



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 25, 2002

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 8383-3/ Sporicidin Brand Disinfectant Solution

DP Barcode: D280104

From: Ian Blackwell, Biologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Through: *for* Emily Mitchell, Team Leader
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

6/25/02

To: Adam Heyward, PM 34 / Adam Heyward
Regulatory Management Branch I
Antimicrobials Division (7510C)

Applicant: Sporicidin International

Formulation From Label:

<u>Active Ingredient(s)</u>	<u>% by wt</u>
Phenol	1.56
Sodium Phenate	0.06
<u>Inert Ingredient(s)</u>	<u>98.38</u>
Total	100.00

(1)

64001

SUMMARY OF INFORMATION REVIEWED AND FINDINGS/CONCLUSIONS:

1. A product efficacy review conducted by EPA contractor DynCorp I&ET has undergone a secondary review by AD/PSB/EET. The contractor's review reflects EPA's Pesticide Assessment Guideline requirements and regulations. The findings are scientifically sound. A copy of that data review is attached to this AD/PSB/EET review.
2. This package included two product efficacy studies. The MRID Numbers are 455569-02 and 455569-03.
3. MRID Number 455569-02: The request to add labeling claims against Methicillin-resistant *Staphylococcus aureus* (ATCC 33591) and Vancomycin-resistant *Enterococcus faecium* (ATCC 51559) is approved.
4. MRID Number 455569-03: The request to add labeling claims against *Stachybotrys chartarum*, *Chaetomium glososum*, and *Aspergillus niger* is denied. The problems with this study are:
 - a. This study did not meet DIS/TSS-6 Guidelines.
 - b. The report did not certify that this study was conducted in accordance with GLPs.
 - c. The study was not conducted using hard, non-porous carriers.
 - d. Testing did not simulate in-use conditions (including contact time)
 - e. Only one lot of product was tested.
 - f. The count of organisms/conidia was not specified.
 - g. The results did not prove that all conidia on all treated agar cultures were killed.
5. The role of microbial contamination in building related illness, specifically that of *Stachybotrys chartarum*, *Penicillium spp*, *Chaetomium globosum* and other related fungi or molds is being investigated by the Antimicrobials Division for the public health implications. AD is consulting with EPA's Office of Air and Radiation, the Centers for Disease Control and Prevention (CDC), academia, industry, and other public health officials to determine the appropriate use conditions for antimicrobial agents against these potentially pathogenic organisms. Once this investigation is completed, guidance will be developed and provided to the regulated community to address this use pattern.
6. The Agency understands that the control of moisture is a key factor in the prevention and remediation of fungi and molds from environmental surfaces. Appropriate label language must be developed to address this issue.
7. In many instances, extensive levels of contamination can only be managed through removal of affected materials. It may be necessary to restrict the use of antimicrobial

products labeled for use against organisms implicated in building related illnesses to certified pesticide applicators as part of an overall remediation process.

8. The latest label included with this submission lists Sporidicin as being effective against *Candida albicans*, *Streptococcus viridans*, and *Proteus mirabilis*; however, no data has been submitted to support these claims. The registrant must remove labeling claims against these three organisms until substantiating data has been reviewed and approved by PSB/AD.
9. The submitted label includes claims against *Pellicularia filamentous*. Before claims against *Pellicularia filamentous* can be approved, the registrant must explain why they seek to make labeling claims against this organism. *Pellicularia filamentous* is a plant pathogen. The registrant must explain its relevance to this product.
10. The submitted label has directions for use of this product to clean and sanitize air ducts. This product has not been approved for use as a sanitizer in air ducts. All claims or directions for use of this product on air ducts must be removed. See the attached Agency letter addressing HVAC issues.
11. The submitted label has directions for the use of this product as a carpet deodorizer and decontaminant. The claim for cleaning, deodorizing and decontaminating carpets is not appropriate for this product because:
 - a. Carpets are considered a porous surface,
 - b. This product is not registered for use as a disinfectant on porous surfaces
 - c. Carpets are not listed on the label for any type of pesticidal application

