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

JAN 4 1985

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Poast®, Reg. No. 7969-58. Toxicological Evaluation of Hydroxymetabolites. EPA Accession No. 251045.

Tox Chem. 72A

FROM: Minnie R. Sochard, Ph.D.
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769C)

Minnie Sochard 11/21/84

TO: Robert Taylor, Product Manager #25
Registration Division (TS-767C)

Rung by necessary

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769C)

Budd 11/21/85

Registrant: BASF Wyandotte Corporation
Parsippany, NJ

Action Requested:

As a condition for the registration of Poast® herbicide (BAS 9052H, Sethoxydim, NP-55) BASF Wyandotte has agreed to perform and submit to TB additional toxicology tests using the hydroxymetabolites of Poast as test chemicals. This submission contains interim reports on subchronic feeding in rats, teratogenicity in rats and mutagenicity in mammalian cell cultures, using the hydroxymetabolite 5-OH-MSO2. In addition, detailed metabolic studies are presented which BASF claims supports the choice of the single hydroxymetabolite, 5-OH-MSO2 as a surrogate to represent all of the metabolites of Poast® for toxicological evaluation.

1. Based on its review of the BASF submission, TB agrees with the registrant in the selection of the hydroxymetabolite 5-OH-MSO2 (also referred to as MU-1) as representative of all of the hydroxymetabolites of the herbicide Poast. (A discussion of this is contained in the Detailed Review of Studies, below.)

2. Summaries of physical and chemical properties of 5-OH-MSO2 and other hydroxymetabolites, provided by the registrant are attached.

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3. Also attached are summaries of selected toxicology data for the parent compound as well as the hydroxymetabolites.

4. Also attached is a discussion of the hydroxymetabolite problem from the March 9, 1983 memorandum by Sochard and Budd (pages 3-5).

5. The interim reports on teratogenicity in rats, and mutagenicity in mammalian cell cultures employing 5-OH-MSO2 as test chemical consist primarily of protocols. The interim report on metabolism in rats using 5-OH-MSO2 contains food consumption and body weight data for the first 13 weeks of the study in addition to the protocol.

Attachments:

OPP:HED:TOX:M.SOCHARD:sb 10/2/84 X72320 #5-D10

3.
2-54

DETAILED REVIEW OF STUDIES

1. Teratogenicity study of MU-1 (5-OH-MSO2) in rats. Appendix A in Accession No. 251045. One page. Study initiated May 9, 1983, Final Report due November, 1983.

   Protocol:

   Four groups of female rats, in groups of 24 per group were dosed with respectively, 0, 40, 100 and 250 mg/kg/day test article. No more details are given in this submission.

2. Mutagenicity Study of MU-1 (5-OH-MSO2) Except Ames Test and Rec-Assay Test. Appendix A in Accession No. 251045, one page. No date, Lab. Number or other information given.

   A. UDS Test - unscheduled end point DNA damage and repair with rat hepatocytes.

   B. Chinese hamster ovary test with end point gene mutation.

   C. Chinese hamster end point chromosomal aberration.

   No further details are given.

3. Subchronic Feeding Study of MU-1 (5-OH-MSO2) in Rats. Appendix A in Accession No. 251045. Study initiated April 5, 1983, Final report due November 1983. One page and 4 tables given. Data is from the first 1.5 months of the study.

   No further details are given.

   Protocol:

   Four groups of male and female F344 rats, 15 animals per sex per group were respectively administered 0, 120, 360, and 1080 ppm test chemical in the diet.

   Results:

   No significant differences were seen within groups of females or males at the end of 4 weeks for net weight gains, although males of the 120 ppm group had slightly greater weight gains compared with males of other dose groups.

No significant differences in food consumption were seen within groups of males or females at the end of 4 weeks. Males appeared to be consuming proportionately less food than females. Preliminary results are tabulated below.

TABLE I

% Weight Gain for Rats at 13 Weeks in Grams

Dose Group	Males	Females
0	85	48
120	89	46
360	87	48
1080	84	47

TABLE II

Mean Food Consumption Changes in Grams

Dose Group	Males	Females
0	+ 0.8	+ 1.6
120	+ 0.4	+ 0.8
360	+ 0.6	+ 1.6
1080	- 0.3	+ 0.4

4. Additional Metabolism and Refined Analytical Chemistry Studies with Parent (NP-55) and Hydroxylated Metabolites of Poast.

