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September 15, 1992

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

The report pertains to N,N'-diphenylmethanimidamide (synonym: N,N-diphenylformamidene) [CAS # 622-15-1] and is being submitted because of effects observed during a subacute study in rats. The title of the report being submitted is: "Basic Toxicity of N,N-Diphenylformamidene". The 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 or 1.0% of the test compound in the diet for four to ten days. Feed intake and body weight gain were decreased at the high-dose level; animals were euthanatized in poor condition on study Day 4. Abnormalities noted at both dose levels included decreased hematocrits and red blood cell counts, abnormal red blood cell morphology, and splenic congestion. Splenic follicular hyperplasia was observed at the low-dose level. In a subsequent feeding study, a no-observed-effect level for the splenic and red blood cell effects was determined to be between 0.01 and 0.1%. The test compound is also a methemoglobin former in rats.

The test compound has been used internally and sold as a pure chemical.

mm  
2/9/95

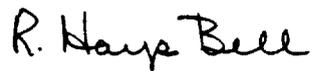


Document Processing Center (TS-790) -- 2

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

RHB:DRG  
Enclosure

125944N

TX-80-55

Basic Toxicity of N,N-Diphenylformamidene

Toxicology Section

Written by: Walter J. Krasavage

May 14, 1980

### Basic Toxicity of N,N-Diphenylformamidene

The approximate acute oral LD50 was 1903 mg/kg and 1796 mg/kg for male rats and mice respectively. Clinical signs included weakness, prostration, severe depression, dyspnea, cyanosis, bloody urine and death within 2-3 days.

When held in contact to the depilated guinea pig skin under an occlusive wrap for 24 hours the compound produced slight skin irritation.

Percutaneous absorption was not evident and the acute dermal LD50 was greater than 1 g/kg. Repeated applications (10) to the clipped backs of guinea pigs produced only slight irritation with very little exacerbation of the response. None of the five guinea pigs tested for allergic skin reactions had a positive response. The compound does not appear to be a skin sensitizer.

Several crystals placed in the conjunctival sacs of six rabbit eyes (three unwashed and three washed) produced slight irritation. The adnexae of all unwashed eyes and one washed eye and the adnexae and 1/2 the cornea of another washed eye showed fluorescein staining.

Two feeding studies were done on this compound because the first study failed to establish a no-effect dose for splenic and red blood cell changes seen.

Groups of five male rats each were fed concentrations of 1.0 and 0.1% in the diet with 1.0% corn oil for 4-10 days. The rats fed 1.0% consumed only a total of 45 grams of diet and lost an average of 23 grams body weight over a four-day period. These animals had slight alopecia, protruding eyes,

orange and dark green colored urine. Because of their weakness and generally poor body condition, they were terminated on day four. The 0.1% concentration provided daily doses of 95 mg/kg and had no effect on body weight gain, feed consumption, liver and kidney weights, while blood cell and differential counts or serum activity of glutamic oxaloacetic and glutamic pyruvic transaminase, alkaline phosphatase, urea nitrogen, lactic dehydrogenase and glucose.

Hemoglobin concentration, hematocrit and erythrocyte count were slightly decreased and abnormal red blood cell morphology was present. The absolute and relative weights of the spleens were moderately increased. At necropsy, slight alopecia, dark eyes and enlarged dark spleens were noted in the 1.0% rats. Large dark spleens were seen in the 0.1% animals. Histopathologic changes included minor to moderate tracheitis (3/5) and moderate splenic congestion (4/5) in the 1.0% rats. Minor to moderate splenic follicular hyperplasia (4/5) and splenic congestion (3/5) were seen in the 0.1% rats, along with increased mean corpuscular volumes, abnormal erythrocyte morphology, decreased hemoglobin concentration, hematocrit, and rbc count.

The site of toxic action was the red blood cells, secondarily, the spleen. A no-effect dose was not established for these changes, therefore an additional repeated feeding study was initiated.

Groups of five male rats each were fed concentrations of 0.1 and 0.01% N,N-diphenylformamidene in the diet with 1.0% corn oil for 10 consecutive days. These concentrations provided daily doses of 98 and 9.7 mg/kg.

The red blood cell and splenic changes seen clinically and histologically in the 0.1% dosed rats in the initial study were reproduced in this study, but were not seen in the low dosed (0.01%) animals, thus establishing a no-effect dose between 0.01 and 0.1% for this compound.

Body weight gain, feed consumption, white blood cell and differential counts, absolute and relative liver and kidney weights and the serum levels of glutamic oxaloacetic and glutamic pyruvic transaminase, lactic dehydrogenase, alkaline phosphatase, urea nitrogen and glucose were not affected by the treatments.