MEMORANDUM

DATE: May 20, 2002

SUBJECT: Efficacy Review for Permicide Brand (Ristex) Germicidal Disinfectant, EPA Reg. No. 008383-00003; DP Barcode: D280104

FROM: DynCorp I&ET

THRU: Ian Blackwell
Antimicrobials Division

TO: Emily Mitchell
Antimicrobials Division

APPLICANT: Sporocidin International, Inc.
Rockville, MD

I BACKGROUND

The product (008383-00003), Sporocidin Brand Disinfectant Solution [formerly known as Permicide Brand (Ristex) Germicidal Disinfectant], is being reviewed as a disinfectant and fungicide, for use on hard, non-porous surfaces. The product is already approved as a disinfectant and fungicide on hard, non-porous surfaces, for use in hospital and medical settings. The applicant is requesting an amendment to their registration to add claims for effectiveness against additional microorganisms, specifically Methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococcus faecium* (VRE), and certain building material molds (i.e., *Stachybotrys chartarum*, *Chaetomium globosum*, and *Aspergillus niger*). The proposed label also identifies a new application for the product; for use in cleaning, deodorizing, and decontaminating carpets. Studies were conducted at MicroBioTest, Inc., 105B Carpenter Drive, Sterling, Virginia, 20164, and the University of Maryland, Department of Cell Biology and Genetics, HJ Patterson Hall, College Park, Maryland 20742-5815.

This data package contained two studies (MRID Nos. 455569-02 and 455569-03), which both contained statements of no data confidentiality, the proposed label, and the last accepted label (approved August 18, 1999).

II USE DIRECTIONS

This product is used as a disinfectant and deodorizer, and is germicidal when used as directed. The product is designed to be used for cleaning, disinfecting and deodorizing hard, non-porous surfaces in hospitals, clinics, medical and veterinary offices, laboratories, industrial clean rooms, homes, nursing homes, ambulances, hotels, restaurants, schools, airplanes, trains, boats, autos, buses, health spas and toilets.

The product is in ready-to-use form. The proposed label directions provided the following information regarding use of the product: Pre-clean surfaces to remove dirt and soil, and wipe

surfaces dry with a paper towel, cloth, or sponge. Thoroughly wet pre-cleaned surfaces, and allow contact times stated for specific organisms at room temperature. Contact times are as follows:

1 minute: HIV-1

3 minutes: *Staphylococcus aureus*, *Salmonella choleraesuis*, *Pseudomonas aeruginosa*, Methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococcus faecium* (VRE), and *Trichophyton mentagrophytes*

10 minutes: *Streptococcus pyogenes*, *Streptococcus salivarius*, *Streptococcus viridans*, *Escherichia coli*, **Herpes simplex types 1/F and 2/G (oral, ocular and genital), Influenza A2 (Japan 305/57 Asian Strain), *Pellicularia filamentosa*, *Penicillium variabile*, *Proteus mirabilis*, *Candida albicans*, Vaccinia, Canine parvovirus, Cytomegalovirus, Coronavirus, Polio type 1 viruses, and *Mycobacterium tuberculosis*

The proposed label directions also included special instructions for cleaning, deodorizing and decontaminating carpets: Spray product onto carpet and allow to dry or apply via machines according to manufacturer's instructions.

The label directions also identified the availability of special instructions (in a Sporicidin Bulletin) for cleaning and decontaminating against HIV-1.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Disinfectants (Against Supplemental Organisms)

Substantiated label claims of effectiveness of a disinfectant against specific microorganisms other than the designated test organism(s) are permitted, provided the target pest is likely to be present in or on the recommended use areas and surfaces and thus may present a potential problem. Effectiveness of disinfectants against specific microorganisms other than those named in the AOAC Use-Dilution Method, AOAC Germicidal Spray Products Test, AOAC Fungicidal Test, and AOAC Tuberculocidal Activity Method, but not including viruses, must be determined by either the AOAC Use-Dilution Method or the AOAC Germicidal Spray Products Test. 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.

