UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

July 28, 2003

MEMORANDUM:

Subject: Efficacy Review EPA Reg.No. 56392-8
Dispatch Hospital Cleaner Disinfectant Towels with Bleach
DP Barcode 289244

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Thru: Emily Mitchell, M.S., Team Leader Emily Mitchell 7/31/03
Efficacy Evaluation Team
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Applicant: Caltech Industries Inc.
Midland, MI 48642

Formulation Label:

Active Ingredient(s)	**%/wt**
Sodium hypochlorite	0.52%
Other ingredients	99.48%
Total	100.0%

I. Background:

The registrant has submitted a data matrix to support added label claims for effectiveness of this towelette product against Methicillin Resistant *Staphylococcus aureus*, Vancomycin Resistant *Enterococcus faecalis, Rotavirus, Hepatitis B Virus, Hepatitis C Virus,* and to add a 30-second exposure time for *Mycobacterium tuberculosis.* A data matrix was

submitted in the package citing data reported for the efficacy testing conducted on a spray product (56392-7) which has the same liquid formulation that has been used to saturate this towelette product. The data package referenced four studies (MRID Nos. 458861-01 through 458861-04) conducted on the ready-to-use spray product DISPATCH® These studies may be found in the data package assigned DP Barcode D289245. No efficacy testing was conducted for the towelette product itself.

II. Use Directions:

The product is designed to be used for disinfecting hard, non-porous surfaces such as tiles. The product may be used on stainless steel, plastic, tile, and porcelain. Directions on the proposed label provided the following information regarding the use of the product as a "one-step" disinfectant: Gloves should be worn. Remove gross soil prior to disinfecting. Wipe surface with towel until completely wet. Allow a contact time of 1 minute at room temperature (68-77°F). Allow a contact time of 30 seconds at room temperature to kill TB. Finally, the label directions noted that: "This product is not to be used as a terminal sterilant/high level disinfectant on any surface or instrument . . . ."

III. Agency Standards for Proposed Change

Disinfectants 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 disinfecting hard surfaces. The standard test methods available for hard surface disinfectants (i.e., AOAC Use-Dilution Method, AOAC Germicidal Spray Products as Disinfectants Method), 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 AOAC Germicidal Spray Products as Disinfectants Method. Agency guidelines further recommend that instead of spraying the inoculated surface of the glass slide, the product should be tested by wiping the surface of the glass slide with the saturated towelette, and then subculturing the slides after a specified holding time. Liquid expressed from the used towelette should also be subcultured. Sixty carriers must be tested with each of 3 product samples, representing 3 different batches, one of which is at least 60 days old. To support products labeled as "disinfectants," killing on 59 out of 60 carriers (for both the slide subculture and the expressed liquid from the towelette) is required to provide effectiveness at the 95% confidence level. The above Agency standards are presented in DIS/TSS-1 and EPA Pesticide Assessment Guidelines, Subdivision G, §91-2(h), Pre-saturated or impregnated towelettes.

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 in developing data for virucides intended for use upon dry inanimate, environmental surfaces (e.g., floors, tables, cleaned dried

medical instruments). 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 batches 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 batches per product per laboratory). The validation of a protocol requires the use of a common positive control disinfectant to be tested concurrently with all new products. For the Hepatitis B Virus protocol, the usual control is BTC-835, a quaternary ammonium compound product obtained from Stepan Company. For the Hepatitis C Virus protocol, the usual control is Bardac 2280, a quaternary ammonium compound obtained from Lonza, Inc. These agents serve as both intra-laboratory and inter-laboratory controls and are used for analyzing the reproducibility of the efficacy data results for the protocol. These Agency standards are tailored from those presented in the Federal Register, Vol. 65, No. 166, Friday, August 25, 2000 and from the August 6, 2002 memorandum entitled "Review of a Protocol for Testing Disinfectants against Hepatitis C Virus Using Bovine Viral Diarrhea Virus."

Supplemental Claims

An antimicrobial agent identified as a "one-step" cleaner-disinfectant, cleaner-sanitizer, or one intended to be effective in the presence of organic soil must be tested for efficacy with an appropriate organic soil load, such as 5 percent serum. This Agency standard is presented in DIS/TSS-2.

