

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

OCT 12 1994

Givaudan-Roure Corporation
125 Delawanna Avenue
Clifton, NJ 07015

Attention: Barbara Lewis
Manager, Product Safety

Subject: Giv-Gard DXN
EPA Registration No. 824-7
Your Submission Dated August 29, 1994.

Your submission has been received by the Agency and the product chemistry information was processed through the Reregistration section and a letter was sent to your attention on September 19, 1994. The purpose of this letter is to followup up on the label review as requested through the reregistration section and bring the label into compliance with current labeling standards.

1. Make the following labeling changes below before you release the product for shipment bearing the amended labeling.

a. The headings "Active Ingredient" and "Inert Ingredients" must be given equal prominence.

b. Delete the word: "by weight".

c. Clarify the correct company address. Our records indicate 100 Delawanna Avenue as the official address on file while the label declares 125 Delawanna Avenue.

d. Revise the word Net to read: Net Contents

e. Place the heading: "Keep out of reach of children" to appear directly above the signal word: Caution (center panel only).

f. Revise the referral statement to read: See side panel for additional precautionary statements.

CONCURRENCES

SYMBOL							
SURNAME							
DATE							

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g. Add the following additional precautionary statement: Wash thoroughly with soap and water after handling.

h. Revise the Environmental Hazards section to comply with PR Notice 93-10.

i. It is preferred that the misuse statement: "It is a violation of Federal law..." be placed directly below the heading; Directions for Use.

j. Include the following two subheading:

Pesticide Disposal
Containter Disposal

These subheadings should be placed in the appropriate location within the Storage Disposal section.

k. The preferred nomenclature for the active ingredient is:

2,6-Dimethyl-m-dioxan-4-ol acetate

1. Add the following statement: A microbiostat/fungistat for use in the manufacture of the following products only: cosmetics, cosmetic lotiions, emulsion paints, jet fuels, liquid soaps, emulsion inks.

2. NOTE: No data review for any proposed uses will be considered under this letter at this time. Previous letters from the product manager team has already addressed the additional information that is required for this product for any new uses.

In order to clarify for the record and based upon the last stamped label for this product dated January 16, 1973. the only acceptable use patterns are:

Cosmetics and cosmetics lotions
Emulsion paints
Emulsion inks
Jet fuels
Liquid soaps

In addition, several use patterns have been deleted as per your letter dated October 23, 1989.

The label and the last stamped bulletin has been adjusted to reflect the above acceptable and deleted use patterns.

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3. A release for shipment of the product bearing the amended labeling constitutes acceptance of these conditions.

4. A stamped copy of the labeling is enclosed for your records.

If you have any questions concerning this letter, contact V. Goncarovs at 703-305-6663.

Sincerely,



Marshall Swindell
Acting Product Manager (31)
Antimicrobial Program Branch
Registration Division (H7505C)

Enclosures

CONCURRENCES

CONCURRENCES							
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SURNAME							
DATE							

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ACCEPTED
with COMMENTS
in EPA Letter Dated:

OCT 12 1994

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

824-7

GIVAUDAN-ROURE

GIV-GARD

(BRAND OF DIMETHOXANE)

PRECAUTIONARY STATEMENTS HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION

Harmful if swallowed, inhaled or absorbed through the skin. Avoid breathing vapors. Avoid contact with skin, eyes or clothing. In case of contact immediately flush eyes or skin with plenty of water. Get medical attention if irritation persists.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to fish and wildlife. Keep out of lakes, ponds or streams. Do not apply directly to water unless in accordance with an NPDES permit. Contact the Regional Office of EPA for guidance. Do not contaminate water by cleaning of equipment or disposal of wastes.

PHYSICAL OR CHEMICAL HAZARDS

Do not use or store near heat or open flame.

NET: GAL. LBS. LOT NO.

Manufactured by: GIVAUDAN-ROURE CORPORATION

GC-1537-A 125 Deanna Avenue
Clifton, N.J. 07014

CAUTION

SEE SIDE PANEL FOR OTHER PRECAUTIONARY STATEMENTS

STATEMENT OF PRACTICAL TREATMENT

If swallowed: Drink a large quantity of water. Do not induce vomiting. Immediately contact physician or Poison Control Center.

