UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: October 13, 2003

SUBJECT: Secondary Review of Contractor's (DynCorp Systems Solutions LLC, A CSC Company), Efficacy Review of Sterilex Ultra Disinfectant Cleaner Solution 1, EPA File Symbol 63761-I,
DP Barcode: D293177
Decision #331549

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APPLICANT: Sterilex Corporation
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FORMULATION:

Active Ingredient(s)	% by wt
n-Alkyl (C12,68%; C14, 32%) ethylbenzyl ammonium chloride	3.00
n-Alkyl (C14, 60%; C16, 30%; C12,5%; C18, 5%) benzyl ammonium chloride	3.00
Hydrogen peroxide	6.30

Internet Address (URL) • http://www.epa.gov

I BACKGROUND

The product, Sterilex Ultra Disinfectant Cleaner Solution 1 (EPA File Symbol 63761-I), is a new product. The applicant requested to register the product as a "one-step" disinfectant (bactericide) for use on hard, non-porous surfaces including for use in household, institutional, industrial, commercial, food and beverage processing, animal care, and hospital or medical environments. The proposed label claims that the product, when mixed with Sterilex Ultra Activator Solution, is effective "in the presence of 400 ppm hard water plus 5% organic serum." Studies were conducted at AppTec Laboratory Services, located at 2540 Executive Drive, St. Paul, MN 55120.

This data package contained a letter from the applicant to EPA (dated July 9, 2003), EPA Form 8570-35 (Data Matrix), three studies (MRID Nos. 460335-02 through 460335-04), Statements of No Data Confidentiality Claims for all three studies, and the proposed label.

Note: The laboratory reports describe studies conducted for the product, Sterilex Ultra-Kleen Liquid. The data package does not contain any information to confirm that the tested product, Sterilex Ultra-Kleen Liquid, is Sterilex Ultra Disinfectant Cleaner Solution 1, which is the subject of this efficacy report

Note: The July 9, 2003 letter from the applicant to EPA states that the product, Sterilex Ultra Disinfectant Cleaner Solution 1 is similar to the EPA-registered product, Ultra Kleen Solution 1 (EPA Reg. No. 63761-3).

Note: The July 9, 2003 letter from the applicant to EPA also indicates that the product, Sterilex Ultra Disinfectant Cleaner Solution1, is substantially similar to a pending product, Sterilex Ultra Liquid B Solution 2 (EPA File Symbol 63761-A). The two products are applied at the same concentration of active ingredients.

II USE DIRECTIONS

The product, when mixed with Sterilex Ultra Activator Solution, is designed to be used for disinfecting hard, non-porous surfaces such as medical machines (x-rays, MRIs, CAT scanners), devices, and equipment; water reservoirs, tubing, tanks, and pipes; tanks; piping systems; floors; walls; counter tops; sinks; appliances; dishes, glassware, silverware, cutlery and other eating and cooking utensils; plastic and other nonporous cutting boards and chopping blocks; coolers, ice chests, and refrigerator bins; food processing equipment; dairy equipment; kitchen equipment; beverage manufacturing and dispensing equipment; ice making machines; furniture; cabinets; garbage cans; telephones; doorknobs; shower stalls, bathtubs, and glazed tiles; whirlpool bathtubs; toilets and urinals; kennel runs and cages; animal waterers and feeders; farm equipment; poultry-house related equipment; and salon/barber tools and instruments. The product may be used on hard, non-porous surfaces made of metal, stainless steel, glazed porcelain, glazed ceramic, sealed stone, fiberglass, plastic (such as polystyrene, polypropylene), porcelain tiling, enameled surfaces, finished woodwork, finished floors, Formica®, vinyl, and plastic upholstery.

The proposed label directions regarding use of the product as a disinfectant, in general, read as follows: "(1) Add 12 oz of Sterilex Ultra Disinfectant Cleaner Solution 1 and 12 oz of Sterilex Ultra Activator Solution to 1 gal. tap water in an appropriate plastic container and stir;

(2) Thoroughly wet surfaces with use-solution by pouring, wiping, brushing, scrubbing, spraying with a coarse trigger sprayer, sponging, using a clean in place (CIP) system, pumping it through the system, drawing it through the system or mopping; (3) allow surfaces to remain wet for at least 10 minutes; (4) wipe or rinse all surfaces thoroughly with potable water." Pre-cleaning of gross filth may be desired.

