Journal of Toxicologic Pathology

Received: January 14, 2020

Accepted: February 7, 2020

J-STAGE Advance Published Date: March 8, 2020
Comparison of longevity and common tumor profiles between Sprague-Dawley and Han Wistar rats

Authors

Ian Taylor
Associate Director, Pathology
Covance CRS Ltd. Eye
Occold
Eye
Suffolk
IP237PX
UK

Vasanthi Mowat
Director of Pathology
Covance CRS Ltd. Huntingdon
Woolley Road
Alconbury
Huntingdon
PE28 4HS
UK

Corresponding author
Ian Taylor
Associate Director, Pathology
Covance CRS Ltd. Eye
Occold
Eye
Suffolk
IP237PX
UK
Tel: +44 (0)1379 672450
E-mail: ian.taylor@covance.com
Longevity - common tumors of Sprague-Dawley and Han Wistar rat

Abstract

The Sprague Dawley (SD) and Han Wistar (HW) are the two most commonly used rat strains in Europe and the US, with the Han Wistar increasing in popularity because of its greater longevity and lower tumor burden. This survey was undertaken at Covance CRS (Huntingdon and Eye) to compare in-house longevity and common spontaneous tumor profiles of the two strains with published data. Data were compiled from 104-week studies started between 2010 and 2017. Mean survival was greater for both sexes of HWs when compared with SDs. Pituitary tumors were the commonest in both strains, with slightly higher incidences and more malignant tumors in SDs of both sexes. Mammary tumors were the second most common tumor in both strains; the incidence being greater in SDs compared to HWs. Benign pheochromocytomas of the adrenal and fibromas of the skin/subcutis were commoner in male SDs than in HWs. Granular cell tumors of the uterine tract were recorded only in SDs, but uterine stromal and glandular tumors were more common in HWs, which also displayed a higher incidence of granulosa cell tumors of the ovaries. Vascular tumors of the mesenteric lymph nodes, thymomas and follicular cell tumors of the thyroids were recorded at a higher incidence in HWs than in SDs. Tumor profiles of other common tumors were broadly similar between the two strains. The results of this survey correlate closely with similar comparisons made at other laboratories, and with data compiled at our laboratories 10 years ago and published as a poster.

Key words: rat, Sprague-Dawley, HAN Wistar, longevity, spontaneous tumors
The data used for collation comprised: 13 Han Wistar (HW) rat studies (16 control groups of 879 males and 879 females in total) obtained from Harlan (UK) Limited, Envigo RMS (UK) or Charles River (UK) Limited; 13 Sprague-Dawley (CD) rat studies (13 control groups of 876 males in total, and 15 control groups of 1016 females in total) obtained from Charles River (UK) Limited. Animals were obtained between ages 7 to 9 weeks and acclimatized for at least 7 days before being placed on a study. They were cage-housed in environmentally controlled (temperature: 20-24ºC and humidity: 40-70%) full barrier buildings and fed a commercially available standard diet (pelleted Rat and Mouse No. 1 Maintenance Diet) ad libitum, with access to water at all times. All studies were conducted in AAALAC-accredited facilities, and in accordance with the UK Animals (Scientific Procedures) Act 1986, which conforms to the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, Council of Europe). Tumours were diagnosed and classified according to the guidelines for proliferative lesions of each organ system published by the Society of Toxicological Pathology/INHAND.
Survival

The overall survival rates for control animals in the studies selected are presented in Table 1. Where necessary, animals were euthanased before scheduled sacrifice in accordance with set humane endpoints for the study type and the company’s guidelines. The mean percentage survival in HW rats was greater than that in SD rats in both sexes, and females showed lower survival than males in both strains.

Common Neoplastic Findings

Tumour incidences in carcinogenicity studies run over the last 7 years at two of our laboratories were collated and profiles compared between HWs and SDs. The results closely reflected a similar survey carried out at different laboratories and published in 2017, despite geographical and husbandry differences. The classification of tumours as common or rare is based on the criteria set out in FDA draft document. Statistical Aspects of the Design, Analysis, and Interpretation of Chronic Rodent Carcinogenicity Studies of Pharmaceuticals. Tumours occurring at an overall incidence of 1% or less are classified as rare; tumours occurring at an overall incidence greater than 1% are classified as common. The findings listed in the tables are those which have reached an overall incidence of greater than 1% in one or more of the strain/sex combinations in the selected studies. For completeness, both the benign and malignant forms of the neoplastic findings are presented, where appropriate, even if both have not reached the 1% threshold.

The overall incidence (with percentage), and range of incidences in individual studies for common tumours in Han Wistar and SD rats are presented in Tables 2 (Males) and 3 (Females).

1. Endocrine System

Tumors of the endocrine system accounted for the largest proportion of spontaneous tumors in rats of both sexes and both strains. Whereas pituitary tumours occurred at a higher incidence in SDs of both
Longevity - common tumors of Sprague-Dawley and Han Wistar rat

sexes, follicular cell tumours of thyroids were more frequent in HWs, with males in particular being more affected. A similar incidence pattern for these tumours has been recorded at other laboratories\(^1\).

