

TABLE 107 - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                    |         |         |              |               |    |
|--------------------|---------|---------|--------------|---------------|----|
| Group              | 1       | 2       | 3            | 4             | 5  |
| Compound           | Control | Control | Palonosetron | Hydrochloride |    |
| Dosage (mg/kg/day) | 0       | 0       | 10           | 30            | 60 |

Printed: 04-DEC-01  
Page: 13

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION                       | SEX:<br>GROUP    | NUMBER OF ANIMALS AFFECTED |     |     |     |     |        |     |     |     |     |
|---|------------------|----------------------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|   |                  | MALE                       |     |     |     |     | FEMALE |     |     |     |     |
|   |                  | -1-                        | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
| *** FROM PREVIOUS PAGE ***                          | NUMBER:          | 56                         | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| GENITAL VESICLES                                    | NUMBER EXAMINED: | 56                         | 56  | 56  | 56  | 64  | 0      | 0   | 0   | 0   | 0   |
| --ABSCERATION                                       |                  | 1                          | 1   | 2   | 3   | 0   | 0      | 0   | 0   | 0   | 0   |
| --DISTENDED   |                  | 0                          | 1   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| --EPITHELIAL HYPERPLASIA                            |                  | 0                          | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| SPINAL C. CERV                                      | NUMBER EXAMINED: | 56                         | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| --GLIOSIS   |                  | 0                          | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   | 0   |
| --CYST(S)   |                  | 1                          | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| SPLEEN  | NUMBER EXAMINED: | 56                         | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| --GROWTH ANOMALY                                    |                  | 0                          | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |
| --MYXAMEDULLARY HEMOPHOYSIS                         |                  | 13                         | 14  | 14  | 12  | 14  | 18     | 20  | 20  | 17  | 19  |
| --INCREASED CELLULARITY OF WHITE PULP - GENERALIZED |                  | 2                          | 6   | 7   | 8   | 9   | 6      | 12  | 9   | 7   | 13  |
| --HEMORRHAGE  |                  | 0                          | 0   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --NECROSIS  |                  | 0                          | 0   | 0   | 0   | 0   | 2      | 0   | 0   | 0   | 0   |
| --AMOEBIASIS  |                  | 0                          | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| STERNUM & MAMMARY                                   | NUMBER EXAMINED: | 56                         | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| --CHONDROID HYPERPLASIA                             |                  | 0                          | 0   | 2   | 1   | 0   | 1      | 0   | 0   | 0   | 0   |
| --INFLAMMATION                                      |                  | 0                          | 0   | 1   | 1   | 0   | 1      | 0   | 0   | 0   | 0   |
| STOMACH L3  | NUMBER EXAMINED: | 56                         | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 61  |
| --CONGESTION  |                  | 0                          | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 0   |
| --SUBMUCOSAL OEDEMA - MUCOSAL REGION                |                  | 2                          | 0   | 5   | 0   | 3   | 4      | 1   | 0   | 3   | 1   |
| --SUBEPITHELIAL INFLAMMATION - MUCOSAL REGION       |                  | 0                          | 0   | 3   | 0   | 2   | 2      | 0   | 2   | 1   | 0   |
| --EPITHELIAL HYPERPLASIA - MUCOSAL REGION           |                  | 0                          | 4   | 3   | 0   | 3   | 3      | 1   | 4   | 1   | 1   |
| --EROSION - MUCOSAL REGION                          |                  | 0                          | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 1   | 0   |
| --ULCERATION - MUCOSAL REGION                       |                  | 0                          | 0   | 0   | 0   | 1   | 1      | 0   | 2   | 0   | 0   |
| --MUCOSAL EROSION - GLANDULAR REGION                |                  | 0                          | 0   | 2   | 1   | 0   | 0      | 1   | 0   | 3   | 2   |

: 197 :

HSH 002/013059 0197

IND 

Page 202

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 107 - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01

Page: 14

Schedule number: E28 002

| ORGAN AND FINDING DESCRIPTION                | NUMBER OF ANIMALS AFFECTED |     |                 |     |                |         |     |                |     |     |
|--|----------------------------|-----|-----------------|-----|----------------|---------|-----|----------------|-----|-----|
|  | Males                      |     |                 |     |                | Females |     |                |     |     |
|  | 1-1                        | 2-2 | 3-3             | 4-4 | 5-5            | 1-1     | 2-2 | 3-3            | 4-4 | 5-5 |
| ** FROM PREVIOUS PAGE **                     | 56                         | 56  | 56              | 56  | 64             | 56      | 56  | 56             | 56  | 64  |
| STOMACH (3)                                  |                            |     |                 |     |                |         |     |                |     |     |
| NUMBER EXAMINED:                             | 56                         | 56  | 56              | 56  | 64             | 56      | 56  | 56             | 56  | 64  |
| --GLANDULAR ATYPICAL HYPERPLASIA             | 2                          | 8   | 7               | 4   | 8              | 2       | 4   | 3              | 2   | 3   |
| --SUBMUCOSAL OEDEMA - GLANDULAR REGION       | 0                          | 0   | 3               | 1   | 1              | 0       | 0   | 0              | 1   | 0   |
| --SUBMUCOSAL INFLAMMATION, GLANDULAR REGION  | 2                          | 3   | 10 <sup>h</sup> | 4   | 4              | 2       | 1   | 2              | 2   | 2   |
| --MUCOSAL ULCERATION - GLANDULAR REGION      | 1                          | 1   | 3               | 0   | 0              | 2       | 1   | 0              | 1   | 1   |
| --EPITHELIAL HYPERPLASIA - GLANDULAR REGION  | 0                          | 0   | 1               | 0   | 0              | 1       | 0   | 0              | 0   | 0   |
| --MUCOSAL MINERALISATION - GLANDULAR REGION  | 0                          | 0   | 0               | 1   | 0              | 0       | 1   | 0              | 2   | 0   |
| --DILATED GLANDS                             | 2                          | 1   | 1               | 0   | 3              | 0       | 1   | 0              | 0   | 2   |
| --PERITONITIS                                | 8                          | 7   | 8               | 7   | 4              | 7       | 6   | 10             | 7   | 8   |
| --ARTERITIS                                  | 0                          | 1   | 0               | 0   | 0              | 0       | 1   | 0              | 0   | 0   |
| --SCUMOUS CYST - LINGVINE RIDGE              | 1                          | 2   | 3               | 1   | 2              | 0       | 0   | 2              | 1   | 0   |
| --METEORISATION - MUSCULARIS                 | 0                          | 0   | 0               | 0   | 0              | 0       | 0   | 0              | 2   | 0   |
| --PERI-CAPSULAR CYST(S)                      | 0                          | 1   | 4 <sup>g</sup>  | 1   | 0              | 0       | 0   | 0              | 0   | 0   |
| --SUBMUCOSAL CYST(S)                         | 0                          | 0   | 0               | 0   | 0              | 0       | 0   | 1              | 0   | 0   |
| TESTES                                       |                            |     |                 |     |                |         |     |                |     |     |
| NUMBER EXAMINED:                             | 56                         | 56  | 56              | 56  | 64             | 0       | 0   | 0              | 0   | 0   |
| --SPERMATOCYTES (S)                          | 11                         | 8   | 4               | 0   | 4 <sup>a</sup> | 0       | 0   | 0              | 0   | 0   |
| --SCIMPIFIED TUBULAR EPITHELIAL DEGENERATION | 26                         | 19  | 19              | 28  | 32             | 0       | 0   | 0              | 0   | 0   |
| --MULTI-FOCAL CYSTIC GLAND CELLS             | 3                          | 0   | 2               | 2   | 2              | 0       | 0   | 0              | 0   | 0   |
| --INTERSTITIAL CELL HYPERPLASIA              | 8                          | 9   | 4               | 14  | 16             | 0       | 0   | 0              | 0   | 0   |
| --CYSTIC TUBULAR HYPERPLASIA                 | 0                          | 0   | 0               | 0   | 1              | 0       | 0   | 0              | 0   | 0   |
| --CONGESTION                                 | 0                          | 0   | 0               | 0   | 1              | 0       | 0   | 0              | 0   | 0   |
| --INFLAMMATION                               | 0                          | 0   | 0               | 1   | 0              | 0       | 0   | 0              | 0   | 0   |
| UTERUS                                       |                            |     |                 |     |                |         |     |                |     |     |
| NUMBER EXAMINED:                             | 51                         | 53  | 52              | 50  | 55             | 55      | 53  | 54             | 55  | 63  |
| --INVOLUTION/ATROPHY                         | 22                         | 18  | 11 <sup>a</sup> | 14  | 14             | 7       | 4   | 7              | 11  | 4   |
| --HAEMORRHAGE                                | 0                          | 0   | 1               | 0   | 0              | 0       | 0   | 3 <sup>g</sup> | 1   | 1   |
| --AMYLOIDOSIS                                | 0                          | 0   | 0               | 0   | 1              | 0       | 0   | 0              | 0   | 0   |
| --EPITHELIAL HYPERPLASIA                     | 1                          | 1   | 2               | 1   | 1              | 0       | 0   | 0              | 0   | 0   |

.. 108 ..

HSH 002/013059 0198

TABLE 107 - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                    |         |         |              |               |    |
|--------------------|---------|---------|--------------|---------------|----|
| Group              | 1       | 2       | 3            | 4             | 5  |
| Compound           | Control | Control | Faloxosetron | Hydrochloride |    |
| Dosage (mg/kg/day) | 0       | 0       | 10           | 30            | 60 |

Printed: 04-DEC-01  
Page: 18

Schedule number: HSE 002

| ORGAN AND FINDING DESCRIPTION        | NUMBER OF ANIMALS AFFECTED |     |     |     |     |             |     |     |     |     |
|--------------------------------------|----------------------------|-----|-----|-----|-----|-------------|-----|-----|-----|-----|
|                                      | SEX: MALE                  |     |     |     |     | SEX: FEMALE |     |     |     |     |
|                                      | GROUP: -1-                 | -2- | -3- | -4- | -5- | -1-         | -2- | -3- | -4- | -5- |
| NUMBER EXAMINED:                     | 56                         | 56  | 56  | 56  | 64  | 56          | 56  | 56  | 56  | 64  |
| ** FROM PREVIOUS PAGE **             |                            |     |     |     |     |             |     |     |     |     |
| <b>TESTES</b>                        | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --INFLAMMATION                       | 0                          | 0   | 2   | 1   | 0   | 0           | 0   | 0   | 0   | 0   |
| --LYMPHOID HYPERPLASIA               | 0                          | 16  | 14  | 9   | 37  | 22          | 29  | 23  | 20  | 34  |
| --INCREASED CELLULARITY - MEDULLA    | 0                          | 0   | 1   | 0   | 0   | 0           | 0   | 1   | 1   | 1   |
| --FOCAL NECROSIS                     | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 0   |
| --GRANULOMA WITH CHOLESTEROL CLEFTS  | 0                          | 0   | 0   | 0   | 0   | 1           | 0   | 0   | 0   | 0   |
| --CYST(S)                            | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 0   | 1   | 0   |
| --ARTERITIS/PERIARTERITIS            | 3                          | 0   | 3   | 3   | 1   | 0           | 0   | 0   | 0   | 0   |
| --RADIOSICROSIS                      | 3                          | 2   | 1   | 0   | 1   | 2           | 4   | 1   | 3   | 0   |
| --THROMBUS/THROMBI                   | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 0   | 1   | 0   |
| --SITE ONLY                          | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 1   | 1   | 0   |
|                                      | 0                          | 1   | 1   | 2   | 2   | 3           | 0   | 1   | 0   | 0   |
| <b>THYROID</b>                       | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --ECTOPIC THYMIC TISSUE              | 0                          | 2   | 0   | 0   | 1   | 0           | 0   | 0   | 2   | 2   |
| --LYMPHOID AGGREGATES                | 1                          | 0   | 0   | 1   | 0   | 3           | 2   | 0   | 2   | 2   |
| --C-CELL HYPERPLASIA                 | 0                          | 0   | 0   | 0   | 1   | 0           | 1   | 0   | 1   | 1   |
| --CYSTIC FOLLICULAR CELL HYPERPLASIA | 5                          | 2   | 4   | 0   | 6   | 2           | 1   | 2   | 2   | 1   |
| --THYROIDITIS                        | 2                          | 1   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 1   |
| --FOLLICULAR DILATATION              | 9                          | 0   | 2   | 7   | 7   | 0           | 0   | 0   | 6   | 4   |
| <b>TONGUE</b>                        | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --INFLAMMATION                       | 1                          | 0   | 0   | 0   | 1   | 2           | 3   | 2   | 1   | 2   |
| --ARTERITIS/PERIARTERITIS            | 0                          | 2   | 0   | 0   | 0   | 1           | 0   | 0   | 2   | 1   |
| <b>TRACHEA</b>                       | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --TRACHEITIS                         | 4                          | 3   | 4   | 1   | 3   | 1           | 4   | 3   | 0   | 2   |
| --ADHESION                           | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 1   | 0   | 0   |
| --CYST(S)                            | 0                          | 0   | 0   | 0   | 1   | 0           | 0   | 0   | 0   | 0   |
| --INFLAMMATORY INFILTRATION          | 0                          | 1   | 0   | 0   | 1   | 0           | 0   | 1   | 1   | 0   |

: 199 :

HSH 002/013059 0199

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 109 - continued.

Histopathology - group distribution of non-neoplastic findings for all animals

Print No: 0022

Group : 1 2 3 4 5  
Compound : Control Control Pelonesetron Hydrochloride  
Dose (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
Page: 16

Schedule number: N2H 002

| ORGAN AND FINDING DESCRIPTION    | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |        |     |     |     |     |
|----------------------------------|------------------------------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|                                  | SEX:                               |     |     |     |     | SEX:   |     |     |     |     |
|                                  | MALE                               |     |     |     |     | FEMALE |     |     |     |     |
| GROUP:                           | -1-                                | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
| NUMBER:                          | 56                                 | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| <b>URINARY BLADDER</b> .....     |                                    |     |     |     |     |        |     |     |     |     |
| NUMBER EXAMINED:                 |                                    |     |     |     |     |        |     |     |     |     |
| --TRANSITIONAL CELL HYPERPLASIA  | 2                                  | 0   | 2   | 2   | 1   | 0      | 0   | 0   | 0   | 0   |
| --LYMPHOID AGGREGATIONS          | 7                                  | 7   | 6   | 9   | 8   | 5      | 8   | 4   | 10  | 10  |
| --LUMINAL DILATATION             | 0                                  | 7   | 4   | 9   | 5   | 0      | 1   | 1   | 0   | 1   |
| --TRANSITIONAL CELL HYPERTROPHY  | 1                                  | 0   | 1   | 1   | 1   | 0      | 0   | 0   | 0   | 0   |
| --PERICAPSULAR INFLAMMATION      | 0                                  | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| --HEMORRHAGE                     | 0                                  | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --EDEMA                          | 1                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --ULCERATION                     | 1                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |
| --REFLUXED SEMINAL COLLOID PLOG  | 0                                  | 0   | 2   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| <b>UTERINE CERVIX</b> .....      |                                    |     |     |     |     |        |     |     |     |     |
| NUMBER EXAMINED:                 |                                    |     |     |     |     |        |     |     |     |     |
| --ARTERITIS/PERIARTERITIS        | 0                                  | 0   | 0   | 0   | 0   | 56     | 56  | 55  | 55  | 64  |
| --MURAL HYPERTROPHY              | 0                                  | 0   | 0   | 0   | 0   | 1      | 1   | 0   | 0   | 0   |
| --MURAL EDEMA                    | 0                                  | 0   | 0   | 0   | 0   | 1      | 1   | 2   | 0   | 2   |
| --INFLAMMATION                   | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 2   | 0   | 1   |
| <b>UTERUS</b> .....              |                                    |     |     |     |     |        |     |     |     |     |
| NUMBER EXAMINED:                 |                                    |     |     |     |     |        |     |     |     |     |
| --SQUAMOUS METAPLASIA            | 0                                  | 0   | 0   | 0   | 0   | 56     | 56  | 55  | 56  | 64  |
| --LUMINAL HEAMORRHAGE            | 0                                  | 0   | 0   | 0   | 0   | 4      | 1   | 3   | 4   | 4   |
| --LUMINAL DILATATION             | 0                                  | 0   | 0   | 0   | 0   | 1      | 5   | 2   | 2   | 1   |
| --ENDOMETRIAL GLAND HYPERPLASIA  | 0                                  | 0   | 0   | 0   | 0   | 39     | 46  | 40  | 40  | 49  |
| --ADENOMYOSIS                    | 0                                  | 0   | 0   | 0   | 0   | 34     | 21  | 20  | 22  | 20  |
| --LIMINAL CELLULAR DEBRIS        | 0                                  | 0   | 0   | 0   | 0   | 7      | 11  | 9   | 9   | 9   |
| --ARTERITIS/PERIARTERITIS        | 0                                  | 0   | 0   | 0   | 0   | 1      | 0   | 0   | 0   | 0   |
| --ENDOMETRIAL HYPERPLASIA, FOCAL | 0                                  | 0   | 0   | 0   | 0   | 2      | 3   | 3   | 4   | 1   |
| --LUMINAL ABSCESS (S)            | 0                                  | 0   | 0   | 0   | 0   | 1      | 1   | 1   | 0   | 0   |
| --ANGIECTASIS                    | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 1   |
| --DECIDUALISATION, FOCAL         | 0                                  | 0   | 0   | 0   | 0   | 1      | 2   | 0   | 0   | 2   |
|                                  | 0                                  | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 1   | 0   |

: 200 :

HSH 002/013058 0200

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10F - continued.

