UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

November 15, 2010

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 70271-13, Pure Bright Germicidal Ultra Bleach; DP Barcode: 383177

From: Tajah Blackburn, PhD, Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P) 11/15/10

To: Wanda Henson, PM 32
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Applicant: KIK International, Inc
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Formulation from the Label:

Active Ingredient(s)	% by wt.
Sodium Hypochlorite	6.0%
Other Ingredients	94.0%
Total	100.0%

I BACKGROUND

The product, Pure Bright Germicidal Ultra Bleach (EPA Reg. No. 70271-13), is an EPA-approved disinfectant (bactericide, fungicide, virucide), sanitizer, mildewcide, and deodorizer for use on hard, non-porous surfaces in household, commercial, institutional, food service, animal care, and hospital or medical environments. In response to the Agency's review (dated August 9, 2010), the registrant is submitting efficacy data to support claims against *Clostridium difficile* spores, and responding to Section VII, Recommendations of the referenced review. In addition to resolution of the issues in the referenced review, the registrant has asked the question, "Are viruses required to be indicated separately within the list of organisms on page 5 of the label?" The study was conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121.

This data package contained a letter from the applicant's representative (dated September 27, 2010), EPA Form 8570-34 (Certification with Respect to Citation of Data), EPA Form 8570-35 (Data Matrix), one study (MRID 482412-01), rationale provided by ATS Labs, Statements of No Data Confidentiality Claims, and the proposed label.

II USE DIRECTIONS

The product is designed for disinfecting and sanitizing hard, non-porous surfaces. The product may be used to treat hard, non-porous surfaces such as appliances, bathtubs, cages, counter tops, cutting boards (hard, non-porous plastic), faucets, floors, furniture, garbage disposals, kennels, mops, shower curtains, shower walls, showers, sinks, toys, trash bins, trash cans, walls, and work surfaces. The proposed label indicates that the product may be used on hard, non-porous surfaces including: glass, glazed ceramic tile, glazed porcelain, linoleum, painted woodwork, and vinyl. Directions on the proposed label provide the following information regarding preparation and use of the product:

> As a disinfectant against Human immunodeficiency virus type 1 (HIV-1), Hepatitis B virus, and Hepatitis C virus in the presence of 5% blood serum: Use 1 ½ cup of the product per 1 gallon of water (5,000 ppm available chlorine). Leave surfaces wet for 5 minutes for HIV and 10 minutes for HBV/HCV. Drain and let air dry.
>
> As a disinfectant against *Clostridium difficile* spores: Clean surfaces by removing gross filth. Apply a 1:5 use solution of the product (~10,000 ppm available chlorine) to surfaces. Let stand for 10 minutes. Rinse and air dry.
>
> As a disinfectant against other label-specified microorganisms: Use ¾ cup of the product per 1 gallon of water (a 1:21 dilution). Wash, rinse, or wipe surfaces. Then, apply use solution. Let stand for 5 minutes. Rinse thoroughly and air dry.
>
> As a sanitizer: Use 1 tablespoon of the product per 1 gallon of water (a 1:257 dilution). Wash, rinse, or wipe surfaces. Then, apply use solution. Let stand for 5 minutes. Air dry.

As a laundry sanitizer: Add 1¼ cup of the product per laundry load (a 1:205 dilution) for a conventional washing machine (16 gallon capacity). Add 2/3 cup of the product per laundry load for an automatic front loading washing machine (8 gallon capacity). Add to pre-soak, wash water. If clothes are in the machine, dilute the product with 1 quart of wash water before adding.

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.

