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PREVENTION AND TOXICS

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Department of
Environmental, Health &
Safety Affairs (DEHSA)

(A)

March 28, 1994
MRS-034-94

Attn: TSCA Section 8(e) Coordinator
Document Processing Center (TS-79C)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460



8EHQ-94-12955
INIT 84/04/94



88940000197

Dear Sir or Madam:

In accordance with the requirements of TSCA Section 8(e), Hoechst Celanese hereby submits a preliminary report for a 2-week inhalation range-finding study of acetic anhydride vapor (CAS No. 108-24-7) in pregnant and non-pregnant rats.

Female rats received 7 exposures of 6 hours (day 13 post coitum) at the maternally toxic 100 ppm dose level. Two of four pregnant females resorbed their entire litter, while the remaining 2 pregnant females sustained viable litters. No similar adverse effects were observed in pregnant females at the 25 ppm dose level. At 100 ppm and 25 ppm dose levels, enlarged lymph nodes were observed in male rats.

This submission contains no confidential business information.

If any further information is required, do not hesitate to contact Dr. Michele R. Sullivan, Director, Product Stewardship at 908-231-4480.

Sincerely,

Michele Sullivan for
Susan Engelman
Vice President, Environmental, Health & Safety Affairs

Encl.

CERTIFIED MAIL/
RETURN RECEIPT REQUESTED



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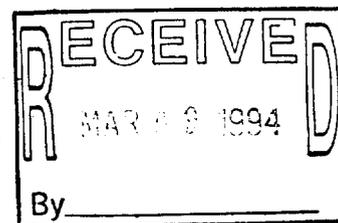
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HUNTINGDON RESEARCH CENTRE
SYNOPSIS
FEBRUARY 1994

Schedule Number: HST/400

Study Title: Acetic Anhydride: 2 weeks repeat dose inhalation toxicity study in male and time mated female rats

Study Director: K Jones

Study Supervisors: P F Bell and T J Kenny

Study Monitor: Dr T Cascieri, Hoechst Celanese Corporation

Date of commencement of treatment: ♂ 17 January 1994
♀ 18 January 1994

Events covered in this synopsis: To termination (2 weeks for males or Day 20 post coitum for females)

STUDY DESIGN

Treatment levels:	No of animals
Group 1: Control	5♂ + 5♀
Group 2: 25 ppm	5♂ + 5♀
Group 3: 100 ppm	5♂ + 5♀
Group 4♂: 400 ppm	5♂
Group 4♀: Untreated	5♀

All data and interpretation are provisional and, as such, may be subject to alteration in subsequent documents.

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1. Exposure at 400 ppm

A single exposure of males at 400 ppm resulted in a severe reaction to treatment.

During the exposure, reactions to treatment in the chamber for the whole group were: eyes half closed/closed, lachrymation, prone posture and exaggerated breathing (Table 2). On examination after exposure all animals exhibited noisy breathing (Appendix 1).

Two males were found dead (numbers 18 and 19) the next day, whilst the remaining three males exhibited gasping, lethargy and brown stained fur. For other parameters group mean bodyweight loss was 45g in one day, whilst food and water consumption was negligible (Tables 3, 5 and 6).

On the basis of such a marked adverse reaction, resulting in very poor condition, the remaining males were sacrificed immediately with no further exposure.

Macroscopic examination of all these males revealed general gaseous distension of the gastrointestinal tract in all animals (Appendix 1).

Due to the adverse reaction to exposure in males, females allocated to this group were not exposed and subsequently sacrificed on Day 13 post coitum.

2. Exposure at 100 ppm

Exposure at 100 ppm resulted in a progressive, marked, adverse reaction to treatment.

Clinical signs during exposure from the onset of treatment for males and females were: eyes closed/half closed, lachrymation, licking inside mouth, gasping and occasional twitching of the head (Table 2). Examination following each exposure revealed noisy respiration with occasional gasping and sneezing in all animals. Additionally, occasional twitching of the head and walking with arched back was seen in females Days 12 and 13 post coitum (Appendix 1).

