EEE BRANCH REVIEW

DATE: IN _____ OUT _____ IN _____ OUT _____ IN 7-3-78 OUT 9-18-78

FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 34292-1

PETITION OR EXP. PERMIT NO. -

DATE DIV. RECEIVED 1-27-78

DATE OF SUBMISSION 1-18-78

DATE SUBMISSION ACCEPTED

TYPE PRODUCTS(S): I, (D,) H, F, N, R, S Bacteriostatic preservative for unfinished textile fibers, fabrics, and threads.

DATA ACCESSION NO(S). 233246

PRODUCT MGR. NO. 31 Tavano

PRODUCT NAME(S) Dow Corning 5700 Antimicrobial Agent

COMPANY NAME Dow Corning Corporation, Midland, Mich.

SUBMISSION PURPOSE Application for amended registration, with data, to add claim "The treatment is bacteriostatic and inhibits the growth of odor-causing bacteria on socks."

CHEMICAL & FORMULATION Active: 3-(trimethoxysilyl)-propyldimethyloctadecyl ammonium chloride 42%

Inert: 58%

200.0 Introduction

200.1 Use:

The subject product is registered as a bacteriostat, fungistat, and algistat for manufacturing use as a preservative for unfinished textile fiber, fabrics, and threads.

200.2 Background Information:

With regard to the above registered claims for the subject product, the required demonstration of efficacy for the registration issued 8-4-75 was based on minimal data showing microbiostatic properties of treated textile fabrics and intrinsic value as a microbiostatic (including bacteriostatic) preservative agent for unfinished textile materials. Actual and/or simulated deterioration/degradation data was not included in the basic registration of 8-4-75, nor has it been subsequently provided.

Thus, efficacy data relative to specific, finished textile products (such as socks), the use patterns of the end articles, warranted claims, dosages, application techniques, duration of efficacy under use conditions, etc. were not provided by the registrant. By agreement with registrant in meeting of January 15, 1975, the registration of the subject product did not include end-use article efficacy.

Several previous efficacy reviews (12-31-74, 5-14-76, 6-2-77, 11-11-77) and meetings have addressed the impregnation of finished articles (including socks), and have delineated the types of efficacy data required for documentation of pesticidal functions (odor control, deterioration, discoloration) intended for impregnated socks. In addition, such residual efficacy is subject to §162.21 (b) of Section 3 Regulations.

The current submission of January 18, 1978 constitutes an application for amended registration to add the claim "The treatment is bacteriostatic and inhibits the growth of odor causing bacteria on socks". The current submission includes proposed labeling

and data package (Accession No. 233246) and was received for scientific review on 7-3-78.

201.0 DATA SUMMARY

201.1 General Comments Regarding Submitted Studies:

Six separate studies are submitted in conjunction with this application. Such studies can be separated into two categories - (A) Human Wear Studies: 3 investigations and (B) Laboratory Studies: 3 investigations. All six studies employed production run socks containing 0.31% active solid on the sock.

(A) Human Wear Studies: The submitted human wear studies are considered to be based on the antimicrobial (medicated and/or cosmetic rather than pesticidal) treatment of the human body, specifically the feet, using socks as the applicator. Subsequent evaluation of such studies in this report is predicated on the following concepts:

(1) that foot odor is often associated with hyperhidrosis of the feet and that microbial metabolism on the skin may be associated with the production of some forms of volatile, foul foot odors on the skin.

(2) that treatment of human skin, such as the foot, with antimicrobial chemicals (direct application or indirect application) may result in inhibition of microbial growth on the skin, and thereby inhibit or reduce the production of volatile, foul odors on the skin.

(3) that inhibiting or lowering the bacterial numbers on the human skin (such as the foot) may lower the numbers of bacteria incidentally transferred to adjacent clothing (such as socks), and that the less foul odor produced on the skin - the less odor that will be available for incidental absorption by adjacent clothing.

(4) that antimicrobial substances or mixtures of substances intended to inhibit the growth of, inactivate, or destroy fungi, bacteria, or viruses in or on living man or other animals are excluded from the purview of FIFRA.

