



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

MEMORANDUM

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: John Lee (31)
Registration Division (TS-767)

SUBJECT: EPA#3876-34; Amended application for Slimicide J-12
(quaternary ammonium plus bis (tributyltin) oxide) for
use in air washers to control microbial fouling.
Caswell Nos.: 16C & 10L

Registrant: Betz Laboratories, Inc.
Somerton Road
Trevose, Pa. 19047

Action Requested:

Betz Laboratories is requesting an amendment of EPA#3876-34 registration to include treatment of industrial air washing systems on their product label. A Woodrow memo of June 25, 1982, requested additional data for the #3876-34 file, which would demonstrate that Slimicide J-12 (#3876-34) would not be present in human work spaces served by air from air washers in which Slimicide J-12 is used.

Recommendations:

1. The addition of industrial air washer use to the Slimicide J-12 product label (EPA#3876-34) is supported toxicologically.

Tests conducted in air washers (included in the present report) show that when four times the maximum recommended Slimicide J-12 application rate listed on the product label was used, organotin could not be detected at the lower limit of methodology sensitivity; which was 0.004, or 0.001 mg/m³, reported by two different testing laboratories, respectively.

The current NIOSH TLV (threshold limit value) established by the ACGIH (American Conference of Government and Industrial Hygienists) is 0.1 mg/m³, or 25 times a 0.004 mg/m³ sensitivity limit utilized in the J-12 air washer tests. Thus, it is highly unlikely that Slimicide J-12 used in industrial air washing systems would present any hazards to humans in work spaces served by air washers in which Slimicide J-12 is used.

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2. Data reviewed in the present report is classified Core-Minimum Data:

- a) Acute Oral Toxicity Evaluation of Slimicide J-12, Rats.
Combined M&F LD₅₀ = 0.59 g/kg
Toxicity Category - III
- b) Acute Dermal Toxicity of Slimicide J-12, Rabbit.
LD₅₀ M = > 8.0, < 16.0 g/kg
LD₅₀ F = > 16.0 g/kg
Toxicity Category - III
- c) Acute Inhalation Toxicity of Slimicide J-12, Rat.
LC₅₀ > 0.057 mg/liter
Toxicity Category - I
- d) Primary Dermal Irritation, Rabbit.
Slimicide J-12 is a moderate skin irritant.
Toxicity Category - III
- e) Department of Transportation Corrosivity (Dermal) Test, Rabbit.
No dermal corrosion.
- f) Primary Eye Irritation Evaluation of Slimicide J-12, Rabbit.
A severe eye irritant (J-12).
Toxicity Category - I
- g) Air Washer Studies to Assess Potential for Human Exposure to Slimicide J-12.
It is very unlikely that humans would be exposed to Slimicide J-12 used in air washers.

3. The product signal word and precautionary statements are satisfactory.

4. No additional toxicity data are required.

Data Review:

The acute data was submitted March 30, 1982. (Woodrow could find no record of any reviews for this data; the Air Washer study was submitted with the present amended application).

1) Acute Oral Toxicity Evaluation of Slimicide J-12, Rat.
Sponsor: Betz Laboratories. Tester: Biosearch, Inc. Project #81-2758A, 3/5/82.

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Test Material - Slimicide J-12:

Active Ingredients

N-Alkyl (C₁₂-5%, C₁₄-60%, C₁₆-30%,
C₁₈-5%) dimethyl benzyl ammonium
chloride ----- 24.0%

Bis (tributyltin) oxide ----- 5.0%

Inert Ingredients* ----- 71.0%

Five groups of 5M and 5F Sprague-Dawley rats each were separately dosed by gavage with 0.125, 0.25, 0.5, 1.0, or 2.0 g/kg body weight. Food (but not water) was withheld overnight prior to dosing.

Animals were permitted food and water ad libitum for the 14 day observation period. Observations included signs of toxicity and mortality on a daily basis. Individual weights were recorded on the day of treatment and on survivors at 14 days post-treatment.