Print No: 0022

Histopathology - Group distribution of non-neoplastic findings for all animals

|                    |         |         |              |               |    |  |
|--------------------|---------|---------|--------------|---------------|----|--|
| Group              | 1       | 2       | 3            | 4             | 5  |  |
| Compound           | Control | Control | Faloxonotran | Hydrochloride |    |  |
| Dosage (mg/kg/day) | 0       | 0       | 10           | 30            | 60 |  |

Printed: 04-DEC-01  
Page: 17

Schedule number: NEW 002

| --- NUMBER OF ANIMALS AFFECTED ---      |                  |      |     |     |     |     |        |     |     |     |     |
|---|------------------|------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
| ORGAN AND FINDING DESCRIPTION           | SEX: GROUP       | MALE |     |     |     |     | FEMALE |     |     |     |     |
|   |                  | -1-  | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
|   | NUMBER           | 56   | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| VAGINA                                  | NUMBER EXAMINED: | 0    | 0   | 0   | 0   | 0   | 56     | 56  | 56  | 56  | 64  |
| --MUCUS AND INFLAMMATORY CELLS IN LUMEN |                  | 0    | 0   | 0   | 0   | 0   | 3      | 2   | 4   | 2   | 2   |
| ABDOMEN                                 | NUMBER EXAMINED: | 0    | 1   | 3   | 1   | 2   | 5      | 2   | 2   | 3   | 3   |
| --SERVIX                                |                  | 0    | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 1   |
| --INFLAMMATION                          |                  | 0    | 0   | 2   | 1   | 0   | 0      | 0   | 0   | 0   | 1   |
| --ADHESION                              |                  | 0    | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 1   |
| --FOCAL NECROSIS                        |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| ADIPOSE TISSUE                          | NUMBER EXAMINED: | 3    | 2   | 2   | 1   | 2   | 9      | 2   | 6   | 4   | 3   |
| --FAT NECROSIS                          |                  | 2    | 1   | 0   | 0   | 1   | 3      | 0   | 1   | 0   | 1   |
| --EDEMA                                 |                  | 0    | 0   | 0   | 0   | 0   | 1      | 1   | 0   | 0   | 0   |
| --INFLAMMATION                          |                  | 2    | 0   | 1   | 0   | 0   | 1      | 0   | 0   | 0   | 0   |
| --ADIPOPHIS                             |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --HAEMOUSAGE                            |                  | 0    | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 0   |
| --MINERALISATION                        |                  | 0    | 0   | 0   | 0   | 0   | 3      | 0   | 0   | 0   | 0   |
| --SPLEENULIS                            |                  | 0    | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| BILE DUCT                               | NUMBER EXAMINED: | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 2   | 0   | 0   |
| --LUMINAL DILATATION                    |                  | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   | 0   |
| BONE                                    | NUMBER EXAMINED: | 2    | 3   | 2   | 2   | 2   | 4      | 1   | 2   | 1   | 1   |
| --CHONDROID HYPERPLASIA                 |                  | 1    | 1   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| --EXOSTOSIS                             |                  | 1    | 0   | 1   | 0   | 1   | 1      | 0   | 2   | 1   | 1   |
| --FRACTURE                              |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --SANDCRASSAGE                          |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| BULBO-URETH. G.                         | NUMBER EXAMINED: | 1    | 2   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --CYSTIC ATROPHY                        |                  | 1    | 2   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |

: 201 :

HSH 002/013059  
0201



APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10F - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                    |         |         |              |               |    |
|--------------------|---------|---------|--------------|---------------|----|
| Group              | 1       | 2       | 3            | 4             | 5  |
| Compound           | Control | Control | Palonosetron | Hydrochloride |    |
| Dosage (mg/kg/day) | 0       | 0       | 10           | 30            | 60 |

Printed: 04-DEC-01

Page: 10

Schedule number: ESH 002

| ORGAN AND FINDING DESCRIPTION             | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |         |     |     |     |     |     |
|---|------------------------------------|-----|-----|-----|-----|---------|-----|-----|-----|-----|-----|
|   | SEX:                               |     |     |     |     | PEDALS: |     |     |     |     |     |
|   | GROUP:                             | -1- | -2- | -3- | -4- | -5-     | -1- | -2- | -3- | -4- | -5- |
| ** FROM PREVIOUS PAGE **                  | NUMBER:                            | 56  | 56  | 56  | 56  | 64      | 56  | 56  | 56  | 56  | 64  |
| BULBO-URETH. G.                           | NUMBER EXAMINED:                   | 1   | 2   | 1   | 0   | 0       | 0   | 0   | 0   | 0   | 0   |
| --INFLAMMATION                            |                                    | 0   | 0   | 1   | 0   | 0       | 0   | 0   | 0   | 0   | 0   |
| CLITORAL GLANDS                           | NUMBER EXAMINED:                   | 0   | 0   | 0   | 0   | 0       | 1   | 0   | 2   | 1   | 0   |
| --KERATIN CYST(S)                         |                                    | 0   | 0   | 0   | 0   | 0       | 1   | 0   | 1   | 1   | 0   |
| --ABSCESSES (AS)                          |                                    | 0   | 0   | 0   | 0   | 0       | 0   | 0   | 0   | 0   | 0   |
| --INFLAMMATION                            |                                    | 0   | 0   | 0   | 0   | 0       | 0   | 0   | 0   | 1   | 0   |
| COAGULATING G.                            | NUMBER EXAMINED:                   | 1   | 1   | 1   | 0   | 1       | 0   | 0   | 0   | 0   | 0   |
| --ABSCISSATION                            |                                    | 1   | 1   | 1   | 0   | 1       | 0   | 0   | 0   | 0   | 0   |
| DIAPHRAGM                                 | NUMBER EXAMINED:                   | 0   | 0   | 0   | 1   | 0       | 0   | 2   | 1   | 1   | 0   |
| --ADHESION                                |                                    | 0   | 0   | 0   | 1   | 0       | 0   | 0   | 0   | 0   | 0   |
| LN AXILLARY                               | NUMBER EXAMINED:                   | 6   | 5   | 13  | 7   | 6       | 7   | 11  | 10  | 10  | 9   |
| --PLASMOCTOSIS                            |                                    | 0   | 0   | 2   | 0   | 1       | 0   | 0   | 1   | 1   | 0   |
| --SINUS HISTIOCYTOSIS                     |                                    | 0   | 0   | 1   | 0   | 0       | 0   | 0   | 0   | 1   | 0   |
| --INCREASED CELLULARITY, PARACORTX        |                                    | 0   | 1   | 0   | 0   | 0       | 0   | 0   | 0   | 1   | 0   |
| --DILATED/CYSTIC SINUSES                  |                                    | 0   | 0   | 0   | 0   | 1       | 0   | 0   | 0   | 0   | 0   |
| --HAMORRHAGE                              |                                    | 1   | 0   | 1   | 0   | 0       | 0   | 0   | 0   | 0   | 0   |
| --SITE ONLY                               |                                    | 0   | 0   | 0   | 0   | 0       | 0   | 0   | 1   | 2   | 1   |
| LN BRONCHIAL                              | NUMBER EXAMINED:                   | 10  | 21  | 28  | 18  | 22      | 19  | 22  | 21  | 18  | 20  |
| --PLASMOCTOSIS                            |                                    | 1   | 1   | 3   | 0   | 2       | 2   | 0   | 0   | 1   | 0   |
| --INCREASED CELLULARITY, GENERALIZED      |                                    | 0   | 2   | 0   | 1   | 1       | 3   | 4   | 3   | 3   | 5   |
| --REACTIVE HISTIOCYTOSIS                  |                                    | 1   | 0   | 1   | 0   | 0       | 0   | 0   | 0   | 0   | 0   |
| --FATTY INFILTRATION                      |                                    | 4   | 6   | 3   | 3   | 5       | 1   | 2   | 2   | 0   | 3   |
| --SINUS HISTIOCYTOSIS/ERYTHROPHAGOCYTOSIS |                                    | 0   | 0   | 1   | 0   | 0       | 0   | 0   | 0   | 1   | 1   |
| --HAISTOCYTOSIS                           |                                    | 0   | 0   | 0   | 0   | 0       | 0   | 0   | 0   | 1   | 0   |

: 202 :

HSH 002/013059  
0202

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10F - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group: 1 2 3 4 5  
 Compound: Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day): 0 0 10 30 40  
 Printed: 04-DEC-01  
 Page: 19

Schedule number: NSH 003

--- NUMBER OF ANIMALS AFFECTED ---

| ORGAN AND FINDING DESCRIPTION            | SEX:             | MALE       |     |     |     |     | FEMALE |     |     |     |     |
|--|------------------|------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|  |                  | GROUP: -1- | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
|  | NUMBER:          | 06         | 06  | 06  | 06  | 04  | 06     | 04  | 06  | 06  | 04  |
| ** FROM PREVIOUS PAGE **                 |                  |            |     |     |     |     |        |     |     |     |     |
| LN BRONCHIAL                             | NUMBER EXAMINED: | 18         | 21  | 25  | 19  | 22  | 19     | 22  | 21  | 19  | 20  |
| --HAEMOSIDEROSIS                         |                  | 0          | 0   | 0   | 0   | 0   | 0      | 1   | 2   | 0   | 0   |
| --SITE ONLY                              |                  | 0          | 0   | 1   | 1   | 0   | 0      | 0   | 0   | 0   | 0   |
| LN THYMICAL                              | NUMBER EXAMINED: | 9          | 10  | 20  | 12  | 7   | 7      | 8   | 5   | 8   | 12  |
| --PLASMOCYTOSIS                          |                  | 1          | 1   | 2   | 1   | 2   | 0      | 0   | 0   | 0   | 1   |
| --INCREASED CELLULARITY, PARACORTX       |                  | 0          | 1   | 3   | 1   | 0   | 1      | 0   | 0   | 0   | 0   |
| --REACTIVE HISTIOCYTOSIS                 |                  | 0          | 1   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --SITE ONLY                              |                  | 0          | 1   | 0   | 1   | 0   | 1      | 0   | 0   | 1   | 2   |
| LN LUMBAR                                | NUMBER EXAMINED: | 14         | 10  | 20  | 11  | 8   | 32     | 24  | 24  | 23  | 23  |
| --PLASMOCYTOSIS                          |                  | 1          | 1   | 2   | 2   | 0   | 1      | 2   | 3   | 1   | 0   |
| --FATTY INFILTRATION                     |                  | 1          | 2   | 2   | 1   | 1   | 2      | 1   | 0   | 1   | 0   |
| --DILATED/CYSTIC SINUSES                 |                  | 2          | 1   | 1   | 1   | 0   | 1      | 0   | 0   | 2   | 0   |
| --SIMUS ENTEROCYTOSIS/ENTEROPHAGOCYTOSIS |                  | 0          | 0   | 0   | 0   | 0   | 2      | 1   | 0   | 0   | 0   |
| --INCREASED CELLULARITY, PARACORTX       |                  | 0          | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| --HAEMOSIDEROSIS                         |                  | 0          | 1   | 1   | 0   | 0   | 1      | 2   | 0   | 2   | 0   |
| --INCREASED CELLULARITY, GENERALISED     |                  | 0          | 0   | 0   | 0   | 0   | 2      | 1   | 0   | 1   | 1   |
| --REACTIVE HISTIOCYTOSIS                 |                  | 0          | 0   | 1   | 0   | 0   | 1      | 0   | 1   | 0   | 0   |
| --EXTRAMEDULLARY HAEMOPOIESIS            |                  | 0          | 0   | 1   | 0   | 0   | 1      | 1   | 1   | 0   | 0   |
| --PIGMENTATION                           |                  | 0          | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |
| --SITE ONLY                              |                  | 0          | 0   | 0   | 0   | 0   | 1      | 1   | 0   | 0   | 1   |
| LN MEDIASTINAL                           | NUMBER EXAMINED: | 4          | 3   | 4   | 1   | 1   | 4      | 2   | 2   | 2   | 1   |
| --PLASMOCYTOSIS                          |                  | 1          | 0   | 3   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --INCREASED CELLULARITY, PARACORTX       |                  | 0          | 0   | 1   | 0   | 0   | 1      | 0   | 0   | 0   | 0   |
| --ANGIECTASIS                            |                  | 0          | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --FATTY INFILTRATION                     |                  | 1          | 2   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --SIMUS ENTEROCYTOSIS/ENTEROPHAGOCYTOSIS |                  | 0          | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |

.. 203 ..

0203  
HSH 002/013059

:

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10P - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                    |         |         |                             |    |    |
|--------------------|---------|---------|-----------------------------|----|----|
| Group              | 1       | 2       | 3                           | 4  | 5  |
| Compound           | Control | Control | Faloxonestron Hydrochloride |    |    |
| Dosage (mg/kg/day) | 0       | 0       | 10                          | 30 | 60 |

Printed: 04-DEC-01  
Page: 20

Schedule number: HSH 003

| ORGAN AND FINDING DESCRIPTION              | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |                  |     |     |     |     |
|--|------------------------------------|-----|-----|-----|-----|------------------|-----|-----|-----|-----|
|  | SEX: -----MALE-----                |     |     |     |     | -----FEMALE----- |     |     |     |     |
|  | GROUP: -1-                         | -2- | -3- | -4- | -5- | -1-              | -2- | -3- | -4- | -5- |
| ** FROM PREVIOUS PAGE **                   | NUMBER:                            | 56  | 56  | 56  | 56  | 56               | 56  | 56  | 56  | 56  |
| LN MEDIASTINAL                             | NUMBER EXAMINED:                   | 4   | 3   | 4   | 1   | 1                | 4   | 2   | 2   | 1   |
| --SITE ONLY                                |                                    | 0   | 0   | 0   | 0   | 0                | 0   | 0   | 0   | 1   |
| LN PANCREATIC                              | NUMBER EXAMINED:                   | 10  | 6   | 19  | 7   | 6                | 14  | 13  | 13  | 7   |
| --PLASMOCYTOSIS                            |                                    | 1   | 0   | 3   | 0   | 0                | 0   | 0   | 2   | 3   |
| --REACTIVE HISTIOCYTOSIS                   |                                    | 1   | 0   | 1   | 0   | 0                | 0   | 0   | 0   | 0   |
| --SINUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                                    | 0   | 1   | 1   | 0   | 0                | 2   | 0   | 1   | 0   |
| --INCREASED CELLULARITY, PARACORTX         |                                    | 0   | 1   | 0   | 0   | 0                | 3   | 0   | 0   | 0   |
| --ANGIECTASIS                              |                                    | 1   | 1   | 1   | 0   | 0                | 0   | 0   | 0   | 0   |
| --HAEMODIARRHOE                            |                                    | 0   | 1   | 0   | 0   | 0                | 0   | 0   | 0   | 0   |
| --EXTRACAPILLARY HAEMOPHYSIS               |                                    | 1   | 0   | 1   | 0   | 1                | 0   | 0   | 0   | 0   |
| --GASTROCYTOSIS                            |                                    | 1   | 0   | 0   | 0   | 0                | 0   | 0   | 0   | 0   |
| --SITE ONLY                                |                                    | 0   | 0   | 0   | 1   | 0                | 1   | 0   | 0   | 0   |
| LN POPLITEAL                               | NUMBER EXAMINED:                   | 2   | 3   | 4   | 3   | 2                | 3   | 3   | 3   | 2   |
| --SINUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                                    | 0   | 0   | 0   | 0   | 0                | 0   | 1   | 0   | 0   |
| LN RENAL                                   | NUMBER EXAMINED:                   | 11  | 14  | 20  | 10  | 9                | 16  | 19  | 11  | 10  |
| --PLASMOCYTOSIS                            |                                    | 0   | 3   | 4   | 2   | 0                | 0   | 2   | 2   | 0   |
| --DILATED/CYSTIC SINUSES                   |                                    | 0   | 2   | 1   | 0   | 0                | 0   | 0   | 0   | 1   |
| --SINUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                                    | 0   | 0   | 2   | 1   | 0                | 2   | 0   | 1   | 0   |
| --HAEMORRHAGE                              |                                    | 0   | 0   | 0   | 0   | 0                | 1   | 0   | 0   | 0   |
| --INCREASED CELLULARITY, GENERALISED       |                                    | 1   | 0   | 0   | 0   | 0                | 1   | 0   | 0   | 1   |
| --ANGIECTASIS                              |                                    | 0   | 1   | 0   | 0   | 0                | 0   | 0   | 0   | 1   |
| --FATTY INFILTRATION                       |                                    | 1   | 0   | 1   | 1   | 3                | 0   | 0   | 0   | 0   |
| --INCREASED CELLULARITY, PARACORTX         |                                    | 0   | 0   | 0   | 0   | 1                | 0   | 0   | 0   | 0   |
| --HAEMODIARRHOE                            |                                    | 0   | 1   | 0   | 0   | 0                | 2   | 0   | 0   | 0   |
| --SINUS HISTIOCYTOSIS                      |                                    | 1   | 0   | 1   | 0   | 0                | 1   | 1   | 0   | 0   |
| --SITE ONLY                                |                                    | 1   | 1   | 0   | 0   | 0                | 0   | 0   | 0   | 0   |