**Pituitary**

The most common tumor in both strains of animal, and both sexes, was benign pituitary adenoma of the pars distalis, with SD rats showing a higher incidence than HW rats in both sexes, and females showing a higher incidence than males in both strains (Male HW – 40.69%; Male SD – 42.31%; Female HW – 58.58%; Female SD – 70.72%). Malignant carcinoma of the pars distalis was rare in male rats of both strains, seen occasionally in female HW rats (0.92%), but occurred commonly in female SD rats (2.08%).

**Thyroids**

Benign and malignant follicular cell tumors were seen at a greater incidence in males of both strains compared to females, while occurring at a higher incidence in HW rats compared to SD rats in both sexes. Benign follicular cell adenoma exceeded the Common threshold in both sexes and both strains (Male HW – 8.10%; Male SD – 2.99%; Female HW – 2.98%; Female SD – 1.68%). Malignant follicular cell carcinoma reached the common threshold in male HW rats only (1.03%). In both strains and both sexes, benign C-Cell adenoma was more common than follicular cell tumors (Male HW – 11.86%; Male SD – 8.27%; Female HW – 8.93%; Female SD – 7.60%). In male HW rats, benign C-Cell adenoma and benign follicular cell adenoma were the second and third most common tumors respectively. Malignant C-Cell carcinoma occurred rarely in HW rats, but reached the common threshold in SD rats of both sexes (Male SD – 1.72%; Female SD – 1.18%)

**Adrenals**

Benign pheochromocytoma was seen at a greater incidence in SD rats of both sexes compared to HW rats, while occurring more commonly in males than females in both strains (Male HW – 4.44%; Male SD – 10.96%; Female HW – 1.37%; Female SD – 2.56%). Malignant pheochromocytoma reached the common threshold in male SD rats only (1.83%). Benign adrenal cortical adenoma was
seen at a lower incidence in comparison to adrenal pheochromocytoma, and at a similar incidence in both sexes and both strains (Male HW – 1.25%; Male SD – 1.37%; Female HW – 1.25%; Female SD – 1.38%). Malignant adrenal cortical carcinoma was not reported in HW rats and were only seen rarely in SD rats.

**Endocrine Pancreas**

Benign islet cell adenoma occurred commonly in both strains, with a higher incidence in SD rats compared to HW rats in both sexes, and at a greater incidence in males compared to females in both strains (Male HW – 6.63%; Male SD – 9.40%; Female HW – 1.48%; Female SD – 2.76%). Malignant islet cell carcinoma exceeded the common threshold in males of both strains but occurred rarely in females. The incidences were comparable in both strains (Male HW – 1.37%; Male SD – 1.83%; Female HW – 0.57%; Female SD – 0.59%).

**Parathyroids**

Benign chief cell adenoma occurred at a greater incidence in males of both strains compared to females, and at a similar incidence in both strains. These tumors were rare in females but exceeded the common threshold in males (Male HW – 1.69%; Male SD – 1.33%; Female HW – 0.12%; Female SD – 0.21%).

2. **Integument and Mammary**

In general, all types of mammary gland and skin tumours were reported more often in SDs than in HWs. Mammary fibroadenoma and adenocarcinoma were recorded at a higher incidence in SDs of both sexes than in HWs, although mammary adenoma showed no significant differences between the strains in either sex.

**Mammary glands**

The second most common tumor type seen in control females were mammary tumors, with SD rats showing a higher incidence of all tumor types compared to HW rats. Benign fibroadenoma was the most commonly occurring tumor (24.94% in HW females and 53.16% in SD females) with a much
higher incidence of malignant adenocarcinoma in female SD rats (29.29%) compared to female HW rats (8.54%). Mammary benign fibroadenoma occurred at a common incidence (1.27%) in male SD rats, but benign adenoma and malignant adenocarcinoma were rare. All mammary tumor types were rare in male HW rats.

**Skin and Subcutis**

In males of both strains, tumors of the skin and subcutis were the second most common neoplastic findings seen in control animals. Benign fibroma was the single most common finding of the integument in male SD rats (12.24%), and apart from benign keratoacanthoma which occurred at a slightly higher incidence in male HW rats (6.83% compared to 5.72% in SD rats), all skin/subcutis tumors occurred at a higher incidence in male SD rats compared to male HW rats. In females of both strains, all skin/subcutis tumors with the exception of benign fibroma (1.14% in HW and 1.38% in SD) fell into the rare classification.

3. **Male and Female reproductive system**

In the female reproductive tract, most tumours occurred more frequently in HWs than in SDs (stromal polyp, adenoma and adenocarcinoma of the uterus and granulosa cell tumours of the ovary), with the exception of benign and malignant granular cell tumours which were recorded only in SDs. The most common neoplastic finding in the female reproductive tract was benign endometrial stromal polyp of the uterus, with a higher incidence in HW rats compared to SD rats (HW – 11.49%; SD – 6.11%). Benign endometrial adenoma and malignant endometrial adenocarcinoma of the uterus reached the common threshold in HW rats (1.02% and 1.71% respectively) but were rare in SD rats. Benign granulosa cell tumor was the only neoplastic finding in the ovaries to reach the common threshold but did so only in HW rats (2.05%). Benign granular cell tumors of the uterine cervix and vagina were seen only in the SD rat, occurring at an incidence of 1.48% and 1.28% respectively. A low incidence of malignant granular cell tumor was reported in the vagina of the SD rat (0.20%).
The interstrain differences in pituitary, mammary and uterine (in females) tumour incidences are thought to relate to differences in hormonal patterns during senescence\(^2\).