A general discussion of new results and conclusions regarding metabolism and chemistry of the parent compound and its metabolites, as well as conclusions regarding their toxicological significance is presented on pages 1-16 of this submission, dated July 20, 1983, BASF Wyandotte Corp., Agricultural Chemicals Group, 100 Cherry Hill Road, Parsippany, NJ 07054. Page 17 of this submission contains the references for the discussion. The references cited are presented in their entirety under the Tab titled "References Cited". These references contain studies for which reviews are presented below.

Soybean products form a significant part of human diet, particularly as milk substitutes for milk-intolerant infants. Since significant amounts of hydroxymetabolites were reported in Poast-treated soybeans, it is essential to understand the metabolism of Poast in soybeans, and to determine exactly how much and what species of hydroxymetabolites as well as parent are metabolized in humans as extrapolated from rat feeding studies.

(For this submission, which also contains several studies dealing with analytical chemistry, only metabolism is reviewed.)

A. Metabolism in Soybeans:

1. Investigation Relating to the Ouestion Whether 6-OH-M2SO2 (MU) is a Metabolite of BAS 9052H in Soybean Seed. Citation Number 8, Page 17 of Accession No. 251044. BASF Lab. Communication No. 1027. Dated March 1983, R. Huber, 9 pages, 3 attachments.

2. Confirmation of the Existence of 6-OH-M2SO2 in Soybeans. Citation Number 7, page 17 of Accession No. 251044. Fine Chemicals Research Laboratory, Nippon Soda Co., Ltd., dated May, 1983. Report No. RD 8341, 5 pages, 1 attachment.

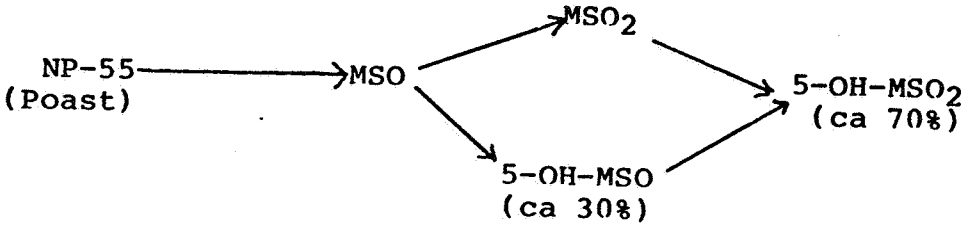
Soybeans treated with Poast in the field under standard conditions were re-analyzed in two different laboratories. Similar procedures were followed by BASF Laboratories and Nippon Soda Co.

The results of the analysis by both laboratories were in agreement and pointed to analytical errors in previous laboratory studies. Previous studies had indicated that 12% of total radioactive residue was 6-OH-M2SO2 (MU). Re-analysis indicated the actual values to be usually not more than 1.0% of total radioactivity recovered. Only one sample was found (BASF Labs) to be 4%. The discrepancy in values between the original and re-analysis results was traced to a protein precipitation step, which favored the artifactual production of 6-OH-M2SO2 from 5-OH-MSO2.

More evidence indicated that the hydroxymetabolite 5-OH-MSO2 (MU-1) is always the predominant hydroxylated residue in soybean seeds (= 35% of total residue) and represents 70-80% of total radioactive recovered material. The hydroxymetabolite 5-OH-MSO (= MU-2) accounts for 20-30% of radioactive recovered material.

The hydroxymetabolites 5-OH-MSO2 (MU-1) and 5-OH-MSO (MU-2) are chemically and biochemically similar (the petitioner indicates this, and presents compelling chemical and metabolism evidence here). As the latter is an intermediate of the former, the selection of 5-OH-MSO2 is logically the representative chemical species on which to base the toxicological evaluation of the hydroxymetabolites of Poast.