Fungicides (Against Pathogenic Fungi, Using a Modified AOAC Use-Dilution Method)

The effectiveness of liquid disinfectants against specific pathogenic fungi must be supported by efficacy data using an appropriate test. The AOAC Use-Dilution Method may be modified to conform with the appropriate elements in the AOAC Fungicidal Test. If the product is intended to be used as a spray product, the AOAC Germicidal Spray Products Test must be employed. The inoculum in the test must be modified to provide a concentration of at least 10^6 conidia per carrier. Ten carriers on each of 2 product samples representing 2 different batches must be

employed in the test. Killing of the specific pathogenic fungi on all carriers is required. These Agency standards are presented in DIS/TSS-6.

Products Controlling Microorganisms of Economic or Aesthetic Significance

Algaecides, slimicides, preservatives, deodorizers, and other products expressly claiming control of microorganisms of economic or aesthetic significance not directly related to human health do not require efficacy data. However, adequate dosage recommendations and complete directions for use must be provided in labeling. These Agency standards are presented in DIS/TSS-16.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 455569-02 "Confirmatory AOAC Use Dilution Test" for Sporidicin Brand Disinfectant Solution, by Shiva D. Rajaram, MicroBioTest, Inc. Study completion date – October 10, 2001.

This study was conducted against Methicillin-resistant *Staphylococcus aureus* (ATCC 33591) and Vancomycin-resistant *Enterococcus faecium* (ATCC 51559). Two lots (Lot Nos. 01512 and 01514) of the product were tested using the Use-Dilution Method as described in the AOAC Official Methods of Analysis, 15th Ed., 1990. A total of ten replicates per microorganism per lot of test product were evaluated using two lots of the test product. Vancomycin-resistant *Enterococcus faecium* (VRE) and Methicillin-resistant *Staphylococcus aureus* (MRSA) cultures dried on stainless steel penicylinders were exposed to the test product at $20 \pm 1^\circ\text{C}$ for 3 minutes. The carriers were removed from the test solution and neutralized. Lethen Broth containing 1% Polysorbate 80 was used as the neutralizer broth. The tubes were incubated at $37 \pm 2^\circ\text{C}$ for 48 ± 2 hours. Controls included: neutralizer effectiveness, carrier counts, viability, bacteriostasis, sterility, Gram stain to confirm challenge microorganisms and resistance profile confirmation. Average colony forming units (CFU) per carrier was recorded as 1.3×10^6 for *Staphylococcus aureus* and 2.2×10^6 for *Enterococcus faecium*.

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

2. MRID 455569-03 "A Preliminary Report, Comparison of Sporidicin Brand Disinfectant Solution and Household Bleach to Control Building Material Molds", by Dr. George A. Bean, University of Maryland. Study completion date – November 19, 2001.

One lot of test product with no indicated lot number was tested against *Stachybotrys chartarum*, *Chaetomium globosum*, and *Aspergillus niger*. No strains (e.g., via ATCC number) were identified. No carrier test was used. Petri dishes containing potato dextrose agar were spray-inoculated with an undeclared amount of a spore suspension of the three molds. Bioassay disks dipped in Sporidicin Brand Disinfectant Solution, Sporidicin Brand First Aid Spray, bleach, or distilled water were placed on the agar surface, 5 disks per plate. Two weeks later, the zones of inhibition were measured. The disks were placed on the agar surface either wet or dried for 24 hours. The experimental controls consisted of the bleach-treated bioassay disks (positive control) and product-free (distilled water) bioassay disks (negative control). The study was submitted with a statement that it was not known whether it had been conducted in accordance with EPA Good Laboratory Practice (GLP) regulations. No quality assurance statement was provided. Results were reported in size of zone of inhibition, and, when applicable, whether there was complete inhibition (100%) or no inhibition (0%). Zones of inhibition were converted to percentages.

