagenic response. In vivo, many factors contribute to the reduction of the bioavailability of H_2O_2 for systemic genotoxic action. The occurrence of genotoxic effects on cells that are in direct contact with H_2O_2 (at the site of application) cannot be excluded (ECETOC 1993).

Subchronic exposure of rats to 0.5–1.5% H_2O_2 produced extensive carious lesions and pathological changes in the peridontium, the intensity of the effect varying with the concentration. There was significant inhibition of body-weight gain (bwg). Seven out of twenty-four rats administered 1.5% H_2O_2 died during the experiment. A no observed effect level (NOEL) for subchronic administration of hydrogen peroxide to rats was determined to be 0.25% in drinking water based on the limited data that was available (ECETOC 1993).

Subchronic exposure of mice to 0.6% hydrogen peroxide in drinking water caused a depression in water consumption and a decrease in body weight gain (ECETOC 1993).

A twelve-week gavage study (5% solution), showed decreased body weight gain, hemoglobin concentration, erythrocyte count, blood corpuscular volume, serum SGOT, SGPT and alkaline phosphatase activity. Organ weight changes were also noted including increased kidney, liver and heart weights and decreased testes and adrenal weights; however, there was no correlating histopathological change.

Rabbits exposed for 6h/d, 5d/wk to 22 ppm (31 mg/m^3) of H_2O_2 vapour during a twelve-week inhalation study exhibited no change aside from bleaching of hair and some nasal irritation. No change was seen in the eyes following an ophthalmoscopic examination,

indicating that vapours did not produce delayed corneal damage. Two dogs exposed to 7 ppm (9.9 mg/m^3) for 6 months exhibited similar results. Hair bleaching and loss were seen after 14 weeks, and sneezing and lacrimation were observed after 23 weeks. There was no significant weight change or alteration in clinical chemistry or hematology. Pathological observation included hyperplasia of the bronchial musculature, collapsed and emphysematous areas in the lungs and thickening of the skin (hair follicles were not destroyed) (ECETOC 1993).

A thirteen-week drinking water toxicity study of hydrogen peroxide in catalase-deficient mice showed animals that received 3000 ppm had depressed water and food consumption and body weight. At 1000 ppm, females exhibited reduced water consumption with slight effects on food consumption, but not on body weight. Hydrogen peroxide administration did not produce any mortality, clinical sign, hematological effect or organ weight effect on brain, liver, kidneys, adrenals, testes, heart or spleen. Histological findings included mild to minimal duodenal mucosal hyperplasia in animals at 1000 and 3000 ppm. The effects were reversible during a 6-week recovery period. The NOELs determined in this study were 26 and 37 mg/kg bw/day for males and females, respectively (Weiner et al. 2000).

In rats, inhalation exposure to hydrogen peroxide (95 mg/m^3 for 30 exposures over 7 weeks), produced signs of nasal irritation and profuse nasal discharge after 2 weeks, and lung and tracheal congestion in all animals after 5 to 7 weeks. No significant microscopic change was found in the tissues. A subchronic inhalation study in mice showed similar toxic signs, but there was increased mortality in the mice.

Chronic exposure of mice to 0.15% H_2O_2 in drinking water produced pathological changes in the liver, kidney, gastro-intestinal tract and spleen with no effect on body weight gain (ECETOC 1993).

Chronic exposure of 0.4% hydrogen peroxide in drinking water to mice caused duodenal tumours, but both the International Agency for Research on Cancer (IARC) and the U.S. Food and Drug Administration (FDA) concluded there was limited or insufficient evidence of carcinogenicity (PRDD2000-02). When hydrogen peroxide was given to mice at 0.1 and 0.4% in drinking water for up to 740 days, a dose-dependent increased incidence of duodenal hyperplasia was noted in the treated groups (0.1% hydrogen peroxide) compared to controls, and the incidence of duodenal carcinomas was higher in female mice at 0.4% hydrogen peroxide compared to control animals. When 0.4% H_2O_2 was administered for six or seven months to female mice, an increased incidence of duodenal tumours was found in mice with low catalase activity (ECETOC, 1993).