Based on the evidence presented above, a new metabolic scheme is presented for the metabolism of Poast in soybeans as follows:



Metabolism in plants is not generally reviewed in Toxicology Branch. However, in view of the necessity for these studies discussed above, they ~~may be~~ are considered. ~~supplementary.~~

~~Core Category: Supplementary.~~

3-1
2-3

B. Metabolism in Rats:

1. Analysis of OH Type Metabolites of NP-55 in Rat Urine. (Obtained from Oiso Laboratory) Citation No. 11 in Accession No. 251045, Dated March 1, 1983. Fine Chemical Research Laboratory. Nippon Soda Co., Ltd. BASF Report No. RD 8324, 4 pages, 2 Tables, 6 attachments.

Protocol:

Three rats (strain, sex, age, weight unspecified) were administered NP-55 (Poast) in the diet at a dose level of 18 mg/kg/day. Urine samples were collected and pooled at 1, 3 and 7 days following initiation of feeding. Pooled samples from days 1, 3 and 7 were chemically extracted and analyzed for the presence of 5-OH-MSO_2, 5-OH-MSO and 6-OH-M_2SO_2 using HPLC. Ouantitation was based on comparison with standards. The formation rate of the hydroxymetabolites were also calculated by comparing metabolites detected against administered parent.

Results:

The findings are summarized in the table below, abstracted in part from the submitted data in RD 8324 and is given below as Table I:

TABLE I

Formation Rate (%) Metabolites in Total/Administered urine in milligrams/amount of NP-55	SAMPLE DAYS		
	1	3	7
5-OH-MSO2 (μg)	1.07	1.04	1.81
5-OH-MSO (μg)	Not Detected	0.07	0.21
6-OH-M2SO2	Not Detected	Not Detected	Not Detected

The data show that continuous feeding of rats at a dose of 18 mg/kg/day of NP-55 in the diet results in metabolic conversion of the chemical to 5-OH-MSO2 and 5-OH-MSO at a ratio of approximately ten-to-one, respectively. No 6-OH-M2SO2 was detected, indicating that under the conditions described above, this metabolite is not formed.

Core Category: Supplementary.

2. Analysis of NP-55 Metabolites in Urine, Obtained from Rats Administered MSO and MSO2. Citation No. 12 in Accession No. 251045. Dated April 29, 1983. Fine Chemicals Research Laboratory, Nippo Soda, Co., Ltd. Report No. RD 8337, 3 pages, 3 Tables, 13 Figures.

Protocol:

Four rats (age, weight, sex, strain unspecified) were orally administered (2 rats per group) MSO or MSO_2 at 18 mg/kg/day. Pooled urines from the paired rats were collected at 24, 48 and 72 hours after dosing. Metabolites were detected following chemical fractionation and analysis by HPLC, using prepared standards for each metabolite for comparison. Analysis for the metabolite 6-OH-M2SO2 was based on a 50 ng standard.

Results:

Refer to Tables I and II below abstracted from Table 2 in RD 8337.

Table I

Analysis of Urine Samples from Rats Administered MSO

	Time After Administration		
Metabolite	24 hours	48 hours	72 hours
MOS	44.1*	42.8	40.1
MSO2	1.7	1.7	2.0
5-OH-MOS	0.07	0.04	0.03
5-OH-MSO2	1.7	2.1	2.1
6-OH-M2SO2	Not detected	Not detected	Not detected

* Values in Percents of Administered Chemical

Table II

Analysis of Urine Samples from
Rats Administered MSO2

	Time After Administration		
Metabolite	24 hours	48 hours	72 hours
MOS	0*	0	0
MSO2	34.8	42.1	45.7
5-OH-MOS	0	0	0
5-OH-MSO2	8.6	10.5	11.6
6-OH-M2SO2	0.04	0.04	0.06

* Values in Percents of Administered Chemical

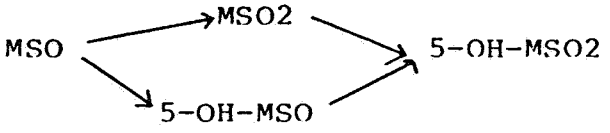
The results indicate that the metabolism of MSO proceeds via the two pathways:

1. MOS ⟶ MSO2 ⟶ 5-OH-MSO2

2. MSO2 ⟶ 5-OH-MSO2 ⟶ 6-OH-M2SO2

No 6-OH-M2SO2 is formed via pathway 1, but feeding ~~results~~ with MSO2 does result in very small amounts of the metabolite 6-OH-M2SO2 via pathway 2. In plants, evidence favors the hypothesis that 6-OH-M2SO2 is an artifact produced during chemical analysis. In rats, loading with the metabolite MSO2 may artifactually induce production of 6-OH-M2SO2. However, since this metabolite can be detected to the value of the 50 ng standard, and no 6-OH-M2SO2 was detected on loading with MSO, this reviewer is of the opinion that 6-OH-M2SO2 is indeed a bona fide metabolite of NP55 in rats, albeit a very minor one.

Therefore, the scheme presented in this submission by the registrant:



Should be amended, to indicate that production of the 6-hydroxymetabolite from 5-OH-MSO2 can occur if the animal is loaded with the precursor MSO2.

Core Category: Supplementary

3. Analysis of 5-OH-MSO2 Related Compound in Urine and Feces Obtained from Rats Administered 5-OH-MSO2. Citation No. 13 in Accession No. 251045. Dated May 1, 1983. Fine Chemicals Research Laboratory, Nippon Soda Co., Ltd., Report No. RD 8338, 3 pages, 2 Tables, 9 Figures.

Protocol:

For this subacute toxicity study, 5-OH-MSO2 was administered in doses of 0, 120, 360 and 1080 ppm in the diet to groups of 3 rats per sex per group. Adult males averaged 234.8 g and females 152.9 g. Samples of urine and feces from each group were collected and pooled for each group, with cage washings added to pooled urine samples. Samples were collected over 24 hour period. Analysis was by differential chemical fractionation and identification of metabolites was by HPLC.

Results:

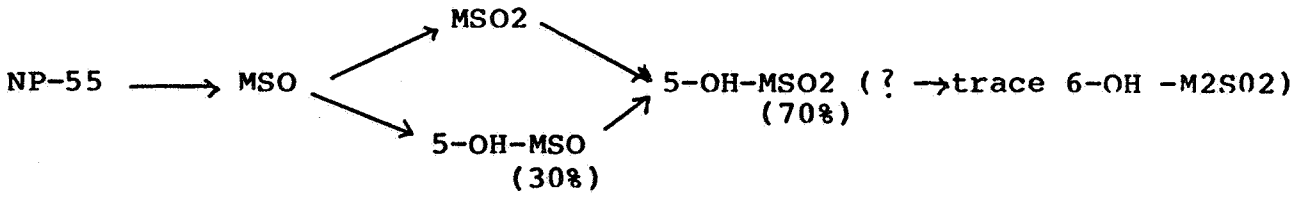
For all animals at 24 hours, recovery of total metabolite administered was about 100% for urine and fecal samples for combined 5-OH-MSO2 and 6-OH-M2SO2 for each dose group. The range of values was from 93.8% to 113.4% (1080 ppm females). For urine samples an average of 72.5% (all animals) was recovered as 5-OH-MSO2, with an average for 6-OH-M2SO2 at 2.0%. Fecal samples yielded an average of 25.8% as 5-OH-MSO2 and 0.09% as 6-OH-M2SO2

Core Category: Supplementary.

Conclusions Regarding Metabolism of Poast (NP-55)

The registrant and this reviewer are in agreement regarding conclusions based on the results of the metabolism studies in soybeans and in rats. The conclusions presented below are this reviewer's:

A. Soybeans: The following metabolic scheme represents metabolism in soybeans:



Reviewer's comments: The above scheme is for soybeans only. It may not represent all seed-bearing plants or monocots.

The hydroxymetabolite 6-OH-M2SO2 appears to be largely an artifact, formed during chemical analysis (Refer to BASF Lab. Commun. No. 1027). However, in report No. RD 8341, a value of 1% of total radioactivity (average) accounted for 6-OH-M2SO2, with only one sample at 4%. Thus the early review (Refer to memorandum of March 9, 1983, Sochard and Budd) which indicated 6-OH-M2SO2 at 12% was based on erroneous data presented by the registrant.