If inhaled: Remove to fresh air and call a physician immediately.

If on skin: Wash thoroughly with soap and water. Flush with large quantities of water.

If in eyes: Flush eyes immediately with plenty of clear water for at least 15 minutes. Immediately contact physician.

If on clothing: Remove contaminated clothing and wash before reuse.

ACTIVE INGRED
Dimethoxane;
6-acetoxy-2, 4-d
INERT INGREDIEN

FOR M.

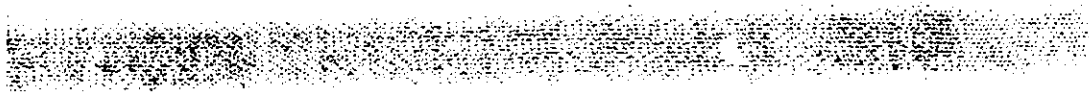
It is a violation of Federal labeling.

Giv-Gard DXN[®] (Brand of D manufacturing use only in industry Givaudan-Roure Corporation



EPA Reg
NOT FOR RESALE

BEST AVAILABLE COPY



GIVAUDAN-ROURE

ARD DXN[®]*

(BRAND OF DIMETHOXANE)

BACTERIOSTAT/FUNGISTAT

STATEMENTS

STATEMENT

Do not induce
poison Control

physician im-

er. Flush with

of clear water
ician.

g and wash

ACTIVE INGREDIENT:

Dimethoxane;
6-acetoxy-2, 4-dimethyl-m-dioxane 87 % by weight

INERT INGREDIENTS: 13 % by weight
100% by weight

**DIRECTIONS FOR USE
FOR MANUFACTURING USE ONLY**

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

Giv-Gard DXN[®] (Brand of Dimethoxane) is a microbial growth inhibiting agent for manufacturing use only in industrial water-based products. It is to be used as directed in Givaudan-Roure Corporation's Technical Bulletin **27A**



*U.S. PAT. 2,167,477

EPA Reg. No. 824-7 EPA Est. No. 824-NJ-1

NOT FOR RESALE

NOT FOR USE IN COSMETICS

STORAGE AND DISPOSAL

Keep container covered. Store in a dry, cool, well-ventilated area avoiding open flames or other sources of ignition.

Do not contaminate water, food or feed by storage or disposal. Open dumping is prohibited. Do not reuse empty container.

Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility. Triple rinse (or equivalent). Then offer for recycling, or reconditioning, or puncture and dispose of in a sanitary landfill, or by other procedures approved by state and local authorities.

KEEP CONTAINER COVERED - STORE IN A DRY PLACE

NON-WARRANTY: Our recommendations for use of this product are based upon tests believed to be reliable. The use of this product being beyond the control of the manufacturer, no guarantee, expressed or implied, is made as to the effects of such or the results to be obtained if not used in accordance with directions and established safe practice. The buyer must assume all responsibility, including injury or damage, resulting from its mis-use as such, or in combination with other materials.

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division

Technical Bulletin #27A

GIV-GARD DIX®
(Brand of Dimethoxane)
Bacteriostat/Fungistat

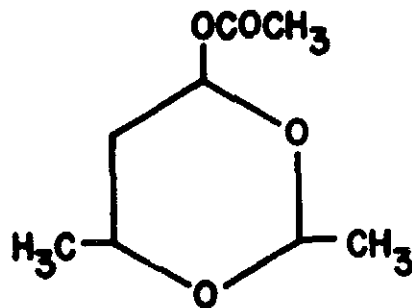
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Physical and Chemical Properties

C₈H₁₄O₄

M. W. 174.2



6-acetoxy-2,4-dimethyl-m-dioxane

Appearance	Clear yellow to light amber liquid
Assay	92% Minimum
Specific Gravity @ 25°/25°C	1.060 - 1.075
Refractive Index @ 20°C	1.429 - 1.435
Boiling Point	66°C - 68°C @ 3mm. Hg.
Freezing Point	Does not freeze at -25°C
Solubility	Soluble in or miscible with water and organic solvents

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*Trademark Reg. U.S. Pat. Off.
U.S. Pat. No. 3,167,477

ACCEPTED
with COMMENTS
in EPA Letter Dated:

OCT 12 1994

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

824-7

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II

Activity

Giv-Gard DXN results from a research program to develop a reliable preservative that will function effectively against the numerous spoilage microorganisms encountered in [REDACTED] various types of emulsions.