Rabbits and rats administered hydrogen peroxide by gavage for 6 months showed decreased body weight and blood lymphocyte concentrations at the highest dose level (50mg/kg bw/day) and increased haemolysis and number of reticulocytes. Other effects included: decreased hepatic catalase activity; increased hepatic succinyl-dehydrogenase

activity; changes in enzyme activity of the stomach, duodenum and cerebrum; and albuminuria. Structural changes were observed in the gastro-intestinal mucosa and focal adiposis at autopsy.

Although details are lacking, the studies provided in the ECETOC report tend to show that hydrogen peroxide causes an inflammatory response in the gastro-duodenal tissue of mice. The inflammatory response is more severe in mice with low catalase activity. This inflammatory response may progress into carcinogenic changes in mice. Papillomas were induced in rats, with no malignant tumour of the fore-stomach seen, even at nearly lethal concentration (1–1.5%). Initiation-promotion studies suggest that it is not an initiator in skin, but may be a weak promoter of intestinal tumours in the rat at high concentrations on the skin or nearly lethal concentrations (1.5%) in drinking water.

The literature suggests that the chemistry of dilute hydrogen peroxide and the anatomy/ physiology of the gastrointestinal tract make it unlikely that orally ingested hydrogen peroxide would reach the duodenum. It also suggests that lesions in animals receiving H_2O_2 in their drinking water may result from decreased water consumption and ingestion of pelleted dry rodent chow (DeSesso et al. 2000).

The available literature was considered insufficient to allow for an adequate evaluation of reproductive toxicity or teratogenic potential. However, it was concluded that studies to evaluate the reproductive toxicity, teratogenicity, or neurotoxicity for hydrogen peroxide were not necessary in view of the rapid decomposition of the active substances to water and oxygen (PRDD2000-02). Hydrogen peroxide and its metabolites are unlikely to accumulate in mammalian organs or tissue long enough to exert significant effects on reproduction and development or induce neurotoxicity.

3.2 Determination of acceptable daily intake (ADI)

In considering the decomposition of hydrogen peroxide, since negligible risk to human health is expected from the ingestion of potatoes treated with hydrogen peroxide, an acceptable daily intake (ADI) is not required (PRDD2000-02). Hydrogen peroxide is used in a wide range of areas, including sanitizing solutions, food processing (sterilization and bleaching), medicines (dermal disinfectant and mouthwash) and cosmetics.

The USEPA has granted an exemption from the requirement of a tolerance for residues of H_2O_2 in or on all food commodities with an application rate of less than or equal to 1% hydrogen peroxide per application on growing and post-harvest crops (USEPA, 1999). This is because hydrogen peroxide degrades into water and oxygen. Decomposition is catalysed by the enzymes catalase and glutathione peroxidase, transition and solid metals, as well as heat and sunlight.

The IARC considers that there is limited evidence in experimental animals for carcinogenicity and considers that hydrogen peroxide is not classifiable regarding its carcinogenicity to humans (Group 3).

3.3 Acute reference dose (ARfD)

An acute reference dose was not established since hydrogen peroxide was considered unlikely to present an acute hazard from a dietary perspective because hydrogen peroxide degrades immediately to oxygen and water. The available literature suggests that there is no significant treatment-related effect to indicate a concern for acute dietary risk assessment.

3.4 Toxicological endpoint selection for occupational risk assessment

Acute toxicology endpoints are considered most appropriate for the occupational risk assessment because:

- hydrogen peroxide is highly reactive and subject to rapid decomposition to water and oxygen upon contact with moisture;
- occupational exposure is expected to be intermittent; and
- this compound is highly corrosive.

The PMRA concurs with the USEPA's assessment that peroxy compounds are corrosive and pose acute risk of severe eye and skin irritation to handlers (USEPA RED FACTS, Peroxy Compounds, December 1993). The corrosive nature alone of these compounds will preclude significant dermal exposure. Further, acute risk from exposure via the inhalation route must also be prevented.

