Summary of Feeding Carcinogenicity Study of 1-Chloro-2,4-Dinitrobenzene in F344 Rats

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Japan Bioassay Laboratory

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Labour of Japan. The tests were conducted by Japan Bioassay Laboratory (JBL) and the report was prepared by JBL and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Labour of Japan on August 19, 1992.

This English Summary was translated by JBL from Japanese complete report.

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Purpose, materials and methods

1-Chloro-2,4-dinitrobenzene (CDNB : CAS No. 97-00-7) is a yellow crystal with a melting point of 51°C. It is insoluble in water and soluble in ether, benzene, carbon disulfide, and hot ethanol.

The carcinogenicity and chronic toxicity of CDNB were examined in F344/DuCrj rats. Groups of test animals were administered CDNB in their diets for 2 years (104 weeks). Each group consisted of either 50 male or 50 female rats. The dietary concentrations of CDNB were 0, 320, 800 or 2000 ppm (w/w). Both sexes were administered each concentration of CDNB. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the CDNB used in these experiments was confirmed by mass spectrometry. It was analyzed by infrared spectrometry, ultraviolet spectrometry and gas chromatography before and after its use to affirm its stability. The concentrations of CDNB in the diet were determined by gas chromatography at the time of preparation and on the 7th day after preparation while stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 2 weeks thereafter. Animals found dead, or in a moribund state, or surviving to the end of the 2-year administration period underwent complete necropsy. Urinalysis was performed near the end of the administration period. Hematology and blood biochemistry analysis were performed at the terminal necropsy: surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five μm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Positive dose-response trends of CDNB induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present study was conducted with reference to the Organisation for Economic Co-operation and Development

(OECD) Good Laboratory Practice and the OECD Guideline for Testing of Chemicals 451 “Carcinogenicity Studies”.

Results

No significant differences in survival rates were found between any of the groups administered CDNB and their respective controls. Yellow urine and yellow coloration of the fur were observed in all the CDNB-fed groups of both sexes in the latter half of the administration period. Body weights were decreased in the males fed 2000 ppm CDNB and females fed 800 and 2000 ppm CDNB throughout the administration period. Body weights were also reduced in females fed 320 ppm CDNB in the latter part of the administration period. Food consumption of males fed 2000 ppm CDNB was decreased throughout the administration period. Food consumption of females fed 2000 ppm CDNB was decreased untill the 70th week of the administration period. Mean corpuscular volume and mean corpuscular hemoglobin were decreased in males fed 2000 ppm CDNB and in all CDNB-fed female groups. Hemoglobin concentration was decreased in females fed 2000 ppm CDNB. Plasma level of urea nitrogen was increased in females fed 800 ppm CDNB and above and glutamic oxaloacetic transaminase was increased in females fed 2000 ppm CDNB. There were no CDNB related changes in urinalysis parameters or organ weights in any of the CDNB administered groups.

The incidence of renal cell adenoma was increased in the 2000 ppm CDNB-fed males. The incidence of adenocarcinoma in the mammary gland was dose dependently increased in CDNB-fed females. The incidence of preputial adenoma was increased in the 2000 ppm CDNB-fed males, however this incidence was similar to the range of JBL historical control data. Non-neoplastic lesions were also found: The incidences of hemosiderin deposition and extramedullary hematopoiesis in the spleen was significantly increased in females fed 800 and 2000 ppm CDNB, and hyperplasia in the forestomach was significantly increased in both males and females fed 2000 ppm CDNB.

Conclusions

There was clear evidence for carcinogenicity of 1-chloro-2,4-dinitrobenzene in male and female rats.

Incidences of selected neoplastic lesions of male rats in the 2-year feed carcinogenicity study of 1-chloro-2,4-dinitrobenzene

Dose (ppm)		0	320	800	2000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
skin/appendage	keratoacanthoma	3 [a)]	0	0	1		
subcutis	fibroma	3	4	6	4		
lung	bronchiolar-alveolar adenoma	3	2	2	4		
liver	hepatocellular adenoma	3	0	2	3		
kidney	renal cell adenoma	0	1	1	6 *	↑ ↑	↑ ↑
pituitary	adenoma	16	21	11	10		↓
thyroid	C-cell adenoma	9	4	7	7		
adrenal	pheochromocytoma	12	8	11	3 *		↓
testis	interstitial cell tumor	41	45	47	45		
mammary	fibroadenoma	1	2	6	2		
preputial gland	adenoma	0	2	4	5 *	↑	↑
peritoneum	mesothelioma	3	1	4	1		
malignant tumor							
spleen	mononuclear cell leukemia	5	2	1	2		

Incidences of selected neoplastic lesions of female rats in the 2-year feed carcinogenicity study of 1-chloro-2,4-dinitrobenzene

Dose (ppm)		0	320	800	2000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
subcutis	fibroma	2	3	2	1		
pituitary	adenoma	21	19	22	17		
thyroid	C-cell adenoma	4	4	6	7		
adrenal	pheochromocytoma	2	5	8	3		
uterus	endometrial stromal polyp	7	6	7	6		
mammary gland	fibroadenoma	10	9	8	10		
clitoral gland	adenoma	1	0	2	3		
malignant tumor							
spleen	mononuclear cell leukemia	8	3	2	4		
mammary gland	adenocarcinoma	1	1	1	5	↑ ↑	↑

[a)] :Numer of examined animal of skin/appendage is 49.

Significant difference

* : p≦0.05		** : p≦0.01		(Fisher test)
↑ : p≦0.05	increase	↑ ↑ : p≦0.01	increase	(Peto, Cochran-Armitage test)
↓ : p≦0.05	decrease	↓ ↓ : p≦0.01	decrease	(Cochran-Armitage test)

SELECTED TABLES

TABLE 10 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN MALE RAT

(TWO-YEAR STUDIES)

