UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

April 3, 2006

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 58779-4, VAPROX® Hydrogen Peroxide Sterilant; DP Barcode: 321541

From: Tajah L. Blackburn, Ph.D., Microbiologist 4/3/06
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Thru: Nancy Whyte, Team Leader
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)
April 3, 2006

To: Marshall Swindell PM 33/Karen Leavy-Munk
Regulatory Management Branch I
Antimicrobials Division (7510C)

Applicant: Steris Corporation
PO Box 147
St. Louis, MO 63166-0147

Formulations from Label:

Active Ingredient(s)	% by wt.
Hydrogen Peroxide.....	35%
Inert Ingredients.....	65%
Total	100%

I BACKGROUND

The product, VAPROX® Hydrogen Peroxide Sterilant (EPA Reg. No. 58779-4), is a registered sterilant for use in industrial environments. The product is to be used only by trained personnel with STERIS Vaporized Hydrogen Peroxide (VHP) application equipment. The applicant requested an amendment to the registration of this product to include applications for sealed enclosures and emergency vehicles in commercial, industrial, and institutional environments. Product labeling now includes a "package insert," which will accompany the container label. Studies were conducted at STERIS Corporation, located at 5960 Heisley Road in Mentor, OH 44060.

This data package contained a letter from the applicant to EPA (dated August 24, 2005), a printed copy of an email message from EPA to the applicant (dated August 19, 2005), EPA Form 8570-4 (Confidential Statement of Formula), four studies (MRID Nos. 466317-01 through 466317-04), Statements of No Data Confidentiality Claims for all four studies, the proposed label, the proposed package insert, and the last accepted label (dated May 19, 2000).

Note: EPA Form 8570-4 (Confidential Statement of Formula) contains Confidential Business Information. Data or information claimed by the applicant to be FIFRA confidential has not been included in this report.

II USE DIRECTIONS

The product is designed for use in sterilizing porous and non-porous surfaces in sealed, dry, pre-cleaned enclosures. Such enclosures might include clean rooms, laboratories, animal research facilities, patient rooms, hotel rooms, offices, cruise ships, recreational facilities, and emergency response vehicles. The proposed label states that the product must be used in STERIS VHP application equipment only. The product is to be applied only by trained personnel. The package insert for the product provides the following directions regarding enclosure preparation and treatment: Remove gross filth and visible soil. Wash soiled surfaces with a compatible detergent. Rinse with potable water. Allow to air dry. Position or connect the VHP application equipment. Seal the enclosure by closing and sealing windows and doors and turning off ventilation systems. Monitor areas adjacent to the enclosure for hydrogen peroxide levels. Reduce the humidity in the enclosure. Inject the product, and maintain the flow of product at a level that maintains the target VHP concentration. Stop injection of the product, and allow the flow of air to reduce VHP concentration to a safe level. Remove sealing materials. Disconnect and remove VHP application equipment. Turn on ventilation systems.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Determination of Initial Decimal Reduction Values (i.e., D-values)

Initial D-values correspond to the time required to achieve a 1-log reduction of test spores. These calculated D-values may then be used to establish theoretical contact times for achieving a 10^6 log reduction. Testing of a sterilant may be conducted according to an EPA-approved protocol such as, "Decimal Reduction Values (D-values)

of *Geobacillus stearothermophilus* Spores Treated with 250 ppm Vaporized Hydrogen Peroxide (VHP®)." In this procedure, plate count data are obtained, a survivor curve is plotted, and D-values are determined by linear regression. Only data falling in the linear region of inactivation on the survivor curve should be evaluated. Populations within 0.5 log of the initial population should be eliminated from the linear regression analysis. Time points demonstrating growth beyond the first zero CFU count may be excluded from analysis. The correlation coefficient of the regression line should lie within the range of 0.8-1.0. See also ASTM E1891-97, Standard Guide for Determination of a Survival Curve for Antimicrobial Agents Against Selected Microorganisms and Calculation of a D-Value and Concentration Coefficient.