The following three human wear type studies were submitted:

(1) Hill Top Research, Study No. 77-1070-70. "Sock Odor Study Comparing Treated and Untreated Socks Following Normal Wear."
(2) Hill Top Research, Study No. 77-1076-11A, "Odor Levels and Population of Bacteria on Socks."
(3) Hill Top Research, Study No. 77-1076-11B, "Bacterial Population of Biogard Treated Socks and Untreated Control Socks."

(B) Laboratory Studies: The following laboratory studies were submitted:

(1) Dow Corning Study No. E-3069-A. "Identification of Bacteria Isolated from Socks".
(2) Dow Corning Study No. E-3069 B. "Anti-bacterial Activity of Biogard Treated Socks and Untreated Control Socks".
(3) Dow Corning Study No. E-3069 C. "The Effect of Various Detergents on the Antimicrobial Activity of Biogard Treated Socks".

201.1.1 Brief description of tests performed and results obtained:

(A) (1) Hill Top Research Study No. 77-1070-10. "Sock Odor Study Comparing Treated and Untreated Socks Following Normal Wear".

Procedure

The details of procedure for this study are available in data file Accession No. 233246. Briefly, 39 male subjects were utilized in a wear study to compare odors of socks following normal wear. Unwashed control socks, washed control socks,

unwashed Biogard treated socks, and washed Biogard treated socks were assigned to subjects on a specific schedule over a four day period. Four judges performed odor evaluations using an odor grading scale of 0-10 (no odor to very intense/ disagreeable odor). Odor evaluations were performed 14 hours subsequent to removal of socks from subjects, during which time worn socks were stored at room temperature in sealed, Whirl-Pak bags. (Sealed storage was necessary to prevent the normally occuring dissipation of absorbed odors). Individual baseline odor evaluations were performed prior to "product study". Since the registrant indicated that unwashed, new, Biogard treated socks contain temporary residual process chemicals that interfere with objectives of the study, results relative to T_1 and C_1 socks (unwashed treated and unwashed control socks) will not be evaluated.

Results

Detailed results presented by registrant are available in data file Accession No. 233246.

Summary:

Baseline odor scores for socks worn during control period =
Mean 4.17 (right sock) 4.26 (left sock)

Individual post-treatment odor scores for all subjects assigned

Socks T_2 and C_2 (washed treated and washed control socks):

Summary of Number of Subjects in Odor Score Category

Odor Score Category	Evaluation 1 Judge 1	Evaluation 1 Judge 2	Evaluation 1 Judge 3	Evaluation 1 Judge 4	Evaluation 2 Judge 1	Evaluation 2 Judge 2	Evaluation 2 Judge 3	Evaluation 2 Judge 4
$T_2 > C_2$	13	6	16	13	16	11	19	12
$T_2 = C_2$	2	9	3	8	3	9	6	10
$T_2 < C_2$	24	24	20	18	20	19	14	17
Total								
$T_2 \geq C_2$	15/39	15/39	19/39	21/39	19/39	20/39	25/39	22/39
$T_2 < C_2$	24/39	24/39	20/39	18/39	20/39	19/39	14/39	17/39

Average

$T_2 \geq C_2$ 19.5/39

$T_2 < C_2$ 19.5/39

Mean Odors Scores: Treated sock 4.56
Control untreated sock 4.91

General purview of individual odor scores for each subject in each of two evaluations by four judges for washed treated and washed untreated socks indicates that for approximately 50% of the subjects - the foul odor absorbed and retained by treated socks was equal to or worse than untreated control control socks. In other words, in approximately 50% of subjects, the Biogard treated socks smelled the same or worse than untreated socks after wearing. These results are not considered conclusive in regard to whether or not antimicrobial treatment of the skin (foot) effectively controls the growth of bacteria and thereby the production of foul odors on the skin, so that less foul odors are absorbed by socks.

(A) (2) Hill Top Research Study No. 77-1076-11A. "Odor Levels and Population of Bacteria on Socks".

