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September 21, 1992

8E HQ - 92 - 12500

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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
Attn: 8(e) Coordinator (CAP Agreement)

Dear Sir or Madam:

Subject: Report submitted in accordance with guidelines established by the U. S. Environmental Protection Agency Registration and Agreement for the TSCA 8(e) Compliance Audit Program

Report submitted by: Eastman Kodak Company
343 State Street
Rochester, NY 14650
(716) 724-4000
CAP Agreement Identification Number (8ECAP-0039)

This report pertains to N-[5-(ethylphenylmethyl)amino-2-[[5-(ethylthio)-1,3,4-thiadiazol-2-yl]azo]phenyl]acetamide (synonym: 3-acetamido-4-(5'-ethylthio-1,3,4-thiadiazol-2'-ylazo)-N-benzyl-N-ethylaniline) [CAS# 67338-62-9] and is being submitted because of effects observed during a study conducted by multiple routes of exposure. The title of the report being submitted is "Basic Toxicity of 3-Acetamido-4-(5'-ethylthio-1,3,4-thiadiazol-2'-ylazo)-N-benzyl-N-ethylaniline". This report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

Groups of five male rats were fed 0.1% (100 mg/kg/day) or 1.0% (950 mg/kg/day) of the test compound in the diet for 12 days. Abnormalities in the high-dose group included increased relative liver weights, decreased absolute and relative kidney and spleen weights, and small spleens. Histopathologic effects in the high-dose group included a decrease in extramedullary hematopoietic response in the spleen and hyperplasia of the thyroid. Thyroid hyperplasia was also seen in the 0.1% dose-group. In a subsequent study, animals were fed 0.1, 0.05 or 0.01% of the test compound in the diet for 27 days. There were no statistically significant differences in absolute or relative thyroid weights. The no-observed-effect level for thyroid hyperplasia was 0.01%.

mm
2/9/95

Document Processing Center (TS-790)--2

Questions regarding this submission should be addressed to:

Mr. William Hart
Eastman Kodak Company
Corporate Health and Environment Laboratories
Rochester, NY 14652-3615
(716)722-5991

Sincerely,

R. Hays Bell

R. Hays Bell, Ph.D.
Vice President
Corporate Health, Safety and Environment
(716)722-5036

RHB:JAF
Enclosure

Basic Toxicity of 3-Acetamio^d-4-(5'-ethylthio-1,3,4-thiadiazol-
2'-ylazo)-N-benzyl-N-ethylaniline

Toxicology Section

October 26, 1977

Basic Toxicity of 3-Acetamido-4-(5'-ethylthio-1,3,4-thiadiazol-2'-ylazo)-N-benzyl-N-ethylaniline

Rats and mice survived oral doses as high as 3200 mg/kg. The only signs noted were weakness and orange colored urine in the mice. The compound caused slight skin irritation and repeated skin exposure over two work weeks only slightly exacerbated the reaction. It elicited a weak allergic contact dermatitis in 2/10 guinea pigs. It caused only slight eye irritation in rabbits.

Rats were placed on diets containing 1.0%, 0.1% or 0.0% of the compound. These diets resulted in the animals eating approximately 950 mg/kg/day, 100 mg/kg/day or no compound for 12 days. The 1.0% group ate normally but gained slightly less weight than the controls. In addition, they developed pink-peach colored urine, hair and skin. This did not occur in the 0.1% group. A hematological profile consisting of hemoglobin concentration, hematocrit, white blood cell count, differential count, red blood cell count, mean corpuscular volume and mean corpuscular hemoglobin concentration was made on each animal and all were normal. Sera were analyzed for the following components and found to be normal: glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, lactic dehydrogenase, alkaline phosphatase, urea nitrogen and glucose. At necropsy, the following organs were weighed: liver, kidney, thyroid gland and spleen. The only changes from controls were found in the 1.0% group and consisted of: increased relative liver weights, decreased absolute and

and relative kidney weights and marked decrease in absolute and relative spleen weights. Gross observation at necropsy revealed small spleens in the 1.0% group only. Microscopically, the spleens showed decreased extramedullary hematopoietic response but not the marrow response indicating some interference in hematopoiesis. The thyroid glands of the experimental animals (both groups) showed minimal or minor evidence of hyperplasia (decreased colloid staining density in the 0.1% group and decreased colloid staining density and a decrease in the number of large follicles in the 1.0% group) indicating an activation of the follicular epithelium. Both the spleen and the thyroid gland appeared to respond to the compound.

