

## **Fexinidazole: 28-day Oral Toxicity Study in the Dog**

Product Name :	Fexinidazole
Study Number:	0505-2007
Study Director/Author:	
Sponsor Reference Study No.:	Not applicable
Status:	Final

## SUMMARY

### Methods

Fexinidazole is a 5-nitroimidazole derivative biologically active against *Trypanosoma* parasites (*T.b. rhodesiense* and *T.b. brucei*).

The test article was given daily for twenty-eight days to five (control and high dose) or three (low and mid dose) beagle dogs/sex/dose at the doses of 0 (control group), 50, 200 and 800 mg/kg/day. The compound was administered orally, by gavage, as a suspension in 5% Tween 80 / 0.5% Methocel in a volume of 10 mL/kg/day. The control group received the vehicle alone (5% Tween 80 in 0.5% Methocel). At the end of the treatment period three animals/sex/group were sacrificed; the remaining animals of the control and high-dose groups were allowed a two-week recovery period.

Body weight was recorded weekly. Clinical signs and food consumption were recorded daily. Electrocardiographic, ophthalmoscopic and clinical pathology examinations were performed pretest and at the end of the treatment and recovery period.

A complete necropsy was performed on animals at the scheduled sacrifices (end of treatment and end of recovery); selected organs were weighed and collected. Histopathological examination was performed on all collected organs/tissues from control and high dose groups and additionally on bone marrow smears, sternum, mammary glands, ovaries and uterus from low and mid dose groups.

Systemic exposure to fexinidazole and of its sulfoxide and sulfone metabolites was evaluated on Days 1, 14 and 28 in the same animals used for the toxicological study.

### Results

No mortality and no treatment-related clinical signs were observed during the study.

A slight to moderate reduction in food intake was observed in four females given 800 mg/kg/day throughout the treatment period. Food intake was normal after the end of the treatment. Concurrently, slight to moderate progressive body weight loss was seen in the same four females. Two males of the high dose group showed a progressive moderate body weight loss without changes in food consumption.

No treatment-related findings were noted at electrocardiographic and ophthalmoscopic examination.

A minimal to slight decrease in lymphocytes was observed mainly at the high dose in both sexes. No meaningful changes were observed at clinical pathology.

At necropsy, no drug-related changes were observed at gross pathology or in organ weights, either at the end of the treatment or after recovery.

At the end of the treatment period, moderately reduced cellularity of the bone marrow, severe involution of the thymus and slight to moderate atrophy of the adipose tissue in the sternal and femoral marrow spaces and in the fat deposits adjacent to the renal pelvis were

noted in a single high dose male. Minimally reduced cellularity was also noted in the bone marrow of one male treated with 200 mg/kg/day. These changes were considered as a consequence of the body weight loss.

At the end of the recovery period, increased severity of involution was noted in the thymus of both sexes compared with controls, secondary to body weight loss.

After single and repeated administrations at the three dose levels, no relevant gender difference in the systemic exposure to fexinidazole was observed. AUCs of fexinidazole increased less than expected assuming dose proportionality in the dose range investigated. No accumulation of fexinidazole was observed.

Fexinidazole was extensively metabolized to the sulfone and sulfoxide derivatives both after single and repeated administration. No accumulation of either metabolite was observed.

Mean  $\pm$ SD systemic exposure to fexinidazole is reported in the following table:

Dose (mg/kg/day)		Male			Female		
		Cmax (ng/mL)	tmax (hour)	AUC0-t(last) (ng-hour/mL)	Cmax (ng/mL)	tmax (hour)	AUC0-t(last) (ng-hour/mL)
50 (n=3)	D1	31.2 $\pm$ 12.4	0.5 $\pm$ 0	140 $\pm$ 147	42.4 $\pm$ 10.6	1 $\pm$ 0.87	237 $\pm$ 105
	D14	26.5 $\pm$ 13	0.5 $\pm$ 0	52.1 $\pm$ 29.4	41.9 $\pm$ 2.2	1.67 $\pm$ 0.58	246 $\pm$ 117
	D28	20.3 $\pm$ 7.89	1 $\pm$ 0	124 $\pm$ 67	36.3 $\pm$ 15.1	1 $\pm$ 0	87.1 $\pm$ 38.1
200 (n=3)	D1	54.9 $\pm$ 10.8	1 $\pm$ 0.87	419 $\pm$ 61.4	84.1 $\pm$ 36.7	1 $\pm$ 0	454 $\pm$ 119
	D14	78.1 $\pm$ 23.5	1 $\pm$ 0.87	452 $\pm$ 41.1	77.7 $\pm$ 50.8	2 $\pm$ 0	443 $\pm$ 217
	D28	57.9 $\pm$ 12.5	1 $\pm$ 0	395 $\pm$ 15.8	73 $\pm$ 12	1 $\pm$ 0	377 $\pm$ 83.5
800 (n=5)	D1	100 $\pm$ 21.2	1.1 $\pm$ 0.55	776 $\pm$ 182	184 $\pm$ 75.6	1.2 $\pm$ 0.45	895 $\pm$ 437
	D14	128 $\pm$ 56.9	1 $\pm$ 0	929 $\pm$ 268	152 $\pm$ 44	1.4 $\pm$ 0.55	1170 $\pm$ 309
	D28	86.2 $\pm$ 38.5	1.2 $\pm$ 0.4	736 $\pm$ 141	101 $\pm$ 47.1	1 $\pm$ 0	956 $\pm$ 378

Mean  $\pm$ SD systemic exposure to the sulfone metabolite is reported in the following table:

Dose (mg/kg/day)		Male			Female		
		Cmax ( $\mu$ g/mL)	tmax (hour)	AUC0-t(last) ( $\mu$ g-hour/mL)	Cmax ( $\mu$ g/mL)	tmax (hour)	AUC0-t(last) ( $\mu$ g-hour/mL)
50 (n=3)	D1	7.17 $\pm$ 1.74	8 $\pm$ 0	126 $\pm$ 28.1	10 $\pm$ 1.6	6.67 $\pm$ 2.31	170 $\pm$ 37.8
	D14	5.57 $\pm$ 2.19	4 $\pm$ 0	78 $\pm$ 35.3	9.98 $\pm$ 1.25	6.67 $\pm$ 2.31	173 $\pm$ 26.9
	D28	7.11 $\pm$ 1.21	8 $\pm$ 0	121 $\pm$ 19.1	6.79 $\pm$ 0.56	3.33 $\pm$ 1.15	107 $\pm$ 22.5
200 (n=3)	D1	17.2 $\pm$ 1.69	13.3 $\pm$ 9.24	338 $\pm$ 50.8	18.1 $\pm$ 3.42	12 $\pm$ 10.6	358 $\pm$ 85.7
	D14	22 $\pm$ 5.59	5.33 $\pm$ 2.31	387 $\pm$ 49.5	21.5 $\pm$ 2.42	5.33 $\pm$ 2.31	381 $\pm$ 61.2
	D28	14 $\pm$ 3.31	4 $\pm$ 4	258 $\pm$ 48	15.4 $\pm$ 2.66	11.7 $\pm$ 10.1	277 $\pm$ 29.9
800 (n=5)	D1	38.6 $\pm$ 2.83	17.6 $\pm$ 8.76	705 $\pm$ 94.9	33.6 $\pm$ 10.9	11.2 $\pm$ 7.16	614 $\pm$ 216
	D14	34.6 $\pm$ 7.42	5.6 $\pm$ 2.19	640 $\pm$ 163	38.6 $\pm$ 4.73	8 $\pm$ 0	667 $\pm$ 67.8
	D28	20.8 $\pm$ 4.14	12.4 $\pm$ 9.81	388 $\pm$ 68.2 <sup>(1)</sup> 601 $\pm$ 29 <sup>(2)</sup>	26 $\pm$ 7.7	7.2 $\pm$ 1.79	477 $\pm$ 145 <sup>(1)</sup> 693 $\pm$ 351 <sup>(2)</sup>

<sup>(1)</sup> AUC0-24; <sup>(2)</sup> n=2

Mean  $\pm$ SD systemic exposure to the sulfoxide metabolite is reported in the following table:

Dose (mg/kg/ day)		Male			Female		
		Cmax ( $\mu$ g/mL)	tmax (hour)	AUC0-t(last) ( $\mu$ g-hour/mL)	Cmax ( $\mu$ g/mL)	tmax (hour)	AUC0-t(last) ( $\mu$ g-hour/mL)
50 (n=3)	D1	3.55 $\pm$ 1.3	1 $\pm$ 0	19.2 $\pm$ 5.82	3.97 $\pm$ 0.74	1.33 $\pm$ 0.58	20 $\pm$ 6.81
	D14	2.24 $\pm$ 0.45	1 $\pm$ 0	8.51 $\pm$ 2.53	3.73 $\pm$ 0.73	1.67 $\pm$ 0.58	18.8 $\pm$ 2.06
	D28	1.83 $\pm$ 0.57	1.67 $\pm$ 0.58	14.2 $\pm$ 2.72	2.72 $\pm$ 0.73	1 $\pm$ 0	9.88 $\pm$ 2.72
200 (n=3)	D1	7.55 $\pm$ 1.03	1.67 $\pm$ 0.58	50.7 $\pm$ 8.61	8.7 $\pm$ 3.95	0.83 $\pm$ 0.29	52.1 $\pm$ 20.6
	D14	8.96 $\pm$ 2.53	2 $\pm$ 0	56.1 $\pm$ 9.96	9.02 $\pm$ 3.69	2 $\pm$ 0	57.2 $\pm$ 24.3
	D28	5.76 $\pm$ 1.17	1.33 $\pm$ 0.58	42.2 $\pm$ 6.46	5.43 $\pm$ 0.34	1 $\pm$ 0	33.8 $\pm$ 1.65
800 (n=5)	D1	13.4 $\pm$ 3.22	1.5 $\pm$ 0.71	104 $\pm$ 11.3	15.6 $\pm$ 4.64	1.6 $\pm$ 0.55	121 $\pm$ 44.4
	D14	12.5 $\pm$ 2.85	1.2 $\pm$ 0.45	113 $\pm$ 39.9	14.8 $\pm$ 5.1	2 $\pm$ 1.22	144 $\pm$ 37.1
	D28	9.35 $\pm$ 3.55	1.6 $\pm$ 0.55	74.3 $\pm$ 14.4 <sup>(1)</sup>	9.48 $\pm$ 3.38	1.4 $\pm$ 0.55	89 $\pm$ 45.2
				121 $\pm$ 33 <sup>(2)</sup>			

<sup>(1)</sup> AUC0-24; <sup>(2)</sup> n=2

## Conclusions

Fexinidazole, given orally to beagle dogs at the doses of 50, 200 and 800 mg/kg/day for 28 consecutive days, was well tolerated.

Slight to moderate body weight loss and reduction in food intake was observed at the dose of 800 mg/kg/day during the treatment period.

A minimal to slight decrease in lymphocytes was seen at the high dose.

Fexinidazole was extensively metabolized to the sulfone and sulfoxide derivatives both after single and repeated administration.

In the conditions applied in the present study, the dose of 200 mg/kg/day can be considered as the NOEL.

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## 1. INTRODUCTION AND OBJECTIVES

The purpose of this study (0505-2007) was to determine the tolerability of and systemic exposure to fexinidazole when given orally for 28 consecutive days to beagle dogs, by gavage. Reversal of possible toxic effects was evaluated in control and high-dose groups over a two-week observation period.

Systemic exposure was assessed in the same animals used for toxicological evaluation.

Fexinidazole is a 5-nitroimidazole derivative, biologically active against *Trypanosoma* parasites (*T.b.rhodesiense* and *T.b. brucei*) and useful in the treatment of the Human African trypanosomiasis (HAT), known as sleeping sickness.

## 2. STUDY SPONSOR

DNDi – Drugs for Neglected Diseases *Initiative*  
1 Place St Gervais  
CH – 1201 Geneva, Switzerland

## 3. TEST FACILITY

Accelera  
.

## 4. REGULATORY REQUIREMENTS

This study was conducted in compliance with:

- Decreto Legislativo 2 Marzo 2007, No. 50;
- Organisation for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP) (as revised in 1997).

The methods employed in this study were those described in the "Standard Operating Procedures" of the laboratories involved.

## 5. SCHEDULE

Experimental Start Date (Randomization Date)	January 24, 2008	
	Males	Females
First Dose (Day 1)	January 29, 2008	January 30, 2008
Last Dose (Day 28)	February 25, 2008	February 26, 2008
Necropsy – Dosing Phase (Day 29-30)	February 26-27, 2008	February 27-28, 2008
Start of recovery (Day 29)	February 26, 2008	February 27, 2008
Necropsy – End of Recovery period (Day 43)	March 11, 2008	March 12, 2008
Experimental Completion Date	March 12, 2008	



## 6. MATERIALS AND METHODS

### 6.1. Test and Control Items

#### 6.1.1. Test Item

Identification	Fexinidazole
Lot/Batch Number	3168-07-01/O
Purity and Expiry	100% October 2008
Storage Conditions	Room temperature, protected from light
Source and Manufacturer	Centipharm (formerly Orgasynth Industries)
Special Handling Precautions	According to MSDS (Material Safety Data Sheet)
The amount of the test article received and used at Accelera, Nerviano Medical Sciences was recorded according to Accelera, Nerviano Medical Sciences' standard procedures.	

#### 6.1.2. Vehicle/Control Item

Identification	5% Tween 80 in 0.5% Methyl cellulose 400 cP (Methocel) suspension in water	
Lot/Batch Number	Tween 80 Methyl cellulose 400 cP	1324202 125K0196
Expiry	Tween 80 Methyl cellulose 400 cP	February 2011 January 2009
Storage Conditions	Room Temperature	
Source and Manufacturer	Tween 80 Methyl cellulose 400 cP	Sigma-Aldrich Sigma-Aldrich
Method of Preparation	On file of ADMET/Preclinical Formulation	

#### 6.1.3. Test Formulation

Type of Formulation	5% Tween 80 in 0.5% Methyl cellulose 400 cP (Methocel) suspension
Method of Preparation	On file at Accelera/Experimental ADMET/Preclinical Formulation
Frequency of Preparation	The suspensions were prepared according to the stability data
Dose Concentrations	5, 20, 80 mg/mL
Storage Conditions	Room temperature
Source and Manufacturer	Accelera/Experimental ADMET/Preclinical Formulation

#### 6.1.4. Test Formulation Analyses

##### 6.1.4.1. Concentration/Homogeneity

Samples (top-middle-bottom, 5 mL each) of each dose suspension prepared for the first and the last week of treatment (Weeks 1 and 4) were collected under stirring for fexinidazole concentration and homogeneity checks; 10 mL were also taken from the vehicle. After collection, samples were directly transferred at room temperature to Accelera/DMPK & ART/Bioanalysis and Analytical Control for analysis. The analyses were performed using a validated HPLC-UV method [1].

### 6.1.4.2. Stability

Stability data indicated that fexinidazole/5% Tween 80 in 0.5% Methyl cellulose 400 cP (Methocel) suspension in the range 0.5-100 mg/mL is stable for 7 days at room temperature or for 14 days at +4°C [1].

All values were found to be within acceptable limits for the solutions.

## 6.2. Test System

Species/Strain or Breed, Source, Sex	Male and female dog/Beagle, Marshall, Europe
Justification of Species	The dog has been used extensively in safety studies and a large amount of biological data is available.
Age	About one year
Weight	6.83 to 9.87 kg
Acclimation	At least 20 days
Selection Criteria	Acceptable findings from pretest observations, body weight, physical examinations, some laboratory examinations
Pretest Animals	20/sex

### 6.2.1. Allocation/Randomization

Animals were randomly assigned to treatment groups based on the most recent pretest body weight. After excluding animals with unacceptable pretest findings, a computer program included in the Xybio Path/Tox system designed to achieve balance with respect to pretest body weights was used to exclude animals from both body weight extremes and randomize the remaining animals to treatment groups.

### 6.2.2. Identification

Animals were identified by individual tattoos and numbered collars (collars could be removed if required).

A color-coded cage card was affixed to each cage and indicated the study number and type, treatment start date, test article, animal number, sex and dose level.

Test Group	Color Code	Animal ID numbers	
		Males	Females
1	White	2516, 2518, 2520 Recovery.: 2527, 2533	2560, 2568, 2572 Recovery: 2575, 2577
2	Yellow	2514, 2521, 2529	2562, 2563, 2576
3	Green	2515, 2523, 2526	2561, 2570, 2567
4	Red	2517, 2519, 2525 Recovery: 2528, 2530	2564, 2565, 2569 Recovery: 2571, 2573

### 6.2.3. Environmental Conditions

Caging	Individual pens – Rooms 11, 12, 13, 18, 19, 20/C
Bedding	None

Temperature	18°C to 21°C
Air changes	15 +/- 5 air changes per hour
Humidity	40% to 70% relative humidity; monitored
Lighting	Approximate 12-hour light, 12-hour dark cycle (light from 6 a.m. to 6 p.m.).
Water	Municipal mains, available ad libitum via an auto-watering system
Diet	Altromin H (A. Rieper, Vandoies, Italy), about 300 g/day

Actual conditions were continuously monitored, recorded and records retained. Release of each lot of feed by the manufacturers was based on analysis of composite samples of each lot, which had met specifications set by the manufacturers. Water was periodically analyzed for chemical and microbial impurities. No contaminants were identified in the food or water, that were deemed to interfere with the results or conclusions of this study.