3.5 Impact on human and animal health arising from exposure to the active substance or to its impurities

3.5.1 Operator exposure assessment

The end-use formulation, BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment, is proposed for use to control storage diseases while potatoes are in storage (Use site Category 12: Stored Food and Feed). Freshly harvested potatoes would be treated in one of two ways: sprayed with diluted product while passing along a conveyor belt, before being loaded into storage bins; or through the humidification water while in the storage bins. The 27% a.i. liquid formulation would be diluted and applied to freshly harvested potatoes before storage, or diluted and injected into the humidification water while in storage. Low occupational exposure would be expected. For potatoes being treated prior to storage, the application equipment is automated. The operator connects the lines to the application equipment and inserts the tubing into the 10 L product container. The system is essentially closed. Product is automatically diluted with water

and sprayed on the potatoes as they pass under a hood and along a conveyor belt. Potatoes automatically fill the storage bins.

There is potential for dermal and inhalation exposure while attaching and disconnecting the tubing from the product container, while levelling off the storage bins when full (arm), and from errant spray from the hooded conveyor belt. Incidental drips may occur when inserting the tubing from the application equipment into the BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment container and disconnecting the equipment.

It is the conclusion of the PMRA that mitigation against acute exposures through labelling is the most appropriate regulatory approach for this active ingredient. Specifically, the label must be modified to specify the following:

- Ensure that hydrogen peroxide air concentrations in the workplace do not exceed the exposure levels established by occupational health and safety authorities in your jurisdiction. If values are unknown, or exceed these levels, wear NIOSH-approved respiratory protection.

- Do not enter treated storage bins until hydrogen peroxide air concentrations are below exposure levels established by occupational health and safety authorities in your jurisdiction. If values are unknown, or exceed these levels, wear NIOSH-approved respiratory protection.

Together with 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 when used with appropriate personal protection.

4.0 Residues

4.1 Residue summary

Nature of the residue in plants
A potato metabolism study is not required, as catalase enzymes reported to be found in potatoes were likely to break down hydrogen peroxide to oxygen and water. Therefore, there is no residue of concern (ROC).

Nature of the residue in animals
Animal metabolism studies are not required since residues of hydrogen peroxide in or on stored potatoes are expected to be negligible. Therefore, no measurable residue of hydrogen peroxide is expected to transfer into animal matrices (meat and milk) when livestock are exposed to treated potato culls and processed potato waste.

Crop field trials
Supervised crop field trials (DACO 7.4.1) and residue decline studies (DACO 7.4.2) were not required. BioSafe OxiDate, having a low concentration of hydrogen peroxide, reacts on contact with the catalase enzymes in potatoes on which it is sprayed and degrades rapidly to oxygen and water. Therefore, residues in or on stored potatoes are expected to be negligible. Hence, no MRL is recommended for promulgation in Table II Division B.15.002(1) of the *Food and Drugs Act* and Regulations.

Processed food/feed
Processing studies (DACO 7.4.5) were not required as residues of hydrogen peroxide in and on treated potatoes are expected to be negligible.

Meat/milk/poultry/eggs
Residues of hydrogen peroxide in and on stored potatoes are expected to be negligible; therefore, when livestock are exposed to treated potato culls and processed potato waste, no measurable residue of hydrogen peroxide is expected to transfer into animal matrices (meat and milk).

Dietary risk assessment
An ADI has not been established by the Health Evaluation Division (HED). It is anticipated that the proposed domestic use of hydrogen peroxide on stored potatoes will not pose a risk to any segment of the population, including infants, children, adults and seniors, when potatoes are subjected to the normal process of washing, peeling and cooking for human consumption.

5.0 Fate and behaviour in the environment

BioSafe OxiDate is an indoor-use oxidizing agent for control of fungal and microbial diseases on potatoes. This use pattern will not result in the release of this product to the environment; therefore non-target organisms will not be exposed. An environmental assessment was not necessary. As a reference, hydrogen peroxide has been previously registered by the PMRA for outdoor use as a bleaching agent in pulp and paper production and a Proposed Regulatory Decision Document is available (*VigorOx*, PRDD2000-02, August 18, 2000).

6.0 Effects on non-target species

Data are not required.

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended uses

BioSafe OxiDate is a hydrogen peroxide based product (27% guarantee) that is currently registered in the U.S. for control of fungal and bacterial diseases of field and stored potatoes, as well as other vegetables. It is proposed for use in Canada on stored potato tubers to control: late blight, early blight, silver scurf, *Fusarium* tuber rot (dry rot) and bacterial soft rot. Applications are to be made at the rate of 1:100 (OxiDate:water), applied through the waters of humidification, and delivered to the tubers as a fine mist or atomized fog. Tubers are to be sprayed before they are placed in the storage bins, then treated daily for the remainder of the storage duration.