B. Rats

1. In rats administered NP-55 (parent) in the diet for 7 days at a dose of 18 mg/kg/day, hydroxymetabolites 5-OH-MSO2 and 5-OH-MSO wre excreted in a ratio of 10:1 with no detectable 6-OH-M2SO2.

The total NP-55 (parent) converted to hydroxymetabolites may now be computed at about 2% (see Table I, Review of RD 8324).

The PMPI computed in an earlier review for a rat metabolism study as 0.0864 (Refer to the memorandum of March 9, 1983 Sochard and Budd) may now be replaced with the presently recalculated value of a new PMPI of 0.22 for hydroxymetabolites. The new MPI was calculated as follows: Using the 2-year chronic feeding/oncogenicity study on rats, a NOEL is found at 360 ppm or 18 mg/kg/day. Using a safety factor of 100, the ADI is 0.18 mg/kg/day. For a 60 kg person, the MPI is 10.8 mg/day. Since evidence from

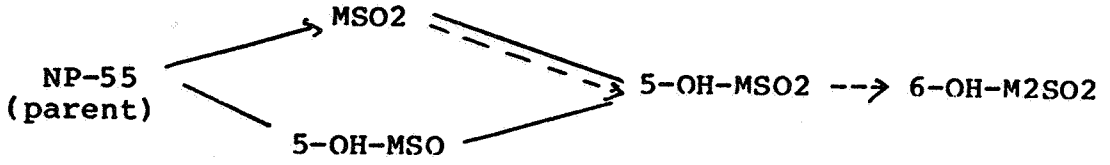
new rat studies indicates that 2% of parent compound is converted to hydroxymetabolites (refer to review of RD 8324), then 2% of the MPI of 10.8 mg/day provides a value of 0.216 mg/day, rounded to 0.22 mg/day for hydroxymetabolites MPI.

2. The metabolism of non-hydroxylated intermediates MOS and MSO2 administered to rats at 18 mg/kg/day yielded results which defined the metabolism of Poast (NP-55) as follows:

1. MSO (Dietary Administration) → MSO2 → 5-OH-MSO2
   MSO2 → 5-OH-MSO → 5-OH-MSO2

2. MSO2 (Dietary Administration) → 5-OH-MSO → 5-OH-MSO2 → 6-OH-M2SO2

Thus the reaction may be written:



When the system is loaded with MSO2, the production of 6-OH-M2SO2 is favored.

3. Results of a subacute feeding study in rats showed that at feeding levels of 120, 360 and 1080 ppm using the major metabolite 5-OH-MSO2, thissame metabolite was recovered from urine at 73% and from feces at 26% as averages for all dosage groups. The average for 6-OH-M2SO2 from urine was 2.0%; the average for fecal samples for 6-OH-M2SO2 was 0.09%.

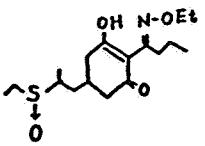
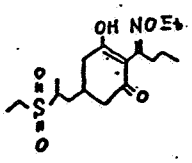
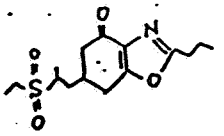
Thus, for rats, NP-55 is largely excreted in urine and feces without further modification. The remainder of the parent chemical is metabolized largely through MSO to 5-OH-MSO2. If the animals are loaded with (greater than the NOEL level) parent or the intermediate MSO2, then production of 6-OH-M2SO2 occurs of very low levels.

Physical and Chemical Properties of Non-Hydroxylated metabolites

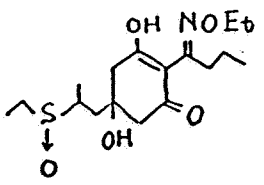
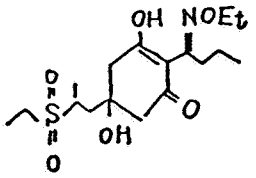
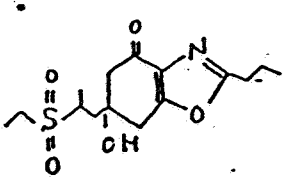
CITATION NUMBER 1