Sanitizers (For Non-Food Contact Surfaces)

The effectiveness of sanitizers for non-food contact surfaces must be supported by data that show that the product will substantially reduce the numbers of test bacteria on a treated surface. The test surface(s) should represent the type(s) of surfaces recommended for treatment on the label, i.e., porous or non-porous. Products that are represented as "one-step sanitizers" should be tested with an appropriate organic soil load, such as 5 percent serum. Tests should be performed with each of 3 product samples, representing 3 different product lots, one of which is at least 60 days old against *Staphylococcus aureus* (ATCC 6538) and either *Klebsiella pneumoniae* (aberrant, ATCC 4352) or *Enterobacter aerogenes* (ATCC 13048 or 15038). Results must show a bacterial reduction of at least 99.9 percent over the parallel control within 5 minutes.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 482412-01 "Standard Quantitative Disk Carrier Test Method," Test Organism: *Clostridium difficile* (spore form) (ATCC 700792), for Pure Bright Germicidal Ultra Bleach, by Becky Lien. Study conducted at ATS Labs. Study completion date – February 5, 2010. Project Number A08850.

This study was conducted against *Clostridium difficile* (spore form) (ATCC 700792). Three lots (Lot Nos. 101820352M, 102431653M, and 102421127M) of the product, Pure Bright Germicidal Ultra Bleach, were tested using the ATSM Standard Quantitative Disk Carrier Test Method (ASTM E2197). At least one of the product lots tested (i.e., Lot No. 101820352M) was at least 60 days old at the time of testing. Use solutions were prepared by adding 10.00 mL of the product and 43.0 to 53.0 mL of filter sterilized tap water. The prepared test substance was titrated and found to be over 10,000 ppm specification. In those situations, 3.0 ml and 4.0 ml of filter sterilized tap water was added to the prepared sample. The final average titration was 9,978, 9,992, and 9,949 ppm. From stock, five 10 ml tube of BHI broth tubes were inoculated with the test organism. The tubes were incubated for 4 days at 35-37°C under anaerobic conditions. Following incubation, the broth culture was vortex-mixed and 80 CDC Anaerobic Blood agar plates were inoculated with 500µl of broth culture. The inoculum was spread over plates. The inoculated plates were incubated for 10 days at 35-37°C under anaerobic conditions. Following incubation, the growth was harvested from the plates by adding 3.0 ml of filter sterile deionized water to each plate, and gently scraping with a sterile cell scraper. The liquid was removed from each plate and transferred to a sterile vessel. The suspension was centrifuge concentrated at 3610 RPM for 20 minutes and the pellet was concentrated in filter sterilized deionized water. An 8X concentration was made. The suspension was centrifuge concentrated a second time at 3600 RPM for 5 minutes. The supernatant was removed and the pellet was resuspended in filter sterilized deionized water (approximately equivalent to the volume of supernatant removed). The suspension was centrifuge concentrated at 3600 RPM for 5 minutes a third time. The supernatant was removed and the pellet was resuspended in filter sterilized deionized water (approximately equivalent to the volume of supernatant removed). The culture was macerated to uniformity. The culture was stored at 2-8°C for approximately 3 months. The target concentration was 2×10^8 spores/ml or greater. The product was not tested in the presence of a 5% organic soil load. Twenty (20) brushed stainless steel disk carriers (1 cm diameter, 0.7 mm thick) per product lot were inoculated with 10 µL of test organism. The carriers were dried in a vacuum desiccator for 5 hours at 19°C. Each carrier was transferred, inoculated side up, to a QCT vial, to which 50 µL of the use solution was added. The carriers remained exposed to the use solution for 10 minutes at 20°C. Following exposure, 10 mL of Letheen Broth with 1.0% sodium thiosulfate was added to each vial to neutralize. The contents of each vial were vortex mixed for 45-60 seconds. As necessary, carriers were scraped with a cell scraper (while flushing the carrier surface with neutralizer) to remove any remaining inoculum from the carrier surface. This represents the 10^0 dilution. The contents of each vial were poured through an individual membrane filter. Each vial was rinsed with saline three times, with each rinse poured through the same membrane filter. Each membrane filter was plated on CDC anaerobic blood agar and incubated for 44.25 hours at 35-37°C. Following incubation, the subcultures were enumerated. Controls included those for initial suspension count, carrier population, purity, sterility, neutralization confirmation, and acid resistance (2 and 5 minutes).