Finally, the proposed label 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 CLAIMS

Confirmatory Efficacy Data Requirements – Disinfectants for Use in Hospital or Medical Environments

Under certain circumstances, an applicant is permitted to rely on previously submitted efficacy data to support an application or amendment for registration of a product and to submit only minimal confirmatory efficacy data on his own product to demonstrate his ability to produce an effective formation. This includes duplicated product formulations. Confirmatory data must be developed on the applicant's own finished product. For hospital disinfectants, 10 carriers on each of 2 samples representing 2 different batches of product must be tested against *Salmonella choleraesuis* (ATCC 10708), *Staphylococcus aureus* (ATCC 6538), and *Pseudomonas aeruginosa* (ATCC 15442) using either the AOAC Use-Dilution Method or the AOAC Germicidal Spray Products as Disinfectants Method. Killing on all carriers is required. The above Agency standards are presented in DIS/TSS-5 enclosure.

Effectiveness of disinfectants against specific microorganisms 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, but not including viruses, must also be determined by the modified version of 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 batches. To support products labeled as "disinfectants" for specific microorganisms (other than those microorganisms named in the above test methods), killing of the specific microorganism on all carriers is required. In addition, plate count data must be submitted for each microorganism to demonstrate that a concentration of at least 10^4 microorganisms survived the carrier-drying step. These Agency standards are presented in DIS/TSS-1 enclosure.

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. These Agency standards are presented in DIS/TSS-2. The hard water tolerance level may differ with the level of antimicrobial activity (e.g., sanitizer vs. disinfectant) claimed. To establish disinfectant efficacy in hard water, all microorganisms (i.e., bacteria, fungi, viruses) claimed to be controlled must be tested by the appropriate Recommended Method at the same hard water tolerance level. These Agency standards are also presented in DIS/TSS-2 enclosure.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 460335-02 "AOAC Use-Dilution Method" for Sterilex Ultra-Kleen Liquid, by Andrea J. Mesaros. Study conducted at AppTec Laboratory Services. Study completion date – July 9, 2002. Project Number 12958.

This study was conducted against *Staphylococcus aureus* (ATCC 6538), *Salmonella choleraesuis* (ATCC 10708), and *Pseudomonas aeruginosa* (ATCC 15442). Solution 1 (Lot No. 1L144) with Solution 2 (Lot No. 1L109) and Solution 1 (Lot No. 1J203) with Solution 2 (Lot No.1J198) of the product, Sterilex Ultra-Kleen Liquid, were tested using the AOAC Use-Dilution Method as described in the AOAC Official Methods of Analysis, 15th Edition, 1990. Fetal bovine serum was added to the culture to achieve a 5% organic soil load. A use solution was prepared by diluting 1 part by volume of Solution 1 and 1 part by volume of Solution 2 with 10 parts by volume of 400 ppm AOAC synthetic hard water (titrated at 394-410 ppm). Ten (10) stainless steel penicylinder carriers were immersed for 15 minutes in a 48-54 hour old suspension of the test organism at a ratio of 1 carrier per 1.0 mL of broth. The carriers were dried for 40 minutes at 35-37°C, and then exposed to 10 mL of the use solution for 10 minutes at 20±1°C. For studies against *Pseudomonas aeruginosa* and *Salmonella choleraesuis*, the carriers were transferred to 10 mL of Letheen Broth to neutralize. For studies against *Staphylococcus aureus*, the carriers were transferred to Letheen Broth with 0.14% Lecithin and 1.0% Tween 80 to neutralize. After 30-60 minutes, the carriers were transferred from primary subculture tubes into secondary subculture tubes containing 10 mL of Letheen Broth (*Pseudomonas aeruginosa* and *Salmonella choleraesuis*) or 10 mL Letheen Broth with 0.14% Lecithin and 1.0% Tween 80 (*Staphylococcus aureus*). All subcultures were incubated for 48±4 hours at 35-37°C. The *Pseudomonas aeruginosa* subcultures were stored at 2-8°C for up to 3 days. Following incubation or incubation and storage, the subcultures were examined for the presence or absence of visible growth. Controls included purity, viability, sterility, neutralization confirmation, and dried carrier counts.