All the above environmental conditions, as well as all the procedures adopted throughout the study for housing and handling the animals were in strict compliance with EEC and Italian Guidelines for Laboratory Animal Welfare.

### 6.3. Experimental Design

The study was performed according to the following experimental scheme:

Test Group	Dose (tentative) (mg/kg/day)	Number of Animals/Group			
		Main Study		Recovery	
		Males	Females	Males	Females
1	0 (vehicle) <sup>a</sup>	3	3	2	2
2	50	3	3	-	-
3	200	3	3	-	-
4	800	3	3	2	2

a: 5% Tween 80 in 0.5% Methyl cellulose 400 cP (Methocel) suspension

Animals were treated orally, by gavage, daily for 28 consecutive days. At the end of the treatment period, all animals from groups 2 and 3 and the first three animals in numerical order from groups 1 and 4 (or otherwise chosen on the basis of the outcome of the study) were sacrificed; the remaining animals were allowed a two-week recovery period.

#### 6.3.1. Dose Administration

Method and Route	Os, gavage
Duration	28 days
Frequency	Once daily, at approximately the same time
Volume	10 mL/kg/day; Individual dose volumes were calculated based on the most recent body weight recorded
Rate	Not applicable
Special Notes	Stir during administration.

### 6.3.2. Dose Justification

The doses were chosen in agreement with the Sponsor on the basis of the results of preliminary oral repeated dose study No. 0338-2007 in which a decrease in food consumption and mild body weight loss were observed in one out of two animals given daily escalating doses of the test article in Phase I of the study (200 mg/kg/day x 4 days +400x4 + 800x4) and in one out of two animals given 800 mg/kg/day for 7 days.

The oral route and the daily administration schedule are those envisaged for the clinical setting.

### 6.4. Clinical and physical examinations

Survival and Moribundity Observations	At least once a day during the pre-test and recovery periods; at least twice a day during the treatment period
Clinical Signs	Every day, at least one session/day
Body Weights	Once pretest, on Day 1, then weekly
Food Consumption	Daily, qualitative, by visual inspection. Only reduced intake was reported.
Electrocardiographic Evaluation	<p>Pretest and at the end of the treatment period (Day 24) and the recovery period (Day 37 or 38). In addition ECG recording was repeated during the pretest period for animal 2568 to further check rhythm.</p> <p>ECGs were recorded from fully conscious manually restrained animals at least from I, II, III, aVR, aVL, aVF and, whenever possible, from precordial leads V1 (rV2), V3 (V2) and V5 (V4).</p> <p>Morphologic review for changes in waveform morphology and for the presence of arrhythmias and interval measurement were conducted on all recordings. The following parameters were measured or computed: heart rate, RR interval, P-R interval, QRS complex width, Q-T interval and Q-T interval corrected for heart rate using Fridericia's formula (<math>QT/RR^{1/3}</math>). In addition P wave width, P, Q, R, S and T wave heights and ST segment deviation were measured, and mean electrical axis computed.</p>
Ophthalmoscopy	<p>Pretest and at the end of the treatment (Day 24) and the recovery period (Day 37 or 38).</p> <p>The examination was performed using an indirect ophthalmoscope and a slit lamp when necessary. Mydriasis was induced by instilling one drop of 0.5% tropicamide (Visumidriatic) solution into each eye. The following were examined: conjunctiva, cornea, sclera, anterior chamber, iris, lens, vitreous body and fundus.</p>

## 6.5. Clinical Pathology

### 6.5.1. Hematology

Collection Intervals	Pretest and at the end of the treatment and recovery periods.
Number of Animals	All animals
Collection Site	Jugular vessels
Anesthesia	None
Fasting Requirements	Overnight (about 16 hours)
Unscheduled Samples	None
Target Blood Volume	0.5 mL
Anticoagulant	8% EDTA solution

#### Hematology Parameters Evaluated

White Blood Cells	Reticulocyte Count (absolute and percent)
Red Blood Cells	Mean Corpuscular Volume reticulocyte (MCVr)
Hemoglobin	Mean Corpuscular Hemoglobin reticulocyte (CHR)
Hematocrit	Mean Corpuscular Hemoglobin Concentration reticulocytes (CHCMr)
Mean Corpuscular Volume	Platelets
Mean Corpuscular Hemoglobin	Mean Platelet Volume
Mean Corpuscular Hemoglobin Concentration	Platelet Distribution Width
Red Cell Distribution Width	Platelet Hematocrit
Hemoglobin Distribution Width	Differential White Blood Cells (absolute and percent)

### 6.5.2. Coagulation

Collection Intervals	Pretest and at the end of the treatment and recovery periods.
Number of Animals	All
Collection Site	Jugular vessels
Anesthesia	None
Fasting Requirements	Overnight (about 16 hours) for scheduled samplings
Unscheduled Sampling	None
Target Blood Volume	About 2.5 mL
Anticoagulant	3.8% sodium citrate solution

#### Coagulation Parameters Evaluated

Activated Partial Thromboplastin Time	Prothrombin Time
Activated Partial Thromboplastin Time Ratio	Prothrombin Time Ratio
Fibrinogen	

### 6.5.3. Clinical Chemistry

Collection Intervals	Pretest and at the end of the treatment and recovery periods.
Number of Animals	All animals
Collection Site	Jugular vessels
Anesthesia	None
Fasting Requirements	Overnight (about 16 hours)
Unscheduled Samples	None
Target Blood Volume	1 mL in tube for serum separation
Anticoagulant	None

**Clinical Chemistry Parameters Evaluated**

Urea	Creatinine
Alanine Aminotransferase	Aspartate Aminotransferase
Alkaline Phosphatase	Total Bilirubin
Albumin	Total Proteins
Glucose	Globulin
Gamma-glutamyl transferase	Total Cholesterol
Triglycerides	Calcium
Phosphorus	Albumin/Globulin Ratio (calculated)
Sodium	Potassium
Chloride	

**6.5.4. Urine Analysis**

Collection Intervals	Pretest and at the end of the treatment and recovery periods.
Number of Animals	All
Method of Collection	Metabolic cages
Sample Requirements	1% Thimerosal (4ml) in each bottle, before collection
Fasting Requirements	Overnight (about 16 hours) for scheduled samplings
Unscheduled Samplings	None

**Urine Parameters Evaluated**

Total Volume	
Macroscopic Appearance (Color, Appearance)	Ketone Bodies
pH	Urobilinogen
White Blood Cells	Bilirubin
Nitrites	Hemoglobin/Red Blood Cells
Proteins	Specific Gravity
Glucose	

**6.6. Post mortem examinations****6.6.1. Unscheduled Deaths**

No animal died during the study.

**6.6.2. Scheduled Necropsy, Tissue Collection, and Tissue Examination**

	End of treatment necropsy	End of recovery necropsy
Sacrifice Schedule	Days 29-30	Day 43
Number of Animals	The first three/group in numerical order	Remaining animals
Method of Euthanasia	Sodium thiopental anesthesia and exsanguination from the femoral vein	
Fasting Requirements	Overnight for scheduled sacrifices	
Terminal Body Weight	All animals	
Macroscopic Examination	All animals	

Organs/tissues from animals surviving to scheduled sacrifice were collected, weighed and examined microscopically (E) according to the following table. Paired organs were weighed together. Relative organ weights were calculated on terminal body weight.