V RESULTS

MRID Number	Organism	No +/Total No. Tested Lot No. 01512	No +/Total No. Tested Lot No. 01514
455569-02	Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	0/10	0/10
	Vancomycin-resistant <i>Enterococcus faecium</i> (VRE)	0/10	0/10

MRID Number	Organism	Sporidicin Brand Disinfectant Solution (no lot number indicated) [results expressed in zone of inhibition (in mm) and percent growth inhibition]	
		Wet	Dry
455569-03	<i>Stachybotrys chartarum</i> <i>Chaetomium globosum</i> <i>Aspergillus niger</i>	complete / 100% complete / 100% complete / 100%	5.6 mm / 46% 8.6 mm / 71% 7.0 mm / 58%

VI CONCLUSIONS

1. The submitted efficacy data (MRID 455569-02) appear to support the use of the product, Sporidicin Brand Disinfectant Solution, as a disinfectant with bactericidal activity when tested against Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant *Enterococcus faecium* (VRE) on hard surfaces for a contact time of 3 minutes. No growth was observed in the 10 carriers per lot.

Discussion of Controls: Neutralization effectiveness testing showed positive growth of the organism in Lethen Broth containing 1% Polysorbate 80. Antibiotic resistance confirmation testing showed complete resistance of the Methicillin-resistant *Staphylococcus aureus* (MRSA) to oxacillin, and for Vancomycin-resistant *Enterococcus faecium* (VRE), a 12 mm zone of inhibition in the presence of a vancomycin-impregnated disk.

2. The submitted efficacy data (MRID 455569-03) do not appear to support the use of the product, Sporidicin Brand Disinfectant Solution, as a disinfectant with fungicidal activity when tested against *Stachybotrys chartarum*, a pathogenic fungi. Although the product demonstrated reduction of this species versus the control solution, the applicant failed to include an affirmation that the study was conducted in accordance with GLPs. Additionally, the study performed was at variance with Agency efficacy study standards in several ways, including the following:

- No carrier test was used (no surface, porous or non-porous, was involved).
- Testing did not simulate in-use conditions (including contact time).
- Only one lot of test product was used.
- The inoculum was not specified (and must be at least 10^6 conidia per carrier).
- Results did not demonstrate that all conidia on all treated carriers were killed.

3. The submitted study data (MRID 455569-03) appear to support the use of the product, Sporidicin Brand Disinfectant Solution, for the control of mold and mildew of economic or aesthetic significance not directly related to human health. Such fungi include the building material fungi *Chaetomium globosum* and *Aspergillus niger*.

VII RECOMMENDATIONS

1. The label claims (as supported by MRID 455569-02) are acceptable regarding the use of the product as a disinfectant against Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant *Enterococcus faecium* (VRE) on hard, non-porous surfaces for a contact time of 3 minutes.

2. The label claims (as supported by MRID 455569-03) are not acceptable regarding the use of the product as a fungicide against *Stachybotrys chartarum* on hard, non-porous surfaces for an unspecified contact time. The applicant has not met the requirements of DIS/TSS-6 or GLPs in performing this study. Prior to approving the proposed label, the Agency needs to request that the applicant conduct a more appropriate study or remove claims against this fungus from the proposed label. See the Conclusions Section of this report for more details.

3. The labels claims (as supported by MRID 455569-03) appear to be acceptable regarding the use of the product to control mold and mildew against *Chaetomium globosum* and *Aspergillus niger*. These molds are building material fungi economic or aesthetic importance. Prior to approving this portion of the label, EPA may want to consider the following:

- The applicant is requesting a change in the wording from “[t]o prevent mold and mildew” to state “[t]o kill mold and mildew.”
- The application instructions have been altered and appear less precise. The text has changed from: “[r]epeat application weekly, or sooner if new growth appears” to “[a]pply product to the contaminated area. Repeat application if new growth appears.”
- The applicant has inserted the phrase “[p]roven effective against ... *Chaetomium globosum* and *Aspergillus niger*.” When listed, these organisms are not identified as being of economic or aesthetic importance (i.e., non-health related).
- No strains (ATCC) of fungi tested were provided.

4. The proposed label includes claims against new fungi and bacteria; however, the data package did not include studies to confirm these claims. The potentially unsupported organisms include the following:

Fungi	Bacteria
<i>Candida albicans</i> <i>Pellicularia filamentosa</i> (name misspelled on proposed label) <i>Penicillium variabile</i> (name misspelled on proposed label)	<i>Proteus mirabilis</i> <i>Streptococcus viridans</i>

Prior to approving the proposed label, EPA may wish to confirm that these additional organisms have been addressed sufficiently in other MRIDs not made available to DynCorp.

