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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Propazine; Evaluation of Mammary Tumors in Female Rats

Tox. Chem. No. 184

TO: Peer Review Committee

FROM: William Dykstra Ph.D., Toxicologist
Section I, Toxicology Branch I/IRS
Health Effects Division (TS-769c)

William Dykstra
11/18/88

THRU: Edwin R. Budd, Section Head
Section I, Toxicology Branch I/IRS
Health Effects Division (TS-769c)

11/19/88

A. Summary

Propazine was fed to male and female Sprague-Dawley rats at doses of 0, 3, 100, and 1000 ppm in a 105 week chronic toxicity/oncogenicity study.

For the female rat, there was a significant increasing linear dose-trend with mortality. The incidence of all mammary tumors combined was significantly increased in the 1000 ppm dose group compared to controls and there was a significant increasing dose-related trend. There was a significant increasing dose-related trend for benign tumors.

B. Statistical Analysis of Mammary Tumors in Female Rats

Propazine, Rat Study - - Female Mammary Tumor Rates and Cochran-Armitage Trend Test and Fisher's Exact Test Results

Dose	0.000	3.000	100.000	1000.000
Benign	19/53	16/55	22/59	25/54
(%)	(36)	(29)	(37)	(46)
	p=0.0463*	p=0.2931	p=0.5158	p=0.1837
Malignant	9/53[c]	17/55	10/58	15/53[c]
(%)	(17)	(31)	(17)	(28)
	p=0.1876	p=0.0706	p=0.5861	p=0.1228
Combined Benign (%) and malignant	28/53	33/55	32/59	40/54
	(53)	(60)	(54)	(74)
	p=0.0087**	p=0.2888	p=0.5161	p=0.0184*

c) First carcinoma occurred at 75 weeks in dose 1000 ppm (papillary carcinoma) and dose 0 (adenocarcinoma).

Note: Significance of trend denoted at Control. Significance of pair-wise comparison with control denoted at Dose level. * $p < 0.05$ ** $p < 0.01$

C. Historical Control Data

Historical Incidence (%) of Mammary Tumors in Females Rats at IRDC

Microscopic Diagnosis	Mean	Range
Adenoma	9.5%	2% - 22%
Fibroadenoma	38.6%	19% - 60%
Adenocarcinoma	11.8%	1% - 29%
Mammary Tumors	50.3%	33% - 68%

D. Conclusions

1. Structure activity for two related triazines (Atrazine and Terbutryn) provides support for association of mammary tumors with this class of chemicals.

2. Propazine induced a dose-related, positive response (without metabolic activation) in V79 Chinese hamster cells (and a weak nondose-related one with activation). Propazine was negative in a Nucleus Anomaly assay and in a DNA damage/repair assay in rat hapatocytes.

3. Propazine was negative for oncogenicity in CD-1 mice. For malignant lymphomas in females, multiplicity of tumors per animal (tumor load) was enhanced relative to dose. This suggests that increased or enhanced metastatic factors may be operating in the mouse.

4. The incidence of all mammary tumors combined was significantly increased in the 1000 ppm dose group compared to controls ($p=0.0184$) and there was a significant increasing dose-related trend ($p=0.0087$).

5. The incidence of all mammary tumors combined at the high-dose (74%) exceeds the range of 33 - 68% of the IRDC historical controls.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PROPAZINE - Second Updated Qualitative Risk Assessment from a Rat 2-Year Chronic Oncogenicity Study.
Caswell No. - 184

FROM: C.J. Nelson, Statistician
Science Support Section
Science Analysis and Coordination Branch, HED (TS-769C)

TO: William Dykstra, Ph.D.
Review Section I
Toxicology Branch I - Insecticide/Rodenticide Support
(TS-769C)

THRU: Richard Levy, M.P.H., Science Advisor
Science Analysis and Coordination Branch, HED (TS-769C)

and

John A Quest, Ph.D., Chief
Science Support Section
Science Analysis and Coordination Branch, HED (TS-769C)

SUMMARY:

Propazine was fed to female Sprague-Dawley rats at doses of 0, 3, 100, and 1000 ppm in a 105 week chronic toxicity /oncogenicity study.

For the female rat, there was a significant increasing linear dose-trend with mortality. The incidence of all mammary tumors combined was significantly increased in the 1000 ppm dose group compared to controls and there was a significant increasing dose-related trend. There was a significant increasing dose-related trend for benign tumors.

