MEMORANDUM

DATE: July 18, 2006

SUBJECT: Efficacy Review for DISPATCH Hospital Cleaner Disinfectant with Bleach, EPA Reg. No. 56392-7; DP Barcode: D328902

FROM: CSC Systems & Solutions LLC (CSS)

THRU: Wallace Powell
Antimicrobials Division

TO: Nancy Whyte
Antimicrobials Division

APPLICANT: Caltech Industries, Inc.
Midland, MI

I BACKGROUND

The product, DISPATCH Hospital Cleaner Disinfectant with Bleach (EPA Reg. No. 56392-7), is an EPA-approved disinfectant (bactericide, fungicide, virucide) and deodorizer for use on hard, non-porous surfaces in commercial, institutional, animal care, and hospital or medical environments. The proposed label indicates that the product disinfects in "one step." The applicant requested to amend the registration of this product to include claims for effectiveness against Avian Flu, Hepatitis A virus, and Norovirus. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 100, in Eagan, MN 55121.

This data package contained a letter from the applicant's representative to EPA (dated April 13, 2006), four studies (MRID Nos. 468154-01 through 468154-04), Statements of No Data Confidentiality Claims for all four studies, and the proposed label.

Note: CSS downloaded the last-accepted label (dated October 18, 2005) from the Internet.

II USE DIRECTIONS

The product is designed to be used for disinfecting hard, non-porous surfaces such as animal equipment, autoclaves, bed railings, blood glucose monitors, cages, chairs, changing tables, counter tops, door knobs, exam tables, fountains, gurneys, hand railings, high chairs, IV poles, medical equipment (exterior surfaces), phlebotomy trays, plastic mattress covers, play pens, stretchers, ultrasound transducers and probes (external surfaces), wash basins, and wheelchairs. The label indicates that the product may be used on hard, non-porous surfaces including: fiberglass, glass, glazed ceramic tile, glazed porcelain, hard plastics, laminated

surfaces, painted surfaces, Plexiglass, stainless steel, and vinyl. Directions on the proposed label provided the following information regarding use of the product as a disinfectant: Remove gross soil prior to disinfecting. Spray 6-8 inches from surface until surface is completely wet. Let stand for 1 minute. Wipe with a clean, damp cloth or paper towel. Allow to air dry. For food contact surfaces, rinse with potable water.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products as Disinfectants Method (for spray disinfectants) must be used. To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of 2 different product lots of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique, using a minimum of four determinations per each dilution assayed. Separate studies are required for each virus. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level. These Agency standards are presented in DIS/TSS-7.

Virucides – Novel Virus Protocol Standards

To ensure that a virus protocol has been adequately validated, data should be provided from at least 2 independent laboratories for each product tested (i.e., 2 product lots per laboratory). These Agency standards are tailored from those presented in the Federal Register, Vol. 65, No. 166, Friday, August 25, 2000.

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. These Agency standards are presented in DIS/TSS-2.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 468154-01 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces, Virus: Avian Influenza A (H3N2) virus (Avian Reassortant)" for Dispatch Hospital Cleaner Disinfectant with Bleach, by Mary J. Miller. Study conducted at ATS Labs. Study completion date – October 4, 2005. Project Number A03121.

This study was conducted against Avian Influenza A (H3N2) virus (Avian Reassortant) (Strain A/Washington/897/80 X A/Mallard/New York/6750/78; ATCC VR-2072), using RMK cells (Rhesus monkey kidney cells; obtained from ViroMed Laboratories, Inc.) as the host system. Two lots (Lot Nos. FF050317 and HF050406) of the product, Dispatch Hospital Cleaner Disinfectant with Bleach, were tested according to ATS Labs Protocol No. SRC36072105.AFLU.2 (copy not provided). The product was received ready-to-use in a trigger sprayer. The stock virus culture was adjusted to contain 5% fetal bovine serum as the organic soil load. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried at 20.0°C at 47% relative humidity for 20 minutes. For each lot of product, separate carriers were sprayed (3 sprays) at a distance of 6-8 inches from the surface until thoroughly wet. The carriers remained exposed to the product for 1 minute at 23.5°C. After exposure, the plates were scraped with a cell scraper to re-suspend the contents. Each virus-disinfectant mixture was passed through a Sephadex column using a syringe plunger. Ten-fold serial dilutions were prepared, using Minimum Essential Medium supplemented with 1% heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, and 2.5 µg/mL amphotericin B. RMK cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The cultures were incubated at 36-38°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 7 days for the presence or absence of unspecified cytopathic effects, cytotoxicity, and viability. Controls included those for dried virus count, cytotoxicity, and neutralization. Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

2. MRID 468154-02 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces, Virus: Hepatitis A virus" for Dispatch Hospital Cleaner Disinfectant with Bleach, by Mary J. Miller. Study conducted at ATS Labs. Study completion date – October 4, 2005. Project Number A03120.