Week-Day on Study	Control Av.Wt.	Control No.of Surviv. <50>	320 ppm Av.Wt.	320 ppm % of cont. <50>	320 ppm No.of Surviv.	800 ppm Av.Wt.	800 ppm % of cont. <50>	800 ppm No.of Surviv.	2000 ppm Av.Wt.	2000 ppm % of cont. <50>	2000 ppm No.of Surviv.
0-0	131 (50)	50/50	131 (50)	100	50/50	131 (50)	100	50/50	131 (50)	100	50/50
1-7	169 (50)	50/50	169 (50)	100	50/50	168 (50)	99	50/50	157 (50)	93	50/50
2-7	201 (50)	50/50	201 (50)	100	50/50	198 (50)	99	50/50	188 (50)	94	50/50
3-7	228 (50)	50/50	228 (50)	100	50/50	226 (50)	99	50/50	215 (50)	94	50/50
4-7	249 (50)	50/50	248 (50)	100	50/50	248 (50)	100	50/50	235 (50)	94	50/50
5-7	266 (50)	50/50	266 (50)	100	50/50	266 (50)	100	50/50	253 (50)	95	50/50
6-7	279 (50)	50/50	280 (50)	100	50/50	280 (50)	100	50/50	266 (50)	95	50/50
7-7	294 (50)	50/50	296 (50)	101	50/50	297 (50)	101	50/50	282 (50)	96	50/50
8-7	305 (50)	50/50	306 (50)	100	50/50	307 (50)	101	50/50	292 (50)	96	50/50
9-7	317 (50)	50/50	319 (50)	101	50/50	319 (50)	101	50/50	303 (50)	96	50/50
10-7	324 (50)	50/50	327 (50)	101	50/50	325 (50)	100	50/50	310 (50)	96	50/50
11-7	333 (50)	50/50	336 (50)	101	50/50	334 (50)	100	50/50	317 (50)	95	50/50
12-7	339 (50)	50/50	342 (50)	101	50/50	339 (50)	100	50/50	323 (50)	95	50/50
13-7	345 (50)	50/50	349 (50)	101	50/50	346 (50)	100	50/50	329 (50)	95	50/50
14-7	350 (50)	50/50	353 (50)	101	50/50	350 (50)	100	50/50	334 (50)	95	50/50
16-7	361 (50)	50/50	364 (50)	101	50/50	360 (50)	100	50/50	342 (50)	95	50/50
18-7	371 (50)	50/50	374 (50)	101	50/50	371 (50)	100	50/50	351 (50)	95	50/50
20-7	380 (50)	50/50	383 (50)	101	50/50	379 (50)	100	50/50	359 (50)	94	50/50
22-7	389 (50)	50/50	393 (50)	101	50/50	389 (50)	100	50/50	367 (50)	94	50/50
24-7	396 (50)	50/50	400 (50)	101	50/50	397 (50)	100	50/50	374 (50)	94	50/50
26-7	404 (50)	50/50	408 (50)	101	50/50	405 (50)	100	50/50	381 (50)	94	50/50
28-7	410 (50)	50/50	415 (50)	101	50/50	412 (50)	100	50/50	387 (50)	94	50/50
30-7	417 (50)	50/50	423 (50)	101	50/50	420 (50)	101	50/50	394 (50)	94	50/50
32-7	422 (50)	50/50	427 (50)	101	50/50	423 (50)	100	50/50	398 (50)	94	50/50
34-7	429 (50)	50/50	432 (50)	101	50/50	431 (50)	100	50/50	403 (50)	94	50/50
36-7	433 (50)	50/50	437 (50)	101	50/50	435 (50)	100	50/50	407 (50)	94	50/50
38-7	438 (50)	50/50	445 (50)	102	50/50	440 (50)	100	50/50	414 (50)	95	50/50
40-7	445 (50)	50/50	450 (50)	101	50/50	447 (50)	100	50/50	419 (50)	94	50/50
42-7	449 (50)	50/50	455 (50)	101	50/50	451 (50)	100	50/50	424 (50)	94	50/50
44-7	453 (50)	50/50	458 (50)	101	50/50	455 (50)	100	50/50	428 (50)	94	50/50
46-7	457 (50)	50/50	462 (50)	101	50/50	459 (50)	100	50/50	431 (50)	94	50/50
48-7	461 (50)	50/50	466 (50)	101	50/50	463 (50)	100	50/50	436 (50)	95	50/50
50-7	460 (50)	50/50	469 (50)	102	50/50	467 (50)	102	50/50	444 (50)	97	50/50
52-7	465 (50)	50/50	470 (50)	101	50/50	467 (50)	100	50/50	440 (50)	95	50/50
54-7	469 (50)	50/50	472 (50)	101	50/50	470 (50)	100	50/50	441 (50)	94	50/50
56-7	473 (50)	50/50	475 (50)	100	50/50	472 (50)	100	50/50	444 (50)	94	50/50
58-7	476 (50)	50/50	478 (50)	100	50/50	474 (50)	100	50/50	447 (50)	94	50/50
60-7	478 (50)	50/50	481 (50)	101	50/50	476 (50)	100	50/50	446 (50)	93	50/50
62-7	481 (50)	50/50	483 (50)	100	50/50	479 (50)	100	50/50	450 (50)	94	50/50
64-7	483 (50)	50/50	487 (50)	101	50/50	480 (50)	99	50/50	451 (50)	93	50/50
66-7	484 (50)	50/50	487 (50)	101	50/50	481 (50)	99	50/50	453 (50)	94	50/50
68-7	485 (50)	50/50	490 (50)	101	50/50	482 (50)	99	50/50	453 (50)	93	50/50
70-7	485 (50)	50/50	491 (50)	101	50/50	483 (50)	100	50/50	455 (50)	94	50/50
72-7	486 (50)	50/50	491 (50)	101	50/50	482 (50)	99	50/50	456 (50)	94	50/50
74-7	488 (50)	50/50	492 (50)	101	50/50	484 (50)	99	50/50	459 (50)	94	50/50
76-7	486 (50)	50/50	490 (50)	101	50/50	483 (50)	99	50/50	457 (50)	94	50/50
78-7	488 (48)	48/50	489 (50)	100	50/50	482 (50)	99	50/50	456 (50)	93	50/50
80-7	486 (48)	48/50	488 (49)	100	49/50	479 (50)	99	50/50	453 (50)	93	50/50
82-7	488 (46)	46/50	482 (49)	99	49/50	476 (50)	98	50/50	450 (50)	92	50/50
84-7	483 (45)	45/50	478 (49)	99	49/50	472 (50)	98	50/50	448 (50)	93	50/50
86-7	479 (45)	45/50	470 (49)	98	49/50	467 (49)	97	49/50	445 (50)	93	50/50
88-7	479 (44)	44/50	475 (46)	99	46/50	462 (49)	96	49/50	440 (49)	92	49/50
90-7	478 (44)	44/50	474 (46)	99	46/50	457 (49)	96	49/50	439 (48)	92	48/50
92-7	475 (44)	44/50	470 (45)	99	45/50	467 (46)	98	46/50	435 (47)	92	47/50
94-7	472 (42)	42/50	464 (44)	98	44/50	463 (46)	98	46/50	436 (46)	92	46/50
96-7	466 (41)	41/50	462 (43)	99	43/50	458 (45)	98	45/50	431 (45)	92	45/50
98-7	469 (39)	39/50	455 (43)	97	43/50	452 (44)	96	44/50	424 (45)	90	45/50
100-7	461 (38)	38/50	440 (41)	95	41/50	444 (43)	96	43/50	418 (43)	91	43/50
102-7	455 (37)	37/50	436 (38)	96	38/50	445 (42)	98	42/50	418 (42)	92	42/50
104-7	445 (36)	36/50	439 (35)	99	35/50	437 (42)	98	42/50	408 (40)	92	39/50

< >:No.of effective animals, ( ):No.of measured animals Av.Wt.: g

TABLE 11 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN FEMALE RAT

(TWO-YEAR STUDIES)

Week-Day on Study	Control Av.Wt.	Control No.of Surviv. <50>	320 ppm Av.Wt.	320 ppm % of cont. <50>	320 ppm No.of Surviv.	800 ppm Av.Wt.	800 ppm % of cont. <50>	800 ppm No.of Surviv.	2000 ppm Av.Wt.	2000 ppm % of cont. <50>	2000 ppm No.of Surviv.
0-0	106 (50)	50/50	106 (50)	100	50/50	106 (50)	100	50/50	106 (50)	100	50/50
1-7	125 (50)	50/50	125 (50)	100	50/50	123 (50)	98	50/50	118 (50)	94	50/50
2-7	140 (50)	50/50	139 (50)	99	50/50	136 (50)	97	50/50	132 (50)	94	50/50
3-7	151 (50)	50/50	150 (50)	99	50/50	147 (50)	97	50/50	142 (50)	94	50/50
4-7	161 (50)	50/50	158 (50)	98	50/50	156 (50)	97	50/50	149 (50)	93	50/50
5-7	169 (50)	50/50	167 (50)	99	50/50	165 (50)	98	50/50	156 (50)	92	50/50
6-7	175 (50)	50/50	172 (50)	98	50/50	169 (50)	97	50/50	160 (50)	91	50/50
7-7	181 (50)	50/50	179 (50)	99	50/50	175 (50)	97	50/50	165 (50)	91	50/50
8-7	185 (50)	50/50	182 (50)	98	50/50	179 (50)	97	50/50	167 (50)	90	50/50
9-7	191 (50)	50/50	187 (50)	98	50/50	184 (50)	96	50/50	171 (50)	90	50/50
10-7	193 (50)	50/50	190 (50)	98	50/50	186 (50)	96	50/50	172 (50)	89	50/50
11-7	198 (50)	50/50	194 (50)	98	50/50	190 (50)	96	50/50	176 (50)	89	50/50
12-7	200 (50)	50/50	195 (50)	98	50/50	192 (50)	96	50/50	178 (50)	89	50/50
13-7	203 (50)	50/50	198 (50)	98	50/50	194 (50)	96	50/50	180 (50)	89	50/50
14-7	204 (50)	50/50	199 (50)	98	50/50	195 (50)	96	50/50	181 (50)	89	50/50
16-7	210 (50)	50/50	203 (50)	97	50/50	198 (50)	94	50/50	184 (50)	88	50/50
18-7	213 (50)	50/50	207 (50)	97	50/50	201 (50)	94	50/50	186 (50)	87	50/50
20-7	216 (50)	50/50	210 (50)	97	50/50	203 (50)	94	50/50	189 (50)	88	50/50
22-7	220 (50)	50/50	213 (50)	97	50/50	206 (50)	94	50/50	191 (50)	87	50/50
24-7	223 (50)	50/50	216 (50)	97	50/50	208 (50)	93	50/50	193 (50)	87	50/50
26-7	227 (50)	50/50	220 (50)	97	50/50	212 (50)	93	50/50	196 (50)	86	50/50
28-7	231 (50)	50/50	222 (50)	96	50/50	215 (50)	93	50/50	197 (50)	85	50/50
30-7	233 (50)	50/50	225 (50)	97	50/50	216 (50)	93	50/50	199 (50)	85	50/50
32-7	236 (50)	50/50	227 (50)	96	50/50	219 (50)	93	50/50	201 (50)	85	50/50
34-7	241 (50)	50/50	230 (50)	95	50/50	222 (50)	92	50/50	205 (50)	85	50/50
36-7	242 (50)	50/50	233 (50)	96	50/50	223 (49)	92	49/50	206 (50)	85	50/50
38-7	246 (50)	50/50	236 (50)	96	50/50	228 (49)	93	49/50	209 (50)	85	50/50
40-7	251 (50)	50/50	240 (50)	96	50/50	231 (49)	92	49/50	212 (50)	84	50/50
42-7	255 (50)	50/50	244 (50)	96	50/50	234 (49)	92	49/50	214 (50)	84	50/50
44-7	256 (50)	50/50	245 (50)	96	50/50	235 (49)	92	49/50	216 (50)	84	50/50
46-7	258 (50)	50/50	247 (50)	96	50/50	237 (49)	92	49/50	218 (50)	84	50/50
48-7	263 (50)	50/50	250 (50)	95	50/50	241 (49)	92	49/50	220 (50)	84	50/50
50-7	266 (50)	50/50	254 (50)	95	50/50	246 (49)	92	49/50	230 (50)	86	50/50
52-7	270 (50)	50/50	256 (50)	95	50/50	246 (49)	91	49/50	226 (49)	84	49/50
54-7	275 (50)	50/50	260 (50)	95	50/50	250 (49)	91	49/50	227 (49)	83	49/50
56-7	279 (50)	50/50	264 (50)	95	50/50	252 (49)	90	49/50	230 (49)	82	49/50
58-7	284 (50)	50/50	267 (50)	94	50/50	255 (49)	90	49/50	233 (49)	82	49/50
60-7	287 (50)	50/50	270 (50)	94	50/50	257 (49)	90	49/50	236 (49)	82	49/50
62-7	291 (50)	50/50	274 (50)	94	50/50	262 (49)	90	49/50	241 (49)	83	49/50
64-7	298 (50)	50/50	281 (50)	94	50/50	267 (49)	90	49/50	245 (49)	82	49/50
66-7	302 (50)	50/50	285 (50)	94	50/50	271 (49)	90	49/50	249 (49)	82	49/50
68-7	306 (50)	50/50	290 (50)	95	50/50	276 (49)	90	49/50	252 (49)	82	49/50
70-7	311 (50)	50/50	296 (50)	95	50/50	281 (49)	90	49/50	257 (49)	83	49/50
72-7	315 (50)	50/50	300 (50)	95	50/50	283 (49)	90	49/50	262 (49)	83	49/50
74-7	316 (49)	49/50	305 (50)	97	50/50	289 (49)	91	49/50	268 (48)	85	48/50
76-7	325 (47)	47/50	309 (50)	95	50/50	292 (49)	90	49/50	270 (48)	83	48/50
78-7	331 (46)	46/50	312 (50)	94	50/50	297 (49)	90	49/50	274 (48)	83	48/50
80-7	331 (46)	46/50	313 (50)	95	50/50	297 (49)	90	49/50	275 (47)	83	47/50
82-7	331 (46)	46/50	315 (50)	95	50/50	299 (49)	90	49/50	277 (47)	84	47/50
84-7	331 (46)	46/50	317 (49)	96	49/50	302 (49)	91	49/50	278 (47)	84	47/50
86-7	333 (46)	45/50	320 (49)	96	49/50	303 (49)	91	49/50	282 (46)	85	45/50
88-7	334 (45)	45/50	321 (49)	96	49/50	301 (48)	90	48/50	285 (45)	85	45/50
90-7	338 (45)	45/50	322 (49)	95	49/50	301 (48)	89	48/50	288 (45)	85	45/50
92-7	340 (44)	44/50	322 (48)	95	48/50	307 (47)	90	47/50	289 (45)	85	45/50
94-7	340 (44)	44/50	329 (46)	97	46/50	308 (47)	91	46/50	291 (45)	86	45/50
96-7	341 (44)	44/50	328 (46)	96	45/50	311 (46)	91	46/50	292 (44)	86	44/50
98-7	341 (44)	44/50	331 (45)	97	45/50	311 (44)	91	44/50	292 (43)	86	43/50
100-7	334 (43)	43/50	332 (45)	99	45/50	309 (44)	93	44/50	290 (42)	87	41/50
102-7	331 (42)	42/50	334 (45)	101	45/50	310 (44)	94	44/50	296 (37)	89	37/50
104-7	327 (42)	42/50	327 (43)	100	43/50	306 (44)	94	44/50	289 (35)	88	35/50