Sterilants for Porous and Non-Porous Surfaces Within Sealed Enclosures and Vehicles (for Bacterial Spores Known to be Highly Resistant to Sterilants and Disinfectants)

The effectiveness of a sterilant within a sealed enclosure or vehicle may be supported by efficacy data from in-use testing (i.e., field testing) conducted according to an EPA-approved protocol such as "End-Use Protocol for Sterilization of Porous and Non-Porous Surfaces within Sealed Enclosures Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology" or "End-Use Protocol for Sterilization of Porous and Non-Porous Surfaces within Emergency Vehicle Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology." Biological Indicators (BIs) must show no growth for the marker organism after 7 days at 55°C. Chemical indicators must show a qualitative color change indicative of hydrogen peroxide exposure. The hydrogen peroxide concentration in the spaces adjacent to the enclosure exterior or vehicle exterior must remain below 1 ppm during the sterilization cycle. Parameters for product application (i.e., temperature, relative humidity, vaporized hydrogen peroxide concentration, contact time) must be met for all four phases of the sterilization cycle.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 466317-01 "Decimal Reduction Values (D-values) of *Geobacillus stearothermophilus* Spores Treated with 250 ppm Vaporized Hydrogen Peroxide (VHP®)" for VAPROX, by Christopher W. Fisher. Study conducted at STERIS Corporation. Study completion date – July 25, 2005. Study Number 05-009.

This study was conducted against *Geobacillus stearothermophilus* spores (ATCC 7953). One lot (Lot No. PE124D) of the product, VAPROX® Hydrogen Peroxide Sterilant, was tested according to EPA-approved Protocol 05-009, "Decimal Reduction Values (D-values) of *Geobacillus stearothermophilus* Spores Treated with 250 ppm Vaporized Hydrogen Peroxide (VHP®)," dated May 2005 (copy provided). The product was tested at a concentration of 250±10% ppm at 20±5°C. No organic load was used in testing. Testing was conducted in triplicate for the following exposure times: 0, 5, 10, 15, 20, 25, and 30 minutes. The emergency vehicle used in the test was a standard U.S. style ambulance, complete with chair, bench, and cabinetry. The inside volume of the vehicle was approximately 13 m^3. Biological indicators (BIs) were prepared by depositing spores of the challenge organism onto stainless steel coupons. The coupons then were packaged into individual Tyvek pouches. The STERIS VHP 1000ED Generation System was attached to ports on the back of the vehicle. The interior of the emergency vehicle was dehumidified to achieve a ≤60% relative humidity

(dehumidification phase). Next, the product was vaporized and injected into the emergency vehicle at a rate sufficient to reach and maintain the 250±10% ppm target concentration (conditioning phase). At this point, the BIs were clipped to a rod and placed into the patient area of the emergency vehicle. The concentration of the vaporized product was maintained at 250 ppm (sterilization phase) and the BIs were exposed to the product for various exposure times (i.e., 0, 5, 10, 15, 20, 25, and 30 minutes) at 20±5°C. Finally, the hydrogen peroxide concentration was lowered to ≤1 ppm (aeration phase). After the exposure time, the BIs were removed from the emergency vehicle and transferred from the Tyvek pouches to tubes containing 10 ml of Tryptic Soy Broth with 0.05% sodium thiosulfate (TSB-N) to neutralize. Each tube was sonicated for 10 minutes and then vortexed for 5 seconds. Ten-fold serial dilutions were performed in sterile deionized water. Aliquots of the dilutions were placed into Petri dishes in triplicate and mixed with melted Tryptic Soy Agar. The plates were allowed to solidify at room temperature. The plates then were incubated at 55°C for 48 hours and enumerated. A survivor curve was plotted. D-values (where D = -1/slope) were determined. Controls included those for initial BI spore population, viability, sterility, and neutralization.

2. MRID 466317-02 "Decimal Reduction Values (D-values) of *Geobacillus stearothermophilus* Spores Treated with 400 ppm Vaporized Hydrogen Peroxide (VHP®)" for VAPROX, by Christopher W. Fisher. Study conducted at STERIS Corporation. Study completion date – July 25, 2005. Study Number 05-007.