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

Note: The applicant provided data for failed trials. In those trials, the neutralization confirmation controls failed to demonstrate growth. Thus, the tests were invalid. These data were not used to evaluate efficacy of the test product. See Attachment I of the laboratory report.

2. MRID 460335-03 "AOAC Use-Dilution Method" for Sterilex Ultra-Kleen Liquid, by Andrea J. Mesaros. Study conducted at AppTec Laboratory Services. Study completion date – April 10, 2002. Project Number 12799.

This study was conducted against *Escherichia coli* O157:H7 (ATCC 35150). Solution 1 (Lot No. 1L144) with Solution 2 (Lot No. 1L109) and Solution 1 (Lot No. 1J203) with Solution 2 (Lot No.1J198) of the product, Sterilex Ultra-Kleen Liquid, were tested using the AOAC Use-Dilution Method as described in the AOAC Official Methods of Analysis, 15th Edition, 1990. Fetal bovine serum was added to the culture to achieve a 5% organic soil load. A use solution was prepared by diluting 1 part by volume of Solution 1 and 1 part by volume of Solution 2 with 10 parts by volume of 400 ppm AOAC synthetic hard water (titrated at 398-399 ppm). Ten (10) stainless steel penicylinder carriers were immersed for 15 minutes in a 48-54 hour old suspension of the test organism, at a ratio of 1 carrier per 1.0 mL of broth. The carriers were

dried for 40 minutes at 35-37°C, and then exposed to 10 mL of the use solution for 10 minutes at 20±1°C. The carriers were transferred to 10 mL of Letheen Broth to neutralize. After 30-60 minutes, the carriers were transferred from primary subculture tubes into secondary subculture tubes containing 10 mL of Letheen Broth. All subcultures were incubated for 48±4 hours at 35-37°C. Certain subcultures were stored at 2-8°C. Following incubation or incubation and storage, the subcultures were examined for the presence or absence of visible growth. Controls included purity, viability, sterility, neutralization confirmation, and dried carrier counts.

Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable. In one protocol amendment, the laboratory report identifies the test product as Sterilex Ultra-Kleen Liquid Solution 1.

3. MRID 460335-04 "AOAC Use-Dilution Method" for Sterilex Ultra-Kleen Liquid, by Andrea J. Mesaros. Study conducted at AppTec Laboratory Services. Study completion date – April 10, 2002. Project Number 12798.

This study was conducted against *Listeria monocytogenes* (ATCC 19111). Solution 1 (Lot No. 1L144) with Solution 2 (Lot No. 1L109) and Solution 1 (Lot No. 1J203) with Solution 2 (Lot No.1J198) of the product, Sterilex Ultra-Kleen Liquid, were tested using the AOAC Use-Dilution Method as described in the AOAC Official Methods of Analysis, 15th Edition, 1990. Fetal bovine serum was added to the culture to achieve a 5% organic soil load. A use solution was prepared by diluting 1 part by volume of Solution 1 and 1 part by volume of Solution 2 with 10 parts by volume of 400 ppm AOAC synthetic hard water (titrated at 398-399 ppm). Ten (10) stainless steel penicylinder carriers were immersed for15 minutes in a 48-54 hour old suspension of the test organism, at a ratio of 1 carrier per 1.0 mL of broth. The carriers were dried for 40 minutes at 35-37°C, and then exposed to 10 mL of the use solution for 10 minutes at 20±1°C. The carriers were transferred to 10 mL of Letheen Broth to neutralize. After 30-60 minutes, the carriers were transferred from primary subculture tubes into secondary subculture tubes containing 10 mL of Letheen Broth. All subcultures were incubated for 48±4 hours at 35-37°C. Certain subcultures were stored at 2-8°C. Following incubation or incubation and storage, the subcultures were examined for the presence or absence of visible growth. Controls included purity, viability, sterility, neutralization confirmation, and dried carrier counts.

Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable. In one protocol amendment, the laboratory report identified the test product as Sterilex Ultra-Kleen Liquid Solution 1.

V RESULTS

MRID Number	Organism	No. Exhibiting Growth/Total No. Tested		Dried Carrier Count (CFU/ carrier)
		Solution 1 (Lot No. 1L144) with Solution 2 (Lot No. 1L109)	Solution 1 (Lot No. 1J203) with Solution 2 (Lot No. 1J198)	
460335-02	*Staphylococcus aureus*	1° = 0/10 2° = 0/10	1° = 0/10 2° = 0/10	1.8×10^6
	Pseudomonas aeruginosa	1° = 0/10 2° = 0/10	1° = 0/10 2° = 0/10	6.0×10^4
	Salmonella choleraesuis	1° = 0/10 2° = 0/10	1° = 0/10 2° = 0/10	5.8×10^4
460335-03	*Escherichia coli* O157:H7 Test Date: 02/22/02	1° = 0/10 2° = 0/10		3.5×10^5
	Test Date: 03/06/02		1° = 0/10 2° = 0/10	1.09×10^6
460335-04	*Listeria monocytogenes* Test Date: 02/22/02	1° = 0/10 2° = 0/10		3.5×10^5
	Test Date: 03/06/02		1° = 0/10 2° = 0/10	2.24×10^6

VI CONCLUSIONS

1. The submitted confirmatory efficacy data (MRID No. 460335-02) do support the use of the tested product, Sterilex Ultra-Kleen Liquid, as a disinfectant with bactericidal activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Salmonella choleraesuis* in the presence of 400 ppm hard water and a 5% organic soil load (fetal bovine serum) on hard, non-porous surfaces for a contact time of 10 minutes at a 1:1:10 dilution. No growth was observed in the subcultures of the required number of carriers (i.e., 10) tested against the required number of product lots (i.e., 2). According to the laboratory report, "all data measurements/controls . . . were within acceptance criteria." Dried carrier counts were at least 10^4. Neutralization confirmation testing showed positive growth of the organisms. Viability controls were positive for growth. Purity controls were reported as pure. Sterility controls (e.g., organic soil, carrier, media) did not show growth.
However, our files shows that the submitted confirmatory data and the referenced basic data are not identical in chemical formulation, and the chemical formulations are considered

substantially different. Therefore, the above submitted confirmatory cannot be referenced as a me-too for the registered product "Ultra-Kleen Solution 1" (EPA reg. No. 63761-3) and is considered unacceptable. Since the submitted confirmatory efficacy data submitted above under item #1 are not applicable for the current product "Sterilex Ultra Disinfectant Cleaner Solution 1" (63761-I), the applicant must generate additional data and resubmit a complete efficacy data package as per (DIS/TSS-1, item c (1) on his/her own finished product and provide to the Agency for an efficacy determination.

2. The submitted efficacy data support the use of the tested product, Sterilex Ultra-Kleen Liquid, as a disinfectant with bactericidal activity against the following microorganisms in the presence of 400 ppm hard water and a 5% organic soil load (fetal bovine serum) on hard, non-porous surfaces for a contact time of 10 minutes at a 1:1:10 dilution:

Escherichia coli O157:H7	MRID No. 460335-03
Listeria monocytogenes	MRID No. 460335-04

No growth was observed in the subcultures of the required number of carriers (i.e., 10) tested against the required number of product lots (i.e., two). According to the laboratory report, "all data measurements/controls . . . were within acceptance criteria." Dried carrier counts were at least 10^4. Neutralization confirmation testing showed positive growth of the organism. Viability controls were positive for growth. Purity controls were reported as pure. Sterility controls (e.g., organic soil, carrier, media) did not show growth.
However, the above acceptance is pending. The submitted additional test data were generated on test substances which are based on study reports listed as "Sterilex Ultra-Kleen Liquid" (MRID Nos. 460335-03 and 460335-04). The applicant needs to provide clarification and/or information as to whether the submitted studies are based on the chemical formulation provided on page #1 of the proposed label "Sterilex Ultra Disinfectant Cleaner Solution 1".

VII RECOMMENDATIONS

The following study-specific recommendations assume that EPA is able to confirm with certainty that the tested product, Sterilex Ultra-Kleen Liquid, is Sterilex Ultra Disinfectant Cleaner Solution 1, which is the subject of this efficacy report.

1. The following comments are only considered temporary recommendations. Until all referenced efficacy data requirements are met, the indicated comments are considered cursory.

