

# Spontaneous Neoplastic Lesions in the CDF<sup>®</sup> (F-344)/CrIBR Rat

February, 1990

Information Compiled by

*Patricia L. Lang, Ph.D.*

Consulting Toxicologist



CHARLES RIVER  
LABORATORIES

## Index

|   | PAGE         |
|---|--------------|
| <b>Introduction</b> .....                                     | 1-3          |
| <b>Glossary Of Synonyms</b> .....                             | 3-4          |
| <b>Key To Abbreviations</b> .....                             | 4            |
| <b>MALE</b>   |              |
| Table 1 Spontaneous Neoplastic Lesions (Summary).....         | 5-7          |
| Table 2 <b>Lymphoreticular</b> Tumors (Expanded).....         | 8            |
| Table 3 Pulmonary Masses (Expanded).....                      | 8            |
| Table 4 Hepatic Masses (Expanded).....                        | 9            |
| Table 5 Testicular Tumors (Expanded).....                     | 9            |
| Table 6 <b>Pituitary</b> Gland Tumors (Expanded).....         | 10           |
| Table 7 Adrenal Gland Tumors (Expanded).....                  | 10           |
| Table 8 <b>Mesotheliomas (Expanded)</b> .....                 | 11           |
| <b>FEMALE</b>   |              |
| <b>Table 9 Spontaneous Neoplastic Lesions (Summary)</b> ..... | <b>12-13</b> |
| Table 10 Lymphoreticular Tumors (Expanded).....               | 14           |
| Table 11 Pulmonary Masses (Expanded).....                     | 14           |
| Table 12 Hepatic Masses (Expanded).....                       | 14           |
| Table 13 Urinary Bladder Tumors (Expanded).....               | 15           |
| Table 14 Uterine Tumors (Expanded).....                       | 15           |
| Table 15 Pituitary Gland Tumors (Expanded).....               | 16           |
| Table 16 Adrenal Gland Tumors (Expanded).....                 | 16           |

## Spontaneous Neoplastic Lesions in the CDF<sup>®</sup> (F-344)ICrIBR Rat

INTRODUCTION—The data in these tables were gathered from chronic toxicology studies designed for product registration. All studies were performed in the United States at contract toxicology laboratories or pharmaceutical facilities.

### I. COMMON STUDY PARAMETERS

Data from 13 groups of control animals are presented in Tables 1 through 16. All studies had the following conditions in common:

- They were 24 months in duration.
- The diet was Purina 5002 Certified Rodent Lab Chow except in studies C (Wayne 86-04) and E (NIH-31).
- The in-life completion dates of the studies ranged from 1980 to 1986.
- Lesions tabulated were assumed to be primary site tumors only.
- CDF<sup>®</sup> (F-344)/CrIBR rats were supplied from Charles River production sites in Portage, MI and Kingston, NY.

The encoded study identification (Study ID), the number of rats housed per cage, and the length of the study to terminal sacrifice of the rats in each study group are as follows:

| Study ID | #/Cage | Study Dates   |
|----------|--------|---------------|
| A        |        | 11/79 - 4/82  |
| B        |        | 11/82 - 12/84 |
| C        | 3      | 1/78 - 3/80   |
| D        | 2      | 4/84 - 4/86   |
| E        | 3      | 1/78 - 2/80   |
| F        |        | 8/81 - 8/83   |
| G        |        | 9/81 - 9/83   |
| H        |        | 9/83 - 9/85   |
|          | 2      | 1/84 - 2/86   |
| J        | 2      | 5/79 - 6/81   |
| K        | 2      | 9/80 - 9/82   |
| L        | 2      | 3/82 - 3/84   |
| M        | 2      | 10/81 - 11/83 |

## II. ENVIRONMENTAL CONDITIONS

Environmental conditions for studies are rarely identical even when two studies are conducted in the same facility. Since these studies were conducted in different laboratories, some variation is inherent in the environmental conditions. The range of the mean room temperatures was 68° to 72°F. The range of the mean relative humidity was 45 to 55 percent. Relative humidity control was not precise in all facilities allowing the relative humidity to drop as low as 30 percent in winter months and to rise as high as 75 percent in the summer.

The photoperiod was maintained at a 12-hour light/dark cycle without twilight. Other environmental conditions were either not stated or were inconsistent between facilities. Information on health assessment monitoring other than that associated with pathologic examination conducted in accordance with scheduled or moribund sacrifices was not available.

Overall, environmental conditions were not considered by those performing and interpreting the studies to have affected the outcome of the studies or the distribution of lesions.

## III. TABLES 1 AND 9

Tables 1 and 9 provide a summary of neoplastic lesions in male and female CDF<sup>o</sup> (F-344)/CrIBR rats. Data in these tables are expressed as follows:

### Numbers Examined (# Examined)

This column was obtained by combining the total numbers of each tissue/organ examined in the control groups of 13 studies. Tumors of the lymphoreticular system are listed on the basis of the number of *animals* examined since these tumors are frequently found in multiple organs. Data from only 10 studies were included in the lymphoreticular tumor data since the data from the remaining three studies were not available in a fashion that allowed its incorporation into this data base.

Autolysis of tissue did not routinely exclude samples from inclusion in the data base since some lesions could be diagnosed despite some autolysis. Tissue numbers were adjusted only if the individual study summary indicated that some were missing or that the tissues were inadequate for evaluation.

### Number of Lesions (# Lesions)

Entries in this column are the total number of occurrences of this lesion in the tissue/organ or animal (i.e., lymphoreticular system) examined. These values were obtained by summing the number of occurrences in all of the studies used.

### Percent

This column represents the mean percent of lesions found in the total population of tissue/organs or animals (i.e., lymphoreticular system) examined. These values were calculated by dividing the total number of lesions by the total number of tissues/organs or animals (i.e., lymphoreticular system) examined and then expressing the result as a percent (i.e., multiplying by 100). The values are expressed to the first decimal place since many values are below 0.5 percent and would be otherwise rounded off to zero.

### Range

The range is the highest and lowest percent reported for a given lesion in the individual study groups. For example, in the case of the kidney of male rats, five renal cell adenomas were found as primary tumors in 964 tissues examined, giving a mean of 0.5 percent for the population. In the 13 control groups represented, there was at least one group with no renal cell adenomas (the low value in the RANGE) and at least one group with as many as 3.3 percent (the high value in the RANGE).

The individual study percentages comprising the range were calculated by dividing the total number of lesions by the total number of tissues/organs or animals (i.e., lymphoreticular system) in each study. Some tissues can be difficult to find in adult animals (e.g., thymus and male mammary gland) unless an obvious lesion exists. It must be remembered that with these tissues the individual group mean percentage may be skewed since the tissue may not have been examined in all animals studied and therefore only those animals with lesions in these tissues may have been recorded.

### Expanded Tables for Selected Tissues/Organs (Tables 2-8 and 10-16)

In compiling these tables it became clear that some lesions were diagnosed differently by dif-

ferent pathologists. Some of the lesions included in the tables may not be considered by all pathologists to represent neoplastic changes. For example, proliferative lesions in the liver of male CDF<sup>®</sup> (F-344)/CrIBR rats included hyperplastic nodules, neoplastic nodules, hepatocellular adenomas, and hepatocellular carcinomas. It was not the goal of the present study, however, to define and categorize lesions whose classification could be argued as being neoplastic, non-neoplastic or preneoplastic.

Due to this lack of uniform classification of lesions, it was decided to present a series of tables separating specific diagnoses by study group. This would allow the readers to interpret the data according to their needs. Organ specific lesions summarized in this manner include proliferative lesions of the lymphoreticular system, lung, liver, testicles, uterus, urinary bladder (female only), pituitary gland, and adrenal glands. In addition, an expanded table showing the distribution of mesotheliomas in all studies is only presented for the males, since none were diagnosed in the females in any study. The mesotheliomas reported in the body cavity (Table 8) were either observed at necropsy or found upon microscopic examination of the viscera. These data were not included in the summary table because an accurate sample size could not be calculated.