204

HSH 002/013059

0204

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10P - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
 Page: 21

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION              | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |        |     |     |     |     |
|--|------------------------------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|  | SEX: -----                         |     |     |     |     | -----  |     |     |     |     |
|  | MALE                               |     |     |     |     | FEMALE |     |     |     |     |
| GROUP:                                     | -1-                                | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
| NUMBER:                                    | 56                                 | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| LN THYMIC .....                            | NUMBER EXAMINED:                   |     |     |     |     |        |     |     |     |     |
| --PLASMOCTOSIS                             | 4                                  | 5   | 12  | 5   | 8   | 21     | 19  | 19  | 19  | 16  |
| --INCREASED CELLULARITY, PARACORTE         | 0                                  | 0   | 0   | 0   | 0   | 1      | 0   | 1   | 1   | 1   |
| --FATTY INFILTRATION                       | 0                                  | 0   | 0   | 0   | 0   | 2      | 2   | 2   | 4   | 2   |
| --SIMUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS | 0                                  | 0   | 1   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --AMIOCYTASIS                              | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| --GUMULON (TS)                             | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| --DILATED/CYSTIC SINUSES                   | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |
| --RADIOICROSIS                             | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 1   | 1   | 0   |
| --INCREASED CELLULARITY, GENERALISED       | 0                                  | 0   | 0   | 0   | 0   | 2      | 0   | 0   | 0   | 0   |
| --SITE ONLY                                | 0                                  | 1   | 0   | 0   | 0   | 0      | 2   | 2   | 0   | 1   |
| MOUSARY A. CHAN .....                      | NUMBER EXAMINED:                   |     |     |     |     |        |     |     |     |     |
| --ACTINAR HYPERPLASIA                      | 3                                  | 1   | 1   | 1   | 0   | 4      | 4   | 1   | 4   | 7   |
| --OCULAR DILATATION                        | 0                                  | 0   | 0   | 0   | 0   | 1      | 0   | 0   | 1   | 0   |
| --INFLAMMATION                             | 3                                  | 0   | 1   | 1   | 0   | 1      | 1   | 0   | 1   | 0   |
| MUSCLE .....                               | NUMBER EXAMINED:                   |     |     |     |     |        |     |     |     |     |
| --GLANGLULAR CHRONIC INFLAMMATION          | 3                                  | 5   | 2   | 4   | 1   | 2      | 1   | 2   | 2   | 3   |
| --TRUNCUS/TROUSI                           | 0                                  | 1   | 1   | 2   | 0   | 0      | 0   | 0   | 0   | 0   |
| --MYOCYIC ABSCESS (ES)                     | 1                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --RADIOICROSIS                             | 1                                  | 0   | 0   | 2   | 1   | 0      | 0   | 0   | 0   | 0   |
| --INFLAMMATION                             | 2                                  | 2   | 0   | 2   | 0   | 0      | 0   | 0   | 0   | 0   |
| --FOCAL NECROSIS                           | 2                                  | 0   | 1   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| --ABSCESS (ES)                             | 1                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| OVIDUCTS .....                             | NUMBER EXAMINED:                   |     |     |     |     |        |     |     |     |     |
| --CYST (S)                                 | 0                                  | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 2   | 1   |

: 205 :

HSH 002/013059  
 0205



APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10F - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                    |         |         |                           |    |    |
|--------------------|---------|---------|---------------------------|----|----|
| Group              | 1       | 2       | 3                         | 4  | 5  |
| Compound           | Control | Control | Faloxestron Hydrochloride |    |    |
| Dosage (mg/kg/day) | 0       | 0       | 10                        | 30 | 60 |

Printed: 04-DEC-01

Page: 22

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION   | NUMBER OF ANIMALS AFFECTED |     |     |     |     |             |     |     |     |     |
|---------------------------------|----------------------------|-----|-----|-----|-----|-------------|-----|-----|-----|-----|
|                                 | SEX: MALE                  |     |     |     |     | SEX: FEMALE |     |     |     |     |
|                                 | GROUP: -1-                 | -2- | -3- | -4- | -5- | -1-         | -2- | -3- | -4- | -5- |
| PAWS                            | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --INFLAMMATION                  | 1                          | 0   | 0   | 1   | 1   | 0           | 0   | 1   | 0   | 0   |
| --KERATIN CYST(S)               | 1                          | 0   | 0   | 1   | 0   | 0           | 0   | 0   | 0   | 0   |
| PENIS/PREPUCE                   | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --TRAUMA                        | 1                          | 0   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 0   |
| --INFLAMMATION                  | 1                          | 0   | 0   | 0   | 2   | 0           | 0   | 0   | 0   | 0   |
| --CONGESTION OF ERECTILE TISSUE | 0                          | 1   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 0   |
| PREPUTIAL GLANDS                | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --ABSCESSEATION                 | 4                          | 6   | 9   | 7   | 3   | 0           | 0   | 0   | 0   | 0   |
| --INFLAMMATION                  | 2                          | 4   | 3   | 5   | 2   | 0           | 0   | 0   | 0   | 0   |
| --CYST(S)                       | 4                          | 3   | 3   | 4   | 2   | 0           | 0   | 0   | 0   | 0   |
| --KERATIN CYST(S)               | 1                          | 3   | 2   | 3   | 1   | 0           | 0   | 0   | 0   | 0   |
| SKIN/SUBCUTIS                   | NUMBER EXAMINED:           |     |     |     |     |             |     |     |     |     |
| --CEDEMA                        | 0                          | 0   | 3   | 1   | 4   | 5           | 4   | 4   | 4   | 1   |
| --EPIDERMAL ULCERATION          | 1                          | 2   | 2   | 2   | 3   | 0           | 5   | 4   | 3   | 4   |
| --INFLAMMATION                  | 1                          | 2   | 4   | 1   | 7   | 0           | 7   | 4   | 4   | 5   |
| --EPIDERMAL HYPERPLASIA         | 1                          | 0   | 3   | 2   | 2   | 1           | 6   | 1   | 2   | 4   |
| --GRANULOMA (TA)                | 0                          | 0   | 0   | 0   | 1   | 0           | 0   | 0   | 0   | 0   |
| --SCAB(S)                       | 0                          | 0   | 2   | 1   | 2   | 0           | 3   | 4   | 3   | 4   |
| --GLANDULAR/DUCTULAR DILATATION | 0                          | 1   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 0   |
| --HEMORRHAGE                    | 0                          | 1   | 0   | 0   | 0   | 0           | 0   | 0   | 0   | 0   |
| --AREA(S) OF PROMINENT COLLAGEN | 0                          | 0   | 0   | 0   | 1   | 0           | 0   | 0   | 0   | 0   |
| --KERATIN CYST(S)               | 0                          | 0   | 0   | 0   | 0   | 0           | 0   | 1   | 0   | 0   |
| --SERACEOUS GLAND HYPERPLASIA   | 0                          | 0   | 0   | 0   | 1   | 0           | 0   | 0   | 0   | 0   |

: 206 :

0206

HSH 002/013059

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10F - continued.

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 1 2 3 4 5  
 Compound : Central Control Pelonecstron Hydrochloride  
 Dose (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01

Page: 23

Schedule Number: R58 002

| ORGAN AND FINDING DESCRIPTION         | NUMBER OF ANIMALS AFFECTED |     |        |     |     |      |     |        |     |     |
|---------------------------------------|----------------------------|-----|--------|-----|-----|------|-----|--------|-----|-----|
|                                       | SEX:                       |     |        |     |     | AGE: |     |        |     |     |
|                                       | MALE                       |     | FEMALE |     |     | MALE |     | FEMALE |     |     |
|                                       | -1-                        | -2- | -3-    | -4- | -5- | -1-  | -2- | -3-    | -4- | -5- |
| NUMBER:                               | 56                         | 56  | 56     | 56  | 64  | 56   | 56  | 56     | 56  | 64  |
| TAIL                                  | NUMBER EXAMINED:           |     |        |     |     |      |     |        |     |     |
| --EPIDERMAL ULCERATION                | 4                          | 4   | 3      | 4   | 4   | 3    | 4   | 3      | 1   | 1   |
| --KERATIN CYST(S)                     | 0                          | 0   | 2      | 2   | 1   | 0    | 1   | 0      | 0   | 0   |
| --INFLAMMATION                        | 0                          | 1   | 0      | 1   | 0   | 1    | 1   | 0      | 0   | 0   |
| --SCAB(S)                             | 0                          | 2   | 2      | 0   | 1   | 0    | 0   | 0      | 0   | 1   |
| --SCAR - NECROSIS                     | 1                          | 1   | 1      | 1   | 1   | 0    | 3   | 1      | 0   | 0   |
| --PIGMENTATION                        | 0                          | 0   | 0      | 0   | 0   | 1    | 0   | 0      | 0   | 0   |
| --EPIDERMAL HYPERPLASIA               | 0                          | 1   | 0      | 0   | 0   | 0    | 1   | 0      | 0   | 0   |
| TESTIS                                | NUMBER EXAMINED:           |     |        |     |     |      |     |        |     |     |
| --NECROBLASTIC EPITHELIAL HYPERPLASIA | 1                          | 0   | 0      | 0   | 0   | 0    | 1   | 1      | 0   | 0   |
| PROSTATE                              | NUMBER EXAMINED:           |     |        |     |     |      |     |        |     |     |
| --ADENOMA                             | 1                          | 0   | 1      | 3   | 1   | 3    | 3   | 0      | 4   | 4   |
| URETERS                               | NUMBER EXAMINED:           |     |        |     |     |      |     |        |     |     |
| --INFLAMMATION                        | 4                          | 3   | 1      | 1   | 1   | 0    | 0   | 2      | 0   | 2   |
| ** END OF LIST **                     | 1                          | 2   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 0   |

: 207 :

HSR 002/013059

0207

IND    
Page 221

NDA 21-372  
Page 79

APPENDIX II

Group Distribution of Neoplastic Incidences in animals of 104-week Mouse Carcinogenicity Study.

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10C

Histopathology - group distribution of neoplastic findings for all animals

Print No: 0018

Group : 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
 Page: 1

Schedule number: N2H 002

--- NUMBER OF ANIMALS AFFECTED ---

| ORGAN AND FINDING DESCRIPTION    | SEX: GROUP       | MALE |     |     |     |     | FEMALE |     |     |     |     |
|----------------------------------|------------------|------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|                                  |                  | -1-  | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
| ** TOP OF LIST **                | NUMBER:          | 56   | 56  | 56  | 56  | 56  | 56     | 56  | 56  | 56  | 56  |
| ADRENAL CTX                      | NUMBER EXAMINED: | 55   | 55  | 55  | 56  | 56  | 56     | 55  | 56  | 56  | 53  |
| --S-SPINDLE CELL ADENOMA         |                  | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 1   | 0   | 0   |
| --S-SUBCAPSULAR CELL ADENOMA     |                  | 1    | 0   | 1   | 1   | 4   | 0      | 0   | 0   | 0   | 0   |
| --S-CORTICAL ADENOMA             |                  | 0    | 0   | 0   | 0   | 2   | 0      | 0   | 0   | 0   | 0   |
| --M-SPINDLE CELL CARCINOMA       |                  | 0    | 0   | 0   | 0   | 0   | 0      | 0   | 1   | 0   | 0   |
| ADRENAL MED                      | NUMBER EXAMINED: | 55   | 55  | 55  | 56  | 56  | 55     | 56  | 56  | 56  | 53  |
| --S-PHACROCHROMOCYTOMA           |                  | 0    | 0   | 0   | 0   | 0   | 0      | 2   | 0   | 0   | 0   |
| --M-MALIGNANT PHACROCHROMOCYTOMA |                  | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   | 0   |
| BRAIN X4                         | NUMBER EXAMINED: | 56   | 56  | 56  | 56  | 56  | 56     | 56  | 56  | 56  | 56  |
| --M-MENINGEAL SARCOMA            |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| CARCIN                           | NUMBER EXAMINED: | 55   | 56  | 55  | 53  | 53  | 53     | 56  | 55  | 53  | 53  |
| --S-LEIOMYOMA                    |                  | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   | 0   |
| --M-ADENOCARCINOMA               |                  | 0    | 0   | 2   | 0   | 2   | 0      | 0   | 0   | 0   | 0   |
| DUODENUM                         | NUMBER EXAMINED: | 54   | 55  | 55  | 52  | 51  | 53     | 54  | 55  | 54  | 50  |
| --S-ADENOMA                      |                  | 0    | 0   | 0   | 0   | 2   | 0      | 0   | 0   | 0   | 0   |
| --M-ADENOCARCINOMA               |                  | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 1   | 0   | 0   |
| GALL BLADDER                     | NUMBER EXAMINED: | 52   | 52  | 53  | 50  | 56  | 54     | 51  | 53  | 52  | 50  |
| --S-PAPILLOMA                    |                  | 1    | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| PANCREATIC ISLET                 | NUMBER EXAMINED: | 56   | 56  | 56  | 56  | 56  | 56     | 56  | 56  | 55  | 54  |
| --S-ADENOMA                      |                  | 5    | 7   | 6   | 4   | 5   | 1      | 5   | 4   | 3   | 2   |
| --M-ADENOCARCINOMA               |                  | 0    | 0   | 0   | 0   | 0   | 1      | 0   | 0   | 0   | 1   |

: 140 :

IND  
 Page 223

HSH 002/013059 0140

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL



TABLE 10C - continued.

Print No: 0010

Histopathology - group distribution of neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Palmoestron Hydrochloride  
 Dose (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
 Page: 2

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION       | NUMBER OF ANIMALS AFFECTED |      |     |     |     |     |        |     |     |     |     |
|-------------------------------------|----------------------------|------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|                                     | SEX GROUP                  | MALE |     |     |     |     | FEMALE |     |     |     |     |
|                                     |                            | -1-  | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
| NUMBER EXAMINED:                    | 56                         | 56   | 56  | 56  | 64  | 56  | 56     | 56  | 56  | 64  |     |
| PLEURUM                             | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --M-ADENOCARCINOMA                  | 0                          | 0    | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   |     |
| KIDNEYS                             | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-TUBULAR ADENOMA                 | 0                          | 0    | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   |     |
| --M-RADIONCARCINOMA                 | 0                          | 1    | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   |     |
| LIVER X 1                           | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-HEPATOCELLULAR ADENOMA          | 16                         | 16   | 16  | 16  | 16  | 16  | 16     | 16  | 16  | 16  |     |
| --M-HEPATOCELLULAR CARCINOMA        | 14                         | 6    | 11  | 6   | 7   | 0   | 0      | 2   | 0   | 0   |     |
| --M-RADIONCARCINOMA                 | 2                          | 1    | 3   | 1   | 3   | 0   | 0      | 0   | 0   | 0   |     |
| LN MENTHERIC                        | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-EMBRYONOMA                      | 1                          | 0    | 0   | 0   | 0   | 0   | 1      | 1   | 0   | 0   |     |
| LUNG X 2                            | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-BRONCHIOALVEOLAR ADENOMA        | 12                         | 17   | 13  | 11  | 19  | 8   | 7      | 11  | 11  | 9   |     |
| --M-BRONCHIOALVEOLAR ADENOCARCINOMA | 4                          | 5    | 3   | 1   | 1   | 4   | 0      | 3   | 0   | 2   |     |
| --M-ANAPLASTIC CARCINOMA            | 0                          | 0    | 0   | 1   | 0   | 0   | 0      | 0   | 0   | 0   |     |
| MURRAY A. CELL                      | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-ADENOMATOUS FIBROSARCOMA        | 0                          | 0    | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   |     |
| --M-ADENOMATOUS FIBROSARCOMA        | 0                          | 0    | 0   | 0   | 0   | 1   | 0      | 2   | 0   | 2   |     |
| --M-FIBROSARCOMA                    | 0                          | 0    | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   |     |
| OVARIES                             | NUMBER EXAMINED:           |      |     |     |     |     |        |     |     |     |     |
| --S-CYSTIC                          | 0                          | 0    | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   |     |
| --S-LIPOMA                          | 0                          | 0    | 0   | 0   | 0   | 1   | 3      | 2   | 8   | 1   |     |
| --S-SERTOLI CELL TUMOR              | 0                          | 0    | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   |     |

141

HSH 002/013059  
 0141

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10C - continued.