Procedure

The details of procedure for this study are available in data file Accession No. 233246. Briefly, the study was conducted with unwashed, untreated control socks containing temporary residual process chemicals. The objective of the study was to determine the relationship between odor intensity and bacterial population on untreated control socks used in a normal wear cycle. Selected socks worn during odor study were examined microbiologically for enumeration of gram positive cocci and gram negative rods present on socks. 40 male subjects were utilized. Odor on socks was determined sometime (undefined) after removal from feet, socks were ranked in order of increased odor scores, and microbiological examination was performed on socks from 20 subjects. Details of time and storage relationships to odor evaluation and microbiological assays were not indicated.

Results

Details of results presented by registrant available in data file Acc. #233246.

Summary: Bacterial Counts from Extraction of Worn, Untreated, Unwashed Socks in order of increasing bacterial numbers.

(a) Subject	Gram Positive Cocci Counts/gm socks	Odor Score
3	0.68×10^5	2.5
14	1.1×10^5	3.3
10	1.3×10^5	3.0
1	2.4×10^5	2.8
32	2.8×10^5	3.8
17	3.4×10^5	3.3
2	4.8×10^5	2.5
5	5.4×10^5	2.3

Continued

Subject	Gram Positive Cocci Counts/gm socks	Odor Score
29	5.4×10^5	4.3
35	12×10^5	5.8
24	13×10^5	6.0
8	14×10^5	7.0
21	17×10^5	4.5
38	29×10^5	6.8
20	32×10^5	4.5
7	34×10^5	6.0
13	38×10^5	5.8
26	44×10^5	5.5
15	86×10^5	2.8
31	180×10^5	not reported

(b)

Subject	Gram Negative rods Counts/gm socks	Odor Score
5	$<2.0 \times 10^1$	2.3
13	$<2.0 \times 10^1$	5.8
17	$<2.0 \times 10^1$	3.3
32	$<2.0 \times 10^1$	3.8
8	4.0×10^1	7.0
15	4.0×10^1	2.8
1	1.0×10^2	2.8
14	1.0×10^2	3.3
10	1.8×10^2	3.0
3	6.4×10^2	2.5
29	1.5×10^3	4.3
26	3.1×10^3	5.5
35	3.5×10^3	5.8
2	1.2×10^4	2.5
24	1.2×10^4	6.0
7	2.7×10^4	6.0
21	5.2×10^4	4.5
20	1.2×10^6	4.5
38	1.9×10^6	6.8

(c)

Subject	Total Counts (Gram Positive and Gram Negative) Counts/gm socks	Odor Score
3	0.69×10^5	2.5
14	1.1×10^5	3.3
10	1.3×10^5	3.0
1	2.4×10^5	2.8
32	2.8×10^5	3.8
17	3.4×10^5	3.3
2	4.9×10^5	2.5
5	5.4×10^5	2.3
29	5.4×10^5	4.3
35	12×10^5	5.8
24	13×10^5	6.0
8	14×10^5	7.0
21	18×10^5	4.5
7	34×10^5	6.0
13	38×10^5	5.8
20	44×10^5	4.5
26	44×10^5	5.5
38	48×10^5	6.8
15	86×10^5	2.8
31	270×10^5	9.8

Summary: No consistent pattern of increased bacterial counts being associated with consistently increasing odor intensity. Detectable levels of bacterial contamination on socks can be recovered, and detectable levels of absorbed odor can be observed. However, the intensity of odors absorbed by socks from the feet does not always parallel the transfer of certain numbers of bacterial contaminants from feet to the socks. Results do not provide conclusive evidence of a consistent relationship between intensity of absorbed odors and transfer of bacterial populations to socks from feet.

(A) (3) Hill Top Research Study No. 77-1076-11B (Revised). "Bacterial Population of Bioguard Treated Socks and Untreated Control Socks".