This study was conducted against Hepatitis A virus (Strain HM-175; obtained from AppTec Laboratory Services, Camden, NJ), using FRhK-4 cells (fetal Rhesus monkey kidney cells; ATCC CRL-1688; propagated in-house) as the host system. Two lots (Lot Nos. FF050317 and HF050406) of the product, Dispatch Hospital Cleaner Disinfectant with Bleach, were tested according to ATS Labs Protocol No. SRC36072105.HAV (copy not provided). The product was received ready-to-use in a trigger sprayer. The stock virus culture contained 5% fetal bovine serum as the organic soil load. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried at 20.5°C at 43% relative humidity for 20 minutes. For each lot of product, separate carriers were sprayed (3 sprays) at a distance of 6-8 inches from the surface until thoroughly wet. The carriers remained exposed to the product for 1 minute at 20.5°C. After exposure, the plates

were scraped with a cell scraper to re-suspend the contents. Each virus-disinfectant mixture was passed through a Sephadex column using a syringe plunger. Ten-fold serial dilutions were prepared, using Minimum Essential Medium supplemented with 10% heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, 2.5 µg/mL amphotericin B, and 2.0 mM L-glutamine. FRhK-4 cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The inoculum was allowed to adsorb and test medium was added to the cultures. The cultures were incubated at 36-38°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 14 days for the presence or absence of unspecified cytopathic effects, cytotoxicity, and viability. Controls included those for dried virus count, cytotoxicity, and neutralization. Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

Note: The applicant provided the data for a failed trial set up on August 11, 2005. In that trial, test virus was observed in the cytotoxicity controls, indicating the presence of virus contamination in the study. Thus, the test was invalid. These data were not used to evaluate efficacy of the test product. See Attachment I of the laboratory report.

3. MRID 468154-03 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces Utilizing Feline Calicivirus as a Surrogate Virus for Norovirus" for Dispatch Hospital Cleaner Disinfectant with Bleach, by Karen M. Ramm. Study conducted at ATS Labs. Study completion date – October 4, 2005. Project Number A03181.

This study, under the direction of Study Director Karen M. Ramm, was conducted against Feline calicivirus (a surrogate for Norovirus; Strain F-9; ATCC VR-782), using CRFK cells (Crandel Reese feline kidney cells; ATCC CCL-94; propagated in-house) as the host system. Two lots (Lot Nos. FF050317 and HF050406) of the product, Dispatch Hospital Cleaner Disinfectant with Bleach, were tested according to ATS Labs Protocol No. SRC36072105.FCAL.2 (copy not provided). The product was received ready-to-use in a trigger sprayer. The stock virus culture contained 5% fetal bovine serum as the organic soil load. Two glass carriers were tested for each product lot against the target virus. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried at 20.5°C at 44% relative humidity for 20 minutes. For each lot of product, separate carriers were sprayed (3 sprays) at a distance of 6-8 inches from the surface. The carriers remained exposed to the product for 1 minute at 23.0°C. After exposure, the plates were scraped with a cell scraper to re-suspend the contents. Each virus-disinfectant mixture was passed through a Sephadex column using a syringe plunger. Ten-fold serial dilutions were prepared, using Minimum Essential Medium supplemented with 5% (v/v) heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, and 2.5 µg/mL amphotericin B. CRFK cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The cultures were incubated at 31-35°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 7 days for the presence or absence of cytopathic effects (i.e., small, rounding of the cells; slight granular look), cytotoxicity, and viability. Controls included those for input virus count, dried virus count, cytotoxicity, and neutralization. Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

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

4. MRID 468154-04 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces Utilizing Feline Calicivirus as a Surrogate Virus for Norovirus – Confirmatory Assay" for Dispatch Hospital Cleaner Disinfectant with Bleach, by Mary J. Miller. Study conducted at ATS Labs. Study completion date – October 4, 2005. Project Number A03122.

This confirmatory study, under the direction of Study Director Mary J. Miller, was conducted against Feline calicivirus (a surrogate for Norovirus; Strain F-9; ATCC VR-782), using CRFK cells (Crandel Reese feline kidney cells; ATCC CCL-94; propagated in-house) as the host system. One lot (Lot No. FF050317) of the product, Dispatch Hospital Cleaner Disinfectant with Bleach, was tested according to ATS Labs Protocol No. SRC36072105.FCAL.1 (copy not provided). The product was received ready-to-use in a trigger sprayer. The stock virus culture contained 5% fetal bovine serum as the organic soil load. Two glass carriers were tested for the single product lot against the target virus. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried at 20.0°C at 45% relative humidity for 20 minutes. For the single product lot, separate carriers were sprayed (3 sprays) at a distance of 6-8 inches from the surface until thoroughly wet. The carriers remained exposed to the product for 1 minute at 23.5°C. After exposure, the plates were scraped with a cell scraper to re-suspend the contents. Each virus-disinfectant mixture was passed through a Sephadex column using a syringe plunger. Ten-fold serial dilutions were prepared, using Minimum Essential Medium supplemented with 5% (v/v) heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, and 2.5 µg/mL amphotericin B. CRFK cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The cultures were incubated at 31-35°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 7 days for the presence or absence of cytopathic effects (i.e., small, rounding of the cells; slight granular look), cytotoxicity, and viability. Controls included those for input virus count, dried virus count, cytotoxicity, and neutralization. Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