A test for methemoglobin formation revealed that this compound is a methemoglobin former. Three rats given 700 mg/kg N,N-diphenylformamide had methemoglobin levels two and four hours later which averaged 19.8 and 28.4% respectively compared to 0.43 and 0.67 for the controls.

WCK:ifp



SUMMARY OF BASIC TOXICITY--2

Repeated Exposure	<u>Feeding</u>	Drinking Water	Gavage	Inhalation
No. rats/group <u>5</u>	No. exposures <u>10</u>	No. days <u>11</u>	Carrier <u>Corn oil 1.0%</u>	
Units of exposure:	<u>%</u>	mg/kg	mg/m <sup>3</sup>	ppm
Exposure concentration:	<u>1.0</u>	<u>0.1</u>	<u>1.0</u>	<u>0.1</u>
Weight gain	<u>+3</u>	<u>N</u>	Hematology:	
Feed intake	<u>+3</u>	<u>N</u>	Hgb.	<u>N</u> <u>+1</u>
Daily dose (mg/kg/day)	<u>--</u>	<u>95</u>	Hct.	<u>+1</u> <u>+1</u>
Signs/behavior	<u>Ab*</u>	<u>N</u>	WBC	<u>+1</u> <u>N</u>
			Diff.	<u>N</u> <u>N</u>
			RBC	<u>+1*</u> <u>+*</u>
			McHc	<u>+1</u> <u>N</u>
			CMV	<u>N</u> <u>+1</u>
			MCH	<u>+1</u> <u>+1</u>

\*Slight alopecia, protruding eyes, orange and dark green urine. All animals terminated on day four because of poor condition.

\*Abnormal red cell morphology

Clinical chemistry:

GOT	<u>N</u>	<u>N</u>
GPT	<u>+1</u>	<u>N</u>
LDH	<u>N</u>	<u>N</u>
AP	<u>+1</u>	<u>N</u>
UN	<u>+1</u>	<u>N</u>
Glucose	<u>+1</u>	<u>N</u>

Organ weight:

Liver		
Abs.	<u>N</u>	<u>N</u>
Rel.	<u>+1</u>	<u>N</u>
Kidney		
Abs.	<u>+1</u>	<u>N</u>
Rel.	<u>N</u>	<u>N</u>
Spleen		
Abs.	<u>N</u>	<u>+2</u>
Rel.	<u>N</u>	<u>+2</u>

Gross pathology: 1.0% - Slight alopecia, dark eyes, enlarged dark spleens  
0.1% - Large dark spleen

Histopathology: 1.0% - Chronic tracheitis, minor to moderate (3/5)  
Moderate spleen congestion (4/5)  
0.1% - Minor - moderate splenic follicular hyperplasia (4/5)  
Splenic congestion (3/5)

Site of toxic action: Red blood cells.

Legend

<u>+</u>	Increased
<u>-</u>	Decreased
<u>1</u>	Slight
<u>2</u>	Moderate
<u>3</u>	Great
<u>N</u>	Normal
<u>ND</u>	Not done

SUMMARY OF BASIC TOXICITY-- 3

Repeated Exposure	<u>Feeding</u>	Drinking Water	Gavage	Inhalation
No. rats/group <u>5</u>	No. exposures <u>10</u>	No. days <u>11</u>	Carrier <u>corn oil 1.0%</u>	
Units of exposure:	<u>%</u>	mg/kg	mg/m <sup>3</sup>	ppm
Exposure concentration:	<u>0.1</u>	<u>.01</u>	<u>0.1</u>	<u>.01</u>
Weight gain	<u>N</u>	<u>N</u>	Hematology:	
Feed intake	<u>N</u>	<u>N</u>	Hgb.	<u>+1</u> <u>N</u>
Daily dose (mg/kg/day)	<u>98</u>	<u>9.7</u>	Hct.	<u>+1</u> <u>N</u>
Signs/behavior	<u>N</u>	<u>N</u>	WBC	<u>N</u> <u>N</u>
*Abnormal red cell morphology, macrocytosis, anisocytosis, poikilocytosis.			Diff.	<u>N</u> <u>N</u>
			RBC	<u>+1*</u> <u>N</u>
			MCV	<u>+1</u> <u>N</u>
			MCH	<u>N</u> <u>N</u>
			MCHC	<u>N</u> <u>N</u>

Clinical chemistry:

GOT	<u>N</u>	<u>N</u>
GPT	<u>N</u>	<u>N</u>
LDH	<u>N</u>	<u>N</u>
AP	<u>N</u>	<u>N</u>
UN	<u>N</u>	<u>N</u>
Glucose	<u>N</u>	<u>N</u>