Progressive and marked bodyweight loss was apparent in both sexes from the onset of treatment (Figure 1, Tables 3 and 4). During the weekend following 5 days of exposure males showed slight bodyweight gain, although on resumption of treatment, marked bodyweight loss was again observed.

Throughout the exposure period food and water consumption were markedly reduced compared with the concurrent control for both sexes (Tables 5 and 6).

On the basis of such marked reactions to treatment it was decided to stop treatment, the males having received 6 times 6 hour exposures, and the females 7 exposures (Day 13 post coitum)(Table 1). At macroscopic examination of the females, 4/5 were confirmed to be pregnant (Table 8). However, two females had resorbed their entire litter, whilst the remaining two females were sustaining viable litters of 11 and 16 foetuses. Visual examination of these foetuses did not reveal any apparent abnormalities.

Macroscopic findings for adults revealed, in particular, enlarged lymph nodes (cervical and/or tracheobronchial) in males and gaseous distension of the gastrointestinal tract in all animals.

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Terminal synopsis - continued

HST/400

3. Exposure at 25 ppm

Exposure at 25 ppm also produced some adverse reaction to treatment which was tolerated until the end of scheduled exposure (Table 1).

As in the higher exposure concentrations, clinical signs whilst in the exposure chamber included eyes half closed/closed, licking inside mouth and occasional twitching of head (Table 2). Following each exposure noisy respiration was observed on most occasions for each sex, persisting to termination for males, but ceasing the day before termination for females.

During the first week of treatment mean bodyweight gain of males was comparable with the controls. However, during the second week of treatment a noticeable divergence from the control group occurred, with a period of weight loss evident (Figure 1, Table 3). Amongst females, reduced bodyweight gain was apparent between Days 8 to 14 of pregnancy compared with the controls. Thereafter the rate of bodyweight gain was similar to the controls, although absolute group mean bodyweight was lower compared with controls at termination (Figure 1, Table 4).

Food and water consumption (Tables 5 and 6) was consistently less than the concurrent controls for both sexes. However, after cessation of treatment recovery of food and water consumption was evident, and parity with the controls was almost regained.

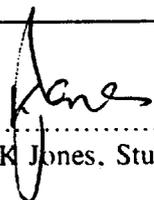
At sacrifice on Day 20 of pregnancy all females including the controls, were pregnant (Table 1). The incidence and pattern of embryofoetal loss, litter size, litter weight and foetal weight were not adversely affected by exposure (Table 7, Appendix 2).

Macroscopic examination of males revealed enlarged lymph nodes (cervical and/or tracheobronchial). No adverse effects of treatment were apparent amongst females (individual data is not supplied with this synopsis).

4. Chamber concentrations (Appendix 3)

Results indicate close agreement between target concentrations and achieved analysed concentrations of test substance.

Next synopsis due: Completion of microscopic examination of males

Signed: 
K Jones, Study Director


P F Bell, Study Supervisor


T J Kenny, Study Supervisor

Date:

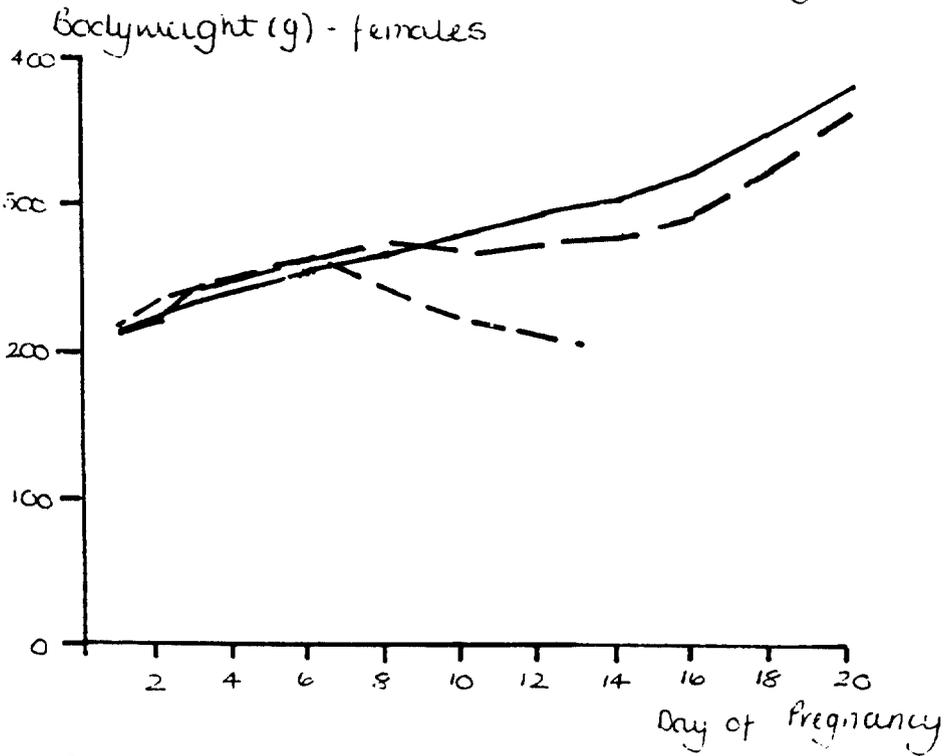
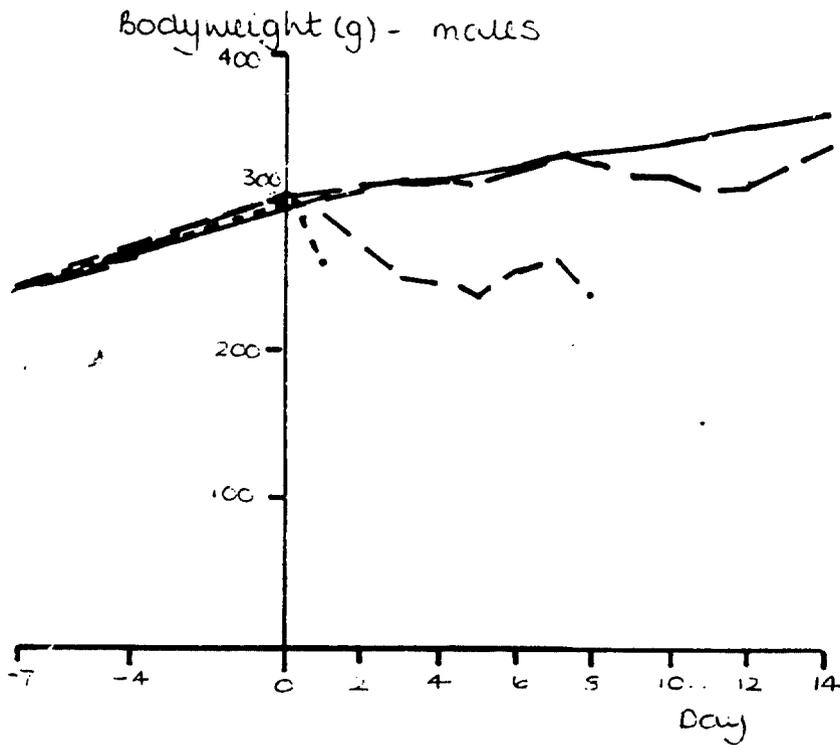
28 February 1994

FIGURE 1

Bodyweight - group mean values

- Control
- 25 ppm
- - - 100 ppm
- - - - 400 ppm

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Females exposed Days 6 to 15 of pregnancy

TABLE 1

Summary of performance

Group: Exposure (ppm):	1 Control	2♂ 25	3♂ 100	4♂ 400	1♀ Control	2♀ 25	3♀ 100	4♀ U
Category	Number of animals							
Allocated	5	5	5	5	5	5	5	5
Exposed	5	5	5	5	5	5	5	0
Dead	0	0	0	2	0	0	0	0
Killed	0	0	5	3	0	0	5	5
Completing study	5	5	0	0	5	5	0	0
Total no. exposures	10	10	6	1	10	10	7	0
Non-pregnant	-	-	-	-	0	0	1	1
Total resorption	-	-	-	-	0	0	2	0
With live young at Day 13	-	-	-	-	0	0	2	4
With live young at Day 20	-	-	-	-	5	5	0	0