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Organ/Tissue	All animals		Examined (mg/kg/day) All animals			
	Collected	Weighed	0	50	200	800
Aorta	X		E			E
Adrenal glands (both)	X	X	E			E
Bone marrow smear	X		E	E (m)	E (m)	E
Brain	X <sup>a</sup>	X	E			E
Diaphragm	X		E			E
Epididymides (both)	X		E			E
Esophagus	X		E			E
Eyes, optic nerve (both)	X		E			E
Heart	X	X	E			E
Duodenum	X		E			E
Jejunum	X		E			E
Ileum	X		E			E
Cecum	X		E			E
Colon	X		E			E
Gallbladder	X		E			E
Femur head	X		E			E
Kidneys (both)	X	X	E			E
Lacrimal glands	X		E			E
Liver	X <sup>a</sup>	X	E			E
Lungs	X		E			E
Lymph node, mandibular	X		E			E
Lymph node, mesenteric	X		E			E
Mammary gland	X		E	E (f)	E (f)	E
Ovaries	X	X	E	E	E	E
Pancreas	X		E			E
Pituitary	X		E			E
Prostate	X	X	E			E
Salivary glands (mandibular, parotids)	X		E			E
Sciatic nerve	X		E			E
Skeletal muscle	X		E			E
Skin	X		E			E
Spinal cord (cervical)	X		E			E
Spleen	X	X	E			E
Sternum	X		E			E
Stomach	X		E			E
Testes (both)	X	X	E			E
Thymus	X	X	E			E
Thyroid glands (with parathyroid glands) <sup>b</sup>	X		E			E
Tongue	X		E			E
Trachea	X		E			E
Urinary bladder	X		E			E
Uterus	X		E	E	E	E
Vagina	X		E	E	E	E
Lesions	X		E	E	E	E

Organ/Tissue	All animals		Examined (mg/kg/day) All animals			
	Collected	Weighed	0	50	200	800
Histological examination was performed on all tissues/organs from dogs of the control and high dose group killed terminally and at the end of the recovery period. For organs/tissues showing treatment-related changes the examination was extended to the other dose-groups as necessary to establish a no-effect level. a Samples of liver and brain were collected and frozen in liquid nitrogen and kept at -80°C as required by the Sponsor b Parathyroid glands examined microscopically if included in the section of thyroid glands  (f) females only (m) males only  Fixatives: Eyes: Davidson's solution Bone Marrow Smears: Methanol-ether All Other Tissues: 10% neutral buffered formalin						

### 6.6.3. Tissue Preparation

Histological sections of all tissues listed in Section 6.6.2 were trimmed, embedded, sectioned, and stained with hematoxylin and erythrosine. Bone marrow smears were prepared and stained with May Grünwald-Giemsa.

All organs/tissues were kept for any further test necessary.

### 6.6.4. Peer review

A pathology peer review was conducted by Anna Maria Giusti. A report was produced and filed with the study raw-data.

## 6.7. Systemic Exposure

The toxicokinetics of fexinidazole and its metabolites M1 (sulfoxide) and M2 (sulfone) were evaluated in accordance with the collection schedule and procedures tabulated below. The bioanalysis were conducted by DMPK & ART – Bioanalysis/Analytical Control, Nerviano.

Dose Levels (Groups)	All groups,
Collection Intervals	Days 1, 14 and 28
Collection Time Points	Days 1 and 14: Predose, 30 minutes, 1, 2, 4, 8 and 24h after dosing (all animals). Day 28: Predose, 30 minutes, 1, 2, 4, 8, 24 (all animals), 48 and 72h after dosing (recovery animals)
Animals/Time Point	See above
Anesthesia	Not required
Collection Volume per Sample	About 1 mL of blood/point.
Collection Site	Peripheral veins (alternate sites may be used if necessary)
Sample Requirements	Blood was put in heparinized plastic tubes kept on a ice-water bath, then centrifuged (10 min, 1200g, +4°C). Two aliquots of about 200 µL each of plasma were stored in a freezer at – 80°C until analysis.



After blood collection, frozen plasma specimens were transferred in plastic boxes to DMPK & ART, Nerviano Medical Sciences. The samples were loaded according to Watson 6.4.0.04 (Thermo Fisher Scientific Waltham, MA, USA).

Plasma samples were analyzed for the quantitation of fexinidazole using a validated LC-MS-MS method by Bioanalysis/Analytical Control, DMPK & ART.

Toxicokinetic calculations were carried out by Pharmacokinetics, DMPK & ART.

The toxicokinetic report is appended to the present report as Appendix 13.

Details of the analytical method and of calculation methods are included in the toxicokinetic report.

## 7. DATA ACQUISITION

Clinical observations, body weights, food consumptions, ECG and ophthalmoscopic examination data, organ weights, gross necropsy observations, histopathologic findings and dose administration documentation were entered directly into the Xybio Path/Tox System or were recorded on appropriate paper forms, and, if appropriate, later entered into the Xybio Path/Tox System. Clinical pathology data were processed according to Clinical Pathology Laboratories procedures.

The limits of a scheduled period were fixed by the “grace days” reported for scheduled determinations.

## 8. STATISTICAL ANALYSIS

### 8.1. Variables

Body weights, clinical chemistry, hematology, ECG data, absolute organ weights, urinalysis (volume and specific gravity only) were statistically analysed.

### 8.2. Methods

Dunnett’s test, included in a customized Xybio package, was used.

## 9. ARCHIVING

The original protocol, the protocol amendment, all raw data, supporting documents, and specimens produced at the Test Facility, and the final report with original signatures were filed in the Archives of Accelera, Nerviano Medical Sciences S.r.l., Nerviano (Italy) for the period of time agreed with the Sponsor (at least 3years) after which the Sponsor will be contacted for instructions regarding dispatch or disposal of the material.

A copy of the protocol, the report with original signatures, a reserve sample and all relevant original documentation of the test item were filed by the Sponsor.

## 10. STUDY DEVIATIONS

1) Report No. 0293-2007-R, mentioned in Paragraph 6.1.4.1 of the protocol. (Homogeneity and Concentration) concerning validation of the analysis method for quantification of fexinidazole, was finalized after start of the study.

2) Only plasma samples taken at 0 and 2h from control animals were analyzed for the presence of Fexinidazole and its metabolites, at variance with Amendment 1 (0505-2007-PA1).

## 11. STUDY PERSONNEL


## 12. RESULTS

### 12.1. Clinical and Physical Examination

#### 12.1.1. Mortality

No mortality was observed during the study.

#### 12.1.2. Clinical Signs

(Table 1, Appendix 2)

No treatment-related clinical signs were observed during the study.

The gastrointestinal disturbances observed (soft stools and/or diarrhea) were considered unrelated to the treatment since they were sporadic, present also during the pretest period and occurring with a similar incidence and severity in control and treated animals.

#### 12.1.3. Body Weight

(Table 2 , Appendix 3, Figure 16.1)

Slight to moderate, progressive body weight loss was observed in one male given 200 mg/kg/day (No. 2523, -10% on Day 28 vs Day 1) and, in the high-dose group, in two males (Nos 2517 and 2530; -10 to -14%) and four females (all except No. 2569; -8 to -15%). A trend towards recovery was observed after the end of the treatment period in female No. 2571 only. Changes in body weight correlated with the decrease in food consumption (see below) in females only.

#### 12.1.4. Food consumption

(Table 1, Appendix 2)

No significant changes in food intake were observed in treated males at any dose. A slight to moderate reduction in food intake was repeatedly observed from Day 2 on, throughout the treatment period, in the same four females given 800 mg/kg/day that showed body weight loss. Female No. 2569 showed only sporadic episodes of slight reduction in food intake. The two females chosen for recovery showed normal food intake after the treatment was discontinued.

#### 12.1.5. Electrocardiographic examination

(Table 3, Appendix 4)

No abnormalities in rhythm and morphology were recorded in any animal.

No meaningful abnormal values were observed in any measured or computed parameters including repolarization parameters, namely QT or QTc interval corrected for heart rate using the Fridericia's formula ( $QT/RR^{1/3}$ ).

The changes observed when the various groups were compared with the control group were not considered to be toxicologically meaningful despite the statistical significance of some differences.

The variations observed in comparison with the pretest values (see table below for mean variations of main parameters) showed no meaningful changes or changes similar to those observed in control animals.

**Main ECG parameters - Differences in comparison with pretest – Mean values**

		Males				Females			
		control	grp2	grp3	grp4	control	grp2	grp3	grp4
<b>Heart rate</b> bpm	<b>pretest</b>	<b>93</b>	<b>82</b>	<b>81</b>	<b>95</b>	<b>95</b>	<b>116</b>	<b>93</b>	<b>102</b>
	Day 24	2	20	16	5	4	-8	19	8
	Day 38	-10			-4	6			0
<b>P-R interval</b> ms	<b>pretest</b>	<b>87</b>	<b>89</b>	<b>97</b>	<b>86</b>	<b>88</b>	<b>83</b>	<b>92</b>	<b>87</b>
	Day 24	-6	-7	-7	0	-5	6	-5	-1
	Day 38	0			15	14			3

<b>QRS complex duration</b> ms	<b>pretest</b>	<b>47</b>	<b>46</b>	<b>55</b>	<b>44</b>	<b>46</b>	<b>51</b>	<b>49</b>	<b>50</b>
	Day 24	0	-1	-2	0	2	-3	4	3
	Day 38	4			7	5			-1
<b>Q-T interval</b> ms	<b>pretest</b>	<b>179</b>	<b>186</b>	<b>190</b>	<b>179</b>	<b>185</b>	<b>180</b>	<b>183</b>	<b>177</b>
	Day 24	10	1	6	18	1	4	9	15
	Day 38	20			24	9			27
<b>Q-Tc interval</b> (QT/RR <sup>1/3</sup> ) ms	<b>pretest</b>	<b>208</b>	<b>204</b>	<b>209</b>	<b>207</b>	<b>214</b>	<b>224</b>	<b>210</b>	<b>211</b>
	Day 24	11	15	18	26	4	0	25	20
	Day 38	14			23	14			30

bpm = beats per minute; ms = milliseconds. Pretest data are reported as absolute values.