7.1.2 Mode of action

OxiDate is a peroxygen formulation, which combines hydrogen dioxide with peroxyacetic acid. The combination of these chemicals allows the hydrogen dioxide to become more active, forming a hydroxyl radical. When this hydroxyl radical comes in contact with a disease organism, it reacts with key enzymes and proteins found in the cell walls, especially those containing sulfhydryl groups. The result is a disruption of cellular respiration and cell death. The oxidizing process leads to the complete breakdown of the OxiDate molecules to produce oxygen, water and other inert elements. It is noted that this reaction occurs immediately on contact with the pathogens found on the surface of the tubers. OxiDate is not a systemic fungicide and will not kill pathogens found deep within the tissues of the tuber.

7.1.3 Effectiveness against pest

7.1.3.1 Description of pest problem

When potatoes are harvested, they may come in contact with fungal or bacterial pathogens found in the soil or in decaying plant tissues. Once the tubers are placed in a storage facility, these pathogens may grow and develop, significantly reducing the marketability of the tubers. In addition, if the diseases are allowed to develop, they become a source of inoculum for the next year's crop if it is used as seed tubers.

Disease: Early blight (*Alternaria solani*)
Early blight is most commonly found as a fungal disease of potato foliage; however, it can infect the tuber itself. Spores are commonly found in the soil and debris of infected fields, or can be transferred from active potato leaf or stem lesions. Physical transference of the spores to the tubers usually occurs during harvest, and the germinating spore usually enters the tuber through cuts, bruises, or surface wounds. Tuber lesions first appear as small, slightly dark and sunken areas that can be circular or

irregular, reaching up to 3/4 inch (19 mm) in diameter. Usually there is a well defined and somewhat raised margin between the infected and healthy tissues, and internally the lesion is expressed as a brown to black corky, dry rot. Lesions usually do not penetrate the tuber more than 1/4 to 3/8 inch (6.4 to 9.5 mm) deep. Once a lesion becomes established, it develops slowly during storage, and may not become severe until quite late in the storage period. Decay of the tuber tissues from early blight may also allow entry of secondary organisms, further damaging stored potatoes.

Disease: Late blight (*Phytophthora infestans*)
Late blight is a devastating disease of potato and can quickly infect above-ground plant tissues, as well as cause tuber rot in storage. If the fungal spores reach a growing tuber (washed down through exposed soil) before harvest, they can germinate and infect it, leading to partially decayed potatoes prior to harvest. Alternatively, during harvest, live spores may be transferred onto the tuber from infected plant tissues. These tubers may not initially display symptoms, but lesions may develop while in storage. Tuber late blight manifests as a shallow, coppery-brown to purple dry-rot that spreads irregularly through the outer ⅛ to ½ inch (3.2 to 12.7 mm) or more of tissue. The surface of the lesion appears brown, dry and sunken, but the skin beneath is granular in texture and tan to coppery-brown in colour. Storage under cool, dry conditions can slow the progress of the disease and little tuber-to-tuber spread of the disease will occur. However, if left to fully develop, the lesions quickly progress to become sunken and desiccated, infecting adjacent healthy tubers. Invasion of secondary fungal or bacterial pathogens into the tuber as a result of the late blight lesions is common, leading to a meltdown of the tubers while in storage.

Disease: Silver scurf (*Helminthosporium solani*)
Silver scurf is considered a seed-borne disease, as it does not manifest itself on the stems or foliage. Newly harvested tubers may appear healthy; however, if they are infected, the disease can be expressed within three to five weeks of storage. An infected tuber can spread spores (conidia) to healthy potatoes when tuber piles are handled or moved for shipping and grading, and released spores may also be spread to other piles via the air circulation system. Sporulation is retarded by cooler storage temperatures, but can still occur at 4°C, and is favoured by high humidity and free water on the tuber surface. The symptoms of silver scurf are mainly cosmetic, including irregular patterns of silvery-metallic discolouration of the periderm that can cover a large portion of the tuber surface. In addition, low tuber weight and shrinkage from water loss can occur. It is a disease that mainly affects the visual quality of the tubers and decreases the value of the crop at market.