Procedure

Details of the procedure for this study are available in data file Accession No. 233246. Briefly, this study was conducted concurrently with study No. 77-1070-70. Selected socks worn during Odor Study 77-1070-70 were examined to determine bacterial population. Socks were removed from subjects' feet and stored in sealed plastic bags for 19 hours prior to microbiological examination - (in order to prevent the normally occurring dissipation of absorbed odors and to provide more suitable bacterial growth and chemical activity conditions than would be found in actual or simulated use conditions). Since the registrant indicates that unwashed, new Bioguard treated and untreated socks contain temporary residual process chemicals that interfere with objectives of the study, results relative to T_1 and C_1 socks (unwashed treated and unwashed control socks) will not be evaluated. From 21 subjects who wore washed Bioguard treated socks (T_2) and washed untreated control socks (C_2), the socks of 5 subjects were selected for microbiological examination. Documentation of neutralization of active ingredient in the microbiological assay procedure is not provided and therefore validity of the bacteriological counts presented is not established.

Results

Subject	Mean Odor Score T_2	Mean Odor Score C_2	Mean Difference $C_2 - T_2$	Washed Treated and Washed Untreated Socks-Bacterial Counts: Gram Positive $x10^5$ T_2	Gram Positive C_2	Gram Positive % Reduction	Gram Negative T_2	Gram Negative C_2	Gram Negative % Reduction
* 21	3.8	5.5	1.7	51	19	0	$1.8x10^3$	$1.1x10^4$	84
* 17	4.8	6.3	1.5	1.2	3.5	66	160 est	460 est	65
* [illegible]	4.0	5.5	1.5	4.0	5.2	23	130 est	$1.4x10^3$	99
* 42	6.5	8.0	1.5	220	180	0	$190x10^5$	$210x10^5$	9.5
* 10	3.3	4.0	0.7	6.4	10	36	70 est	130 est	46
14	2.0	2.7	0.7						
37	5.3	6.0	0.7						
18	5.5	6.0	0.5						
9	5.5	6.0	0.5						
33	6.5	7.0	0.5						
25	7.5	7.8	0.3						
22	2.5	2.5	0.0						
26	6.5	6.5	0.0						
13	6.5	6.3	-0.2						
2	3.3	3.0	-0.3						
34	6.3	6.0	-0.3						
41	6.3	6.0	-0.3						
1	3.0	2.3	-0.7						
[illegible]	3.8	2.8	-1.0						
[illegible]	4.3	3.3	-1.0						
38	8.8	7.8	-1.0						

* Chosen for microbiological assay.

Summary: $T_2 \geqq C_2$ in 10 out of 21 subjects. (mean odor score). $T_2 < C_2$ in 11 out of 21 subjects. Only this group employed for the microbiological assays. 4 of 5 subjects chosen were in this group and were those in which mean odor score $C_2 > T_2$ by more than one odor unit.

40% of the five subjects (2 out of 5) showed no reduction whatsoever (0%) of the predominant skin bacterial floragram positive cocci, under the test conditions. The remaining 60% of subjects (3) showed varying (23-66%) degrees of gram positive

bacterial reduction under test conditions. The reduction of gram negative rods under test conditions varied widely from 9.5% to 99%, with the bacterial counts on 3 out of 5 subjects being estimates.

None of the odor evaluations or microbiological assays were performed under conditions that represented assay of skin derived odors and bacterial contamination of socks immediately after wearing, or under conditions that represented actual or simulated environmental conditions shortly after wearing. The microbiological study included only those subjects in which the odor of control sock exceeded odor of treated sock by more than one odor unit. Neutralization of the active ingredient in microbiological assays is not indicated. Even under these conditions there was no indication of a consistent pattern of bacterial reduction on the skin, and no consistent pattern of decreased odor intensity absorption by socks from skin associated with increased bacterial reduction on the skin. In other words, the results do not indicate that a consistent pattern of increased bacterial reduction is associated with a consistent pattern of decreased odor intensity absorption. The results provide some indication that if worn socks are immediately placed in sealed containers and stored there for 19 hours, varying levels of absorbed, retained odors and varying levels of bacterial reduction (0% - 99%) can be detected, but these observations cannot be associated with any intended use benefit.

(B) (1) Dow Corning Study E-3069-A. "Identification of Bacteria Isolated From Socks".