2. The applicant has provided confirmatory data, and referenced efficacy data previously submitted to EPA for the products, Ultra Kleen Solution 1 (EPA Reg. No. 63761-3) and Sterilex Ultra Liquid B Solution 2 (EPA File Symbol 63761-A)(MRID Nos. 4456047-06 & 45587-06 in support of the product, Sterilex Ultra Disinfectant Cleaner Solution 1; however, the chemical formulations of the referenced data report were found not to be substantially similar or identical, as such, the proposed referenced product cannot be rely upon to support a "me-too" registration. Therefore, the proposed label claims (as supported by MRID No. 460335-02) are not acceptable regarding the use of the product, Sterilex Ultra Disinfectant Cleaner Solution 1 when mixed with Sterilex Ultra Activator Solution (Solution 2), as a disinfectant against

Pseudomonas aeruginosa, *Staphylococcus aureus*, and *Salmonella choleraesuis* in the presence of 400 ppm hard water and for preclean, hard, non-porous surfaces for a contact time of at least 10 minutes at a 1:1:10 dilution.

2. The proposed label claims are not acceptable, as one-step disinfectant, however, regarding the use of the product, Sterilex Ultra Disinfectant Cleaner Solution 1 when mixed with Sterilex Ultra Activator Solution (Solution 2), as a disinfectant against the following microorganisms in the presence of 400 ppm hard water and a 5% organic soil load on hard, non-porous surfaces for a contact time of at least 10 minutes at a 1:1:10 dilution are acceptable:

Escherichia coli O157:H7	MRID No. 460335-03
Listeria monocytogenes	MRID No. 460335-04

The proposed label lists the organism, *Escherichia coli* [see page 2 of the proposed label]. The applicant needs to change *Escherichia coli* to *Escherichia coli* O157:H7. Efficacy data were provided for *Escherichia coli* O157:H7, not *Escherichia coli*.

3. Based on the proposed use sites listed on the upper panel of page #3 which infers that the product is recommended for athletic facilities, locker rooms, dressing rooms, shower and bath areas, the label must indicate the type of microorganism intended to be controlled by the product which should be associated with a specific level of antimicrobial activity. The use of the product in the above mentioned areas implicates a claim of fungicidal activity which is not provided on the front panel. In order to substantiate the effectiveness for these use sites, the applicant must submit and satisfy the efficacy data requirements as specified in item #1 of DIS/TSS-6 enclosure.

4. On the bottom of page #2, under the directions for use, the use of the product for the disinfection of dental lines is not acceptable. The applicant must submit a proposed protocol for an efficacy determination for this particular use pattern. Until a protocol is submitted for an efficacy determination, the proposed use pattern is considered <u>unacceptable</u>. However, the Agency does allow the use of the product as a cleaner or as a deodorizer for dental unit water lines.

5. In order to avoid the appearance of heightened efficacy, the proposed product <u>name</u> "Sterilex Ultra Disinfectant Cleaner Solution 1" must be revised to reflect a name that does not include the wording <u>Ultra</u>. A name that implies broader effectiveness or a higher level of efficacy than has been demonstrated is unacceptable.

6. A cursory review of referenced efficacy data for (MRID Nos. 455876-06 and 456047-06) show that the data were developed in the absence of a 5% organic soil. If your true intent is for product effectiveness in the presence of soil "one-step disinfectant hospital disinfectant", the basic referenced data or generated data must be reflective of the data requirements specified in item c of DIS/TSS-1 enclosure and items 4, 6, and 7 of DIS/TSS-2 enclosure. If the applicant does not referenced or provide the applicable efficacy data tested in the presence of a 5% organic soil, the proposed label will have to be revised to include a statement that the proposed product is effective only on "preclean, hard, nonporous, surfaces". For specifics and guidance on this label comment, refer to item #3 of DIS/TSS-15 enclosure.

7. All of the above label comments are considered cursory statements, until the efficacy data requirements are met and satisfied, then, the Agency will provide the registrant proposed label a more detailed and complete label review.

8. In the future, the product actual test use dilution which is used to generate applicable and acceptable efficacy data must be reflective and consistent with the test dilution listed on the product proposed label.