**Testes**

Benign adenoma of the Leydig cells was common, occurring at a similar incidence in both strains (HW – 2.05%; SD – 2.97%).

4. **Central Nervous System**

Benign granular cell tumor of the brain was common in HW rats of both sexes, but rare in SD rats (Male HW – 3.07%; Male SD – 0.91%; Female HW – 1.37%; Female SD – 0.89%). Malignant granular cell tumor was rare in both strains and both sexes. The incidence of malignant astrocytoma exceeded the common threshold in male SD rats only (1.37%).

5. **Hematopoietic system**

The most marked differences between the strains were in the lymphoreticular system. Benign thymoma and haemangioma of the mesenteric lymph nodes occurred more frequently in HW rats of both sexes than in SD rats; the higher incidence of these tumours is characteristic of HW rats\(^1\).

**Thymus**

Benign thymoma occurred commonly in HW rats of both sexes, with a higher incidence in females than males (Male HW – 3.14%; Male SD – 0.24%; Female HW – 7.81%; Female SD – 0.20%). Malignant thymoma was rare in both sexes and strains.

**Hematolymphoreticular system**

The only systemic neoplastic finding to reach the common threshold was malignant lymphoma in males of both strains (Male HW – 1.71%; Male SD – 1.37%; Female HW – 0.57%; Female SD – 0.39%).

**LN Mesenteric**

Benign hemangioma of the mesenteric lymph nodes occurred at a higher incidence in males compared to females and in HW rats of both sexes compared to SD rats (Male HW – 4.91%; Male
SD – 1.15%; Female HW – 0.80%; Female SD – 0.00%). Malignant hemangiosarcoma was rare in males of both strains and were not reported in females.

6. Digestive system

Liver

Benign hepatocellular adenoma had a relatively low incidence in both strains and reached the common threshold in male SD rats and female HW rats only (Male HW – 0.91%; Male SD – 1.83%; Female HW – 1.14%; Female SD – 0.98%). Malignant hepatocellular carcinoma was rare.
Exocrine pancreas

Benign acinar cell adenoma had a relatively low incidence in both strains and sexes and reached the common threshold in male SD rats only (Male HW – 0.11%; Male SD – 1.72%; Female HW – 0.11%; Female SD – 0.20%). Malignant acinar cell adenocarcinoma was rare in males of both strains, and not reported in females.

7. Respiratory system

Lungs

Benign bronchioloalveolar adenoma had a relatively low incidence in both strains and sexes and reached the common threshold in male HW rats only (Male HW – 1.02%; Male SD – 0.23%; Female HW – 0.00%; Female SD – 0.10%). Malignant bronchioloalveolar carcinoma was rare.

Disclosure of Potential Conflicts of Interest: The authors declare that there is no conflict of interest.
References

1. Weber K. Differences in Types and Incidence of Neoplasms in Wistar Han and Sprague-Dawley Rats. Toxicol Pathol. 45:64-75. 2017.

2. Vidal JD. The Impact of Age on the Female Reproductive System: A Pathologist’s Perspective. Toxicol Pathol. 45: 206-215. 2017.
Longevity - common tumors of Sprague-Dawley and Han Wistar rat

Table 1 – Mean percentage survival

| Animals surviving to scheduled euthanasia\(^a\) |
|-----------------------------------------------|
|                                              |
| Percentage survival (%)                      |
| Male HW Rats                                  |
| mean   | min  | max  |                      |
| 69.6%  | 56.4%| 85.0%|                      |
| Female HW Rats                                |
| mean   | min  | max  |                      |
| 65.5%  | 49.1%| 80.0%|                      |
| Male SD Rats                                  |
| mean   | min  | max  |                      |
| 41.9%  | 27.7%| 52.9%|                      |
| Female SD Rats                                |
| mean   | min  | max  |                      |
| 37.0%  | 23.1%| 51.4%|                      |