#### IV. SYNONYMOUS TERMS

In general, the diagnoses included in Tables 1 and 9 were the terms also used in the 13 studies in the data base. However, synonymous diagnoses were occasionally encountered in different sets of data. In such cases, the preferred diagnostic term listed in Tables 1 and 9 was substituted for the original term used in the studies. The following table lists these preferred diagnoses that were used in formulating Tables 1 and 9. This tabulated glossary of terms lists the preferred diagnosis under each tissue/organ followed by its synonyms. For example, in the lymphoreticular system, large granular lymphocyte leukemia was the preferred diagnosis used in Tables 1 and 9, but the synonymous diagnoses reported in some of the control data included mononuclear cell leukemia and myelomonocytic leukemia. The number of tumors reported in Tables 1 and 9 included all those listed as either the preferred diagnoses or synonymous diagnoses in all 13 studies. In cases where many diagnoses were used to describe a single lesion/tumor, the information was presented in expanded tables in which each diagnosis is separated by study group (see previous explanation).

The following is a listing of preferred and synonymous diagnoses:

#### GLOSSARY OF SYNONYMS

##### **Lymphoreticular System:**

LARGE GRANULAR LYMPHOCYTE LEUKEMIA = mononuclear cell leukemia;  
myelomonocytic leukemia

HISTIOCYTIC SARCOMA = reticulum cell sarcoma

##### **Mammary Gland:**

CARCINOMA = adenocarcinoma; adenocarcinoma, acini

FIBROADENOMA = adenoma/adenofibroma/fibroma; acinar fibroadenoma; fibroadenoma, acini

ADENOMA = acinar cell adenoma; adenoma, acini

##### **Bone:**

OSTEOSARCOMA = osteogenic sarcoma

##### **Lung:**

BRONCHIOLAR/ALVEOLAR HYPERPLASIA = adenomatous/alveolar cell hyperplasia

BRONCHIOLAR/ALVEOLAR ADENOMA = alveolar adenoma; adenoma  
(not otherwise specified)

BRONCHIOLAR/ALVEOLAR CARCINOMA = carcinoma (not otherwise specified)

## GLOSSARY OF SYNONYMS

### **Stomach:**

SQUAMOUS PAPILLOMA, NONGLANDULAR MUCOSA = papilloma (nonglandular area)

### **Pancreas (Endocrine):**

ISLET CELL CARCINOMA = islet cell adenocarcinoma

### **Pancreas (Exocrine):**

ACINAR CELL CARCINOMA = carcinoma; adenocarcinoma

### **Kidney:**

RENAL CELL ADENOMA = tubular cell adenoma; renal tubular cell adenoma; adenoma  
(not otherwise specified)

RENAL CELL CARCINOMA = tubular cell carcinoma; renal adenocarcinoma; carcinoma  
(not otherwise specified)

### **Testis:**

INTERSTITIAL (LEYDIG) CELL TUMOR (Benign) = Leydig cell tumor (benign); interstitial cell  
tumor (benign)

INTERSTITIAL (LEYDIG) CELL TUMOR (Not Otherwise Specified) = interstitial cell tumor  
(not otherwise specified)

MESOTHELIOMA (Malignant) = mesothelioma, tunic (malignant);  
mesothelioma, capsule (malignant)

### **Uterus:**

PAPILLARY ADENOMA = adenomatous polyp

ENDOMETRIAL STROMAL SARCOMA = stromal cell sarcoma

ADENOCARCINOMA (Not Otherwise Specified) = carcinoma (not otherwise specified)

### **Ovary:**

GRANULOSA/THECA CELL TUMOR (Not Otherwise Specified) = thecoma

### **Pituitary Gland:**

ADENOMA, PARS DISTALIS = adenoma, anterior (pars distalis)

CARCINOMA, PARS DISTALIS = carcinoma, anterior (pars distalis);  
adenocarcinoma, anterior (pars distalis)

### **Thyroid Gland:**

FOLLICULAR CELL CARCINOMA = follicular carcinoma/adenocarcinoma

C-CELL ADENOMA = clear cell adenoma; parafollicular cell adenoma

MEDULLARY CARCINOMA = parafollicular cell adenocarcinoma; parafollicular cell carcinoma;  
C-cell carcinoma; clear cell carcinoma

### **Adrenal Gland:**

CORTICAL ADENOCARCINOMA = cortical carcinoma

PHEOCHROMOCYTOMA (Malignant) = medullary carcinoma

## KEY TO ABBREVIATIONS

The following abbreviations are used in conjunction with many of the tables:

|     |   |
|-----|---|
| NOS | Not otherwise specified                         |
| M   | Malignant                                       |
| B   | Benign  |
| +   | Number of animals examined                      |
| *   | Listed with neoplastic lesions in some studies. |

**TABLE 1 (SUMMARY)**  
**CDF° (F-344)/CrIBR RATS - 24 MONTHS**  
**SPONTANEOUS NEOPLASTIC LESIONS**  
**MALE**

| LOCATION & LESION                    | # TISSUES<br>EXAM. | # LESIONS  | PERCENT | RANGE  |
|--------------------------------------|--------------------|------------|---------|--------|
| <b>HEMATOPOIETIC SYSTEM</b>          |                    |            |         |        |
| LYMPH NODES                          | 921                |            |         |        |
| THYMUS                               | 858                |            |         |        |
| thymoma                              |                    | 1          | 0.1     | 0- 2.8 |
| SPLEEN                               | 954                |            |         |        |
| hemangioma                           |                    | 1          | 0.1     | 0- 0.8 |
| hemangiosarcoma                      |                    | 3          | 0.3     | 0- 1.1 |
| fibrosarcoma                         |                    | 1          | 0.1     | 0- 1.4 |
| leiomyoma                            |                    | 1          | 0.1     | 0- 1.4 |
| BONE MARROW                          | 934                |            |         |        |
| LYMPHORETICULAR TUMORS               | + 846              |            |         |        |
| malignant lymphoma, lymphocytic      |                    | 16         | 1.9     | 0- 7.1 |
| lymphoid cell leukemia               |                    | 9          | 1.1     | 0-12.9 |
| lymphosarcoma/lymphoid cell leukemia |                    | 1          | 0.1     | 0- 1.4 |
| large granular lymphocyte leukemia   |                    | <b>140</b> | 16.5    | 0-31.3 |
| myelogenous leukemia                 |                    | 5          | 0.6     | 0- 4.0 |
| histiocytic sarcoma                  |                    | 5          | 0.6     | 0- 2.9 |
| histiocytoma (M)                     |                    | 1          | 0.1     | 0- 0.8 |
| fibrous histiocytoma (M)             |                    | 3          | 0.4     | 0- 2.8 |
| erythroid leukemia                   |                    | 1          | 0.1     | 0- 0.8 |
| lymphoreticular tumor (M)(NOS)       |                    | 1          | 0.1     | 0- 1.4 |
| <b>INTEGUMENTARY SYSTEM</b>          |                    |            |         |        |
| SKIN/SUBCUTIS                        | 948                |            |         |        |
| squamous cell papilloma              |                    | 7          | 0.7     | 0- 5.7 |
| papilloma (NOS)                      |                    | 3          | 0.3     | 0- 2.8 |
| squamous cell carcinoma              |                    | 2          | 0.2     | 0- 1.6 |
| basal cell adenoma                   |                    | 4          | 0.4     | 0- 2.9 |
| basal cell carcinoma, subcutis       |                    |            | 0.1     | 0- 0.8 |
| sebaceous adenoma                    |                    |            | 0.1     | 0- 1.7 |
| adnexal gland adenoma (NOS)          |                    | 1          | 0.1     | 0- 1.4 |
| trichoepithelioma                    |                    | 1          | 0.1     | 0- 1.4 |
| keratoacanthoma                      |                    | 11         | 1.2     | 0- 3.3 |
| preputial gland adenocarcinoma       |                    | 1          | 0.1     | 0- 1.4 |
| fibroma, skin                        |                    | 12         | 1.3     | 0- 6.7 |
| fibroma, subcutis                    |                    | 19         | 2.0     | 0-13.9 |
| fibrosarcoma, skin                   |                    | 5          | 0.5     | 0- 1.7 |
| fibrosarcoma, subcutis               |                    | 3          | 0.3     | 0- 2.8 |
| neurofibroma, subcutis               |                    |            | 0.1     | 0- 1.4 |
| lipoma, skin                         |                    | 1          | 0.1     | 0- 1.4 |
| lipoma, subcutis                     |                    | 3          | 0.3     | 0- 1.4 |
| hemangioma, subcutis                 |                    | 1          | 0.1     | 0- 1.4 |
| hemangiopericytoma (B)               |                    |            | 0.1     | 0- 1.7 |
| osteosarcoma                         |                    |            | 0.1     | 0- 1.3 |
| sarcoma, skin, undifferentiated      |                    | 2          | 0.2     | 0- 1.7 |
| sarcoma, subcutis, undifferentiated  |                    |            | 0.1     | 0- 1.4 |
| MAMMARY GLAND                        | 826                |            |         |        |
| adenoma                              |                    | 9          | 1.1     | 0- 8.3 |
| fibroadenoma                         |                    | 21         | 2.5     | 0- 5.8 |
| fibroma                              |                    | 19         | 2.3     | 0-10.8 |
| fibrosarcoma                         |                    | 1          | 0.1     | 0- 2.8 |
| myxosarcoma                          |                    | 1          | 0.1     | 0- 2.8 |
| <b>MUSCULOSKELETAL SYSTEM</b>        |                    |            |         |        |
| SKELETAL MUSCLE                      | 953                |            |         |        |
| fibrosarcoma                         |                    | 1          | 0.1     | 0- 1.4 |
| BONE                                 | 953                |            |         |        |
| osteosarcoma                         |                    | 3          | 0.3     | 0- 2.2 |
| odontogenic tumor (M)(NOS)           |                    | 1          | 0.1     | 0- 1.4 |
| <b>RESPIRATORY SYSTEM</b>            |                    |            |         |        |
| NASAL TURBINATES                     | 760                |            |         |        |
| papillary adenoma                    |                    | 1          | 0.1     | 0- 1.4 |
| TRACHEA                              | 832                |            |         |        |