5. The proposed label includes changes to the directions for using the product to clean air ducts. The last accepted label identifies how the product is to be used for cleaning air ducts; the proposed label identifies how the product is to be used for cleaning and sanitizing air ducts. Prior to approving the proposed label, EPA may want to confirm whether efficacy data previously submitted for this product supports this new claim to sanitize. The applicant also eliminated the phrase “[r]inse surfaces after application” in the directions for using the product to clean air (and sanitize) ducts. Prior to approving the proposed label, EPA may wish to confirm whether rinsing would or would not be appropriate.

6. DynCorp notes that the newly listed use, as a carpet deodorizer, does not require efficacy data. Nonetheless, the proposed label does not provide adequate dosage recommendations and complete directions for use, which are required by DIS/TSS-16.



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

March 14, 2002

SUBJECT: Use of Disinfectants and Sanitizers in Heating, Ventilation,
Air Conditioning, and Refrigeration Systems

The purpose of this letter is to bring to your attention several concerns that the Agency has regarding the possible use of sanitizer and/or disinfectant products, and possibly other types of antimicrobial products, to treat the surfaces of heating, ventilation, air conditioning, and refrigeration systems (HVAC&R), typically as part of air duct cleaning. First, although the directions for use of most of these products permit use on hard, non-porous surfaces, such directions may not specifically include the use of the product in HVAC&R systems.

We are particularly concerned about this possibility because the Agency has not assessed the potential exposure and risks to building occupants or applicators from the use of these products in or on any surfaces that are part of HVAC&R systems in circumstances where the labels do not specifically authorize use in HVAC&R systems. Also, the Agency has not assessed whether such products are efficacious when used in HVAC&R systems. Therefore, users cannot assume that EPA registration of these products reflects any conclusions about their safety or effectiveness in this situation. Even in circumstances where labels do list HVAC&R systems as a possible use, we are concerned that the Agency has not received and reviewed adequate data to fully evaluate risks to building occupants or product efficacy in that use pattern.

An additional source of concern arises because some pesticide products also bear labels which identify the product as HVAC&R "cleaners," which could further increase the likelihood that users incorrectly make pesticidal use of such products or make incorrect assumptions about the status of EPA review, evaluation, and conclusions about them.

We believe that all these factors may contribute to possibly unlawful and/or uninformed use of these products, which could have implications for public health and safety and for consumer protection.

In the absence of adequate data and the associated review and evaluation of the registration process, use of these products in HVAC&R systems could lead to significant exposures in indoor environments with potentially unreasonable adverse effects. One indication of the potential scope of the problem is the fact that the National Antimicrobial Information Network has reported to us that it received about 150 calls related to the possible application of antimicrobial pesticide products in HVAC&R systems in a recent 18 month period.

We are writing to you because we believe you would share our concerns about the possibility that these products may be being used as pesticides in a manner not authorized by the label and not contemplated by the pesticide registration process. We also believe that you wish to ensure that these products are not being used in a manner which might be harmful to applicators and/or building occupants.

We recommend that you advise your members not to apply disinfectant, sanitizer or other antimicrobial products to treat HVAC&R systems if such product does not include specific directions for HVAC&R use. The Agency believes that it is important that you ensure that members of your association are not applying products to HVAC&R systems which are not registered for that use. We intend to further evaluate this use to determine the potential exposure and risks as well as the efficacy criteria which are required before pesticide products are registered to be used in HVAC&R systems.

We recognize that it is important to address the labeling of these products, and we intend to work with pesticide registrants to assure that these product labels clearly communicate the uses which EPA has (and has not) authorized. We also expect to assure that appropriate evaluations of risk and effectiveness accompany any authorized uses in these systems. However, we felt it was important to inform you of these issues promptly, without waiting for any further revisions of these product labels and the conditions for their registration.

We hope you will find this information of value to you and your company as part of your approach to serving your customers. Feel free to contact Tracy Lantz at (703) 308-6415 if you have any questions.

Sincerely,

/S/

Marcia E. Mulkey, Director
Office of Pesticide Programs