< >:No.of effective animals, ( ):No.of measured animals Av.Wt.: g

TABLE 12 FOOD CONSUMPTION IN MALE RAT

(TWO-YEAR STUDIES)

Week-Day on Study	Control Av.FC.	Control No.of Surviv. <50>	320 ppm Av.FC.	320 ppm % of cont. <50>	320 ppm No.of Surviv.	800 ppm Av.FC.	800 ppm % of cont. <50>	800 ppm No.of Surviv.	2000 ppm Av.FC.	2000 ppm % of cont. <50>	2000 ppm No.of Surviv.
1-7	14.3 (50)	50/50	13.9 (50)	97	50/50	13.6 (50)	95	50/50	11.3 (49)	79	50/50
2-7	15.3 (50)	50/50	15.2 (50)	99	50/50	15.1 (50)	99	50/50	14.2 (50)	93	50/50
3-7	15.8 (50)	50/50	15.6 (50)	99	50/50	15.6 (49)	99	50/50	14.9 (50)	94	50/50
4-7	15.7 (50)	50/50	15.6 (50)	99	50/50	15.7 (50)	100	50/50	14.8 (50)	94	50/50
5-7	15.7 (50)	50/50	15.7 (50)	100	50/50	15.8 (50)	101	50/50	14.9 (50)	95	50/50
6-7	15.2 (50)	50/50	15.4 (50)	101	50/50	15.4 (50)	101	50/50	14.8 (50)	97	50/50
7-7	15.5 (50)	50/50	15.8 (50)	102	50/50	15.5 (50)	100	50/50	15.2 (50)	98	50/50
8-7	15.4 (50)	50/50	15.6 (50)	101	50/50	15.3 (50)	99	50/50	14.5 (50)	94	50/50
9-7	15.5 (50)	50/50	15.4 (50)	99	50/50	15.5 (50)	100	50/50	14.6 (50)	94	50/50
10-7	15.1 (50)	50/50	15.3 (50)	101	50/50	15.0 (50)	99	50/50	14.5 (50)	96	50/50
11-7	15.1 (50)	50/50	15.1 (50)	100	50/50	14.9 (50)	99	50/50	14.6 (50)	97	50/50
12-7	14.7 (50)	50/50	15.1 (50)	103	50/50	14.8 (50)	101	50/50	14.1 (50)	96	50/50
13-7	14.8 (50)	50/50	14.8 (50)	100	50/50	14.6 (50)	99	50/50	14.2 (50)	96	50/50
14-7	14.5 (50)	50/50	14.5 (50)	100	50/50	14.4 (50)	99	50/50	14.1 (50)	97	50/50
16-7	14.5 (50)	50/50	14.6 (50)	101	50/50	14.7 (50)	101	50/50	14.1 (50)	97	50/50
18-7	14.7 (50)	50/50	14.9 (50)	101	50/50	14.9 (50)	101	50/50	14.1 (50)	96	50/50
20-7	15.0 (50)	50/50	15.0 (50)	100	50/50	14.9 (50)	99	50/50	14.3 (50)	95	50/50
22-7	15.0 (50)	50/50	15.1 (50)	101	50/50	15.0 (50)	100	50/50	14.3 (50)	95	50/50
24-7	15.4 (50)	50/50	15.4 (50)	100	50/50	15.5 (50)	101	50/50	14.8 (50)	96	50/50
26-7	15.8 (50)	50/50	15.9 (50)	101	50/50	15.9 (50)	101	50/50	15.3 (50)	97	50/50
28-7	15.5 (50)	50/50	15.6 (50)	101	50/50	15.7 (50)	101	50/50	14.9 (50)	96	50/50
30-7	15.4 (50)	50/50	15.6 (50)	101	50/50	15.5 (50)	101	50/50	15.1 (50)	98	50/50
32-7	15.3 (50)	50/50	15.4 (50)	101	50/50	15.3 (50)	100	50/50	14.9 (50)	97	50/50
34-7	16.1 (50)	50/50	15.9 (50)	99	50/50	16.1 (50)	100	50/50	15.5 (50)	96	50/50
36-7	15.7 (50)	50/50	15.9 (50)	101	50/50	15.8 (50)	101	50/50	15.6 (50)	99	50/50
38-7	15.7 (50)	50/50	15.9 (50)	101	50/50	16.0 (50)	102	50/50	15.5 (50)	99	50/50
40-7	16.0 (50)	50/50	16.1 (50)	101	50/50	15.9 (50)	99	50/50	15.2 (50)	95	50/50
42-7	15.9 (50)	50/50	16.1 (50)	101	50/50	15.9 (50)	100	50/50	15.6 (50)	98	50/50
44-7	16.1 (50)	50/50	16.0 (50)	99	50/50	16.0 (50)	99	50/50	15.6 (50)	97	50/50
46-7	15.9 (50)	50/50	16.1 (50)	101	50/50	15.9 (50)	100	50/50	15.6 (50)	98	50/50
48-7	15.9 (50)	50/50	16.2 (50)	102	50/50	16.1 (50)	101	50/50	15.1 (50)	95	50/50
52-7	15.8 (50)	50/50	15.7 (50)	99	50/50	15.5 (50)	98	50/50	15.0 (50)	95	50/50
54-7	16.0 (50)	50/50	15.9 (50)	99	50/50	15.8 (50)	99	50/50	15.1 (50)	94	50/50
56-7	16.0 (50)	50/50	16.1 (50)	101	50/50	15.7 (50)	98	50/50	15.3 (50)	96	50/50
58-7	15.9 (50)	50/50	16.1 (50)	101	50/50	15.8 (50)	99	50/50	15.4 (50)	97	50/50
60-7	15.9 (50)	50/50	16.2 (50)	102	50/50	15.9 (50)	100	50/50	15.3 (50)	96	50/50
62-7	16.1 (50)	50/50	16.1 (50)	100	50/50	15.8 (50)	98	50/50	15.7 (50)	98	50/50
64-7	15.8 (50)	50/50	16.1 (50)	102	50/50	15.6 (50)	99	50/50	15.0 (50)	95	50/50
66-7	15.7 (50)	50/50	16.0 (50)	102	50/50	15.6 (50)	99	50/50	15.3 (50)	97	50/50
68-7	15.5 (50)	50/50	15.9 (50)	103	50/50	15.7 (50)	101	50/50	15.1 (50)	97	50/50
70-7	15.1 (50)	50/50	15.5 (50)	103	50/50	15.2 (50)	101	50/50	14.9 (50)	99	50/50
72-7	15.3 (50)	50/50	15.6 (50)	102	50/50	14.9 (50)	97	50/50	15.0 (50)	98	50/50
74-7	15.7 (50)	50/50	15.7 (50)	100	50/50	15.6 (50)	99	50/50	14.9 (50)	95	50/50
76-7	14.9 (50)	50/50	15.4 (50)	103	50/50	15.0 (50)	101	50/50	14.6 (50)	98	50/50
78-7	15.3 (48)	48/50	15.4 (50)	101	50/50	15.4 (50)	101	50/50	14.8 (50)	97	50/50
80-7	15.4 (48)	48/50	15.4 (49)	100	49/50	15.3 (50)	99	50/50	14.8 (50)	96	50/50
82-7	15.2 (47)	46/50	15.2 (49)	100	49/50	15.3 (50)	101	50/50	14.8 (50)	97	50/50
84-7	15.6 (46)	45/50	15.5 (49)	99	49/50	15.4 (50)	99	50/50	15.1 (50)	97	50/50
86-7	15.5 (45)	45/50	15.0 (49)	97	49/50	14.9 (49)	96	49/50	14.8 (50)	95	50/50
88-7	15.3 (44)	44/50	15.3 (46)	100	46/50	14.7 (49)	96	49/50	14.1 (50)	92	49/50
90-7	15.6 (44)	44/50	15.8 (46)	101	46/50	15.0 (49)	96	49/50	14.8 (48)	95	48/50
92-7	15.2 (44)	44/50	15.7 (45)	103	45/50	15.6 (46)	103	46/50	14.6 (47)	96	47/50
94-7	15.2 (43)	42/50	15.4 (45)	101	44/50	15.6 (46)	103	46/50	14.6 (46)	96	46/50
96-7	15.6 (33)	41/50	15.8 (43)	101	43/50	15.0 (46)	96	45/50	14.4 (45)	92	45/50
98-7	15.3 (40)	39/50	15.3 (43)	100	43/50	14.5 (44)	95	44/50	14.3 (45)	93	45/50
100-7	15.2 (39)	38/50	14.3 (42)	94	41/50	14.6 (43)	96	43/50	14.4 (43)	95	43/50
104-7	14.6 (36)	36/50	15.2 (35)	104	35/50	14.2 (41)	97	42/50	13.8 (41)	95	39/50