U Not exposed

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TABLE 2
Clinical signs during exposure

Group / exposure ppm	Observation	Exposure number																		
		Male					Female													
		1	2	3	4	5	6	7	8	9	10									
1 Control	No abnormality detected	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2 25	No abnormality detected Eyes half closed/ closed Licking inside mouth Occasional twitching of head	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3 100	Eyes half closed/ closed Licking inside mouth Lacrimation Gaspings Exaggerated breathing of head Occasional twitching of head	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
4 400	Prone posture Eyes half closed/ closed Lacrimation Exaggerated breathing	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Females allocated to the high dose group were not exposed on the basis of the adverse response seen in males after one exposure. The remaining high exposure males were sacrificed prior to exposure no. 2.

Intermediate dose animals were sacrificed prior to exposure no. 7 for males and exposure no. 8 for females, due to poor condition (treatment related)

TABLE 3

Bodyweight - group mean daily values (g)

Day	Group / exposure (ppm)			
	1♂ Control	2♂ 25	3♂ 100	4♂ 400
-7	236	239	241	239
-4	264	266	269	267
E 0	295	303	307	305
1	303	308	292	260
2	309	313	270	
3	315	315	250	
4	315	316	248	
5 X	319	213	238	
6 X	325	324	254	
7	331	334	263	
8	335	326	239	
9	338	319		
10	342	319		
11	348	310		
12 X	352	313		
13 X	354	325		
14 X	361	335		

E First day of exposure
X Animals withdrawn from exposure

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TABLE 4

Bodyweight during pregnancy - group mean values

Group/ exposure (ppm)	No. of animals	Bodyweight (g) at Day of pregnancy											
		1	2	3	6E	8	10	12	14	16	18	20	
1 Control	5	213	225	235	253	264	279	293	302	321	350	380	
2 25	5	213	222	237	260	270	265	271	276	294	323	361	
3 100	4	217	231	243	264	246	221	213	205	S			
4 U	4	217	227	242	261	278	288	304	311	S			

E First day of exposure
S Bodyweight at sacrifice Day 13 of pregnancy
U not exposed

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TABLE 5

Food consumption - group mean values (g/rat/day)

Males

Day	Group / exposure (ppm)			
	1♂ Control	2♂ 25	3♂ 100	4♂ 400
P	30	32	31	32
1	32	31	19	1
2	29	29	8	
3	30	26	3	
4	28	25	7	
5	29	22	4	
6 X	28	28	15	
7 X	30	31	20	
8	28	22	8	
9	27	16		
10	28	18		
11	29	16		
12	30	19		
13 X	29	27		
14 X	29	30		

P Pre- exposure mean

E First day of exposure

X Animals withdrawn from exposure

Females

Day post coitum	Group / exposure (ppm)			
	1♀ Control	2♀ 25	3♀ 100	4♀ U
1	23	20	23	20
2	21	22	22	23
3- 5	23	23	25	24
6- 7	24	22	11	26
8- 9	25	18	5	25
10-11	26	18	5	28
12-13	25	17	14@	32@
14-15	28	20		
16-17	30	26		
18-19	28	26		

Females exposed Days 6 to 15 post coitum inclusive

U Not exposed

@ Day 12 only, animals sacrificed Day 13

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TABLE 6

Water consumption - group mean values (g/rat/day)

Males

Day	Group / exposure (ppm)			
	1♂ Control	2♂ 25	3♂ 100	4♂ 400
P	32	34	34	34
1	33	34	25	3
2	30	31	11	
3	32	29	6	
4	30	31	14	
5	31	25	45	
6 X	32	34	29	
7 X	33	35	32	
8	31	27	8	
9	30	21		
10	32	27		
11	33	20		
12	36	28		
13 X	32	40		
14 X	30	36		

