

**Experiment Number:** 99920-93  
**Test Type:** SPECIAL STUDY  
**Route:** DOSED FEED  
**Species/Strain:** Rat/CD

**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS  
ABRIDGED) (a)**

**Test Compound:** ENDOCRINE DISRUPTOR(Ethinyl Estradiol)  
**CAS Number:** 57-63-6

**Date Report Requested:** 10/23/2014  
**Time Report Requested:** 11:55:22  
**First Dose M/F:** NA / NA  
**Lab:** NCTR

**C Number:** MG96006  
**Lock Date:** 12/02/2008  
**Cage Range:** All  
**Date Range:** All  
**Reasons For Removal:** All  
**Removal Date Range:** All  
**Treatment Groups:** All  
**Study Gender:** Both  
**PWG Approval Date** NONE

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 Test Type: SPECIAL STUDY  
 Route: DOSED FEED  
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**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)**

Test Compound: ENDOCRINE DISRUPTOR(Ethinyl Estradiol)  
 CAS Number: 57-63-6

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 First Dose M/F: NA / NA  
 Lab: NCTR

CD Rat MALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPB TO CTL	F3/50PPB TO CTL
<b>Disposition Summary</b>					
Animals Initially In Study	50		49	50	50
Early Deaths					
Moribund Sacrifice	13		16	13	12
Natural Death	7		6	6	3
Survivors					
Terminal Sacrifice	30		27	31	35
Animals Examined Microscopically	50		49	50	50

ALIMENTARY SYSTEM

Esophagus	(50)		(48)	(50)	(50)
Intestine Large, Cecum	(45)		(43)	(47)	(47)
Intestine Large, Colon	(45)		(43)	(48)	(48)
Adenoma	2 (4%)			1 (2%)	
Intestine Large, Rectum	(45)		(44)	(48)	(48)
Anus, Sarcoma				1 (2%)	
Intestine Small, Duodenum	(44)		(43)	(47)	(47)
Adenocarcinoma	2 (5%)				
Intestine Small, Ileum	(44)		(38)	(47)	(47)
Intestine Small, Jejunum	(44)		(41)	(45)	(46)
Liver	(49)		(47)	(50)	(49)
Cholangiocarcinoma	2 (4%)				
Cholangioma	1 (2%)			1 (2%)	
Hepatocellular Adenoma	1 (2%)				1 (2%)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Mesentery	(4)		(0)	(6)	(3)
Squamous Cell Carcinoma, Metastatic, Uncertain Primary Site				1 (17%)	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors

\* Number of animals with any tissue examined microscopically

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CD Rat MALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPB TO CTL	F3/50PPB TO CTL
Oral Mucosa	(3)		(8)	(4)	(6)
Squamous Cell Carcinoma	3 (100%)		4 (50%)	1 (25%)	5 (83%)
Pancreas	(47)		(48)	(49)	(49)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Salivary Glands	(48)		(49)	(49)	(50)
Stomach, Forestomach	(46)		(48)	(49)	(49)
Squamous Cell Carcinoma			1 (2%)		
Stomach, Glandular	(45)		(46)	(47)	(47)
<b>CARDIOVASCULAR SYSTEM</b>					
Blood Vessel	(50)		(49)	(50)	(50)
Heart	(50)		(49)	(50)	(50)
Endocardium, Schwannoma Malignant			1 (2%)		
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
<b>ENDOCRINE SYSTEM</b>					
Adrenal Cortex	(49)		(49)	(49)	(50)
Adenoma	1 (2%)		1 (2%)	1 (2%)	
Adrenal Medulla	(49)		(48)	(49)	(50)
Bilateral, Pheochromocytoma Benign				1 (2%)	
Pheochromocytoma Benign	4 (8%)		4 (8%)	5 (10%)	1 (2%)
Pheochromocytoma Malignant	1 (2%)			2 (4%)	1 (2%)
Islets, Pancreatic	(48)		(48)	(50)	(50)
Adenoma	2 (4%)		1 (2%)	3 (6%)	1 (2%)
Parathyroid Gland	(47)		(44)	(50)	(46)
Adenoma	1 (2%)		1 (2%)		
Pituitary Gland	(49)		(48)	(49)	(50)
Pars Distalis, Adenoma	24 (49%)		20 (42%)	18 (37%)	26 (52%)