The LD₅₀ was calculated according to the Thompson Moving Average Method as modified by Weil (Biometrics, Sept., 1952, Vol. 8, No. 3, pp 249-263).

Results:

Dose (g/kg)	Number Dead/Number Treated		
	Males	Females	Total
0.125	0/5	0/5	0/10
0.250	0/5	1/5	1/10
0.500	2/5	2/5	4/10
1.000	4/5	4/5	8/10
2.000	5/5	5/5	10/10

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No unusual behavior signs were noted..

LD₅₀ Males = 0.62 (0.40-0.95) g/kg 19/20 CL

LD₅₀ Females = 0.55 (0.29-1.02) g/kg 19/20 CL

Combined M & F LD₅₀ = 0.59 (0.35-0.99) g/kg 19/20 CL

Toxicity Category - III

Classification: Core-Minimum Data

2) Acute Dermal Toxicity of Slimicide J-12, Rabbit. Sponsor: Betz Laboratories. Tester: Biosearch, Inc. Project#81-2758A, 3/5/82.

Test Material: Slimicide J-12

Four groups of 4M and 4F NZW rabbits each were separately treated with 2.0, 4.0, 8.0, or 16.0 g/kg, by the dermal route. The animals were weighed on the day of dosing, and prior to sacrificing 14 days post-treatment. Prior to dose application, the animals backs were clipped free of hair and the backs of one-half of the animals were abraded.

Treated areas were covered with gauze patches. An impervious wrapping was applied over the patches to secure the test material. Animals were observed 2x daily for signs of toxicity and mortality. Gross autopsies were performed on all dead animals and on survivors 14 days post-treatment.

Results:

Dose g/kg	Number Dosed	Number Dead/Number Treated		Total
		Males	Females	
2.0	2A*	0/2	0/2	0/4
2.0	2U**	0/2	0/2	0/4
4.0	2A	0/2	0/2	0/4
4.0	2U	0/2	0/2	0/4
8.0	2A	0/2	1/2	1/4
8.0	2U	0/2	0/2	0/4
16.0	2A	1/2	0/2	1/4
16.0	2U	2/2	0/2	2/4

*A = Abraded

**U = Unabraded

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The skin of the animals at treatment sites appeared to display severe erythema and moderate edema after 24 hours exposure to test material at all dose levels tested. Forty-eight hours post treatment, treated skin appeared necrotic; this necrotic condition persisted through the 14 day observation period.

The gross autopsies did not reveal any remarkable changes.

Acute dermal LD₅₀:

Male Rabbits = > 8.0, < 16.0 g/kg

Female Rabbits = > 16.0 g/kg

Toxicity Category - III

Classification: Core-Minimum Data

3) Acute Inhalation Toxicity of Slimicide J-12, Rat.

Sponsor: Betz Laboratories. Tester: Biosearch, Inc. Project#81-2758A, 3/5/82.

Test Material: Slimicide J-12

Two groups of 5M and 5F Sprague-Dawley rats each were acclimated to laboratory conditions for 5 days prior to use in the inhalation study. One group of rats was exposed by the inhalation route for 1 hour to the maximum amount of test material possible in a 260 liter plexiglass exposure chamber, while the second group was similarly exposed for 1 hour to a chamber concentration somewhat less than the first group was exposed to.

The aerosols were generated by a six jet collision nebulizer (BGI Incorporated) Waltham, Mass.). Nominal concentrations were determined by dividing the difference in test material reservoir weight during animal exposure by the total amount of air passed through the exposure chamber. The actual exposure chamber concentration and particle size determinations were made by withdrawing chamber aerosol samples for 5 minutes into Anderson Cascade Samplers at the rate of 1 cubic foot of atmosphere per minute. The amount of aerosol impacting on each plate of the Anderson Sampler was determined by weighing; these values, in conjunction with the known Sampler plate pore sizes, permitted calculation of the mass median aerodynamic diameter of test aerosols and animal exposure concentrations.