Disease: *Fusarium* dry rot (*Fusarium solani* and *F. roseum*)
These *Fusarium* organisms are almost universally present in cultivated soils. Entry of the pathogens into the tuber occurs mainly through cuts or bruises (mechanical damage) in the tuber surface, or through wounds created by other organisms. The symptoms of *Fusarium* dry rot include sunken, wrinkled areas of firm, brown rot that can cover a large portion of the tuber surface. The infection can move deep into the tuber, creating

large pockets of decay. The development of *Fusarium* dry rot is retarded by low storage temperatures; however, if temperatures increase, the infection can continue to spread.

Disease: Bacterial soft rot (*Erwinia carotovora*)
The causative agent of bacterial soft rot (*Erwinia carotovora* var *carotovora*) is commonly found living freely in the soil. The bacteria are usually introduced to the tuber during harvest, handling, or washing and they enter via lenticels, cracks, or any injury. Symptoms begin at the surface of the tuber (usually near an eye) and progress inwards, producing rotted tissues that are wet and cream to tan in colour. Infected tissues are distinctly separated from healthy tissues by a dark brown to black margin. Shallow, necrotic spots on the surface are distinct, caused by the organism's entry through lenticels. In the early stages of decay there is no odour; however, as secondary organisms invade the infected tissues, a foul smell may develop. The disease develops under favourable conditions (adverse temperatures, mechanical damage and free water on the tuber surface), usually affecting tubers previously invaded by other diseases. Development of soft rot may not be apparent until later on in storage and can pass from tuber to tuber, infecting adjacent healthy potatoes.

7.1.3.2 Efficacy trials

Two studies were conducted to test the efficacy of BioSafe OxiDate on stored potatoes for silver scurf, *Fusarium* dry rot and bacterial soft rot. Data on tuber early blight and tuber late blight were not reviewed. The first study was a long-term (eight-month) trial conducted in 1998 in the U.S., which tested OxiDate at the rate of 1:100, applied daily for the entire trial. Disease incidence (DI) on tubers was assessed once every four weeks for silver scurf, *Fusarium* dry rot and bacterial soft rot. Tubers were not inoculated in this experiment; however, adequate disease pressures were evident. By month eight, disease pressures in the untreated check treatment reached 12% DI for silver scurf (peaking at 20% in month three), 20% for soft rot and 15% for *Fusarium* dry rot. Results suggest that by the end of the eight-month assessment period, OxiDate controlled the DI of silver scurf by 92.5–100%, soft rot by 64–100% and *Fusarium* tuber rot by 81–100%. Although the frequency of OxiDate application was greater than what is proposed, this trial was conducted under true storage conditions, using application equipment that would be used under normal operating conditions. Comments on how the extended use of OxiDate affected metal surfaces were not mentioned in this study. This trial demonstrated that good control of silver scurf, soft rot and *Fusarium* dry rot was achieved with daily applications of OxiDate at the rate of 1:100.

The second trial was conducted in 2001 in New Brunswick. BioSafe was tested at two rates, 1:50 and 1:100 over a storage period of four months. Percent disease severity (DS), the percentage of surface area covered with disease, was assessed after two weeks of daily applications, then every four weeks. Also assessed were tuber sprouting, glucose content, sucrose content and French fry colour. It is noted that the product was applied according to the proposed label directions, and tubers were inoculated

(separately) with silver scurf, *Fusarium* dry rot and soft rot pathogens. Results for each assessment date were presented as means for the two potato varieties (Shepody and Norland). The disease control levels for both BioSafe rates were lower than those found in the first trial.

i. Silver scurf

On the initial disease assessment date there was a large difference in % DS between the untreated check (UTC) (8%) and the two OxiDate treatments (16.3% for the 1:50 treatment and 17.6% for the 1:100 treatment). By the second assessment date, these differences were no longer apparent, as the disease had progressed rapidly on the UTC tubers. By the final assessment date, the UTC tubers reported 83.6% DS, 75.1% for the 1:100 OxiDate treatment and 67.6% for the 1:50 OxiDate treatment. While both OxiDate rates resulted in lower DS values compared to the UTC tubers, the differences among the three treatments were modest. For the 1:50 rate, percent disease control (relative to the UTC) ranged between 17 and 25%, while for the 1:100 rate, it was between 0 and 18.9%. Trends indicated that the 1:50 OxiDate rate provided slightly better disease control than the 1:100 rate. In general, BioSafe OxiDate provided low to moderate control of Silver Scurf for this trial, and both rates would be consistent with levels considered to be “disease suppression”.