BACKGROUND:

This is the third evaluation of a chronic rat study (see Levy memo dated 4/1/87 and Nelson memo dated 8/30/88). The sponsor had the lab re-evaluate the tumors and clarify some questions. The counts for mammary tumors decreased by 6 for the malignant tumors and increased by 5 for the benign tumors in the 1000 ppm dose group. There were more animals the last time than this time. Most animals that were not examined for the tumor of interest were not included.

Propazine was fed to male and female Sprague-Dawley rats at doses of 0, 3, 100, and 1000 ppm in a 105 week chronic toxicity/oncogenicity study. Approximately 5 animals of each sex were sacrificed after 52 weeks and 57 weeks of continuous dosing in the control and 1000 ppm dose group. The 57 week animals are not included in this memo. The study was conducted by IRDC for Ciba-Geigy. The IRDC report number was 382-007. Data was extracted from an addendum to the final report dated October 27, 1980. Test animals were assigned randomly to the following groups:

Table 1. Experimental Design for Rat Chronic Study

			Time of Sacrifice (weeks)			
Dose	Total Number		52		57 *	
(ppm)	Male	Female	Male	Female	Male	Female
Control	70	70	5	5	5	5
3	60	60				
100	60	60				
1000	70	70	5	5	5	5

* Compound-withdrawal group fed a control diet for 4 weeks and then sacrificed and necropsied (See Dykstra memo dated 6/8/81).

SURVIVAL ANALYSIS:

Ten animals were not examined in the compound withdrawal group in the control and 1000ppm groups and 2 rats from the other two groups. There were actually 61 rats assigned to the 100 ppm group.

For the female rat there was a significant increasing linear dose-trend with mortality ($p = 0.0037$, Table 2x). Table 2 from the last memo is included. These results disagree with the previous two memos, where the 100ppm dose group had significantly lower mortality than the control group.

Test for mortality were made using the Thomas, Breslow, and Gart procedure.

TABLE 2. PROPAZINE, RAT Study-- FEMALE Mortality Rates+ and Cox or Generalized K/W Test Results

	WEEK							
DOSE(PPM)	1-26	27-52	53 a	53-57	57 a	58-78	79-105 a	TOTAL
0.000	1/68 (1)	2/67 (3)	4/4	1/61 (2)	4/4	8/56 (14)	12/48 (25)	24/60 ** (40)
3.000	0/60 (0)	2/60 (3)	0/0	2/58 (3)	0/0	1/56 (2)	18/55 (33)	23/60 (38)
100.000	1/61 (2)	0/60 (0)	0/0	0/60 (0)	0/0	1/60 (2)	14/59 (24)	16/61 * (26)
1000.000	3/68 (4)	0/65 (0)	5/5	1/60 (2)	5/5	5/54 (9)	24/49 (49)	33/58 (57)

\+ Number of animals that died during the interval/Number of animals alive at the beginning of the interval.
( ) Per cent

a Interim sacrifice was conducted at 53 and 57 weeks. Final sacrifice occurred at week 105.

Note: Time intervals were selected for display purposes only. Significance of trend denoted at Control. Significance of pair-wise comparison with control denoted at Dose level. * denotes $p < 0.05$ and ** denotes $p < 0.01$

TABLE 2x. PROPAZINE, RAT Study-- FEMALE Mortality Rates and Cox or Generalized K/W Test Results

	WEEK						
DOSE(PPM)	1-26	27-52	53 a	53-57	58-78	79-105 a	TOTAL
0.000	1/63 (2)	2/62 (3)	4/4	0/56 (0)	8/56 (14)	12/48 (25)	23/59 ** (39)
3.000	0/60 (0)	2/60 (3)	0/0	2/58 (3)	1/56 (2)	18/55 (33)	23/60 (38)
100.000	1/60 (2)	0/59 (0)	0/0	0/59 (0)	1/59 (2)	14/58 (24)	16/60 (27)
1000.000	3/63 (5)	0/60 (0)	5/5	1/55 (2)	5/54 (9)	24/49 (49)	33/58 (57)

TUMOR ANALYSIS:

Using the present data set, no pair-wise survival disparities were detected, but there was a statistically significant increasing dose-trend with mortality. Hence the Cochran-Armitage test for trend and the Fisher's exact test for pair-wise differences between control and treated groups was used. The tumors are incidental in context (see Levy Memo dated April 1, 1987). Both malignant mammary tumors and all mammary tumors combined were analyzed. The two malignant mammary tumors were papillary carcinoma and adenocarcinoma. The two benign mammary tumors were fibroadenoma, and adenoma (Table 3x). Table 3 from the previous memo is included for comparison.

