UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OCT 19 1998

MEMORANDUM

SUBJECT: **A "Me TOO" Registration of Oxidate Broad Spectrum Algicide/Fungicide® (EPA File Symbol No. 070299-E) Containing 27.18% Hydrogen Peroxide as its Active Ingredient and A Pesticide Petition (PP# 8F4996) for an Exemption from the Requirement of a Tolerance for Residues of Hydrogen Peroxide in or on all Food Commodities: Chemical Nos. 000595; Case No. 062477: Review of Product Chemistry and Toxicology Studies. MRID Nos. 443402-01, 443142-01, 441160-01, -02, -03, -04, and -05; Submission No.: S547816; DP Barcode: D249870**

FROM: **Freshteh Toghrol, Ph.D., Senior Chemist** F. Toghrol
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511W)

TO: **Anne Ball, Regulatory Action Leader**
Microbial Pesticides Branch
Biopesticides & Pollution Prevention Division (7511W)

ACTION REQUESTED:

BioSafe Systems Inc., submits a petition (PP# 8F4996) and requests an exemption from the requirement of a tolerance for residues of Hydrogen Peroxide in or on all food commodities, when applied as a pesticide to growing agricultural crops. Additionally, the registrant requests a "Me Too" registration for registration of an end-use product Oxidate Broad Spectrum Algicide/Fungicide® (EPA File Symbol No. 070299-E) Containing 27.18% Hydrogen Peroxide (H_2O_2)as its active ingredient. The end-use product will be used as a food use bactericide/algicide/ fungicide on growing food commodities (beans, broccoli, cauliflower, cabbage, cucurbits, onions, peppers, potatoes (including seed potatoes), tomatoes, apples, filberts, bananas, grapes, peaches, plums, cherries, nectarines, and prunes. To support this registration, the registrant has referenced product chemistry and toxicological studies MRID Nos. 443402-01, 443142-01, 441160-01, -02, -03, -04, and -05.

7. The registrant also submitted toxicity information indicating that this level of hydrogen peroxide has no adverse effects on groundwater or human health. Additionally, hydrogen peroxide is considered as GRAS by FDA 21 CFR §184.1366, and is used at concentrations of 0.04% in whey processing and 0.05% in cheese making. The FDA also permits the use of Hydrogen peroxide as a food additive, in toothpaste, or in mouthwash. Since the end-use product is a food use product and contains 0.5% hydrogen peroxide at the time of application, it should not have an adverse effect on humans or the environment.

8. There is also an exemption from the requirement of a tolerance for residues of Hydrogen peroxide up to 120 PPM in or on raw agricultural commodities (fruits, tree nuts, cereal grains, herb, and spices)and in processed commodities when applied as antimicrobial agent (see Federal Register: May 6, 1998 Volume 63, No. 87; this Final Rule is to amend 40 CFR 180 Section 180.1197).

9. The registrant Biosafe Systems has submitted a petition for hydrogen peroxide tolerance exemption (PP# 8F4996). BPB has no objection to this tolerance exemption, to be read as follows: An exemption from the requirement of a tolerance for residues of hydrogen peroxide in or on all food commodities, when applied as an Algicide, Fungicide, and bactericide at the rate of ≤1% Hydrogen peroxide per application on growing crops.

10. The Agency has concluded that no apparent acute toxicity and subchronic toxicity endpoints exist to suggest a significant toxicity for the proposed food use. A RfD (chronic toxicity) for hydrogen peroxide has not been estimated because of its short half life and lack of any residues of toxicological concern (see FR 180.1197 May 6, 1998 Volume 63 No. 87 pages 24955-24963 and Reregistration Eligibility Decision (RED dated December 1993)for Peroxy Compounds (including Hydrogen peroxide).

11a. BPB previously granted data waivers for avian acute oral and acute dietary toxicity studies based on the registrant's representation that "... no direct environmental exposure to birds is expected to occur." Although there is a potential for exposure to birds when the end-use product is applied (in aqueous solution) to the outdoor sites listed on the proposed label (turf and outdoor ornamental plants, shrubs and trees, hydrogen peroxide will react on contact with the surface on which it is sprayed and rapidly degrade to oxygen and water (See memo by Russell S. Jones to Anne Ball, dated 1/29/98).