< >:No.of effective animals,( ):No.of measured animals Av.FC.: g

TABLE 13 FOOD CONSUMPTION IN FEMALE RAT

(TWO-YEAR STUDIES)

Week-Day on Study	Control Av.FC.	Control No.of Surviv. <50>	320 ppm Av.FC.	320 ppm % of cont. <50>	320 ppm No.of Surviv.	800 ppm Av.FC.	800 ppm % of cont. <50>	800 ppm No.of Surviv.	2000 ppm Av.FC.	2000 ppm % of cont. <50>	2000 ppm No.of Surviv.
1-7	10.9 (50)	50/50	10.6 (50)	97	50/50	10.2 (50)	94	50/50	9.6 (50)	88	50/50
2-7	11.1 (50)	50/50	10.9 (50)	98	50/50	10.7 (50)	96	50/50	10.2 (50)	92	50/50
3-7	11.2 (50)	50/50	11.3 (50)	101	50/50	10.9 (50)	97	50/50	10.4 (50)	93	50/50
4-7	11.1 (50)	50/50	11.1 (50)	100	50/50	10.9 (50)	98	50/50	10.1 (50)	91	50/50
5-7	11.5 (50)	50/50	11.3 (50)	98	50/50	11.0 (50)	96	50/50	10.3 (50)	90	50/50
6-7	11.1 (49)	50/50	10.9 (50)	98	50/50	10.8 (50)	97	50/50	9.9 (50)	89	50/50
7-7	11.2 (50)	50/50	11.1 (50)	99	50/50	11.0 (50)	98	50/50	10.3 (50)	92	50/50
8-7	10.8 (50)	50/50	10.5 (50)	97	50/50	10.6 (50)	98	50/50	9.6 (50)	89	50/50
9-7	11.1 (49)	50/50	10.6 (50)	95	50/50	11.0 (49)	99	50/50	9.9 (50)	89	50/50
10-7	10.8 (50)	50/50	10.5 (50)	97	50/50	10.7 (50)	99	50/50	10.0 (50)	93	50/50
11-7	10.9 (50)	50/50	11.0 (50)	101	50/50	11.1 (50)	102	50/50	10.1 (50)	93	50/50
12-7	10.7 (50)	50/50	10.5 (50)	98	50/50	10.7 (50)	100	50/50	9.7 (50)	91	50/50
13-7	10.9 (50)	50/50	10.6 (49)	97	50/50	11.3 (50)	104	50/50	9.8 (48)	90	50/50
14-7	10.4 (50)	50/50	10.3 (50)	99	50/50	10.7 (50)	103	50/50	9.6 (50)	92	50/50
16-7	10.6 (50)	50/50	10.7 (50)	101	50/50	10.8 (50)	102	50/50	9.8 (50)	92	50/50
18-7	10.5 (50)	50/50	10.6 (50)	101	50/50	10.5 (50)	100	50/50	9.8 (50)	93	50/50
20-7	10.5 (50)	50/50	10.6 (50)	101	50/50	10.8 (49)	103	50/50	10.1 (50)	96	50/50
22-7	10.7 (50)	50/50	10.4 (50)	97	50/50	10.7 (50)	100	50/50	9.8 (50)	92	50/50
24-7	11.1 (50)	50/50	10.8 (50)	97	50/50	11.3 (50)	102	50/50	10.2 (50)	92	50/50
26-7	11.4 (50)	50/50	11.4 (50)	100	50/50	11.7 (50)	103	50/50	10.8 (50)	95	50/50
28-7	11.0 (50)	50/50	11.1 (50)	101	50/50	11.5 (50)	105	50/50	10.4 (50)	95	50/50
30-7	11.0 (48)	50/50	10.9 (50)	99	50/50	11.2 (50)	102	50/50	10.5 (50)	95	50/50
32-7	11.3 (50)	50/50	11.1 (50)	98	50/50	11.2 (50)	99	50/50	10.5 (50)	93	50/50
34-7	12.0 (50)	50/50	11.8 (50)	98	50/50	11.8 (50)	98	50/50	10.8 (50)	90	50/50
36-7	11.4 (50)	50/50	11.4 (50)	100	50/50	11.6 (49)	102	49/50	10.6 (50)	93	50/50
38-7	11.6 (50)	50/50	11.7 (50)	101	50/50	12.1 (49)	104	49/50	10.7 (50)	92	50/50
40-7	12.0 (50)	50/50	11.9 (50)	99	50/50	11.9 (49)	99	49/50	10.9 (50)	91	50/50
42-7	12.0 (50)	50/50	11.8 (50)	98	50/50	11.9 (49)	99	49/50	11.1 (50)	93	50/50
44-7	12.2 (50)	50/50	12.0 (50)	98	50/50	12.3 (49)	101	49/50	11.4 (50)	93	50/50
46-7	11.7 (50)	50/50	11.6 (50)	99	50/50	11.9 (48)	102	49/50	10.8 (50)	92	50/50
48-7	12.2 (50)	50/50	12.1 (50)	99	50/50	12.4 (49)	102	49/50	11.2 (50)	92	50/50
52-7	12.1 (50)	50/50	12.2 (50)	101	50/50	11.9 (49)	98	49/50	10.8 (49)	89	49/50
54-7	12.4 (50)	50/50	12.2 (50)	98	50/50	12.0 (49)	97	49/50	11.0 (49)	89	49/50
56-7	12.5 (50)	50/50	12.2 (50)	98	50/50	11.9 (49)	95	49/50	11.0 (49)	88	49/50
58-7	12.6 (50)	50/50	12.3 (50)	98	50/50	12.3 (49)	98	49/50	11.5 (49)	91	49/50
60-7	12.6 (50)	50/50	12.4 (50)	98	50/50	12.4 (49)	98	49/50	11.5 (49)	91	49/50
62-7	12.5 (50)	50/50	12.7 (50)	102	50/50	12.5 (49)	100	49/50	12.0 (49)	96	49/50
64-7	12.5 (50)	50/50	12.7 (50)	102	50/50	12.5 (49)	100	49/50	11.8 (49)	94	49/50
66-7	12.5 (50)	50/50	12.8 (50)	102	50/50	12.5 (49)	100	49/50	11.9 (49)	95	49/50
68-7	12.4 (50)	50/50	12.8 (50)	103	50/50	12.5 (49)	101	49/50	11.7 (49)	94	49/50
70-7	12.5 (50)	50/50	12.5 (50)	100	50/50	12.2 (49)	98	49/50	11.5 (49)	92	49/50
72-7	12.4 (50)	50/50	12.6 (50)	102	50/50	13.2 (49)	106	49/50	12.0 (49)	97	49/50
74-7	12.0 (50)	49/50	12.8 (50)	107	50/50	12.5 (49)	104	49/50	11.8 (49)	98	48/50
76-7	12.2 (47)	47/50	12.2 (50)	100	50/50	12.1 (49)	99	49/50	11.5 (48)	94	48/50
78-7	12.4 (47)	46/50	12.5 (50)	101	50/50	12.5 (49)	101	49/50	11.9 (48)	96	48/50
80-7	12.4 (46)	46/50	12.3 (50)	99	50/50	12.3 (49)	99	49/50	12.0 (47)	97	47/50
82-7	12.4 (46)	46/50	12.6 (50)	102	50/50	12.7 (49)	102	49/50	12.0 (47)	97	47/50
84-7	12.3 (46)	46/50	12.5 (50)	102	49/50	12.7 (49)	103	49/50	12.0 (47)	98	47/50
86-7	12.5 (46)	45/50	12.9 (49)	103	49/50	12.6 (49)	101	49/50	12.2 (46)	98	45/50
88-7	12.3 (45)	45/50	12.4 (49)	101	49/50	11.8 (48)	96	48/50	11.8 (45)	96	45/50
90-7	13.1 (45)	45/50	12.7 (49)	97	49/50	12.2 (48)	93	48/50	12.2 (45)	93	45/50
92-7	12.7 (45)	44/50	12.6 (48)	99	48/50	13.2 (47)	104	47/50	11.8 (45)	93	45/50
94-7	12.8 (44)	44/50	13.1 (47)	102	46/50	12.9 (47)	101	46/50	12.0 (45)	94	45/50
96-7	13.0 (44)	44/50	13.1 (46)	101	45/50	13.1 (46)	101	46/50	11.8 (44)	91	44/50
98-7	12.5 (44)	44/50	13.2 (45)	106	45/50	13.2 (46)	106	44/50	11.7 (43)	94	43/50
100-7	11.7 (44)	43/50	13.4 (45)	115	45/50	12.6 (44)	108	44/50	11.6 (42)	99	41/50
104-7	11.9 (40)	42/50	12.7 (44)	107	43/50	12.1 (44)	102	44/50	11.7 (35)	98	35/50

