

US EPA ARCHIVE DOCUMENT

4-28-89

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EPA No.: 68D80056  
DYNAMAC No.: 167-B  
TASK No.: 1-67B  
April 28, 1989

DATA EVALUATION RECORD

ACAROSAN - MOIST POWDER

Mutagenicity--Escherichia coli  
Mammalian Microsome Mutagenicity Assay

APPROVED BY:

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Program Manager  
Dynamac Corporation

Signature: Robert J. Weir  
Date: 4/28/89

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ACAROSAN- MOIST POWDER

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REVIEWED BY:

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DATA EVALUATION RECORD

CHEMICAL: Acarosan.

STUDY TYPE: Escherichia coli mammalian activation mutagenicity assay.

ACCESSION/MRID NUMBER: 408453-10.

TEST MATERIAL: Acarosan-Moist Powder.

SYNONYM(S)/CAS No.: Not listed.

SPONSOR: Gesellschaft fur Hausbiologische Forschung, Mainz, F.R.G.

TESTING FACILITY: Cytotest Cell Research GmbH and Co., Darmstadt, F.R.G.

TITLE OF REPORT: Escherichia coli Reverse Mutation Assay with Acarosan-Moist Powder.

AUTHOR(S): Timm, A.

STUDY NUMBER(S): 118506.

REPORT ISSUED: November 26, 1987.

CONCLUSIONS-Executive Summary:

Under the conditions of two independent Escherichia coli/mammalian-microsome plate incorporation assays, 10.0, 100.0, 333.3, 1000.0, and 5000.0 µg/plate acarosan-moist powder did not induce a cytotoxic or mutagenic effect in E. coli WP<sub>2</sub> uvrA either in the presence or absence of S9 activation. The highest assayed dose was not completely soluble and, therefore, represents the limit of solubility. It was concluded, therefore, that acarosan-moist powder was assayed to an appropriate concentration with no evidence of mutagenicity in this test system.

Study: Acceptable.

A. MATERIALS:

1. Test Material: Name: Acarosan-moist powder  
Description: White solid  
Lot No.: Prod. Mai 1987. purity: Listed as a mixture  
Contaminants: None reported  
Solvent used: Dimethylsulfoxide (DMSO)  
Other comments: Test material was not fully soluble at 50 mg/mL in DMSO.

2. Control Materials:  
Negative: Bacteria  
Solvent/final concentration: 100 µg/plate  
Positive: Nonactivation:  
Methyl methanesulfonate (MMS) 10 µL/plate  
  
Activation:  
2-Aminoanthracene (2-AA) 10 µg/plate.

3. Activation: S9-derived from:

<input checked="" type="checkbox"/>	Aroclor 1254	<input checked="" type="checkbox"/>	induced	<input checked="" type="checkbox"/>	rat	<input checked="" type="checkbox"/>	liver
<input type="checkbox"/>	phenobarbital	<input type="checkbox"/>	noninduced	<input type="checkbox"/>	mouse	<input type="checkbox"/>	lung
<input type="checkbox"/>	none			<input type="checkbox"/>	hamster	<input type="checkbox"/>	other
<input type="checkbox"/>	other			<input type="checkbox"/>	other		

4. Test Organism Used: E. coli WP<sub>2</sub> uvrA.

Test organisms were properly maintained. Yes.  
Checked for appropriate genetic markers (normal spontaneous mutation rate). Yes.

5. Test Compound Concentrations Used:

Preliminary cytotoxicity/mutagenicity assay: 1, 3, 10, 33, 100, 333, 1000, and 5000  $\mu\text{g}/\text{plate}$  with or without S9 activation.

Repeat mutation assay: 10.0, 100.0, 333.3, 1000.0, and 5000.0  $\mu\text{g}/\text{plate}$  with or without S9 activation.

B. TEST PERFORMANCE:

1. Type of E. coli Assay:       x     Standard plate test  
     Pre-incubation ( ) minutes  
     "Prival" modification  
     Spot test  
     Other (describe).