Organ weight:

Liver		
Abs.	<u>N</u>	<u>N</u>
Rel.	<u>N</u>	<u>N</u>
Kidney		
Abs.	<u>N</u>	<u>N</u>
Rel.	<u>N</u>	<u>N</u>
Spleen		
Abs.	<u>+2</u>	<u>N</u>
Rel.	<u>+2</u>	<u>N</u>

Gross pathology: 0.1% - Large dark spleens  
0.01% - None

Histopathology: 0.1% - Moderate splenic congestion (3/5)  
0.01% - None

Site of toxic action: Red cell and spleen at 0.1%  
None identified at 0.01%

Legend

<u>+</u>	Increased
<u>-</u>	Decreased
<u>1</u>	Slight
<u>2</u>	Moderate
<u>3</u>	Great
<u>N</u>	Normal
<u>ND</u>	Not done



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

R. Hays Bell, Ph.D.  
Vice President, Corporate Health, Safety, and Environment  
Eastman Kodak Company  
343 State Street  
Rochester, New York 14650

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

12506A  
Enclosure



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### Triage of 8(e) Submissions

Date sent to triage: 12/14/95

NON-CAP

CAP

Submission number: 12506A

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 1,2

pages 1,2,7,8,9

Notes:

Contractor reviewer: PRR

Date: 3/13/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:

Submission # BEHQ-0992-12506 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:

- 063 REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION OF WORKER CONCERNS
- 0404 LABEL/MSDS CHANGES
- 0405 PROCESS/HANDLING CHANGES
- 0406 APP/USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 09/15/92 OTS DATE: 09/24/92 CSRAD DATE: 02/09/95

CHEMICAL NAME: \_\_\_\_\_

CAS#

622-15-1

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	<u>0243</u> 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. 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	<u>0247</u> DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	<u>0248</u> 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
<u>0211</u> 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

YES

CAS SR

NO

IN TERMINI

ONGOING REVIEW

YES (DROP/REFER)

NO (CONTINUE)

REFER

SPECIES

RAT  
MUS  
GP  
RBT

TOXICOLOGICAL CONCERN:

LOW ATOX ~~LOW~~

MED SBT0X

HIGH

USE:

Internal

PRODUCTION:

COMMENTS

12506A

L

Acute oral toxicity in rats and mice is of low concern. Single oral doses to rats and mice resulted in LD<sub>50</sub> value of 1903 and 1796, respectively. Clinical signs included weakness, prostration, severe depression, dyspnea, cyanosis, and bloody urine.

L

Dermal irritation in guinea pigs is of low concern. A single application to depilated guinea pig skin produced slight irritation. Repeated applications (10 doses) to the clipped backs of guinea pigs produced only slight irritation with very little exacerbation of the response.

L

Acute dermal toxicity is of low concern. A single dermal application to guinea pig skin at 1000 mg/kg resulted in no deaths.

L

Dermal sensitization is of low concern. None of the five guinea pigs tested had a positive response.

L

Eye irritation is of low concern. Application to the conjunctival sac of six rabbit eyes (3 washed/3 unwashed) resulted in slight irritation. Fluorescein staining was observed in the adnexae (3/3 unwashed, 2/3 washed) and cornea (1/3 washed).

M

Subacute oral toxicity in rats is of moderate concern. Repeated oral doses were given to male rats (5/dose) at levels of 0.1 and 1.0% in the diet for 4-10 days. The high-dose rats exhibited severe weight loss, decreased food consumption, slight alopecia, and protruding eyes; the animals were sacrificed on day 4 due to poor condition. The group fed 0.1% in diet (95 mg/kg/day) for 10 days had normal body weight gain, feed consumption, liver and kidney weights, and serum chemistry. In these animals, hemoglobin concentration, hematocrit, and erythrocyte count were slightly decreased and abnormal red blood cell morphology was present. Absolute and relative spleen weights were moderately increased. Histopathological changes included minor to moderate tracheitis (3/5) and moderate splenic congestion (4/5) in the high-dose group. Minor to moderate splenic follicular hyperplasia (4/5) and splenic congestion (3/5) were seen in the low-dose group. In a subsequent study, repeated oral doses were given to male rats (5/dose) at levels of 0.01 and 0.1% in the diet (9.7 and 98 mg/kg/day, respectively) for 10 days. The red blood cell and splenic changes seen in the 0.1%-dosed rats in the previous study were reproduced, but these effects were not seen in the 0.01%-dose group.