Monsanto

The Agricultural Group
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

January 18, 1995

Company Sanitized

COMPANY SANITIZED

A

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

8EHQ-95-13317

88950000106

95 JAN 31 PM 3:12

RECEIVED

OPPT Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Subject: Submission of Information pertaining to Acylamino pyrimidine II

Attention: Section 8(e) Coordinator

Dear Sir:

At this time, Monsanto Company is submitting to the TSCA 8(e) coordinator preliminary information pertaining to a chronic rat study, ML-94-118, with [ ]. We have given the generic name acylamino pyrimidine II to this chemical substance.

In this study, [ ] is being administered in the diet to rats of both sexes at concentrations of 0, 50, 500, 5000, and 20000 ppm. This study is currently in the ninth of twenty-four months.

Preliminary results indicate that excessive mortality has occurred in the high level males (20,000 ppm dietary level). As of January 3, 1995, 22 of 60 males have died or become moribund at this level compared with only one control male. The apparent cause of the great majority of deaths has been kidney, urinary bladder and/or ureteral calculi and or the resulting damage therefrom. Abundant urinary chemical crystals were observed in nearly all animals of both sexes at the 20,000 and 5000 ppm dietary levels at the six month urinalysis.

2/17/95

The chemical structure and name for acylamino pyrimidine are provided below. The CAS Registry number is [ ].

Chemical Name: [ ]

This chemical substance, acylamino pyrimidine II, is currently being evaluated in research and development. It is not in commerce. Monsanto claims all information within the brackets [ ] as TSCA Confidential Business Information of Monsanto Company.

Sincerely,

Robert W. Street
Manager, Regulatory Affairs

TSCA 8(e) [375].SAN

STUDY NO: 94051 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 1

PATHOLOGY SECTION

STUDY TYPE: CH SPECIES: RAT SUBSTANCE: [redacted] PRINTED: 4-JAN-95

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	MALE				
	MN	M1	M2	M3	M4
NO. IN GROUP AT RISK:	1	1	0	0	22
		50	500	500W	2000
AORTA					
-ABNORMAL CONSISTENCY, RIGID/FIRM	0	0	0	0	1
PERITONEAL CAV.					
-ABNORMAL CONTENTS	0	0	0	0	1
EYE(S)					
-CORNEAL OPACITY	0	0	0	0	1
-ABNORMAL DISCHARGE/ENCRUSTATION	0	0	0	0	2
HEART					
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	1
KIDNEY(S)					
-HYDRONEPHROSIS	1	0	0	0	18
-ENLARGED	0	0	0	0	13
-CALCULUS	0	0	0	0	14
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	1
-MASS/NODULE	0	0	0	0	2
-DILATED PELVIS	0	0	0	0	4
-EDEMA, PERIRENAL	0	0	0	0	1
LIVER					
-ABNORMAL COLOR, BROWN/YELLOW/TAN	1	0	0	0	0
-ENLARGED	0	1	0	0	5
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	1
LY.NODE,MESENT.					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	1
-ENLARGED/PROMINENT	0	0	0	0	3
NOSE/TURBINATES					
-ABNORMAL DISCHARGE/ENCRUSTATION	0	0	0	0	2

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	MALE				
	MN	M1	M2	M3	M4
NO. IN GROUP AT RISK:	1	1	0	0	22
PAWS/FEET					
-ENLARGED/SWOLLEN	0	0	0	0	1
LY.NODE,PANCR.					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	1
-ENLARGED/PROMINENT	0	0	0	0	1
PROSTATE					
-ENLARGED	0	0	0	0	1
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	1
PARATHYROID(S)					
-ENLARGED/PROMINENT	0	0	0	0	1
SKIN					
-EDEMA	0	0	0	0	1
LY.NODE,SUBMAX.					
-ENLARGED/PROMINENT	0	1	0	0	4
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	2
SPLEEN					
-ATROPHY/SMALL	0	0	0	0	5
-ABNORMAL COLOR, PALE	0	0	0	0	1
STOMACH					
-FOCUS, RED/PURPLE/BLACK	0	0	0	0	4
-ULCERATION/EROSION	0	0	0	0	1
-DILATED/DISTENDED	0	0	0	0	1
SEM. VESICLE(S)					
-ATROPHY/SMALL	1	0	0	0	0
-ENLARGED/DILATED/DISTENDED	0	0	0	0	2

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	MALE				
	MN	M1	M2	M3	M4
NO. IN GROUP AT RISK:	1	1	0	0	22
SEM. VESICLE(S)					
-ABNORMAL CONSISTENCY, SOFT	0	0	0	0	1
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	1
THYROID(S)					
-ENLARGED	0	0	0	0	1
LY.NODE,THYMIC					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	2
-ENLARGED/PROMINENT	0	0	0	0	2
URINARY BLADDER					
-ENLARGED/DILATED/DISTENDED	0	0	0	0	19
-ABNORMAL CONTENTS	0	0	0	0	9
-CALCULUS	0	0	0	0	15
-FOCUS, RED/PURPLE/BLACK	0	0	0	0	1
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	2
URETER(S)					
-CALCULUS	0	0	0	0	4
-DILATED/DISTENDED	0	0	0	0	6
GROSS CONDITION					
-EMACIATED	0	0	0	0	1
ORAL CAVITY					
-MALOCCLUSION	0	0	0	0	1