\(^a\) Mean percentage survival represents the average survival calculated from the total number of control groups for each sex/strain combination. The range presented is based on the control groups within each sex/strain combination with the lowest and highest percentage survival.
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|                | HAN WISTAR RATS |                           | SD RATS |                           |
|----------------|-----------------|---------------------------|---------|---------------------------|
|                | totals          | range of percentages     | totals  | range of percentages     |
| number of animals | 879             | min    | max    | 876                     | min    | max    |
| **ENDOCRINE SYSTEM** |                 |                    |         |                          |
| Pituitary      |                 |                    |         |                          |
| No examined    | 870             | 865             |         |                           |
| **Adenoma, Pars Distalis** |       |                    |         |                          |
| incidence      | 354             | 366             | 15.0%   | 66.7%                    |
| percentage     | 40.69%          | 29.7%           | 42.31%  | 60.0%                    |
| **Carcinoma, Pars Distalis** |       |                    |         |                          |
| incidence      | 0               | 2               | 0.00%   | 2.8%                     |
| percentage     | 0.00%           | 0.00%           | 0.23%   | 0.0%                     |
| **Thyroids**   |                 |                    |         |                          |
| No examined    | 877             | 871             |         |                           |
| **Adenoma, Follicular Cell** |       |                    |         |                          |
| incidence      | 71              | 26              | 0.0%    | 11.4%                    |
| percentage     | 8.10%           | 2.99%           | 0.00%   | 11.4%                    |
| **Carcinoma, Follicular Cell** |       |                    |         |                          |
| incidence      | 9               | 5               | 1.03%   | 3.2%                     |
| percentage     | 1.03%           | 0.57%           | 0.00%   | 3.2%                     |
| **Adenoma, C-Cell** |       |                    |         |                          |
| incidence      | 104             | 72              | 3.6%    | 20.6%                    |
| percentage     | 11.86%          | 8.27%           | 0.00%   | 20.6%                    |
| **Carcinoma, C-Cell** |       |                    |         |                          |
| incidence      | 5               | 15              | 0.00%   | 5.7%                     |
| percentage     | 0.57%           | 1.72%           | 0.00%   | 5.7%                     |
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|                         | HAN WISTAR RATS | SD RATS |
|-------------------------|-----------------|---------|
|                         | totals          | range of percentages | totals | range of percentages |
|                         | min  | max  | min  | max  | min  | max  |
| number of animals       | 879  | 876  |      |      |      |      |
| **Adrenals**            |      |      |      |      |      |      |
| No examined             | 879  | 876  |      |      |      |      |
| **Adenoma, Cortical**   |      |      |      |      |      |      |
| incidence               | 11   | 12   |      |      |      |      |
| percentage              | 1.25%| 0.0% | 4.0% | 1.37%| 0.0% | 8.3% |
| **Carcinoma, Cortical** |      |      |      |      |      |      |
| incidence               | 0    | 0    |      |      |      |      |
| percentage              | 0.00%| 0.0% | 0.0% | 0.00%| 0.0% | 0.0% |
| **Pheochromocytoma, Benign** |      |      |      |      |      |      |
| incidence               | 39   | 96   |      |      |      |      |
| percentage              | 4.44%| 0.0% | 12.0%| 10.96%| 0.0% | 21.7%|
| **Pheochromocytoma, Malignant** |      |      |      |      |      |      |
| incidence               | 7    | 16   |      |      |      |      |
| percentage              | 0.80%| 0.0% | 5.5% | 1.83%| 0.0% | 4.3% |
| **Endocrine Pancreas**  |      |      |      |      |      |      |
| No examined             | 875  | 872  |      |      |      |      |
| **Adenoma, Islet Cell** |      |      |      |      |      |      |
| incidence               | 58   | 82   |      |      |      |      |
| percentage              | 6.63%| 1.7% | 12.0%| 9.40%| 3.1% | 14.3% |
| **Carcinoma, Islet Cell** |      |      |      |      |      |      |
| incidence               | 12   | 16   |      |      |      |      |
| percentage              | 1.37%| 0.0% | 9.1% | 1.83%| 0.0% | 4.7% |
| **Parathyroids**        |      |      |      |      |      |      |
| No examined             | 827  | 828  |      |      |      |      |
| **Adenoma, Chief Cell** |      |      |      |      |      |      |
| incidence               | 14   | 11   |      |      |      |      |
| percentage              | 1.69%| 0.0% | 5.4% | 1.33%| 0.0% | 7.5% |
Longevity - common tumors of Sprague-Dawley and Han Wistar rat

Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

| MAMMARY Glands | HAN WISTAR RATS | SD RATS |
|-----------------|-----------------|--------|
| number of animals | 879 | 876 |

**INTEGUMENT AND MAMMARY**

| Mammary Glands | HAN WISTAR RATS | SD RATS |
|-----------------|-----------------|--------|
| No examined | 850 | 869 |

| Mammary Adenoma | incidence | percentage | incidence | percentage |
|------------------|-----------|------------|-----------|------------|
|                  | 1         | 0.12%      | 3         | 0.35%      |
|                  | 0.0%      | 0.0%       | 1.8%      | 0.0%       |

| Mammary Fibroadenoma | incidence | percentage | incidence | percentage |
|----------------------|-----------|------------|-----------|------------|
|                      | 2         | 0.24%      | 11        | 1.27%      |
|                      | 0.0%      | 0.0%       | 2.0%      | 0.0%       |
|                      |           |            | 1.8%      | 0.0%       |

| Mammary Adenocarcinoma | incidence | percentage | incidence | percentage |
|------------------------|-----------|------------|-----------|------------|
|                        | 0         | 0.00%      | 6         | 0.69%      |
|                        | 0.0%      | 0.0%       | 0.0%      | 1.6%       |

