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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

August 9, 1999

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 11631-U / AlphaSan RC 7000
DP Barcode: D253513
Case No: 062543

To: Marshall Swindell, PM 33 / Tony Kish
Regulatory Management Branch
Antimicrobials Division (7510C)

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

Through: for Karen Hicks, Team Leader
Chemistry and Toxicology Team
Efficacy and Science Support Branch
Antimicrobials Division (7510C)

Michele E. Wingfield, Chief
Efficacy and Science Support Branch
Antimicrobials Division (7510C)
8/18/99

Applicant: Milliken Swindell

FORMULATION FROM LABEL:

	% by wt.
Active Ingredient(s):	
Silver sodium hydrogen zirconium phosphate	31
Other Ingredient(s):	69
Total:	100%

BACKGROUND: Milliken Chemical has submitted an acute oral toxicity study, a primary skin irritation study and a primary eye irritation study in support of "AlphaSan RC 7000". These studies were conducted by Huntingdon Research Centre, Ltd., of Cambridgeshire, England. The MRID numbers are 446183-02 through 446183-04. The registrant has also requested a waiver of the acute dermal toxicity, acute inhalation toxicity and skin (dermal) sensitization studies.

The justification for the waiver requests is as follows:

"During testing it was found that the RC 2000 active ingredient in AlphaSan RC 7000 elicited no toxicological response from test animals and organisms at the limit dose. Similarly, the second component in the formulation, [redacted] is well known to be of no toxicological concern."

RECOMMENDATIONS: ESSB findings are:

1. The acute oral toxicity, primary eye irritation and primary skin irritation studies are acceptable. The test material is listed as "Novaron AGZ330" in these studies; however, the cover page of these studies lists the test material as AlphaSan RC 7000.

2. As stated in the 9/10/98 letter to the registrant from Marshall Swindell, the decision as to the necessity for acute toxicity studies for AlphaSan RC 7000 will be contingent upon acute toxicity data reviews for products AlphaSan RC 2000 and 5000. Apparently, these studies have not been submitted to, or reviewed by EPA/OPP yet. The information given for these waiver requests does not support a waiver for a dermal sensitization study.

   ESSB would like to point out that waiving acute toxicity studies because one or more ingredients are considered to be of low toxicity is very unusual. Typically, a registrant may support the requirements for acute toxicity studies by one of three methods:

   a. Submitting studies conducted on the product: Submitting acute toxicity studies conducted on the actual registration product is the most specific and readily accepted method of supporting this requirement.
   b. A Waiver: In this case, a study is waived because it cannot be conducted. For example, a product that comes in the form of petrolatum (Vaseline) or a solid like a table cloth cannot be made into an aerosol for an acute inhalation toxicity study. Such products would have the acute inhalation toxicity study waived.
   c. Data Citation: In this instance, a product demonstrates that it is chemically identical to, or greatly chemically similar to, another product for which the EPA has acute toxicity data. The registrant may cite data conducted on the other product.

   In this case, the registrant is trying to use yet another method to bypass having to have acute toxicity studies conducted. The registrant may wish to have further communications

with one of AD's acute toxicity reviewers to determine what steps should be taken to cite data conducted on one of the registrant's other products. (This matter is not readily explained. It depends upon factors such as: the percentage of active and inert ingredients in the products and the categories of each acute toxicity study.) If the registrant prefers to use the data citations listed in this submission, they will have to submit detailed supporting data (study reports, MSDSs, data summary from texts on toxicology apply to these specific chemicals, etc.). However, this is not a standard method of supporting acute toxicity requirements and will not be as readily accepted as one of the approved OPP/EPA methods of supporting a product.