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	---- FEMALE ----				
	FM	F1	F2	F3	F4
NO. IN GROUP AT RISK:	0	0	0	0	3
AORTA					
-ABNORMAL CONSISTENCY, RIGID/FIRM	0	0	0	0	0
PERITONEAL CAV.					
-ABNORMAL CONTENTS	0	0	0	0	0
EYE(S)					
-CORNEAL OPACITY	0	0	0	0	0
-ABNORMAL DISCHARGE/ENCRUSTATION	0	0	0	0	0
HEART					
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	0
KIDNEY(S)					
-HYDRONEPHROSIS	0	0	0	0	2
-ENLARGED	0	0	0	0	0
-CALCULUS	0	0	0	0	2
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	0
-MASS/NODULE	0	0	0	0	0
-DILATED PELVIS	0	0	0	0	1
-EDEMA, PERIRENAL	0	0	0	0	0
LIVER					
-ABNORMAL COLOR, BROWN/YELLOW/TAN	0	0	0	0	0
-ENLARGED	0	0	0	0	0
-FOCUS, BROWN/YELLOW/TAN	0	0	0	0	0
LY.NODE,MESENT.					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
-ENLARGED/PROMINENT	0	0	0	0	0
NOSE/TURBINATES					
-ABNORMAL DISCHARGE/ENCRUSTATION	0	0	0	0	1

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	---- FEMALE ----				
	FM	F1	F2	F3	F4
NO. IN GROUP AT RISK:	0	0	0	0	3
PAWS/FEET					
-ENLARGED/SWOLLEN	0	0	0	0	0
LY.NODE,PANCR.					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
-ENLARGED/PROMINENT	0	0	0	0	0
PROSTATE					
-ENLARGED	0	0	0	0	0
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
PARATHYROID(S)					
-ENLARGED/PROMINENT	0	0	0	0	0
SKIN					
-EDEMA	0	0	0	0	0
LY.NODE,SUBMAX.					
-ENLARGED/PROMINENT	0	0	0	0	0
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
SPLEEN					
-ATROPHY/SMALL	0	0	0	0	1
-ABNORMAL COLOR, PALE	0	0	0	0	0
STOMACH					
-FOCUS, RED/PURPLE/BLACK	0	0	0	0	1
-ULCERATION/EROSION	0	0	0	0	0
-DILATED/DISTENDED	0	0	0	0	0
SEM. VESICLE(S)					
-ATROPHY/SMALL	0	0	0	0	0
-ENLARGED/DILATED/DISTENDED	0	0	0	0	0

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: UNSCHEDULED DEATHS

	---- FEMALE ----				
	FM	F1	F2	F3	F4
NO. IN GROUP AT RISK:	0	0	0	0	3
SEM. VESICLE(S)					
-ABNORMAL CONSISTENCY, SOFT	0	0	0	0	0
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
THYROID(S)					
-ENLARGED	0	0	0	0	0
LY.NODE,THYMIC					
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
-ENLARGED/PROMINENT	0	0	0	0	0
URINARY BLADDER					
-ENLARGED/DILATED/DISTENDED	0	0	0	0	1
-ABNORMAL CONTENTS	0	0	0	0	0
-CALCULUS	0	0	0	0	2
-FOCUS, RED/PURPLE/BLACK	0	0	0	0	0
-ABNORMAL COLOR, RED/PURPLE/BLACK	0	0	0	0	0
URETER(S)					
-CALCULUS	0	0	0	0	1
-DILATED/DISTENDED	0	0	0	0	1
GROSS CONDITION					
-EMACIATED	0	0	0	0	1
ORAL CAVITY					
-MALOCCLUSION	0	0	0	0	0

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

Robert W. Street
Manager, Regulatory Affairs
Monsanto Company
The Agricultural Group
800 North Lindbergh Boulevard
St. Louis, Missouri 63167

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 24 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

13317A

Recycled/Recyclable
Printed with Soy/Canola Ink on paper that contains at least 50% recycled fiber

IM

Triage of 8(e) Submissions

Date sent to triage: 5/28/96

Submission number: 13317A

NON-CAP CAP

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** — **pages** 1,2

Notes:

Contractor reviewer : PDR **Date:** 4/21/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0195 - 13317 (S) SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Monsanto Company (Agricultural Group)

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 01/18/95 OTS DATE: 01/31/95 CSRAD DATE: 02/17/95

CHEMICAL NAME: Acylamino pyrimidine II

CAS# Confident

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	(0248)	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	(0224)	PROD/COMP/CHEM ID	01 02 (04)	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
(0215)	CHRONIC TOX (ANIMAL)	(01) 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	RAT	LOW	R&D	
CAS SR	NO	NO (CONTINUE)		MED		
	(DETERMINE)	REFER		HIGH		

Interim study

COMMENTS: Non-Cap Rats received acylamino pyridine at concentrations of 0, 50, 500 5000 and 20000 ppm for 9 months/2 yr. The deaths occurred at 20000 ppm. Renal effects and urinary crystals were seen at the 2 top dose levels. The NOAEL seems to be 500 ppm.