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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:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: Robert J. Weir

Date: 4/28/89

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Mammalian Microsome Mutagenicity Assay

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 Hausbiologishe 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_2 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:

x Aroclor 1254	x induced	x rat	x liver
___ phenobarbital	___ noninduced	___ mouse	___ lung
___ none		___ hamster	___ other
___ other		___ other	

4. Test Organism Used: E. coli WP_2 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 µg/plate with or without S9 activation.

Repeat mutation assay: 10.0, 100.0, 333.3, 1000.0, and 5000.0 µg/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_2 uvrA. Eight concentrations of the test material ranging from 1 to 5000 µg/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 µg/plate of the test material; the report stated that at 1000 µg/plate and lower, the test material was "completely dissolved." Although revertant colonies of E. coli WP_2 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 µL MMS/-S9 and 10 µg/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 µg/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_2 uvrA.

Representative results from both assays are presented in Table 1.

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

Substance	S9 Activation	Dose/plate	Revertants per plate of E. coli WP_2 uvrA[a] Initial Assay	Repeat Assay
Negative Control				
Bacteria	-	--	33 ± 3.5	30 ± 0.6
	+	--	35 ± 1.0	35 ± 3.0
Solvent Control				
Dimethyl sulfoxide	-	--	32 ± 3.2	34 ± 2.6
	+	--	35 ± 4.5	34 ± 2.1
Positive Control				
Methylmethane-sulfonate	-	10 µL	520 ± 63.6	1425 ± 115.0
2-Aminoanthracene	+	10 µg	377 ± 62.2	447 ± 42.3
Test Material				
Acarosan-Moist powder	-	5000 µg[b]	22 ± 6.0	34 ± 4.0
	+	5000 µg	23 ± 4.5	28 ± 10.6

[a]Means and standard deviations of the counts of triplicate plates.

[b]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_2 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

Page_____ is not included in this copy.

Pages 9 through 15 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

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____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

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✓ FIFRA registration data.

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