UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

May 5, 2011

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 67619-12, CPPC Tsunami;
DP Barcode: 387066

From: Tajah L. Blackburn, Ph.D., Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

To: Wanda Henson PM32
Regulatory Management Branch II
Antimicrobials Division (7510P)

Applicant: The Clorox 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 towelette product, CPPC Tsunami (EPA Reg. No. 67619-12), is an EPA-approved disinfectant (bactericide, fungicide, virucide), mildewcide, and deodorizer for use on hard, non-porous surfaces in household, commercial, institutional, industrial, food service, animal care, and hospital or medical environments. The applicant requested to amend the registration of this product to add new claims for effectiveness as a disinfectant against *Clostridium difficile* – spore form. The label states that the product is effective in the presence of 5% blood serum. Studies were conducted at BioScience Laboratories, Inc., located at 300 N. Willson Avenue, in Bozeman, MT 59715.

This data package contained a letter from the applicant to EPA (dated February 4, 2011), EPA Form 8570-1 (Application for Pesticide), EPA Form 8570-34 (Certification with Respect to Citation of Data), EPA Form 8570-35 (Data Matrix), three studies (MRID 483771-01 through 483771-03), Statements of No Data Confidentiality Claims for all three studies, and the proposed label.

Note: The laboratory reports describe studies conducted for the product, F2010.0203. The applicant's letter to EPA (dated February 4, 2011) states that the tested product, F2010.0203, is the product, CPPC Tsunami (identical to CSF A10), which is the subject of this efficacy report.

II USE DIRECTIONS

The product is designed for disinfecting hard, non-porous surfaces. The product may be used to treat hard, non-porous surfaces, including: air vent exteriors, appliances, automatic feeders, bathroom fixtures, bathtubs, bed frames, bed pans, bed railings, booster chairs, cabinet handles, cabinets, cages, carts, ceilings, cellular phones, chairs, closet handles, computer keyboards and monitors, counters, cribs, desk tops, diaper changing stations, diaper pails, dictating equipment, dish racks, doorknobs, drain boards, drawers, examination tables, faucets, feed racks, floors, food cases and trays, fountains, garbage cans, hampers, hand railings, headsets, high chairs, hospital equipment (e.g., gurneys, IV stands, stretchers, wheelchairs), lamps, mattress covers, outdoor furniture (excluding wood frames and upholstery), pens, pipes, playpens, shelves, shower fixtures, shower stalls, sinks, sneeze guards, stalls, tables, telecommunication equipment, telephones, television remote controls, towel dispensers, toys, troughs, urinal surfaces, vanity tops, veterinary equipment, walls, wash basins, and watering appliances. The proposed label indicates that the product may be used on hard, non-porous surfaces, including: baked enamel, chrome, Formica, glass, glazed ceramic, glazed porcelain, laminated surfaces, linoleum, Marlite, plastic, porcelain enamel, stainless steel, synthetic marble, and vinyl. Directions on the proposed label provide the following information regarding preparation and use of the product as a disinfectant against *Clostridium difficile* spores: Fecal matter/waste must be thoroughly cleaned from surfaces/objects before disinfection. 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 be cleaned last. Do not reuse soiled cloths. Wipe surface to be disinfected. Use enough wipes for treated surface to remain visibly wet for 5 minutes. Let air dry. Gross filth should be removed prior to disinfecting.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Antimicrobial Products for Use on Hard Surfaces Using Pre-saturated or Impregnated Towelettes

Towelette products represent a unique combination of antimicrobial chemical and applicator, pre-packaged as a unit in fixed proportions. As such, the complete product, as offered for sale, should be tested according to the directions for use to ensure the product's effectiveness in treating hard surfaces. The standard test methods available for hard surface disinfectants and sanitizers, if followed exactly, would not closely simulate the way a towelette product is used. Agency guidelines recommend that a simulated-use test be conducted by modifying the standard test methods. Agency guidelines further recommend that instead of spraying the inoculated surface of the carrier, the product should be tested by wiping the surface of the carrier with the saturated towelette, and then subculturing the slides after a specified holding time. Performance standards of the standard test methods must be met. These Agency standards are presented in EPA Pesticide Assessment Guidelines, Subdivision G, §91-2(h), Pre-saturated or impregnated towelettes; and the April 12, 2001 EPA Memorandum, Draft Interim Guidance for Non-Residual Sanitization of Hard Inanimate Food Contact Surfaces Using Pre-Saturated Towelettes.