Physical and Chemical Properties of
NP-55 Related Compounds

Copied Directly from Submission, Accession No. 251045

	MSO	MSO_2	$M2SO_2$
Structural formula			
Molecular weight	343	359	313
Appearance	Colorless oil	White Crystals	White Crystals
Melting point	-	64-66° C	93.5 - 95.0°C
Refractive index	n_D^{24} = 1.5256	-	-
Solubility in water (27°C,pH5.5)	1.92 g/100 ml	0.22	1.12
Stability in buffer solutions (5 ppm) Half-life			
at pH 3, 25°C	45 hrs	36 hrs	
pH 3, 50°C	2 hrs	1.9 hrs	
pH 6, 50°C	6 days	7.3 days	
pH 9, 50°C	>45 days	>45 days	
pH14, 50°C	>33 days	>33 days	
Stability in dil. HCl solution(5 ppm) Half-life			
at pH 3, 37°C	8 hrs	7.9	>900
pH 6, 37°C	287.5 hrs	302.6	>900
O/W Partition coefficient (range, all conditions)	0.03-21.5	0.04-40.8	1.6-3.6
Dissoc. constant	4.45	4.38	nd

Copied Directly from Submission

Synonyms	5-OH-MSO mu-2	5-OH-MSO_2 mu-1	6-OH-$M2SO_2$ mu
Structural formula			
Molecular weight	359	375	329
Appearance		White crystal	Colorless oil
Melting point		91.0 -92.3°C	
Refractive index			
Solubility in water(27°C,pH 5.5)		0.54	1.84
Stability in dil.HCl solution (5 ppm) Half-life			
at pH 3, 37°C	6.3 hrs	9.0 hrs.	>900
pH 6, 37°C	252.9 hrs	360.8 hrs	>900
O/W Partition coefficient (range, all conditions)	0.06 - 4.0	0.02 - 13.0	0.08 - 2.2
Dissoc. constant	4.10	4.03	nd

Summary of Toxicity Data

1. Summary of selected toxicology data considered for these actions:

a) Data on Technical NP-55

STUDY	RESULTS	TOX CATEGORY	CORE CLASSIFICATION
Acute Oral LD50, Rat	3.125 gms/kg - males 2.676 gms/kg - females	III	Guidelines
Acute Dermal LD50, Rat	> 5.0 gms/kg, males & females	III	Guidelines
Acute Inhalation LC50, Rat (4 hours)	6.03 mg/L, males 6.28 mg/L, females	III	Guidelines
Primary Eye Irritation, Rabbit	No irritation	IV	Guidelines
Primary Dermal Irritation, Rabbit	No irritation	IV	Guidelines
Dermal Sensitization, Guinea Pig	Negative	-	Minimum
14-Week Mouse Feeding Study	NOEL = 300 ppm	-	Minimum
14-Week Rat Feeding Study	NOEL = 300 ppm	-	Guidelines
Six Month Dog Feeding Study	NOEL = 20 mg/kg/day (males and females) LEL = 177 mg/kg/day - males 223 mg/kg/day - females (values based on analysis of diet and food) Non-specific anemia, liver effects, possible kidney effects.	-	Guidelines

TUDY	RESULTS	TOX CATEGORY	CORE CLASSIFICATION
2-Year Mouse Chronic Feeding/Oncogenicity Study	NOEL = 120 ppm (=18 mg/kg/day) LEL = 360 ppm (non-neoplastic liver lesions) Not oncogenic in BDF1 mice.	-	
	As a chronic feeding study	-	Guidelines
	As an oncogenic study	-	Guidelines
2-Year Rat Chronic Feeding/Oncogenicity Study	NOEL $\geq$ 360 ppm (highest dose tested, (= 18 mg/kg/day)	-	
	As a chronic feeding study	-	Guidelines
	As an oncogenic study	-	Guidelines
Teratology Study, Rats	Teratogenicity NOEL: 250 mg/kg/day (highest dose tested) (Maternal NOEL = 40 mg/kg/day Maternal LEL = 100 mg/kg/day, [significantly decreased adrenal weight]).	-	Guidelines
Teratology Study, Rabbits	No terata up to and including 160 mg/kg/day. Effects observed at 480 mg/kg/day (increased number of a variety of random effects including skeletal, visceral abnormalities, reduced fetal weight, changes in male/ female ratios) considered due to extreme toxicity in dams and not to test material. Maternal NOEL = 160 mg/kg/day. Maternal LEL = 480 mg/kg/day (severe weight loss, 5/16 deaths, 6/16 abortions, reduction in number of litters and viable fetuses).	-	Minimum