**Skin and Subcutis**

| Skin and Subcutis | HAN WISTAR RATS | SD RATS |
|-------------------|-----------------|--------|
| No examined | 879 | 874 |

| Tumor, Basal Cell, Benign | incidence | percentage | incidence | percentage |
|---------------------------|-----------|------------|-----------|------------|
|                           | 3         | 0.34%      | 11        | 1.26%      |
|                           | 0.0%      | 0.0%       | 2.0%      | 0.0%       |
|                           |           |            | 1.8%      | 0.0%       |

| Tumor, Basal Cell, Malignant | incidence | percentage | incidence | percentage |
|------------------------------|-----------|------------|-----------|------------|
|                              | 1         | 0.11%      | 1         | 0.11%      |
|                              | 0.0%      | 0.0%       | 1.8%      | 0.0%       |
|                              |           |            | 1.5%      | 0.0%       |

| Fibroma | incidence | percentage | incidence | percentage |
|---------|-----------|------------|-----------|------------|
|         | 25        | 2.84%      | 107       | 12.24%     |
|         | 0.0%      | 0.0%       | 10.9%     | 2.9%       |
|         |           |            | 21.5%     |            |

| Fibrosarcoma | incidence | percentage | incidence | percentage |
|--------------|-----------|------------|-----------|------------|
|              | 11        | 1.25%      | 15        | 1.72%      |
|              | 0.0%      | 0.0%       | 4.0%      | 0.0%       |
|              |           |            | 4.2%      |            |

| Keratoacanthoma | incidence | percentage | incidence | percentage |
|-----------------|-----------|------------|-----------|------------|
|                 | 60        | 6.83%      | 50        | 5.72%      |
|                 | 0.0%      | 0.0%       | 13.3%     | 0.0%       |
|                 |           |            | 11.7%     |            |

| Lipoma | incidence | percentage | incidence | percentage |
|--------|-----------|------------|-----------|------------|
|        | 17        | 1.93%      | 20        | 2.29%      |
|        | 0.0%      | 0.0%       | 6.0%      | 0.0%       |
|        |           |            | 5.6%      |            |
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|                  | HAN WISTAR RATS | SD RATS |
|------------------|-----------------|---------|
|                  | totals          | range of percentages | totals | range of percentages |
|                  | min | max | min | max |
| number of animals| 879 | 879 | 876 | 876 |
| Skin and Subcutis (cont’d) |          |          |      |      |
| No examined      | 879 |       | 874 |       |
| Liposarcoma      |     |      |     |      |
| incidence        | 1   |       | 1   |       |
| percentage       | 0.11% | 0.0% | 2.0% | 0.11% | 0.0% | 1.5% |
| Adenoma, Sebaceous Cell |      |      |      |      |
| incidence        | 1   |       | 9   |       |
| percentage       | 0.11% | 0.0% | 2.0% | 1.03% | 0.0% | 3.1% |
| Carcinoma, Sebaceous Cell |    |      |      |      |
| incidence        | 2   |       | 2   |       |
| percentage       | 0.23% | 0.0% | 1.9% | 0.23% | 0.0% | 1.7% |
| Papilloma, Squamous Cell |     |      |      |      |
| incidence        | 5   |       | 13  |       |
| percentage       | 0.57% | 0.0% | 2.0% | 1.49% | 0.0% | 4.2% |
| Carcinoma, Squamous Cell |    |      |      |      |
| incidence        | 4   |       | 6   |       |
| percentage       | 0.46% | 0.0% | 3.8% | 0.69% | 0.0% | 6.9% |

**REPRODUCTIVE SYSTEM**

**Testes**

|                  | HAN WISTAR RATS | SD RATS |
|------------------|-----------------|---------|
|                  | totals          | range of percentages | totals | range of percentages |
|                  | min | max | min | max |
| No examined      | 878 |       | 875 |       |
| Adenoma, Leydig Cell |      |      |      |      |
| incidence        | 18  |       | 26  |       |
| percentage       | 2.05% | 0.0% | 6.0% | 2.97% | 0.0% | 8.6% |
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|                            | HAN WISTAR RATS | SD RATS |
|-----------------------------|----------------|---------|
| number of animals           | 879            | 876     |

**CENTRAL NERVOUS SYSTEM**

**Brain**

| Tumor, Granular Cell, Benign | incidence | percentage | total | percentages | range of percentages |
|-------------------------------|-----------|------------|-------|-------------|----------------------|
| No examined                   | 879       | 876        |       |             |                      |
| Tumor, Granular Cell, Benign  | 27        | 3.07%      | 8     | 0.0%        | 9.1%                 |
| Tumor, Granular Cell, Malignant| 3         | 0.34%      | 1     | 0.0%        | 2.0%                 |
| Astrocytoma                   | 7         | 0.80%      | 12    | 0.0%        | 5.0%                 |

**HEMATOPOIETIC SYSTEM**

**Thymus**

| Thymoma, Benign | incidence | percentage | total | percentages | range of percentages |
|-----------------|-----------|------------|-------|-------------|----------------------|
| No examined     | 860       | 831        |       |             |                      |
| Thymoma, Benign | 27        | 3.14%      | 2     | 0.0%        | 6.3%                 |
| Thymoma, Malignant| 2         | 0.23%      | 2     | 0.0%        | 3.4%                 |