The acute toxicity profile for File Symbol 11631-U is currently:

acute oral toxicity	IV	acceptable
acute dermal toxicity		Outstanding/requested
acute inhalation toxicity		Outstanding/requested
primary eye irritation	IV	acceptable
primary skin irritation	IV	acceptable
dermal sensitization		Outstanding/requested

LABELING:

No precautionary labeling can be recommended for this product until the registrant has satisfied the requirements for acute toxicity data for File Symbol 11631-U.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Product Manager: 33
MRID No.: 446183-02

Reviewer: I. Blackwell
Study Completion Date: 2/17/95
Study No.: TSI 78a/940765/AC

Testing Laboratory : Huntingdon Research Centre, Ltd.
Authors : Lewis A. McRae and Jacqueline Cahill

Quality Assurance (40 CFR §160.12): Included

Test Material: Novaron AGZ330; "white powder" (AlphaSan RC 7000; EPA reg. no. 11631-U)

Species: HSD/OLA:Sprague-Dawley (CD)) rat
Age: four to seven weeks
Weight: 201-235 g
Source: Harlan Olac Ltd.

Conclusion:

1. **LD_{50} (mg/kg):** **Males** > 5,000 mg/kg
Females > 5,000 mg/kg
Combined > 5,000 mg/kg

2. **The estimated LD_{50} is greater than 5,000 mg/kg**

3. **Tox. Category**: IV **Classification**: acceptable

Procedure (Deviations from §81-1):

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5,000	0/5	0/5	0/10

Observations: Piloerection (only).

Gross Necropsy: No macroscopic abnormalities.

4

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 33
MRID No.: 446183-04

Reviewer: Ian Blackwell
Study Completion Date: 7/14/97
Study No.: TSI 112/972049/SE

Testing Laboratory: Huntingdon Research Centre, Ltd.
Author(s): Brenda Parcell, M.I.A.T.

Quality Assurance (40 CFR §160.12): Included

Test Material: Novaron AGZ330; "white powder" (AlphaSan RC 7000)
Dosage: 0.1 mL (≃ 62 mg)
Species: New Zealand White rabbits
Sex: 3 males
Weight: 2.0-2.7 kg
Age: 9-12 weeks
Source: Harlan U.K.

Summary:

1. **Toxicity Category**: IV

2. **Classification**: acceptable

Procedure (Deviations From §81-4):
☞The lab did not report on the presence of (or lack thereof) ocular discharge.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	0/3	0/3	0/3	0/3	—	—	—	---
Iritis	0/3	0/3	0/3	0/3	—	—	—	—
Conjunctivae								
Redness	1/3	0/3	0/3	0/3	—	—	—	—
Chemosis	0/3	0/3	0/3	0/3	—	—	—	—
Discharge	—	—	—	—	—	—	—	---

--- = no observations at this point

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 33
MRID No.: 446183-03

Reviewer: Ian Blackwell
Study Completion Date: 2/3/95
Study No.: TSI 79/940809/SE

Testing Laboratory: Huntingdon Research Centre, Ltd.
Author: Brenda Parcell

Quality Assurance (40 CFR §160.12): Included

Test Material: Novaron AGZ330; "white powder" (AlphaSan RC 7000)
Dosage: 0.5 g
Species: New Zealand White (albino) rabbit
Age: 10-13 weeks
Sex: 6 males
Weight: 2.3-3.0 kg
Source: Frosfield (U.K.) Ltd.

Summary:

1. **Toxicity Category**: IV
2. **Classification**: acceptable

Procedure (Deviations From §81-5): None

Results: No erythema or edema was observed.

Special Comments: None

ACUTE TOX ONE-LINER

1. PC CODE: 072560

2. CURRENT DATE: August 9, 1999

3. TEST MATERIAL: Silver sodium hydrogen zirconium phosphate ... 31%

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
acute oral toxicity / rat / Huntingdon Research Centre / **TSI 78a/940765/AC** / 2-17-95	446183-02	LD_{50} > 5,000 mg/kg	IV	A
primary eye irritation / rabbit / Huntingdon Research Centre / **TSI 112/972049/SE** / 7-14-97	446183-04	Redness in 1/6 at 1 hour.	IV	A
primary skin irritation / rabbit / Huntingdon Research Centre / **TSI 79/940809/SE** / 2-3-95	446183-03	No erythema or edema was observed.	IV	A

A = Acceptable
U = Unacceptable
S = Supplementary
V = self-Validated