P Pre- exposure mean

E First day of exposure

X Animals withdrawn from exposure

Females

Days	Group / exposure (ppm)			
	1♀ Control	2♀ 25	3♀ 100	4♀ U
1	37	36	42	36
2	34	40	43	37
3- 5	32	39	44	33
6- 7	29	30	20	32
8- 9	32	27	12	30
10-11	33	26	11	32
12-13	32	27	15@	33@
14-15	40	34		
16-17	43	47		
18-19	41	53		

Females exposed Days 6 to 15 post coitum inclusive

U Not exposed

@ Day 12 only, animals sacrificed Day 13

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TABLE 7

Litter data - group mean values - Day 20 sacrifice

Category	Group/Exposure (ppm)	
	1 Control	2 25
With live young	5	5
Corpora lutea / Dam	14.6	14.6
Implantations / Dam	14.0	14.4
Pre-imp loss %	3.8	1.3
E.D.E.S	1.4	0.6
L.E.D.S	0.0	0.0
Total E.D.S	1.4	0.6
Post-imp loss %	9.9	4.2
Live young / Dam	12.6	13.8
Litter weight	50.31	52.09
Mean foetal weight	3.99	3.78
EMBRYONIC DEATHS		
Total	0	2
	1	3
	2	-
	3	-
=> 4	-	-
Early	0	2
	1	3
	2	-
	3	-
=> 4	-	-
Late	0	5
	1	-
	2	-
	3	-
=> 4	-	-

E.D.E.S Early embryonic deaths
L.E.D.S Late embryonic deaths

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TABLE 8

Litter data - group mean values - Day 13 sacrifice

Category	Group/Exposure(ppm)	
	3 100	4 Untreated
Pregnant dams	4	4
Corpora lutea / Dam	14.5	15.3
Implantations / Dam	14.3	14.5
Pre-imp loss %	1.5	4.4
E.D.E.S	7.5	2.0
Post-imp loss %	53.9	12.0
Live young / Dam	6.8	12.5
Litter weight	NR	NR
Mean foetal weight	NR	NR
EMBRYONIC DEATHS		
Total (early)	0	2
	1	1
	2	-
	3	-
=> 4	2	1

E.D.E.S Early embryonic deaths
NR Not recordable

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 11♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1-8
Sneezing 4
Gasping 5, 6, 9
Brown staining around snout 5

KILLED DAY 9

MACROSCOPIC FINDINGS

LYMPH NODES - CERVICAL
Enlarged: 7mm
LYMPH NODES - DEEP CERVICAL
Enlarged: 6mm
LUNGS
Not collapsed
LYMPH NODES - TRACHEOBRONCHIAL
Enlarged: 3mm
ADIPOSE TISSUE
Minimal
SMALL INTESTINE
Gaseous distension: (Minimal)
CAECUM
Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 12♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1-8
Sneezing 4
Gasping 4, 5, 9

KILLED DAY 9

MACROSCOPIC FINDINGS

LYMPH NODES - CERVICAL
Enlarged: 8mm
LYMPH NODES - DEEP CERVICAL
Enlarged: 3mm
ADIPOSE TISSUE
Minimal
STOMACH
Contents minimal
Gaseous distension
SMALL INTESTINE
Gaseous distension
CAECUM
Gaseous distension: (Severe)

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 13♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1-9
Sneezing 4
Gasping 5
Brown staining around snout 5

KILLED DAY 9

MACROSCOPIC FINDINGS

LYMPH NODES - CERVICAL
 Enlarged: 8mm
LYMPH NODES - DEEP CERVICAL
 Enlarged: 5mm
LUNGS
 Not collapsed
ADIPOSE TISSUE
 Minimal
LIVER
 Pale subcapsular area/s: (One) Left lobe 2mm
STOMACH
 Contents minimal
 Gaseous distension
SMALL INTESTINE
 Gaseous distension
CAECUM
 Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 14♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1-8
Sneezing 4,5
Gasping 4,5,9