The approximate, static 96 hour LC_{50} was found to be greater than 100 mg/l for fathead minnows and snails, 6.5 mg/l for daphnids and 3.2 mg/l for flatworms. Germination, hypocotyl growth and root growth of ryegrass, radish and lettuce were unaffected by a saturated aqueous solution. Young corn, marigold, lettuce and radish plants were unaffected by a saturated aqueous solution. The Industrial Laboratory, Kodak Park, reported a COD of 1.30 g O_2 /g sample. BOD and TOD tests could not be run because of the insolubility of the compound.

Summary of Basic Toxicity

Chemical 3-Acetamido-4-(5'-ethylthio-1,3,4-thiadiazol-2'-ylazo)-N-benzyl-N-
ethylaniline

Date 10-26-77

LD₅₀ (mg/kg) P.O. Rats >3200 Mice >3200*

Remarks:
*Orange colored urine

Skin Irritation (covered) Slight Moderate Strong Absorption: Not evident

Remarks:

Eye Irritation

	Slight	Moderate	Strong	<u>Fluorescein stain</u>	
				Cornea	Adnexa
No. washed	3/3				
No. unwashed	3/3				

Remarks:

Skin Sensitization Potential No. guinea pigs 10

None 8/10 Weak 2/10 Moderate Potent

Remarks:

Repeated (10 days) Skin Application (uncovered) No. guinea pigs 10

Remarks:
Day 1: Slight (5/10) to moderate (5/10) erythema. Day 10: Severe (10/10) erythema. Slight exacerbation of reaction.

Other Tests

Summary of Basic Toxicity--2

Repeated Feeding No. rats/group 5 No. days 12 Carrier corn oil

	<u>1.0 %</u>	<u>0.1 %</u>	<u>1.0 %</u>	<u>0.1 %</u>
Weight gain	<u>+1</u>	<u>N</u>	Hematology	
Feed intake	<u>N</u>	<u>N</u>	Hgb.	<u>N</u> <u>N</u>
Signs/behavior	<u>*</u>	<u>N</u>	Hct.	<u>N</u> <u>N</u>
*Pink-peach colored urine, hair, skin			WBC	<u>N</u> <u>N</u>
Clinical Chemistry:			Diff.	<u>N</u> <u>N</u>
			No. RBC, MCV, MCHC normal in 1.0% and 0.1%	
			Organ Weight:	
GOT	<u>N</u>	<u>N</u>		1.0% 0.1%
GPT	<u>N</u>	<u>N</u>	Liver	Spleen
LDH	<u>N</u>	<u>N</u>	Abs.	<u>N</u> <u>N</u>
AP	<u>N</u>	<u>N</u>	Rel.	<u>+2</u> <u>N</u> <u>+3</u> <u>N</u>
UN	<u>N</u>	<u>N</u>	Kidney	
Gluc.	<u>N</u>	<u>N</u>	Abs.	<u>+2</u> <u>N</u>
			Rel.	<u>+1</u> <u>N</u>
			Thyroid	
			Abs.	<u>N</u> <u>N</u>
			Rel.	<u>N</u> <u>N</u>

Pathology

Gross: Small spleens, 1.0% only.
Microscopic: See pathologist's report.