**Hematolymphoreticular System**

| Malignant Lymphoma | incidence | percentage | total | percentages | range of percentages |
|--------------------|-----------|------------|-------|-------------|----------------------|
| No examined        | 879       | 876        |       |             |                      |
| Malignant Lymphoma | 15        | 1.71%      | 12    | 0.0%        | 5.5%                 |
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|               | HAN WISTAR RATS | SD RATS |
|---------------|-----------------|--------|
|               | totals          | range of percentages | totals | range of percentages |
|               | min | max | min | max |
| number of animals | 879 | 876 |
| LN Mesenteric  |     |     |     |     |
| No examined    | 875 | 871 |
| Hemangioma     |     |     |     |     |
| incidence      | 43  | 10  |
| percentage     | 4.91% | 0.0% | 23.3% | 1.15% | 0.0% | 4.7% |
| Hemangiosarcoma|     |     |     |     |
| incidence      | 7   | 2   |
| percentage     | 0.80% | 0.0% | 6.0% | 0.23% | 0.0% | 1.5% |
| DIGESTIVE SYSTEM|    |    |    |    |
| Liver          |     |     |     |     |
| No examined    | 878 | 876 |
| Adenoma, Hepatocellular |     |     |     |     |
| incidence      | 8   | 16  |
| percentage     | 0.91% | 0.0% | 5.8% | 1.83% | 0.0% | 6.2% |
| Carcinoma, Hepatocellular |     |     |     |     |
| incidence      | 1   | 5   |
| percentage     | 0.11% | 0.0% | 2.0% | 0.57% | 0.0% | 2.8% |
| Exocrine Pancreas|    |    |    |    |
| No examined    | 875 | 872 |
| Adenoma, Acinar Cell |     |     |     |     |
| incidence      | 1   | 15  |
| percentage     | 0.11% | 0.0% | 1.7% | 1.72% | 0.0% | 4.6% |
| Adenocarcinoma, Acinar Cell |     |     |     |     |
| incidence      | 1   | 1   |
| percentage     | 0.11% | 0.0% | 1.9% | 0.11% | 0.0% | 1.6% |
Table 2 – Incidence and range of common neoplastic findings in male Han Wistar and Sprague-Dawley rats

|                             | HAN WISTAR RATS | SD RATS |
|-----------------------------|-----------------|---------|
|                             | totals          | range of percentages | totals | range of percentages |
|                             | min  | max   | min  | max   |
| number of animals           | 879  |       | 876  |       |
| RESPIRATORY SYSTEM          |       |       |       |       |
| Lungs                       |       |       |       |       |
| No examined                 | 879  |       | 876  |       |
| Adenoma, Bronchioloalveolar| incidence   | 9      | 2    |
|                             | percentage   | 1.02%  | 0.0% | 3.6%  | 0.23%  | 0.0% | 1.5% |
| Carcinoma, Bronchioloalveolar| incidence | 2      | 1    |
|                             | percentage   | 0.23%  | 0.0% | 3.6%  | 0.11%  | 0.0% | 1.5% |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

FEMALES

| System                      | Number of Animals | HAN WISTAR RATS | SD RATS |
|-----------------------------|-------------------|-----------------|---------|
|                             | totals            | range of percentages | totals | range of percentages |
|                             | min | max | min | max |
| Endocrine System            | 879 | 1016 |
| Pituitary                   | No examined      | 874             | 1011 |
| Adenoma, Pars Distalis      | incidence        | 512             | 715 |
|                             | percentage       | 58.58% | 40.7% | 74.6% | 70.72% | 58.6% | 84.3% |
| Carcinoma, Pars Distalis    | incidence        | 8               | 21 |
|                             | percentage       | 0.92% | 0.0% | 5.8% | 2.08% | 0.0% | 8.3% |
| Thyroids                    | No examined      | 873             | 1013 |
| Adenoma, Follicular Cell    | incidence        | 26              | 17 |
|                             | percentage       | 2.98% | 0.0% | 10.0% | 1.68% | 0.0% | 6.9% |
| Carcinoma, Follicular Cell  | incidence        | 4               | 2 |
|                             | percentage       | 0.46% | 0.0% | 2.0% | 0.20% | 0.0% | 1.5% |
| Adenoma, C-Cell             | incidence        | 78              | 77 |
|                             | percentage       | 8.93% | 4.0% | 16.9% | 7.60% | 2.9% | 15.7% |
| Carcinoma, C-Cell           | incidence        | 2               | 12 |
|                             | percentage       | 0.23% | 0.0% | 1.9% | 1.18% | 0.0% | 4.3% |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                | HAN WISTAR RATS | SD RATS |
|----------------|-----------------|---------|
|                | totals          | range of percentages | totals | range of percentages |
|                | min | max | min | max |
| number of animals | 879 | 1016 |
| **Adrenals**    |                 |                   |       |                   |
| No examined     | 879 | 1014 |
| **Adenoma, Cortical** | 11 | 14 | 1.25% | 0.0% | 5.0% | 1.38% | 0.0% | 3.1% |
| Incidence       | percentage     |                   |       |                   |
| Carcinoma, Cortical | 2 | 4 | 0.23% | 0.0% | 2.0% | 0.39% | 0.0% | 1.5% |
| Incidence       | percentage     |                   |       |                   |
| Pheochromocytoma, Benign | 12 | 26 | 1.37% | 0.0% | 3.3% | 2.56% | 0.0% | 7.1% |
| Incidence       | percentage     |                   |       |                   |
| Pheochromocytoma, Malignant | 3 | 6 | 0.34% | 0.0% | 3.6% | 0.59% | 0.0% | 4.3% |
| Incidence       | percentage     |                   |       |                   |
| **Endocrine Pancreas** |                 |                   |       |                   |
| No examined     | 877 | 1014 |
| Adenoma, Islet Cell | 13 | 28 | 1.48% | 0.0% | 6.1% | 2.76% | 0.0% | 6.2% |
| Incidence       | percentage     |                   |       |                   |
| Carcinoma, Islet Cell | 5 | 6 | 0.57% | 0.0% | 3.6% | 0.59% | 0.0% | 4.3% |
| Incidence       | percentage     |                   |       |                   |
| **Parathyroids** |                 |                   |       |                   |
| No examined     | 824 | 962 |
| Adenoma, Chief Cell | 1 | 2 | 0.12% | 0.0% | 2.0% | 0.21% | 0.0% | 1.6% |
| Incidence       | percentage     |                   |       |                   |
Longevity - common tumors of Sprague-Dawley and Han Wistar rat

Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                        | HAN WISTAR RATS | SD RATS |
|------------------------|-----------------|---------|
|                        | totals          | range of percentages | totals | range of percentages |
|                        | min | max |          | min | max |
| number of animals      | 879 | 1016 |
| INTEGUMENT AND         |      |      |          |      |      |
| MAMMARY               |      |      |          |      |      |
| Mammary Glands        |      |      |          |      |      |
| No examined            | 878 | 1014 |
| Mammary Adenoma       | 34  | 51   | 3.87% 0.0% 13.3% | 5.03% 0.0% 11.3% |
| Mammary Fibroadenoma   | 219 | 539  | 24.94% 8.3% 42.0% | 53.16% 43.1% 69.2% |
| Mammary Adenocarcinoma| 75  | 297  | 8.54% 0.0% 17.3% | 29.29% 18.5% 41.5% |
| Skin and Subcutis      |      |      |          |      |      |
| No examined            | 879 | 1014 |
| Tumor, Basal Cell, Benign | 2    | 0     | 0.23% 0.0% 2.0% | 0.00% 0.0% 0.0% |
| Tumor, Basal Cell, Malignant | 0    | 1     | 0.00% 0.0% 0.0% | 0.10% 0.0% 1.5% |
| Fibroma                | 10  | 14   | 1.14% 0.0% 5.5% | 1.38% 0.0% 6.3% |
| Fibrosarcoma           | 8   | 6    | 0.91% 0.0% 4.0% | 0.59% 0.0% 3.1% |
| Keratoacanthoma        | 8   | 2    | 0.91% 0.0% 7.3% | 0.20% 0.0% 1.4% |
| Lipoma                 | 4   | 8    | 0.46% 0.0% 1.8% | 0.79% 0.0% 5.7% |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                            | HAN WISTAR RATS | SD RATS |
|-----------------------------|-----------------|---------|
| **FEMALES**                 | totals          | range of percentages | totals | range of percentages |
| number of animals           | 879             | 1016     |
| **Skin and Subcutis (cont’d)** |          |          |
| No examined                 | 879             | 1014     |
| **Liposarcoma**            | incidence       | percentage |         |         |
|                            | 0               | 0.00% 0.0% 0.0% | 0       | 0.00% 0.0% 0.0%    |
| **Adenoma, Sebaceous Cell**| incidence       | percentage |         |         |
|                            | 0               | 0.00% 0.0% 0.0% | 0       | 0.00% 0.0% 0.0%    |
| **Carcinoma, Sebaceous Cell** | incidence       | percentage |         |         |
|                            | 1               | 0.11% 0.0% 1.9% | 0       | 0.00% 0.0% 0.0%    |
| **Papilloma, Squamous Cell** | incidence       | percentage |         |         |
|                            | 2               | 0.23% 0.0% 2.0% | 2       | 0.20% 0.0% 1.5%    |
| **Carcinoma, Squamous Cell** | incidence       | percentage |         |         |
|                            | 2               | 0.23% 0.0% 2.0% | 2       | 0.20% 0.0% 1.7%    |