Other values or notes reported in the tables or appendices were deemed to be spontaneous because one or more of the following conditions apply: they were present at the pre-test examinations, without any dose and/or time relationship and, in our experience, are those commonly occurring under the experimental conditions or are well-known normal features of the dog heart rhythm such as respiratory sinus arrhythmia.

### 12.1.6. Ophthalmoscopic examination

(Table 4, Appendix 5)

No treatment-related changes were noted during the study.

The only alteration recorded (female dog No. 2575, small areas of corneal opacity in the right eye at the end of the treatment and recovery period) was unilateral and involved a control animal.

## 12.2. Clinical pathology

### 12.2.1. Hematology

(Table 5, Appendix 6)

No clear treatment-related changes were recorded during the study.

On Day 28 a minimal to slight (about 25%) variable decrease in lymphocytes was recorded in males dosed at 200 and 800 mg/kg/day. The same parameter showed a minimal (9 to 16%) variable decrease in all dosed females without dose-relationship. Recovery occurred on Day 42 in high-dose animals. In other groups recovery could not be ascertained. Neutrophils were slightly (about 20%) decreased in males dosed at 200 mg/kg/day. Recovery could not be ascertained.

### 12.2.2. Coagulation

(Table 6, Appendix 7)

No treatment-related changes were recorded during the study.

### 12.2.3. Clinical chemistry

(Table 7, Appendix 8)

No clear treatment-related changes were recorded during the study.

On Day 28, a minimal (about 2-fold) increase in alkaline phosphatase was observed in high-dose male No. 2525. Recovery could not be ascertained.

A minimal (about 1.5-fold) increase in total cholesterol was recorded in high-dose female No. 2564 at the end of the treatment period. Recovery could not be ascertained.

In male No. 2528 given the high dose gamma-glutamyl transferase was minimally (about 1.4-fold) increased starting from Day 28 up to Day 42.

### 12.2.4. Urinalysis

(Tables 8 and 9, Appendix 9)

No treatment-related changes were recorded during the study.

## 12.3. Post-mortem examinations

### 12.3.1. Organ Weights

(Tables 10 and 11, Appendices 10 and 11)

#### **End of treatment (Days 29-30)**

The increases in mean absolute and relative weights of the ovaries observed in treated animals, without dose-relationship, are considered of doubtful toxicological significance and are further discussed in the histopathology section.

Other variations in mean weights, sometimes noted in treated animals, reflect the remarkable individual variability observed also in controls.

#### **Final Phase Sacrifice (Day 43)**

The changes observed in mean absolute and relative organ weights were not considered toxicologically significant due to the low number of animals available for evaluation and to individual variability.

### 12.3.2. Gross Pathology

(Table 12, Appendix 12)

#### **End of treatment (Days 29-30)**

Fairly good general condition, clear liquid content in the peritoneal cavity or small thymus were occasionally observed in treated animals as well as in controls.

A generalized increase in size of lymph nodes was noted in male No. 2523, receiving 200 mg/kg/day of the test compound.

#### **Final Phase Sacrifice (Day 43)**

Fairly good general condition was noted in one male treated with 800 mg/kg/day (No. 2530). Small prostate was noted in the same animal as well as in one control male (No. 2533).

### 12.3.3. Histopathology

(Table 13, Appendix 12)

#### End of treatment (Days 29-30)

Changes considered as indirectly related to treatment with the test compound were observed in the hematopoietic system.

Moderately reduced cellularity of the bone marrow and severe involution of the thymus were noted in a high dose male (No. 2517), accompanied by atrophy of the adipose tissue with grades ranging from slight to moderate in the sternal and femoral marrow spaces and in the fat deposits adjacent to the renal pelvis. Minimally reduced cellularity was also noted in the bone marrow of one male treated with 200 mg/kg/day (No. 2523). The changes observed in the bone marrow in both animals, and in the thymus and adipose tissue in the high-dose male were interpreted as a consequence of body weight loss.

#### Final Phase Sacrifice (Day 43)

No clear treatment related changes were noted in the hematopoietic system of high-dose animals at the end of the recovery period. The increased severity of involution noted in the thymus of both sexes compared with controls was considered related to body weight loss.

Additional changes of doubtful toxicological significance were noted as follows.

At the end of treatment period, corpora lutea were observed in all females at 200 and 800 mg/kg/day dose levels and in two out of three females treated with 50 mg/kg/day (Table 14). The situation of the stage of estrus of female animals is summarized in Table 15. The stage of estrus was assessed on the base of the comprehensive microscopic appearance of ovaries, uterus and vagina [5]. All three control animals sacrificed at the end of the treatment were immature. On the contrary, the majority of the treated animals sacrificed at the same timepoint were in diestrus, while one low dose was in estrus and one was in metestrus. The significance of this finding is discussed later (see 13.Discussion).

## 12.4. Systemic Exposure Evaluation

(Appendix 13)

### Day 1

Mean  $\pm$ SD systemic exposure to Fexinidazole is reported in the following table

Dose mg/kg	Male			Female		
	C <sub>max</sub> ng/mL	t <sub>max</sub> hour	AUC <sub>0-t</sub> (last) ng·hour/mL	C <sub>max</sub> ng/mL	t <sub>max</sub> hour	AUC <sub>0-t</sub> (last) ng·hour/mL
50 (n=3)	31.2 $\pm$ 12.4	0.5 $\pm$ 0	140 $\pm$ 147	42.4 $\pm$ 10.6	1 $\pm$ 0.87	237 $\pm$ 105
200 (n=3)	54.9 $\pm$ 10.8	1 $\pm$ 0.87	419 $\pm$ 61.4	84.1 $\pm$ 36.7	1 $\pm$ 0	454 $\pm$ 119
800 (n=5)	100 $\pm$ 21.2	1.1 $\pm$ 0.55	776 $\pm$ 182	184 $\pm$ 75.6	1.2 $\pm$ 0.45	895 $\pm$ 437

At each dose, no relevant gender difference was observed in terms of  $C_{max}$  and  $AUC_{0-t(last)}$  values. The maximal plasma concentrations of fexinidazole were promptly achieved, on average at 1 hour post dosing.  $AUC_{0-t(last)}$  values of fexinidazole increased with the dose

Mean  $\pm$ SD systemic exposure to the sulfone metabolite is reported in the following table

Dose mg/kg	Male			Female		
	$C_{max}$ $\mu$ g/mL	$t_{max}$ Hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL
50 (n=3)	7.17 $\pm$ 1.74	8 $\pm$ 0	126 $\pm$ 28.1	10 $\pm$ 1.6	6.67 $\pm$ 2.31	170 $\pm$ 37.8
200 (n=3)	17.2 $\pm$ 1.69	13.3 $\pm$ 9.24	338 $\pm$ 50.8	18.1 $\pm$ 3.42	12 $\pm$ 10.6	358 $\pm$ 85.7
800 (n=5)	38.6 $\pm$ 2.83	17.6 $\pm$ 8.76	705 $\pm$ 94.9	33.6 $\pm$ 10.9	11.2 $\pm$ 7.16	614 $\pm$ 216

At each dose, the levels of the metabolite were similar in males and females.  $T_{max}$  values of the metabolite were achieved later than for the parent compound. The systemic exposure to the metabolite increased with the dose.

The systemic exposure to the sulfone metabolite was definitely higher than that to the parent compound.

Mean  $\pm$ SD systemic exposure to the sulfoxide metabolite is reported in the following table

Dose mg/kg	Male			Female		
	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL
50 (n=3)	3.55 $\pm$ 1.3	1 $\pm$ 0	19.2 $\pm$ 5.82	3.97 $\pm$ 0.74	1.33 $\pm$ 0.58	20 $\pm$ 6.81
200 (n=3)	7.55 $\pm$ 1.03	1.67 $\pm$ 0.58	50.7 $\pm$ 8.61	8.7 $\pm$ 3.95	0.83 $\pm$ 0.29	52.1 $\pm$ 20.6
800 (n=5)	13.4 $\pm$ 3.22	1.5 $\pm$ 0.71	104 $\pm$ 11.3	15.6 $\pm$ 4.64	1.6 $\pm$ 0.55	121 $\pm$ 44.4

At each dose, the levels of the metabolite were similar in males and females. The maximal plasma concentrations of the sulfoxide metabolite were rapidly achieved, on average 1 - 2 hours post dosing.

