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September 28, 1992

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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-(2-methoxyphenyl)-3-oxobutanamide (synonym: acetoacet-o-anisidide) [CAS# 92-15-9] 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 Acetoacet-o-Anisidide". This report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

Groups of five rats were fed 0.1 or 1.0% of the test compound in the diet for fourteen days. Abnormalities observed at the high-dose level included: decreased body weight gain, red blood cell count, hemoglobin concentration and hematocrit; changes in red blood cell morphology; and increased serum aspartate aminotransferase, urea nitrogen, and glucose. Gross and histopathologic abnormalities included darkening of the spleen and splenic congestion. A slight decrease in serum glucose and splenic congestion were observed at the low-dose level.

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

Kodak
Official Sponsor of the 1992 Olympic Games

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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

Basic Toxicity of Acetoacet-o-Anisidide

The oral LD_{50} was 1903 mg/kg and 1600 mg/kg for male and female rats respectively. Animals showed signs which ranged from a slight weakness to prostration, ataxia and rough hair coats. Rats given 1500 mg/kg orally did not develop methemoglobinemia. Application of the compound to the depilated abdomen of guinea pigs for 24 hours under an impervious cuff produced a slight irritation with no evidence of percutaneous absorption. The topical LD_{50} was greater than 1 g/kg. Repeated application to the clipped backs of guinea pigs for 10 days did not exacerbate the irritative response. Skin sensitization was not induced in ten guinea pigs tested using the established procedure. Eye irritation produced by instillation of the compound into the conjunctival sacs of six rabbits, three of which when promptly washed, was slight. Retention of fluorescein dye was observed in the nictitating membrane of 1/3 unwashed eyes. No staining was observed in the washed eyes.

Three groups of five rats administered the test compound incorporated in their diet at 0.0%, 0.1%, and 1.0% with 1% corn oil for 14 days consumed 0 mg/kg/dav, 75 mg/kg/day, or 709 mg/kg/day, respectively. There was a slight decrease in weight gain for the high dosed, but not in feed consumption in either of the dose groups.

No mortality or unusual clinical signs were observed during the study other than nonspecific corneal opacity observed in a single animal.

Absolute and relative kidney and liver weights of treated animals were not significantly different from those of the control animals with the exception of a slight increase in relative liver weights in animals fed the high dose. This alteration was due to the lower body weights of the animals in that group and was not considered to be biologically significant.

Hematological changes caused by feeding of the compound at the high dose included slight decreases in red blood cell count, hemoglobin concentration and hematocrit. Red cell morphologic abnormalities present in blood from high dosed animals included macrocytosis, poikilocytosis, polychromasia, anisocytosis, spherocytosis and the presence of target cells and Howell-Jolly bodies. Hematologic parameters which were unaffected included red blood cell indices, platelets, white blood cell count and differential white blood cell count. None of the hematological parameters were altered in animals fed the low dose with the exception of the differential white blood cell count, which reflected a slight decrease in lymphocytes and an increase in polymorphonuclear leukocytes.

Alterations in blood chemistry in animals fed the high dose included slight increases in serum aspartate aminotransferase and urea nitrogen and a slight decrease in glucose. A slight increase in serum glucose was observed in animals fed the low dose. All other clinical chemistries were comparable between control and treated groups: this included serum alanine aminotransferase, lactic dehydrogenase, alkaline phosphatase, and creatinine. None of the alterations in clinical chemistry were considered biologically significant.

Gross pathology examination revealed minor to moderate darkening of the spleen in 4/5 animals and a single enlarged spleen. Histopathologic examination revealed minor to moderate splenic congestion in 4/5 high dosed and minor splenic congestion in 3/5 low dosed animals. Background lesions not related to treatment were observed in the liver, kidneys and lungs.

The site of toxic action for this compound was determined to be the red blood cell. Congestion of the spleen also occurred in what appears to be a secondary response to the toxic effects in the red blood cell.

SUMMARY OF BASIC TOXICITY

Chemical Acetoacet-o-Anisidide

Date 9/29/82

GAVAGE LD50 (mg/kg) **Rats (M)** 1903 (1355-2672) **Rats (F)** 1600 (1080-2368)

Remarks: Slight weakness to prostration, ataxia and rough hair coat.

INHALATION LC50 (mg/m^3, ppm) **Rats (M)** _____

Remarks: ND

GUINEA PIG SKIN IRRITATION

Occluded, Single Dose

No. responding:

Slight 5/5 Moderate Strong Severe

Remarks:

Open, Repeated (10 Doses) No. animals 5

Remarks: No exacerbation observed

Skin Absorption Not evident Dermal LD50 >1 g/kg

Acute Skin Irritation
Slight
Moderate
Strong

Estimated Corrosivity
No
Questionable
Yes

GUINEA PIG SKIN SENSITIZATION

No. responding:	None	Weak	Moderate	Potent
	10			

Remarks:

Estimated Human Risk
Low
Moderate
High

RABBIT EYE IRRITATION

No. responding:	Slight	Moderate	Strong	Severe	Fluorescein stain Cornea	Fluorescein stain Adnexa
Unwashed	3/3				0/3	1/3
Washed	3/3				0/3	0/3

Remarks:

Acute Eye Irritation
Slight
Moderate
Strong

OTHER TESTS

1500 mg/kg p.o. produced no methemoglobinemia.

SUMMARY OF BASIC TOXICITY--2

REPEATED EXPOSURE

Feeding (%); Drinking Water (%); Gavage (mg/kg); Inhalation (mg/m^3, ppm)

No. rats/group 5 No. of Treatment(s) 14 Days of Experiment 15 Carrier 1.0% Corn oil

Exposure concentration:	1.0	0.1
Weight gain	↓1	N
Feed intake	N	N
Daily dose (mg/kg/day)	709	75
Clinical signs	N	N

Clinical chemistry:		
AST (GOT)	↑1	N
ALT (GPT)	N	N
LDH	N	N
AP	N	N
Creatinine	N	N
UN	↑1	N
Glucose	↓1	↑1

Hematology:	1.0	0.1
RBC	↓1*	N
Hgb.	↓1	N
Hct.	↓1	N
RBC Ind.	N	N
Platelets	N	N
WBC	N	N
Diff.	N	Ab**

*Macrocytosis, poikilocytosis, polychromasia, anisocytosis, and spherocytosis in 4 or 5 animals. Target cells and Howell-Jolly bodies in 2 and 1 animals.

**↑1 polys, ↓1 lymphocytes.

Organ weight:		
Liver		
Abs.	N	N
Rel.	↑1	N
Kidney		
Abs.	N	N
Rel.	N	N

Gross pathology:

4/5 animals in the high dose had enlarged and/or dark spleens.

Histopathology:

Histopathologic examination revealed a minor to moderate splenic congestion in 4/5 high dosed and a minor splenic congestion in 3/5 low dosed rats.

Site of toxic action:

The red blood cell, with congestion of the spleen occurring secondarily.

Legend

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

1/27/81