**REPRODUCTIVE SYSTEM**

**Ovaries**

|                            | HAN WISTAR RATS | SD RATS |
|-----------------------------|-----------------|---------|
| No examined                 | 879             | 1013    |
| **Tumor, Granulosa Cell, Benign** | incidence       | percentage |         |         |
|                            | 18              | 2.05% 0.0% 5.0% | 2       | 0.20% 0.0% 1.5%    |
| **Tumor, Granulosa Cell, Malignant** | incidence       | percentage |         |         |
|                            | 4               | 0.46% 0.0% 3.3% | 2       | 0.20% 0.0% 1.4%    |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                      | HAN WISTAR RATS |                                           | SD RATS |                                           |
|----------------------|-----------------|-------------------------------------------|---------|-------------------------------------------|
|                      | totals          | range of percentages                      | totals  | range of percentages                      |
|                      |                 | min | max    |                 | min | max    |
| number of animals    | 879             | 1016 |        | 878             | 1014 |        |
| **Uterine Cervix**   |                 |     |        |                 |     |        |
| No examined          | 878             | 1014 |        |                 |     |        |
| **Tumor, Granular Cell, Benign** |       |       |        | **Tumor, Granular Cell, Malignant** |       |       |        |
| incidence            | 0               | 15  |        | 0               | 0   |        |
| percentage           | 0.00%           | 1.48%| 0.0% | 0.00%           | 0.0%| 7.1%  |
| **Uterus**           |                 |     |        |                 |     |        |
| No examined          | 879             | 1014 |        |                 |     |        |
| **Polyp, Endometrial Stromal** |       |       |        | **Sarcoma, Endometrial Stromal** |       |       |        |
| incidence            | 101             | 62  |        | 3               | 1   |        |
| percentage           | 11.49%          | 6.11%| 18.3%| 0.34%           | 0.10%| 1.4%  |
| **Adenoma, Endometrium** |             |       |        | **Adenocarcinoma, Endometrium** |       |       |        |
| incidence            | 9               | 5   |        | 15              | 8   |        |
| percentage           | 1.02%           | 0.0% | 6.7% | 1.71%           | 0.0% | 4.6%  |
| **Vagina**           |                 |     |        |                 |     |        |
| No examined          | 878             | 1014 |        |                 |     |        |
| **Tumor, Granular Cell, Benign** |       |       |        | **Tumor, Granular Cell, Malignant** |       |       |        |
| incidence            | 0               | 13  |        | 0               | 2   |        |
| percentage           | 0.00%           | 1.28%| 0.0% | 0.00%           | 0.20%| 2.8%  |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|系统 | 细胞类型 | 雌性 | HAN WISTAR RATS | SD RATS |
|---|---|---|---|---|
| | | | 总数 | 范围 | 百分比 | 总数 | 范围 | 百分比 |
| | | 个数 | | 最低 | 最高 | | 最低 | 最高 |
| | | | | | |
|中央神经系统 | 脑 | 879 | | 1016 | |
| | 脑肿瘤，良性 | 肿瘤类型 | 是否存在 | 12 | 9 | 0.89% | 0.0% | 5.7% |
| | 肿瘤类型 | 百分比 | 1.37% | 0.0% | 5.5% |
| | 脑肿瘤，恶性 | 肿瘤类型 | 是否存在 | 1 | 0 | 0.00% | 0.0% | 0.0% |
| | 肿瘤类型 | 百分比 | 0.0% | 0.0% | 1.8% |
| | 脑胶质瘤 | 肿瘤类型 | 是否存在 | 1 | 9 | 0.89% | 0.0% | 2.9% |
| | 肿瘤类型 | 百分比 | 0.11% | 0.0% | 1.7% |
| | | | | | |
|造血系统 | 胸腺 | 871 | | 989 | |
| | 胸腺瘤，良性 | 肿瘤类型 | 是否存在 | 68 | 2 | 0.20% | 0.0% | 2.9% |
| | 肿瘤类型 | 百分比 | 7.81% | 0.0% | 18.0% |
| | 胸腺瘤，恶性 | 肿瘤类型 | 是否存在 | 5 | 1 | 0.10% | 0.0% | 1.4% |
| | 肿瘤类型 | 百分比 | 0.57% | 0.0% | 6.8% |
| | | | | | |
| | | | | | |
|血液淋巴系统 | 恶性淋巴瘤 | 肿瘤类型 | 是否存在 | 5 | 4 | 0.39% | 0.0% | 3.1% |
| | 肿瘤类型 | 百分比 | 0.57% | 0.0% | 4.0% |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                      | HAN WISTAR RATS | SD RATS |
|----------------------|----------------|---------|
| **FEMALES**          |                |         |
| number of animals    | 879            | 1016    |
| LN Mesenteric        |                |         |
| No examined          | 879            | 1012    |
| Hemangioma           |                |         |
| incidence            | 7              | 0       |
| percentage           | 0.80%          | 0.0%    |
|                     | 3.6%           | 0.0%    |
| Hemangiosarcoma      |                |         |
| incidence            | 0              | 0       |
| percentage           | 0.00%          | 0.0%    |
|                     | 0.0%           | 0.0%    |
| **DIGESTIVE SYSTEM** |                |         |
| Liver                |                |         |
| No examined          | 879            | 1016    |
| Adenoma, Hepatocellular |            |         |
| incidence            | 10             | 10      |
| percentage           | 1.14%          | 0.0%    |
|                     | 3.8%           | 0.98%   |
| Carcinoma, Hepatocellular |        |         |
| incidence            | 1              | 0       |
| percentage           | 0.11%          | 0.0%    |
|                     | 1.7%           | 0.0%    |
| Exocrine Pancreas    |                |         |
| No examined          | 877            | 1014    |
| Adenoma, Acinar Cell |                |         |
| incidence            | 1              | 2       |
| percentage           | 0.11%          | 0.0%    |
|                     | 1.8%           | 0.20%   |
| Adenocarcinoma, Acinar Cell |       |         |
| incidence            | 0              | 0       |
| percentage           | 0.00%          | 0.0%    |
|                     | 0.0%           | 0.0%    |
Table 3 – Incidence and range of common neoplastic findings in female Han Wistar and Sprague-Dawley rats

|                  | HAN WISTAR RATS | SD RATS |
|------------------|-----------------|---------|
|                  | number of animals |         |
| Females          | 879             | 1016    |
| **RESPIRATORY SYSTEM** |               |         |
| **Lungs**        |                 |         |
| No examined      | 879             | 1016    |
| **Adenoma, Bronchioalveolar** | 0            | 1       |
| incidence        | 0               | 1       |
| percentage       | 0.00%           | 0.0%    |
| **Carcinoma, Bronchioalveolar** | 0            | 1       |
| incidence        | 0               | 1       |
| percentage       | 0.00%           | 0.0%    |