IV. Summary of Submitted Studies:

1. MRID 458861-01 "Initial Virucidal Effectiveness Test Using Duck Hepatitis B Virus" for XC20003.05, by Shiva D. Rajaram. Study conducted at MicroBioTest, Inc. Study completion date – November 21, 2002. Laboratory Project Identification Number 338-145.

This study, under the direction of Study Director M. Khalid Ijaz, was conducted against the Duck Hepatitis B virus (strain not specified; obtained from HepadnaVirus Testing, Inc.) using primary duck hepatocytes as the host system. The study protocol followed MicroBioTest Protocol "Initial Virucidal Effectiveness Test Using Duck Hepatitis B Virus," July 25, 2002 (copy provided). Two lots (Lot Nos. IF020625 and HF020501) of the ready-to-use spray product, XC20003.05, were tested. Serum, at a concentration of at least 5%, was present in the virus stock. Two glass carriers were tested for each product lot against the target virus. Films of virus were made by spreading 0.2 mL of stock virus on the bottoms of separate sterilized Petri dishes. The virus films were dried for 30-60 minutes at room temperature. For each lot of

product, the ready-to-use product was sprayed at a distance of 6-8 inches until the virus films were thoroughly wet. The product was allowed to remain for 1 minute at 23±2°C. After the contact period, the virus-disinfectant mixture was neutralized with 2.0 mL of fetal bovine serum and the mixture was scraped from the surface of the dish with a cell scraper. Each sample (0.5 mL) was loaded onto pre-spun Sephacryl columns and spun to obtain the eluate. Ten-fold serial dilutions were prepared, using Liebovitz-15 complete tissue culture medium (CCM). Primary duck hepatocytes were inoculated in quadruplicate with an unspecified amount of each dilution and incubated at 37±2°C in 5±1% CO_2 for 20-30 hours for viral adsorption. Post-adsorption, the media was aspirated and the cells were washed with CCM. The cells then were refed with CCM. The plates were incubated for an additional 7-14 days at 37±2°C in 5±1% CO_2. CCM was replaced with fresh CCM on alternate days. The plates were assayed by indirect immunofluorescence assay. Host cells were fixed with ethanol, stained and read for infectivity, and enumerated as Most Probable Number (MPN). Controls included cell viability, virus stock titer, plate recovery, column titer, neutralizer effectiveness, cytotoxicity, and data consistency. Stepan Company's BTC 835 (Lot No. 7-39358) was used as the data consistency control at two concentrations, 175±15 ppm (titrated at 164.6 ppm) and 350±15 ppm (titrated at 338.5 ppm).
Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.
Note: The laboratory report [pages 7 and 11] incorrectly refers to the data consistency control as BTC 385.

2. MRID 458861-02 "Confirmatory Virucidal Effectiveness Test Using Duck Hepatitis B Virus" for XC20003.05, by Shiva D. Rajaram. Study conducted at MicroBioTest, Inc. Study completion date – December 23, 2002. Laboratory Project Identification Number 338-146.

This study, under the direction of Study Director John C. Pugh, was conducted against the Duck Hepatitis B virus (strain not specified; obtained from HepadnaVirus Testing, Inc.) using primary duck hepatocytes as the host system. The study protocol followed MicroBioTest Protocol "Confirmatory Virucidal Effectiveness Test Using Duck Hepatitis B Virus," July 11, 2002 (copy provided). One lot (Lot No. HF020501) of the ready-to-use spray product, XC20003.05, was tested. Serum, at a concentration of at least 5%, was present in the virus stock. Two glass carriers were tested for the product lot against the target virus. Films of virus were made by spreading 0.2 mL of stock virus on the bottoms of separate sterilized Petri dishes. The virus films were dried for 30-60 minutes at room temperature. For each lot of product, the ready-to-use product was sprayed at a distance of 6-8 inches until the virus films were thoroughly wet. The product was allowed to remain for 1 minute at 23±2°C. After the contact period, the virus-disinfectant mixture was neutralized with an unspecified amount of fetal bovine serum and the mixture was scraped from the surface of the dish with a cell scraper. Each sample (0.5 mL) was loaded onto pre-spun Sephacryl columns and spun to obtain the eluate. The samples were aseptically removed from the columns and dispensed into dilution tubes containing Liebovitz-15 complete tissue culture medium (CCM). Ten-fold serial dilutions were prepared in CCM. Primary duck hepatocytes were inoculated in quadruplicate with an unspecified amount of each dilution and incubated at 37±2°C in 5±1% CO_2 overnight for viral adsorption. On the following day, CCM was replaced with fresh CCM followed by replacement of CCM on alternate days. The plates were incubated for an additional 7-14 days at 37±2°C in 5±1% CO_2. The plates were assayed by immunofluorescence assay. Host cells were fixed with ethanol, stained, washed with PBS, and read for infectivity. Host cells were enumerated as