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.

Supplemental Claims

An antimicrobial agent identified as a "one-step" disinfectant or as effective in the presence of organic soil must be tested for efficacy with an appropriate organic soil load, such as 5 percent serum.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 483771-01 "A Quantitative Hard Surface Disinfection Evaluation of One Test Formulation Versus Spores of *Clostridium difficile*" (ATCC 43598), for CPPC Tsunami, F2010.0203, by Terri Eastman. Study conducted at BioScience Laboratories, Inc. Study completion date – January 24, 2011. Laboratory Study Number 101123-204 A.

This study was conducted against spores of *Clostridium difficile* (ATCC 43598; spore suspension; obtained from the Centre for Research on Environmental Microbiology, University of Ottawa, Canada). One lot (10CGW2) of the product, CPPC Tsunami, F2010.0203, was tested using the ASTM E 2197-02, Standard Quantitative Disk Carrier Test Method for Determining the Bactericidal, Virucidal, Fungicidal, Mycobactericidal and Sporicidal Activities of Liquid Chemical Germicides (modified). The product lot tested was at least 60 days old at the time of testing. One use solution (Test Solution #1, 10CGW2L) was obtained by expressing the liquid from a number of disinfectant wipes using a centrifuge; this use solution was used within 3 hours of its collection. A second use solution (Test Solution #2, 10CGW2E) was obtained by expressing the liquid from a "retained sample" of the disinfectant wipes; this use solution was diluted prior to its use. [Details regarding the dilution of the expressed liquid were not provided.] The culture of the challenge microorganism, obtained from the Centre for Research on Environmental Microbiology, was certified to contain ~1 x 10^9 CFU/mL. Use solutions were not tested in the presence of an organic soil load. Ten (10) sterile stainless steel disk carriers (1 cm in diameter; thickness not reported) for the single product lot were inoculated with 10 µL of a culture of the test organism. The carriers were dried in a desiccator containing anhydrous calcium chloride, under vacuum, for ~22 hours at room temperature. Each carrier was transferred, inoculated side up, to a sterile 15 mL vial, to which 50 µL of the use solution was added. In addition, three carriers were treated with 50 µL of a control solution (i.e., 0.9% Sodium Chloride Irrigation, USP [SCI]). The test and control carriers remained exposed to the appropriate solution for 4.5 minutes at ambient temperature (22.1-23.1°C). Following exposure, 9.95 mL of Butterfield's Phosphate Buffer solution with product neutralizers was added to each vial to neutralize. The contents of each vial were shaken vigorously and/or vortex mixed for ~1 minute. The contents of each vial containing a carrier treated with the use solution were vacuum-filtered using separate, sterile analytical filter units with 0.45 µm pore-size membranes. Each vial was rinsed with 15 mL of SCI three times, with each rinse poured through the same membrane filter. Each filter unit was also rinsed with ~40 mL of SCI, with the rinsate filtered. [The contents of each vial containing a carrier treated with the control solution were also filtered and plated.] Each membrane filter was plated on Brain Heart Infusion Agar modified for *Clostridium* species and incubated for 7 days at 30±2°C under anaerobic conditions. Following incubation, the subcultures were examined for the presence or absence of visible growth and colonies were enumerated. Controls included those for viable carrier count, purity, sterility, neutralizer efficacy verification, and acid resistance at 2, 5, and 10 minutes.

Note: Protocol deviations/amendments were observed in the current study.

2. MRID 483771-02 "A Quantitative Hard Surface Disinfection Evaluation of One Test Formulation Versus Spores of *Clostridium difficile*" (ATCC 43598), for CPPC Tsunami, F2010.0203, by Terri Eastman. Study conducted at BioScience Laboratories, Inc. Study completion date – January 24, 2011. Laboratory Study Number 101123-204 B.

