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SUMMARY TABLE 1a - GUTHION - Acute Oral Toxicity.

Species	Sex	No. of Animals	Type of Material	Application Method	LD_{50} mg/kg (Technical)	LD_{50} mg/kg (Formulation)	Report Number
Rats	F	40	50% WP	Suspended in water.	12.5	25	24933
Rats	F	16	2% Dust	20% ethanol and 80% propylene glycol	-	>50	27457
Rats	M	24	1 lb/gal EC Form. 70-17-32 Batch 70-17-86A	Diluted in water.	-	96.7	27449
Rats	F	8	1 lb/gal EC Form. 70-17-32 Batch 70-17-86A	Diluted in water.	-	50	27498
Rats	M	32	1 lb/gal EC Form. 70-17-32 Batch 70-17-86B	Diluted in water.	-	100.8	27449
Rats	F	8	1 lb/gal EC Form. 70-17-32 Batch 70-17-86B	Diluted in water.	-	58	27498
Rats	F	48	2 lb/gal SC	Diluted in water.	-	40-45	24198
Rats	M	-	Technical	Suspended in peanut oil.	13	-	25529
Rats	F	-	Technical	Suspended in peanut oil.	11	-	25529
Rats	F	29	62.5% WP	Suspended in water.	-	14.8	28476
Rats	M	24	62.5% WP	Suspended in water.	-	23.6	28476

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SUMMARY TABLE 3a - GUTHION - Acute Dermal Toxicity

Species	Sex	No. of Animals	Type of Material	Application Method	Dose mg/kg	LD_{50} mg/kg (AI)	LD_{50} mg/kg (Form.)	Observations	Report Number
Rats	F	8	2% Dust	Taped to back for 24 hours.	2000	-	-	Two animals died.	27457
Rats	M	24	1 lb/gal EC Form. 70-17-32 Batch 70-17-86A	Undiluted.	-	-	816.1	-	27449
Rats	M	24	1 lb/gal EC Form. 70-17-32 Batch 70-17-86B	Undiluted.	-	-	345.3	-	27449
Rats	F	16	2 lb/gal SC	Undiluted.	-	-	~350-375	-	24198
Rats	F	-	Technical	Diluted in xylene.	-	220	-	-	25529
Rats	M	-	Technical	Diluted in xylene.	-	220	-	-	25529
Rabbits	-	2	62.5% WP ?	Taped to the clipped backs of the animals for 24 hours.	1000	-	-	No deaths or symptoms.	28476

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SUMMARY TABLE 4 - GUTHION - Acute Inhalation Toxicity (Continued)

Species	Sex	No. of Animals	Type of Material	Exposure Time (Minutes)	Chamber Concentration Microgram/l	Observations	Report Number
Mice	F	4	2% Dust	60	2,000	No symptoms or mortality.	[illegible]
Mice	F	4	2% Dust	60	20,000	No symptoms or mortality.	27316
Rats	M	6	2 lb/gal SC Form. 11013 Batch 9050085	60	2,000	5/6	27345
Mice	M	10	2 lb/gal SC Form. 11013 Batch 9050085	60	2,000	2/10	27347
Rats	M	6	2 lb/gal LC Form. 11013 Batch 9050090	60	2,000	4/6	27346
Mice	M	10	2 lb/gal LC Form. 11013 Batch 9050090	60	2,000	10/10	27348

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SUMMARY TABLE 4a - GUTHION - Acute Inhalation Toxicity

Species	Sex	No. of Animals	Type Material	Exposure Time (Minutes)	Chamber Concentration Microgram/l	Observations	Report Number
Rats	F	6	Technical	60/day/5 days	10	No cholinesterase depression.	26254
Rats	F	6	Technical	60/day/10 days	10	No cholinesterase depression.	26254
Rats	F	6	Technical	60/dau/5 days	25	No cholinesterase depression	26254
Rats	F	6	Technical	60/day/10 days	25	No cholinesterase depression.	26254
Rats	F	6	Technical	60/day/5 days	50	No cholinesterase depression.	26254
Rats	F	6	Technical	60/day/10 days	50	Cholinesterase depression.	26254
Rats	F	4	62.5% WP	60	2,000	No toxic symptoms.	28735
Rats	M	4	62.5% WP	60	2,000	No toxic symptoms.	28735
Rats	F	4	62.5% WP	60	5,000	Three animals died.	28735
Rats	M	4	62.5% WP	60	5,000	No toxic symptoms.	28735
Rats	M	36	1 lb/gal EC Form. 70-17-32 Batch 70-17-86A	60	2,000 2,500 3,000	0/6 No. dead/ No. tested. 1/6 No. dead/ No. tested. 4/6 No. dead/ No. tested.	27449 27449 27449
Rats	F	36	1 lb/gal EC Form. 70-17-32 Batch 70-17-86A	60	2,000 2,500	1/6 No. dead/ No. tested. 3/6 No. dead/ No. tested.	27498 27498
Rats	M	12	1 lb/gal EC Form. 70-17-32 Batch 70-17-86B	60	2,000 2,500 3,000	0/6 No. dead/ No. tested. 1/6 No. dead/ No. tested. 3/6 No. dead/ No. tested.	27449 27449 27449
Rats	F	12	1 lb/gal EC Form 70-17-32 Batch 70-17-86B	60	2,000 2,600	1/6 No. dead/ No. tested. 2/6 No. dead/ No. tested.	27498 27498

SUMMARY TABLE 4a - GUTHION - Acute Inhalation Toxicity (Continued)

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Species	Sex	No. of Animals	Type of Material	Exposure Time (Minutes)	Chamber Concentration Microgram/l	Observations	Report Number
Rats	F	4	2% Dust	60	2,000	No symptoms or mortality.	27316
Rats	F	4	2% Dust	60	20,000	No symptoms or mortality.	27316

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From IF 1166

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SUPPLEMENT TO

SYNOPSIS OF

GUTHION

TOXICOLOGY DATA

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A. Acute Oral Toxicity

9. A study was conducted on the acute oral toxicity of GUTHION 50% W.P. to adult female rats. From the mortality the LD_{50} was estimated to be ~25 mg GUTHION 50% W.P./kg. This is equivalent to 12.5 mg GUTHION/kg (Report No. 24933).

10. A GUTHION 2% Dust formulation was administered to female rats at 50 and 500 mg formulation/kg. There were no deaths at 50 mg/kg while 500 mg formulation resulted in the death of seven out of eight animals dosed (Report No. 27457).

11. Two formulations of GUTHION 1 lb/gal E.C. were diluted with water and administered to adult male rats. One formulation was prepared with emulsifier and one was prepared without emulsifier. The LD_{50} was 96.7 and 100.8 mg formulation/kg, respectively (Report No. 27449). The same formulations of GUTHION 1 lb/gal EC were diluted with water and administered to adult female rats. The LD_{50} of these formulations was approximately 50 and 58 mg/kg, respectively (Report No. 27498).

12. The oral LD_{50} of a 2 lb/gal S.C. formulation is 40-45 mg formulation/kg to adult female rats (Report No. 24198).

13. The oral LD_{50} of the technical grade compound administered in peanut oil to male and female rats was 13 and 11 mg/kg, respectively (Report No. 25529).

14. A formulation of GUTHION 22% Emulsifiable Concentrate was orally tested on domestic animals. The following maximal nontoxic oral doses were found (Report No. 25425).

Newborn Calves	0.5 mg/kg
Yearling Cattle	2.5 mg/kg
Sheep	5.0 mg/kg
Goats	2.5 mg/kg

15. GUTHION technical was administered to 14 head of mixed bred heifers at a dose of 3.6 mg/kg for 6 days via gelatin capsule. This treatment resulted in the death of five animals (Report No. 23065).

16. A formulation of GUTHION 62.5% W.P. suspended in water had an oral LD_{50} of 14.8 and 23.6 mg formulation/kg to female and male rats, respectively (Report No. 28476).

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Synopsis (Continued)

C. Acute Dermal Toxicity

6. The dermal toxicity of a GUTHION 2% Dust formulation was studied by taping 2000 mg formulation/kg to the clipped backs of adult female rats for 24 hours. This treatment resulted in the death of two of the eight animals dosed (Report No. 27457).

7. Two formulations of GUTHION 1 lb/gal E.C., one with emulsifier and one without emulsifier, was applied to adult male rats. The LD_{50} was 816.1 and 845.3 mg formulations/kg, respectively (Report No. 27449).

8. The dermal LD_{50} of a GUTHION 2 lb/gal S.C. was found to be ∿350-375 mg/kg to adult female rats (Report No. 24198).

9. When the technical grade compound was placed in xylene the dermal LD_{50} to male and female rats was 220 mg/kg (Report No. 25529).

10. A GUTHION 62.5% W.P. was taped to the clipped backs of rabbits for 24 hours. This treatment did not result in symptoms or death of the animals so treated (Report No. 28476).

D. Acute Inhalation Toxicity

6. The acute inhalation toxicity of two GUTHION 1 lb/gal E.C., one with emulsifier and one without emulsifier, was studied on adult male rats. The exposure time was 60 minutes. The LC_{50} was ∿3000 mgm for both formulations (Report No. 27449). The result of inhalation toxicity tests on females at the same airborne concentrations for males show the females to be more susceptible to both formulations (Report No. 27498).

7. Female rats and mice were exposed to concentrations of 2000 and 20,000 mg GUTHION 2% Dust for 60 minutes. There were no symptoms or mortality from the exposure (Report No. 27316).

8. A formulation of GUTHION 2 lb/gal S.C. (Formula 11013 and Batch No. 9050085) and a GUTHION 2 lb/gal L.C. (Formula 11013 and Batch No. 9050090) were both studied at concentrations of 2000 mgm to male mice and rats for 60 minute exposures. Both formulations resulted in the death of more than 50% of the animals (Report No. 27346).

9. Groups of adult female rats were exposed to chamber concentrations of 10, 25, or 50 mgm GUTHION/1 for 60 minutes a day for 5 or 10 days. Only the group exposed at 50 mgm/1 for 10 days demonstrated cholinesterase depression (Report No. 26254).

10. A study was conducted where groups of male and female rats were exposed to 2000 or 5000 mgm/1 of GUTHION 62.5% W.P. for 60 minutes. There were no symptoms or deaths following exposure to concentrations of 2000 mgm/1. Three out of four female rats exposed to concentrations of 5000 mgm/1 died. The remainder of the animals exposed to this concentration remained asymptomatic throughout the study (Report No. 28735).

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J. Antidotes

1. Atropine is an effective antidote for GUTHION intoxication (Reports Nos. 987, 29454, and 27089). When 50 mg 2-PAM was administered prior to GUTHION, the 2-PAM provided complete protection from one LD_{50} of GUTHION and the protection was slightly enhanced by atropine (Report No. 5724). In another study 2-PAM increased the antidotal effects of atropine (Report No. 27759).

K. Potentiation Studies

1. In one study potentiation of toxicity occurred when GUTHION was administered simultaneously with Ethion (Report No. 10320). In a second study GUTHION and Ethion did not potentiate the toxicity of each other (Report No. 27985).

   In a series of studies, potentiation of toxicity did not occur when GUTHION was given simultaneously with a series of anticholinesterase compounds (Reports Nos. 7880, 12299, 12300, 15983, 15990, and 24673).

L. General Pharmacology

1. A study was conducted where the acute toxicity of a number of organic-phosphorus compounds was measured in normal rats and mice. The same group of compounds were studied in rats and mice which had undergone induction of hepatic microsomal enzymes by dosing with phenobarbital. The toxicity of GUTHION was nearly the same in both groups of mice. The intraperitoneal LD_{50} of GUTHION was 8.7 mg/kg in the control rats and 11.4 mg/kg in the rats that underwent enzyme induction (Report No. 24413).

2. Technical grade GUTHION is a poor inhibitor of mammalian, avian or fish brain cholinesterase. The oxygen analogue is a potent inhibitor. It is interesting to note that avian brain cholinesterase is more refractile than mammalian brain cholinesterase to depression by the oxygen analogue (Report No. 23311). The acute oral LD_{50} of GUTHION to chickens varies from 100 to 275 mg/kg (Reports Nos. 16263 and 19324).

3. A copy of Report No. 29454 is included to complete the file on the toxicology of GUTHION. This is the published work of Dr. K. P. DuBois.. The results of the studies reported in this paper are included in various other reports by Dr. DuBois (Report No. 29454).

M. Human Toxicity

1. Human oral cholinesterase "no effect" dose studies are in progress. In these studies five individuals are used as test subjects while two serve as controls. Plasma and erythrocyte cholinesterase is measured twice weekly and during an approximately four-week treatment period. The following doses were orally administered to human volunteers: 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 6, 8, 9, 10, and 12 mg/day. There was no cholinesterase depression found at any of the dose levels studied (Reports Nos. 23886 and 25553).

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