UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

March 29, 2011

MEMORANDUM

Subject: Efficacy Review for 777-99, Brace
DP Barcode: 386281

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

3/31/11

To: Jacqueline Campbell PM 34/ Stacey Grisgby
Regulatory Management Branch II
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Applicant: Reckitt Benckiser, Inc.
Morris Corporate Center IV
399 Interspace Parkway
Parsippany, NJ 07054

Formulation from the Label:

Active Ingredient(s)	% by wt.
Alkyl (50% C_{14}, 40% C_{12}, 10% C_{16}) Dimethyl Benzyl Ammonium Saccharinate	0.10%
Ethanol	58.00%
Other Ingredients	41.90%
Total	100.00%

I BACKGROUND

The product, BRACE (EPA Reg. No. 777-99), is an EPA-approved disinfectant (bactericide, tuberculocide, fungicide, virucide), sanitizer, mildewcide, and deodorizer for use on hard, non-porous surfaces in household, institutional, commercial, food preparation, animal care, and hospital or medical environments. Per the registrant's letter, the current submission was provided to address:

- Typographical/grammatical errors
- Additional claims that were previously submitted as a Notification since the last EPA Stamped Accepted label
- Per the comments on the last EPA Stamped label, we added "as a spot sanitizer" to the Soft Surface sanitization claims
- Removed all references to "heavy fabrics"
- Removed the asterisks on the Deodorizing claims—since these claims are non-public health claims a qualifier not required
- Added alternate qualifier statements for the Disinfection claims
- Alternate H1N1 claims as supported by efficacy data previously submitted
- Added the claim, Rhinovirus (a leading cause of the common cold)
- Added claims based on efficacy data provided
- Revised the Storage and Disposal Instructions

Efficacy data was generated at ATS Labs located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN, 55121. The data package contained a letter from the registrant (dated January 3, 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), 3 efficacy studies (MRID Nos. 483395-01, -03, and 483627-01), Statement of No Data Confidentiality for each study, and the proposed label.

II USE DIRECTIONS

The product is designed for disinfecting hard, non-porous surfaces, including: appliances, bathtubs, bed frames, bed springs, bidets, blinds, cabinets, cages, chairs, changing tables, clean-up carts, counters, cribs, cuspidors, desks, diaper pails, dish pails, doorknobs, drains, dressing carts, drinking fountains, examination tables, faucets, fixtures, floors, furniture, garbage cans, garbage pails, highchairs, kennels, lamps, laundry hampers, light switches, linen carts, litter boxes, mattress covers, mirrors, outdoor patio furniture, pens, recycling bins, remote controls, salad bar sneeze guards, showers, sinks, sports equipment, stretchers, tables, telephones, toilets, tools, toys, urinal exteriors, walls, wheelchairs, whirlpool interiors, and windows. The proposed label indicates that the product may be used on hard, non-porous surfaces including: crystal, enamel, glass, glazed ceramic, glazed porcelain, glazed tile, laminated surfaces, linoleum, marble (synthetic), Marlite, metal (i.e., brass, chrome, copper, stainless steel, tin), Parquet, plastic, sealed granite, and vinyl. Directions on the proposed label provide the following information regarding use of the product as a disinfectant:

Disinfectant: Pre-clean surfaces prior to use. Hold container upright 6-8 inches from surface. Spray 2 to 3 seconds until covered with mist. Let stand for 10 minutes then allow to air dry.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Disinfectants for Use on Hard Surfaces in Hospital or Medical Environments (Additional Bacteria)

The effectiveness of disinfectants against specific bacteria other than those named in the AOAC Use-Dilution Method, AOAC Germicidal Spray Products as Disinfectants Method, AOAC Fungicidal Test, and AOAC Tuberculocidal Activity Method, must be determined by either the AOAC Use-Dilution Method or the AOAC Germicidal Spray Products as Disinfectants Method. Ten carriers must be tested against each specific microorganism with each of 2 product samples, representing 2 different product lots. To support products labeled as "disinfectants" for specific bacteria (other than those bacteria named in the above test methods), killing of the specific microorganism on all carriers is required.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 483395-03 "AOAC Germicidal Spray Method", by Matthew Sathe. Study conducted at ATS Labs. Study completion date – November 19, 2010. Project Number A10383.