Print No: 0016

Histopathology - group distribution of neoplastic findings for all animals

Group 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 60  
 Printed: 04-DEC-01  
 Page: 3

Schedule number: BSH 002

| ORGAN AND FINDING DESCRIPTION | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |       |     |     |     |     |     |
|-------------------------------|------------------------------------|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|
|                               | SEX:                               |     |     |     |     | FOLE: |     |     |     |     |     |
|                               | GROUP:                             | -1- | -2- | -3- | -4- | -5-   | -1- | -2- | -3- | -4- | -5- |
| ** FROM PREVIOUS PAGE **      | NUMBER:                            | 56  | 56  | 56  | 56  | 56    | 56  | 56  | 56  | 56  | 56  |
| OVARIES                       | NUMBER EXAMINED:                   | 0   | 0   | 0   | 0   | 0     | 56  | 56  | 56  | 56  | 56  |
| --S-SARCOMA                   |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 1   | 1   | 0   | 0   |
| --S-GRANULOSA CELL TUMOR      |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 0   | 0   | 1   | 0   |
| --S-LEIOMYOMA                 |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 0   | 0   | 1   | 0   |
| --S-FUNCTIONAL ADENOMA        |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 0   | 0   | 1   | 0   |
| --M-GRANULOSA CELL TUMOR      |                                    | 0   | 0   | 0   | 0   | 0     | 1   | 0   | 0   | 1   | 0   |
| --S-THCA/GRANULOSA CELL TUMOR |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 1   | 0   | 0   | 0   |
| PANCREAS                      | NUMBER EXAMINED:                   | 56  | 56  | 56  | 56  | 56    | 56  | 56  | 56  | 56  | 56  |
| --S-ACINAR CELL ADENOMA       |                                    | 1   | 0   | 0   | 0   | 0     | 0   | 0   | 0   | 0   | 0   |
| --S-ISLET CELL ADENOMA        |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 0   | 1   | 0   | 0   |
| PARATHYROID                   | NUMBER EXAMINED:                   | 49  | 42  | 41  | 47  | 50    | 42  | 44  | 42  | 42  | 56  |
| --S-ADENOMA                   |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 0   | 1   | 0   | 0   |
| PITUITARY                     | NUMBER EXAMINED:                   | 56  | 55  | 55  | 56  | 56    | 56  | 56  | 56  | 56  | 56  |
| --S-ADENOMA, PART DISTALIS    |                                    | 0   | 0   | 0   | 0   | 0     | 0   | 3   | 0   | 1   | 2   |
| EDENAL VESICLES               | NUMBER EXAMINED:                   | 56  | 56  | 56  | 56  | 56    | 0   | 0   | 0   | 0   | 0   |
| --S-ADENOMA                   |                                    | 0   | 0   | 0   | 0   | 1     | 0   | 0   | 0   | 0   | 0   |
| --M-CARCINOSARCOMA            |                                    | 0   | 1   | 0   | 0   | 0     | 0   | 0   | 0   | 0   | 0   |
| SPLEEN                        | NUMBER EXAMINED:                   | 56  | 56  | 56  | 56  | 56    | 56  | 56  | 56  | 56  | 56  |
| --S-SARCOMA                   |                                    | 0   | 0   | 0   | 1   | 0     | 0   | 1   | 0   | 0   | 0   |
| --M-SARCOMATOSARCOMA          |                                    | 2   | 0   | 0   | 0   | 1     | 0   | 0   | 0   | 0   | 0   |
| --M-STROMAL CELL SARCOMA      |                                    | 0   | 0   | 1   | 0   | 0     | 0   | 0   | 0   | 0   | 0   |
| STOMACH 13                    | NUMBER EXAMINED:                   | 56  | 56  | 56  | 56  | 56    | 56  | 56  | 56  | 56  | 56  |
| --S-ADENOMA                   |                                    | 1   | 0   | 0   | 0   | 0     | 0   | 0   | 0   | 0   | 0   |

: 142 :

HSR 002/013059 0142

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10C - continued.

Print No: 0018

Histopathology - group distribution of neoplastic findings for all animals

Group : 1 2 3 4 5  
Compound : Control Control Palonosetron Hydrochloride  
Doseage (ug/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
Page: 4

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION          | NUMBER OF ANIMALS AFFECTED |     |     |     |     |        |     |     |     |     |     |
|--|----------------------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|
|  | MALE                       |     |     |     |     | FEMALE |     |     |     |     |     |
|  | SEX GROUP                  | -1- | -2- | -3- | -4- | -5-    | -1- | -2- | -3- | -4- | -5- |
| ** FROM PREVIOUS PAGE **               | NUMBER                     | 56  | 56  | 56  | 56  | 64     | 56  | 56  | 56  | 56  | 64  |
| STOMACH                                | NUMBER EXAMINED:           | 56  | 56  | 56  | 56  | 64     | 56  | 56  | 56  | 56  | 64  |
| --SQUAMOUS CELL PAPILLOMA              |                            | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   | 0   |
| --M-ANAPLASTIC CARCINOMA               |                            | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   | 0   |
| --M-ADENOCARCINOMA                     |                            | 0   | 0   | 0   | 0   | 1      | 0   | 0   | 0   | 0   | 0   |
| TESTES                                 | NUMBER EXAMINED:           | 56  | 56  | 56  | 56  | 64     | 0   | 0   | 0   | 0   | 0   |
| --S-INTERSTITIAL (LEYDIG) CELL ADENOMA |                            | 0   | 1   | 1   | 0   | 0      | 0   | 0   | 0   | 0   | 0   |
| --S-ADENOMA, SEVE TESTIS               |                            | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 0   | 0   |
| --S-LEIOMYOMA                          |                            | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   | 0   |
| THYROID                                | NUMBER EXAMINED:           | 56  | 56  | 56  | 56  | 64     | 56  | 56  | 56  | 56  | 64  |
| --S-FOLLICULAR CELL ADENOMA            |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   | 1   |
| --M-FOLLICULAR CELL CARCINOMA          |                            | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   | 0   |
| TONGUE                                 | NUMBER EXAMINED:           | 56  | 56  | 56  | 56  | 64     | 56  | 56  | 56  | 56  | 64  |
| --M-SQUAMOUS CELL CARCINOMA            |                            | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   | 0   |
| UTERINE CERVIX                         | NUMBER EXAMINED:           | 0   | 0   | 0   | 0   | 0      | 56  | 56  | 56  | 56  | 64  |
| --S-LEIOMYOMA                          |                            | 0   | 0   | 0   | 0   | 0      | 0   | 1   | 0   | 0   | 1   |
| --M-LEIOMYOSARCOMA                     |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   | 0   |
| UTERUS                                 | NUMBER EXAMINED:           | 0   | 0   | 0   | 0   | 0      | 56  | 56  | 56  | 56  | 64  |
| --S-SARCOMA                            |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   | 1   |
| --S-LEIOMYOMA                          |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 2   | 1   | 0   |
| --S-ENDOMETRIAL POLYP                  |                            | 0   | 0   | 0   | 0   | 0      | 0   | 3   | 2   | 1   | 0   |
| --S-ENDOMETRIAL ADENOMA                |                            | 0   | 0   | 0   | 0   | 0      | 5   | 13  | 6   | 3   | 7   |
| --M-ENDOMETRIAL ADENOCARCINOMA         |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   | 1   |
| --M-MALIGNANT SEROSARCOMA              |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   | 0   |
| --M-SARCOMA                            |                            | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 1   | 1   |

: 143 :

HSH 002/013059 0143

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 10C - continued.

Print No: 0010

Histopathology - group distribution of neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Paclitaxel Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 50

Printed: 04-DEC-01  
 Page: 3

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION   | --- NUMBER OF ANIMALS AFFECTED --- |     |        |     |     |      |     |        |     |     |
|---------------------------------|------------------------------------|-----|--------|-----|-----|------|-----|--------|-----|-----|
|                                 | SEX:                               |     |        |     |     | AGE: |     |        |     |     |
|                                 | MALE                               |     | FEMALE |     |     | MALE |     | FEMALE |     |     |
| GROUP:                          | -1-                                | -2- | -3-    | -4- | -5- | -1-  | -2- | -3-    | -4- | -5- |
| NUMBER:                         | 84                                 | 86  | 84     | 84  | 84  | 86   | 86  | 86     | 86  | 84  |
| ** FROM PREVIOUS PAGE **        |                                    |     |        |     |     |      |     |        |     |     |
| UTERUS                          | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --M-LEIOMYOSARCOMA              | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 0   |
| --M-ENDOMETRIAL STROMAL SARCOMA | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 1   | 0   |
| VAGINA                          | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --M-EPITHELIOID SARCOMA         | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 0   |
| ADIPOSER                        | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --M-ANGIOLIPOMA                 | 0                                  | 1   | 2      | 1   | 2   | 2    | 2   | 2      | 2   | 2   |
| --M-OSTEOGENIC                  | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 1      | 0   | 0   |
| BONE                            | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --M-MALIGNANT FIBROSARCOMA      | 2                                  | 2   | 2      | 2   | 2   | 4    | 1   | 2      | 1   | 1   |
| HEMATOPOIETIC TUMOR             | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --M-MYELOID LEUKEMIA            | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 0   |
| --M-MALIGNANT LYMPHOMA          | 1                                  | 1   | 0      | 0   | 1   | 0    | 0   | 0      | 0   | 1   |
| --M-MEGAKARYOCYTIC LEUKEMIA     | 2                                  | 5   | 0      | 0   | 1   | 7    | 12  | 10     | 8   | 9   |
| --M-EPITHELIOID SARCOMA         | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 1   |
| --M-PLASMOCYTIC LYMPHOMA        | 0                                  | 0   | 0      | 0   | 2   | 2    | 2   | 2      | 1   | 2   |
| HEMANGIOMA                      | 4                                  | 0   | 7      | 1   | 2   | 7    | 4   | 6      | 3   | 8   |
| HEMANGIOMA OF SKIN              | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --S-HEMANGIOMA                  | 3                                  | 1   | 1      | 1   | 0   | 4    | 4   | 1      | 4   | 7   |
| --M-CARCINOMA                   | 0                                  | 0   | 0      | 0   | 0   | 1    | 0   | 0      | 0   | 0   |
| --M-ADENOCARCINOMA              | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 1   |
| --M-HEMANGIOMA                  | 0                                  | 0   | 0      | 0   | 0   | 0    | 0   | 0      | 1   | 0   |
| MUSCLE                          | NUMBER EXAMINED:                   |     |        |     |     |      |     |        |     |     |
| --S-FIBROMA                     | 3                                  | 2   | 2      | 4   | 1   | 2    | 1   | 2      | 2   | 3   |
|                                 | 0                                  | 1   | 0      | 0   | 0   | 0    | 0   | 0      | 0   | 0   |

144

HSH 002/013059 0144

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL



TABLE 10C - continued.

Print No: 0018

Histopathology - group distribution of neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dosage (mg/kg/day) : 0 0 10 30 60

Printed: 04-DEC-01  
 Page: 6

Schedule number: HSH 002

| ORGAN AND FINDING DESCRIPTION | --- NUMBER OF ANIMALS AFFECTED --- |     |     |     |     |        |     |     |     |     |
|-------------------------------|------------------------------------|-----|-----|-----|-----|--------|-----|-----|-----|-----|
|                               | SEX:                               |     |     |     |     | SEX:   |     |     |     |     |
|                               | MALE                               |     |     |     |     | FEMALE |     |     |     |     |
|                               | -1-                                | -2- | -3- | -4- | -5- | -1-    | -2- | -3- | -4- | -5- |
|                               | NUMBER:                            |     |     |     |     |        |     |     |     |     |
| ** FROM PREVIOUS PAGE **      | 56                                 | 56  | 56  | 56  | 64  | 56     | 56  | 56  | 56  | 64  |
| MUSCLE                        |                                    |     |     |     |     |        |     |     |     |     |
| --M-FIBROSARCOMA              | 3                                  | 5   | 2   | 4   | 1   | 2      | 1   | 2   | 2   | 3   |
| --M-LEIOMYOSARCOMA            | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
|                               | 0                                  | 1   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| SKIN/SUBCUTIS                 |                                    |     |     |     |     |        |     |     |     |     |
| --S-KEPATOACANTHOMA           | 3                                  | 12  | 12  | 12  | 21  | 11     | 12  | 11  | 12  | 16  |
| --S-SQUAMOUS CELL PAPILLOMA   | 1                                  | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| --M-FIBROUS HISTIOCYTOMA      | 0                                  | 0   | 0   | 0   | 0   | 0      | 1   | 0   | 0   | 0   |
| --M-UNDIFFERENTIATED SARCOMA  | 0                                  | 0   | 1   | 0   | 0   | 0      | 0   | 1   | 0   | 0   |
| --M-REARDOYOSARCOMA           | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 1   |
| --M-POLYOMYXOID SARCOMA       | 1                                  | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 0   |
| --M-FIBROSARCOMA              | 0                                  | 1   | 1   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |
| THORAX                        |                                    |     |     |     |     |        |     |     |     |     |
| --M-REARDOYOSARCOMA           | 1                                  | 0   | 1   | 3   | 1   | 5      | 3   | 9   | 4   | 4   |
| --M-OSTEOSARCOMA              | 1                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 0   | 0   |
| --M-UNDIFFERENTIATED SARCOMA  | 0                                  | 0   | 0   | 1   | 0   | 0      | 0   | 0   | 0   | 0   |
| --M-FIBROSARCOMA              | 0                                  | 0   | 0   | 0   | 1   | 0      | 0   | 0   | 0   | 0   |
| ** END OF LIST **             | 0                                  | 0   | 0   | 0   | 0   | 0      | 0   | 0   | 1   | 0   |

: 145 :

HSH 002013059 0145

IND   
Page 234

MUA 21-372  
Page 00

APPENDIX III

Group Distribution of Non Neoplastic Incidences in animals of 104 week Rat Carcinogenicity

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F

Print No 0023

Histopathology - group distribution of non-neoplastic findings for all animals

Group            1        2        3        4        5  
 Compound        Control Control Palonosetron Hydrochloride  
 Dose (mg/kg/day): 0        0        15        30/45    62/90

Printed: 85-NOV-81  
 Page: 1

Schedule number: N88 001

----- NUMBER OF ANIMALS AFFECTED -----

| ORGAN AND FINDING DESCRIPTION               | SEX GROUP | -----MALE----- |      |     |      |       |
|---|-----------|----------------|------|-----|------|-------|
|   |           | 1              | 2    | 3   | 4    | 5     |
| <b>ADRENAL CXT</b>                          |           |                |      |     |      |       |
| NUMBER EXAMINED                             |           | 65             | 65   | 65  | 65   | 65    |
| --CORTICAL CONGESTION                       |           | 0              | 2    | 0   | 1    | 1     |
| --CORTICAL VACUOLATION                      |           | 0              | 16   | 15  | 12   | 11    |
| --CORTICAL HYPERTROPHY                      |           | 11 d           | 23 s | 14  | 10 d | 12 d  |
| --CORTICAL FIBROSIS                         |           | 1              | 0    | 0   | 2    | 0     |
| --CORTICAL CYSTIC/HAEMORRHAGIC DEGENERATION |           | 0              | 0    | 11  | 12   | 12    |
| --CORTICAL HYPERPLASIA, FOCAL               |           | 0              | 6    | 0   | 10   | 3     |
| --LOWA GLOMERULOSA - HYPERTROPHY, FOCAL     |           | 10             | 15   | 13  | 4    | 1 dfa |
| --MADNESICERIN DEPOSITION                   |           | 1              | 0    | 0   | 1    | 0     |
| --EXTRAMEDULLARY HAEMOPHOSES                |           | 0              | 0    | 2   | 1    | 1     |
| --EXTRA-CAPSULAR CORTICAL TISSUE            |           | 0              | 0    | 0   | 1    | 0     |
| <b>ADRENAL MED</b>                          |           |                |      |     |      |       |
| NUMBER EXAMINED                             |           | 65             | 65   | 65  | 65   | 65    |
| --MEDULLARY HYPERPLASIA, FOCAL              |           | 1              | 4    | 6   | 12   | 0     |
| --CORTICAL CYSTIC/HAEMORRHAGIC DEGENERATION |           | 1              | 0    | 1   | 0    | 2     |
| --FIBROSIS                                  |           | 0              | 0    | 0   | 0    | 2     |
| <b>AORTA</b>                                |           |                |      |     |      |       |
| NUMBER EXAMINED                             |           | 65             | 64   | 65  | 65   | 65    |
| --MEDIAL MINERALISATION                     |           | 0              | 0    | 0   | 1    | 0     |
| <b>BRAIN X</b>                              |           |                |      |     |      |       |
| NUMBER EXAMINED                             |           | 65             | 65   | 65  | 65   | 65    |
| --DEPRESSION DUE TO ENLARGED PITUITARY      |           | 10             | 6    | 22  | 16   | 20 an |
| --DILATED VENTRICLES                        |           | 1              | 1    | 7 h | 3    | 4     |
| --SUB-MENINGEAL HAEMORRHAGE                 |           | 1              | 0    | 0   | 0    | 1     |
| --MINERALISATION                            |           | 0              | 0    | 0   | 3 p  | 0     |
| <b>CARCUM</b>                               |           |                |      |     |      |       |
| NUMBER EXAMINED                             |           | 65             | 65   | 65  | 65   | 65    |
| --MUCOSAL CHRONIC INFLAMMATION              |           | 2              | 0    | 0   | 1    | 0     |
| --MUCOSAL ULCERATION                        |           | 2              | 0    | 0   | 0    | 1     |

150

TABLE 11F - continued

Print No. 0033

Histopathology - group distribution of non-neoplastic findings for all animals

Group                    1            2            3            4            5  
 Compound            Control Control Palonosipron Hydrochloride  
 Dose (mg/kg/day):    0            0            10          10:45       60:00

Printed: 05-MAY-01

Page: 2

Schedule number: N3H 091

..... N U M B E R   O F   A N I M A L S   A F F E C T E D .....