For the female rats, there was a significant increasing trend between benign tumor incidence and dose but there were no significant pair-wise comparisons between the control and dosed groups. The incidence of malignant mammary tumors was not significantly increased in any dosed group compared to controls and there was no significant trend. The incidence of all mammary tumors combined was significantly increased in the 1000 ppm dose group compared to controls ($p = 0.0184$) and there was a significant increasing dose-related trend ($p = 0.0087$.

TABLE 3. PROPAZINE, RAT Study-- FEMALE Mammary Tumor Rates+ and Peto's Prevalence Test Results

DOSE		0.	3.	100.	1000.
Benign		19/53	16/55	22/59 a	20/54
	(%)	(36)	(29)	(37)	(37)
	(p)	0.3292	0.2931	0.5158	0.5292
Malignant		9/56 b	17/55	10/58	21/53 b
	(%)	(16)	(31)	(17)	(40)
	(p)	0.0029**	0.0496 *	0.4708	0.0028 **
Combined Benign and Malignant		28/56	33/55	32/59	41/59
	(%)	(50)	(60)	(54)	(69)
	(p)	0.0015 **	0.3011	0.4575	0.0015 **

\+ Number of tumor bearing animals / number of animals at risk. (Excluding animals that died before the observation of the first tumor).
( ) Per cent

a) First Adenoma (Fibroadenoma) occurred at 71 weeks in dose 1000 ppm.
b) First Carcinoma occurred at 75 weeks in dose 1000 ppm (Papillary adenocarcinoma & carcinoma) and dose 0 (carcinoma, adenocarcinoma).

TABLE 3x. PROPAZINE, RAT Study-- FEMALE Mammary Tumor Rates+ and Cochran-Armitage Trend Test and Fisher's Exact Test Results

DOSE		0.000	3.000	100.000	1000.000
Benign		19/53	16/55	22/59 a	25/54
	(%)	(36)	(29)	(37)	(46)
		p= 0.0463*	p= 0.2931	p= 0.5158	p= 0.1837
Malignant		9/53 c	17/55	10/58	15/53 c
	(%)	(17)	(31)	(17)	(28)
		p= 0.1876	p= 0.0706	p= 0.5861	p= 0.1228
Combined Benign and Malignant		28/53	33/55	32/59	40/54
	(%)	(53)	(60)	(54)	(74)
		p= 0.0087**	p= 0.2888	p= 0.5161	p= 0.0184*

c) First Carcinoma occurred at 75 weeks in dose 1000 ppm (Papillary carcinoma) and dose 0 (adenocarcinoma).

Note: Significance of trend denoted at Control. Significance of pair-wise comparison with control denoted at Dose level. * $p < 0.05$ ** $p < 0.01$

REFERENCES:

Armitage, P. Tests for Linear Trends in Proportions and Frequencies. Biometrics 11, 375-386, 1955.

Cochran, W.G. Some Methods for Strengthening the Common Chi-Square Test. Biometrics 10, 417-451, 1954.

Thomas, D G, N Breslow, and J J Gart, Trend and Homogeneity Analyses of Proportions and Life Table Data, Computers and Biomedical Research 5, 373-381, 1977.

Peto, R., M Pike, N Day, R Gray, P Lee, S Parish, J Peto, S Richard, and J Wahrendorf. Guidelines for Simple, Sensitive, Significant Tests for Carcinogenic Effects in Long-term Animal Experiments. In: Monographs on the long-term and short-term screening assays for carcinogens: a critical appraisal. IARC Monographs, Supplement 2. Lyon, France: International Agency for Research on Cancer, pp. 311-426, 1980.

EPA Cancer Guidelines, F. R. 51:33993-34014, 1986.