Microbial growth inhibiting agents commonly in use in industry today may or may not offer optimum preservative action, depending upon factors such as pH, type of emulsifier, or a loss of material into the oil phase of an emulsion system. There is considerable need for an agent that will remain in the water phase of such systems and continue to exert its biological activity over a broad pH range. Needless to say, the product should exert action against a broad spectrum of microorganisms and especially against the Gram negative bacteria which are the major organisms involved in bacterial spoilage problems.

Bacteriological evaluation of Giv-Gard DXN demonstrated microbial growth inhibiting activity in various products against both Gram positive and Gram negative bacteria, as well as against several yeasts and fungi at concentrations in the range of 0.03% to 0.1%. The minimum concentrations of Giv-Gard DXN, inhibiting various organisms in conventional microbiological tests are shown in Table I.

Giv-Gard DXN functions effectively over a wide pH range and in a wide variety of formulations. Giv-Gard DXN is not inactivated by the presence of nonionic surfactants, and thus, will probably be of great interest in the preservation of cosmetics. Compatibility with systems containing amides or amines warrants careful examination since Giv-Gard DXN may cause discoloration in such systems.

(2)

Giv-Gard DXN has been added to a number of heavily contaminated commercial products resulting in the death of the spoilage organisms within twenty-four to forty-eight hours. It has been shown to be particularly effective in controlling Pseudomonas contamination in nonionic cosmetic lotions, emulsion paints, [REDACTED] at a level of 0.1%. Experimental evidence indicates that Giv-Gard DXN may control the molds and bacteria encountered in jet fuels and liquid soaps. Giv-Gard DXN is being successfully used to control bacterial slime formation [REDACTED] [REDACTED] in the preservation of emulsion inks.

The lethal action towards Pseudomonas may be seen in Figure I which depicts the death of the test organism in a nonionic cosmetic emulsion. It may be noted that there was an approximate 90% kill within six hours after inoculation.

The action of Giv-Gard DXN in 5% Tween-80® solution against representative organisms is shown in Table II. It may be noted that virtual elimination of the contaminant was obtained by the end of twenty-four hours. Giv-Gard DXN performs equally well in actual cosmetic formulations as seen in Table III. Giv-Gard DXN effectively reduced the bacterial contamination whereas methyl p-hydroxybenzoate failed in some instances.

Giv-Gard DXN being water soluble, can readily be dissolved in aqueous systems; it is also miscible with many oils and solvents. It is suggested that Giv-Gard DXN be used at about 0.1% as an experimental starting point. The addition of 1.0% liquid sodium xylene sulfonate aids in the preparation of a 10.0% Giv-Gard DXN stock solution.

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III

Stability

Giv-Gard DXN is stable in storage. When added to an aqueous system, the ester group hydrolyzes to produce acetic acid which causes a slight lowering of the pH. This effect may be compensated for by the addition of an appropriate alkaline material. The acetic acid produced plays no part in the preservative action of the product. The ester is offered because of the difficulty of isolating and purifying the free alcohol.

IV

Toxicological Properties

The acute oral toxicity (LD_{50}) of Giv-Gard DXN in rats was found to be 1.9 ml./kg. Using the Repeated Insult Patch Test Method of Shelanski and Shelanski (Proceedings of the Scientific Section Toilet Goods Association #19, May 1953) on fifty-two subjects, a 1% aqueous solution did not produce irritation or sensitization; at a concentration of 1% or less, it is therefore considered to be safe for use in cosmetic preparations coming in contact with the human skin. When a 1% aqueous solution was applied to the eyes of three albino rabbits, no irritation occurred; the cornea, iris and conjunctivae were normal throughout the seven day observation period. The procedure was that suggested by Draize and described in "Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics," published by the Association of Food and Drug Officials of the United States.