< >:No.of effective animals, ( ):No.of measured animals Av.FC.: g

Table 14 CLINICAL OBSERVATION (104W-SUMMRY) -RATS-

Findings	Male				Female			
	2000ppm S(DM)*	800ppm S(DM)	320ppm S(DM)	0ppm S(DM)	2000ppm S(DM)	800ppm S(DM)	320ppm S(DM)	0ppm S(DM)
COLORED(着色)	39(11)	42(8)	25(7)	0(0)	35(12)	38(3)	10(1)	1(0)
YELLOW URINE(黄色尿)	39(11)	42(8)	35(12)	0(0)	35(13)	44(5)	43(6)	1(0)
SOILED PERI GENITALIA(尿による外陰部周囲の汚染)	25(9)	5(2)	0(9)	0(6)	35(14)	32(5)	27(6)	18(4)
HUNCHBACK POSITION(円背位)	15(7)	8(6)	4(10)	1(6)	31(13)	22(5)	13(6)	7(3)
INTERNAL MASS(内部腫瘤)	0(0)	5(0)	2(0)	0(0)	0(3)	0(1)	1(1)	3(0)
EXTERNAL MASS(外部腫瘤)								
M.NOSE(鼻腫瘤)	2(0)	1(0)	1(0)	1(0)	0(0)	1(0)	0(0)	0(0)
M.EYE(眼腫瘤)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(0)	0(0)
M.PERI MOUTH(口周囲腫瘤)	0(0)	2(1)	4(1)	5(1)	1(0)	2(0)	0(0)	4(0)
M.ORAL CAVITY(口腔内部腫瘤)	0(0)	2(0)	1(0)	0(0)	0(0)	0(0)	0(0)	0(0)
M.PERI EAR(耳根部腫瘤)	0(1)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
M.HEAD(頭部腫瘤)	1(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
M.NECK(頸部腫瘤)	0(1)	1(0)	0(0)	1(0)	1(1)	1(0)	0(0)	0(0)
M.FORLIMB(前肢腫瘤)	0(0)	0(0)	0(0)	0(1)	0(0)	1(0)	0(0)	2(0)
M.BREAST(胸部腫瘤)	5(1)	5(0)	3(1)	2(1)	6(4)	4(0)	4(1)	6(1)
M.ABDOMEN(腹部腫瘤)	10(2)	10(3)	5(2)	3(1)	8(2)	6(3)	3(1)	9(1)
M.ANTERIOR.DORSUM(背側前部腫瘤)	2(1)	1(1)	1(2)	2(2)	0(1)	1(0)	1(0)	2(0)
M.POSTERIOR.DORSUM(背側後部腫瘤)	1(0)	4(0)	1(0)	2(1)	1(0)	0(0)	0(0)	1(0)
M.HINDLIMB(後肢腫瘤)	2(0)	2(0)	3(1)	0(0)	0(0)	1(1)	0(1)	0(0)
M.GENITALIA(外陰部腫瘤)	2(1)	4(1)	1(1)	1(0)	5(4)	6(2)	5(3)	12(1)
M.TAIL(尾腫瘤)	6(0)	6(1)	11(4)	12(1)	3(1)	1(0)	3(0)	0(0)
NO.of Animals with EXTERNAL MASS	20(6)	21(5)	19(8)	18(5)	16(8)	17(3)	16(5)	21(3)
NO.of Survival Animals (Dead & Moribund Animals)	39(11)	42(8)	35(15)	36(14)	35(15)	44(6)	43(7)	42(8)
NO.of Observed Animals	50	50	50	50	50	50	50	50

* : S=Survival Animals (DM=Dead & Moribund Animals)

TABLE 15 NEOPLASTIC LESIONS (KIDNEY) INCIDENCE AND STATISTICAL ANALYSIS : RAT:MALE

Group Name	Control	320 ppm	800 ppm	2000 ppm
SITE : kidney				
TUMOR : renal cell adenoma				
Overall Rates(a)	0/50 (0.0)	1/50 (2.0)	1/50 (2.0)	6/50 (12.0)
Adjusted Rates(b)	0.0	2.70	2.38	15.38
Terminal Rates(c)	0/36 (0.0)	0/35 (0.0)	1/42 (2.4)	6/39 (15.4)
Standard Rates(d)	P=-------			
Prevalence Rates(d)	P=0.0014**			
Combind analysis(d)	P=-------			
Cochran-Armitage Test(e)	P=0.0011**			
Fisher Exact Test(e)		P=0.4950	P=0.4950	P=0.0190*

TABLE 16 NEOPLASTIC LESIONS (PREPUTIAL/CLITORAL GLAND) INCIDENCE AND STATISTICAL ANALYSIS : RAT:MALE

Group Name	Control	320 ppm	800 ppm	2000 ppm
SITE : preputial/clitral gland				
TUMOR : adenoma				
Overall Rates(a)	0/50 (0.0)	2/50 (4.0)	4/50 (8.0)	5/50 (10.0)
Adjusted Rates(b)	0.0	5.71	7.14	10.00
Terminal Rates(c)	0/36 (0.0)	2/35 (5.7)	3/42 (7.1)	3/39 (7.7)
Standard Rates(d)	P=0.3989			
Prevalence Rates(d)	P=0.0231*			
Combind analysis(d)	P=0.0286*			
Cochran-Armitage Test(e)	P=0.0318*			
Fisher Exact Test(e)		P=0.2574	P=0.0638	P=0.0360*

TABLE 17 NEOPLASTIC LESIONS (MAMMARY GLAND) INCIDENCE AND STATISTICAL ANALYSIS : RAT:FEMALE

Group Name	Control	320 ppm	800 ppm	2000 ppm
SITE : mammary gland				
TUMOR : adenocarcinoma				
Overall Rates(a)	1/50 (2.0)	1/50 (2.0)	1/50 (2.0)	5/50 (10.0)
Adjusted Rates(b)	0.0	2.33	0.0	10.87
Terminal Rates(c)	0/42 (0.0)	1/35 (2.3)	0/44 (0.0)	3/35 (8.6)
Standard Rates(d)	P=0.7109			
Prevalence Rates(d)	P=0.0015**			
Combind analysis(d)	P=0.0137*			
Cochran-Armitage Test(e)	P=0.0205*			
Fisher Exact Test(e)		P=0.2475	P=0.2475	P=0.1210

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimate tumor incidence at the end of study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneth the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combind analysis : Death analysis + Incidental tumor test
(e):The Cochran-Armitage and Fisher's exact test compare directly the overall incidence rates.
? :The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value beyond the estimated P-value.
------:There is no data which should be statistic analysis.

TABLE 18 C A U S E O F D E A T H : R A T

Sex	Male				Female			
Group Name	Control	320ppm	800ppm	2000ppm	Control	320ppm	800ppm	2000ppm
Number of Dead/Moribund Animal	14	15	8	11	8	7	6	15
cardiovascular lesion	1							
digestive system lesion	1							
respiratory system lesion					1			1
hepatic lesion		1						
renal lesion	2		1					
pneumonia				1				
chronic nephropathy	1	2		2				
Tumor death : leukemia	2	1	1	1	1	1	1	3
: subcutis	2		3	2		1		
: bone marrow	1							
: spleen	1			1				
: liver		1						
: pancreas	1							1
: pituitary gland	1	7		1	3		1	3
: ovary								2
: uterus					1	1	1	2
: adrenal				1				
: mammary gland		1			2	2	2	1
: preputial/clitoral gland			1			2	1	
: brain			1	1				1
: retroperitoneum								1
: Zymbal gland				1				
: vertebra		1	1					
: peritoneum	1	1						