| ORGAN AND FINDING DESCRIPTION          | SEX GROUP        | MALE |     |     |     |        |
|--|------------------|------|-----|-----|-----|--------|
|  |                  | -1-  | -2- | -3- | -4- | -5-    |
| NUMBER EXAMINED:                       | NUMBER:          | 05   | 05  | 05  | 05  | 05     |
| ** FROM PREVIOUS PAGE **               |                  |      |     |     |     |        |
| CÆCUM                                  | NUMBER EXAMINED: | 05   | 05  | 05  | 05  | 05     |
| --SUBMUCOSAL INFLAMMATION              |                  | 0    | 0   | 0   | 2   | 1      |
| --LUMINAL DILATATION                   |                  | 0    | 1   | 0   | 1   | 0      |
| --PERITONITIS                          |                  | 0    | 1   | 0   | 0   | 0      |
| COLON                                  | NUMBER EXAMINED: | 05   | 05  | 05  | 05  | 05     |
| --LUMINAL DILATATION                   |                  | 0    | 0   | 0   | 1   | 1      |
| --PERITONITIS                          |                  | 0    | 1   | 0   | 0   | 0      |
| DUODENUM                               | NUMBER EXAMINED: | 05   | 05  | 05  | 05  | 05     |
| --MUCOSAL CHRONIC INFLAMMATION         |                  | 3    | 0   | 2   | 1   | 0      |
| --PERITONITIS                          |                  | 0    | 1   | 0   | 0   | 0      |
| ESTROUS CYCLES                         | NUMBER EXAMINED: | 05   | 05  | 05  | 05  | 05     |
| --HYPOSPERMIA                          |                  | 9    | 11  | 6   | 5   | 50 cfs |
| --INFLAMMATION                         |                  | 1    | 0   | 0   | 0   | 1      |
| --SPERMATOCELE                         |                  | 1    | 0   | 2   | 0   | 0      |
| --CYST                                 |                  | 0    | 1   | 0   | 0   | 0      |
| --PERITONITIS                          |                  | 0    | 1   | 0   | 0   | 0      |
| EYES                                   | NUMBER EXAMINED: | 05   | 05  | 05  | 05  | 05     |
| --KERATITIS                            |                  | 1    | 0   | 0   | 0   | 0      |
| --RETINA - LOSS OF OUTER NUCLEAR LAYER |                  | 1    | 1   | 1   | 0   | 0      |
| --INFLAMMATORY CELLS, ANTERIOR CHAMBER |                  | 1    | 0   | 0   | 0   | 0      |
| --LENTICULAR DEGENERATION              |                  | 2    | 1   | 1   | 0   | 0      |
| --RETINAL ATROPHY                      |                  | 0    | 0   | 2   | 0   | 0      |
| --RETINAL DETACHMENT                   |                  | 1    | 0   | 0   | 0   | 0      |

0 0

359

TABLE IIP - continued

Form No. 1023

Histopathology - group distribution of non-neoplastic findings for all groups

Group 1 2 3 4 5  
 Compound Control Control Polymyxin Hydrochloride  
 Dosage mg/kg/day 0 0 13 20-45 53-60  
 Printed 01-NOV-61  
 Page 3  
 Module number 001 001

--- R E S U L T S - O F - A N I M A L S - S P E C I F I C ---

| ORGAN AND FINDING DESCRIPTION          | GROUP           | SPECIMEN |    |    |    |    |
|--|-----------------|----------|----|----|----|----|
|  |                 | 1        | 2  | 3  | 4  | 5  |
| <b>PERICARDIUM</b>                     | NUMBER EXAMINED | 45       | 45 | 45 | 45 | 45 |
| -- FIBRIN DEPOSITION                   |                 | 0        | 0  | 0  | 0  | 1  |
| -- OSTEONECROSIS                       |                 | 0        | 0  | 1  | 0  | 1  |
| -- ERYTHROSIS                          |                 | 0        | 1  | 0  | 0  | 0  |
| -- OSTEOMYELITIS                       |                 | 0        | 1  | 0  | 0  | 0  |
| <b>PAROTID GLANDS</b>                  | NUMBER EXAMINED | 45       | 45 | 45 | 45 | 45 |
| -- ACINUS HYPERPLASIA                  |                 | 0        | 0  | 0  | 0  | 1  |
| -- ACINUS ATROPHY                      |                 | 1        | 0  | 0  | 0  | 0  |
| -- ACINUS NECROSIS                     |                 | 1        | 0  | 0  | 0  | 1  |
| -- LYMPHOCYTIC INFILTRATION            |                 | 2        | 2  | 1  | 1  | 2  |
| -- SQUAMOUS                            |                 | 0        | 1  | 1  | 1  | 1  |
| -- INFLAMMATION                        |                 | 1        | 1  | 1  | 1  | 2  |
| <b>HEART, ATRIUM</b>                   | NUMBER EXAMINED | 45       | 45 | 45 | 45 | 45 |
| -- CHRONIC MYOCARDITIS                 |                 | 0        | 0  | 1  | 0  | 2  |
| -- FIBROSIS                            |                 | 0        | 0  | 1  | 0  | 0  |
| <b>HEART, VENTRICLE</b>                | NUMBER EXAMINED | 45       | 45 | 45 | 45 | 45 |
| -- CHRONIC MYOCARDITIS                 |                 | 10       | 17 | 20 | 12 | 17 |
| -- VALVULAR HYPERTROPHY                |                 | 1        | 0  | 0  | 0  | 0  |
| -- VALVULAR ENDOCARDITIS, BACTERIAL    |                 | 1        | 0  | 0  | 0  | 0  |
| -- INFILTRATION OF CORONARY EPICARDIUM |                 | 1        | 2  | 0  | 1  | 1  |
| -- ENDOCARDIAL FIBRINIZATION           |                 | 1        | 0  | 1  | 0  | 0  |
| <b>ILEUM</b>                           | NUMBER EXAMINED | 45       | 45 | 45 | 45 | 45 |
| -- MUCOSAL DILATATION                  |                 | 0        | 0  | 0  | 0  | 1  |
| -- PERITONITIS                         |                 | 0        | 1  | 0  | 1  | 0  |

360

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11P - continued.

Print No 0023

Histopathology - group distribution of non-neoplastic findings for all animals

Group 1 2 3 4 5  
 Compound Control Control Poloxabuton Hydrochloride  
 Doseage (mg/kg/day) 0 0 11 10/45 67/91

Printed: 05-MAY-03  
 Page 4

Schedule number N9H 001

| ORGAN AND FINDING DESCRIPTION                 | NUMBER OF ANIMALS AFFECTED |     |    |    |    |    |
|---|----------------------------|-----|----|----|----|----|
|   | SEX GROUP                  | SEX |    |    |    |    |
|   |                            | ♂   | ♀  | ♂  | ♀  | ♂  |
| <b>JEJUNUM</b>                                | NUMBER EXAMINED            | 65  | 65 | 65 | 65 | 65 |
| --INTUSSUSCEPTION                             |                            | 0   | 0  | 0  | 1  | 0  |
| --PERITONITIS                                 |                            | 0   | 1  | 0  | 0  | 0  |
| <b>KIDNEYS</b>                                | NUMBER EXAMINED            | 65  | 65 | 65 | 65 | 65 |
| --HYPERPLASIA, PAPILLARY EPITHELIUM           |                            | 0   | 10 | 6  | 13 | 3  |
| --HYPERPLASIA, PELVIC EPITHELIUM              |                            | 3   | 2  | 4  | 1  | 1  |
| --TUBULAR HYPERPLASIA, SIMPLE                 |                            | 0   | 1  | 1  | 1  | 0  |
| --PROGRESSIVE (RENAL) NEPHROPATHY             |                            | 17  | 19 | 19 | 15 | 24 |
| --CORTICAL TUBULAR BASOPHILIA                 |                            | 17  | 19 | 10 | 14 | 13 |
| --HYDROMEPHROSIS                              |                            | 4   | 6  | 3  | 7  | 3  |
| --GLOMERULO-NEPHROPATHY                       |                            | 1   | 1  | 0  | 0  | 0  |
| --CORTICAL MINERALISATION                     |                            | 0   | 0  | 0  | 1  | 0  |
| --MINERALISATION, PAPILLARY/PELVIC EPITHELIUM |                            | 1   | 3  | 1  | 3  | 0  |
| --PELVIC CALCULUS/ST                          |                            | 1   | 3  | 1  | 0  | 0  |
| --PELVES - INFLAMMATION                       |                            | 1   | 2  | 2  | 0  | 2  |
| --PERIVASCULAR LYMPHOID AGGREGATIONS          |                            | 1   | 0  | 0  | 0  | 0  |
| --CORTICAL CYST(S)                            |                            | 3   | 4  | 4  | 3  | 4  |
| --MEDULLARY CYST(S)                           |                            | 2   | 4  | 7  | 8  | 3  |
| --PAPILLARY CYST                              |                            | 1   | 0  | 0  | 1  | 0  |
| --CORTICAL TUBULAR NECROSIS                   |                            | 1   | 0  | 0  | 0  | 0  |
| --DILATED MEDULLARY TUBULES                   |                            | 0   | 0  | 0  | 1  | 0  |
| --CORTICAL TUBULES WITH STALINE DROPLETS      |                            | 0   | 0  | 0  | 0  | 1  |
| --CORTICAL SCARRING                           |                            | 1   | 3  | 3  | 1  | 1  |
| --PAPILLA - INFLAMMATION                      |                            | 1   | 0  | 0  | 0  | 0  |
| --PAPILLARY NECROSIS                          |                            | 1   | 0  | 0  | 0  | 1  |
| --CORTICAL PURULENT INFLAMMATION              |                            | 1   | 0  | 0  | 0  | 0  |
| --PYELONEPHRITIS                              |                            | 0   | 1  | 0  | 0  | 0  |

361



APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11P - continued.

Print No. 0023

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Polonium Chloride Hydrochloride  
 Dose (mg/kg/day) : 0 0 15 10/45 65/90

Printed 05-NOV-81  
 Page 9

Schedule Number: NSB 031

| ORGAN AND FINDING DESCRIPTION              | NUMBER OF ANIMALS AFFECTED |    |    |    |    |
|--|----------------------------|----|----|----|----|
|  | SEX                        |    |    |    |    |
|  | 1-                         | 2- | 3- | 4- | 5- |
| <b>L N RESIDENTIAL</b>                     | <b>NUMBER EXAMINED</b>     |    |    |    |    |
| --SINUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS | 1                          | 3  | 0  | 3  | 0  |
| --AGGREGATIONS OF HISTIOCYTES              | 30                         | 27 | 37 | 22 | 18 |
| --MACROPHAGOSIS                            | 0                          | 0  | 1  | 0  | 0  |
| --LYMPHADENITIS                            | 0                          | 1  | 0  | 0  | 1  |
| --ANGIECTASIS                              | 1                          | 5  | 0  | 1  | 0  |
| --DILATED/CESTIC SINUSES                   | 0                          | 3  | 0  | 0  | 0  |
| --SINUS HISTIOCYTOSIS                      | 1                          | 0  | 1  | 3  | 5  |
| --HISTIOCYTOSIS                            | 0                          | 0  | 0  | 1  | 0  |
| --NECROSIS                                 | 0                          | 0  | 1  | 0  | 0  |
| <b>LACRYMAL GLANDS</b>                     | <b>NUMBER EXAMINED</b>     |    |    |    |    |
| --INTERSTITIAL LYMPHOCYTE AGGREGATES       | 2                          | 1  | 0  | 1  | 1  |
| --ARTERITIS                                | 0                          | 0  | 0  | 1  | 0  |
| --ACINAR VACUOLATION                       | 0                          | 0  | 0  | 0  | 1  |
| --BACTERIEMISATION                         | 13                         | 22 | 24 | 14 | 9  |
| --ACINAR NECROSIS                          | 1                          | 0  | 0  | 0  | 0  |
| <b>LIVER K S</b>                           | <b>NUMBER EXAMINED</b>     |    |    |    |    |
| --FOCAL NECROSIS                           | 5                          | 3  | 1  | 3  | 1  |
| --BILE DUCT PROLIFERATION                  | 9                          | 11 | 11 | 0  | 7  |
| --DIFFUSE FATTY VACUOLATION                | 1                          | 0  | 0  | 0  | 1  |
| --HEPATOCTE VACUOLATION, MEDIAN CLEFT      | 3                          | 1  | 3  | 3  | 3  |
| --HEPATOCTE VACUOLATION, PERIPORAL         | 5                          | 1  | 7  | 3  | 3  |
| --HEPATOCTE VACUOLATION, CENTILOBULAR      | 0                          | 1  | 7  | 2  | 0  |
| --HEPATOCTE VACUOLATION, FOCAL             | 0                          | 1  | 1  | 0  | 0  |
| --HEPATOCTE VACUOLATION, GENERALISED       | 0                          | 1  | 1  | 0  | 0  |
| --HEPATOCTE VACUOLATION, REGIONAL          | 0                          | 1  | 0  | 1  | 0  |
| --BASOPHILIC FOCI/FOCE                     | 0                          | 1  | 0  | 1  | 0  |

367

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 119 - continued

Print No 3633

Histopathology - group distribution of non-neoplastic findings for all animals

Group  
Compound Control Control Poloxosiron Hydrochloride  
Doseage mg/kg/days 0 0 15 30/35 10/35

Printed: 05-NOV-01  
Page 6

Study Number: 888 001

| ORGAN AND FINDING DESCRIPTION               | --- NUMBER OF ANIMALS AFFECTED --- |    |    |    |    |
|---|------------------------------------|----|----|----|----|
|   | SEX: ..... FOLE.....               |    |    |    |    |
|   | GROUP                              | 01 | 02 | 03 | 04 |
| ** FROM PREVIOUS PAGE **                    |                                    |    |    |    |    |
| LIVER L 1                                   | NUMBER EXAMINED                    | 01 | 02 | 03 | 04 |
| --CLEAR CELL FOCUS/FOCI                     |                                    | 14 | 15 | 23 | 24 |
| --REGIMONILIC FOCUS/FOCI                    |                                    | 0  | 2  | 2  | 2  |
| --FOCAL CONGESTION                          |                                    | 4  | 12 | 27 | 13 |
| --INFLAMMATION PORTAL                       |                                    | 1  | 0  | 1  | 0  |
| --INCREASED SLOUGH                          |                                    | 2  | 0  | 1  | 0  |
| --STRUCTURAL DILATATION, FOCAL              |                                    | 1  | 0  | 1  | 0  |
| --FIBROSIS, CENTRILOBULAR                   |                                    | 0  | 1  | 1  | 0  |
| --FUCAL PELANGIOECTASIS                     |                                    | 0  | 10 | 0  | 1  |
| --MULTINUCLEATE HEPATOCYTES                 |                                    | 0  | 0  | 1  | 0  |
| --CONGESTION, CENTRILOBULAR                 |                                    | 0  | 0  | 1  | 0  |
| --PELLOID HEPATIS                           |                                    | 12 | 12 | 14 | 11 |
| --HEPATOCYTE HYPERPLASIA, CENTRILOBULAR     |                                    | 0  | 0  | 1  | 0  |
| --HEPATO-DIAPHRAGMATIC BRIDGES              |                                    | 0  | 1  | 1  | 0  |
| --BILIRUBIN CYSTS, MULTICUCULAR             |                                    | 0  | 0  | 0  | 1  |
| --INFLAMMATION, FOCAL                       |                                    | 0  | 1  | 2  | 1  |
| --HEPATOCYTE NECROSIS, LOBAR, PORTION       |                                    | 0  | 0  | 0  | 1  |
| --PROMINENT IN FLUDDER CELLS                |                                    | 0  | 0  | 0  | 1  |
| --EXTRACELLULAR HAEMOPHOESIS                |                                    | 0  | 0  | 0  | 1  |
| --HAEMORRHAGE                               |                                    | 0  | 0  | 1  | 0  |
| --CHOLANGIOPLASIA                           |                                    | 0  | 0  | 0  | 1  |
| --REGIMONILIC HYPERPLASIA                   |                                    | 0  | 0  | 0  | 1  |
| LN PARACORTICAL                             | NUMBER EXAMINED                    | 01 | 02 | 03 | 04 |
| --PLASMACYTOSIS                             |                                    | 2  | 1  | 0  | 1  |
| --DILATED/CYSTIC SINUSSES                   |                                    | 2  | 1  | 2  | 2  |
| --SERIES ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                                    | 0  | 0  | 2  | 1  |
| --DISSEMINATION OF HISTIOCYTES              |                                    | 0  | 0  | 0  | 1  |
| --PROMINENT GERMINAL CENTRES                |                                    | 0  | 0  | 0  | 1  |

11  
12  
13

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 117 - continued.