**TABLE 1 (SUMMARY)**  
**CDF° (F-344)/CrIBR RATS - 24 MONTHS**  
**SPONTANEOUS NEOPLASTIC LESIONS**  
**MALE (Continued)**

| LOCATION & LESION                       | # TISSUES<br>EXAM. | # LESIONS | PERCENT | RANGE  |
|---|--------------------|-----------|---------|--------|
| LUNG                                    | 956                |           |         |        |
| * bronchiolar/alveolar hyperplasia      |                    | 4         | 0.4     | 0- 3.2 |
| bronchiolar/alveolar adenoma            |                    | 22        | 2.3     | 0- 6.7 |
| bronchiolar/alveolar carcinoma          |                    | 4         | 0.4     | 0- 2.2 |
| squamous cell carcinoma                 |                    | 1         | 0.1     | 0- 0.8 |
| <b>CIRCULATORY SYSTEM</b>               |                    |           |         |        |
| HEART                                   | 956                |           |         |        |
| AORTA                                   | 826                |           |         |        |
| <b>DIGESTIVE SYSTEM</b>                 |                    |           |         |        |
| SALIVARY GLAND                          | 940                |           |         |        |
| adenoma (NOS)                           |                    | 1         | 0.1     | 0- 1.4 |
| fibrosarcoma                            |                    | 1         | 0.1     | 0- 0.8 |
| sarcoma, undifferentiated               |                    | 1         | 0.1     | 0- 1.7 |
| ESOPHAGUS                               | 751                |           |         |        |
| STOMACH                                 | 944                |           |         |        |
| squamous papilloma, nonglandular mucosa |                    | 3         | 0.3     | 0- 1.7 |
| SMALL INTESTINE                         | 936                |           |         |        |
| adenoma (NOS)                           |                    | 2         | 0.2     | 0- 1.7 |
| adenocarcinoma (NOS)                    |                    | 2         | 0.2     | 0- 1.7 |
| leiomyoma                               |                    | 2         | 0.2     | 0- 3.3 |
| LARGE INTESTINE                         | 941                |           |         |        |
| adenoma (NOS)                           |                    | 2         | 0.2     | 0- 1.4 |
| polypoid adenoma                        |                    | 2         | 0.2     | 0- 1.7 |
| LIVER                                   | 956                |           |         |        |
| * hyperplastic nodule                   |                    | 4         | 0.4     | 0- 2.9 |
| neoplastic nodule                       |                    | 27        | 2.8     | 0-20.8 |
| hepatocellular adenoma                  |                    | 8         | 0.8     | 0- 4.3 |
| hepatocellular carcinoma                |                    | 6         | 0.6     | 0- 3.3 |
| PANCREAS (EXOCRINE)                     | 944                |           |         |        |
| acinar cell adenoma                     |                    | 3         | 0.3     | 0- 1.7 |
| acinar cell carcinoma                   |                    | 2         | 0.2     | 0- 6.7 |
| PANCREAS (ENDOCRINE)                    | 944                |           |         |        |
| islet cell adenoma                      |                    | 88        | 9.3     | 0-20.0 |
| islet cell carcinoma                    |                    | 6         | 0.6     | 0- 4.3 |
| <b>URINARY SYSTEM</b>                   |                    |           |         |        |
| KIDNEY                                  | 964                |           |         |        |
| renal cell adenoma                      |                    | 5         | 0.5     | 0- 3.3 |
| renal cell carcinoma                    |                    | 5         | 0.5     | 0- 2.8 |
| transitional cell carcinoma             |                    | 4         | 0.4     | 0- 2.9 |
| angioma (NOS)                           |                    |           | 0.1     | 0- 3.3 |
| sarcoma, undifferentiated               |                    |           | 0.1     | 0- 1.4 |
| URINARY BLADDER                         | 921                |           |         |        |
| papillary adenoma (NOS)                 |                    | 2         | 0.2     | 0- 2.9 |
| transitional cell carcinoma, urethra    |                    |           | 0.1     | 0- 1.4 |
| <b>REPRODUCTIVE SYSTEM</b>              |                    |           |         |        |
| TESTIS                                  | 946                |           |         |        |
| interstitial (Leydig) cell tumor (B)    |                    | 534       | 56.4    | 0-93.1 |
| interstitial (Leydig) cell tumor (NOS)  |                    | 207       | 21.9    | 0-86.2 |
| mesothelioma (M)                        |                    | 13        | 1.4     | 0- 7.1 |
| mesothelioma (NOS)                      |                    | 3         | 0.3     | 0- 1.6 |
| PROSTATE                                | 938                |           |         |        |
| adenoma (NOS)                           |                    | 3         | 0.3     | 0- 1.6 |
| <b>ENDOCRINE SYSTEM</b>                 |                    |           |         |        |
| PITUITARY GLAND                         | 901                |           |         |        |
| chromophobe adenoma                     |                    | 15        | 1.7     | 0-20.0 |
| adenoma, pars distalis                  |                    | 136       | 15.1    | 0-35.8 |
| adenoma, anterior lobe (NOS)            |                    | 8         | 0.9     | 0-13.3 |
| adenoma (NOS)                           |                    | 42        | 4.7     | 0-23.1 |
| adenoma with cellular atypia            |                    | 2         | 0.2     | 0- 1.9 |
| carcinoma, pars distalis                |                    | 11        | 1.2     | 0- 6.8 |
| carcinoma (NOS)                         |                    | 2         | 0.2     | 0- 2.6 |