SELECTED FIGURES

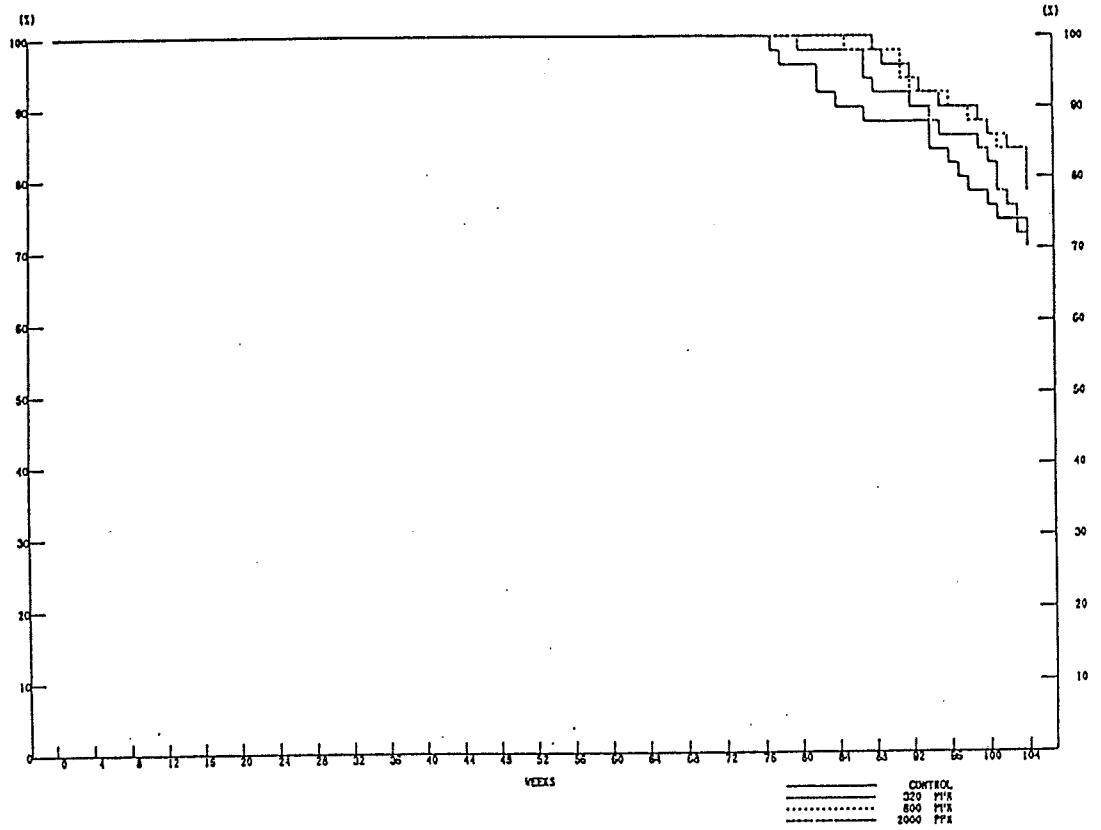


FIGURE 2 SURVIVAL ANIMAL RATE : RAT:MALE(TWO-YEAR STUDIES)

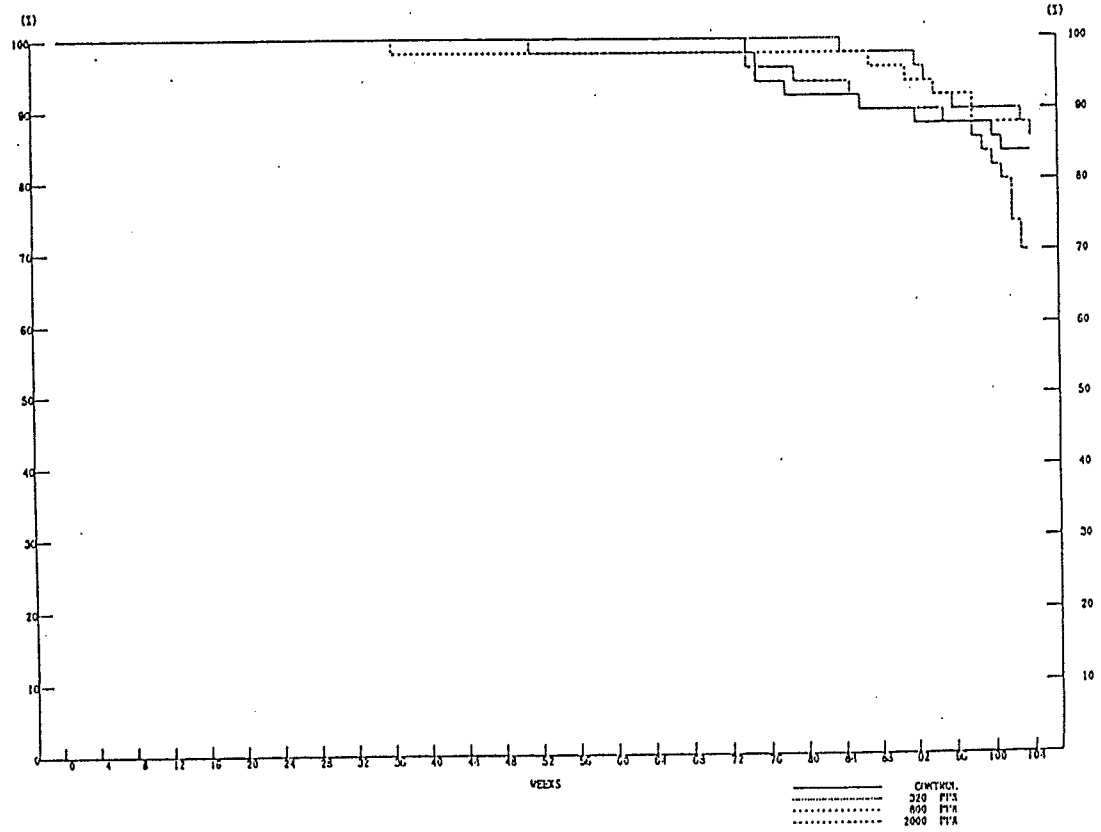


FIGURE 3 SURVIVAL ANIMAL RATE : RAT:FEMALE(TWO-YEAR STUDIES)

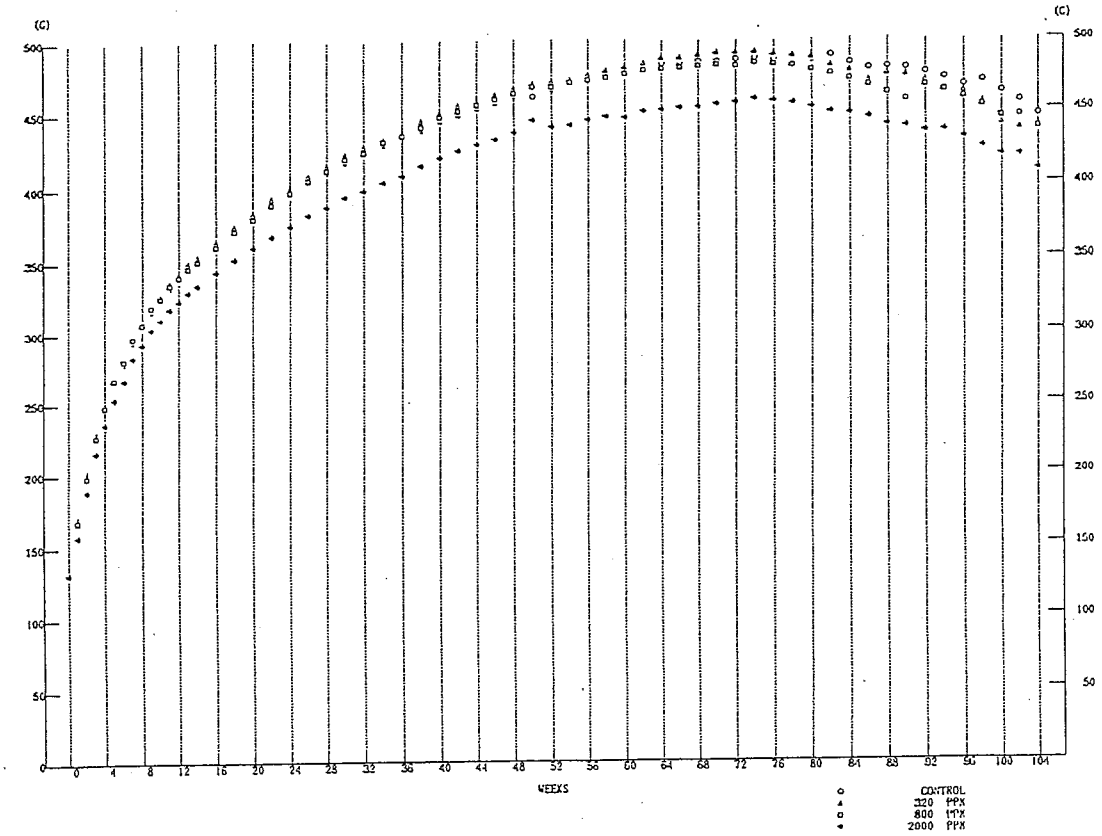


FIGURE 4 BODY WEIGHT CHANGES : RAT:MALE(TWO-YEAR STUDIES)