This study was conducted against *Klebsiella pneumoniae* NDM-1 positive (CDC 1000527). Two lots (Lot Nos. 1325-186 and 1325-181 of the product, Formula 1338-016 were tested according to ATS Labs Protocol No. REK01100510.GS.3 (copy provided). The product was received ready-to-use. Testing was conducted in the presence of 5% fetal bovine serum as the organic soil load. Glass slides were inoculated with 10 µl of culture. The inoculum was uniformly spread over the entire surface of the slide contained in the Petri dish. The dish was covered immediately. The slides were allowed to dry for 30 minutes at 35-37°C at a 61% relative humidity. Carriers were sprayed individually with the test substance for 3 seconds at a distance 6-8 inches from the carrier surface. Each carrier remained in contact with the test substance for 10 minutes at room temperature (21.0°C) at a 20% relative humidity. Following exposure, the remaining liquid was drained off. Each medicated carriers was then transferred using sterile forceps at identical staggered intervals to 20 ml aliquots of Letheen Broth. All subcultures and controls were incubated for 47.5 hours at 35-37°C. Subcultures were examined for the presence or absence of growth. Controls included those for purity, sterility, viability, neutralization confirmation, and carrier population.

Note—Antibiotic sensitivity testing was performed using a representative organism from the day of testing to verify the stated antibiotic resistance pattern. This testing was performed at the University of Minnesota Physicians Outreach Laboratory in Minneapolis, Minnesota. The testing was not conducted under Good Laboratory Practices.

Note—Lot 1325-181 exceeds the lower certified limits for both active ingredients.

2. MRID 483395-01 "AOAC Germicidal Spray Method", by Becky Lien. Study conducted at ATS Labs. Study completion date – October 19, 2010. Project Number A10151.

This study was conducted against *Escherichia coli* with extended beta-lactamase resistance (ESBL) (ATCC BAA-196). Two lots (Lot Nos. 1325-186 and 1325-181) of the product, Formula 1338-016 were tested according to ATS Labs Protocol No. REK01081310.GS.1 (copy provided). The product was received ready-to-use. Testing was conducted in the presence of 5% fetal bovine serum as the organic soil load. Glass slides were inoculated with 10 µl of culture. The inoculum was uniformly spread over the entire surface of the slide contained in the Petri dish. The dish was covered immediately. The slides were allowed to dry for 40 minutes at 35-37°C at a 42% relative humidity. Carriers were sprayed individually with the test substance for 3 seconds at a distance 6-8 inches from the carrier surface. Each carrier remained in contact with the test substance for 10 minutes at room temperature (21.0°C) at 35% relative humidity. Following exposure, the remaining liquid was drained off. Each medicated carriers was then transferred using sterile forceps at identical staggered intervals to 20 ml aliquots of Letheen Broth. All subcultures and controls were incubated for 46 hours at 35-37°C. Subcultures were examined for the presence or absence of growth. Controls included those for purity, sterility, viability, neutralization confirmation, and carrier population.

Note—ATS Labs used the AB BIODISK Etest Method to verify the antimicrobial susceptibility patter of *Escherichia coli* with extended beta-lactamase resistance (ESBL). The organism was grown on TSA with 5% sheep blood and used to make a suspension equal to a 0.5 McFarland standard in 0.85% sterile saline. The test organism suspension was streaked onto a Mueller Hinton agar plate. The Etest strip containing Cefotaxime and Cefotaxime +Clavulanic acid and the Etest strip containing Ceftazidime and Ceftazidime +Clavulanic acid were both place on the inoculated Mueller Hinton agar plate. The plates were inoculated for 16.5 hours at 35-37°C. Following incubation, the minimum inhibitory concentration values were read. Two quality control strains were run concurrently with the test organism to confirm validity of the assay. The interpretation of the MIC values for the test organism were determined using the Reading and Interpretation section included in the attached reference for AB specifications for the Etest ESBL.

Note—Lot 1325-181 exceeds the lower certified limits for both active ingredients.

3. MRID 483627-01 "AOAC Germicidal Spray Method", by Becky Lien. Study conducted at ATS Labs. Study completion date – November 8, 2010. Project Number A10150.

This study was conducted against *Klebsiella pneumoniae* (ATCC BAA-1705). Two lots (Lot Nos. 1325-186 and 1325-181) of the product, Formula 1338-016 were tested according to ATS Labs Protocol No. REK01081710.GS (copy provided). The product was received ready-to-use. Testing was conducted in the presence of 5% fetal bovine serum as the organic soil load. Glass slides were inoculated with 10 µl of culture. The inoculum was uniformly spread over the entire surface of the slide contained in the Petri dish. The dish was covered immediately. The slides were allowed to dry for 30 minutes at 35-37°C at a 44% relative humidity. Carriers were sprayed individually with

the test substance for 3 seconds at a distance 6-8 inches from the carrier surface. Each carrier remained in contact with the test substance for 10 minutes at room temperature (21.0°C) at 44% relative humidity. Following exposure, the remaining liquid was drained off. Each medicated carriers was then transferred using sterile forceps at identical staggered intervals to 20 ml aliquots of Letheen Broth. All subcultures and controls were incubated for 46.5 hours at 35-37°C. Subcultures were examined for the presence or absence of growth. Controls included those for purity, sterility, viability, neutralization confirmation, and carrier population.

Note—Following incubation, a culture suspension of E. coli (ATCC 25922) was prepared using a sterile swab and sterile 0.85% saline to equal a 0.5 McFarland Turbidity Standard. A 1:10 dilution of the *E. coli* culture suspension was prepared using sterile 0.85% saline. A lawn plate was generated on Mueller Hinton Agar plate.

A 10 µg meropenem disk was aseptically placed in the center of the Mueller Hinton Agar plate inoculated with *E. coli* (ATCC 25922). In a straight line, a sterile inoculating loop was used to streak the positive control (Klebsiella pneumoniae ATCC BAA-1705), the test organism (*Klebsiella pneumonia* ATCC BAA-1705), and the negative control (*Klebsiella pneumoniae* ATCC BAA-1706). The plates were then incubated for 16-24 hours at 35-37°C in the inverted position. Following incubation, the plates was examined for a cloverleaf type identification at the intersection of the test organism and the *E. coli* within the zone of inhibition of the carbapenemase susceptibility disk. The presence of the cloverleaf indentation indicates a positive Modified Hodge test result and confirms that the test organism produces a carbapenemase, and is therefore carbapenem resistant. The absence of the cloverleaf type indentation indicates that the organism does not produce a carbapenemase, and is therefore susceptible to carbapenem.

Note—Lot 1325-181 exceeds the lower certified limits for both active ingredients.

V RESULTS

MRID Number	Organism	No. Exhibiting Growth/ Total No. Tested		Carrier Population (CFU/ Carrier)
		Formula 1338-016, Lot No. 1325-186	Formula 1338-016, Lot No. 1325-181	
483395-01	*Escherichia coli* with extended beta-lactamase resistance (ESBL) (ATCC BAA-196)	0/10	0/10	1.05×10^5
483395-03	*Klebsiella pneumoniae* NDM-1 positive (CDC 1000527)	0/10	0/10	8.71×10^4
483627-01	*Klebsiella pneumoniae* Carbapenem Resistant (ATCC BAA-1705)	0/10	0/10	6.17×10^5

VI CONCLUSIONS

1. The submitted efficacy data do not support the use of the product, Formula # 1338-016, as a disinfectant against the following microorganisms on hard, non-porous surfaces in the presence of a 5% organic soil load for a 10-minute contact time:

Escherichia coli with extended beta-lactamase resistance (ESBL)	MRID 483395-01
Klebsiella pneumoniae NDM-1 positive (CDC 1000527)	MRID 483395-03
Klebsiella pneumoniae Carbapenem Resistant	MRID 483627-01

Neutralization confirmation testing showed positive growth of the microorganism. Purity controls were reported as pure. Viability controls were positive for growth. Sterility controls did not show growth. While complete killing was observed in the subcultures of the tested lots, Lot No. 1325-181 was not tested at the lower certified limits.

Note—The submitted data packages identified Formula# 1338-016 as the EPA Reg. No. 777-99, the subject of this current submission.

VII RECOMMENDATIONS

1. The proposed label claims are unacceptable regarding the use of the product, BRACE, as a disinfectant against the following microorganisms on pre-cleaned, hard, non-porous surfaces for a 10-minute contact time in the presence of 5% organic soil:

Escherichia coli with extended beta-lactamase resistance (ESBL)	ATCC BAA-196
Klebsiella pneumoniae NDM-1 positive	CDC 1000527
Klebsiella pneumoniae Carbapenem Resistant	ATCC BAA-1705

Efficacy data must be generated using a product lot at the lower certified limits.

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

- On the proposed label, the claim for "Superbug" is unacceptable. The Agency has not defined bacteria that constitute "superbug". Until such time, this claim must be removed from the label.
- On the proposed label, remove references to "Childhood infections", as the Agency has not determined pathogens associated with this claim.
- The claim "fast-acting" has not been quantitated by the Agency. Until such time, these claims are unacceptable.
- For the claim Respiratory Syncytial Virus (RSV), replace "the leading cause of lower respiratory infections in children" with "a leading cause of lower respiratory infection in children"