**TABLE 1 (SUMMARY)**  
**CDF® (F-344)CrIBR RATS - 24 MONTHS**  
**SPONTANEOUS NEOPLASTIC LESIONS**  
**MALE (Continued)**

| LOCATION & LESION               | # TISSUES<br>EXAM. | k LESIONS | PERCENT | RANGE  |
|---------------------------------|--------------------|-----------|---------|--------|
| <b>THYROID GLAND</b>            | 945                |           |         |        |
| follicular cell adenoma         |                    | 21        | 2.2     | 0- 6.4 |
| follicular cell carcinoma       |                    | 6         | 0.6     | 0- 2.8 |
| C-cell adenoma                  |                    | 80        | 8.5     | 0-14.3 |
| medullary carcinoma             |                    | 18        | 1.9     | 0- 8.3 |
| <b>PARATHYROID GLAND</b>        | 750                |           |         |        |
| adenoma                         |                    | 8         | 1.1     | 0- 3.0 |
| <b>ADRENAL GLAND</b>            | 952                |           |         |        |
| cortical adenoma                |                    | 4         | 0.4     | 0- 4.3 |
| cortical adenocarcinoma         |                    | 1         | 0.1     | 0- 1.3 |
| pheochromocytoma (B)            |                    | 64        | 6.7     | 0-24.3 |
| pheochromocytoma (M)            |                    | 5         | 0.5     | 0- 2.2 |
| pheochromocytoma (NOS)          |                    | 4         | 0.4     | 0- 3.2 |
| <b>NERVOUS SYSTEM</b>           |                    |           |         |        |
| <b>BRAIN</b>                    | 954                |           |         |        |
| astrocytoma                     |                    | 7         | 0.7     | 0- 4.4 |
| papillary ependymoma            |                    | 1         | 0.1     | 0- 0.8 |
| glioma (NOS)                    |                    | 1         | 0.1     | 0- 0.8 |
| oligodendroglioma (M)           |                    | 2         | 0.2     | 0- 1.7 |
| granular cell tumor (B)         |                    | 2         | 0.2     | 0- 1.7 |
| <b>NERVES</b>                   | 833                |           |         |        |
| <b>SPECIAL SENSES</b>           |                    |           |         |        |
| <b>EYE</b>                      | 925                |           |         |        |
| blastoma, retina                |                    | 1         | 0.1     | 0- 0.9 |
| <b>HARDERIAN/LACRIMAL GLAND</b> | 380                |           |         |        |

**TABLE 2 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**LYMPHORETICULAR TUMORS**  
**MALE**

| <b>STUDY IDENTIFICATION</b>        | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| <b># ANIMALS EXAMINED</b>          | 72       | 72       | 126      | 70       | 126      | 70       | 80       | 90       | 70       | 70       |
| <b>LESION</b>                      |          |          |          |          |          |          |          |          |          |          |
| malignant lymphoma, lymphocytic    |          |          | 7        |          | 9        |          |          |          |          |          |
| %                                  |          |          | 5.6      |          | 7.1      |          |          |          |          |          |
| lymphoid cell leukemia             |          |          |          |          |          |          |          |          |          | 9        |
| %                                  |          |          |          |          |          |          |          |          |          | 12.9     |
| lymphosarcoma/lymphoid leukemia    |          | 1        |          |          |          |          |          |          |          |          |
| %                                  |          | 1.4      |          |          |          |          |          |          |          |          |
| large granular lymphocyte leukemia |          |          |          | 21       |          | 16       |          | 10       | 13       |          |
| %                                  |          |          |          | 30.0     |          | 22.9     |          | 11.1     | 18.6     |          |
| mononuclear cell leukemia          | 21       | 15       |          |          |          |          | 25       |          |          |          |
| %                                  | 29.2     | 20.8     |          |          |          |          | 31.3     |          |          |          |
| myelomonocytic leukemia            |          |          | 13       |          | 6        |          |          |          |          |          |
| %                                  |          |          | 10.3     |          | 4.8      |          |          |          |          |          |
| myelogenous leukemia               |          |          |          |          | 5        |          |          |          |          |          |
| %                                  |          |          |          |          | 4.0      |          |          |          |          |          |
| histiocytic sarcoma                |          | 1        |          |          |          |          | 1        |          | 2        |          |
| %                                  |          | 1.4      |          |          |          |          | 1.3      |          | 2.9      |          |
| reticulum cell sarcoma             | 1        |          |          |          |          |          |          |          |          |          |
| %                                  | 1.4      |          |          |          |          |          |          |          |          |          |
| histiocytoma (M)                   |          |          |          |          |          | 1        |          |          |          |          |
| %                                  |          |          |          |          |          | 0.8      |          |          |          |          |
| fibrous histiocytoma (M)           | 2        | 1        |          |          |          |          |          |          |          |          |
| %                                  | 2.8      | 1.4      |          |          |          |          |          |          |          |          |
| erythroid leukemia                 |          |          |          |          |          | 1        |          |          |          |          |
| %                                  |          |          |          |          |          | 0.8      |          |          |          |          |
| lymphoreticular tumor (M)(NOS)     |          | 1        |          |          |          |          |          |          |          |          |
| %                                  |          | 1.4      |          |          |          |          |          |          |          |          |

**TABLE 3 (EXPANDED)**  
**CDF® (F-344)/CrIBR RATS - 24 MONTHS**  
**PULMONARY MASSES**  
**MALE**

| <b>STUDY IDENTIFICATION</b>        | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| <b># TISSUES EXAMINED</b>          | 72       | 72       | 126      | 60       | 126      | 30       | 30       | 60       | 70       | 80       | 90       | 70       | 70       |
| <b>LESION</b>                      |          |          |          |          |          |          |          |          |          |          |          |          |          |
| * bronchiolar/alveolar hyperplasia |          |          | 4        |          |          |          |          |          |          |          |          |          |          |
| %                                  |          |          | 3.2      |          |          |          |          |          |          |          |          |          |          |
| alveolar adenoma                   |          |          | 4        |          |          |          |          |          | 3        |          | 5        |          |          |
| %                                  |          |          | 3.2      |          |          |          |          |          | 4.3      |          | 5.6      |          |          |
| bronchiolar/alveolar adenoma       |          |          |          |          |          |          |          | 2        |          | 1        | 1        |          |          |
| %                                  |          |          |          |          |          |          |          | 3.3      |          | 1.3      | 1.1      |          |          |
| adenoma (NOS)                      | 1        |          |          |          | 4        | 1        |          |          |          |          |          |          |          |
| %                                  | 1.4      |          |          |          | 3.2      | 3.3      |          |          |          |          |          |          |          |
| bronchiolar/alveolar carcinoma     |          |          | 1        |          | 1        |          |          |          |          |          |          |          |          |
| %                                  |          |          | 0.8      |          | 0.8      |          |          |          |          |          |          |          |          |
| carcinoma (NOS)                    |          |          |          |          |          |          |          |          |          |          |          | 2        |          |
| %                                  |          |          |          |          |          |          |          |          |          |          |          | 2.2      |          |
| squamous cell carcinoma            |          |          | 1        |          |          |          |          |          |          |          |          |          |          |
| %                                  |          |          | 0.8      |          |          |          |          |          |          |          |          |          |          |

**TABLE 4 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**HEPATIC MASSES**  
**MALE**

| STUDY IDENTIFICATION<br># TISSUES EXAMINED | A    | B   | C   | D   | E   | F   | G   | H   | I   | J   | K   | L   | M   |
|--|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| LESION                                     |      |     |     |     |     |     |     |     |     |     |     |     |     |
| * hyperplastic nodule                      |      |     |     |     |     |     |     |     |     |     | 2   | 2   |     |
| %  |      |     |     |     |     |     |     |     |     |     | 2.2 | 2.9 |     |
| neoplastic nodule                          | 15   |     | 6   |     | 1   |     |     |     |     | 1   |     |     | 4   |
| %  | 20.8 |     | 4.8 |     | 0.8 |     |     |     |     | 1.3 |     |     | 5.7 |
| hepatocellular adenoma                     |      |     |     | 2   |     |     | 1   | 1   | 3   |     |     | 1   |     |
| %  |      |     |     | 3.3 |     |     | 3.3 | 1.7 | 4.3 |     |     | 1.4 |     |
| hepatocellular carcinoma                   | 2    | 2   | 1   |     |     | 1   |     |     |     |     |     |     |     |
| %  | 2.8  | 2.8 | 0.8 |     |     | 3.3 |     |     |     |     |     |     |     |