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CD Rat MALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPB TO CTL	F3/50PPB TO CTL
Pars Intermed, Adenoma			1 (2%)	1 (2%)	
Thyroid Gland	(48)		(49)	(50)	(50)
C Cell, Adenoma				1 (2%)	
C Cell, Carcinoma	3 (6%)			3 (6%)	1 (2%)
Follicular Cel, Adenoma			1 (2%)		
<b>GENERAL BODY SYSTEM</b>					
Tissue NOS	(0)		(0)	(0)	(1)
Sarcoma					1 (100%)
<b>GENITAL SYSTEM</b>					
Coagulating Gland	(47)		(49)	(48)	(50)
Carcinoma, Metastatic, Uncertain Primary Site					1 (2%)
Schwannoma Malignant					1 (2%)
Ductus Deferens	(0)		(0)	(0)	(1)
Epididymis	(49)		(49)	(50)	(50)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Penis	(0)		(0)	(0)	(1)
Preputial Gland	(49)		(49)	(50)	(49)
Carcinoma			1 (2%)		1 (2%)
Squamous Cell Carcinoma	2 (4%)		3 (6%)	4 (8%)	7 (14%)
Prostate, Dorsal/Lateral Lobe	(43)		(38)	(41)	(43)
Schwannoma Malignant					1 (2%)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (3%)		
Prostate, Dorsal/lateral Lobe	(7)		(10)	(9)	(7)
Prostate, Ventral Lobe	(49)		(48)	(50)	(50)
Schwannoma Malignant					1 (2%)

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Rete Testes	(46)		(45)	(43)	(44)
Seminal Vesicle	(44)		(44)	(47)	(47)
Testes	(50)		(49)	(50)	(50)
Interstit Cell, Adenoma			1 (2%)		1 (2%)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
<hr/>					
HEMATOPOIETIC SYSTEM					
Bone Marrow	(49)		(49)	(50)	(50)
Lymph Node	(14)		(16)	(13)	(16)
Lymph Node, Mandibular	(46)		(48)	(50)	(49)
Lymph Node, Mesenteric	(44)		(46)	(49)	(48)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Spleen	(49)		(48)	(49)	(50)
Sarcoma					1 (2%)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Thymus	(47)		(45)	(47)	(45)
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
<hr/>					
INTEGUMENTARY SYSTEM					
Mammary Gland	(42)		(42)	(40)	(45)
Adenocarcinoma					2 (4%)
Adenoma					1 (2%)
Fibroadenoma			2 (5%)		1 (2%)
Fibroma	1 (2%)		1 (2%)		
Skin	(50)		(49)	(50)	(50)
Basal Cell Adenoma	2 (4%)			1 (2%)	
Carcinoma					1 (2%)

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Fibroma				1 (2%)	2 (4%)
Keratoacanthoma			2 (4%)	3 (6%)	1 (2%)
Lipoma			2 (4%)		2 (4%)
Sarcoma	1 (2%)				1 (2%)
Schwannoma Malignant				1 (2%)	
<b>MUSCULOSKELETAL SYSTEM</b>					
Bone	(0)		(1)	(1)	(0)
Cranium, Squamous Cell Carcinoma, Deep Invasion			1 (100%)		
Bone, Femur	(49)		(49)	(50)	(50)
Skeletal Muscle	(3)		(4)	(3)	(0)
Diaphragm, Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (25%)		
<b>NERVOUS SYSTEM</b>					
Brain	(0)		(0)	(0)	(1)
Cranial Nerve, Schwannoma Malignant					1 (100%)
Brain, Brain Stem	(49)		(49)	(50)	(50)
Reticulosis Malignant					1 (2%)
Brain, Cerebellum	(49)		(49)	(50)	(50)
Granular Cell Tumor Malignant				1 (2%)	
Brain, Cerebrum	(49)		(49)	(50)	(50)
Granular Cell Tumor Malignant				1 (2%)	
Meninges, Granular Cell Tumor Benign					1 (2%)
Osteoma	1 (2%)				
Peripheral Nerve	(2)		(4)	(2)	(0)
<b>RESPIRATORY SYSTEM</b>					
Lung	(47)		(48)	(48)	(50)
Alveolar/Bronchiolar Adenoma				1 (2%)	