Procedure

Procedural details for this study are available in data file Accession No. 233246. Briefly, 6 pairs of orlon/nylon untreated socks were utilized. Three males and three females each wore one pair of socks for 12 hours, then placed socks in sealed plastic bags where they were stored until microbiological examination the following day. Microbiological examination included extraction with sterile Letheen Broth and selective plating on

MacConkey Agar, Mannitol Salt Agar, and Tryptic-Soy Agar. Isolates were "reisolated" for purification and identification.

Results

The following microorganisms were isolated from worn socks:

Gram positive cocci:	Micrococcus sp. Staph epidermidis Staph aureus (pigmented) Staph aureus (non-pigmented)
Gram negative rods:	Enterobacter aglomerans Acinetobacter calcoaceticus

Summary: The above gram positive and gram negative bacteria appear to be skin flora capable of being transferred from the skin to the socks, and appear to be capable of survival under the ideal storage conditions of the study.

(B) (2) Dow Corning Study E-3069-B. "Antibacterial Activity of Bioguard Treated Socks and Untreated Control Socks".

Procedure

Procedural details available in data file Accession No. 233246. Briefly, the objective of this study was to determine the activity of the subject product against the bacteria isolated from socks in Dow Corning Study E-3069-A above, using AATCC Method 100-1974. Nine treated and 9 untreated socks were utilized. Evidence of neutralization of active ingredient in assay procedure not provided.

Results

Organism	Sample	# Remaining Bacteria at: 0 Time	6 Hours	% Bacterial Reduction
Micrococcus sp.	Control	350,000	215,500	38%
	Bioguard	254,000	2,700	99%
Staph. epidermidis	Control	85,000	58,000	32%
	Bioguard	82,000	3,000	96%
E. aglomerans	Control	175,000	1,355,000	0%
	Bioguard	170,000	16,500	90%
A. calcoaceticus	Control	86,000	3,500	96%
	Bioguard	76,000	1,000	99%
E. aglomerans	Control	159,000	1,410,000	0%
	Bioguard	149,000	48,000	69%
Micrococcus sp.	Control	172,000	305,000	0%
	Bioguard	173,000	0	100%
Micrococcus sp.	Control	187,000	395,000	0%
	Bioguard	197,500	200	99%
S. aureus (pigm.)	Control	265,000	200,000	25%
	Bioguard	245,000	200	99%
S. aureus (nonpigm.)	Control	170,000	63,000	63%
	Bioguard	197,000	900	99%

Summary: Results indicate that under the test conditions (sealed storage under ideal conditions for 6 hours), treated fabrics exert varying levels of antibacterial reduction (69-100%) in a 6 hour exposure period against specific microorganisms isolated from socks. These results are somewhat questionable since the method utilized did not take into consideration the percent die-off of test organisms on untreated control fabrics, which in this study ranged from 0% to 96%. Also, evidence of neutralization of active ingredients in assay was not provided.

In general, the results are indicative of some level of intrinsic (not practical benefit) value of treated socks against the bacteria isolated from worn socks. Such intrinsic, presumptive results could provide a basis for proceeding with the required simulated-use studies to demonstrate the claimed effectiveness in the use pattern proposed.

(B) (3) Dow Corning Study E-3069-C. "The Effect of Various Detergents on the Antimicrobial Activity of Bioguard Treated Scoks".

Procedure

Procedural details available in data file Accession No. 233246. Briefly, Bioguard treated socks and untreated control socks (number of socks not indicated) were laundered through 10 cycles according to AATCC Method 124-1975 using various detergents. A set of treated and untreated socks was laundered in water only. Subsequent to laundering, socks were tested according to AATCC Method 100-1974 against Klebsiella pneumoniae ATCC 4352.

Results

Sample	Detergent	# Bacteria Remaining at: 0 Time	6 Hours	% Reduction
Control	Water Only	214,000	201,000	6.1%
Bioguard	Water Only	205,000	900	99.6%
Control	Tide	198,000	245,000	0%
Bioguard	Tide	202,000	1,600	99.2%
Control	Arm & Hammer	189,000	191,000	0%
Bioguard	Arm & Hammer	199,000	2,100	98.9%
Control	Dynamo	201,000	189,000	6%
Bioguard	Dynamo	208,000	2,950	98.6%
Control	Cheer	192,000	180,000	6.3%
Bioguard	Cheer	199,000	1,500	99.2%

Summary: Again, this study did not address die-off of test organisms in untreated control socks in 6 hours, and documentation of neutralization of active ingredients in assay was not provided. In general, the data appears to indicate a retention of the active ingredient through various wash procedures, under conditions of testing. Such data provides intrinsic, presumptive evidence (not practical benefit) of chemical retention and could provide a basis for proceeding with the required simulated-use studies to demonstrate claimed effectiveness in the use pattern proposed.