Most Probable Number (MPN). Controls included cell viability, virus stock titer, plate recovery, column titer, neutralizer effectiveness, cytotoxicity, and data consistency. Stepan Company's BTC 835 (Lot No. 931539) was used as the data consistency control at two concentrations, 175±15 ppm (titrated at 175.4 ppm) and 350±15 ppm (titrated at 350.9 ppm).
Note: The study was conducted according to GLP standards with the following exception: Not all data was recorded promptly in strict compliance with GLP standards.
Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.

3. MRID 458861-03 "Virucidal Effectiveness Test Using Bovine Viral Diarrhea Virus (BVDV) (Surrogate for human Hepatitis C virus)" for XC20003.05, by Shiva D. Rajaram. Study conducted at MicroBioTest, Inc. Study completion date – November 18, 2002. Laboratory Project Identification Number 338-153.

This study, under the direction of Study Director M. Khalid Ijaz, was conducted against the Bovine viral diarrhea virus (strain not specified; obtained from American BioResearch Laboratories) using MDBK cells (ATCC CCL-22) as the host system. The study protocol followed MicroBioTest Protocol "Virucidal Effectiveness Test Using Bovine viral diarrhea virus (BVDV) (Surrogate for human Hepatitis C virus)" (undated; copy provided). Two lots (Lot Nos. LF020807 and IF020625) of the ready-to-use spray product, XC20003.05, were tested. Serum, at a concentration of at least 5%, was present in the virus stock. Two glass carriers were tested for each of the product lots against the target virus. Films of virus were made by spreading 0.2 mL of stock virus on the bottoms of separate sterilized Petri dishes. The virus films were dried for 30-60 minutes at room temperature. For each lot of product, the ready-to-use product was sprayed at a distance of 6-8 inches until the virus films were thoroughly wet; approximately 2.0 mL of the product was used. The product was allowed to remain for 1 minute at 23±2°C. After the contact period, the virus-disinfectant mixture was neutralized with 2.0 mL of horse serum and the mixture was scraped from the surface of the dish with a cell scraper. Each sample (0.5 mL) was loaded onto pre-spun Sephacryl columns and spun to obtain the eluate. Ten-fold serial dilutions were prepared, using Minimum Essential Media Eagle's containing 5% horse serum. MDBK cells were inoculated in quadruplicate with an unspecified amount of each dilution and incubated at 37±2°C in 5±1% CO_2 for 3-5 days. The plates were assayed by direct immunofluorescence assay. Host cells were fixed with alcohol, stained and read for infectivity, and enumerated as Most Probable Number (MPN). Controls included cell viability, virus stock titer, plate recovery, column titer, neutralizer effectiveness, cytotoxicity, and data consistency. Lonza Inc.'s Bardac 2280 (Lot No. 5081-170A) was used as the data consistency control at two concentrations, 50±5 ppm (titrated at 50 ppm) and 350±15 ppm (titrated at 348.6 ppm).
Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.
Note: Information on page 14 of the laboratory report notes a contact period of 10 minutes. The laboratory report references a contact time of 1 minute in all other places. This appears to be a simple typographical error.

4. MRID 458861-04 "Confirmatory Virucidal Effectiveness Test Using Bovine Viral Diarrhea Virus (BVDV) (Surrogate for human Hepatitis C virus)" for XC20003.05, by Shiva D. Rajaram. Study conducted at MicroBioTest, Inc. Study completion date – November 22, 2002. Laboratory Project Identification Number 338-154.