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SUBJECT: PROPAZINE - Updated Qualitative Risk Assessment from a Rat 2-Year Chronic Oncogenicity Study.
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FROM: C.J. Nelson, Statistician C J Nelson 8/11/88
Science Support Section
Science Analysis and Coordination Branch, HED (TS-769C)

TO: William Dykstra, Ph.D.
Review Section I
Toxicology Branch - Insecticide, Rodenticide Support (TS-769C)

THRU: Richard Levy, M.P.H.,Leader-Biostatistics Team
Science Support Section 8-29-88
Science Analysis and Coordination Branch, HED (TS-769C)

and

John A Quest, Ph.D., Chief JA Quest 8/30/88
Science Support Section
Science Analysis and Coordination Branch, HED (TS-769C)

SUMMARY:

Propazine was fed to female Sprague-Dawley rats at doses of 0, 3, 100, and 1000 ppm in a 105 week chronic toxicity /oncogenicity study.

For the female rat The 100 ppm dose group had significantly lower mortality than the control and there was a significant increasing linear trend with dose. The incidence of malignant mammary tumors and all mammary tumors combined was significantly increased in the 1000 ppm dose group compared to controls and there was a significant increasing dose-related trend for both analyses. The 3 ppm dose group was significantly increased compared to control for malignant mammary tumors.

BACKGROUND:

This is a re-evaluation of a chronic rat study (see Levy memo dated 4/1/87). There were disparities between the reviewers counts and the companies. The company then had the lab re-evaluate the tumors and clarify some questions. The counts for mammary tumors in the above referenced memo changed from 1 to 2 animals for most dose groups except in the 3 ppm dose for malignant, which changed from 8 to 17.

Propazine was fed to male and female Sprague-Dawley rats at doses of 0, 3, 100, and 1000 ppm in a 105 week chronic toxicity/oncogenicity study. Approximately 5 animals of each sex were sacrificed after 52 weeks and 57 weeks of continuous dosing in the control and 1000 ppm dose group. The study was conducted by IRDC for Ciba-Geigy. The IRDC report number was 382-007. Data was extracted from a final report dated April 28, 1980. Test animals were assigned randomly to the following groups:

Table 1. Experimental Design for Rat Chronic Study

			Time of Sacrifice (weeks)			
Dose	Total Number		52		57 *	
(ppm)	Male	Female	Male	Female	Male	Female
Control	70	70	5	5	5	5
3	60	60				
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1000	70	70	5	5	5	5

* Compound-withdrawal group fed a control diet for 4 weeks and then sacrificed and necropsied (See Dykstra memo dated 6/8/81).

SURVIVAL ANALYSIS:

Ten animals were not examined in the compound withdrawal group in the control and 1000ppm groups and 2 rats from the other two groups. There were actually 61 rats assigned to the 100 ppm group.

For the female rat the 100ppm dose group had significantly lower mortality than the control ($p = 0.0405$) and there was a significant linear trend with dose ($p = 0.0029$) (Table 2). These results essentially agree with the previous Levy memo.

Test for mortality were made using the Thomas, Breslow, and Gart procedure.

TABLE 2. PROPAZINE, RAT Study-- FEMALE Mortality Rates+ and Cox or Generalized K/W Test Results

	WEEK							
DOSE(PPM)	1-26	27-52	53 a	53-57	57 a	58-78	79-105 a	TOTAL
0.000	1/68 (1)	2/67 (3)	4/4	1/61 (2)	4/4	8/56 (14)	12/48 (25)	24/60 ** (40)
3.000	0/60 (0)	2/60 (3)	0/0	2/58 (3)	0/0	1/56 (2)	18/55 (33)	23/60 (38)
100.000	1/61 (2)	0/60 (0)	0/0	0/60 (0)	0/0	1/60 (2)	14/59 (24)	16/61 * (26)
1000.000	3/68 (4)	0/65 (0)	5/5	1/60 (2)	5/5	5/54 (9)	24/49 (49)	33/58 (57)

\+ Number of animals that died during the interval/Number of animals alive at the beginning of the interval.

( ) Per cent

a Interim sacrifice was conducted at 53 and 57 weeks. Final sacrifice occurred at week 105.