KILLED DAY 9

MACROSCOPIC FINDINGS

LYMPH NODES - CERVICAL

Enlarged: 7mm

LYMPH NODES - DEEP CERVICAL

Enlarged: 6mm

LUNGS

Not collapsed

ADIPOSE TISSUE

Minimal

LIVER

Pale subcapsular area/s - median cleft: (One) 2mm

Swollen: Anterior caudate lobe

Small: Posterior caudate lobe

Pale: Posterior caudate lobe

Haemorrhagic: Anterior caudate lobe

STOMACH

Contents minimal

Gaseous distension

SMALL INTESTINE

Gaseous distension

CAECUM

Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 15♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1-8
Sneezing 4
Gasping 5,9

KILLED DAY 14

MACROSCOPIC FINDINGS

SKIN ALOPECIA
Hindlimb/s: (Minimal , Diffuse)
LYMPH NODES - CERVICAL
Enlarged: 7mm
LYMPH NODES - DEEP CERVICAL
Enlarged: 4mm
LUNGS
Not collapsed
LYMPH NODES - TRACHEOBRONCHIAL
Enlarged: 3mm
GASTRO-INTESTINAL TRACT
Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 400 ppm
Rat No/Sex: 16♂ (Intercurrent)

CLINICAL SIGNS (Days)

Brown staining around snout 1,2
Yellow staining of urogenital region 1
Noisy respiration 1
Gasping 2
Brown staining under chin 2
Brown staining under front paws 2
Lethargic 2

KILLED DAY 2

MACROSCOPIC FINDINGS

FUR

Stained - perinasal region: (Red , Brown)
Stained - perioral region: (Red , Brown)

STOMACH

Empty

CAECUM

Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 400 ppm
Rat No/Sex: 17♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1
Brown staining around snout 2
Gasping 2
Brown staining under chin 2
Brown staining under front paws 2
Lethargic 2

KILLED DAY 2

MACROSCOPIC FINDINGS

FUR Stained - perinasal region: (Brown)
STOMACH Empty
CAECUM_s Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride

Dosage Level: 400 ppm

Rat No/Sex: 18♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1

DEAD DAY 2

MACROSCOPIC FINDINGS

Found dead

FUR

Stained - perinasal region: (Minimal , Red , Brown)

SUBCUTIS

Congested

STOMACH

Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 400 ppm
Rat No/Sex: 19♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1
Brown staining around snout 1

DEAD DAY 2

MACROSCOPIC FINDINGS

Found dead

FUR

 Stained - perinasal region: (Brown)

 Stained - perioral region: (Brown)

 Stained - forepaw/s: (Brown)

LUNGS

 Congested

STOMACH

 Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 400 ppm
Rat No/Sex: 20♂ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 1
Brown staining around snout 1, 2
Gasping 2
Brown staining under chin 2
Brown staining under front paws 2

KILLED DAY 2

MACROSCOPIC FINDINGS

LYMPH NODES - CERVICAL

Enlarged: 9mm

STOMACH

Gaseous distension

SMALL INTESTINE

Gaseous distension

CAECUM

Gaseous distension

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 31♀ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 6-13
Sneezing 8
Gasping 8, 9, 10
Walking with arched back 12, 13
Occasionally twitching head 12, 13

KILLED DAY 13 POST COITUM

MACROSCOPIC FINDINGS

LUNGS

a few haemorrhagic areas (minimal) (2x2mm)

NON-PREGNANT

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 32♀ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 6-13
Sneezing 8
Gasping 9, 10
Brown staining under chin 9
Brown staining around snout 9, 10
Walking with arched back 12, 13
Occasionally twitching head 12, 13

KILLED DAY 13 OF PREGNANCY

MACROSCOPIC FINDINGS

LUNGS -
 a, few small red fluid filled cysts (1x1mm)
OVARIES -
 contained 13 corpora lutea
UTERUS -
 contained 11 live young, 2 embryonic deaths

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 33♀ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 6-12
Sneezing 8
Brown staining under chin 8, 9
Gasping 9, 10, 11, 13
Brown staining around snout 9, 10, 11, 13
Walking with arched back 12, 13
Occasionally twitching head 12, 13
Yellow staining urogenital region 12
Swollen abdomen 13