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Our recommendations for use of this product are based upon tests believed to be reliable. The use of this product being beyond the control of the manufacturer, no guarantee, expressed or implied, is made as to the effects of such or the results to be obtained if not used in accordance with directions and established safe practice. The buyer must assume all responsibility, including injury or damage, resulting from its misuse as such, or in combination with other materials.

CAUTION: Harmful if swallowed! Do not get in eyes, on skin, or on clothing. In case of contact, immediately flush skin or eyes with water. If irritation persists, get medical attention. Do not reuse empty drum. Return to drum reconditioner or destroy by perforating or crushing and burying in a safe place away from water supplies.

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TABLE I

BACTERIOSTATIC AND FUNGISTATIC SPECTRUM OF GIV-GARD DXN®

<u>Organism</u>	<u>M.I.C. (ug/ml)*</u>
Staphylococcus aureus	1250
Bacillus subtilis	625
Pseudomonas aeruginosa	625
Pseudomonas fluorescens	625
Bacterium ammoniagenes	625
Escherichia coli	625
Aerobacter aerogenes	625
Salmonella typhosa	625
Salmonella choleraesuis	312
Shigella sonnei	625
Saccharomyces cerevisiae	2500
Pityrosporum ovale	625
Candida albicans	1250
Aspergillus niger	1250
Aspergillus flavus	1250
Aspergillus terreus	1250
Aspergillus oryzae	1250
Penicillium piscarium	625
Penicillium species (unknown)	1250

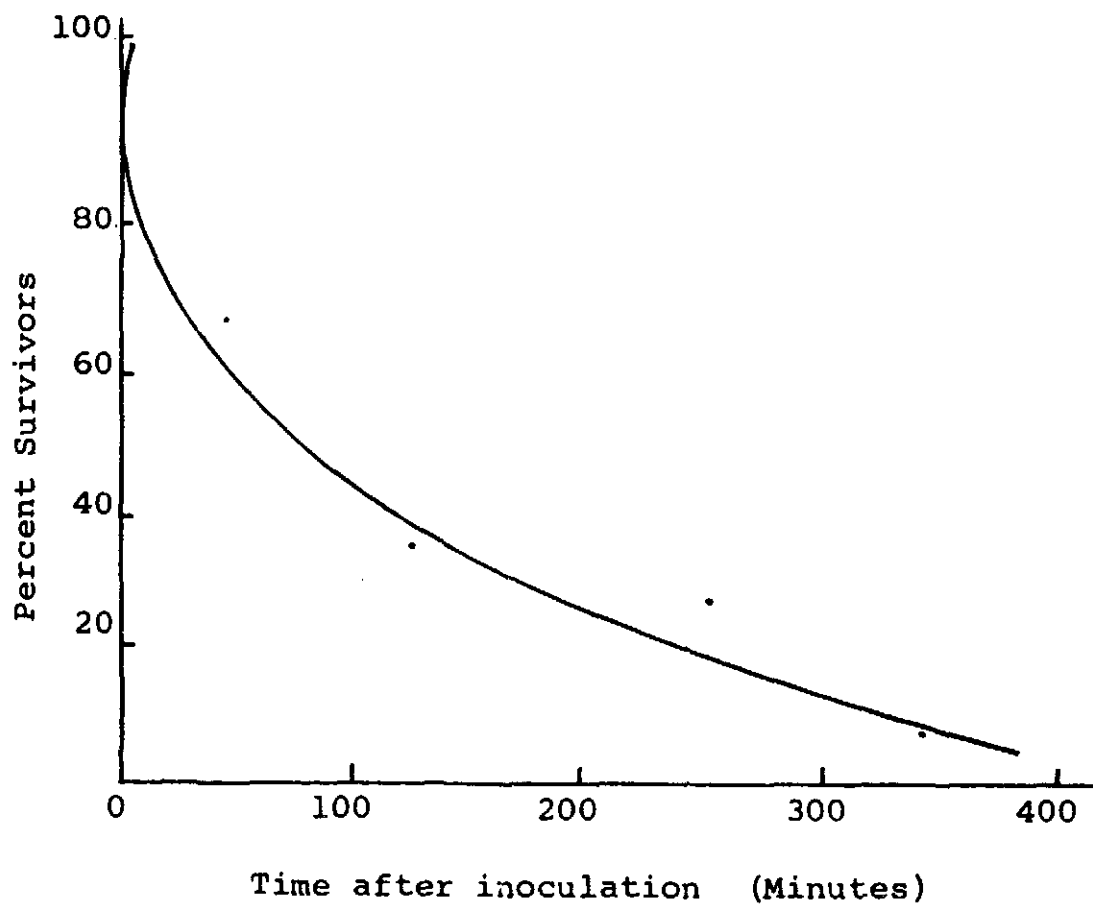
*Minimal inhibitory concentration in ug/ml agar by two-fold serial dilution technique. Bacteria on Dextrose Tryptone Extract Agar, 3 days at 34°C. Mold and yeasts on Sabouraud's Dextrose 5 days at 30°C.