The systemic exposure to the metabolite increased with the dose (Figures 26 - 27).

The systemic exposure to the metabolite was definitely higher than that to the parent compound.

#### Repeated dosing

Day 14 and Day 28 mean  $\pm$ SD systemic exposure to fexinidazole is reported in the following table

Dose mg/kg/day	Male			Female		
	$C_{max}$ ng/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ ng·hour/mL	$C_{max}$ ng/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ ng·hour/mL
	Day 14					
50 (n=3)	26.5 $\pm$ 13	0.5 $\pm$ 0	52.1 $\pm$ 29.4	41.9 $\pm$ 2.2	1.67 $\pm$ 0.58	246 $\pm$ 117
200 (n=3)	78.1 $\pm$ 23.5	1 $\pm$ 0.87	452 $\pm$ 41.1	77.7 $\pm$ 50.8	2 $\pm$ 0	443 $\pm$ 217
800 (n=5)	128 $\pm$ 56.9	1 $\pm$ 0	929 $\pm$ 268	152 $\pm$ 44	1.4 $\pm$ 0.55	1170 $\pm$ 309
	Day 28					
50 (n=3)	20.3 $\pm$ 7.89	1 $\pm$ 0	124 $\pm$ 67	36.3 $\pm$ 15.1	1 $\pm$ 0	87.1 $\pm$ 38.1
200 (n=3)	57.9 $\pm$ 12.5	1 $\pm$ 0	395 $\pm$ 15.8	73 $\pm$ 12	1 $\pm$ 0	377 $\pm$ 83.5
800 (n=5)	86.2 $\pm$ 38.5	1.2 $\pm$ 0.4	736 $\pm$ 141	101 $\pm$ 47.1	1 $\pm$ 0	956 $\pm$ 378

At each dose, the levels of fexinidazole were similar in both genders after administration on Day 14 and Day 28. The maximal plasma concentrations of fexinidazole were achieved, on average, 1 - 2 hours post dosing. The systemic exposure to fexinidazole increased with the dose (Figures 22 - 23).  $C_{max}$  and  $AUC_{0-t(last)}$  accumulation ratios were about 1.

Day 14 and Day 28 mean  $\pm$ SD systemic exposure to the sulfone metabolite is reported in the following table

Dose mg/kg/day	Male			Female		
	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL
	Day 14					
50 (n=3)	5.57 $\pm$ 2.19	4 $\pm$ 0	78 $\pm$ 35.3	9.98 $\pm$ 1.25	6.67 $\pm$ 2.31	173 $\pm$ 26.9
200 (n=3)	22 $\pm$ 5.59	5.33 $\pm$ 2.31	387 $\pm$ 49.5	21.5 $\pm$ 2.42	5.33 $\pm$ 2.31	381 $\pm$ 61.2
800 (n=5)	34.6 $\pm$ 7.42	5.6 $\pm$ 2.19	640 $\pm$ 163	38.6 $\pm$ 4.73	8 $\pm$ 0	667 $\pm$ 67.8
	Day 28					
50 (n=3)	7.11 $\pm$ 1.21	8 $\pm$ 0	121 $\pm$ 19.1	6.79 $\pm$ 0.56	3.33 $\pm$ 1.15	107 $\pm$ 22.5
200 (n=3)	14 $\pm$ 3.31	4 $\pm$ 4	258 $\pm$ 48	15.4 $\pm$ 2.66	11.7 $\pm$ 10.1	277 $\pm$ 29.9
800 (n=5)	20.8 $\pm$ 4.14	12.4 $\pm$ 9.81	388 $\pm$ 68.2 <sup>(1)</sup>	26 $\pm$ 7.7	7.2 $\pm$ 1.79	477 $\pm$ 145 <sup>(1)</sup>
			601 $\pm$ 29 <sup>(2)</sup>			693 $\pm$ 351 <sup>(2)</sup>
<sup>(1)</sup> AUC <sub>0-24</sub> ; <sup>(2)</sup> n=2						

At each dose, the levels of the metabolite were similar in both genders.  $T_{max}$  values of the metabolite were achieved later than for the parent compound. On Day 28 after 800 mg/kg/day, mean  $\pm$ SD apparent terminal half-lives were 6.7  $\pm$ 0.7 and 7.8  $\pm$ 0.7 (n=2) hours in males and females, respectively. After the three doses, systemic exposure to the metabolite increased with the dose (Figures 24 - 25). Accumulation ratios, in terms of both  $C_{max}$  and  $AUC_{0-t(last)}$ , were about 1.

The systemic exposure to the metabolite was remarkably higher than that to the parent compound.

Day 14 and Day 28 mean  $\pm$ SD systemic exposure to the sulfoxide metabolite is reported in the following table

Dose mg/kg/day	Male			Female		
	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g·hour/mL
	Day 14					
50 (n=3)	2.24 $\pm$ 0.45	1 $\pm$ 0	8.51 $\pm$ 2.53	3.73 $\pm$ 0.73	1.67 $\pm$ 0.58	18.8 $\pm$ 2.06
200 (n=3)	8.96 $\pm$ 2.53	2 $\pm$ 0	56.1 $\pm$ 9.96	9.02 $\pm$ 3.69	2 $\pm$ 0	57.2 $\pm$ 24.3
800 (n=5)	12.5 $\pm$ 2.85	1.2 $\pm$ 0.45	113 $\pm$ 39.9	14.8 $\pm$ 5.1	2 $\pm$ 1.22	144 $\pm$ 37.1
	Day 28					
50 (n=3)	1.83 $\pm$ 0.57	1.67 $\pm$ 0.58	14.2 $\pm$ 2.72	2.72 $\pm$ 0.73	1 $\pm$ 0	9.88 $\pm$ 2.72
200 (n=3)	5.76 $\pm$ 1.17	1.33 $\pm$ 0.58	42.2 $\pm$ 6.46	5.43 $\pm$ 0.34	1 $\pm$ 0	33.8 $\pm$ 1.65
800 (n=5)	9.35 $\pm$ 3.55	1.6 $\pm$ 0.55	74.3 $\pm$ 14.4 <sup>(1)</sup>	9.48 $\pm$ 3.38	1.4 $\pm$ 0.55	89 $\pm$ 45.2
			121 $\pm$ 33 <sup>(2)</sup>			
<sup>(1)</sup> AUC <sub>0-24</sub> ; <sup>(2)</sup> n=2						

At each dose, the levels of the metabolite were similar in both genders. The maximal plasma concentrations of the sulfoxide metabolite were promptly achieved, on average, 1 - 2 hours



post dosing. On Day 28 after 800 mg/kg/day, mean  $\pm$ SD apparent terminal half-lives were  $9.4 \pm 5.4$  (n=2) hours in males. After the three doses, the systemic exposure to the metabolite increased with the dose (Figures 26 - 27). Accumulation ratios, in terms of both  $C_{max}$  and  $AUC_{0-t(last)}$ , were about 1.

The systemic exposure to the metabolite was remarkably higher than that to the parent compound.

### 13. DISCUSSION

Fexinidazole was given daily for twenty-eight days to five (control and high dose) or three (low and mid dose) beagle dogs/sex/dose at the doses of 0 (control group), 50, 200 and 800 mg/kg/day. The compound was administered orally, by gavage, as a suspension in 5% Tween 80 / 0.5% Methocel in a volume of 10 mL/kg/day. The control group received the vehicle alone (5% Tween 80 in 0.5% Methocel).

No drug-related changes were observed at electrocardiographic and ophthalmoscopic examination.

No mortality and no drug-related clinical signs were observed.

Slight to moderate, progressive body weight loss was observed in a few males and in the majority of females given 800 mg/kg/day. A slight to moderate reduction in food intake was seen during the treatment period in the same females given 800 mg/kg/day that showed body weight loss, with normalization during the recovery period.

Similar effects on body weight and food consumption were observed in a previous repeated dose toxicity study in the dog with this same compound [2], [3].

A minimal to slight decrease in lymphocytes was observed mainly at the high dose in both sexes. Other changes observed at hematology and clinical chemistry were not dose-related or present only in single instances and thus considered of no toxicological relevance.

No clear cut treatment-related histological changes were identified in animals treated with the test compound when compared with controls.