**TABLE 5 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**TESTICULAR TUMORS**  
**MALE**

| STUDY IDENTIFICATION<br># TISSUES EXAMINED | A    | B    | C    | D    | E    | F    | G    | H    | I    | J    | K    | L    | M    |
|--|------|------|------|------|------|------|------|------|------|------|------|------|------|
| LESION                                     |      |      |      |      |      |      |      |      |      |      |      |      |      |
| Leydig cell tumor (B)                      |      |      |      | 51   |      |      |      |      | 46   | 11   | 67   | 52   | 49   |
| % <sub>70</sub>                            |      |      |      | 85.0 |      |      |      |      | 65.7 | 13.8 | 74.4 | 74.3 | 70.0 |
| interstitial cell tumor (B)                | 56   | 53   |      |      |      | 27   | 26   | 53   |      | 43   |      |      |      |
| % <sub>10</sub>                            | 78.9 | 73.6 |      |      |      | 93.1 | 86.7 | 88.3 |      | 53.8 |      |      |      |
| interstitial cell tumor (NOS)              |      |      | 101  |      | 106  |      |      |      |      |      |      |      |      |
| %  |      |      | 83.5 |      | 86.2 |      |      |      |      |      |      |      |      |
| mesothelioma (M)                           |      | 1    |      |      |      |      |      |      |      |      |      |      | 1    |
| %  |      | 1.4  |      |      |      |      |      |      |      |      |      |      | 1.4  |
| mesothelioma, tunic (M)                    |      |      |      |      |      |      |      |      | 5    |      | 4    | 1    |      |
| %  |      |      |      |      |      |      |      |      | 7.1  |      | 4.4  | 1.4  |      |
| mesothelioma, capsule (M)                  |      |      |      |      |      |      |      |      | 1    |      |      |      |      |
| %  |      |      |      |      |      |      |      |      | 1.4  |      |      |      |      |
| mesothelioma (NOS)                         | 1    |      |      |      | 2    |      |      |      |      |      |      |      |      |
| %  | 1.4  |      |      |      | 1.6  |      |      |      |      |      |      |      |      |

**TABLE 6 (EXPANDED)**  
**CDF® (F-344)1CrIBR RATS - 24 MONTHS**  
**PITUITARY GLAND TUMORS**  
**MALE**

| STUDY IDENTIFICATION<br># TISSUES EXAMINED | A    | B    | C    | D    | E    | F   | G    | H    | I    | J    | K    | L    | M    |
|--|------|------|------|------|------|-----|------|------|------|------|------|------|------|
| <b>LESION</b>                              |      |      |      |      |      |     |      |      |      |      |      |      |      |
| chromophobe adenoma                        | 1    | 14   |      |      |      |     |      |      |      |      |      |      |      |
| %  | 1.5  | 20.0 |      |      |      |     |      |      |      |      |      |      |      |
| adenoma, pars distalis                     | 24   |      |      | 17   |      |     |      |      | 14   | 17   | 24   | 24   | 16   |
| %  | 35.8 |      |      | 28.8 |      |     |      |      | 20.0 | 22.1 | 26.7 | 34.3 | 23.2 |
| adenoma, anterior lobe (NOS)               |      |      |      |      |      |     |      | 8    |      |      |      |      |      |
| %  |      |      |      |      |      |     |      | 13.3 |      |      |      |      |      |
| adenoma (NOS)                              |      |      | 18   |      | 16   | 2   | 6    |      |      |      |      |      |      |
| %  |      |      | 16.2 |      | 15.0 | 7.7 | 23.1 |      |      |      |      |      |      |
| adenoma with cellular atypia               |      |      |      |      | 2    |     |      |      |      |      |      |      |      |
| %  |      |      |      |      | 1.9  |     |      |      |      |      |      |      |      |
| carcinoma, pars distalis                   | 3    |      |      |      |      |     |      |      | 2    |      |      |      |      |
| %  | 4.5  |      |      |      |      |     |      |      | 2.9  |      |      |      |      |
| adenocarcinoma, pars distalis              |      |      |      | 4    |      |     |      |      |      |      | 1    | 1    |      |
| %  |      |      |      | 6.8  |      |     |      |      |      |      | 1.1  | 1.4  |      |
| carcinoma (NOS)                            |      |      |      |      |      |     |      |      |      | 2    |      |      |      |
| %  |      |      |      |      |      |     |      |      |      | 2.6  |      |      |      |

**TABLE 7 (EXPANDED)**  
**CDF® (F-344)1CrIBR RATS - 24 MONTHS**  
**ADRENAL GLAND TUMORS**  
**MALE**

| STUDY IDENTIFICATION<br># TISSUES EXAMINED | A    | B   | C | D    | E   | F | G | H   | I    | J   | K   | L   | M    |
|--|------|-----|---|------|-----|---|---|-----|------|-----|-----|-----|------|
| <b>LESION</b>                              |      |     |   |      |     |   |   |     |      |     |     |     |      |
| cortical adenoma                           | 3    |     |   |      |     |   |   |     |      | 1   |     |     |      |
| %  | 4.3  |     |   |      |     |   |   |     |      | 1.3 |     |     |      |
| cortical adenocarcinoma                    |      |     |   |      |     |   |   |     |      | 1   |     |     |      |
| %  |      |     |   |      |     |   |   |     |      | 1.3 |     |     |      |
| pheochromocytoma (B)                       | 17   | 2   |   | 6    | 7   |   |   | 2   | 8    | 6   | 4   | 5   | 7    |
| %  | 24.3 | 2.8 |   | 10.0 | 5.6 |   |   | 3.3 | 11.4 | 7.5 | 4.4 | 7.1 | 10.0 |
| pheochromocytoma (M)                       |      | 1   |   |      |     |   |   |     |      | 1   | 2   |     | 1    |
| %  |      | 1.4 |   |      |     |   |   |     |      | 1.3 | 2.2 |     | 1.4  |
| pheochromocytoma (NOS)                     |      |     |   | 4    |     |   |   |     |      |     |     |     |      |
| %  |      |     |   | 3.2  |     |   |   |     |      |     |     |     |      |

**TABLE 8 (EXPANDED)**  
**CDF° (F-344)ICrIBR RATS - 24 MONTHS**  
**MESOTHELIOMAS**  
**MALE**

| <b>STUDY IDENTIFICATION</b>         | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| <b># TISSUES EXAMINED</b>           | 71       | 72       | 121      | 60       | 123      | 29       | 30       | 60       | 70       | 80       | 90       | 70       | 70       |
| <b>LESION</b>                       |          |          |          |          |          |          |          |          |          |          |          |          |          |
| mesothelioma (M), testis            |          | 1        |          |          |          |          |          |          | 6        |          | 4        | 1        | 1        |
|                                     |          | 1.4      |          |          |          |          |          |          | 8.6      |          | 4.4      | 1.4      | 1.4      |
| mesothelioma (NOS), testis          | 1        |          |          |          | 2        |          |          |          |          |          |          |          |          |
| %a                                  | 1.4      |          |          |          | 1.6      |          |          |          |          |          |          |          |          |
| <b># ANIMALS EXAMINED</b>           | 72       | 72       | 126      |          | 126      |          |          |          | 70       | 80       | 90       | 70       | 70       |
| mesothelioma (M), multiple organs   |          |          |          |          |          |          |          |          |          | 2        |          |          |          |
| %o                                  |          |          |          |          |          |          |          |          |          | 2.5      |          |          |          |
| mesothelioma (NOS), multiple organs |          |          | 2        |          |          |          |          |          |          |          |          |          |          |
|                                     |          |          | 1.6      |          |          |          |          |          |          |          |          |          |          |
| mesothelioma (M), peritoneal cavity | 1        |          |          |          |          |          |          |          |          |          |          |          |          |
| %                                   | 1.4      |          |          |          |          |          |          |          |          |          |          |          |          |

— = Accurate sample size could not be determined in some studies.