V RESULTS

MRID No. 482412-01

Test Organism	Carrier#	Number of Survivors/Carrier	Log_{10} of Number Survivors/Carrier	Average Log_{10}	CFU/Carrier
Clostridium difficile	1	2.8×10^6	6.45	6.43	2.96×10^6
	2	2.5×10^6	6.40		
	3	2.7×10^6	6.43		

Lot Number #101820352M					
Test Organism	Carrier #	#Survivors/Test carrier (Log_{10})	Geometric Mean Test carriers (Avg Log_{10})	Geometric Mean Control Carriers (Average Log_{10})	Percent Reduction (Log_{10} reduction)
Clostridium difficile	1-10	<1 (<0.0)	<1 (<0.0)	2.96×10^6 (6.43)	>99.9999% (>6.4)
Lot Number #102431653M					
Clostridium difficile	1-10	<1 (<0.0)	<1 (<0.0)	2.96×10^6 (6.43)	>99.9999% (>6.4)
Lot Number #102421127M					
Clostridium difficile	1-10	<1 (<0.0)	<1 (<0.0)	2.96×10^6 (6.43)	>99.9999% (>6.4)

VI CONCLUSIONS

A. Conclusions Regarding Use of the Product as a Disinfectant Against *Clostridium difficile* Spores

1. The submitted efficacy data (MRID No. 482412-01) support the use of a 9,978, 9,992, and 9,949 ppm available chlorine use solution of the product, Pure Bright Germicidal Ultra Bleach, as a disinfectant against *Clostridium difficile* on pre-cleaned surfaces for a 10-minute contact time. A 6-log reduction in viable spores was reported by the laboratory. At least one of the product lots tested was at least 60 days old at the time of testing. *Clostridium difficile* test spores showed resistance to acid for >2 minutes. Carrier population counts were $>10^6$ spores/carrier. Neutralization confirmation testing met the acceptance criterion of growth within 1 log_{10} of the numbers control. Purity controls were reported as pure. Sterility controls did not show growth.

B. Conclusions Regarding Use of the Product as a Sanitizer

1. The submitted efficacy data partially support the use of a 1:257 use solution of the product, Pure Bright Germicidal Ultra Bleach, as a sanitizer against the following microorganisms on pre-cleaned, hard, non-porous, non-food contact surfaces for a 5-minute contact time:

The registrant must explain the test protocol deviations: (1) culture was incubated for 48±4-hour which differs from the 18-24 hour old suspension requirement as specified in DIS/TSS-10; and (2) carriers were dried for 20 minutes instead of 40 minute-drying time as specified in DIS/TSS-10. Bacterial reductions of at least 99.9 percent over the parallel control were observed within 5 minutes. At least one of the product lots tested was at least 60 days old at the time of testing. The zero-time control count demonstrated an average of at least 7.5×10^5 surviving organisms, which is the criterion set forth in ASTM 1153. Neutralization confirmation testing met the acceptance criterion of growth within 1 $\log_{10}$ of the numbers control. Purity controls were reported as pure. Sterility controls did not show growth. According to the letter provided by ATS Labs, (1) DIS/TSS-10 from 1976 does note the use of an 18-24 hour culture, the more recent ASTM method reference (E1153) and re-approved in 2003 states that a 48 hour culture be used, therefore in effect superseding DIS/TSS-10. It has been our experience that the culture suspension prepared per ASTM 1153 reproducibly and consistently generates a carrier population of > 10^6 CFU/carrier. When the product being tested is an acceptable sanitizer, this challenge level is more than sufficient to demonstrate the required ≥99.9% reduction; (2) ATS labs specifies a range of drying of 20-40 minutes. In order to assure organism viability and to comply with the drying parameter outlined in ASTM E1153, the carriers are dried with the Petri dish lids slightly ajar when testing with the standard organisms. Subsequently, the organism film does dry onto the carriers in a shorter period of time than stated in DIS/TSS-10. This does not negatively impact the organism challenge in that the carrier population control performed with representative carriers during testing consistently demonstrates an acceptable challenge level of >10^6 CFU/carrier.