Print No. 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                  |         |         |                             |       |       |                          |
|------------------|---------|---------|-----------------------------|-------|-------|--------------------------|
| Group            | 1       | 2       | 3                           | 4     | 5     |                          |
| Compound         | Control | Control | Polioxybenzyl Hydrochloride |       |       | Printed: 03-MOV-01       |
| Dose (mg/kg/day) | 0       | 0       | 15                          | 30/25 | 60/30 | Page: 1                  |
|                  |         |         |                             |       |       | Schedule number: RSH 001 |

... NUMBER OF ANIMALS AFFECTED ...

| ORGAN AND FINDING DESCRIPTION                  | NUMBER                 | SEX  |        |    |    |    |
|--|------------------------|------|--------|----|----|----|
|  |                        | MALE | FEMALE |    |    |    |
|  |                        | 1    | 2      | 3  | 4  | 5  |
| <b>LUNGS</b>                                   | <b>NUMBER EXAMINED</b> | 65   | 65     | 65 | 65 | 65 |
| --ACCUMULATION OF ALVEOLAR MACROPHAGES         |                        | 14   | 10     | 23 | 29 | 10 |
| --ALVEOLAR HEMORRHAGE                          |                        | 0    | 0      | 3  | 2  | 1  |
| --ALVEOLAR OSSIFIC METAPLASIA                  |                        | 0    | 2      | 0  | 2  | 1  |
| --ALVEOLAR EDEMA                               |                        | 0    | 0      | 0  | 3  | 0  |
| --ALVEOLAR EPITHELIAL HYPERPLASIA              |                        | 2    | 2      | 2  | 2  | 2  |
| --PERIVASCULAR LYMPHOID AGGREGATES             |                        | 2    | 4      | 2  | 5  | 6  |
| --CHILIBESTER CLEFT GRANULOMATIS               |                        | 1    | 3      | 1  | 1  | 2  |
| --ARTERITIS                                    |                        | 0    | 0      | 0  | 0  | 1  |
| --ARTERIAL WALL MINERALIZATION                 |                        | 0    | 0      | 0  | 1  | 2  |
| --BRONCHOLAR METAPLASIA OF ALVEOLAR EPITHELIUM |                        | 1    | 1      | 0  | 0  | 0  |
| --PERIBRONCHOLAR INFLAMMATION                  |                        | 1    | 0      | 0  | 0  | 1  |
| --PNEUMONITIS                                  |                        | 1    | 2      | 0  | 0  | 1  |
| --PERIBRONCHOLAR LYMPHOID AGGREGATES           |                        | 0    | 0      | 0  | 0  | 1  |
| --MESOTHELIAL HYPERPLASIA                      |                        | 0    | 0      | 0  | 0  | 1  |
| <b>MAMMARY &amp; CAUD</b>                      | <b>NUMBER EXAMINED</b> | 65   | 65     | 65 | 65 | 65 |
| --SECRETORY ACTIVITY                           |                        | 6    | 2      | 0  | 11 | 10 |
| --GALACTOCYTES                                 |                        | 0    | 0      | 2  | 3  | 2  |
| --KERATIN CYST                                 |                        | 0    | 0      | 0  | 0  | 1  |
| <b>ESOPHAGUS</b>                               | <b>NUMBER EXAMINED</b> | 65   | 65     | 65 | 65 | 65 |
| --ULCERATION                                   |                        | 0    | 0      | 0  | 1  | 0  |
| --INFLAMMATION                                 |                        | 0    | 0      | 0  | 1  | 0  |
| <b>OPTIC NERVE</b>                             | <b>NUMBER EXAMINED</b> | 64   | 65     | 65 | 65 | 64 |
| --INFLAMMATION                                 |                        | 0    | 0      | 1  | 0  | 1  |
| --GLIOSIS                                      |                        | 0    | 0      | 0  | 1  | 0  |

364

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 127 - continued

Brinc No. 0033

Histopathology - gross distribution of non-neoplastic findings for all animals

Group 1 2 3 4 5  
Compound Control Control Poloxoneuron Hydrochloride  
Dose (mg/kg/day) 0 0 15 10/45 10/90

Printed: 03-MAY-01  
Page: 8

Schedule number: MSH 001

| ORGAN AND FINDING DESCRIPTION              | NUMBER OF ANIMALS AFFECTED |      |      |        |        |
|--|----------------------------|------|------|--------|--------|
|  | SEX GROUP                  | SEX  |      |        |        |
|  |                            | MALE | MALE | FEMALE | FEMALE |
| NUMBER                                     | 05                         | 05   | 05   | 05     | 05     |
| <b>PANCREAS</b>                            |                            |      |      |        |        |
| NUMBER EXAMINED                            | 05                         | 05   | 05   | 05     | 05     |
| --DUKE HYPERPLASIA                         | 1                          | 2    | 1    | 2      | 0      |
| --ACINAR CELL HYPERPLASIA, FOCAL           | 2                          | 5    | 1    | 0      | 1      |
| --ISLET CELL HYPERPLASIA                   | 0                          | 1    | 1    | 1      | 3      |
| --ACINAR ATROPHY WITH CHRONIC INFLAMMATION | 2                          | 1    | 1    | 4      | 1      |
| --DUCTECTAL INFLAMMATION/FIBROSIS          | 1                          | 1    | 0    | 1      | 0      |
| --ACINAR CELL HYPERSTROPHY, FOCAL          | 1                          | 1    | 1    | 0      | 0      |
| --INFLAMMATION                             | 4                          | 1    | 0    | 0      | 2      |
| --NECROSIS                                 | 3                          | 2    | 1    | 0      | 0      |
| <b>PANCREATITIS</b>                        |                            |      |      |        |        |
| NUMBER EXAMINED                            | 05                         | 05   | 05   | 05     | 05     |
| --HYPERPLASIA                              | 0                          | 0    | 0    | 0      | 0      |
| <b>PIYOSITIS</b>                           |                            |      |      |        |        |
| NUMBER EXAMINED                            | 05                         | 05   | 05   | 05     | 05     |
| --HYPERPLASIA - DUCT DISTALIS, FOCAL       | 5                          | 0    | 4    | 0      | 0      |
| --HYPERPLASIA - PAMP INTERMEDIA, FOCAL     | 1                          | 3    | 0    | 1      | 2      |
| --MULTIFOCAL NECROSIS                      | 2                          | 2    | 0    | 0      | 0      |
| --VACUOLATED CELLS - DUCT DISTALIS, FOCAL  | 2                          | 2    | 1    | 0      | 1      |
| --DEVELOPMENTAL CYST(S)                    | 2                          | 0    | 2    | 0      | 1      |
| --CHOLESTASIS                              | 1                          | 1    | 1    | 4      | 1      |
| --MUCORRHOEA                               | 0                          | 1    | 0    | 0      | 1      |
| <b>PROSTATE</b>                            |                            |      |      |        |        |
| NUMBER EXAMINED                            | 05                         | 04   | 05   | 05     | 05     |
| --ACINAR HYPERPLASIA, FOCAL                | 1                          | 0    | 1    | 1      | 1      |
| --DIFFUSE HYPERPLASIA                      | 0                          | 1    | 0    | 0      | 0      |
| --NECROSIS                                 | 0                          | 1    | 0    | 0      | 0      |
| --INFLAMMATION                             | 0                          | 2    | 5    | 0      | 2      |
| --MUCORRHOEA                               | 0                          | 0    | 0    | 0      | 2      |
| --ACINAR DILATATION                        | 0                          | 1    | 0    | 1      | 0      |

365



APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F - continued

Print No 0273

Pathopathology - group distribution of non-neoplastic findings for all animals

|                  |         |         |              |             |             |
|------------------|---------|---------|--------------|-------------|-------------|
| Group            | 1       | 2       | 3            | 4           | 5           |
| Compound         | Control | Control | Palonosetron | Hydroxyzole | Hydroxyzole |
| Dose (mg/kg/day) | 0       | 0       | 10           | 32/45       | 45/90       |

Printed 05-NOV-01  
Page: 0

Schedule Number: 000 001

| ORGAN AND FINDING DESCRIPTION                       | NUMBER          | SEX  |     |        |     |     |
|---|-----------------|------|-----|--------|-----|-----|
|   |                 | MALE |     | FEMALE |     |     |
|   |                 | -1-  | -2- | -3-    | -4- | -5- |
| RECTUM  | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --LYMPHOID HYPERPLASIA                              |                 | 2    | 1   | 0      | 0   | 0   |
| SMALL INTESTINE                                     | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --MUCOSAL DEGENERATION                              |                 | 0    | 3   | 10     | 0   | 0   |
| Salivary Glands                                     | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --LYMPHOID AGGREGATES                               |                 | 0    | 0   | 1      | 0   | 0   |
| --INFLAMMATION                                      |                 | 0    | 1   | 0      | 0   | 0   |
| SPLEEN  | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --DEGENERATE FIBRES                                 |                 | 0    | 0   | 11     | 11  | 0   |
| --CHOLESTEROL CLEFTS                                |                 | 0    | 0   | 0      | 0   | 1   |
| --VASCULAR MINERALISATION                           |                 | 0    | 1   | 0      | 0   | 0   |
| THYROID GLANDS                                      | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --EPITHELIAL HYPERPLASIA                            |                 | 0    | 1   | 0      | 0   | 0   |
| --ACUTE INFLAMMATION                                |                 | 0    | 0   | 1      | 0   | 0   |
| --CHRONIC INFLAMMATION                              |                 | 2    | 0   | 0      | 1   | 1   |
| --ABSENCE OF COLLOID                                |                 | 1    | 0   | 3      | 1   | 0   |
| --REDUCED COLLOID                                   |                 | 2    | 1   | 0      | 2   | 0   |
| --PERITONITIS                                       |                 | 0    | 1   | 0      | 0   | 0   |
| SPLEEN  | NUMBER EXAMINED | 65   | 65  | 65     | 65  | 65  |
| --EPITHELIAL NEOPLASIA                              |                 | 2    | 1   | 2      | 2   | 0   |
| --MADHOGENESIS                                      |                 | 4    | 0   | 0      | 0   | 0   |
| --PERITONITIS                                       |                 | 0    | 2   | 0      | 0   | 0   |
| --INCREASED CELLULARITY OF WHITE PULP - GENERALISED |                 | 0    | 0   | 0      | 0   | 1   |
| --CAPSULA THICKENING                                |                 | 0    | 0   | 0      | 0   | 1   |

366

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL



APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11P - continued

Print No 7023

Histopathology - group distribution of non-neoplastic findings for all animals

Group                    1                    2                    3                    4                    5  
Compound                Control Control Polonastrox Hydrochloride  
Doseage (mg/kg/day):    0                    0                    15                    10/15                    52/90

Printed 02-09-51  
Page 11

Schedule Number NYN 001

| ORGAN AND FINDING DESCRIPTION             | NUMBER OF ANIMALS AFFECTED |         |         |         |         |          |
|---|----------------------------|---------|---------|---------|---------|----------|
|   | SEX                        |         |         |         |         |          |
|   | GROUP                      | 1-      | 2-      | 3-      | 4-      | 5-       |
| STOMACH                                   | NUMBER EXAMINED:           | 65      | 65      | 65      | 65      | 65       |
| --MINERALISATION OF MUSCULARIS MUCOSA     |                            | 1       | 1       | 2       | 0       | 0        |
| --SACCHARINAGE                            |                            | 1       | 0       | 0       | 1       | 0        |
| --PROLIFERATION                           |                            | 0       | 1       | 0       | 0       | 0        |
| --ATROPHY                                 |                            | 0       | 1       | 0       | 0       | 0        |
| TESTES                                    | NUMBER EXAMINED:           | 65      | 65      | 65      | 65      | 65       |
| --DEGENERATION OF EPIDIDYMUS (EPIDIDYMUS) |                            | 14      | 14      | 14      | 10      | 60 of 65 |
| --ATROPHY                                 |                            | 1       | 0       | 0       | 0       | 0        |
| --SEMIPERFORATE FIBULAR DILATATION        |                            | 0       | 3       | 0       | 0       | 0        |
| --SPERMATOCELE GRANULOMATA                |                            | 0       | 1       | 0       | 0       | 0        |
| --SEMIPERFORATE FIBULAR MINERALISATION    |                            | 0       | 1       | 0       | 0       | 0        |
| --MACROCYTIC                              |                            | 0       | 1       | 0       | 0       | 0        |
| THYROID                                   | NUMBER EXAMINED:           | 63      | 65      | 63      | 65      | 66       |
| --EPITHELIAL HYPERPLASIA                  |                            | 0       | 0       | 0       | 0       | 1 of 66  |
| --NODULARITY                              |                            | 1       | 0       | 2       | 1       | 1        |
| --ATROPHY                                 |                            | 0       | 1       | 0       | 0       | 0        |
| --CYSTIC                                  |                            | 2       | 0       | 3       | 0       | 1 of 66  |
| --LYMPHOCTOXYCITIS                        |                            | 0       | 0       | 0       | 0       | 1        |
| --SITE ONLY                               |                            | 7 of 63 | 1 of 65 | 7 of 63 | 7 of 65 | 7 of 66  |
| UTERUS                                    | NUMBER EXAMINED:           | 65      | 64      | 65      | 65      | 64       |
| --C-CELL HYPERPLASIA                      |                            | 2       | 0       | 0       | 0       | 13 of 64 |
| --CYTIC FOLLICULAR CELL HYPERPLASIA       |                            | 2       | 4       | 3       | 1       | 1        |
| --FOLLICULAR DILATATION                   |                            | 4       | 0       | 0       | 3       | 1        |
| --PROLIFERATE ULTIMOPHARYNGEAL CYSTIC     |                            | 0       | 1       | 0       | 0       | 1        |
| --FOLLICULAR ATROPHY                      |                            | 0       | 0       | 0       | 0       | 1        |
| --FOLLICULAR CELL HYPERPLASIA             |                            | 0       | 1       | 0       | 0       | 0        |

NYN

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F - continued.

Print No 2573

Histopathology - group distribution of non-neoplastic findings for all animals

| Group            | 1       | 2       | 3            | 4             | 5     |
|------------------|---------|---------|--------------|---------------|-------|
| Compound         | Control | Control | Palonosetron | Hydrochloride |       |
| Dose (mg/kg/day) | 0       | 0       | 15           | 10/15         | 40/10 |

Printed: 03-NOV-01  
Page 12

.....

----- NUMBER OF ANIMALS AFFECTED -----

| ORGAN AND FINDING DESCRIPTION   | NUMBER EXAMINED        | SEX  |     |     |     |     |
|---------------------------------|------------------------|------|-----|-----|-----|-----|
|                                 |                        | MALE |     |     |     |     |
|                                 |                        | -1-  | -2- | -3- | -4- | -5- |
| <b>TONGUE</b>                   | <b>NUMBER EXAMINED</b> | 69   | 63  | 61  | 65  | 64  |
| --VASCULAR MINERALIZATION       |                        | 1    | 0   | 0   | 0   | 0   |
| --ARTERITIS                     |                        | 0    | 0   | 0   | 1   | 0   |
| --HEMORRHAGE                    |                        | 1    | 0   | 1   | 0   | 1   |
| <b>URINARY BLADDER</b>          | <b>NUMBER EXAMINED</b> | 65   | 65  | 61  | 61  | 61  |
| --TRANSITIONAL CELL HYPERPLASIA |                        | 3    | 2   | 1   | 0   | 0   |
| --LUMINAL DILATATION            |                        | 0    | 2   | 2   | 1   | 1   |
| --ULCERATION                    |                        | 1    | 0   | 0   | 0   | 0   |
| --INFLAMMATION                  |                        | 2    | 2   | 1   | 0   | 1   |
| <b>ABDOMEN</b>                  | <b>NUMBER EXAMINED</b> | 0    | 2   | 1   | 1   | 2   |
| --PERITONITIS                   |                        | 0    | 1   | 0   | 0   | 1   |
| --ARTERITIS                     |                        | 0    | 1   | 0   | 0   | 0   |
| <b>ADIPOSE TISSUE</b>           | <b>NUMBER EXAMINED</b> | 1    | 1   | 1   | 0   | 6   |
| --HEMORRHAGE                    |                        | 1    | 0   | 0   | 0   | 0   |
| --FAT NECROSIS                  |                        | 0    | 2   | 2   | 0   | 1   |
| --ACUTE INFLAMMATION            |                        | 1    | 0   | 0   | 0   | 0   |
| --CONGESTION                    |                        | 0    | 0   | 1   | 0   | 0   |
| --HEPATITIS                     |                        | 0    | 1   | 0   | 0   | 0   |
| <b>BILE DUCT</b>                | <b>NUMBER EXAMINED</b> | 2    | 0   | 0   | 2   | 2   |
| --LUMINAL DILATATION            |                        | 2    | 0   | 0   | 2   | 2   |
| --EPITHELIAL HYPERPLASIA        |                        | 1    | 0   | 0   | 0   | 0   |
| --ARTERITIS                     |                        | 1    | 0   | 0   | 0   | 0   |
| <b>BONE</b>                     | <b>NUMBER EXAMINED</b> | 2    | 1   | 2   | 4   | 1   |
| --HEPATITIS                     |                        | 2    | 0   | 2   | 3   | 0   |



TABLE 11F - continued.

