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DATA EVALUATION RECORD

ACAROSAN - MOIST POWDER

Mutagenicity--Salmonella typhimurium/Mammalian Microsome  
Mutagenicity Assay

APPROVED BY:

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Signature: Robert J. Weir

Date: 4-28-89

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Date: 6/5/89

DATA EVALUATION RECORD

CHEMICAL: Acarosan.

STUDY TYPE: Salmonella/mammalian activation mutagenicity assay.

ACCESSION NUMBER: 408453-11.

TEST MATERIAL: Acarosan-Moist Powder.

SYNONYMS/CAS NO. Not listed.

SPONSOR: Gesellschaft fur Hausbiologische Forschung, Mainz, FRG.

TESTING FACILITY: Cytotest Cell Research GmbH and Co., Darmstadt, FRG.

✓ TITLE OF REPORT: Salmonella typhimurium reverse mutation assay with Acarosan-Moist Powder.

AUTHOR(S): Timm, A.

STUDY NUMBER(S): 111508.

REPORT ISSUED: September 30, 1987.

CONCLUSION(S) - Executive Summary: Under the conditions of two independent Salmonella typhimurium/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 mutagenic effect in S. typhimurium strains TA1535, TA1537, TA1538, TA98, and TA100 either in the presence or absence of S9 activation. Compound precipitation was noted at the highest assayed dose (5000 µg/plate) and a weak but reproducible cytotoxic effect was seen in strain TA100 at this level without S9 activation. It was concluded, therefore, that acarosan-moist powder was assayed up to an appropriate concentration with no evidence of mutagenicity.

Study: Acceptable.

A. MATERIALS:

1. Test Material: Name: Acaroson-Moist Powder  
Description: White solid  
Lot #: Prod. Mai 1987; purity: Listed as a mixture  
Contaminants: None reported  
Solvent used: Dimethylsulfoxide (DMSO)  
Other comments: The test material was not completely soluble at a concentration of 50 mg/mL in DMSO.
  
2. Control Materials:  
Negative: Bacteria  
Solvent/final concentration: 100 µL/plate  
Positive: Nonactivation:  
Sodium azide 10 µg/plate TA100, TA1535  
4-Nitro-o-phenylene-diamine (4-NPA)  
50 µg/plate TA98, TA1538, TA1537  
  
Activation:  
2-Aminoanthracene (2-AA) 10 µg/plate all strains.
  
3. Activation: S9 derived from  

<u>  x  </u>	Aroclor 1254	<u>  x  </u>	induced	<u>  x  </u>	rat	<u>  x  </u>	liver
<u>      </u>	phenobarbital	<u>      </u>	noninduced	<u>      </u>	mouse	<u>      </u>	lung
<u>      </u>	none	<u>      </u>		<u>      </u>	hamster	<u>      </u>	other
<u>      </u>	other	<u>      </u>		<u>      </u>	other	<u>      </u>	

If other, describe below. Describe S9 composition (if purchased, give details).

4. Test Organism Used: S. typhimurium strains  

<u>      </u>	TA97	<u>  x  </u>	TA98	<u>  x  </u>	TA100	<u>      </u>	TA102	<u>      </u>	TA104
<u>  x  </u>	TA1535	<u>  x  </u>	TA1537	<u>  x  </u>	TA1538;	list any others:			

Test organisms were properly maintained: Yes  
Checked for appropriate genetic markers (rfa mutation, R factor): Yes

5. Test Compound Concentrations Used:

Preliminary Assay: 1, 3, 10, 33, 100, 333, 1000, and 5000 µg/plate with or without S9 activation with strains TA98 and TA100.

Mutation Assays: 10.0, 100.0, 333.3, 1000.0, and 5000.0 µg/plate with or without S9 activation in all strains.



TABLE 1. Representative Results of the Initial *Salmonella typhimurium* Mutagenicity Assay with Acarosan-Moist Powder

Substance	S9 Acti- vation ( $\mu\text{g}/\text{plate}$ )	Dose ( $\mu\text{g}/\text{plate}$ )	Revertants per Plate of Bacterial Tester Strain <sup>a</sup>				
			TA1535	TA1537	TA1538	TA98	TA100
<b>Negative Control</b>							
Bacteria	-	--	15 $\pm$ 0.6	10 $\pm$ 2.5	14 $\pm$ 0.0	28 $\pm$ 6.6	143 $\pm$ 11.1
	+	--	11 $\pm$ 3.5	7 $\pm$ 2.6	23 $\pm$ 2.1	46 $\pm$ 6.7	144 $\pm$ 8.2
<b>Solvent Control</b>							
Dimethyl- sulfoxide	-	--	13 $\pm$ 3.8	14 $\pm$ 5.0	18 $\pm$ 2.0	23 $\pm$ 7.0	133 $\pm$ 21.4
	+	--	13 $\pm$ 5.5	7 $\pm$ 2.0	21 $\pm$ 3.1	37 $\pm$ 6.0	138 $\pm$ 1.7
<b>Positive Control</b>							
Sodium azide	-	10	883 $\pm$ 47.4	--	--	--	797 $\pm$ 20.2
4-Nitro-o- phenylene-diamine	-	50	--	395 $\pm$ 35.2	1689 $\pm$ 125.7	2036 $\pm$ 209.0	--
2-Aminoanthracene	+	10	151 $\pm$ 29.7	252 $\pm$ 19.1	1390 $\pm$ 68.9	1237 $\pm$ 92.1	2265 $\pm$ 212.0
<b>Test Material</b>							
Acarosan- moist powder	-	5000 <sup>b</sup>	9 $\pm$ 3.1	11 $\pm$ 5.0	8 $\pm$ 1.2	13 $\pm$ 4.9	73 $\pm$ 12.7
	+	5000	13 $\pm$ 4.0	9 $\pm$ 3.1	24 $\pm$ 4.6	46 $\pm$ 9.6	120 $\pm$ 16.4