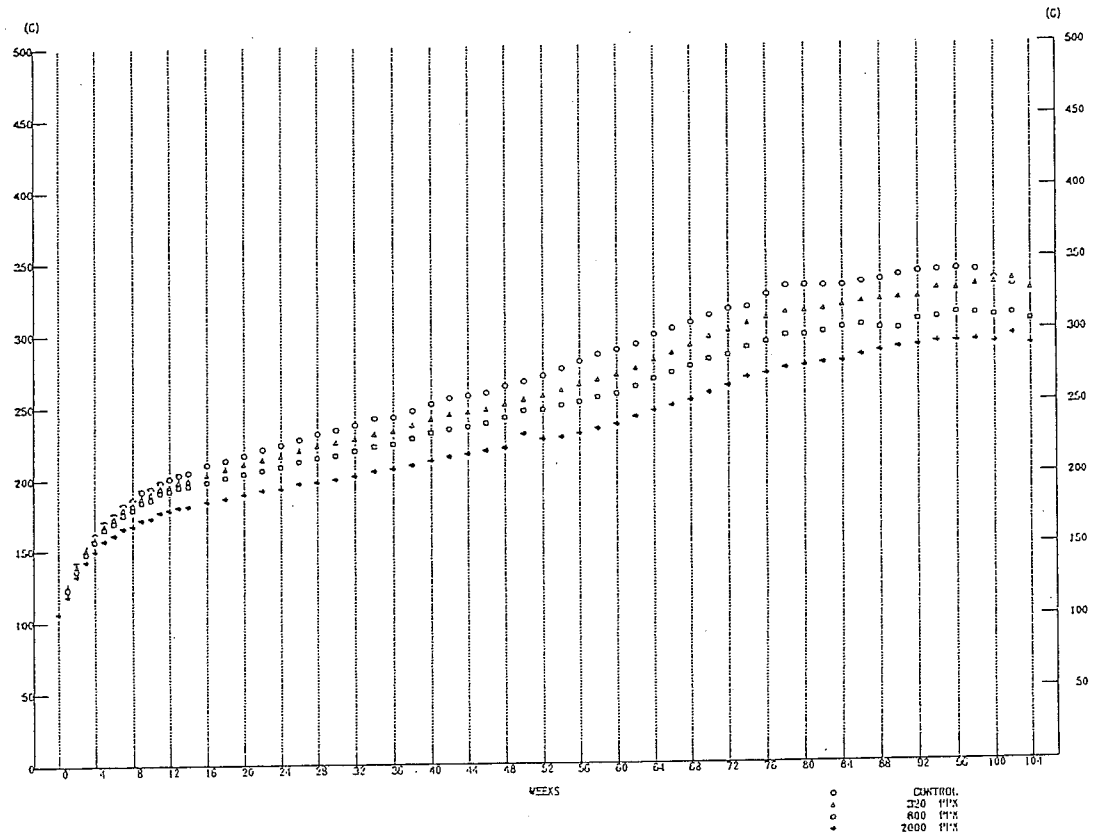


FIGURE 5 BODY WEIGHT CHANGES : RAT:FEMALE(TWO-YEAR STUDIES)

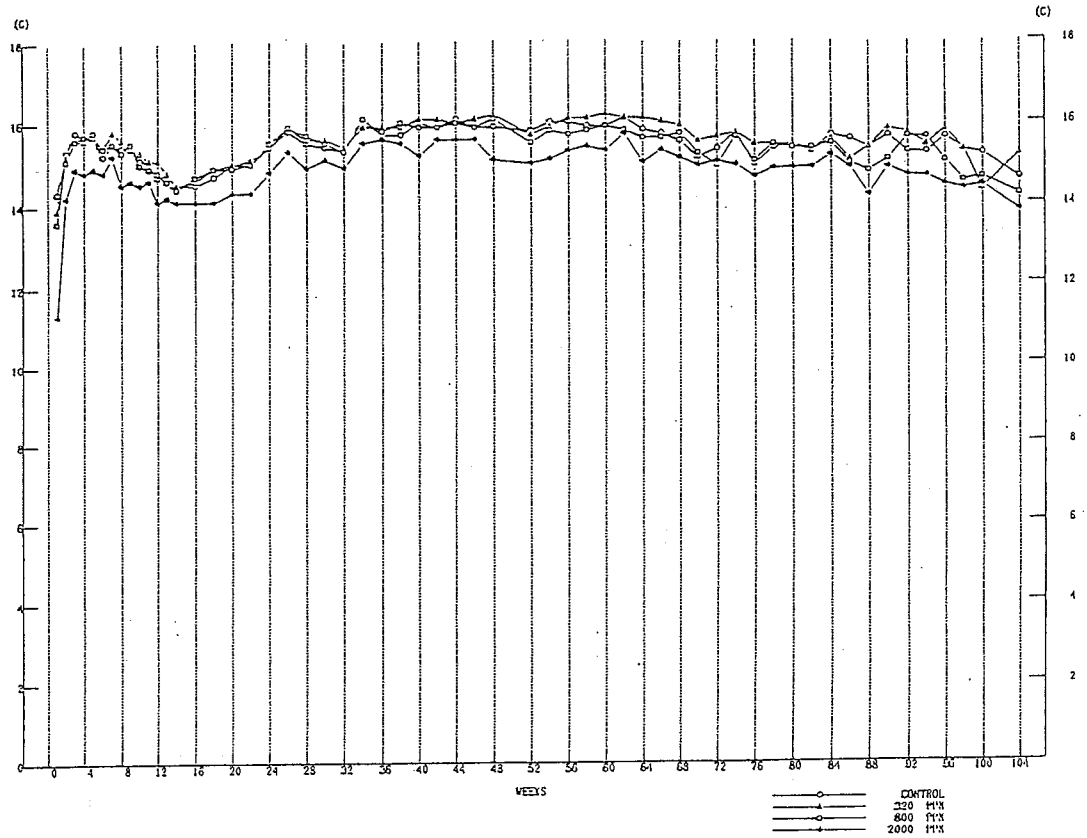


FIGURE 6 FOOD CONSUMPTION : RAT:MALE(TWO-YEAR STUDIES)

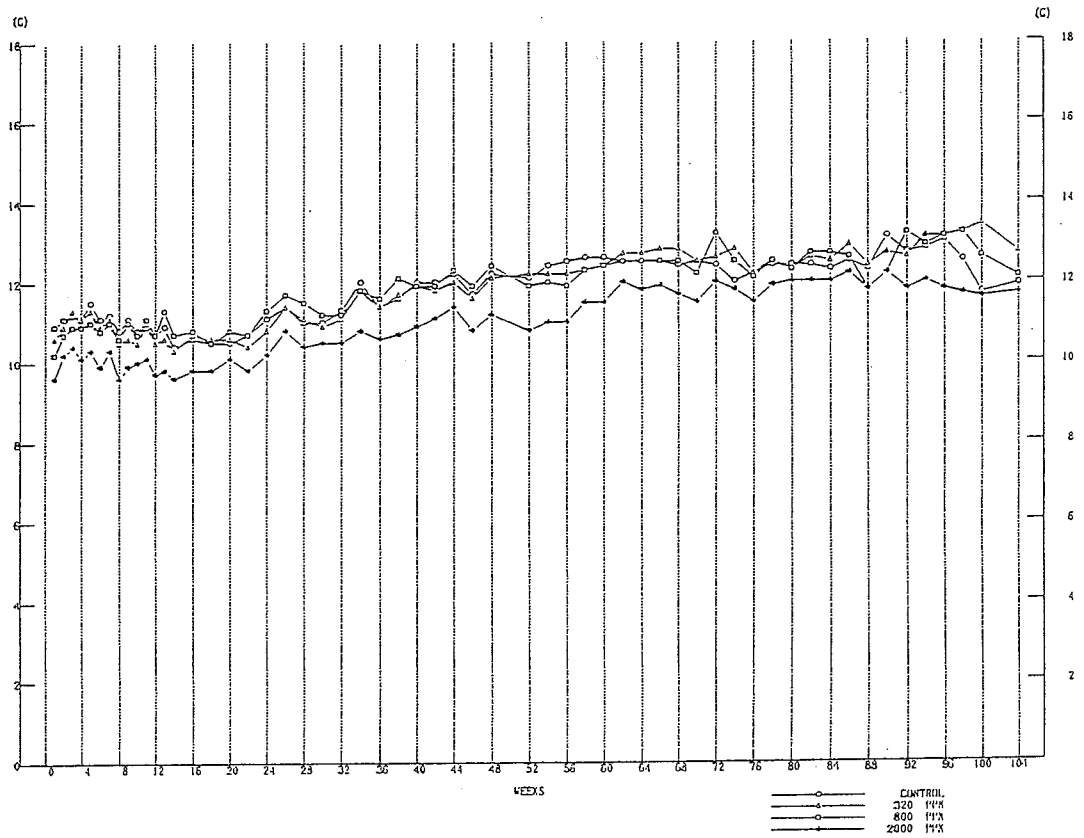


FIGURE 7 FOOD CONSUMPTION : RAT:FEMALE(TWO-YEAR STUDIES)