This study was conducted against spores of *Clostridium difficile* (ATCC 43598; spore suspension; obtained from the Centre for Research on Environmental Microbiology, University of Ottawa, Canada). One lot (10CGW7) of the product, CPPC Tsunami, F2010.0203, was tested using the ASTM E 2197-02, Standard Quantitative Disk Carrier Test Method for Determining the Bactericidal, Virucidal, Fungicidal, Mycobactericidal and Sporicidal Activities of Liquid Chemical Germicides (modified). A use solution was obtained by expressing the liquid from a number of disinfectant wipes using a centrifuge; this use solution was used within 3 hours of its collection. The culture of the challenge microorganism, obtained from the Centre for Research on Environmental Microbiology, was certified to contain ~1 x 10^9 CFU/mL. The use solution was not tested in the presence of an organic soil load. Ten (10) sterile stainless steel disk carriers (1 cm in diameter; thickness not reported) for the single product lot were inoculated with 10 µL of a culture of the test organism. The carriers were dried in a desiccator containing anhydrous calcium chloride, under vacuum, for ~22 hours at room temperature. Each carrier was transferred, inoculated side up, to a sterile 15 mL vial, to which 50 µL of the use solution was added. In addition, three carriers were treated with 50 µL of a control solution (i.e., 0.9% Sodium Chloride Irrigation, USP [SCI]). The test and control carriers remained exposed to the appropriate solution for 4.5 minutes at ambient temperature (22.1-23.1°C). Following exposure, 9.95 mL of Butterfield's Phosphate Buffer solution with product neutralizers was added to each vial to neutralize. The contents of each vial were shaken vigorously and/or vortex mixed for ~1 minute. The contents of each vial containing a carrier treated with the use solution were vacuum-filtered using separate, sterile analytical filter units with 0.45 µm pore-size membranes. Each vial was rinsed with 15 mL of SCI three times, with each rinse poured through the same membrane filter. Each filter unit was also rinsed with ~40 mL of SCI, with the rinsate filtered. [The contents of each vial containing a carrier treated with the control solution were also filtered and plated.] Each membrane filter was plated on Brain Heart Infusion Agar modified for *Clostridium* species and incubated for 7 days at 30±2°C under anaerobic conditions. Following incubation, the subcultures were examined for the presence or absence of visible growth and colonies were enumerated. Controls included those for viable carrier count, purity, sterility, neutralizer efficacy verification, and acid resistance at 2, 5, and 10 minutes.

Note: Protocol deviations/amendments were observed in the current study.

3. MRID 483771-03 "A Quantitative Hard Surface Disinfection Evaluation of One Test Formulation Versus Spores of *Clostridium difficile*" (ATCC 43598), for CPPC Tsunami, F2010.0203, by Terri Eastman. Study conducted at BioScience Laboratories, Inc. Study completion date – January 24, 2011. Laboratory Study Number 101123-204 C.

This study was conducted against spores of *Clostridium difficile* (ATCC 43598; spore suspension; obtained from the Centre for Research on Environmental Microbiology, University of Ottawa, Canada). One lot (10CGW8) of the product, CPPC Tsunami, F2010.0203, was tested using the ASTM E 2197-02, Standard Quantitative Disk Carrier Test Method for Determining the Bactericidal, Virucidal, Fungicidal, Mycobactericidal and Sporicidal Activities of Liquid Chemical Germicides (modified). A use solution was obtained by expressing the liquid from a number of disinfectant wipes using a centrifuge; this use solution was used within 3 hours of its collection. The culture of the challenge microorganism, obtained from the Centre for Research on Environmental Microbiology, was certified to contain ~1 x 10^9 CFU/mL. The use solution was not tested in the presence of an organic soil load. Ten (10) sterile stainless steel disk carriers (1 cm in diameter; thickness not reported) for the single product lot were inoculated with 10 µL of a culture of the test organism. The carriers were dried in a desiccator containing anhydrous calcium chloride, under vacuum, for ~22 hours at room temperature. Each carrier was transferred, inoculated side up, to a sterile 15 mL vial, to which 50 µL of the use solution was added. In addition, three carriers were treated with 50 µL of a control solution (i.e., 0.9% Sodium Chloride Irrigation, USP [SCI]). The test and control carriers remained exposed to the appropriate solution for 4.5 minutes at ambient temperature (22.1-23.1°C). Following exposure, 9.95 mL of Butterfield's Phosphate Buffer solution with product neutralizers was added to each vial to neutralize. The contents of each vial were shaken vigorously and/or vortex mixed for ~1 minute. The contents of each vial containing a carrier treated with the use solution were vacuum-filtered using separate, sterile analytical filter units with 0.45 µm pore-size membranes. Each vial was rinsed with 15 mL of SCI three times, with each rinse poured through the same membrane filter. Each filter unit was also rinsed with ~40 mL of SCI, with the rinsate filtered. [The contents of each vial containing a carrier treated with the control solution were also filtered and plated.] Each membrane filter was plated on Brain Heart Infusion Agar modified for *Clostridium* species and incubated for 7 days at 30±2°C under anaerobic conditions. Following incubation, the subcultures were examined for the presence or absence of visible growth and colonies were enumerated. Controls included those for viable carrier count, purity, sterility, neutralizer efficacy verification, and acid resistance at 2, 5, and 10 minutes.

Note: Protocol deviations/amendments were observed in the current study.

V RESULTS

MRID Number	Organism		Test Carriers	Control Carriers	Log Reduction
			(Mean log_{10} Density)		
483771-01	*Clostridium difficile* – spore form	10CGW2L 10CGW2E	0.0 0.0	6.8 6.8	6.8 6.8
483771-02	*Clostridium difficile* – spore form	10CGW7	0.0	6.8	6.8
483771-03	*Clostridium difficile* – spore form	10CGW8	0.0	6.8	6.8

VI CONCLUSIONS

1. The submitted efficacy data (MRID 483771-01 through 483771-03) do not support the use of the expressed liquid of the towelette product, CPPC Tsunami, F2010.0203, as a disinfectant against *Clostridium difficile* on pre-cleaned, hard, non-porous surfaces for a 4.5-minute contact time. The registrant needs to provide information pertaining to (a) the number of towelettes used to obtain the expressed liquid; (b) define retained sample as stated in MRID No. 483771-01 (Lot# 10CGW2E); (c) provide clarity regarding the dilution of the expressed liquid as stated in the MRID No. 483771-01; (d) explain the change in filter pore size from 0.22 µm to 0.45 µm; and (e) identify the aged lot. At least a 6-log reduction in viable spores was observed. Neutralizer efficacy verification testing showed growth of the "test" population not more than 0.25 log_{10} less than the average control population. Purity controls were reported as pure. The sterility controls did not show growth. Acid resistance testing met the acceptance criterion of growth following a 2-minute exposure.

2. The data package failed to include a wetness determination study to justify/determine the contact time. The study is required to determine the acceptability of the proposed claims.

VII RECOMMENDATIONS

1. The proposed label claims are unacceptable regarding the use of the product, CPPC Tsunami, as a disinfectant against *Clostridium difficile* spores on hard, non-porous surfaces in the presence or absence of 5% organic soil for a 5-minute contact time. Testing was not conducted in the presence of a light or moderate organic soil load. Directions for disinfecting against *Clostridium difficile* must include a pre-cleaning step. Label claims regarding *Clostridium difficile* must clearly refer to pre-cleaned surfaces. Furthermore, the deficient elements identified in the Conclusion section must be addressed before the acceptability of the proposed claims can be determined. Upon submission, review and acceptance of the deficient elements, the ATCC# for *Clostridium difficile* must be changed from 70092 to 43598, consistent with the tested strain. Until such time, any and all claims pertaining to *Clostridium difficile* spores must be removed from the proposed label.

2. The following revisions to the proposed label are required:

- Under the "Precautionary Statements" section of the proposed label, change

"before eating, drinking, chewing gum, or using tobacco" to read "before eating, drinking, chewing gum, using tobacco, or using the toilet."

- On the proposed label, remove the term "leading" or add "a leading" causative agent of the common cold. The term "leading" alone is unacceptable.

- The contact time for bloodborne pathogens on page 3 of the proposed label is 1 minute. While the contact time for bloodborne pathogens on page 6 of the proposed label is 30 seconds.

- On page 5, revise the claim "[30 second] broad spectrum no-rinse disinfectant for non-food contact surfaces" as some contact times extend beyond 30 seconds.

- On page 5, remove the claims "kills many common bacteria and viruses". The Agency has not determined the bacteria and viruses that may satisfy this claim.

- On page 6, remove the term Hospital Associated Infections [HAIs]. The Agency has not determined which microorganisms can support this claim.

- On page 7, under use directions for Farm Premise and Poultry House Disinfection, revise the item #5 "Wipe all surfaces using enough wipes to keep surfaces visibly wet for 1 minute" as some contact times extend beyond 1 minute.

- On page 8, revise the claim "[appropriate] [perfect] [ideal] [for Terminal Cleaning Patient Discharge[s] [ing]" must make reference to the room or surfaces in the room. Claim as currently written implies that the towelette can be used on the patient.