202.0 COMMENTS REGARDING PROPOSED EFFICACY:

The submitted Human Wear Studies are not considered conclusive in regard to whether or not antibacterial treatment of the skin (foot) with Bioguard treated socks effectively controls the growth of bacteria on the skin, and production of foul odors on the skin, so that less intense foul odors are absorbed by socks. These wear studies are not considered conclusive in regard to a consistent relationship between intensity of absorbed odors from the feet and transfer of certain bacterial numbers from the feet to socks, with or without Bioguard treated socks. (Refer to Section 201.0 above for detailed discussion). Therefore, it cannot be concluded that Bioguard treated socks are an effective drug and/or cosmetic antibacterial treatment for the human body. Also, note that this use pattern is not subject to purview under FIFRA.

The submitted laboratory studies identify specific bacteria isolated from worn socks, and provide presumptive evidence of intrinsic value of the active ingredient as an antibacterial agent against such bacteria. Also, presumptive evidence of retention of active ingredient through a limited number of laundering cycles is presented. However, this presumptive, intrinsic value laboratory data does not substantiate the claimed pesticidal efficacy of the subject product in the use pattern

proposed, but rather serves as a basis for proceeding with the required simulated-use laboratory study previously delineated.

203.0 DATA REQUIRED TO DOCUMENT PROPOSED EFFICACY OF PRODUCT IN PROPOSED USE PATTERN:

To substantiate the pesticidal claim "The treatment is bacteriostatic and inhibits the growth of odor causing bacteria on socks", the following type of study must be conducted:

(1) A controlled, simulated-use laboratory study which demonstrates that offensive sock odor is microbiologically produced in/on socks, and that Dow Corning 5700 treatment controls this problem. This demonstration should show that the specific types of bacteria that were found to contaminate socks in the in-use wear study (E-3069-A), when inoculated into/onto socks under laboratory conditions, are in fact responsible for the production of offensive sock odor at the claimed site -- that is, in/on socks. Therefore, control studies in this laboratory test should demonstrate bacterial growth (by quantitative plate count procedures and employing appropriate neutralizer) and offensive odor production in/on untreated socks. Test studies should demonstrate control of bacterial growth (by quantitative plate count procedures and employing appropriate neutralizer) and control of offensive odor production in/on Dow Corning 5700 treated socks. Odor evaluations and plate counts should be conducted concurrently.

(2) Test and control socks should be initially challenged and subsequently rechallenged, at appropriate intervals and for an appropriate time period, with those elements and under environmental conditions that can be associated with actual use conditions.

It is suggested that any proposed protocols designed to demonstrate the above effectiveness be submitted to this Agency for comment <u>prior</u> to initiation of testing.

204.0 SUPPLEMENTAL SUMMARY COMMENTS:

In summary, it is important to note that what must be documented to support efficacy of the subject product in the proposed pesticidal use pattern, for the proposed pesticidal function, is basically a rather limited laboratory study (as indicated above in 203.0) to show:

(a) that socks are the site of growth of specific target pests and that such growth results in the production of offensive odor in/on socks per se.

(b) that the proposed treatment of socks, per se, with Dow Corning 5700 controls bacterial growth and odor production at this site.

It is also important to note that human wear studies, either alone or combined with laboratory studies, do not permit distinction between the human body and the sock as the site of the pest problem and site of control. To support a pesticidal use pattern and function, studies must be based on reproduction of the pest problem and control of the pest problem in/on/at sites <u>other</u> than the human body.

Doris Jean Jenkins

Doris Jean Jenkins
September 18, 1978
Microbiologist - Technical Support Section
Disinfectants Branch