**TABLE 9 (SUMMARY)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**SPONTANEOUS NEOPLASTIC LESIONS**  
**FEMALE**

| LOCATION & LESION                       | # TISSUES<br>EXAM. | <sup>a</sup> LESIONS | PERCENT | RANGE  |
|---|--------------------|----------------------|---------|--------|
| <b>HEMATOPOIETIC SYSTEM</b>             |                    |                      |         |        |
| LYMPH NODES                             | 905                |                      |         |        |
| THYMUS                                  | 863                |                      |         |        |
| thymoma                                 |                    | 1                    | 0.1     | 0- 3.3 |
| adenoma (NOS)                           |                    | 1                    | 0.1     | 0- 1.2 |
| ultimobranhial cyst carcinoma           |                    | 1                    | 0.1     | 0- 0.9 |
| SPLEEN                                  | 951                |                      |         |        |
| angioma (NOS)                           |                    | 1                    | 0.1     | 0- 3.3 |
| BONE MARROW                             | 924                |                      |         |        |
| LYMPHORETICULAR TUMORS                  | + 846              |                      |         |        |
| malignant lymphoma, lymphocytic         |                    | 6                    | 0.7     | 0- 2.4 |
| lymphoid cell leukemia                  |                    | 11                   | 1.3     | 0-15.7 |
| lymphosarcoma                           |                    | 2                    | 0.2     | 0- 0.8 |
| large granular lymphocyte leukemia      |                    | 88                   | 10.4    | 0-26.4 |
| histiocytic sarcoma                     |                    | 1                    | 0.1     | 0- 1.4 |
| <b>INTEGUMENTARY SYSTEM</b>             |                    |                      |         |        |
| SKIN/SUBCUTIS                           | 946                |                      |         |        |
| squamous cell papilloma                 |                    | 1                    | 0.1     | 0- 1.1 |
| papilloma (NOS)                         |                    | 4                    | 0.4     | 0- 3.3 |
| squamous cell carcinoma                 |                    | 2                    | 0.2     | 0- 1.4 |
| basal cell adenoma                      |                    | 1                    | 0.1     | 0- 1.1 |
| sebaceous adenoma                       |                    | 1                    | 0.1     | 0- 1.7 |
| keratoacanthoma                         |                    | 3                    | 0.3     | 0- 3.3 |
| calcifying epithelioma                  |                    | 1                    | 0.1     | 0- 1.4 |
| fibroma, skin                           |                    | 4                    | 0.4     | 0- 1.7 |
| fibroma, subcutis                       |                    | 7                    | 0.8     | 0- 5.0 |
| fibrosarcoma                            |                    | 2                    | 0.2     | 0- 1.7 |
| fibrous histiocytoma (NOS), skin        |                    | 1                    | 0.1     | 0- 1.4 |
| fibrous histiocytoma (NOS), subcutis    |                    | 1                    | 0.1     | 0- 1.4 |
| lipoma                                  |                    | 1                    | 0.1     | 0- 3.3 |
| myxosarcoma, subcutis                   |                    | 1                    | 0.1     | 0- 1.3 |
| sarcoma, undifferentiated               |                    | 1                    | 0.1     | 0- 1.4 |
| MAMMARY GLAND                           | 915                |                      |         |        |
| adenoma                                 |                    | 12                   | 1.3     | 0- 6.7 |
| cystadenoma                             |                    | 1                    | 0.1     | 0- 0.8 |
| carcinoma                               |                    | 14                   | 1.5     | 0- 4.3 |
| squamous cell carcinoma                 |                    | 1                    | 0.1     | 0- 0.8 |
| squamous cell carcinoma, teat           |                    | 1                    | 0.1     | 0- 1.4 |
| fibroadenoma                            |                    | 110                  | 12.0    | 0-32.7 |
| fibroma                                 |                    | 2                    | 0.2     | 0- 1.4 |
| <b>MUSCULOSKELETAL SYSTEM</b>           |                    |                      |         |        |
| SKELETAL MUSCLE                         | 951                |                      |         |        |
| fibrosarcoma                            |                    | 1                    | 0.1     | 0- 3.3 |
| BONE                                    | 947                |                      |         |        |
| <b>RESPIRATORY SYSTEM</b>               |                    |                      |         |        |
| NASAL TURBINATES                        | 757                |                      |         |        |
| TRACHEA                                 | 828                |                      |         |        |
| LUNG                                    | 953                |                      |         |        |
| * bronchiolar/alveolar hyperplasia      |                    | 1                    | 0.1     | 0- 0.8 |
| bronchiolar/alveolar adenoma            |                    | 3                    | 0.3     | 0- 1.7 |
| <b>CIRCULATORY SYSTEM</b>               |                    |                      |         |        |
| HEART                                   | 954                |                      |         |        |
| fibroma                                 |                    | 1                    | 0.1     | 0- 0.8 |
| AORTA                                   | 830                |                      |         |        |
| <b>DIGESTIVE SYSTEM</b>                 |                    |                      |         |        |
| SALIVARY GLAND                          | 936                |                      |         |        |
| ESOPHAGUS                               | 753                |                      |         |        |
| STOMACH                                 | 939                |                      |         |        |
| squamous papilloma, nonglandular mucosa |                    | 2                    | 0.2     | 0- 1.4 |
| SMALL INTESTINE                         | 938                |                      |         |        |
| LARGE INTESTINE                         | 934                |                      |         |        |
| LIVER                                   | 954                |                      |         |        |
| neoplastic nodule                       |                    | 22                   | 2.3     | 0-23.6 |
| hepatocellular adenoma                  |                    | 8                    | 0.8     | 0- 3.3 |
| hepatocellular carcinoma                |                    | 2                    | 0.2     | 0- 1.3 |

**TABLE 9 (SUMMARY)**  
**CDF° (F-344)1CrIBR RATS - 24 MONTHS**  
**SPONTANEOUS NEOPLASTIC LESIONS**  
**FEMALE (Continued)**