ii. *Fusarium* dry rot

On the initial assessment date there was no difference in % DS for *Fusarium* dry rot between the two OxiDate rates and the check treatment. Disease pressures in the UTC steadily increased throughout the storage period, reaching a maximum of 18.6% by the final assessment date. Percent DS for OxiDate-treated potatoes for both rates demonstrated lower DS values compared to the UTC on each assessment date (values ranged from 37 to 59% for the 1:50 rate and 18.5 to 33% for the 1:100 rate). When the two OxiDate rates were compared, there was a consistent trend of lower % DS values for the 1:50 rate; however, these differences were not strong. By the final assessment date, OxiDate at the 1:50 rate was assessed at 10.2% DS (45% disease control over the UTC) and at the 1:100 rate was 12.5% DS (32% disease control over the UTC). These results demonstrate that BioSafe OxiDate at both rates provided moderate control of *Fusarium* dry rot on stored potatoes when used according to the product directions

iii. Bacterial soft rot

The disease pressures for soft rot were very low for the duration of the trial, despite inoculation of the tubers with the pathogen. For the first two assessments, there was no sign of tuber infection in any of the treatments. On the third assessment date soft rot had appeared in the UTC and the 1:100 rate treatments, although there was less than 1% DS for each. For the last assessment, DS values had reached 2.68% in the UTC, 1.74% in the 1:100 treatment and 0.33% in the 1:50 treatment. Again, trends indicated that the 1:50 OxiDate rate provided better disease control levels than the 1:100 rate. The disease

pressures in this trial were too low to accurately assess the level of disease control for the two rates, although the 1:50 rate appeared to delay the appearance of the disease more than the 1:100 rate. It is unknown whether similar levels of disease control would be found under conditions of high disease pressures.

7.2 Economics

Not assessed.

7.3 Sustainability

7.3.1 Survey of alternatives (chemical and non-chemical)

Currently, no product is registered for use against fungal or bacterial diseases of stored potatoes.

7.3.2 Compatibility with current management practices, including integrated pest management

Not assessed.

7.3.3 Contribution to risk reduction

Currently, no product is registered for control of fungal or bacterial pathogens on stored potato tubers. Introducing a new product that could reduce the source of disease inoculum on seed tubers would lead to a reduced need for fungicides once the tubers are planted in the field.

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

Data were not provided on this. Because OxiDate kills pathogens on contact, then quickly breaks down, it is unlikely to lead to resistance development in pathogen population. At this time FRAC (the Fungicide Resistance Action Committee) has not determined the Fungicide Group that hydrogen peroxide falls into, and has not made specific resistance management recommendations.

7.4 Phytotoxicity to target plants

No phytotoxic symptom nor product residue was noted on tubers treated with OxiDate.

7.5 Observations on undesirable or unintentional side effects (non-target effects)

In the second trial, the effects of BioSafe OxiDate on tuber sprouting, sucrose levels, glucose levels and French fry colour were assessed. OxiDate was demonstrated to have

no inhibiting effects on tuber sprouting. In addition, although differences between treatments were apparent for the number of sprouts per tuber, there was no consistent trend associated with the OxiDate rate used. It must be noted that neither of the trials tested for adverse interactive effects of OxiDate and growth inhibitors (e.g., Chlorpropham) that are commonly used in commercial storage facilities to inhibit tuber sprouting. The more concentrated rate (1:50) produced longer sprouts but this was not quantified. While differences among treatments occurred, the reported values for glucose and sucrose content were within acceptable ranges. In addition, tubers treated with the 1:100 OxiDate rate had a slightly lighter French fry colour, which is desirable for the French fry industry.

The second study stated that BioSafe OxiDate had a corrosive effect on metal objects that came in direct contact with it. This suggests potential for damage to any metal machinery that delivers OxiDate via the waters of humidification, or to the metal fasteners commonly found on wooden storage bins that will be subjected to OxiDate. A warning should be added to the label to indicate to the user the product's potential corrosive nature to metal objects. Further trials should be conducted to clarify the extent of corrosion associated with daily applications of OxiDate.