Form No 0023

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Palonosetron Hydrochloride  
 Dose (mg/kg/day) : 0 0 11 30/65 60/90

Printed 05-MAY-01  
 Page 13

Schedule number: N88 001

| ORGAN AND FINDING DESCRIPTION            | GROUP           | NUMBER OF ANIMALS AFFECTED |    |    |    |    |
|--|-----------------|----------------------------|----|----|----|----|
|  |                 | 1-                         | 2- | 3- | 4- | 5- |
| <b>*** FROM PREVIOUS PAGE ***</b>        |                 |                            |    |    |    |    |
| <b>BONE</b>                              |                 |                            |    |    |    |    |
| **OSTEOARTHRITIS                         | NUMBER EXAMINED | 2                          | 1  | 2  | 4  | 3  |
|  |                 | 1                          | 0  | 0  | 3  | 1  |
| <b>COAGULATING B</b>                     | NUMBER EXAMINED | 0                          | 1  | 0  | 2  | 0  |
| **ACUTE INFLAMMATION                     |                 | 0                          | 0  | 0  | 1  | 0  |
| **EPITHELIAL HYPERPLASIA                 |                 | 0                          | 0  | 0  | 1  | 0  |
| <b>LN AXILLARY</b>                       | NUMBER EXAMINED | 10                         | 10 | 21 | 10 | 22 |
| **AGGREGATIONS OF HISTIOCYTES            |                 | 0                          | 0  | 0  | 0  | 1  |
| **DILATED/CYSTIC SINUSES                 |                 | 0                          | 1  | 0  | 0  | 0  |
| **SITE ONLY                              |                 | 0                          | 0  | 1  | 0  | 0  |
| <b>LN BRONCHIAL</b>                      | NUMBER EXAMINED | 3                          | 1  | 4  | 1  | 2  |
| **DILATED/CYSTIC SINUSES                 |                 | 1                          | 0  | 0  | 0  | 0  |
| **SITE ONLY                              |                 | 0                          | 0  | 1  | 0  | 0  |
| <b>LN CERVICAL</b>                       | NUMBER EXAMINED | 1                          | 1  | 0  | 0  | 0  |
| **PROMINENT GERMINAL CENTRES             |                 | 1                          | 0  | 0  | 0  | 0  |
| <b>LN THYROIDAL</b>                      | NUMBER EXAMINED | 5                          | 12 | 10 | 12 | 12 |
| **SITE ONLY                              |                 | 1                          | 0  | 3  | 1  | 0  |
| <b>LN LUNG</b>                           | NUMBER EXAMINED | 10                         | 9  | 12 | 6  | 10 |
| **DILATED/CYSTIC SINUSES                 |                 | 0                          | 2  | 6  | 3  | 0  |
| **SINUS ENTHRACTIONIS/ENTHROPHAGOCYTOSIS |                 | 1                          | 0  | 1  | 0  | 1  |
| **GAUDEMIOGENESIS                        |                 | 0                          | 0  | 3  | 0  | 0  |
| **PLASMOCYTOSIS                          |                 | 1                          | 0  | 0  | 0  | 0  |

370

TABLE 117 - continued

Print No. 0031

Histopathology - gross distribution of non-neoplastic findings for all animals

|                    |         |         |                          |       |       |
|--------------------|---------|---------|--------------------------|-------|-------|
| Group              | 1       | 2       | 3                        | 4     | 5     |
| Compound           | Control | Control | Debenzoate Hydrochloride |       |       |
| Dosage (mg/kg/day) | 0       | 0       | 25                       | 10/11 | 10/90 |

Printed 03-MAY-81  
Page 14

Schedule number: 85H 001

| ORGAN AND FINDING DESCRIPTION                     | NUMBER OF ANIMALS AFFECTED |      |      |        |        |        |
|---|----------------------------|------|------|--------|--------|--------|
|   | SEX GROUP                  | SEX  |      |        |        |        |
|   |                            | MALE | MALE | FEMALE | FEMALE | FEMALE |
|   | 1                          | 2    | 3    | 4      | 5      |        |
| <b>UP GASTROINTESTINAL</b>                        |                            |      |      |        |        |        |
| NUMBER EXAMINED                                   | 1                          | 1    | 1    | 2      | 0      |        |
| --SIMPLE ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS       | 0                          | 0    | 1    | 0      | 0      |        |
| <b>UP PANCREATIC</b>                              |                            |      |      |        |        |        |
| NUMBER EXAMINED                                   | 0                          | 11   | 10   | 0      | 10     |        |
| --AGGREGATIONS OF DISTICTYTES                     | 0                          | 0    | 0    | 0      | 1      |        |
| --LYMPHADENITIS                                   | 0                          | 0    | 0    | 0      | 1      |        |
| --SIMPLE ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS       | 0                          | 1    | 1    | 0      | 0      |        |
| --NADPHOCYTOXIS                                   | 0                          | 0    | 2    | 0      | 0      |        |
| --DILATED/CYSTIC SINUSES                          | 0                          | 2    | 0    | 0      | 0      |        |
| --EXTENDED/ILLARY NADPHOCYTOXIS                   | 0                          | 0    | 1    | 0      | 1      |        |
| --SIMPLE DISTICTYPTOSIS                           | 0                          | 0    | 0    | 0      | 1      |        |
| --SITE ONLY                                       | 0                          | 0    | 0    | 1      | 0      |        |
| <b>UP PULMONARY</b>                               |                            |      |      |        |        |        |
| NUMBER EXAMINED                                   | 4                          | 4    | 4    | 3      | 0      |        |
| --SIMPLE ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS       | 0                          | 1    | 0    | 0      | 0      |        |
| --PLASMOCYTOSIS                                   | 2                          | 0    | 0    | 0      | 2      |        |
| <b>UP RENAL</b>                                   |                            |      |      |        |        |        |
| NUMBER EXAMINED                                   | 3                          | 7    | 6    | 5      | 0      |        |
| --SIMPLE ERYTHROCYTOSIS                           | 0                          | 0    | 0    | 1      | 0      |        |
| --DILATED/CYSTIC SINUSES                          | 1                          | 1    | 0    | 1      | 0      |        |
| --LYMPHADENITIS                                   | 0                          | 0    | 0    | 0      | 1      |        |
| --SIMPLE ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS       | 1                          | 1    | 3    | 1      | 0      |        |
| --NADPHOCYTOXIS                                   | 0                          | 0    | 1    | 0      | 0      |        |
| --SITE ONLY                                       | 0                          | 0    | 2    | 0      | 0      |        |
| <b>UP SPLEEN</b>                                  |                            |      |      |        |        |        |
| NUMBER EXAMINED                                   | 4                          | 4    | 4    | 0      | 3      |        |
| --ERYTHROCYTES AND ERYTHROPHAGOCYTOSIS IN SINUSES | 1                          | 1    | 1    | 0      | 0      |        |
| --LYMPHADENITIS                                   | 1                          | 0    | 0    | 0      | 1      |        |
| --DILATED/CYSTIC SINUSES                          | 2                          | 2    | 1    | 0      | 0      |        |

371

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F - continued

Print No: 0575

Histopathology - group distribution of non-neoplastic findings for 031 animals

Group: 1 Control, 2 Control, 3 Poloxosetron Hydrochloride 15 mg/kg/day, 4 Poloxosetron Hydrochloride 30 mg/kg/day, 5 Poloxosetron Hydrochloride 45 mg/kg/day

Printed: 03-NOV-01  
Page: 33

Schedule number: HSE 001

| ORGAN AND FINDING DESCRIPTION               | SEX: -----MALE----- |       |     |     |     |     |
|---|---------------------|-------|-----|-----|-----|-----|
|   | NUMBER              | GROUP |     |     |     |     |
|   |                     | -1-   | -2- | -3- | -4- | -5- |
| SPLEEN                                      | NUMBER EXAMINED     | 4     | 4   | 4   | 0   | 3   |
| --CYTAMUCILLARY NUCLEOPOIISIS               |                     | 0     | 0   | 0   | 0   | 1   |
| --SITE ONLY                                 |                     | 0     | 0   | 1   | 0   | 0   |
| MANDIBULAR GLAND                            | NUMBER EXAMINED     | 4     | 7   | 10  | 15  | 18  |
| --SECRETORY ACTIVITY                        |                     | 1     | 2   | 6   | 6   | 10  |
| --CALACTOCYTE(S)                            |                     | 1     | 2   | 2   | 3   | 5   |
| MISCELLANEOUS                               | NUMBER EXAMINED     | 1     | 1   | 1   | 0   | 0   |
| --CRANIAL HEMORRHAGE                        |                     | 1     | 1   | 0   | 0   | 0   |
| MUSCLE                                      | NUMBER EXAMINED     | 9     | 9   | 8   | 7   | 7   |
| --HEMORRHAGE                                |                     | 0     | 1   | 0   | 0   | 0   |
| --MYOFIBRE DEGENERATION                     |                     | 2     | 2   | 1   | 6   | 5   |
| NASAL TURBINATES                            | NUMBER EXAMINED     | 0     | 1   | 0   | 0   | 1   |
| --INFLAMMATION                              |                     | 0     | 0   | 0   | 0   | 1   |
| PAWS  | NUMBER EXAMINED     | 11    | 11  | 7   | 9   | 12  |
| --EPIDERMAL HYPERPLASIA                     |                     | 0     | 1   | 1   | 0   | 2   |
| --ULCERATIVE PODODERMATITIS                 |                     | 0     | 0   | 1   | 0   | 0   |
| --OEDEMA                                    |                     | 0     | 2   | 2   | 0   | 0   |
| --ULCERATION                                |                     | 2     | 2   | 2   | 0   | 0   |
| --SUBCUTANEOUS INFLAMMATION                 |                     | 2     | 1   | 0   | 0   | 1   |
| --HYPERKERATOSIS                            |                     | 2     | 0   | 1   | 0   | 2   |
| --ABSCESS                                   |                     | 0     | 1   | 0   | 0   | 0   |
| PREPUITAL GLANDS                            | NUMBER EXAMINED     | 0     | 1   | 2   | 3   | 3   |
| --DUCT(S) DISTENDED WITH SECRETORY MATERIAL |                     | 0     | 0   | 0   | 1   | 1   |

TABLE III - continued

Print No 0523

Histopathology - group distribution of non-neoplastic findings for all animals

| Group            | 1       | 2       | 3                          | 4     | 5     |
|------------------|---------|---------|----------------------------|-------|-------|
| Compound         | Control | Control | Polonosetron Hydrochloride |       |       |
| Dose (mg/kg/day) | 0       | 0       | 15                         | 30/45 | 60/90 |

Printed: 03-MOV-01  
Page 16

Schedule Number NBR 001

| ORGAN AND FINDING DESCRIPTION       | --- NUMBER OF ANIMALS AFFECTED --- |       |     |     |     |     |
|-------------------------------------|------------------------------------|-------|-----|-----|-----|-----|
|                                     | SEX                                | MALE  |     |     |     |     |
|                                     |                                    | GROUP | -1- | -2- | -3- | -4- |
|                                     | NUMBER                             | 45    | 65  | 65  | 55  | 65  |
| ** FROM PREVIOUS PAGE **            |                                    |       |     |     |     |     |
| PREPUTIAL GLANDS                    | NUMBER EXAMINED                    | 0     | 1   | 2   | 2   | 3   |
| --ABSCESSTION                       |                                    | 0     | 0   | 2   | 2   | 2   |
| SKIN                                | NUMBER EXAMINED                    | 20    | 37  | 35  | 37  | 39  |
| --EPIDERMAL HYPERPLASIA             |                                    | 2     | 2   | 2   | 1   | 1   |
| --PINNA - HYPERPLASTIC CARILAGE     |                                    | 1     | 0   | 0   | 0   | 2   |
| --DIFFUSE DERMATITIS (INFLAMMATION) |                                    | 2     | 2   | 1   | 0   | 0   |
| --ULCER(S)                          |                                    | 2     | 4   | 0   | 0   | 0   |
| --SCAB(S)                           |                                    | 2     | 2   | 4   | 0   | 2   |
| --KERATIN CYST(S)                   |                                    | 2     | 2   | 5   | 8   | 11  |
| --DERMAL COLLAGEN DEPOSITION        |                                    | 10    | 11  | 11  | 8   | 6   |
| --ABCESS                            |                                    | 0     | 0   | 0   | 0   | 1   |
| --KERATIN GRANULOMATA               |                                    | 0     | 0   | 0   | 1   | 2   |
| --CRUST(S)                          |                                    | 0     | 0   | 0   | 0   | 1   |
| PAWL                                | NUMBER EXAMINED                    | 18    | 18  | 24  | 31  | 33  |
| --EPIDERMAL HYPERPLASIA             |                                    | 3     | 9   | 10  | 17  | 21  |
| --KERATIN CYST                      |                                    | 1     | 1   | 0   | 0   | 3   |
| --PYLREMATOSIS                      |                                    | 0     | 1   | 4   | 1   | 13  |
| --FOLLICULAR ABSCESTION             |                                    | 0     | 5   | 10  | 9   | 19  |
| --SCAB(S)                           |                                    | 1     | 12  | 18  | 17  | 33  |
| --CRUST(S)                          |                                    | 0     | 1   | 0   | 1   | 0   |
| --EPIDERMAL ULCERATION              |                                    | 2     | 0   | 0   | 1   | 2   |
| --DERMATITIS (INFLAMMATION)         |                                    | 2     | 5   | 1   | 12  | 14  |
| --EPIDERMAL NECROSIS                |                                    | 1     | 0   | 0   | 0   | 0   |
| URETERS                             | NUMBER EXAMINED                    | 1     | 1   | 0   | 0   | 1   |
| --INFLAMMATION                      |                                    | 1     | 0   | 0   | 0   | 0   |
| --LUMINAL DILATATION                |                                    | 0     | 0   | 0   | 0   | 1   |
| ** END OF LIST **                   |                                    |       |     |     |     |     |

373

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F - continued

Print No: 0022

Histopathology - group distribution of non-neoplastic findings for all animals

|                  |         |         |              |               |       |
|------------------|---------|---------|--------------|---------------|-------|
| Group            | 1       | 2       | 3            | 4             | 5     |
| Compound         | Control | Control | Pelamocortin | Hydrochloride |       |
| Dose (mg/kg/day) | 0       | 0       | 10           | 10/45         | 50/45 |

Printed 01-MOV-81

Page 1

Schedule number: 15H 0015

| ORGAN AND FINDING DESCRIPTION               | NUMBER OF ANIMALS AFFECTED |      |      |        |        |        |
|---|----------------------------|------|------|--------|--------|--------|
|   | SEX GROUP                  | SEX  |      |        |        |        |
|   |                            | MALE | MALE | FEMALE | FEMALE |        |
| NUMBER                                      | 1-                         | 2-   | 3-   | 4-     | 5-     |        |
| ADRENAL CTR                                 | NUMBER EXAMINED:           | 45   | 45   | 45     | 45     | 45     |
| --CORTICAL CYSTIC/HAEMORRHAGIC DEGENERATION |                            | 41   | 51   | 51     | 14     | 28 eff |
| --CORTICAL VASCULATION                      |                            | 2    | 2    | 0      | 6      | 6      |
| --CORTICAL NECROSIS                         |                            | 1    | 2    | 0      | 1      | 0      |
| --CORTICAL HYPERTROPHY                      |                            | 7    | 9    | 10     | 11     | 12     |
| --CORTICAL HYPERPLASIA, FOCAL               |                            | 6    | 5    | 5      | 0      | 0      |
| --CORTICAL MINERALISATION                   |                            | 0    | 0    | 1      | 1      | 0      |
| --CORTICAL FIBROSIS                         |                            | 1    | 1    | 0      | 0      | 0      |
| --PIGMENTED MACROPHAGES                     |                            | 1    | 0    | 0      | 0      | 1      |
| --FOCAL GLOMERULOSA - HYPERTROPHY, FOCAL    |                            | 10   | 19   | 11     | 2      | 8 eff  |
| --EXTRAMEDULLARY HAEMOPHOISIS               |                            | 0    | 0    | 1      | 2      | 1      |
| ADRENAL MED                                 | NUMBER EXAMINED:           | 45   | 45   | 45     | 45     | 45     |
| --MEDULLARY HYPERPLASIA, FOCAL              |                            | 2    | 3    | 5      | 3      | 11 med |
| --MINERALISATION                            |                            | 0    | 0    | 0      | 1      | 0      |
| BRAIN R 4                                   | NUMBER EXAMINED:           | 45   | 45   | 45     | 45     | 45     |
| --DEPRESSION DUE TO ENLARGED PITUITARY      |                            | 10   | 28   | 20     | 20     | 12 deg |
| --DILATED VENTRICLES                        |                            | 5    | 7    | 10     | 0      | 5      |
| --SAHCHORRAE                                |                            | 0    | 0    | 1      | 0      | 0      |
| CARCIN                                      | NUMBER EXAMINED:           | 45   | 45   | 45     | 45     | 45     |
| --LUMINAL DILATATION                        |                            | 1    | 0    | 0      | 0      | 1      |
| --ARTERITIS/VEINARTERITIS                   |                            | 0    | 0    | 1      | 0      | 0      |
| --SUBMUCOSAL INFLAMMATION                   |                            | 0    | 0    | 0      | 1      | 0      |
| COLON                                       | NUMBER EXAMINED:           | 45   | 45   | 45     | 45     | 45     |
| --LUMINAL DILATATION                        |                            | 1    | 0    | 0      | 0      | 0      |

374

TABLE 11P - continued.