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Schwannoma Malignant, Metastatic, Skin				1 (2%)	
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		
Squamous Cell Carcinoma, Metastatic, Uncertain Primary Site				1 (2%)	
Thymoma Malignant, Metastatic, Uncertain Primary Site					1 (2%)
Nose	(49)		(48)	(49)	(50)
Osteosarcoma					1 (2%)
Trachea	(49)		(49)	(50)	(50)
<b>SPECIAL SENSES SYSTEM</b>					
Ear	(0)		(0)	(1)	(1)
Neural Crest Tumor					1 (100%)
Squamous Cell Papilloma				1 (100%)	
Eye	(46)		(47)	(48)	(50)
Iris, Melanoma Benign					1 (2%)
Retrobulbar, Squamous Cell Carcinoma, Deep Invasion	1 (2%)				
Harderian Gland	(49)		(48)	(50)	(50)
Lacrimal Gland	(1)		(1)	(2)	(1)
Zymbal's Gland	(1)		(0)	(2)	(0)
Carcinoma	1 (100%)			1 (50%)	
Squamous Cell Carcinoma				1 (50%)	
<b>URINARY SYSTEM</b>					
Kidney	(49)		(48)	(50)	(50)
Liposarcoma					1 (2%)
Sarcoma			1 (2%)		
Squamous Cell Carcinoma, Metastatic, Stomach, Forestomach			1 (2%)		

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Urethra	(3)		(1)	(1)	(0)
Urinary Bladder	(49)		(48)	(49)	(50)
SYSTEMIC LESIONS					
Multiple Organ	*(50)		*(49)	*(50)	*(50)
Leukemia Mononuclear			1 (2%)	1 (2%)	
Lymphoma Malignant	2 (4%)		1 (2%)	1 (2%)	

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CD Rat MALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPB TO CTL	F3/50PPB TO CTL
<b>Tumor Summary for MALE</b>					
Total Animals with Primary Neoplasms (b)	41		34	31	37
Total Primary Neoplasms	58		51	57	68
Total Animals with Benign Neoplasms	33		30	25	31
Total Benign Neoplasms	40		37	39	39
Total Animals with Malignant Neoplasms	14		13	14	19
Total Malignant Neoplasms	18		14	18	28
Total Animals with Metastatic Neoplasms			1	2	2
Total Metastatic Neoplasms			12	3	2
Total Animals with Malignant Neoplasms Uncertain Primary Site				1	2
Total Animals with Neoplasms Uncertain - Benign or Malignant					1
Total Uncertain Neoplasms					1

\*\*\*END OF MALE DATA\*\*\*

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CD Rat FEMALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPBTO CTL	F3/50PPBTO CTL
<b>Disposition Summary</b>					
Animals Initially In Study	52		50	50	50
Early Deaths					
Moribund Sacrifice	24		19	23	21
Natural Death	1		2	5	3
Survivors					
Moribund Sacrifice				1	2
Terminal Sacrifice	27		29	21	24
Animals Examined Microscopically	52		50	50	50
<b>ALIMENTARY SYSTEM</b>					
Esophagus	(52)		(49)	(50)	(50)
Intestine Large, Cecum	(51)		(49)	(49)	(50)
Intestine Large, Colon	(52)		(50)	(50)	(50)
Intestine Large, Rectum	(51)		(49)	(50)	(50)
Adenoma	1 (2%)				
Intestine Small, Duodenum	(52)		(49)	(50)	(50)
Intestine Small, Ileum	(52)		(49)	(49)	(50)
Intestine Small, Jejunum	(51)		(49)	(48)	(50)
Carcinoma			1 (2%)	1 (2%)	
Leiomyoma			1 (2%)		
Liver	(52)		(50)	(50)	(50)
Adenocarcinoma, Metastatic, Uterus	1 (2%)				
Carcinoma, Metastatic, Intestine Small, Jejunum			1 (2%)		
Cholangiocarcinoma	1 (2%)		1 (2%)		
Cholangioma					1 (2%)
Hepatocellular Adenoma	2 (4%)				
Hepatocellular Carcinoma			1 (2%)		

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Nephroblastoma, Metastatic, Kidney	1 (2%)				
Mesentery	(3)		(3)	(4)	(4)
Adenocarcinoma, Metastatic, Uterus	1 (33%)				
Nephroblastoma, Metastatic, Kidney	1 (33%)				
Oral Mucosa	(2)		(4)	(7)	(2)
Fibrous Histiocytoma				1 (14%)	
Squamous Cell Carcinoma	2 (100%)		1 (25%)	2 (29%)	1 (50%)
Pancreas	(52)		(49)	(50)	(50)
Adenocarcinoma, Metastatic, Uterus	1 (2%)				
Salivary Glands	(52)		(50)	(50)	(50)
Stomach, Forestomach	(52)		(49)	(50)	(50)
Adenocarcinoma, Metastatic, Uterus	1 (2%)				
Squamous Cell Carcinoma					1 (2%)
Squamous Cell Papilloma	1 (2%)			2 (4%)	
Stomach, Glandular	(52)		(49)	(50)	(50)
Leiomyosarcoma	1 (2%)				
Tongue	(0)		(1)	(0)	(0)
<b>CARDIOVASCULAR SYSTEM</b>					
Blood Vessel	(52)		(50)	(50)	(50)
Heart	(52)		(50)	(50)	(50)
<b>ENDOCRINE SYSTEM</b>					
Adrenal Cortex	(52)		(50)	(50)	(50)
Adenoma	2 (4%)		2 (4%)	1 (2%)	
Adrenal Medulla	(52)		(50)	(50)	(50)
Pheochromocytoma Benign					1 (2%)
Islets, Pancreatic	(52)		(49)	(50)	(50)
Adenoma	1 (2%)				1 (2%)