Animals were observed for mortality and toxic signs 2x per day for 14 days following test exposures. Animal weights were recorded on the day of exposure and at days 7 and 14 post-exposure. Gross autopsies were performed on all animals that died during the observation period, and on all survivors.

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Results:

Nominal concentrations and mortality for the two dose levels used were:

<u>Nominal Concentration</u>	<u>Mortality</u> (5M & 5F)
2.38 mg/liter	0/10
5.55 mg/liter	4/10 (2 males & 2 females)

No adverse symptoms were observed during the 1 hour exposure to 2.38 mg/liter, and none during the 14 day observation period for these animals.

All the animals exposed to the 5.55 mg/liter aerosol concentration showed ruffled fur and appeared slightly legarthic. One animal died sometime during the first 24 hours post exposure. Three animals were found dead six days post-exposure. Twenty-four hours post-exposure, surviving animals had a red discharge around the nose which persisted for about 7 days. Gross pathologic examination did not reveal any remarkable findings for animals that died during the experiment, or survivors.

Actual chamber aerosol concentrations and particle sizes:

<u>Nominal Concentration</u>	<u>Actual Chamber Concentration</u> (Anderson Sampler)	<u>Particle Signs</u>
2.38 mg/L	0.003 mg/L	<0.43 u mmD*
5.55 mg/L	0.057 mg/L	1.3 u mmD*

*Mass median aerodynamic diameter.

NOTE: The large differences between the nominal and actual test chamber aerosol concentrations could possibly be approximately accurate; aerosols generated with nebulizers are largely devoid of larger particle sizes, due to impingement of the aerosol almost immediately upon generation to permit escape of small particles and constant refluxing of large particles. Betz Laboratories also states that the active ingredients quite likely "plated out" onto various surfaces with which J-12 comes into contact while being recirculated in the system water.

LC₅₀ > 0.057 mg/liter
Toxicity Category - I
Classification: Core-Minimum Data

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4) Primary Dermal Irritation, Rabbit. Sponsor: Betz Laboratories. Tester: Biosearch, Inc. Project#81-2758A, 11/3/81.

Test Material: Slimicide J-12

The backs and flanks of 6 NZW rabbits were clipped free of hair prior to abrading one side of each animals back. One-half ml of undiluted Slimicide J-12 was applied to one intact and one abraded skin site on each rabbit; treatment sites were then covered with gauze patches. The gauze patches were then wrapped with impervious wrapping. Twenty-four hours post-treatment, the treatment sites were examined and scored according to Draize for erythema and edema. The treated sites were scored again at 72 hours and were examined again 7 days post-treatment, due to persisting irritation.

Results:

The dermal scores were evaluated according to the method of Draize; the P.I. score = 4.12, which indicates that Slimicide J-12 is a moderate skin irritant.

Toxicity Category - III
Classification: Core-Minimum Data

5) Department of Transportation Corrosivity (Dermal) Test, Rabbit. Sponsor: Betz Laboratories. Tester: Biosearch, Inc. Project#81-2758A, 10/29/81.

Test Material: Slimicide J-12

The backs and flanks of 6 NZW rabbits were clipped free of hair. One-half ml of Slimicide J-12, undiluted was applied to a 1" x 1" intact skin site (the skin was not abraded). Two, one inch x 1", single layer gauze patches were placed on treated sites. The gauze patches were then held in place with impervious wrapping. Wrappings were removed at the end of a four hour exposure period and the treated sites were examined. The sites were then washed with water and examined again at twenty-four and forty-eight hours.

Corrosion was positive if tissue destruction or irreversible alteration occurred:

Destruction - any ulceration or necrosis.

Sloughing of epidermis, edema, erythema, or fissuring did not constitute corrosivity.

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Results:

Very slight to well defined erythema and very slight to slight edema occurred; however, no dermal corrosion was noted.

Classification: Core-Minimum Data

6) Primary Eye Irritation Evaluation of Slimicide J-12,
Rabbit. Sponsor: Betz Laboratories. Tester: Biosearch, Inc.
Project#81-2758A, 11/17/81.