This study was conducted against *Geobacillus stearothermophilus* spores (ATCC 7953). One lot (Lot No. PE124D) of the product, VAPROX® Hydrogen Peroxide Sterilant, was tested according to EPA-approved Protocol 05-007, "Decimal Reduction Values (D-values) of *Geobacillus stearothermophilus* Spores Treated with 400 ppm Vaporized Hydrogen Peroxide (VHP®)," dated April 2005 (copy provided). The product was tested at a concentration of 400±10% ppm at 20±5°C. No organic load was used in testing. Testing was conducted in triplicate for the following exposure times: 0, 2, 4, 6, 8, 10, 12, and 14 minutes. The emergency vehicle used in the test was a standard U.S. style ambulance, complete with chair, bench, and cabinetry. The inside volume of the vehicle was approximately 13 m^3. Biological indicators (BIs) were prepared by depositing spores of the challenge organism onto stainless steel coupons. The coupons then were packaged into individual Tyvek pouches. The STERIS VHP 1000ED Generation System was attached to ports on the back of the emergency vehicle. The interior of the emergency vehicle was dehumidified to achieve a ≤60% relative humidity (dehumidification phase). Next, the product was vaporized and injected into the emergency vehicle at a rate sufficient to reach and maintain the 400±10% ppm target concentration (conditioning phase). At this point, the BIs were clipped to a rod and placed into the patient area of the emergency vehicle. The concentration of the vaporized product was maintained at 400 ppm (sterilization phase) and the BIs were exposed to the product for various exposure times (i.e., 0, 2, 4, 6, 8, 10, 12, and 14 minutes) at 20±5°C. Finally, the hydrogen peroxide concentration was lowered to ≤1 ppm (aeration phase). After the exposure time, the BIs were removed from the emergency vehicle and immediately, aseptically transferred from the Tyvek pouches to tubes containing 10 ml of Tryptic Soy Broth with 0.05% sodium thiosulfate (TSB-N) to neutralize. Each tube was sonicated for 10 minutes and then vortexed for 5 seconds. Ten-fold serial dilutions were performed in sterile deionized water. Aliquots of the

dilutions were placed into Petri dishes in triplicate and mixed with melted Tryptic Soy Agar. The plates were allowed to solidify at room temperature. The plates then were incubated at 55°C for 48 hours and enumerated. A survivor curve was plotted. D-values (where D = -1/slope) were determined. Controls included those for initial BI spore population, viability, sterility, and neutralization.

3. MRID 466317-03 "Sterilization of Porous and Non-Porous Surfaces within Sealed Enclosures Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology, Test Organism: *Geobacillus stearothermophilus* ATCC 7953 Spores," by Derek A. Price. Study conducted at STERIS Corporation. Study completion date – July 29, 2005. Study Number 04-037.

This field study was conducted against *Geobacillus stearothermophilus* spores (ATCC 7953). One lot (Lot No. PE124D) of the product, VAPROX® Hydrogen Peroxide Sterilant, was tested according to EPA-approved Protocol 04-037, "End-Use Protocol for Sterilization of Porous and Non-Porous Surfaces within Sealed Enclosures Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology," dated June 2005 (copy provided). The product was tested at a concentration of 250±10% ppm. No organic load was used in testing. Testing was conducted for a 90-minute exposure time at 23±5°C. The sealed enclosure used in the study was a 6.25 m x 6.27 m room, with a 1.98 m x 2.62 m alcove at one corner. The room height was 2.53 m. The room was carpeted and painted, and contained fixed (e.g., cabinets, counters) and removable objects (e.g., mattress and box springs, chair, wooden dresser, wooden table). Sixty-six (66) biological indicators (BIs) were prepared by depositing spores of the challenge organism onto coupons (coupon material not specified). The inside volume of the room was approximately 4000 ft^3 (112 m^3). Doors of the room were sealed to prevent vaporized hydrogen peroxide leakage. The distribution of hydrogen peroxide vapor during testing was assisted with fans. The coupons then were packaged into individual Tyvek pouches. BIs and Chemical Indicators (CIs) were placed in the sealed enclosure, including room corners. The STERIS VHP 1000ED Generation System was positioned in the sealed enclosure. The interior of the sealed enclosure was dehumidified to achieve a ≤60% relative humidity (dehumidification phase). Next, the product was vaporized and injected into the sealed enclosure at a rate sufficient to reach and maintain the 250 ppm target concentration (conditioning phase). The concentration of the vaporized product was maintained at 250±10% ppm (sterilization phase) and the BIs and CIs were exposed to the product for 90 minutes at 23±5°C. Finally, the hydrogen peroxide concentration was lowered to ≤1 ppm (aeration phase). Then, the BIs and CIs were removed from the sealed enclosure. The BIs were aseptically transferred from the Tyvek pouches to containers containing Tryptic Soy Broth with 0.05% sodium thiosulfate (TSB-N) to neutralize. CIs were inspected. Serial dilutions of the BIs were prepared and enumerated using the pour plate method; the plates were incubated at 55°C for 7 days. Controls included a negative control (i.e., test system sterility) and those for initial BI spore population, viability, and neutralization.

Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.

4. MRID 466317-04 "Sterilization of Porous and Non-Porous Surfaces within Emergency Vehicle Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology, Test Organism: *Geobacillus stearothermophilus* ATCC 7953 Spores," by Melvin J. Long. Study conducted at STERIS Corporation. Study completion date – July 25, 2005. Study Number 04-038.

This field study was conducted against *Geobacillus stearothermophilus* spores (ATCC 7953). One lot (Lot No. PE124D) of the product, VAPROX® Hydrogen Peroxide Sterilant, was tested according to EPA-approved Protocol 04-038, "End-Use Protocol for Sterilization of Porous and Non-Porous Surfaces within Emergency Vehicle Using STERIS Vaporized Hydrogen Peroxide (VHP®) Technology," dated April 2005 (copy provided). The product was tested at a concentration of 400±10% ppm. No organic load was used in testing. Testing was conducted for a 30-minute exposure time at 20±5°C. The emergency vehicle used in the test was a standard U.S. style ambulance, complete with chair, bench, and cabinetry. The inside volume of the vehicle was approximately 13 m^3 (460 ft^3). Doors and the ventilation system of the vehicle were sealed to prevent vaporized hydrogen peroxide leakage. The distribution of hydrogen peroxide vapor during testing was assisted with fans. Sixteen (16) biological indicators (BIs) were prepared by depositing spores of the challenge organism onto coupons (coupon material not specified). The coupons then were packaged into individual Tyvek pouches. BIs and Chemical Indicators (CIs) were placed into the cab and patient areas of the emergency vehicle. The STERIS VHP 1000ED Generation System was attached to the sealed vehicle. The interior of the vehicle was dehumidified to achieve a ≤60% relative humidity at 20±5°C (dehumidification phase). Next, the product was vaporized and injected into the emergency vehicle at a rate sufficient to reach and maintain the 400 ppm target concentration (conditioning phase). The concentration of the vaporized product was maintained at 400±10% ppm (sterilization phase) and the BIs and CIs were exposed to the product for 30 minutes at 20±5°C. Finally, the hydrogen peroxide concentration was lowered to ≤1 ppm (aeration phase). Then, the BIs and CIs were removed from the emergency vehicle. The BIs were aseptically transferred from the Tyvek pouches to containers containing Tryptic Soy Broth with 0.05% sodium thiosulfate (TSB-N) to neutralize. CIs were inspected. Serial dilutions of the BIs were prepared and enumerated using the pour plate method; the plates were incubated at 55°C for 7 days. Controls included a negative control (i.e., test system sterility), and those for initial BI spore population, viability, and neutralization.

Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.

V RESULTS

MRID Number	Organism	Results				Initial BI Spore Population (avg log CFU/ coupon)
		Lot No. PE124D				
		Conc.	R^2 Value	Line Slope	D-value	
466317-01	*Geobacillus stearothermophilus*	250 ppm	0.9909	-0.0761	13	5.75
466317-02	*Geobacillus stearothermophilus*	400 ppm	0.8176	-0.66	1.5	5.93

MRID Number	Organism	No. Exhibiting Growth/ Total No. Tested	Enumeration Results (avg CFU/coupon)
		Lot No. PE124D	
466317-03	*Geobacillus stearothermophilus*	0/66	1.00×10^6
466317-04	*Geobacillus stearothermophilus*	0/16	1.42×10^6

VI CONCLUSIONS

1. The submitted test data (MRID Nos. 466317-01 and 466317-02) support the determination of D-values for *Geobacillus stearothermophilus* spores housed on biological indicators when exposed to the product, VAPROX® Hydrogen Peroxide (using the STERIS VHP 1000 ED Generation System), at a 250 ppm and 400 ppm concentration. D-values were determined, in triplicate, to be 13 and 1.5 minutes, respectively. R^2 values (correlation coefficients) were within the acceptance range of 0.8-1.0. BIs contained a minimum of 10^6 spores of the challenge organism. Neutralization testing showed positive growth of the challenge microorganism. The viability controls were positive for growth. The sterility controls did not show growth.

Note: The laboratory reports did not provide the expiration date of the biological indicator lot.

Note: The laboratory reports did not provide data collected to monitor relative humidity, temperature, and hydrogen peroxide concentrations during the four phases of the sterilization cycle. It is assumed that these parameters met product application standards.

2. The submitted efficacy data (MRID No. 466317-03) support the use of the product, VAPROX® Hydrogen Peroxide Sterilant, when used in conjunction with the STERIS VHP

1000ED Generation System, against *Geobacillus stearothermophilus* on porous and non-porous surfaces in a 4000 ft^3 sealed enclosure at a 250 ppm concentration for a 90-minute exposure time. BIs showed no growth for the marker organism after 7 days at 55°C. **The number of BIs tested (i.e., 66) was appropriate based on the formula [(m^3-10)/2]+15, where m^3 is the inside volume of the sealed enclosure.** BIs contained a minimum of 10^6 spores of the challenge organism. Chemical indicators showed a qualitative color change indicative of hydrogen peroxide exposure. The hydrogen peroxide concentration in the spaces adjacent to the sealed enclosure exterior remained below 1 ppm during the sterilization cycle. Parameters for product application (i.e., temperature, relative humidity, vaporized hydrogen peroxide concentration, contact time) were met for all four phases of the sterilization cycle. Neutralizer testing showed positive growth of the challenge microorganism. The viability controls were positive for growth. The negative (i.e., sterility) controls did not show growth.

Note: The incubation time for the negative and neutralizer controls deviated from the signed protocol. A 7-day incubation time was specified. On page 15 of the laboratory report, the actual incubation time is reported as 48 hours. The laboratory report did not identify or discuss this deviation. The protocol deviation does not invalidate the test results.

Note: The BIs were actually exposed to some level of vaporized hydrogen peroxide for 90 minutes (conditioning phase) plus 90 minutes (sterilization phase) plus 404 minutes (aeration phase). This is inconsistent with the 90-minute contact time prescribed on the label.

Note: The laboratory report did not provide the expiration date of the biological indicator lot.

3. The submitted efficacy data (MRID No. 466317-04) support the use of the product, VAPROX® Hydrogen Peroxide Sterilant, when used in conjunction with the STERIS VHP 1000ED Generation System, against *Geobacillus stearothermophilus* on porous and non-porous surfaces in a 460 ft^3 emergency vehicle at a 400 ppm concentration for a 30-minute exposure time. BIs showed no growth for the marker organism after 7 days at 55°C. The number of BIs tested (i.e., 16) was appropriate based on the formula [(m^3-10)/2]+15, where m^3 is the inside volume of the vehicle. BIs contained a minimum of 10^6 spores of the challenge organism. Chemical indicators showed a qualitative color change indicative of hydrogen peroxide exposure. The hydrogen peroxide concentration in the spaces adjacent to the emergency vehicle exterior remained below 1 ppm during the sterilization cycle. Parameters for product application (i.e., temperature, relative humidity, vaporized hydrogen peroxide concentration, contact time) were met for all four phases of the sterilization cycle. Neutralizer testing showed positive growth of the challenge microorganism. The viability controls were positive for growth. The negative (i.e., sterility) controls did not show growth.

Note: The incubation time for the negative and neutralizer controls deviated from the signed protocol. A 7-day incubation time was specified. On page 15 of the laboratory report, the actual incubation time is reported as 48 hours. The laboratory report did not identify or discuss this deviation. The protocol deviation does not invalidate the test results.

Note: The BIs were actually exposed to some level of vaporized hydrogen peroxide for 22 minutes (conditioning phase) plus 30 minutes (sterilization phase) plus 85 minutes (aeration phase). This is inconsistent with the 30-minute contact time prescribed on the label.

Note: The laboratory report did not provide the expiration date of the biological indicator lot.

VII RECOMMENDATIONS

1. The package insert for the product, VAPROX® Hydrogen Peroxide Sterilant, claims that the product was developed for the VHP Generator and validated for both $2ft^3$ and 40 ft^3 on pre-cleaned, dry, porous and non-porous surfaces in sealed enclosures using an Association of Official Analytical Chemists (AOAC) sporicidal test protocol to validate sterilization when applied at 2.2 grams per minute for 90 minutes. These label claims are acceptable.

2. The package insert for the product, VAPROX® Hydrogen Peroxide Sterilant, claims that the product is effective on exposed, pre-cleaned, dry, porous and non-porous surfaces in sealed enclosures when used with STERIS VHP application equipment under the following conditions:

- As a sterilant, sporicide, bactericide, virucide, and fungicide for sealed enclosures up to 4,000 ft^3, when applied at a minimum of 250 ppm for 90 minutes

- As a sterilant, sporicide, bactericide, virucide, and fungicide for sealed enclosures up to 4,000 ft^3 when applied at a minimum of 400 ppm for 30 minutes

- As a Sterilant, Sporicide, Bactericide, Virucide, and Fungicide when used in a validated application in accordance with VAPROX sterilant use instructions.

Data provided by the applicant support these claims.

3. The package insert for the product, VAPROX® Hydrogen Peroxide Sterilant, claims that the product is effective on exposed, pre-cleaned, dry, porous and non-porous surfaces in sealed enclosures when used with STERIS VHP application equipment as a sterilant, sporicide, bactericide, virucide, and fungicide when used in a validated application in accordance with product use instructions. Previously submitted efficacy data support these claims.

4. The applicant must make the following revisions to the label:

- On page 1, change "For use as a microbial sterilant in sealed, dry, pre-cleaned enclosures.... " to read "For use as a microbial sterilant in sealed, dry, pre-cleaned enclosures up to 4000 ft^3 . . . ." The Agency requested this change in an email message to the applicant (dated August 19, 2005).

- Under the "Directions for Use," insert language similar to the following: "See package insert for complete directions on cleaning, sealing, and using the

product for validated and un-validated applications." The Agency requested this change in an email message to the applicant (dated August 19, 2005).

5. The applicant may want to make the following revisions to the package insert, as appropriate:

- Add page numbers to the package insert.

- Revise the Index of the package insert so that the section titles on the Index match, word-for-word, the section titles on each page of the package insert. For example, change "Efficacy and Use Applications" on the Index to read "Efficacy."

- Add section numbers before the section titles on each page of the package insert, so that the numbering system on the Index carries through the pages of the package insert. For example, change "VAPROX Application Process" to read "Section 1. VAPROX Application Process."

- Change all references to the equipment user manual to read "Operator Manual VHP 100P HO Biodecontamination System." The package insert refers to this user manual as "VHP User's Equipment Manual" on page 1, "VHP Generator Equipment User's Manual" on pages 1 and 4, "Equipment User's Manual" on page 2, and "User's Manual for VHP Generating Unit" on page 6.

- Include instructions for disposing of equipment and materials used to pre-clean surfaces.

- Include instructions for dismantling a sealed enclosure, disposing of materials used to seal an enclosure, and cleaning equipment (e.g., VHP application equipment, sensors and probes) used during treatment.

- In the "Applications to Sealed Enclosures Requiring Validation of Use Conditions" section, change "Sites Not Requiring In Use Validation" to read "Set Concentration and Contact Time Application to Sealed Enclosures of Up to 4,000 ft^3."

- In the "System Characterization" section, change "time required to aeration of the enclosure" to read "time required to aerate the enclosure."

- In the "System Characterization" section, revise the last sentence to read: To achieve reproducible results, Standard Operating Procedures (SOPs) must be written to identify and characterize the contents of an enclosure and describe the physical preparation of the enclosure for treatment.

- In the "Process Development" section, change "dependant" to read "dependent."

- On page 6 (two places), change "fans maybe placed" to read "fans may be placed." Also change (two places) "STERIZATION" to read "STERILIZATION." Also, change (two places) "to reduce levels of hydrogen

peroxide at or below 1 ppm" to read "to reduce levels of hydrogen peroxide to at or below 1 ppm."

- In a previous electronic transmittance from the Agency (dated August 19, 2005), Michele Wingfield requested that adhesive tape be added to the list of articles used for sealing the enclosures.

Notes to PM

1. Oscillating fans were used in both field tests to distribute the product. Fans appear to be significant in the delivery of the vaporized H_2O_2. The proposed label suggests that the use of fans is optional. Verbiage should be changed to strongly encourage the use of fans in these use conditions.

2. Should the registrant recommend a placement strategy for optimal VHP delivery based on the diffusion rate of the H_2O_2? Is vaporized H_2O_2 product dense, thus requiring dispersion to occur from an elevated area, or is mere diffusion sufficient to disperse vaporized H_2O_2? The presence of an oscillating device (i.e., fan) may potentially resolve this diffusion/dispersion issue, if this is indeed an issue.