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Parathyroid Gland	(48)		(45)	(47)	(44)
Pituitary Gland	(52)		(50)	(50)	(50)
Pars Distalis, Adenoma	32 (62%)		30 (60%)	36 (72%)	32 (64%)
Thyroid Gland	(52)		(49)	(50)	(50)
Bilateral, C Cell, Adenoma					1 (2%)
C Cell, Adenoma	1 (2%)		1 (2%)	1 (2%)	1 (2%)
C Cell, Carcinoma	1 (2%)			1 (2%)	
GENERAL BODY SYSTEM					
Tissue NOS	(0)		(0)	(1)	(1)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung					1 (100%)
Squamous Cell Carcinoma, Deep Invasion				1 (100%)	
GENITAL SYSTEM					
Clitoral Gland	(50)		(50)	(49)	(48)
Adenoma			1 (2%)	1 (2%)	2 (4%)
Ovary	(51)		(50)	(50)	(50)
Granulosa Cell Tumor Benign			1 (2%)	1 (2%)	2 (4%)
Granulosa Cell Tumor Malignant			1 (2%)		
Sertoli Cell Tumor Benign			2 (4%)	1 (2%)	
Oviduct	(51)		(49)	(50)	(50)
Uterus	(52)		(50)	(50)	(50)
Endometrium, Adenocarcinoma	4 (8%)		1 (2%)		
Endometrium, Adenoma	1 (2%)		1 (2%)	2 (4%)	
Leiomyoma					1 (2%)
Nephroblastoma, Metastatic, Kidney	1 (2%)				
Polyp Stromal	1 (2%)		7 (14%)	2 (4%)	5 (10%)
Vagina	(51)		(50)	(50)	(50)
Nephroblastoma, Metastatic, Kidney	1 (2%)				

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<b>HEMATOPOIETIC SYSTEM</b>					
Bone Marrow		(52)	(50)	(50)	(50)
Schwannoma Malignant, Metastatic, Skin	1 (2%)				
Lymph Node		(10)	(17)	(10)	(5)
Lymph Node, Mandibular		(51)	(50)	(50)	(50)
Carcinoma, Metastatic, Zymbal'S Gland				1 (2%)	
Lymph Node, Mesenteric		(51)	(49)	(50)	(49)
Nephroblastoma, Metastatic, Kidney	1 (2%)				
Spleen		(52)	(50)	(50)	(50)
Thymus		(50)	(45)	(46)	(49)
<b>INTEGUMENTARY SYSTEM</b>					
Mammary Gland		(52)	(50)	(50)	(50)
Adenocarcinoma	6 (12%)		4 (8%)	6 (12%)	10 (20%)
Adenocarcinoma, Multiple			2 (4%)	3 (6%)	
Fibroadenoma	17 (33%)		13 (26%)	21 (42%)	13 (26%)
Fibroadenoma, Multiple	19 (37%)		21 (42%)	19 (38%)	24 (48%)
Skin		(52)	(50)	(50)	(50)
Basal Cell Adenoma					1 (2%)
Ear, Basal Cell Adenoma			1 (2%)		
Fibroma			2 (4%)		1 (2%)
Fibrous Histiocytoma				1 (2%)	
Lipoma	1 (2%)				
Sarcoma	1 (2%)			1 (2%)	1 (2%)
Schwannoma Malignant	1 (2%)				
<b>MUSCULOSKELETAL SYSTEM</b>					
Bone		(0)	(1)	(0)	(0)
Bone, Femur		(52)	(50)	(50)	(50)

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors

\* Number of animals with any tissue examined microscopically

Experiment Number: 99920-93

Test Type: SPECIAL STUDY

Route: DOSED FEED

Species/Strain: Rat/CD

**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)**

Test Compound: ENDOCRINE DISRUPTOR(Ethinyl Estradiol)