11b. The proposed label for Oxidate (EPA Symbol No. 070299-E) also contains the following statements: Keep out of lakes, ponds and streams. This product is toxic to birds and fish. Do not apply directly to water. This product is highly toxic to bees and other beneficial insects exposed to direct contact on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds while bees are actively visiting the treatment area. Do not apply this product or allow it to drift to crops where beneficial insects

[redacted] part of an integrated pest management strategy.

11c. Based on the conclusions above (11a and 11b), BPB supports the registration of the end-use product Oxidate (EPA Symbol No. 070299-E), containing 27.18% hydrogen peroxide as its active ingredient. Additionally, BPB has no objection to the establishment of an exemption from the requirement of a tolerance for hydrogen peroxide to be used in or on all food commodities.

Note To RAL

Please note that the registrant has miscalculated the amount of hydrogen peroxide in the product at the time of application in the Notice of filing, as 0.25 - 1.5 (also see the conclusion 4 above).

SUMMARY OF CHEMISTRY DATA

(151-10) Product Identity: MRID 441160-01

Hydrogen peroxide (CAS No. 7722-84-1), empirical formula H_2O_2 is the active ingredient. The manufacturer of hydrogen peroxide is [redacted] The end-use product is used as an algicide/fungicide/bactericide. There is a Reregistration Eligibility Decision (RED dated December 1993)for Peroxy Compounds (including Hydrogen peroxide), in which hydrogen peroxide is used as an indoor pesticide.

The registrant submitted information regarding product identity and disclosure of ingredients for the end-use product (MRID 441160-01). The data are identical to the registered non-food end-use product contains 27.18% hydrogen peroxide. At the time of application, the end-use product will be diluted with water (1:50,1:100, and 1:300), and the level of hydrogen peroxide will not exceed 0.54%.

CHEMICAL AND PHYSICAL PROPERTIES (63-1 through 21) MRID 441160-01 & -02

Guideline	Type of Data	Description
63-2	Color	Colorless
63-3	Physical state	Liquid
63-4	Odor	Moderately pungent
63-5	Melting point	N/A for end-use product
63-6	Boiling point	100 °C/ N/A for end-use product
63-7	Specific gravity	1.091 at 22°C
63-8	Solubility	Soluble in water
63-9	Vapor pressure	N/A for end-use product
63-10	Dissociation constant	N/A for end-use product
63-11	Octanol/water partition	N/A for end-use product
63-12	pH	1.05 at 25°C
63-13	Stability	N/A for end-use product
63-14	Oxidizing or reducing	strong oxidizing agent
63-15	Flammability	Non-flammable
63-16	Explodability	Not explosive
63-17	Storage	stability unstable at 50°C for 30 days
63-18	Viscosity	0.78 cs. at 22°C
63-19	Miscibility	N/A
63-20	Corrosion characteristics	Moderately corrosive
63-21	Dielectric breakdown	N/A: Not for use in, on, or around voltage

BPPD's Comments

All necessary information was submitted and was appropriate.

SUMMARY OF TOXICITY DATA

While the end-use product at the time of application only contains 0.5% hydrogen peroxide, the registrant has submitted toxicology information from open literature for solutions containing a range of concentrations of hydrogen peroxide. The studies demonstrate that hydrogen peroxide is toxic at high levels, but that a 0.5% concentration has no negative impact on human skin, eyes, and respiratory systems. However, since the pH of the end-use product is 1.05, BPPD will assume toxicity category I for skin and eye irritation. Therefore, the proposed label language "corrosive" for concentrated end-use product, which causes eye and skin damage or irritation is acceptable.

Results of Studies Using Lower Levels of Hydrogen Peroxide

The registrant submitted toxicology information from open literature demonstrating that solutions containing 6% hydrogen peroxide have an acute oral LD_{50} => 5000 mg/kg in rats (toxicity category III), an acute dermal LD_{50} => 10000 mg/kg in rabbits (toxicity category IV), and an inhalation LC_{50} of 4 mg/l (toxicity category IV). Such solutions are mild irritants to rabbit skin and cause severe irreversible corneal injury in half of the exposed rabbits (toxicity category I). Since the level of hydrogen peroxide in Zero Tolerance® will be 0.5%, which is much less than 6%, the level of toxicity of this product will be even lower than the levels submitted by the registrant.