| LOCATION & LESION                | # TISSUES<br>EXAM. | N LESIONS | PERCENT | RANGE  |
|----------------------------------|--------------------|-----------|---------|--------|
| <b>PANCREAS (EXOCRINE)</b>       | 947                |           |         |        |
| acinar cell carcinoma            |                    | 1         | 0.1     | 0- 1.4 |
| squamous cell carcinoma          |                    | 1         | 0.1     | 0- 1.7 |
| <b>PANCREAS (ENDOCRINE)</b>      | 947                |           |         |        |
| islet cell adenoma               |                    | 19        | 2.0     | 0- 6.7 |
| <b>URINARY SYSTEM</b>            |                    |           |         |        |
| <b>KIDNEY</b>                    | 964                |           |         |        |
| renal cell adenoma               |                    | 1         | 0.1     | 0- 0.8 |
| nephroblastoma                   |                    | 1         | 0.1     | 0- 1.4 |
| liposarcoma                      |                    | 1         | 0.1     | 0- 1.4 |
| <b>URINARY BLADDER</b>           | 909                |           |         |        |
| transitional cell papilloma      |                    | 1         | 0.1     | 0- 0.8 |
| transitional cell adenoma        |                    | 1         | 0.1     | 0- 0.8 |
| papillary adenoma (NOS)          |                    | 1         | 0.1     | 0- 1.4 |
| carcinoma (NOS)                  |                    | 1         | 0.1     | 0- 1.4 |
| leiomyoma                        |                    | 1         | 0.1     | 0- 1.8 |
| <b>REPRODUCTIVE SYSTEM</b>       |                    |           |         |        |
| <b>UTERUS</b>                    | 950                |           |         |        |
| endometrial stromal polyp        |                    | 136       | 14.3    | 0-41.7 |
| polyp (NOS)                      |                    | 4         | 0.4     | 0-13.3 |
| papillary adenoma                |                    | 20        | 2.1     | 0-26.4 |
| adenoma (NOS)                    |                    | 19        | 2.0     | 0- 5.6 |
| endometrial adenoma              |                    | 2         | 0.2     | 0- 3.3 |
| polypoid fibroma                 |                    | 1         | 0.1     | 0- 0.8 |
| carcinomatous polyp              |                    | 1         | 0.1     | 0- 1.4 |
| adenocarcinoma (NOS)             |                    | 79        | 8.3     | 0-36.0 |
| fibroma                          |                    | 1         | 0.1     | 0- 1.4 |
| endometrial stromal sarcoma      |                    | 9         | 0.9     | 0- 7.1 |
| leiomyoma                        |                    | 5         | 0.5     | 0- 3.2 |
| leiomyosarcoma                   |                    | 7         | 0.7     | 0- 1.7 |
| <b>OVARY</b>                     | 937                |           |         |        |
| granulosa/theca cell tumor (NOS) |                    | 6         | 0.6     | 0- 4.3 |
| granulosa cell tumor (B)         |                    | 2         | 0.2     | 0- 3.3 |
| <b>ENDOCRINE SYSTEM</b>          |                    |           |         |        |
| <b>PITUITARY GLAND</b>           | 878                |           |         |        |
| chromophobe adenoma              |                    | 24        | 2.7     | 0-32.4 |
| adenoma, pars distalis           |                    | 153       | 17.4    | 0-51.4 |
| adenoma (NOS)                    |                    | 78        | 8.9     | 0-35.0 |
| chromophobe carcinoma            |                    | 1         | 0.1     | 0- 1.1 |
| carcinoma, pars distalis         |                    | 20        | 2.3     | 0-10.2 |
| carcinoma (NOS)                  |                    | 3         | 0.3     | 0- 2.6 |
| <b>THYROID GLAND</b>             | 936                |           |         |        |
| adenoma (NOS)                    |                    |           | 0.1     | 0- 3.4 |
| follicular cell adenoma          |                    | 12        | 1.3     | 0- 4.3 |
| follicular cell carcinoma        |                    | 5         | 0.5     | 0- 1.4 |
| C-cell adenoma                   |                    | 49        | 5.2     | 0-13.3 |
| medullary carcinoma              |                    | 8         | 0.9     | 0- 4.2 |
| <b>PARATHYROID GLAND</b>         | 643                |           |         |        |
| adenoma                          |                    | 3         | 0.2     | 0- 1.7 |
| <b>ADRENAL GLAND</b>             | 954                |           |         |        |
| cortical adenoma                 |                    | 10        | 1.0     | 0- 4.2 |
| cortical adenocarcinoma          |                    | 3         | 0.3     | 0- 1.7 |
| pheochromocytoma (B)             |                    | 9         | 0.9     | 0- 4.2 |
| pheochromocytoma (M)             |                    | 3         | 0.3     | 0- 1.7 |
| pheochromocytoma (NOS)           |                    | 2         | 0.2     | 0- 0.8 |
| <b>NERVOUS SYSTEM</b>            |                    |           |         |        |
| <b>BRAIN</b>                     | 954                |           |         |        |
| astrocytoma                      |                    | 5         | 0.5     | 0- 2.9 |
| oligodendroglioma                |                    | 1         | 0.1     | 0- 1.7 |
| glioma (NOS)                     |                    | 1         | 0.1     | 0- 0.8 |
| <b>NERVES</b>                    | 829                |           |         |        |
| <b>SPECIAL SENSES</b>            |                    |           |         |        |
| <b>EYE</b>                       | 915                |           |         |        |
| <b>HARDERIAN/LACRIMAL GLAND</b>  | 379                |           |         |        |

**TABLE 10 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**LYMPHORETICULAR TUMORS**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b>        | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| # ANIMALS EXAMINED                 | 72       | 72       | 126      | 70       | 126      | 70       | 80       | 90       | 70       | 70       |
| <b>LESION</b>                      |          |          |          |          |          |          |          |          |          |          |
| malignant lymphoma, lymphocytic    |          |          | 3        |          | 3        |          |          |          |          |          |
| %                                  |          |          | 2.4      |          | 2.4      |          |          |          |          |          |
| lymphoid cell leukemia             |          |          |          |          |          |          |          |          |          | 11       |
| %                                  |          |          |          |          |          |          |          |          |          | 15.7     |
| lymphosarcoma                      |          |          | 1        |          | 1        |          |          |          |          |          |
| %                                  |          |          | 0.8      |          | 0.8      |          |          |          |          |          |
| large granular lymphocyte leukemia |          |          |          | 8        |          | 7        |          | 12       | 6        |          |
| %                                  |          |          |          | 11.4     |          | 10.0     |          | 13.3     | 8.6      |          |
| mononuclear cell leukemia          | 19       | 8        |          |          |          |          |          | 18       |          |          |
| %                                  | 26.4     | 11.1     |          |          |          |          |          | 22.5     |          |          |
| myelomonocytic leukemia            |          |          | 6        |          | 4        |          |          |          |          |          |
| %                                  |          |          | 4.8      |          | 3.2      |          |          |          |          |          |
| histiocytic sarcoma                |          |          |          |          |          |          |          |          |          | 1        |
| %                                  |          |          |          |          |          |          |          |          |          | 1.4      |

**TABLE 11 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**PULMONARY MASSES**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b>        | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| # TISSUES EXAMINED                 | 72       | 72       | 125      | 60       | 125      | 30       | 30       | 60       | 70       | 80       | 90       | 69       | 70       |
| <b>LESION</b>                      |          |          |          |          |          |          |          |          |          |          |          |          |          |
| * bronchiolar/alveolar hyperplasia |          |          | 1        |          |          |          |          |          |          |          |          |          |          |
| %                                  |          |          | 0.8      |          |          |          |          |          |          |          |          |          |          |
| alveolar adenoma                   |          |          |          | 1        |          |          |          |          |          |          | 1        |          |          |
| %                                  |          |          |          | 0.8      |          |          |          |          |          |          | 1.1      |          |          |
| bronchiolar/alveolar adenoma       |          |          |          |          |          |          |          | 1        |          |          |          |          |          |
| %                                  |          |          |          |          |          |          |          | 1.7      |          |          |          |          |          |

**TABLE 12 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**HEPATIC MASSES**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b> | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| # TISSUES EXAMINED          | 72       | 72       | 126      | 60       | 125      | 30       | 30       | 60       | 70       | 80       | 90       | 69       | 70       |
| <b>LESION</b>               |          |          |          |          |          |          |          |          |          |          |          |          |          |
| neoplastic nodule           | 17       | 1        |          |          | 1        |          |          |          |          | 1        |          |          | 2        |
| %                           | 23.6     | 1.4      |          |          | 0.8      |          |          |          |          | 1.3      |          |          | 2.9      |
| hepatocellular adenoma      |          |          | 3        |          | 1        | 1        |          |          | 1        |          |          |          | 2        |
| %                           |          |          | 2.4      |          | 0.8      | 3.3      |          |          | 1.4      |          |          |          | 2.9      |
| hepatocellular carcinoma    |          |          |          |          | 1        |          |          |          |          | 1        |          |          |          |
| %                           |          |          |          |          | 0.8      |          |          |          |          | 1.3      |          |          |          |