KILLED DAY 13 OF PREGNANCY

MACROSCOPIC FINDINGS

FUR -
brown staining nasal region
yellow staining anogenital region
ABDOMEN -
distended
LUNGS -
a few haemorrhagic areas (1mm)
STOMACH -
gaseous distension
GASTROINTESTINAL TRACT -
gaseous distension
OVARIES -
contained 17 corpora lutea
UTERUS -
contained 16 live young
All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 34♀ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 6-13
Sneezing 8
Gasping 8, 9, 10
Brown staining under chin 9
Brown staining around snout 9
Walking with arched back 12, 13
Occasionally twitching head 12, 13

KILLED DAY 13 OF PREGNANCY

MACROSCOPIC FINDINGS

LUNGS
a few small red fluid filled cysts (1x2mm)
ILEUM
gaseous distension
CAECUM
gaseous distension
COLON
gaseous distension
OVARIES -
contained 14 corpora lutea
UTERUS -
contained 14 embryonic deaths

All the other organs and tissues appeared normal.

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APPENDIX 1

Compound: acetic anhydride
Dosage Level: 100 ppm
Rat No/Sex: 35♀ (Intercurrent)

CLINICAL SIGNS (Days)

Noisy respiration 6-13
Sneezing 8
Gasping 9, 10
Red staining urogenital region 12
Brown staining urogenital region 13
Walking with arched back 12, 13
Occasionally twitching head 12, 13

KILLED DAY 13 OF PREGNANCY

MACROSCOPIC FINDINGS

LUNGS

a few small red fluid filled cysts (1x2mm)

UROGENITAL

brown staining

OVARIES -

contained 14 corpora lutea

UTERUS -

contained 14 embryonic deaths

All the other organs and tissues appeared normal.

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APPENDIX 2

Foetal abnormalities at autopsy - individual observations

Animal number	Litter size	Foetus number	Observations
Group 1: Control - Day 20			
22	14	(13)	Subcutaneous oedema, marked. (M)
Group 2: 25ppm - Day 20			
No abnormalities detected			
Group 3: 100ppm - Day 13			
No abnormalities detected			
Group 4: untreated - Day 13			
No abnormalities detected			

(M) Indicates probable malformation.
Only litters with abnormal foetuses are reported.

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APPENDIX 3

Chamber concentration of acetic anhydride (ppm)

Exposure number	Group		
	2 (Low dose)	3 (Inter. dose)	4 (High dose)
1 Males only	20	102	410
	20	102	397
	21	103	391
	23	104	420
	23	105	411
	23	107	410
Mean	22	104	407
2	22	96	
	19	101	
	20	98	
	23	103	
	22	101	
	23	104	
Mean	22	100	
3	23	99	
	21	91	
	26	96	
	22	100	
	25	102	
	25	(56)	
	25		
Mean	24	98	
4	21	99	
	23	99	
	25	101	
	24	101	
	27	103	
	25	106	
Mean	24	102	

1 Injection error - value excluded from mean

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APPENDIX 3

Chamber concentration of acetic anhydride (ppm)

Exposure number	Group		
	2 (Low dose)	3 (Inter. dose)	4 (High dose)
5	21	103	
	21	101	
	26	107	
	26	102	
	25	108	
	24	108	
Mean	24	105	
6 Females only	26	108	
	27	110	
	26	108	
	27	105	
	24	108	
	24	107	
Mean	26	108	
7 Females only	25	106	
	24	108	
	26	110	
	24	111	
	30	111	
	27	112	
Mean	26	110	
8	25	109	
	23	107	
	25	106	
	24	108	
	27	112	
	25	104	
Mean	25	108	

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APPENDIX 3

Chamber concentration of acetic anhydride (ppm)

Exposure number	Group		
	2 (Low dose)	3 (Inter. dose)	4 (High dose)
9	24 24 24 24 23 25		
Mean	24		
10	28 32 21 22 21 23 23 24		
mean	24		
11	20 27 28 25 23 23		
Mean	24		
12 Males only	21 24 24 22 21 23 22 21 23		
Mean	22		
Mean: Females	24	105	
Mean: Males	24	103	407

² sample lost through GC fault