Results of Studies Using Higher Levels of Hydrogen Peroxide

The registrant also submitted toxicology information from open literature demonstrating that solutions containing 50% hydrogen peroxide have an acute oral LD_{50} => 500 mg/kg in rats (toxicity category II), an acute dermal LD_{50} => 1000 mg/kg in rabbits (toxicity category II). No deaths resulted after an 8-hour exposure of rats to saturated vapors of 90% hydrogen peroxide LC_{50} = 4 mg/l (2000 PPM). Solutions containing 50% hydrogen peroxide are also extremely irritating (corrosive) to rabbit eyes (toxicity category I), with a maximum primary dermal irritation in rabbits (toxicity category I). Weak direct mutagenicity responses were seen for hydrogen peroxide in Ames tests with *Salmonella typhimurium* strains TA97, TA98, TA102, and TA1537, in a 20-minute preincubation test with strains TA97, TA98, TA100, TA102, TA1537, and TA1538, and in a liquid incubation modification using strain TA1537. Additional information regarding immunotoxicity, developmental toxicity, and chronic toxicity (at various concentrations of hydrogen peroxide) was submitted from the open literature.

The Agency has concluded that for the propose food use no apparent acute toxicity and subchronic toxicity end point exist to suggest a significant toxicity. A RfD (chronic toxicity) for hydrogen peroxide has not been estimated because of its short half life and lack of any residues.of toxicological concern. Additionally, Hydrogen peroxide is generally recognized as safe (GRAS) by FDA, it meets the Food Chemicals Codex and is used at 0.05% in milk and 0.04% in whey 0.15% in starch and corn syrup, and 1.25% emulsifiers containing fatty acid esters as bleaching agent 21 CFR 180. 1336. Also as sanitizing solution for use on food processing equipment and in sterilizing polymeric food-contact surface 21 CFR 178.1010 and it is used in washing or assist in the lye peeling of fruits and vegetable (21 CFR 173.315).

There is also an exemption from the requirement of a tolerance for residues of Hydrogen peroxide up to 120 PPM in or on raw agricultural commodities (fruits, tree nuts, cereal grains, herb, and spices)and in processed commodities when applied as antimicrobial agent (see Federal Register: May 6, 1998 Volume 63, No. 87; this Final Rule is to amend 40 CFR 180 Section 180.1197).

CONFIDENTIAL APPENDIX

PRODUCT CHEMISTRY

Guideline 151-10: Product Identity

The active ingredients in the product are 27.18% hydrogen peroxide H_2O_2 , is also known as hydrogen dioxide.

Guideline No. 151-11: Manufacturing Process

The active ingredient is commercially available from suppliers (the registrant obtained its supply of [redacted] and hydrogen peroxide from [redacted]). Additionally, the manufacturing process of both these compounds is well known and can be found in the open literature.

Formulation:

Name	Purpose In formulation	Formulation
[redacted] hydrogen peroxide Final concentration in the formulation	Active ingredient	[redacted] 27.18%
% inert ingredient		
[redacted]		

PRODUCT INGREDIENT SOURCE INFORMATION IS NOT INCLUDED

INERT INGREDIENT INFORMATION IS NOT INCLUDED

BPPD's Comment: The submitted information satisfy the requirements of 40 CFR 158.690 (Guideline No. 151-11).

Guideline Nos. 151-13 and 151-15: Analysis of Samples and Certification of Ingredient Limits

The hydrogen peroxide content of each end-use product sample was determined using the titration method. The product was diluted 100 times, and 20 ml of the diluted product was mixed with 20 ml of diluted sulfuric acid (1:15). The mixture was titrated with 0.1 N potassium permanganate, until the solution demonstrated a persistent pink color for 15 seconds. Analysis of five batches of this solution demonstrated.

The registrant has also submitted a CSF (dated 7/7/98) for the end-use product.

Guideline No. 151-16: Analytical Method

The titration method was used to determine the percentage of hydrogen peroxide present in the end-use product. This method is acceptable.

BPPD's Comment: The submitted information regarding the analytical method satisfies the requirements of 40 CFR 158.690 (Guideline No. 151-16).

c: Ftoghrol, A.Ball, BPPD Subject File
. Toghrol; BPPD; CM2-902; Tel: 703-308-7014; 10/16/98