V RESULTS

MRID Number	Organism	Results			Dried Virus Control ($TCID_{50}$/0.1 mL)
			Lot No. FF050317	Lot No. HF050406	
468154-01	Avian Influenza A (H3N2) virus	10^{-1} to 10^{-8} dilutions	Complete inactivation	Complete inactivation	$10^{6.5}$
		$TCID_{50}$/0.1 mL	$\leq 10^{0.5}$	$\leq 10^{0.5}$	
468154-02	Hepatitis A virus	10^{-1} to 10^{-8} dilutions	Complete inactivation	Complete inactivation	$10^{6.5}$
		$TCID_{50}$/0.1 mL	$\leq 10^{0.5}$	$\leq 10^{0.5}$	

MRID Number	Organism	Results			Dried Virus Control ($TCID_{50}$/0.1 mL)
			Lot No. FF050317	Lot No. HF050406	
468154-03	Feline calicivirus	10^{-1} to 10^{-4} dilutions	Complete inactivation	Complete inactivation	$10^{6.25}$ and $10^{5.75}$
		$TCID_{50}$/0.1 mL	$\leq 10^{0.5}$	$\leq 10^{0.5}$	
468154-04	Feline calicivirus	10^{-1} to 10^{-4} dilutions	Complete inactivation	---	$10^{6.75}$ and $10^{6.5}$
		$TCID_{50}$/0.1 mL	$\leq 10^{0.5}$		

VI CONCLUSIONS

1. The submitted efficacy data support the use of the product, DISPATCH Hospital Cleaner Disinfectant with Bleach, as a disinfectant with virucidal activity against the following microorganisms on hard, non-porous surfaces in the presence of a 5% organic soil load for a contact time of 1 minute:

Avian Influenza A (H3N2) virus	MRID No. 468154-01
Hepatitis A virus	MRID No. 468154-02
Feline calicivirus (a surrogate for Norovirus)	MRID Nos. 468154-03 and -04

Recoverable virus titers of at least 10^4 were achieved. Cytotoxicity was not observed. Complete inactivation (no growth) was indicated in all dilutions tested. In studies against Feline calicivirus, confirmatory testing was performed under a different study director. The confirmatory study used one lot of product not the standard two.

VII RECOMMENDATIONS

1. The proposed label claims that the product, DISPATCH Hospital Cleaner Disinfectant with Bleach, is an effective "one-step" disinfectant on hard, non-porous surfaces against Avian Flu Virus (H3N2), Hepatitis A Virus, and Norovirus for a contact time of 1 minute. Data provided by the applicant support these claims.

2. The following claim [on page 1 of the proposed label] should be deleted or revised: "Meets OSHA Bloodborne Pathogen Standards." These standards relate to requirements for employers of workers exposed to blood or other potentially infectious materials.

3. The proposed label indicates that the product may be used on fiberglass surfaces [see page 2 of the proposed label]. Fiberglass is a porous surface. This general reference to fiberglass surfaces should be deleted. Specific fiberglass surfaces (e.g., fiberglass bathtubs) may be listed on the product label.

4. Storage and disposal information on the proposed label should be revised as follows:

   - Under the "Storage and Disposal" heading on page 4 of the proposed label, insert the following statement: "Do not contaminate water, food, or feed by storage or disposal." EPA has historically required labels for all non-household products to include this statement.

   - Under the "Storage and Disposal" section on page 4 of the proposed label, reinsert the following statement, which was included on the last-accepted label: "In case of spill, flood areas with large quantities of water." Product labels must include instructions on what to do if a container is leaking or a product spill has occurred.

   - Revise the label's current disposal statement according to information provided in PR Notice 83-3 for plastic containers: "Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or by incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke."

5. Making the following changes would improve the proposed label:

   - Under the "To Clean and Disinfect in a Veterinary Application" on page 2 of the proposed label, after the phrase ". . . traversed by animals," insert: "Empty all feeding and watering equipment."

   - Under the "To Clean and Disinfect in a Veterinary Application" on page 2 of the proposed label, after the phrase ". . . to remain wet for one minute," insert: "Immerse all halters, ropes and other types of equipment used in handling and restraining animals, as well as forks, shovels, and scrapers used for removing litter and manure."

   - On page 3 of the proposed label, change "Critical and semi-critical devices must be followed by . . ." to read "Cleaning of critical and semi-critical devices must be followed by . . . ."