Note: Time intervals were selected for display purposes only. Significance of trend denoted at Control. Significance of pair-wise comparison with control denoted at Dose level. * denotes $p < 0.05$ and ** denotes $p < 0.01$

TUMOR ANALYSIS:

Since survival disparities exist and the tumors are incidental in context (see Rich Levy Memo dated April 1, 1987), the Peto Prevalence Method for adjusting for differences in time-to-death with tumor was used. Both malignant mammary tumors and all mammary tumors combined were analyzed. The two malignant mammary tumors were 1) papillary adenocarcinoma and carcinoma and 2) carcinoma-adenocarcinoma. The five benign mammary tumors were fibroadenoma, papillary adenoma, cystadenoma, adenoma, and ductular adenoma (Table 3). A table of all combinations of mammary tumors was provided to the reviewer and copies are available to anyone who is interested.

For the female rats, there were no significant pair-wise comparisons with control and no significant trend for adenomas. The incidence of malignant mammary tumors was significantly increased in the 3 ppm and 1000 ppm dose groups compared to controls ($p = 0.0496$ and $p = 0.0028$, respectively). The incidence of all mammary tumors combined was significantly increased in the 1000 ppm dose groups compared to controls ($p = 0.0015$). There was a significant increasing dose-related trend for both analyses ($p = 0.0029$ and $= 0.0015$, respectively).

TABLE 3. PROPAZINE, RAT Study-- FEMALE Mammary Tumor Rates+ and Peto's Prevalence Test Results

DOSE		0.	3.	100.	1000.
Benign		19/53	16/55	22/59 a	20/54
	(%)	(36)	(29)	(37)	(37)
	(p)	0.3292	0.2931	0.5158	0.5292
Malignant		9/56 b	17/55	10/58	21/53 b
	(%)	(16)	(31)	(17)	(40)
	(p)	0.0029**	0.0496 *	0.4708	0.0028 **
Combined Benign and Malignant		28/56	33/55	32/59	41/59
	(%)	(50)	(60)	(54)	(69)
	(p)	0.0015 **	0.3011	0.4575	0.0015 **

\+ Number of tumor bearing animals / number of animals at risk. (Excluding animals that died before the observation of the first tumor).
( ) Per cent

a) First Adenoma (Fibroadenoma) occurred at 71 weeks in dose 1000 ppm.
b) First Carcinoma occurred at 75 weeks in dose 1000 ppm (Papillary adenocarcinoma & carcinoma) and dose 0 (carcinoma, adenocarcinoma).

Note: Significance of trend denoted at Control. Significance of pair-wise comparison with control denoted at Dose level. * $p < 0.05$ ** $p < 0.01$

REFERENCES:

Thomas, D G, N Breslow, and J J Gart, Trend and Homogeneity Analyses of Proportions and Life Table Data, Computers and Biomedical Research 5, 373-381, 1977.

Peto, R., M Pike, N Day, R Gray, P Lee, S Parish, J Peto, S Richard, and J Wahrendorf. Guidelines for Simple, Sensitive, Significant Tests for Carcinogenic Effects in Long-term Animal Experiments. In: Monographs on the long-term and short-term screening assays for carcinogens: a critical appraisal. IARC Monographs, Supplement 2. Lyon, France: International Agency for Research on Cancer, pp. 311-426, 1980.

EPA Cancer Guidelines, F. R. 51:33993-34014, 1986.

This is a table showing all lesions that the reviewer requested to be coded. Each animal will appear once and only once in the individual tumor lines. All animals with a particular lesion appear in the total lines (benign, malignant, and combined). Fibroadenoma is shown separately while all other benign consists of papillary adenoma, cystadenoma, adenoma, and ductular adenoma which are all adenomas.

TABLE 5. PROPAZINE, RAT Study-- FEMALE Mammary Tumor Rates

Dose (ppm)	0.	3.	100.	1000.
Number on Study	70	60	61	70
Number Not Examined	10	2	2	10
Number Examined	60	58	59	60
ADENOMAS ONLY				
FIBROADENOMA	15/60 (25)	13/58 (22)	18/59 (31)	14/60 (23)
PAPILLARY ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	1/60 (2)
CYSTADENOMA	1/60 (2)	0/58 (0)	0/59 (0)	0/60 (0)
ADENOMA	1/60 (2)	3/58 (5)	1/59 (2)	0/60 (0)
DUCTULAR ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	1/60 (2)
FIBROADENOMA AND PAPILLARY ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	2/60 (3)
FIBROADENOMA AND CYSTADENOMA	1/60 (2)	0/58 (0)	3/59 (5)	0/60 (0)
FIBROADENOMA AND ADENOMA	1/60 (2)	0/58 (0)	0/59 (0)	1/60 (2)
FIBROADENOMA AND DUCTULAR ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	1/60 (2)
TOTAL ANIMALS WITH ADENOMAS	19/60 (32)	16/58 (28)	22/59 (37)	20/60 (33)