Print No. 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Poloxetron Hydrochloride  
 Dosage (mg/kg/day): 0 0 15 30/45 10/60

Printed 03-MAY-01  
 Page 2

Schedule number N8H 001A

--- NUMBER OF ANIMALS AFFECTED ---

| ORGAN AND FINDING DESCRIPTION          | SEX              |     |     |     |     |
|--|------------------|-----|-----|-----|-----|
|  | GROUP            | -1- | -2- | -3- | -5- |
|  | NUMBER           | 65  | 65  | 65  | 65  |
| <b>EYES</b>                            | NUMBER EXAMINED  | 65  | 65  | 65  | 65  |
| --PANOPTHALMITIS                       |                  | 0   | 0   | 0   | 1   |
| --IRITIS                               |                  | 0   | 0   | 0   | 1   |
| --INFLAMMATORY CELLS, ANTERIOR CHAMBER |                  | 1   | 0   | 1   | 2   |
| --IRIS - INFLAMMATION                  |                  | 0   | 0   | 0   | 1   |
| --IRITIS                               |                  | 1   | 0   | 0   | 0   |
| --ASPIHAL ATROPHY                      |                  | 1   | 0   | 1   | 0   |
| --KERATITIS                            |                  | 1   | 0   | 1   | 2   |
| --LENTICULAR DEGENERATION              |                  | 0   | 0   | 0   | 1   |
| --SCLERITIS                            |                  | 0   | 0   | 0   | 2   |
| <b>PERIARTIC JOINTS</b>                | NUMBER EXAMINED: | 65  | 65  | 65  | 65  |
| --OSTEOCLEROSIS                        |                  | 0   | 0   | 0   | 1   |
| --MADON - MYELOFIBROSIS                |                  | 0   | 0   | 1   | 0   |
| <b>MARROW CLAND</b>                    | NUMBER EXAMINED: | 65  | 65  | 65  | 65  |
| --ACINAE HYPERPLASIA                   |                  | 0   | 0   | 1   | 2   |
| --HAEMORRHAGE                          |                  | 0   | 0   | 1   | 1   |
| --INFLAMMATION                         |                  | 0   | 0   | 1   | 2   |
| --ABSCISS                              |                  | 0   | 0   | 0   | 1   |
| --LYMPHOCTIC INFILTRATION              |                  | 2   | 0   | 0   | 0   |
| <b>HEART, VENTRICLE</b>                | NUMBER EXAMINED: | 65  | 65  | 65  | 65  |
| --CHRONIC MYOCARDITIS                  |                  | 61  | 39  | 24  | 28  |
| --ENDOCARDITIS                         |                  | 1   | 0   | 0   | 0   |
| --MINERALISATION OF CHORDAE TENDINAE   |                  | 1   | 0   | 0   | 0   |
| <b>JEJUNUM</b>                         | NUMBER EXAMINED: | 65  | 65  | 65  | 65  |
| --NECROSIS                             |                  | 0   | 0   | 0   | 1   |

0 0



TABLE 31F - continued

Fract No 2C72

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Polamoxon Hydrochloride  
 Doseage (mg/kg/day): 0 0 15 10/45 60/10

Printed 05-NOV-03

Page 3

Module Number HSN 001A

--- NUMBER OF ANIMALS AFFECTED ---

| ORGAN AND FINDING DESCRIPTION                 | SEX  |    |        |    |    |
|---|------|----|--------|----|----|
|   | MALE |    | FEMALE |    |    |
|   | 1-   | 2- | 3-     | 4- | 5- |
| .. FROM PREVIOUS PAGE ..                      |      |    |        |    |    |
| <b>JEJUNUM</b>                                |      |    |        |    |    |
| NUMBER EXAMINED                               | 05   | 05 | 05     | 05 | 05 |
| --DIVERGICULUM                                | 0    | 0  | 0      | 1  | 0  |
| --LUMINAL DILATATION                          | 1    | 0  | 0      | 0  | 0  |
| <b>PITNEY'S</b>                               |      |    |        |    |    |
| NUMBER EXAMINED                               | 05   | 05 | 05     | 05 | 05 |
| --PROGRESSIVE FIBRILE METAPLASIA              | 0    | 0  | 1      | 10 | 10 |
| --CORTICAL TUBULAR BASOPHILIA                 | 0    | 0  | 0      | 0  | 1  |
| --HYPERPLASIA, PAPILLARY EPITHELIUM           | 14   | 11 | 8      | 10 | 10 |
| --HYPERPLASIA, PELVIC EPITHELIUM              | 3    | 1  | 0      | 5  | 2  |
| --TUBULAR HYPERPLASIA, SIMPLE                 | 0    | 0  | 0      | 1  | 1  |
| --CORTICAL TUBULAR COLLAPSE                   | 0    | 0  | 0      | 1  | 0  |
| --MINERALISATION, PAPILLARY-PELVIC EPITHELIUM | 10   | 9  | 7      | 4  | 1  |
| --CORTICO-MEDULLARY MINERALISATION            | 3    | 2  | 1      | 1  | 0  |
| --MINERALISATION, MEDULLA                     | 0    | 0  | 0      | 0  | 1  |
| --MINERALISATION, PAPILLA                     | 0    | 0  | 0      | 0  | 1  |
| --PELVIC CALCULUS                             | 1    | 5  | 1      | 0  | 0  |
| --CORTICAL TUBULAR DILATATION                 | 0    | 1  | 1      | 0  | 0  |
| --DILATED MEDULLARY TUBULES                   | 0    | 0  | 1      | 1  | 1  |
| --CORTICAL TUBULES WITH HYALINE COAGULUM      | 1    | 6  | 3      | 0  | 0  |
| --CORTICAL TUBULAR SEGMENT                    | 0    | 0  | 1      | 0  | 0  |
| --CORTICAL FLAPPING                           | 0    | 0  | 0      | 2  | 0  |
| --CORTICAL CYST(S)                            | 1    | 0  | 0      | 1  | 1  |
| --MEDULLARY CYST(S)                           | 0    | 2  | 4      | 2  | 1  |
| --PAPILLARY CYST(S)                           | 0    | 3  | 1      | 0  | 1  |
| --RENAL - INFLAMMATION                        | 2    | 1  | 0      | 0  | 0  |
| --OBSTRUCTION                                 | 0    | 1  | 0      | 0  | 0  |
| --PERIVASCULAR LYMPHOIC AGGREGATIONS          | 0    | 0  | 0      | 0  | 1  |
| --CAPSULAR INFLAMMATION                       | 0    | 0  | 0      | 1  | 0  |
| --INTERSTITIAL INFLAMMATION                   | 0    | 1  | 0      | 0  | 0  |

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

TABLE 11F - continued.

Report No. 0022

Histopathology - group distribution of non-neoplastic findings for all animals

Group : 1 2 3 4 5  
 Compound : Control Control Poloxoneuron Hydrocortisone  
 Doseage mg/kg/day: 0 0 15 30/45 45/90

Printed: 25-NOV-63  
 Page 4

Schedule number N9H 001A

| ORGAN AND FINDING DESCRIPTION              | SEX GROUP       | NUMBER OF ANIMALS AFFECTED |    |    |    |         |
|--|-----------------|----------------------------|----|----|----|---------|
|  |                 | FEMALE                     |    |    |    |         |
|  |                 | 1                          | 2  | 3  | 4  | 5       |
| * FROM PREVIOUS PAGE *                     |                 |                            |    |    |    |         |
| KIDNEYS                                    | NUMBER EXAMINED | 45                         | 45 | 45 | 45 | 45      |
| --HYDRONEPHROSIS                           |                 | 9                          | 7  | 3  | 0  | 7       |
| LIVER MESENTERIC                           | NUMBER EXAMINED | 45                         | 45 | 45 | 45 | 45      |
| --AGGREGATIONS OF HISTIOCYTES              |                 | 37                         | 33 | 31 | 10 | adh def |
| --SIMUS HISTIOCYTOSIS                      |                 | 1                          | 2  | 3  | 3  | 17 def  |
| --SIMUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                 | 1                          | 2  | 1  | 2  | 0 adh   |
| --MADNOSIDIOSIS                            |                 | 0                          | 0  | 0  | 2  | 0 adh   |
| --DILATED/CYSTIC SIMUS                     |                 | 1                          | 0  | 0  | 2  | 2       |
| --MNOICTASIS                               |                 | 2                          | 0  | 1  | 1  | 1       |
| --MNSTOCTOSIS                              |                 | 0                          | 0  | 1  | 0  | 2       |
| LACRYMAL GLANDS                            | NUMBER EXAMINED | 45                         | 45 | 45 | 45 | 45      |
| --INTERSTITIAL LYMPHOID AGGREGATES         |                 | 0                          | 1  | 0  | 1  | 0       |
| LIVER R S                                  | NUMBER EXAMINED | 45                         | 45 | 45 | 45 | 45      |
| --BASOPHILIC FOCUS/FOCI                    |                 | 43                         | 42 | 45 | 44 | 31 0    |
| --CLEAR CELL FOCUS/FOCI                    |                 | 9                          | 13 | 21 | 29 | 25 adh  |
| --EOSINOPHILIC FOCUS/FOCI                  |                 | 3                          | 2  | 0  | 1  | 1       |
| --BILE DUCT PROLIFERATION                  |                 | 9                          | 0  | 0  | 0  | 0       |
| --HEPATOCTYE MICROBIS, LOBAR, TORION       |                 | 1                          | 0  | 0  | 0  | 0       |
| --HEPATOCTYE MICROBIS, CENTRILOBULAR       |                 | 0                          | 0  | 0  | 1  | 0       |
| --FOCAL NECROSIS                           |                 | 4                          | 3  | 2  | 1  | 2       |
| --HEPATOCTYE VACUOLATION - MEDIAN CLEFT    |                 | 1                          | 5  | 7  | 7  | 0 adh   |
| --HEPATOCTYE VACUOLATION, GENERALISED      |                 | 0                          | 3  | 0  | 0  | 0       |
| --HEPATOCTYE VACUOLATION, CENTRILOBULAR    |                 | 1                          | 0  | 2  | 1  | 1       |
| --HEPATOCTYE VACUOLATION, FOCAL            |                 | 0                          | 0  | 0  | 2  | 1       |
| --HEPATOCTYE VACUOLATION, MIDSMAL          |                 | 0                          | 0  | 2  | 0  | 1       |

377

TABLE 11F - continued.

Print No 0032

Histopathology - group distribution of non-neoplastic findings for all animals

Group                    1                    2                    3                    4                    5  
 Compound                Control Control Polameteron Hydrochloride  
 Doseage (mg/kg/day):    0                    0                    15                    30/43                    60/10

Printed 05-NOV-01  
 Page: 5

Schedule number N88 001A

| ORGAN AND FINDING DESCRIPTION              | NUMBER OF ANIMALS AFFECTED |     |        |     |     |    |
|--|----------------------------|-----|--------|-----|-----|----|
|  | Males                      |     | FEMALE |     |     |    |
|  | -1-                        | -2- | -3-    | -4- | -5- |    |
| .....                                      | NUMBER                     | 65  | 65     | 65  | 65  | 65 |
| ** FROM PREVIOUS PAGE **                   |                            |     |        |     |     |    |
| LIVER X 5                                  | NUMBER EXAMINED            | 65  | 65     | 65  | 65  | 65 |
| --HEPATOCTE VACUCLATION, PERIPORTAL        |                            | 13  | 10     | 7   | 9   | 0  |
| --FOCAL TELANGIECTASIS                     |                            | 0   | 0      | 0   | 10  | 6  |
| --EXTRAMEDULLARY HEMOPHOESIS               |                            | 1   | 2      | 0   | 2   | 0  |
| --FOCAL CONGESTION                         |                            | 11  | 0      | 15  | 15  | 6  |
| --CONGESTION, CENTRAL                      |                            | 0   | 0      | 3   | 2   | 3  |
| --PIGMENT IN MACROPHAGES                   |                            | 0   | 1      | 1   | 1   | 3  |
| --HEPATO-DIAPHRAGMATIC BERNIA              |                            | 1   | 0      | 0   | 1   | 0  |
| --PELLOSID HEPATIS                         |                            | 0   | 1      | 2   | 1   | 1  |
| --NANODIAPHRAGM, FOCAL                     |                            | 1   | 0      | 0   | 1   | 1  |
| --INFLAMMATION, PORTAL                     |                            | 1   | 0      | 0   | 1   | 0  |
| --BILIARY CYSTS, SINGLE                    |                            | 0   | 0      | 0   | 1   | 1  |
| --BILIARY CYSTS, MULTILOCULAR              |                            | 0   | 0      | 1   | 1   | 1  |
| --CAPSULAR ADHESIONS                       |                            | 0   | 0      | 0   | 1   | 1  |
| --FIBROSIS, PORTAL BRIDGING                |                            | 0   | 0      | 0   | 1   | 0  |
| --VASCULAR MEDIAL HYPERTROPHY              |                            | 0   | 0      | 6   | 1   | 0  |
| LIVER X 10                                 | NUMBER EXAMINED            | 65  | 65     | 65  | 65  | 65 |
| --PLASMACTOSIS                             |                            | 1   | 0      | 1   | 1   | 7  |
| --SINUS ERYTHROCYTOSIS/ERYTHROPHAGOCYTOSIS |                            | 1   | 1      | 2   | 2   | 0  |
| --DILATED/CYSTIC SINUSES                   |                            | 2   | 0      | 3   | 2   | 2  |
| --SINUS ERYTHROCYTOSIS                     |                            | 0   | 0      | 0   | 0   | 1  |
| --NANODIAPHRAGM                            |                            | 0   | 0      | 1   | 0   | 0  |
| LUNGS X 2                                  | NUMBER EXAMINED            | 65  | 65     | 65  | 65  | 65 |
| --ALVEOLAR HEMORRHAGE                      |                            | 2   | 0      | 2   | 4   | 1  |
| --ACCUMULATION(S) OF ALVEOLAR MACROPHAGES  |                            | 13  | 17     | 8   | 13  | 21 |
| --ALVEOLAR BRONCHIOLAR METAPLASIA          |                            | 0   | 0      | 0   | 0   | 1  |
| --ALVEOLAR EPITHELIAL HYPERPLASIA          |                            | 0   | 1      | 2   | 2   | 1  |

378

TABLE IIF - continued.

Print No 3022

Histopathology - group distribution of non-neoplastic findings for all Animals

|                  |         |         |                            |       |       |                   |
|------------------|---------|---------|----------------------------|-------|-------|-------------------|
| Group            | 1       | 2       | 3                          | 4     | 5     |                   |
| Compound         | Control | Control | Palonosetron Hydrochloride |       |       | Printed 05-NOV-01 |
| Dose (mg/kg/day) | 0       | 0       | 10                         | 10/45 | 40/40 | Page 6            |

Schedule number N88 001A

..... NUMBER OF ANIMALS AFFECTED .....

| ORGAN AND FINDING DESCRIPTION         | SEX GROUP       | FEMALE |     |     |     |     |
|---------------------------------------|-----------------|--------|-----|-----|-----|-----|
|                                       |                 | 1-1    | 2-1 | 3-1 | 4-1 | 5-1 |
| *1 FROM PREVIOUS PAGE *               | NUMBER          | 65     | 65  | 65  | 65  | 65  |
| UTERUS                                | NUMBER EXAMINED | 65     | 65  | 64  | 65  | 65  |
| **ALVEOLAR OEDEMA                     |                 | 0      | 0   | 0   | 0   | 1   |
| **ALVEOLAR OBSCURE METAPLASIA         |                 | 1      | 0   | 1   | 0   | 1   |
| **ENDOMETRIA                          |                 | 0      | 0   | 0   | 0   | 1   |
| **ENDOMETRITIS                        |                 | 0      | 0   | 0   | 0   | 3   |
| **PERIVASCULAR LYMPHOCYTE AGGREGATES  |                 | 0      | 1   | 0   | 0   | 3   |
| **PERIVASCULAR OEDEMA                 |                 | 0      | 0   | 0   | 0   | 1   |
| **CHOLESTEROL CLEFT GRANULOMATIS      |                 | 0      | 1   | 1   | 0   | 3   |
| **ARTERIAL MEDIAL HYPERTHROPHY        |                 | 0      | 1   | 0   | 1   | 0   |
| **FOREIGN BODY GRANULOMATIS           |                 | 1      | 1   | 0   | 0   | 1   |
| MAMMARY GLAND                         | NUMBER EXAMINED | 65     | 65  | 65  | 65  | 64  |
| **ACTINAL HYPERPLASIA                 |                 | 11     | 15  | 12  | 10  | 22  |
| **SECRETORY ACTIVITY                  |                 | 31     | 31  | 29  | 35  | 18  |
| **GALACTOCELE(SIS)                    |                 | 7      | 1   | 6   | 6   | 1   |
| OPTIC NERVE                           | NUMBER EXAMINED | 64     | 65  | 65  | 65  | 64  |
| **MACROPHAGE                          |                 | 1      | 0   | 1   | 0   | 0   |
| **GLIOSIS                             |                 | 6      | 5   | 3   | 3   | 3   |
| OVARIES                               | NUMBER EXAMINED | 65     | 65  | 65  | 65  | 64  |
| **FOLLICULAR MATURATION               |                 | 0      | 0   | 1   | 0   | 0   |
| **CYST                                |                 | 0      | 0   | 0   | 0   | 1   |
| **LUTEAL CYST                         |                 | 1      | 0   | 1   | 1   | 0   |
| **LUTEAL CYST                         |                 | 0      | 3   | 5   | 4   | 2   |
| **FOLLICULAR CYST                     |                 | 0      | 14  | 11  | 0   | 0   |
| **SERVICIPITHELIUM CELL PROLIFERATION |                 | 11     | 9   | 13  | 11  | 9   |
| **NO CORPORA LUTEA                    |                 | 0      | 0   | 14  | 0   | 5   |
| **SPARSE CORPORA LUTEA                |                 | 0      | 0   | 1   | 0   | 1   |

379

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL