UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

August 29, 2010

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 67619-12, CPPC Tsunami
DP Barcode: 378468

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Applicant: Clorox Professional Products Company
PO Box 493
Pleasanton, CA 94566-0803

Formulation from the Label:

Active Ingredient(s)	% by wt.
Sodium Hypochlorite	0.55%
Other Ingredients	99.45%
Total	100.00%

I BACKGROUND

The product, CPPC Tsunami (EPA Reg. No. 67619-12) is a registered disinfectant (bactericide, virucide, tuberculocide, and fungicide) on hard, non-porous surfaces in hospitals, veterinary offices, dental practices, colleges, schools, health clubs, and food service establishments. The current data package is submitted to support claims against *Clostridium difficile* spores. Efficacy testing was conducted at Bioscience Laboratories, located at 300 N. Wilson Avenue, in Bozeman, MT and at Antimicrobial Test Laboratories, located at 3000 Joe DiMaggio Blvd., Suite #32, in Round Rock, TX.

The data package contained a letter from the registrant (dated May 6, 2010), EPA Form 8570-1 (Application for Pesticide), EPA Form 8570-34 (Certification with Respect to Citation of Data), EPA Form 8570-35 (Data Matrix), two efficacy studies (MRID No. 480900-01 and -02), Statement of No Data Confidentiality for both studies, and the proposed label.

II USE DIRECTIONS

The product is for use on carts, blood pressure monitors, footboards, glucometers, IV stands, bed pans, cabinet handles, desk tops, coated pillows, coated mattresses, pipes, light lens covers, animal equipment, stalls, troughs, freezers, and hoods composed of glass, glazed ceramic tiles, laminated surfaces, chrome, stainless steel, and vinyl. Directions on the proposed label provided the following directions for use of the product against *Clostridium difficile* spores:

Wipe surface to be disinfected. Use enough wipes for treated surfaces to remain visibly wet for 5 minutes. Let air dry. Gross filth should be removed prior to disinfecting. **Special Instruction for Cleaning Prior to Disinfection against Clostridium difficile spores.** Personal Protection: Wear appropriate barrier protection such as gloves, gowns, masks, or eye covering. Cleaning Procedure: Fecal matter/waste must be thoroughly cleaned from surfaces/objects before disinfection by application with product. Cleaning is to include vigorous wiping and/or scrubbing, until all visible soil is removed. Special attention is needed for high-touch surfaces. Surfaces in patient rooms are to be cleaned in an appropriate manner, such as from right to left or left to right, on horizontal surfaces, and top to bottom, on vertical surfaces to minimize spreading of the spores. Restrooms are to cleaned last. Do not reuse soiled cloths.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Sporicidal Disinfectant against *Clostridium difficile*

The Agency has established interim guidance for the efficacy evaluation of antimicrobial products (e.g., dilutable products, ready-to-use products, spray products, towelettes) that are labeled for use to treat hard, non-porous surfaces in healthcare settings contaminated with spores of *Clostridium difficile.* The effectiveness of such a product must be substantiated by data derived from one of the following four test methods: Most recent version (2006) of AOAC Method 966.04: AOAC Sporicidal Activity of Disinfectants Test, Method I for *Clostridium sporogenes*; AOAC Method 2008.05: Quantitative Three Step Method (Efficacy of Liquid Sporicides Against Spores of *Bacillus subtilis* on a Hard Nonporous Surface); ASTM E 2414-05: Standard Test

Method for Quantitative Sporicidal Three Step Method (TSM) to Determine Efficacy of Liquids, Liquid Sprays, and Vapor or Gases on Contaminated Carrier Surfaces; or ASTM E 2197-02: Standard Quantitative Carrier Test Method to Evaluate the Bactericidal, Fungicidal, Mycobactericidal, and Sporicidal Potencies of Liquid Chemical Germicides. Modifications to each test method will be necessary to specifically accommodate spores of *Clostridium difficile*. Because *Clostridium difficile* is an obligate anaerobe, testing should ensure adequate incubation conditions for the recovery of viable spores. The following toxigenic strains of *Clostridium difficile* may be used for testing: ATCC 700792, ATCC 43598, or ATCC 43599. All products must carry a pre-cleaning step, thus no organic soil should be added to the spore inoculum. Results must show a minimum 6 log reduction of viable spores in 10 minutes or less. Control carrier counts must be greater than 10^6 spores/carrier.

IV SYNOPSIS OF SUBMITTED EFFICACY STUDIES

1. MRID No. 480900-01, "A Quantitative Hard Surface Disinfection Evaluation of One Test Formulation Versus Spores of Clostridium difficile" by Terri Eastman. Study Completion Date—April 22, 2010. Testing Facility—Bioscience Laboratories. Laboratory Study Number—091246-204 F.

The study was conducted against *Clostridium difficile* spores (ATCC# 43598). Three lots (Lot Nos. 09CGW3, 09CGW1, and 09CGW2) of the product, CPPC Tsunami F2004.0147 were tested using ASTM E2197-02, Standard of Quantitative Disk Carrier Test Method for Determining the Bactericidal, Virucidal, Fungicidal, Mycobactericidal and Sporicidal Activities of Liquid Chemical Germicides, as specified by the US EPA in Guidance for the Efficacy Evaluation of Products with Sporicidal Claims Against *Clostridium difficile* (February 5, 2009). One lot (Lot No. 09CGW3) was ≥60 days old at the time of testing. Four sterile pipette tips (100 µl – 1000 µl capacity) were transferred into the bottom of a sterile 50 ml centrifuge tube, so that the tips were pointing downward. A technician donned sterile powder-free gloves prior to handling the disinfectant wipes, and changed gloves prior to handling wipes of a different batch/lot. A canister containing a batch/lot of disinfectant wipes was opened, and a wipe was pulled through the center "donut" of the opening in the lid. The first three wipes from each canister were removed and discarded, and the next wipe was the first to be used for testing. The wipe was folded and placed into the centrifuge tube so that it rested on top of the pipette tips. The tubes containing the wipe were centrifuged at approximately 3000 rpm for approximately 10 minutes in order to express the fluid from the wipes. The wipe was aseptically removed from the centrifuge tube immediately following centrifugation and discarded. These procedures were repeated, until a quantity of liquid sufficient for testing had been collected. The pipettes tips were aseptically removed from the centrifuge tube. Liquid from different wipes of the same lot were combined to achieve the necessary volume for testing. Sterilized stainless steel disks were inoculated with 0.01 ml of aliquot spore suspension. Approximately 50 carriers were inoculated. The Petri plates containing the inoculated carriers were transferred to desiccators, and dried under vacuum for approximately 18.5 hours at room temperature. Prior to testing, the combined test solution and control solution (0.9% Sodium Chloride Irrigation, USP) were placed in a water bath at 20±1°C for no less than 15 minutes. Post-drying, 30 inoculated carriers were treated with the test solution, and 6 carriers were treated with the control solution. Each carrier was transferred inoculated side-up to

a sterile 15 ml vial. A 0.05ml (50 µl) aliquot of test formulation or control solution was transferred onto the surface of the inoculated carrier. Each carrier was exposed to the solution for 4 minutes and 30 seconds. Post-exposure, 9.95 ml aliquots of neutralizing solution (Butterfield's Phosphate Buffer solution with product neutralizers) was added to each vial. The vials were shaken vigorously and/or vortex mixed for approximately (10^0 dilution). The procedure was repeated in sequential fashion until 10 contaminated carriers had been treated with each lot of the test formulation liquid, and 6 inoculated carriers had been treated with the control solution. For the control solution, serial 10-fold dilution (10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, and 10^{-5}) of the neutralizing solution from each carrier treated with the control solution were prepared in sterile 0.9% sodium chloride irrigation, USP (SCI). Aliquots of 1.0 ml of the 10^{-1}, 10^{-3}, 10^{-4}, and 10^{-5} dilutions were each vacuum-filtered using separate sterile analytical filter units with 0.45µm pore-size membranes. Each filter unit was rinsed with approximately 100 mL of SCI, and the rinsate was filtered. Each membrane filter was transferred, up-side-up, to the surface of BHI agar modified for *Clostridium* species (BHIAY) contained in Petri plates. For test carriers, the entire fluid volume of each 100 dilution vial was vacuum-filtered using separate sterile analytical filter units with 0.45µm pore-size membranes. Each vial was rinsed three times with 15 ml SCI, and the rinsate was filtered. Each filter unit was rinsed with approximately 40 ml of SCI, and the rinsate was filtered. Each membrane filter was transferred to the surface of BHIAY agar. The plates were incubated anaerobically at 30±2°C. Final plate counts were recorded after 7 days. Controls included those for HCl resistance, purity, sterility, and neutralization effectiveness confirmation.

2. **MRID No. 480900-02, "Custom Towelette Wetness Test," by Ashley Rex. Study Completion Date—April 21, 2010. Amended Report Date—May 4, 2010. Testing Facility—Antimicrobial Test Laboratories. Study Identification Number—GLP1030.**

The purpose of this study was to determine the residual wetness of test carriers following treatment and a 5 minute contact time. Three lots (Lot Nos. 09CGW1, 09CGW2, and 09CGW3) of the product EPA Reg. No. 67619-12 CPPC, Tsunami F2004.0147 were tested using the study design approved by the EPA for Caltech Industries, Inc. (now owned by the Clorox Company) for observing and measuring the surface wetness imparted by using a disinfectant towelette (protocol attached). The test carriers were composed of new Formica (Black Matte Finish, e.g. style 909-58) cut to a 12 inch by 12 inch size. The test carriers were wiped with a damp cloth and allowed to air dry prior to initiation of the study in order to remove dust. The back of each test carrier was labeled with a unique identifier (e.g. "A," "B," "C,") by permanent marker. The exposure portion of the test was controlled by a calibrated timer. One towelette was used to wipe each test carrier (one wipe treated one 12" x 12" carrier). Three (3) towelettes were evaluated per lot. To begin the study, laboratory staff initiated the video recording of the study. The first test carrier was weighed prior to treatment using a calibrated laboratory balance with an accuracy of 0.01 g. The test carrier was placed on a flat lab bench so that it created a square shape in front of the test operator. Ten (10) towelettes were removed from the towelette package to demonstrate wetness throughout the towelette container. The next towelette was used for the initial test carrier. For the second carrier, 10 more towelettes were removed and the next towelette was used. For the third carrier, another 10 towelettes were removed and then the next towelette was used for that test. The towelette container was securely closed between

removals of each set of 11 test towelettes. The towelette was unfolded. The towelette was folded in half twice, once along the length and once along the width. The towelette was placed on the top left corner of the test carrier. The test carrier was wiped in an up and down motion, each stroke slightly overlapping the last; until the entire test carrier was completely covered (7 total strokes with the wipe were used on each 12" x 12" carrier). After the entire test surface area was treated, the timer was started. The carrier was placed on the balance and the initial wet weight of the test carrier was recorded. The test carrier was allowed to sit undisturbed for the 5 minute contact time. Upon completion of the contact time, the final wet weight of the test carrier was recorded. Immediately after weighing, a single sheet of unfolded cigarette paper was wiped across the test surface to assist in visualization of wetness for the laboratory technician and video camera due to the clear colorless nature of the test substance. Visual wetness of the cigarette paper was defined as wetness. The paper wetness was observed and recorded.

V RESULTS

Lot Number	Carrier Number	CFU/carrier Post-Exposure	Log_{10} CFU/carrier	Mean Log_{10} Density	Mean Log_{10} Reduction
09CGW3 (60-day sample)	1-10	<1.00	0.0	0.0	6.0
09CGW1	1-10	<1.00	0.0	0.0	6.0
09CGW2	1-10	<1.00	0.0	0.0	6.0

Carrier No	CFU/carrier Post Exposure	Log_{10} Carrier	Mean Log10 Density
1	7.70×10^5	5.9	6.0
2	9.90×10^5	6.0	
3	1.180×10^6	6.1	
4	8.80×10^5	5.9	
5	9.60×10^5	6.0	
6	1.14×10^6	6.1	

HCl Resistance

Test Strain	Exposure Time Results (+/-)*		
	2 Minutes	5 Minutes	10 Minutes
Clostridium difficile spores	+	+	+

Visual Wetness

Test Lot Number	Carrier Number	Visual Wetness Confirmed
09CGW1	1	Yes
	2	Yes
	3	Yes
09CGW2	1	Yes
	2	Yes
	3	Yes
09CGW3	1	Yes
	2	Yes
	3	Yes

Test Lot#	Carrier#	Initial Carrier Dry Weight	Initial Carrier Wet Weight	Final Carrier Weight	Remaining Test Substance Weight	Wetness Confirmation
09CGW1	1	109.3	109.97	109.64	0.34	Yes
	2	106.99	107.7	107.28	0.29	Yes
	3	108.46	108.99	108.69	0.23	Yes

Test Lot#	Carrier#	Initial Carrier Dry Weight	Initial Carrier Wet Weight	Final Carrier Weight	Remaining Test Substance Weight	Wetness Confirmation
09CGW2	1	106.46	107.13	106.74	0.28	Yes
	2	107.76	108.42	108.05	0.29	Yes
	3	110.03	110.62	110.2	0.17	Yes

Test Lot#	Carrier#	Initial Carrier Dry Weight	Initial Carrier Wet Weight	Final Carrier Weight	Remaining Test Substance Weight	Wetness Confirmation
09CGW3	1	111.19	111.62	111.29	0.10	Yes
	2	109.05	109.44	109.12	0.07	Yes
	3	112.22	112.57	112.3	0.08	Yes

VI CONCLUSIONS

1. The submitted efficacy data (MRID No. 480900-01) is unacceptable regarding the use of the product, CPPC Tsunami as a sporicide against *Clostridium difficile* spores in the absence of organic soil for a contact time of 5 minutes. No information was provided regarding spore purity (consistent with the August 21, 2009 DER, "the Agency recommends at least 90% spores for spore purity" and stated in the November 14, 2009 DER; "the percentage of spores must be ≥90% to confirm the purity of the spore suspension. If this value is not achieved, additional steps will be taken to further concentrate/purify the preparation"). Additionally, carrier counts did not consistently

achieve the ≥ 1x 10^6 spore/carrier-requirement (consistent with the August 21, 2009 DER and stated in the November 14, 2009 DER; "each control carrier must yield enough CFU to indicate the presence of ≥10^6 viable spores. This is essential to meet the product performance criterion of a spore kill of ≥10^6)". The acceptance criterion for HCl resistance (i.e. the acceptance criterion is growth following a 2 minute HCl exposure) was achieved.

2. The wetness determination (as described in MRID No. 480900-01) demonstrated weight and visual wetness endpoints for confirming wetness consistent with the proposed contact time. The submitted efficacy data is acceptable.

VII RECOMMENDATION

1. In the absence of acceptable efficacy data, claims against *Clostridium difficile* spores are unacceptable regarding the use of the product, CPPC Tsunami at a contact time of 5 minutes. The efficacy test relied on the test protocols/revised protocols provided by Caltech Industries (recently purchased by Clorox).

2. When acceptable efficacy data is provided, the following label claims must be revised or removed:

- Attacks *Clostridium difficile*;
- Fast-acting disinfectants and "fast disinfection";
- Gold-standard disinfection; Most-trusted;
- Passes requirements for killing *Clostridium difficile*;
- Rapidly kills;
- Quick;
- To break down;

The Agency has not determined testing parameters consistent with these proposed claims.