MALIGNANT with or without BENIGN

PAPILLARY CARCINOMA	2/60 (3)	4/58 (7)	2/59 (3)	4/60 (7)
PAPILLARY CARCINOMA AND ADENOCARCINOMA	0/60 (0)	0/58 (0)	0/59 (0)	4/60 (7)
PAPILLARY CARCINOMA AND ADENOCARCINOMA, AND FIBROADENOMA	0/60 (0)	1/58 (2)	1/59 (2)	0/60 (0)
PAPILLARY CARCINOMA AND FIBROADENOMA	0/60 (0)	2/58 (3)	0/59 (0)	1/60 (2)
PAPILLARY CARCINOMA AND PAPILLARY ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	1/60 (2)
PAPILLARY CARCINOMA AND FIBROADENOMA AND PAPILLARY ADENOMA	1/60 (2)	0/58 (0)	0/59 (0)	1/60 (2)
PAPILLARY CARCINOMA AND FIBROADENOMA AND ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	2/60 (3)
ADENOCARCINOMA	2/60 (3)	4/58 (7)	4/59 (7)	3/60 (5)
ADENOCARCINOMA AND FIBROADENOMA	4/60 (7)	6/58 (10)	2/59 (3)	2/60 (3)
ADENOCARCINOMA AND ADENOMA	0/60 (0)	0/58 (0)	1/59 (2)	3/60 (5)
ADENOCARCINOMA AND FIBROADENOMA AND ADENOMA	0/60 (0)	0/58 (0)	0/59 (0)	1/60 (2)
TOTAL ANIMALS WITH CARCINOMA AND/OR ADENOMAS	9/60 (15)	17/58 (29)	10/59 (17)	21/60 (35)

NOTE: 1) Papillary Carcinoma was listed on the data sheets as Papillary Adenocarcinoma and Carcinoma.
2) Adenocarcinoma was listed on the data sheets as Carcinoma, Adenocarcinoma.

TABLE 3. PROPAZINE, RAT Study-- FEMALE Mammary Tumor Incidence

Dose (ppm)	0.	3.	100.	1000.
ADENOMAS ONLY				
FIBROADENOMA	15/60 (25)	13/58 (22)	18/59 (31)	14/60 (23)
Other Benign a	2/60 (3)	3/58 (5)	1/59 (2)	2/60 (3)
Fibroadenoma and Other Benign	2/60 (3)	0/58 (0)	3/59 (5)	4/60 (7)
TOTAL ANIMALS WITH ADENOMAS	19/60 (32)	16/58 (28)	22/59 (37)	20/60 (33)
MALIGNANT with or without BENIGN				
PAPILLARY CARCINOMA b Only or with one or more Benign Tumors	3/60 (5)	6/58 (10)	2/59 (3)	9/60 (15)
PAPILLARY CARCINOMA AND ADENOCARCINOMA Only or with one or more Benign Tumors	0/60 (0)	1/58 (2)	1/59 (1)	4/60 (7)
ADENOCARCINOMA c Only or with one or more Benign Tumors	6/60 (10)	10/58 (17)	7/59 (12)	9/60 (15)
TOTAL ANIMALS WITH one or more CARCINOMAs	9/60 (15)	17/58 (29)	10/59 (17)	21/60 (35)
TOTAL ANIMALS WITH Benign or Malignant Tumors	28/60 (47)	33/58 (57)	32/59 (54)	41/60 (68)

NOTE: a) Other Benign is Papillary Adenoma, Cystadenoma, Adenoma, and Ductular Adenoma
b) Papillary Carcinoma was listed on the data sheets as Papillary Adenocarcinoma and Carcinoma.
c) Adenocarcinoma was listed on the data sheets as Carcinoma, Adenocarcinoma.

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Chemical:	**Propazine**
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Memo Date:	***11/19/88***
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Accession Number:	**412-03-0019**

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01/09/2003