<sup>a</sup>Means  $\pm$  standard deviations of the counts of triplicate plates.

<sup>b</sup>Highest assayed dose with or without S9 activation; results for lower doses (10.0, 100.0, 333.3, and 1000.0  $\mu\text{g}/\text{plate}$  +/- S9 with all strains and additional doses of 1 and 3  $\mu\text{g}/\text{plate}$  +/- S9 with TA98 and TA100) did not indicate a mutagenic effect.

Representative results from the second assay are shown in Table 2. An  $\approx \leq 30\%$  reduction in TA100 His<sup>+</sup> revertant colonies was seen after exposure to 1000 and 5000  $\mu\text{g}/\text{plate}$  -S9. No cytotoxicity was observed for the other tester strains with or without S9 activation. The findings further indicated, in agreement with the results of the initial trial, that acarosan-moist powder was not mutagenic in this test system. All strains responded to the mutagenic action of the appropriate nonactivated and S9-activated positive controls.

The study author concluded that "acarosan-moist powder is considered to be nonmutagenic in this Salmonella typhimurium 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, assayed to the limit of solubility, induced a reproducible weak cytotoxic effect in TA100 under nonactivated conditions at the highest assayed dose (5000  $\mu\text{g}/\text{plate}$ ) but was not mutagenic in two independent assays either with or without S9 activation.

The sensitivity of the test system to detect direct-acting mutagens and promutagens was clearly demonstrated for all strains under nonactivated and S9-activated conditions. 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 September 30, 1987.
6. CBI APPENDIX: Appendix A, Materials and Methods, CBI pp. 9-15.

TABLE 2. Representative Results of the Second Salmonella typhimurium Mutagenicity Assay with Acarosan-Moist Powder

Substance	S9 Acti- vation	Dose ( $\mu\text{g}/\text{plate}$ )	Revertants per Plate of Bacterial Tester Strain <sup>a</sup>				
			TA1535	TA1537	TA1538	TA98	TA100
<u>Negative Control</u>							
Bacteria	-	--	25 $\pm$ 6.4	13 $\pm$ 2.6	14 $\pm$ 3.1	26 $\pm$ 3.5	101 $\pm$ 10.8
	+	--	13 $\pm$ 3.0	16 $\pm$ 3.1	30 $\pm$ 3.2	37 $\pm$ 1.2	115 $\pm$ 10.1
<u>Solvent Control</u>							
Dimethyl- sulfoxide	-	--	25 $\pm$ 1.2	11 $\pm$ 1.5	14 $\pm$ 9.0	31 $\pm$ 3.5	102 $\pm$ 7.9
	+	--	11 $\pm$ 2.5	19 $\pm$ 5.0	22 $\pm$ 4.0	24 $\pm$ 9.5	105 $\pm$ 8.1
<u>Positive Control</u>							
Sodium azide	-	10	1203 $\pm$ 32.0	---	---	---	1243 $\pm$ 42.9
4-Nitro-o- phenylene-diamine	-	50	---	239 $\pm$ 28.8	1721 $\pm$ 195.4	2295 $\pm$ 162.8	---
2-Aminoanthracene	+	10	328 $\pm$ 22.8	325 $\pm$ 25.5	1314 $\pm$ 359.2	1381 $\pm$ 73.3	2215 $\pm$ 291.6
<u>Test Material</u>							
Acarosan- Moist Powder	-	5000 <sup>b</sup>	21 $\pm$ 3.8	11 $\pm$ 2.1	14 $\pm$ 5.3	24 $\pm$ 6.7	44 <sup>c</sup> $\pm$ 6.7
	+	5000	16 $\pm$ 1.5	16 $\pm$ 8.5	30 $\pm$ 8.0	22 $\pm$ 2.1	93 $\pm$ 6.1

<sup>a</sup>Means  $\pm$  standard deviations of the counts of triplicate plates.

<sup>b</sup>Highest assayed dose with or without S9 activation; results for lower doses (10.0, 100.0, 333.3, and 1000.0  $\mu\text{g}/\text{plate}$  +/-S9) did not indicate a mutagenic effect.

<sup>c</sup>Revertant counts of TA100 were also reduced following exposure to 1000  $\mu\text{g}/\text{plate}$ /-S9 (75  $\pm$  10.4 revertants/plate).

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:

- Identity of product inert ingredients.
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  - The product confidential statement of formula.
  - Information about a pending registration action.
  - FIFRA registration data.
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