PHOTOGRAPHS

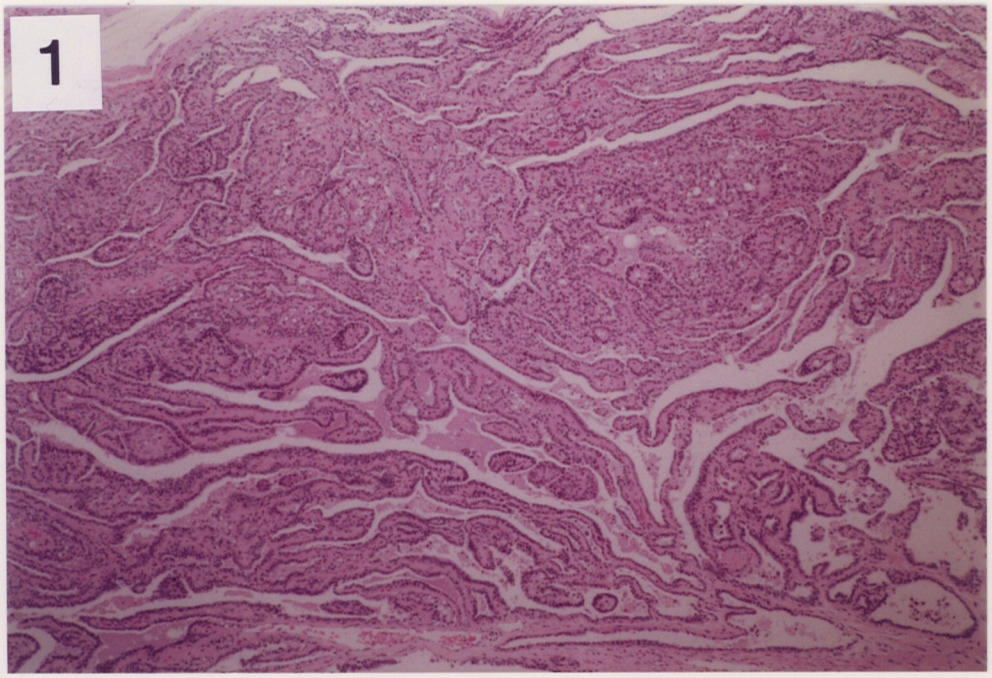
PHOTOGRAPH 1 MAMMARY GLAND, ADENOCARCINOMA
104-WEEK STUDY, RAT, FEMALE, 2000ppm, ANIMAL No. 0095-2350
(H. E., X60)

PHOTOGRAPH 2 KIDNEY, RENAL CELL ADENOMA : A
104-WEEK STUDY, RAT, MALE, 2000ppm, ANIMAL No. 0095-1315
(H. E., X150)

PHOTOGRAPH 3 KIDNEY, EOSINOPHILIC DROPLET ; PROXMAL TUBULE : A
104-WEEK STUDY, RAT, MALE, 2000ppm, ANIMAL No. 0095-1331
(H. E., X300)

PHOTOGRAPH 4 SPLEEN, EXTRAMEDULLARY HEMATOPOIESIS : A
DEPOSIT OF HEMOSIDERIN (MODERATE) : B
104-WEEK STUDY, RAT, MALE, 800ppm, ANIMAL No. 0095-1242
(H. E., X150) WHITE PULP : C

PHOTOGRAPH 5 STOMACH, HYPERPLASIA ; FORESTOMACH:A
104-WEEK STUDY, RAT, MALE, 2000ppm, ANIMAL No. 0095-1309
(H. E., X60)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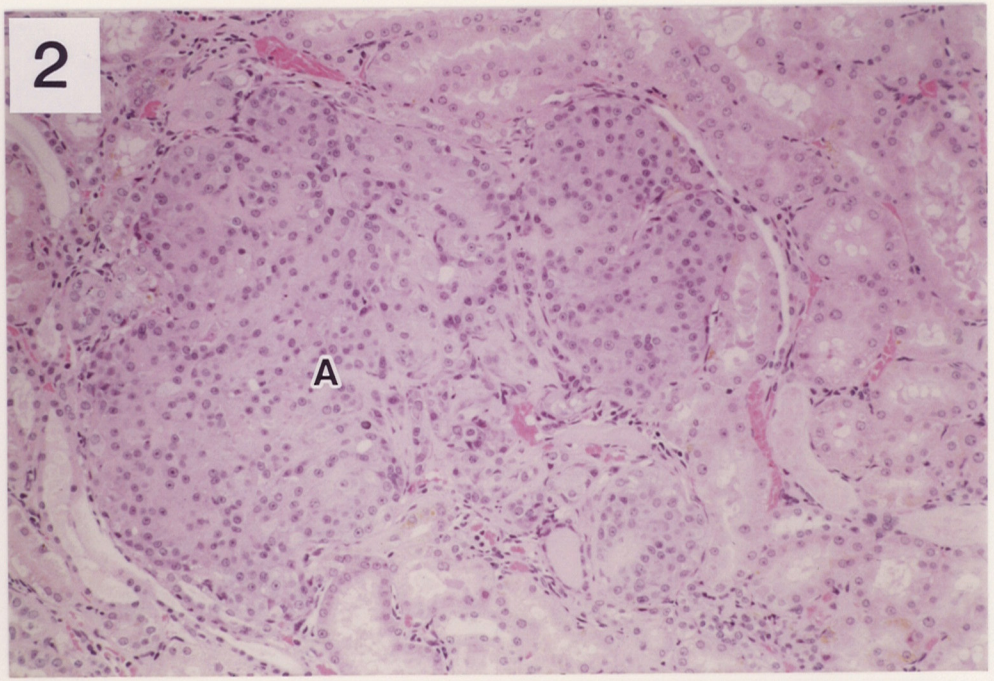
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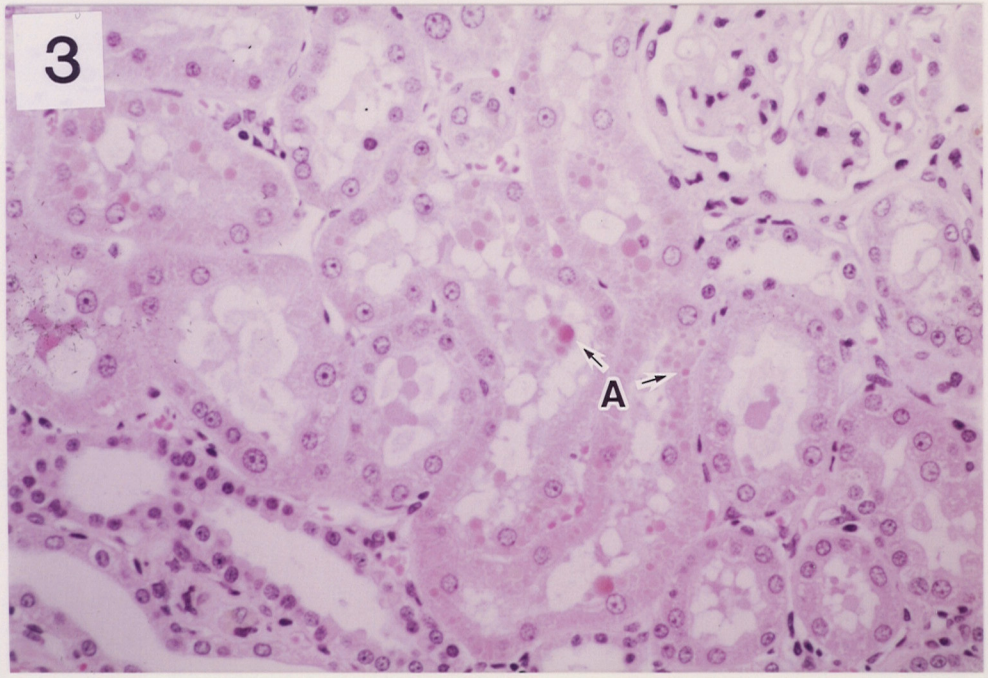
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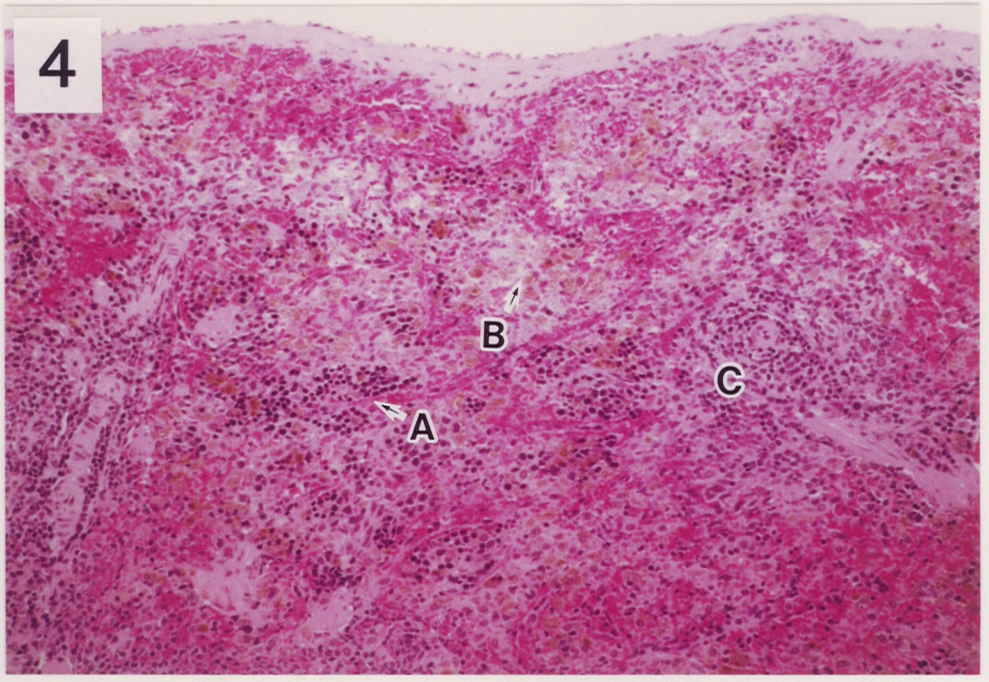
4
B
C
A


5
A