Test Material:

One-tenth ml of undiluted Slimicide J-12 was instilled into the right eye of each of 9 NZW rabbits; untreated eyes served as controls. The treated eyes of six rabbits remained unwashed. The remaining three rabbits had treated eyes washed for 1 minute, beginning 30 seconds after treatment.

Treated eyes were examined at one, two, three, four, seven, fourteen and twenty-one days post-treatment. The eyes were scored for irritation during the examinations according to the method of Draize.

Results:

The eyes of rabbits 1 through 6 were not washed:

	<u>Ocular Scores</u> (Day of Examination)						
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>7</u>	<u>14</u>	<u>21</u>
Average ocular irritation score	105.7	106.7	106.0	106.3	105.7	105.7	106.0

The eyes of rabbits 7 through 9 were washed:

	Ocular Scores (Day of Examination)						
	1	2	3	4	7	14	21
Average ocular irritation score	90.7	105.3	104.7	105.3	105.3	100.7	98.0

NOTE: Washing treated eyes apparently did not affect the severity of irritation; corneal opacity persisted through 21 days of observation.

Toxicity Category: I

Classification: Core-Minimum Data

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7) Air Washer Studies to Assess Potential for Human Exposure to Slimicide J-12. Sponsor: Betz Laboratories. Tester: Betz Laboratories (no study no.), October 14, 1982.

Test Material: Slimicide J-12

Slimicide J-12 was added to the sump of an Air Washer facility in use at the Betz Laboratories in Trevose, Pa. in attempts to determine whether the microbicide would become entrained in the treated air washer effluent air and constitute a hazard to humans working in closed spaces serviced by the Air Washer. In lieu of performing simulated air washer toxic potential studies according to the "Protocol for Human Hazard Evaluation of Microbicides Used in Industrial Air Washing Systems to Control Biological Fouling" prepared by the Agency, the Betz Co. elected to perform actual air washer tests to determine whether Slimicide J-12 was present in work-space air that had been treated in an air washing device that utilized Slimicide J-12 to control microbial fouling.

Air Washer Specifications:

Air flow: 22,800 CFM
Spray water flow: 110 gpm
Cooling capacity (by design): 1170.4 MBH
Humidification (by design): 4.0 pounds/hour
Total Capacity: 185 gallons of water
The device did utilize mist eliminators.

Before beginning the experiment, the sump contents were removed and replaced with potable water; to eliminate previously employed slimicide.

Three different concentrations of Slimicide J-12 were separately added to the sump water, beginning with the lowest concentration, followed by a second and a third concentration:

<u>Test Amount of J-12 Added</u>	<u>(PPM)</u>	<u>Length of Air Washer Water Spray</u>
0.1 pound/1000 gal.	12	4 hours
0.9 pounds/1000 gal.	108	4 hours
4.0 pounds/1000 gal.	480	4 hours

NOTE: The Slimicide J-12 product label recommends air washer system treatment at a range of 0.1 to 1.0 pounds per 1000 gallons of water in the system (12 to 120 ppm) depending on the severity of the microbial contamination. Thus, the highest concentration recommended on the product label is 1/4 of the highest concentration tested in the present experiments.

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Water (sump) samples were taken at one hour and at 4 hours after each addition of Slimicide J-12, excepting the first trial where a 4 hour sample only was taken. Immediately following removal of a 4 hour sample, the next level of test Slimicide J-12 was added to the system sump.

Air sampling was done continuously throughout each of the three four-hour runs; the sampling tubes were changed for each successive air sample.

The air samples were analyzed by two different laboratories "A and B" (the tester did not specify the names of the laboratories). The continuous air samples were collected concurrently with operation of the air washing system.

Slimicide J-12 contains quaternary ammonium and bis (tributyltin) oxide active ingredients. Evaluation of the aerosol samples reported organo tin, and tributyltin oxide, while the sump water analyses measured quaternary ammonium compound, organo tin, and tributyltin oxide.

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Results:

TABLE #1

LABORATORY "A"

1 Hour Air Concentrations of Organo-Tin (O-Sn) and n-butyl Tin Oxide (TBTO)

	mg/m ³ O-Sn	mg/m ³ TBTO (Calc.)
Background Levels		
Workplace	<0.004	<0.01
Trial 1 (see Table #3)		
Workplace	<0.004	<0.01
Trial 2 (see Table #3)		
Workplace	<0.004	<0.01
Trial 3 (see Table #3)		
Workplace	<0.004	<0.01
Mist Generated from a 600 ppm Aqueous Solution Positive Control in Lab Hood	0.080	0.199

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TABLE #2LABORATORY "B"4 Hour Air Concentrations of Organo-Tin (O-Sn) and Tributyl Tin Oxide

	mg/m ³ O-SN	mg/m ³ TBTO (Calc.)
Background Levels		
Workplace	0.001	0.002
Trial 1 (see Table #3)		
Workplace	0.001	0.004
Trial 2 (see Table #3)		
Workplace	0.001	0.002
Trial 3 (see Table #3)		
Workplace	0.001	0.004
Mist Generated from a 600 ppm Aqueous Solution		
Positive Control in Lab Hood	0.129	0.323

NOTE: The values shown in Tables 1 and 2 represent the lower limits of method sensitivity reported by the two different laboratories that analyzed the air washer air samples. The Betz Corporation analyzed the quat and tin components of sump water samples.

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TABLE #3

TRIAL #1

Concentration Based
On Amount of J-12
Added to H₂O

Concentration in H₂O (Sump)
Based on Analytical Data

Time Hrs.	0	4			
Lbs. J-12 added(1)	0.1	(4.02 based on Sn)			
ppm J-12 added	12.0	(<8.33 based on Quat)			
		(0.201 based on Sn)			
ppm TBTO added	0.6	0.08			
ppm O-Sn(2) added	0.23	<2.0			
ppm Quat	2.88	(0.964 based on Sn)			
Time Hrs.	4	5	8		
Lbs. J-12 added(1)	0.9	(95.4 based on Sn)	(40.6 based on Sn)		
ppm J-12 added	108+	(45.8 based on Quat)	(<8.33 based on Quat)		
		(4.77 based on Sn)	(2.03 based on Sn)		
ppm TBTO added	5.4+	1.90	0.81		
ppm O-Sn(2) added	2.14+	11.0	<2.0		
ppm Quat	25.92+	(22.9 based on Sn)	(9.74 based on Sn)		
Time Hrs.	8	9	12		
Lbs. J-12 added(1)	4.0	(296 based on Sn)	(190.8 based on Sn)		
ppm J-12 added	408+	(302 based on Quat)	(148 based on Quat)		
		(14.8 based on Sn)	(9.54 based on Sn)		
ppm TBTO added	24+	5.9	0.81		
ppm O-Sn(2) added	9.36+	73.5	<2.0		
ppm Quat	115.2+	(71.04 based on Sn)	(45.8 based on Sn)		

(1) per 1000 gallons of water in system
(2) O-Sn means organotin

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Conclusions:

One of the test trials for organotin detection resulted in 0.004 mg organotin/m³ (laboratory "A"), while the method used by the other laboratory ("B") could detect organotin at 0.001 mg/m³; therefore any organotin, if present in work spaces serviced by air washer air from an air washing device using Slimicide J-12 at 4x the label recommended highest dosage rate, was present at <0.004 mg/m³.

The current NIOSH TLV for organotin is 0.1 mg/m³, which is far greater (25x) than the 0.004 lower limit of detection possible used by one of the analyzing laboratories for Slimicide J-12 4-hour air test samples.

Therefore it is very unlikely that humans working in areas serviced by air from Industrial Air Washers utilizing Betz Slimicide J-12 would be exposed to airborne hazardous materials.

Study Classification: Core-Minimum Data

William S. Woodrow

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6/6/83

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