Agency's Response: The Agency does not always observe these deviations (1) culture was incubated for 48±4-hour which differs from the 18-24 hour old suspension requirement as specified in DIS/TSS-10; and (2) carriers were dried for 20 minutes instead of 40 minute-drying time as specified in DIS/TSS-10. These deviations are noted, and the claims are now acceptable.

VII RECOMMENDATION

A. Use of the Product as a Disinfectant against *Clostridium difficile* Spores

1. The proposed label claims are acceptable regarding the use of a 1:5 dilution (~10,000 ppm available chlorine) of the product, Pure Bright Germicidal Ultra Bleach as disinfectant against *Clostridium difficile* spores (ATCC 700792) on pre-cleaned, hard, non-porous surfaces for a 10-minute contact time. Acceptable efficacy data support this claim.

B. Use of the Product as a Sanitizer

1. The proposed label claims that a 1 tablespoon product per gallon water use solution (a 1:257 dilution) of the product, Pure Bright Germicidal Ultra Bleach, is an effective sanitizer against the following microorganisms on pre-cleaned, hard, non-porous, non-food contact surfaces for a 5-minute contact time:

Enterobacter aerogenes (ATCC 13048)
Staphylococcus aureus (ATCC 6538)

These claims are **acceptable** as they are supported by the submitted data.

VIII REGISTRANT'S RESPONSE TO AGENCY'S RECOMMENDATIONS

1. Agency's Recommendation: On page 4 of the proposed label, remove the claims "powerful", "original disinfectant", "and smart way to disinfect" as these claims are misleading and/or difficult to assess.
Registrant's Response: KIK used the same claims already approved by EPA: see page 7 (column 3) of the EPA stamped label for Clorox's EPA Reg. No. 5813-50 dated 11/25/09; the label states "Powerful germ killer" and "The smart way to disinfect." As this language has been approved by EPA in the past, KIK has not made the change. KIK has deleted the claim "The original disinfectant."
Agency's Response: No additional information is required.

2. Agency's Recommendation: On page 6 of the proposed label, the claims "purest white", "whitest white", and "more valuable" are unacceptable. The Agency has not determined how to measure/quantitate this claim.
Registrant's Response: The terms of "purest white" and "whitest white" are non-pesticidal laundry claims. These are common claims on non-EPA registered as well as EPA registered bleach labels. There are many examples of this type of claim, including on Clorox's EPA-approved label discussed above. EPA does not need to be able to measure or quantitated the claims, as they are non-pesticidal. The other claim listed is "More Value [than before]" and this refers to size of container, and also is in the nonpesticidal section. Therefore, KIK has not made any changes to those claims.
Agency's Response: No additional information is required.

3. Agency's Recommendation: All allergen claims must be qualified as non-living or include the non-living description before the term "allergen".
Registrant's Response: "Non-living" has been added or used as a qualifier wherever the word "allergen" occurs except on page 4 where the label says "Kills the source of mold allergens." The symbol refers readers to the organism *Aspergillus brasiliensis*. The product kills Aspergillus and many people are allergic to *Aspergillus*, so the statement is correct and does not need to be modified.
Agency's Response: On page 4 of the proposed label, the Agency considers allergens are "non-living"; therefore the claim "Kills the source of mold allergens" is not acceptable.

Additional Comments

1. In response to the question, "Are viruses required to be indicated separately within the list of organisms on page 5 of the label", the response is "no". Viruses typically have the term "virus" associated with their names. For ease of use, thoroughness, registrant often separate viruses in a separate category.