CAS Number: 57-63-6

Date Report Requested: 10/23/2014

Time Report Requested: 11:55:22

First Dose M/F: NA / NA

Lab: NCTR

CD Rat FEMALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPBTO CTL	F3/50PPBTO CTL
Skeletal Muscle	(3)		(4)	(0)	(1)
Diaphragm, Adenocarcinoma, Metastatic, Uterus	1 (33%)				
Diaphragm, Granulosa Cell Tumor Malignant, Metastatic, Ovary			1 (25%)		
Diaphragm, Nephroblastoma, Metastatic, Kidney	1 (33%)				
<b>NERVOUS SYSTEM</b>					
Brain, Brain Stem	(52)		(50)	(50)	(50)
Brain, Cerebellum	(51)		(50)	(50)	(50)
Astrocytoma Malignant					1 (2%)
Brain, Cerebrum	(52)		(50)	(50)	(50)
Peripheral Nerve	(0)		(1)	(0)	(1)
Spinal Cord	(0)		(1)	(0)	(1)
<b>RESPIRATORY SYSTEM</b>					
Lung	(52)		(50)	(50)	(50)
Adenocarcinoma, Metastatic, Mammary Gland				1 (2%)	1 (2%)
Alveolar/Bronchiolar Adenoma	1 (2%)				1 (2%)
Alveolar/Bronchiolar Carcinoma					1 (2%)
Carcinoma, Metastatic, Thyroid Gland	1 (2%)			1 (2%)	
Carcinoma, Metastatic, Zymbal'S Gland				1 (2%)	
Nose	(52)		(50)	(50)	(50)
Trachea	(52)		(49)	(50)	(50)
<b>SPECIAL SENSES SYSTEM</b>					
Ear	(0)		(0)	(2)	(0)
Neural Crest Tumor				2 (100%)	
Eye	(52)		(50)	(49)	(50)

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b - Primary tumors: all tumors except metastatic tumors

\* Number of animals with any tissue examined microscopically

Experiment Number: 99920-93

Test Type: SPECIAL STUDY

Route: DOSED FEED

Species/Strain: Rat/CD

**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)**

Test Compound: ENDOCRINE DISRUPTOR(Ethinyl Estradiol)

CAS Number: 57-63-6

Date Report Requested: 10/23/2014

Time Report Requested: 11:55:22

First Dose M/F: NA / NA

Lab: NCTR

CD Rat FEMALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPBTO CTL	F3/50PPBTO CTL
Harderian Gland	(52)		(50)	(50)	(50)
Squamous Cell Carcinoma, Deep Invasion				1 (2%)	
Zymbal's Gland	(0)		(0)	(1)	(0)
Carcinoma				1 (100%)	
URINARY SYSTEM					
Kidney	(52)		(50)	(50)	(50)
Lipoma	1 (2%)				
Liposarcoma					1 (2%)
Nephroblastoma	1 (2%)				1 (2%)
Renal Tubule, Adenoma				1 (2%)	1 (2%)
Urinary Bladder	(52)		(49)	(49)	(50)
Transit Epithe, Papilloma					1 (2%)
SYSTEMIC LESIONS					
Multiple Organ	*(52)		*(50)	*(50)	*(50)
Histiocytic Sarcoma				1 (2%)	
Leukemia Mononuclear	1 (2%)				
Lymphoma Malignant				1 (2%)	1 (2%)
Mesothelioma Malignant			1 (2%)	1 (2%)	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors

\* Number of animals with any tissue examined microscopically

Experiment Number: 99920-93  
 Test Type: SPECIAL STUDY  
 Route: DOSED FEED  
 Species/Strain: Rat/CD

**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)**

Test Compound: ENDOCRINE DISRUPTOR(Ethinyl Estradiol)  
 CAS Number: 57-63-6

Date Report Requested: 10/23/2014  
 Time Report Requested: 11:55:22  
 First Dose M/F: NA / NA  
 Lab: NCTR

CD Rat FEMALE	F3	0PPB	F3/2PPB TO CTL	F3/10PPBTO CTL	F3/50PPBTO CTL
<b>Tumor Summary for FEMALE</b>					
Total Animals with Primary Neoplasms (b)	50		48	48	48
Total Primary Neoplasms	100		96	112	107
Total Animals with Benign Neoplasms	46		47	46	44
Total Benign Neoplasms	81		83	88	89
Total Animals with Malignant Neoplasms	15		12	16	16
Total Malignant Neoplasms	19		13	22	18
Total Animals with Metastatic Neoplasms	5		3	3	2
Total Metastatic Neoplasms	14		4	4	2
Total Animals with Malignant Neoplasms Uncertain Primary Site					
Total Animals with Neoplasms Uncertain - Benign or Malignant				2	
Total Uncertain Neoplasms				2	

**\*\* END OF REPORT \*\***

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors

\* Number of animals with any tissue examined microscopically