STUDY	RESULTS	TOX CATEGORY	CORE CLASSIFICATION
Two Generation Reproductive Study, Rats	No reproductive effects. NOEL = 360 ppm	-	Guidelines
Mutagenicity Studies:			
i. Rec-assays and forward mutations, B. subtilis, E. coli, S. typhimurium	Negative at concentrations of chemical to 100%	-	Minimum
ii. Mouse host-mediated assay - S. typhimurium	Negative at up to 2.5 gms/kg bw/day of chemical.	-	Minimum
Metabolism Study - Rats	Tissue accumulation of chemical negligible and excretion extremely rapid, assuming DMSO vehicle doesn't affect storage or excretion of the chemical.	-	Guidelines
b) Data on Formulated Product - BAS 9052 OH (EPA #7969 - LI)			
Acute Oral LD50, Rat	4918.7 mg/kg	III	Guidelines
Acute Dermal LD50, Rat	>4000 mg/kg	III	Guidelines
Acute Inhalation LC50, Rat	>7.6 mg/L	III	Guidelines
Primary Eye Irritation, Rabbit Study No. 1	P.I. = 32 (24-hrs.); 35 (48-hrs.); 29 (72 hrs.) (scarring in 5/6 animals at 8 days, corneal opacity, in one animal at 8 days).	I	Minimum
		TOX	CORE
Primary Eye Irritation, Rabbit Study No. 2 (~~present review~~)	P.I. indexes - Washed eyes = 6.0, 6.0, 1.3, 0.7 and 0.0 at respectively 24, 48, 72 hrs. and 4 and 7 days.	I	Minimum
Primary Eye Irritation Rabbit Study No. 3	P.I. index = 35	II	Guidelines

STUDY	RESULTS	TOX CATEGORY	CORE CLASSIFICATI
	Unwashed eyes = 32.0, 31.0, 28, 17.6, 7.7 at respectively, 24, 48, 72 hrs and 4 and 7 days.		
Primary Dermal Irritation, Rabbit	P.I. = 4.0 Tox. Category I (numerical score indicates moderately irritating but 1 animal with necrosis & 5/6 with severe scaling at 8 days upgrades category to I).	I	Minimum
Primary Dermal Irritation, Rabbit (above study)	A re-review at Company request, and consultation with TB reviewer and pathologist L. Kasza, D.V.M. has justified a change in Tox Category	II	Minimum

Tox Chem No. 72A — File Last Updated 3/9/83 — Current Date 11/20/84

Study/Lab/Study #/Date	Material	EF Accession No.	Results - Post: Hydroxymetabolites	TOX Category	CORE Grade
Acute Oral - Rats 10/30/80 NISSO Inst. Life Sciences PART I TESTS	Technical* 98-99% mSO	249241	> 5000 mg/kg, males and females	IV	Guidelines
	mSO_2		> 5,000 mg/kg, males + females	IV	Guidelines
	m1S		> 5,000 mg/kg, males + females	IV	Guidelines
	$m1SO_2$		> 5,000 mg/kg, males + females	IV	Guidelines
	m2S		> 5,000 mg/kg, males + females	IV	Guidelines
	$m2SO_2$		> 5,000 mg/kg, males + females	IV	Guidelines
	m1SO		≤ 5,000 mg/kg, males + females	III	~~Guidelines~~ minimum
	m2SO		≤ 5,000 mg/kg, males + females	III	~~Guidelines~~ minimum
Part II Tests	m1SO		≤ 3080 (2953-3175) mg/kg, males	III	Guidelines
	m2SO		55-73 (4942-7435) mg/kg, males	IV	Guidelines
Part III Tests	mu-1(5-OH-mSO)		> 5,000 mg/kg, males	IV	Guidelines
	* all preparations tested were dissolved in 1% Carboxymethyl cellulose with Tween 80				

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