7.6 Conclusions

Based on the submitted efficacy data, the use of BioSafe OxiDate on stored tubers to control silver scurf, *Fusarium* dry rot and bacterial soft rot can be supported if applied on a daily basis at the rate of 1:100, until a growth regulator (e.g., Chlorpropham) is applied. If a growth regulator is applied, OxiDate applications must be discontinued for the remainder of the storage period (see Table 7.6.1). Further studies are required to test for any adverse interactive effect of OxiDate and growth inhibitors on tuber sprouting. Data were not provided to support the claims of control of tuber early blight or late blight. OxiDate, when applied at the diluted application rate of 1:100, appears to have a corrosive effect on metal objects. The extent of this corrosion is unknown and further trials should determine the extent of the corrosion and the potential damage to application machinery or storage bin fasteners.

7.6.1 Summary

Table 7.6.1 Supported label claims (based on efficacy assessment)

Pest claims	Controls silver scurf, *Fusarium* dry rot and bacterial soft rot on stored potato tubers.
Product rate	Apply to tubers as they enter the storage facility, followed by daily applications at the dilution rate of 1:100 (OxiDate:water).

Application method	Apply the diluted OxiDate through the waters of humidification. The product will be delivered to the tubers as a fine mist or atomized fog. Apply for at least 20 min per day, based on a humidification airflow rate of 0.6 cfm. BioSafe test strips should be placed periodically around the tubers to determine if a longer application period is needed. Apply OxiDate daily until a growth regulator is applied, then discontinue OxiDate use. If a growth regulator is not used on the stored tubers, then OxiDate can continue to be applied for the remainder of the storage period.
Resistance management	No specific action is recommended at this time.

8.0 Toxic Substances Management Policy (TSMP) considerations

Active ingredient
BioSafe OxiDate contains the active ingredient hydrogen peroxide, which is rapidly transformed to water and oxygen; therefore, environmental exposure, persistence and bioaccumulation are not of concern. On this basis, the PMRA concluded that BioSafe OxiDate does not meet the criteria for Track-1 classification under the TSMP.

Refer to Regulatory Directive DIR99-03, *The PMRA's Strategy for Implementing the Toxic Substances Management Policy*, March 12, 1999.

Microcontaminants
The technical active ingredient does not contain any impurity that is known to meet the criteria for Track-1 classification under the TSMP.

9.0 Regulatory decision

Technical hydrogen peroxide and the end-use product BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment have been granted temporary registration for the control of *Fusarium* tuber rot, bacteria soft rot and silver scurf on potatoes before and during storage, under Section 17 of the PCP Regulations, subject to the generation of the following studies:

- Laboratory trial to determine the interactive effects of end-use product on tubers treated with growth inhibitors (at label rates) with regard to tuber sprouting.
- Small-scale efficacy trial in a commercial potato storage facility and potential for adverse effects e.g., corrosion of equipment/machinery.

List of abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
bwg	body-weight gain
CAS	Chemical Abstracts Service
d	day(s)
DACO	data code
DI	disease incidence
DNA	deoxyribonucleic acid
DS	disease severity
ECETOC	European Centre for Ecotoxicology of Chemicals
FDA	Food and Drug Administration (U.S.)
FDA	*Food and Drugs Act* (Canada)
FRAC	Fungicide Resistance Action Committee
h	hour(s)
Hb	hemoglobin
HED	Health Evaluation Division
IARC	International Agency for Research on Cancer
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
LD_{50}	median lethal dose
LC_{LO}	lethal concentration, low
mg	milligram
mm	millimetre
MRL	maximum residue level
NIOSH	National Institute for Occupational Safety and Health
NOEL	No observable effect level
PMRA	Pest Management Regulatory Agency (Health Canada)
ppm	parts per million
PRDD	Proposed Regulatory Decision Document
RED	Reregistration Eligibility Document
ROC	residue of concern
SGOT	Serum aspartate amino-transferase
SGPT	Serum alanine amino-transferase
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
U.S.	United States (of America)
UTC	untreated check
UV	ultraviolet
µg	microgram
µL	micro litre
USEPA	Environmental Protection Agency

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