2. Preliminary Assay: Cytotoxicity and mutagenicity of acarosan were assessed concurrently in E. coli WP<sub>2</sub> uvrA. Eight concentrations of the test material ranging from 1 to 5000  $\mu\text{g}/\text{plate}$ , negative, solvent (DMSO), and the positive controls (MMS or 2-AA) were assayed in the presence and absence of S9 activation. Triplicate plates were prepared for each treatment and/or dose level. Compound precipitation was observed on plates containing 5000  $\mu\text{g}/\text{plate}$  of the test material; the report stated that at 1000  $\mu\text{g}/\text{plate}$  and lower, the test material was "completely dissolved." Although revertant colonies of E. coli WP<sub>2</sub> uvrA were lower than the concurrent control at the three highest doses with or without S9 activation, the counts were within the normal range of plating variability and, therefore, not considered to indicate a cytotoxic effect.

Similarly, no appreciable increase in reversion to tryptophan prototrophy occurred at any nonactivated or S9 activated dose of the test material. In contrast, increases in mutant colonies were seen following exposure to the positive controls ( 10  $\mu\text{L}$  MMS/-S9 and 10  $\mu\text{g}/\text{plate}$  2AA +S9).

3. Repeat Mutation Assay: The repeat assay was conducted as described with five test material concentrations (10.0, 100.0, 333.3, 1000.0, and 5000.0  $\mu\text{g}/\text{plate}$  in the presence or absence of S9 activation. Results of the second assay compared favorably with the initial finding indicating that acarosan-moist powder was neither cytotoxic nor mutagenic in E. coli WP<sub>2</sub> uvrA.

Representative results from both assays are presented in Table 1.

TABLE 1. Representative Results of the Escherichia coli Mutagenicity Assays with Acaroson-Moist Powder

Substance	S9 Acti- vation	Dose/ plate	Revertants per plate of <u>E. coli WP<sub>2</sub> uvrA<sup>a</sup></u>	
			Initial Assay	Repeat Assay
<u>Negative Control</u>				
Bacteria	-	--	33 ± 3.5	30 ± 0.6
	+	--	35 ± 1.0	35 ± 3.0
<u>Solvent Control</u>				
Dimethyl sulfoxide	-	--	32 ± 3.2	34 ± 2.6
	+	--	35 ± 4.5	34 ± 2.1
<u>Positive Control</u>				
Methylmethane-sulfonate	-	10 µL	520 ± 63.6	1425 ± 115.0
2-Aminoanthracene	+	10 µg	377 ± 62.2	447 ± 42.3
<u>Test Material</u>				
Acarosan-Moist powder	-	5000 µg <sup>b</sup>	22 ± 6.0	34 ± 4.0
	+	5000 µg	23 ± 4.5	28 ± 10.6

<sup>a</sup>Means and standard deviations of the counts of triplicate plates.

<sup>b</sup>Highest assayed dose and compound precipitation was observed at this level; results for lower doses (1, 3, 10, 33, 100, 333, and 1000 µg/plate +/-S9 in the initial assay and 10.0, 100.0, 333.3, and 1000.0 µg/plate +/-S9 in the repeat assay) were comparable to the solvent control values.

The author concluded that "acarosan-moist powder was not mutagenic in the Escherichia coli reverse mutation assay."

4. Reviewers' Discussion/Conclusions: We assess that the study was properly conducted and that the author's interpretation of the data was correct. Acarosan-moist powder was neither cytotoxic nor mutagenic when assayed up to the limit of solubility. The results further show that the sensitivity of the test system to detect a mutagenic effect was adequately demonstrated in both trials as indicated by the response of E. coli WP<sub>2</sub> uvrA to the direct-acting and promutagenic positive controls. It was concluded, therefore, that the study provides acceptable evidence that acarosan-moist powder is not mutagenic in this test system.
  
5. Quality Assurance : A quality assurance statement was signed and dated November 26, 1987.
  
6. CBI Appendix: Appendix A, Materials and Methods, CBI pp. 9-15.



APPENDIX A  
Materials and Methods

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Pages 9 through 15 are not included.

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The material not included contains the following type of information:

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  - Identity of product impurities.
  - Description of the product manufacturing process.
  - Description of quality control procedures.
  - Identity of the source of product ingredients.
  - Sales or other commercial/financial information.
  - A draft product label.
  - The product confidential statement of formula.
  - Information about a pending registration action.
  - FIFRA registration data.
  - The document is a duplicate of page(s) \_\_\_\_\_.
  - The document is not responsive to the request.
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