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FIGURE I SURVIVAL CURVE OF PSEUDOMONAS AERUGINOSA
IN NONIONIC LOTION CONTAINING 0.1% GIV-GARD DXN



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TABLE II

INHIBITORY ACTION OF GIV-GARD DXN IN A 5% TWEEN® 80 SOLUTION
AGAINST DIFFERENT GRAM NEGATIVE BACTERIA

Culture	Preservative Conc. =0.1%	Bacterial Counts per ml.		
		Initial	After 24 hrs.	After 5 days
Pseudomonas aeruginosa	GIV-GARD DXN	1,590,000	0	0
	None	1,800,000	4,800,000	30,000,000
Escherichia coli	GIV-GARD DXN	340,000	0	0
	None	420,000	89,000,000	35,000,000
Culture #25*	GIV-GARD DXN	75,000	0	0
	None	74,000	89,000,000	24,000,000
Culture #20*	GIV-GARD DXN	31,000	0	0
	None	37,000	10,000	12,400

*Gram negative isolates recovered from spoiled cosmetic lotion.

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TABLE III

INHIBITORY EFFECT OF GIV-GARD DXN IN DIFFERENT NONIONIC FORMULATIONS

AGAINST

PSEUDOMONAS AERUGINOSA

Lotion No.	Preservative Conc. =0.1%	pH	Initial	BACTERIAL COUNTS PER ML.	
				After 24 hrs.	After 48 hrs.
I	None	8.0	990,000	12,000	0
	Giv-Gard DXN	7.9	2,200,000	0	0
	MP*	8.0	1,540,000	42,000	0
II	None	7.7	3,800,000	30,000,000	30,000,000
	Giv-Gard DXN	7.7	740,000	0	0
	MP	7.7	1,000,000	24,000,000	520,000
III	None	5.5	3,900,000	30,000,000	30,000,000
	Giv-Gard DXN	4.8	1,500,000	0	0
	MP	5.5	2,400,000	100	960,000
IV	None	6.7	2,650,000	30,000,000	30,000,000
	Giv-Gard DXN	5.0	130,000	0	0
	MP	6.7	3,000,000	590,000	3,100,000
V	None	5.5	2,850,000	30,000,000	30,000,000
	Giv-Gard DXN	4.6	1,800,000	0	0
	MP	5.5	2,850,000	0	0

*Methyl p-hydroxybenzoate

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TABLE IV

COMPOSITIONS OF NONIONIC LOTIONS REFERRED

TO IN THIS REPORT

LOTION	I	II	III	IV	V	"D"
Mineral Oil	37.5	37.5	35.0	25.0		5.0
Petroleum	6.0	7.5				
Lanolin	3.0		1.0		0.5	
Beeswax	12.0	2.0				
Borax	0.5					
G-11®			0.5			
Cetyl Alcohol			1.0			
Giv-Tan® F				1.5		
Stearic Acid					7.0	3.0
Sorbo® 70% Solution					10.0	
Water	35.0	46.5	55.5	63.5	79.5	87
Arlacel® -83	3.0	2.0				
Arlacel® -20	1.0					
Arlacel® -60				4.0		1.5
Arlacel® -80			2.1		0.5	
Tween® -20	2.0					
Tween® -60				6.0	2.5	3.5
Tween® -80			4.9			
Atlas® G-1425		4.5				