This study, under the direction of Study Director John C. Pugh, was conducted against the Bovine viral diarrhea virus (strain not specified; obtained from American BioResearch Laboratories) using MDBK cells (ATCC CCL-22) as the host system. The study protocol followed MicroBioTest Protocol "Confirmatory Virucidal Effectiveness Test Using Bovine viral diarrhea virus (BVDV) (Surrogate for human Hepatitis C virus)" (undated; copy provided). One lot (Lot No. LF020807) of the ready-to-use spray product, XC20003.05, was tested. Serum, at a concentration of at least 5%, was present in the virus stock. Two glass carriers were tested for the product lot against the target virus. Films of virus were made by spreading 0.2 mL of stock virus on the bottoms of separate sterilized Petri dishes. The virus films were dried for 30-60 minutes at room temperature. For each lot of product, the ready-to-use solution was sprayed (three times) at a distance of 6-8 inches; approximately 2.0 mL of the product was used. The product was allowed to remain for 1 minute at 23±2°C. After the contact period, the virus-disinfectant mixture was neutralized with 2.0 mL of horse serum and the mixture was scraped from the surface of the dish with a cell scraper. Each sample (0.5 mL) was loaded onto pre-spun Sephacryl columns and spun to obtain the eluate. Ten-fold serial dilutions were prepared, using Minimum Essential Media Eagle's containing 5% horse serum. MDBK cells were inoculated in quadruplicate with an unspecified amount of each dilution and incubated at 37±2°C in 5±1% CO_2 for 3-5 days. The plates were assayed by direct immunofluorescence assay. Host cells were fixed with alcohol, stained and read for infectivity, and enumerated as Most Probable Number (MPN). Controls included cell viability, virus stock titer, plate recovery, column titer, neutralizer effectiveness, cytotoxicity, and data consistency. Lonza Inc.'s Bardac 2280 (Lot No. 5081-170A) was used as the data consistency control at two concentrations, 50±5 ppm (titrated at 50 ppm) and 350±15 ppm (titrated at 348.6 ppm).
Note: The study was conducted according to GLP standards with the following exception: Not all data were initialed and dated promptly in strict compliance with GLP standards.
Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.
Note: Information on page 14 of the laboratory report notes a contact period of 10 minutes. The laboratory report references a contact time of 1 minute in all other places. This appears to be a simple typographical error.

V. Labeling:

1. The last accepted label states that the product (the spray product) kills *Mycobacterium tuberculosis* in two minutes. This is not supported by efficacy testing conducted by the Agency laboratory and must be removed. The minimum exposure time allowed by the Agency for this organism is one minute.

VI. Comments and Recommendations:

1. The proposed label claims <u>are not acceptable</u> regarding the use of the product, DISPATCH® Hospital Cleaner Disinfectant Towels with Bleach, as a virucide against the following organisms in the presence of a 5% organic soil load (serum) on hard, non-porous surfaces for a contact time of 1 minute:

Hepatitis B virus	MRID Nos. 458861-01 and -02
Hepatitis C virus	MRID Nos. 458861-03 and -04

Efficacy data for a towelette product must be obtained using a towelette and

subculturing expressed liquid from the used towelette; these conditions were not included in MRID Nos. 458861-01 through 458861-04. Efficacy data for a duplicated formulation are permissible only when, among other conditions, directions for use are identical in substance. A spray product and a towelette product do not have identical directions for use.

2. The proposed label claims <u>are not acceptable</u> regarding the use of the product DISPATCH® Hospital Cleaner Disinfectant Towels with Bleach as a disinfectant against the following organisms in the presence of a 5% organic soil load (serum) on hard, non-porous surfaces for the contact times noted:

Organism	Contact Time
Enterococcus faecalis Vancomycin Resistant	1 minute
Mycobacterium tuberculosis	1 minute
Staphylococcus aureus MRSA	1 minute
Rotavirus	1 minute

For the reasons stated above, the applicant may not rely on efficacy data developed for the spray product registered as EPA Reg. No. 56392-7 . The applicant must submit efficacy data developed for the towel product itself; this data must include results from the subculturing of expressed liquid from the used towel product.

3. No label claims for the effectiveness of this towelette product against the above listed organisms are allowed until efficacy testing has been conducted and approved by the Agency.