Repeated Inhalation ND Conc. _____ No. rats _____ No. days _____

Wt. change _____ Signs/behavior _____

Hemat.: Hgb. _____ Hct. _____ WBC _____ Diff. _____

Clinic. Chem.: GOT _____ GPT _____ LDH _____ AP _____ UN _____ Gluc. _____

Pathology

Static 96 hour LC₅₀ mg/l µl/l Added to aquaria in acetone

Fathead minnows >100 Daphnids 6.5 Snails >100 Flatworms 3.2

No effect concn. mg/l µl/l

	Germination	Hypocotyl Growth	Root Growth
Ryegrass	<u>>1000*</u>	<u>>1000</u>	<u>>1000</u>
Radish	<u>"</u>	<u>"</u>	<u>"</u>
Lettuce	<u>"</u>	<u>"</u>	<u>"</u>

Remarks:

*Saturated aqueous solution

Summary of Basic Toxicity--3

No effect concn.	<u>mg/l</u>	<u>µl/l</u>	Early Plant Growth
Marigold			<u>1000</u>
Radish			<u>1000</u>
Corn			<u>1000*</u>
Lettuce			<u>1000</u>

Remarks:

*Slight growth inhibition. Normal at 100 mg/l.

Industrial Laboratory (g O₂/g sample)

BOD₅ * BOD₂₀ * TOD * COD 1.30

*Insoluble

Historical

Control Data (5/77)

	Mean	SD	Extremes
GPT	70	16	29-135
GOT	174	32	114-304
LDH	1410	494	459-3135
AP	669	170	341-1166
UN	19.0	2.9	9.0-29.0
Glucose	141	17.6	94-216
Hgb	14.6	1.1	10.5-18.7
Hct	45.8	3.4	35-58
WBC	13,955	4330	6700-46,500
Poly	18.4	7.4	4-50
Band	2.1	2.1	0-11
Lymph	78.1	8.5	44-95

Legend

- ↑ Increased
- ↓ Decreased
- 1 Slight
- 2 Moderate
- 3 Great
- N Normal
- ND Not done

Compound 77-122 (cont.)--2
October 18, 1977

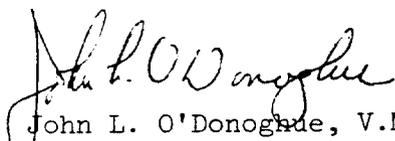
Spontaneous lesions (cont.):

	Number of animals affected	
	1.0%	0.0%
Kidney-focal mononuclear infiltrates: minimal	2/5	0/5
Kidney-regeneration tubular epithelium: minimal	2/5	1/5
Kidney-pelvis dilated: minor	0/5	2/5
Urinary bladder-coagulum present	2/5	2/5
Stomach: heterotopic non-glandular epithelium: present	1/5	0/5
Pancreas: focal degeneration exocrine cells: minor	0/5	1/5
Tongue: focal mononuclear infiltrate: minimal	0/5	1/5
Adrenal gland: focal mononuclear infiltrate: minor	0/5	1/5
Eye: persistent hyaloid vasculature: present	1/5	0/5
Eye: retinal rosettes: present	0/5	1/5

Compound related changes were present in the spleen and thyroid. In the spleen, the reduction in size noted on autopsy examination correlated with a decrease in extramedullary hematopoiesis in the spleen. In this instance, the extramedullary hematopoietic response but not the marrow response is less in treated (1.0%) than in control animals indicating some interference in the hematopoietic response.

The thyroids from the 1.0, 0.1 and 0.0% groups were examined. Those from the 1.0% group had minimal evidence of thyroid hyperplasia in 4/5 rats and minor evidence in 1/5 while the 0.1% group had minimal evidence of hyperplasia in 5/5 rats. These changes consisted of decreased colloid staining density in the 0.1% group and decreased colloid staining density and a decrease in the number of large follicles in the 1.0% group indicating an activation of the follicular epithelium. Thyroid weights (absolute and relative) were comparable amongst all three dose levels:

	<u>1.0%</u>	<u>0.1%</u>	<u>0.0%</u>
Absolute weight(g) \bar{x} ±SD	0.024±0.0047	0.021±0.0053	.025±0.0057
Relative weight(%) \bar{x} ±SD	1.0±0.13	0.82±0.206	1.0±0.25
n	4	4	4


John L. O'Donoghue, V.M.D.
Toxicology Section

Health, Safety, and Human Factors Laboratory

JO'D:bdo



July 12, 1978

Compound 77-122 N-[5-(ethylphenylmethyl)amino-2-[[5-(ethylthio)-1,3,4-thiadiazol-2-yl]azo]phenyl]acetamide

Twenty male Charles River CD rats were fed 0.1, 0.05, 0.01 or 0% of Compound 77-122 in their diet for 27 days. All were killed one day later by inhalation of carbon dioxide. Thyroid glands were weighed, fixed in 10% buffered formalin, embedded in Paraplast, cut at 5 μ m, stained with hematoxylin-eosin and examined by light microscopy.