**TABLE 13 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**URINARY BLADDER TUMORS**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b> | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| <b>4 TISSUES EXAMINED</b>   | 68       | 72       | 105      | 60       | 119      | 28       | 28       | 57       | 70       | 76       | 90       | 69       | 67       |
| <b>LESION</b>               |          |          |          |          |          |          |          |          |          |          |          |          |          |
| transitional cell papilloma |          |          |          |          |          |          |          |          |          |          |          |          |          |
| %                           |          |          |          |          | 0.8      |          |          |          |          |          |          |          |          |
| transitional cell adenoma   |          |          |          |          |          |          |          |          |          |          |          |          |          |
| %                           |          |          |          |          | 0.8      |          |          |          |          |          |          |          |          |
| papillary adenoma (NOS)     |          |          |          |          |          |          |          |          |          |          |          |          |          |
| carcinoma (NOS)             |          |          |          |          |          |          |          |          |          |          |          |          |          |
| leiomyoma                   |          |          |          |          |          |          |          |          |          |          |          |          |          |
| %                           |          |          |          |          |          |          |          |          |          |          |          |          |          |

**TABLE 14 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**UTERINE TUMORS**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b> | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| <b>4 TISSUES EXAMINED</b>   | 71       | 72       | 125      | 60       | 124      | 30       | 30       | 60       | 70       | 79       | 90       | 69       | 70       |
| <b>LESION</b>               |          |          |          |          |          |          |          |          |          |          |          |          |          |
| endometrial stromal polyp   |          |          |          | 25       |          |          |          | 6        | 17       | 19       | 25       | 21       | 23       |
| <sub>0</sub> <sub>10</sub>  |          |          |          | 41.7     |          |          |          | 10.0     | 24.3     | 24.1     | 27.8     | 30.4     | 32.9     |
| polyp (NOS)                 |          |          |          |          |          |          | 4        |          |          |          |          |          |          |
| %                           |          |          |          |          |          |          | 13.3     |          |          |          |          |          |          |
| papillary adenoma           | 1        | 19       |          |          |          |          |          |          |          |          |          |          |          |
| <sub>0</sub> <sub>10</sub>  | 1.4      | 26.4     |          |          |          |          |          |          |          |          |          |          |          |
| adenoma (NOS)               |          |          | 5        |          | 7        |          |          |          |          |          | 5        | 1        | 1        |
| %                           |          |          | 4.0      |          | 5.6      |          |          |          |          |          | 5.6      | 1.4      | 1.4      |
| endometrial adenoma         |          |          |          |          |          |          |          | 2        |          |          |          |          |          |
| %                           |          |          |          |          |          |          |          | 3.3      |          |          |          |          |          |
| polypoid fibroma            |          |          | 1        |          |          |          |          |          |          |          |          |          |          |
| %                           |          |          | 0.8      |          |          |          |          |          |          |          |          |          |          |
| carcinomatous polyp         | 1        |          |          |          |          |          |          |          |          |          |          |          |          |
| %                           | 1.4      |          |          |          |          |          |          |          |          |          |          |          |          |
| adenocarcinoma (NOS)        | 1        | 2        | 45       |          | 29       |          |          |          |          |          | 1        |          |          |
| %                           | 1.4      | 2.8      | 36.0     |          | 23.4     |          |          |          |          |          | 1.1      |          |          |
| carcinoma (NOS)             |          |          |          |          |          |          |          |          |          |          |          |          | 1        |
| %                           |          |          |          |          |          |          |          |          |          |          |          |          | 1.4      |
| fibroma                     | 1        |          |          |          |          |          |          |          |          |          |          |          |          |
| %                           | 1.4      |          |          |          |          |          |          |          |          |          |          |          |          |
| endometrial stromal sarcoma | 1        |          |          |          |          |          |          |          | 1        |          | 1        | 1        | 5        |
| %                           | 1.4      |          |          |          |          |          |          |          | 1.4      |          | 1.1      | 1.4      | 7.1      |
| leiomyoma                   |          |          |          |          | 4        |          |          | 1        |          |          |          |          |          |
| %                           |          |          |          |          | 3.2      |          |          | 1.7      |          |          |          |          |          |
| leiomyosarcoma              |          | 1        |          | 1        | 2        |          |          | 1        |          | 1        |          | 1        |          |
| %                           |          | 1.4      |          | 1.7      | 1.6      |          |          | 1.7      |          | 1.3      |          | 1.4      |          |

**TABLE 15 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**PITUITARY GLAND TUMORS**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b>   | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| # TISSUES EXAMINED            | 70       | 71       | 95       | 59       | 93       | 29       | 30       | 60       | 68       | 78       | 89       | 68       | 68       |
| <b>LESION</b>                 |          |          |          |          |          |          |          |          |          |          |          |          |          |
| chromophobe adenoma           | 1        | 23       |          |          |          |          |          |          |          |          |          |          |          |
| %                             | 1.4      | 32.4     |          |          |          |          |          |          |          |          |          |          |          |
| adenoma, pars distalis        | 36       |          |          | 21       |          |          |          |          | 26       |          | 27       | 23       | 20       |
| %                             | 51.4     |          |          | 35.6     |          |          |          |          | 37.1     |          | 30.0     | 33.8     | 29.4     |
| adenoma (NOS)                 |          |          | 12       |          | 7        | 6        | 8        | 21       |          | 24       |          |          |          |
| %                             |          |          | 12.6     |          | 7.5      | 20.7     | 26.7     | 35.0     |          | 30.8     |          |          |          |
| chromophobe carcinoma         |          |          |          |          | 1        |          |          |          |          |          |          |          |          |
| %                             |          |          |          |          | 1.1      |          |          |          |          |          |          |          |          |
| carcinoma, pars distalis      | 2        |          |          |          |          |          |          |          | 1        |          |          |          | 2        |
| %                             | 2.9      |          |          |          |          |          |          |          | 1.4      |          |          |          | 2.9      |
| adenocarcinoma, pars distalis |          |          |          | 6        |          |          |          |          |          |          | 7        | 2        |          |
| %                             |          |          |          | 10.2     |          |          |          |          |          |          | 7.8      | 2.9      |          |
| carcinoma (NOS)               |          |          |          |          | 1        |          |          |          |          | 2        |          |          |          |
| %                             |          |          |          |          | 1.1      |          |          |          |          | 2.6      |          |          |          |

**TABLE 16 (EXPANDED)**  
**CDF® (F-344)ICrIBR RATS - 24 MONTHS**  
**ADRENAL GLAND TUMORS**  
**FEMALE**

| <b>STUDY IDENTIFICATION</b> | <b>A</b> | <b>B</b> | <b>C</b> | <b>D</b> | <b>E</b> | <b>F</b> | <b>G</b> | <b>H</b> | <b>I</b> | <b>J</b> | <b>K</b> | <b>L</b> | <b>M</b> |
|-----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| # TISSUES EXAMINED          | 72       | 72       | 126      | 60       | 126      | 30       | 30       | 60       | 70       | 79       | 90       | 69       | 70       |
| <b>LESION</b>               |          |          |          |          |          |          |          |          |          |          |          |          |          |
| cortical adenoma            | 3        |          | 1        | 1        | 3        |          |          |          | 1        |          |          |          | 1        |
| %                           | 4.2      |          | 0.8      | 1.7      | 2.4      |          |          |          | 1.4      |          |          |          | 1.4      |
| cortical adenocarcinoma     | 1        |          |          | 1        |          |          |          |          | 1        |          |          |          |          |
| %                           | 1.4      |          |          | 1.7      |          |          |          |          | 1.4      |          |          |          |          |
| pheochromocytoma (B)        | 3        | 1        |          | 1        |          |          |          | 1        |          | 1        | 1        | 1        |          |
| %                           | 4.2      | 1.4      |          | 1.7      |          |          |          | 1.7      |          | 1.3      | 1.1      | 1.4      |          |
| pheochromocytoma (M)        | 1        |          |          | 1        |          |          |          |          |          | 1        |          |          |          |
| %                           | 1.4      |          |          | 1.7      |          |          |          |          |          | 1.3      |          |          |          |
| pheochromocytoma (NOS)      |          |          | 1        |          | 1        |          |          |          |          |          |          |          |          |
| %                           |          |          | 0.8      |          | 0.8      |          |          |          |          |          |          |          |          |