On gross examination, the only abnormality noted was a pink discoloration of the skin of the tail. No statistically significance difference in absolute or relative thyroid weights was found (t-test at 5% significance level).

On histologic examination, minimal thyroid hyperplasia was found in:

0.1% - 4/5*
0.05% - 4/5
0.01% - 0/5
0% - 0/5

*Number of samples with finding over total number of samples examined.

The criteria for classifying a positive response was the same as that used in Toxicology Section Report TL-77-88. The severity of the effect was not altered by increasing the exposure time from 12 days (TL-77-88) to 27 days. The no effect level for the thyroid change is between 0.01% and 0.05% in the diet.

John L. O'Donoghue, V.M.D.
Toxicology Section, B-306
Health, Safety, and Human Factors Laboratory

JO'D:bdo



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

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Vice President, Corporate Health, Safety, and Environment
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343 State Street
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 06 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

12500A



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Triage of 8(e) Submissions

Date sent to triage: 12/14/95

NON-CAP

CAP

Submission number: 12500A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

~~EXO~~ ~~AQ/ATO~~

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:

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Notes:		
Contractor reviewer:	<u>POK</u>	Date: <u>3/13/95</u>



CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8EHQ-0992-12500 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Eastman Kodak Company

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/IN PROGRESS
 0403 NOTIFICATION OF WORKER RIGHTS
 0404 LABEL/MSDS CHANGES
 0405 PROCESS/HANDLING CHANGES
 0406 APP/USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

SUB. DATE: 09/21/92 OTS DATE: 09/24/92 CSRAD DATE: 02/09/95

CHEMICAL NAME:

CASE#
67338-62-9

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	<u>0220</u> ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCC/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		
<u>0212</u> ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
<u>0213</u> SUB ACUTE TOX (ANIMAL)	01 02 04	<u>0228</u> 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 ATOX (oral, eye irr.), SEN
CAS SR NO NO (CONTINUE) MUS MED ATOX (dermal irr.), SBTOX
IN TERMINI REFER GP HIGH RBT
CONFIDENTIAL FISH

12500A

L

Acute oral toxicity in rats and mice is of low concern. Single oral doses to rats and mice at levels up to 3200 mg/kg resulted in no deaths. Clinical signs were limited to weakness in the mice.

M

Dermal irritation in guinea pigs is of moderate concern. Application of the substance resulted in slight irritation. Repeated application (10 doses) to ten guinea pigs resulted in slight exacerbation of the reaction. Slight (5/10) to moderate (5/10) erythema was noted at day 1, and severe erythema was noted at day 10 (10/10).

L

Dermal sensitization in guinea pigs is of low concern. The compound elicited a weak allergenic contact dermatitis in 2/10 guinea pigs.

L

Eye irritation in rabbits is of low concern. Application to rabbit eyes (3 washed/3 unwashed) resulted in slight irritation.

~~M~~ L

Subacute oral toxicity in rats is of ~~moderate~~ ^{Low} concern. Rats received dietary doses of 0, 950, or 100 mg/kg/day for 12 days. Clinical signs were limited to reduced weight gain and discolored urine, hair, and skin in the high-dose group. Hematology and serum chemistry were not altered. The high-dose animals had increased relative liver weights, decreased absolute and relative kidney weights, and marked decrease in absolute and relative spleen weights. Gross necropsy revealed small spleens in the high-dose group. Microscopically, the spleens showed decreased extramedullary hematopoietic response. Hyperplasia of the thyroid (decreased colloid staining density and/or decrease in the number of follicles) was noted in both treatment groups.