The minimally to moderately reduced cellularity in the bone marrow observed in one male treated with 200 mg/kg/day and in one high dose male (No. 2517), and the severe involution of the thymus observed in the high dose male were considered as changes secondary to body weight loss, which was more prominent in this last male with respect to other males given the same dose. This interpretation would be further supported by the occurrence of atrophy of the adipose tissue, noted in the animal treated with the high dose, both in the marrow spaces of the sternum and femur [4] and in the fat deposits adjacent to the renal pelvis.

At the end of treatment period, corpora lutea were observed in all females at 200 and 800 mg/kg/day dose levels and in two out of three females treated with 50 mg/kg/day, while they were not present in the ovaries of control females, correlating with the increase in absolute and relative weight of the ovaries and with the differences in the stage of estrus noted in treated animals compared to controls.

The odd distribution of the stage of estrus within the groups, in animals with a quite homogeneous age at the time of necropsy (about 9.5 month), could suggest an effect of the test compound in terms of induction of estrus in treated animals, independently from the dose administered. Nevertheless, the two control animals sacrificed after recovery were both in diestrus and thus already cycling (i.e., mature) two weeks before, at the time of the end-of-treatment sacrifice, thus re-equilibrating the distribution of estrus stage with the treated groups at that time.

On the base of these considerations, the distribution observed in animals at the end of treatment is considered most likely due to the incidental occurrence of immature animals only in the control group and there is not a clear influence of the test compound on the stage of estrus of the animals in the study.

After single and repeated administrations at the three dose levels, no relevant gender difference in the systemic exposure to fexinidazole was observed. AUCs of fexinidazole increased less than expected assuming dose proportionality in the dose range investigated. No accumulation of fexinidazole was observed.

Fexinidazole was extensively metabolized to the sulfone and sulfoxide derivatives after both single and repeated administration. No accumulation of either metabolite was observed.

## 14. CONCLUSIONS

Fexinidazole, given orally to beagle dogs at the doses of 50, 200 and 800 mg/kg/day for 28 consecutive days, was well tolerated.

Slight to moderate body weight loss and reduction in food intake was observed at the dose of 800 mg/kg/day during the treatment period.

A minimal to slight decrease in lymphocytes was seen at the high dose.

Fexinidazole was extensively metabolized to the sulfone and sulfoxide derivatives both after single and repeated administration.

In the condition applied in the present study, the dose of 200 mg/kg/day can be considered as the NOEL.

## 15. REFERENCES

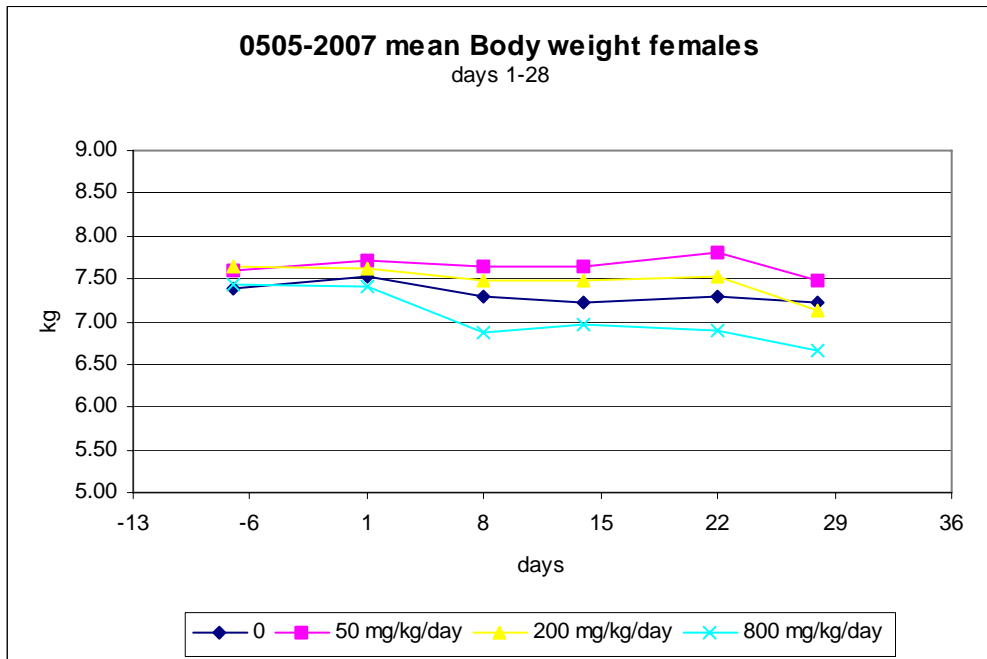
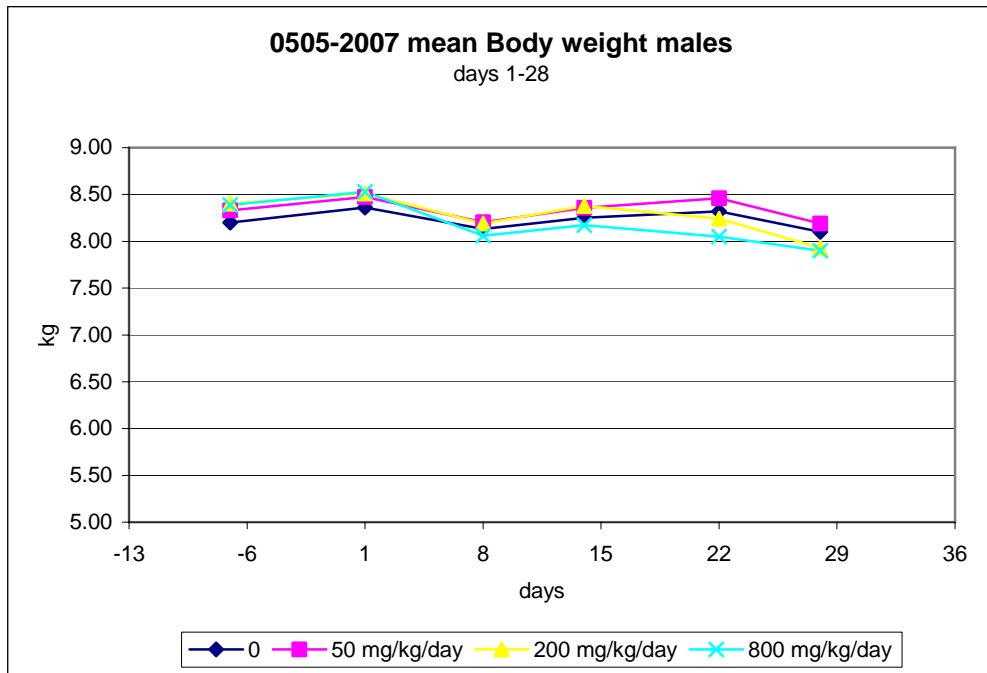
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## 16. FIGURES

### 16.1. Body weight

(during treatment period)



## **TABLES**

***Table 1 Clinical Signs***

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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days -8--1	Group Number Number of Animals <sup>+</sup>	M a l e s							
		1		2		3		4	
		5		3		3		5	
		a	(b)	a	(b)	a	(b)	a	(b)
Normal									
	NORMAL/NO SIGNIFICANT SIGNS	5	(6.6)	3	(7.3)	3	(6.7)	5	(7.4)
GASTRO-INTESTINAL FUNCTIONS									
	DIARRHEA	1	(2.0)	0	(0.0)	0	(0.0)	0	(0.0)
	SOFT STOOL	4	(1.3)	1	(2.0)	3	(1.3)	2	(1.5)
Group 1:Vehicle		Group 2:50 mg/kg/day		Group 3:200 mg/kg/day		Group 4:800 mg/kg/day			

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign

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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days -8--1	Group Number Number of Animals <sup>+</sup>	F e m a l e s							
		1		2		3		4	
		5	3	3	5				
		a	(b)	a	(b)	a	(b)	a	(b)
Normal									
NORMAL/NO SIGNIFICANT SIGNS		5	(7.8)	3	(7.3)	3	(6.7)	5	(7.6)
GASTRO-INTESTINAL FUNCTIONS									
SOFT STOOL		1	(1.0)	1	(2.0)	2	(2.0)	1	(1.0)
FOOD/WATER INTAKE									
REDUCED FOOD INTAKE		0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Group 1:Vehicle	Group 2:50 mg/kg/day	Group 3:200 mg/kg/day		Group 4:800 mg/kg/day					

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign



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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days 1-30	Group Number Number of Animals <sup>+</sup>	M a l e s								
		1		2		3		4		
		5		3		3		5		
		a	(b)	a	(b)	a	(b)	a	(b)	
Normal										
	NORMAL/NO SIGNIFICANT SIGNS	5	(29.6)	3	(29.0)	3	(29.3)	5	(29.6)	
GASTRO-INTESTINAL FUNCTIONS										
	DIARRHEA	3	(1.7)	1	(5.0)	0	(0.0)	4	(1.3)	
	SOFT STOOL	5	(6.4)	2	(6.5)	1	(3.0)	5	(4.0)	
FOOD/WATER INTAKE										
	REDUCED FOOD INTAKE	2	(1.0)	1	(6.0)	1	(3.0)	1	(1.0)	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign

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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days 1-30	Group Number Number of Animals <sup>+</sup>	F e m a l e s								
		1		2		3		4		
		5	3	3	5					
		a	(b)	a	(b)	a	(b)	a	(b)	
Normal										
	NORMAL/NO SIGNIFICANT SIGNS	5	(29.6)	3	(29.3)	3	(29.3)	5	(29.4)	
GASTRO-INTESTINAL FUNCTIONS										
	DIARRHEA	3	(2.3)	0	(0.0)	1	(4.0)	2	(1.0)	
	EMESIS OF FOOD	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)	
	SOFT STOOL	5	(2.6)	2	(2.0)	2	(5.0)	3	(1.0)	
FOOD/WATER INTAKE										
	REDUCED FOOD INTAKE	1	(1.0)	1	(1.0)	2	(2.5)	5	(12.8)	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign

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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days 31-43	Group Number Number of Animals <sup>+</sup>	M a l e s								
		1		2		3		4		
		5		3		3		5		
		a	(b)	a	(b)	a	(b)	a	(b)	
Normal										
	NORMAL/NO SIGNIFICANT SIGNS	2	(12.0)	0	(0.0)	0	(0.0)	2	(12.5)	
GASTRO-INTESTINAL FUNCTIONS										
	DIARRHEA	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)	
	SOFT STOOL	2	(1.0)	0	(0.0)	0	(0.0)	0	(0.0)	
Group 1:Vehicle		Group 2:50 mg/kg/day		Group 3:200 mg/kg/day		Group 4:800 mg/kg/day				

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign

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Table 1  
Group Incidence of Clinical Signs

Study Number: 0505-2007

Fexinidazole

Study Days 31-43	Group Number Number of Animals <sup>+</sup>	F e m a l e s							
		1		2		3		4	
		5		3		3		5	
		a	(b)	a	(b)	a	(b)	a	(b)
Normal									
NORMAL/NO SIGNIFICANT SIGNS		2	(12.0)	0	(0.0)	0	(0.0)	2	(12.0)
GASTRO-INTESTINAL FUNCTIONS									
SOFT STOOL		2	(1.0)	0	(0.0)	0	(0.0)	2	(1.0)
Group 1:Vehicle	Group 2:50 mg/kg/day	Group 3:200 mg/kg/day				Group 4:800 mg/kg/day			

Key: + = Number of animals alive at start of interval  
a = Number of animals affected  
(b) = Mean number of animal days that the group displayed the sign

***Table 2 Body Weights***

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Table 2  
Body Weights (kg)

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Study Day	M a l e s								
			-8"	1#	8	14	22	28	35	40	
1	Vehicle	N	5	5	5	5	5	5	5	2	2
		Mean	8.20	8.36	8.14	8.25	8.32	8.10	7.58	7.71	
		Sdev	0.444	0.436	0.410	0.423	0.472	0.411	0.240	0.153	
2	50 mg/kg/day	N	3	3	3	3	3	3	3	0	0
		Mean	8.33	8.47	8.20	8.36	8.46	8.19	-	-	
		Sdev	1.160	1.163	1.165	1.155	1.271	1.081	-	-	
3	200 mg/kg/day	N	3	3	3	3	3	3	3	0	0
		Mean	8.40	8.51	8.19	8.37	8.24	7.93	-	-	
		Sdev	0.691	0.482	0.642	0.479	0.531	0.351	-	-	
4	800 mg/kg/day	N	5	5	5	5	5	5	5	2	2
		Mean	8.39	8.53	8.06	8.17	8.05	7.90	7.55	7.75	
		Sdev	0.734	0.954	0.993	1.049	1.010	1.117	1.131	1.039	

Note: " = Pretest phase; # = Test period

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Table 2  
Body Weights (kg)

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Study Day	F e m a l e s							
			-8"	1#	8	14	22	28	35	40
1	Vehicle	N	5	5	5	5	5	5	2	2
		Mean	7.37	7.52	7.29	7.22	7.29	7.23	8.06	8.21
		Sdev	0.471	0.592	0.621	0.737	0.783	1.020	0.445	0.426
2	50 mg/kg/day	N	3	3	3	3	3	3	0	0
		Mean	7.60	7.70	7.65	7.63	7.80	7.49	-	-
		Sdev	0.674	0.872	0.762	0.847	0.784	0.803	-	-
3	200 mg/kg/day	N	3	3	3	3	3	3	0	0
		Mean	7.65	7.63	7.48	7.48	7.52	7.13	-	-
		Sdev	0.960	0.807	0.808	0.862	0.770	0.809	-	-
4	800 mg/kg/day	N	5	5	5	5	5	5	2	2
		Mean	7.42	7.41	6.87	6.96	6.90	6.65	6.81	6.95
		Sdev	0.391	0.546	0.670	0.671	0.677	0.659	0.601	0.592

Note: " = Pretest phase; # = Test period

***Table 3 ECG Examinations***



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Table 3  
Incidence of ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

Study Day	Group:	M a l e s			
		1	2	3	4
-5					
ECG Notes	/No ECG abnormalities detected	1	0	0	2
	/Respiratory Sinus Arrhythmia	4	3	3	3
24					
ECG Notes	/No ECG abnormalities detected	1	3	1	2
	/Respiratory Sinus Arrhythmia	4	0	2	3
38					
ECG Notes	/No ECG abnormalities detected	0	0	0	1
	/Respiratory Sinus Arrhythmia	2	0	0	1

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 3

Incidence of ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

Study Day	Group:	F e m a l e s			
		1	2	3	4
-5					
ECG Notes	/No ECG abnormalities detected	2	2	0	3
	/Respiratory Sinus Arrhythmia	3	1	3	2
24					
ECG Notes	/No ECG abnormalities detected	1	2	0	3
	/Respiratory Sinus Arrhythmia	4	1	3	2
38					
ECG Notes	/No ECG abnormalities detected	2	0	0	1
	/Respiratory Sinus Arrhythmia	0	0	0	1
Group 1:Vehicle		Group 2:50 mg/kg/day		Group 3:200 mg/kg/day	
				Group 4:800 mg/kg/day	

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Table 3  
Day -5 ECG Examinations  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
Heart rate bpm	N	5	3	3	5	5	3	3	5	
	Mean	93.	82.	81.	95.	95.	116.	93.	102.	
	Sdev	6.2	28.0	19.8	25.6	21.5	16.2	19.7	20.5	
R-R interval ms	N	5	3	3	5	5	3	3	5	
	Mean	642.	780.	769.	672.	664.	523.	658.	599.	
	Sdev	41.8	221.6	184.0	204.8	176.5	70.9	124.6	102.4	
P wave duration ms	N	5	3	3	5	5	3	3	5	
	Mean	38.	37.	37.	39.	41.	37.	38.	36.+	
	Sdev	1.8	1.5	4.4	3.0	3.4	2.1	1.7	2.3	
P-R interval ms	N	5	3	3	5	5	3	3	5	
	Mean	87.	89.	97.	86.	88.	83.	92.	87.	
	Sdev	5.8	9.3	2.1	8.5	12.8	2.5	5.8	11.3	
QRS complex duration ms	N	5	3	3	5	5	3	3	5	
	Mean	47.	46.	55.	44.	46.	51.	49.	50.	
	Sdev	11.7	2.6	9.0	1.3	7.0	7.2	5.5	10.6	
Q-T interval ms	N	5	3	3	5	5	3	3	5	
	Mean	179.	186.	190.	179.	185.	180.	183.	177.	
	Sdev	1.8	11.5	13.6	6.8	6.5	1.2	10.1	6.4	
Q-T interval (Fridericia) ms	N	5	3	3	5	5	3	3	5	
	Mean	208.	204.	209.	207.	214.	224.	210.	211.	
	Sdev	5.7	8.6	10.3	19.9	14.3	10.6	2.7	8.7	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test

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 Table 3  
 Day -5 ECG Examinations  
 Pretest phase

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
Mean Electrical Axis degree	N	5	3	3	5	5	3	3	5
	Mean	45.	51.	59.	38.	46.	44.	42.	50.
	Sdev	60.1	12.2	12.2	11.7	32.1	10.0	28.4	24.8
P wave amplitude mV	N	5	3	3	5	5	3	3	5
	Mean	0.30	0.36	0.35	0.41	0.32	0.39	0.44	0.37
	Sdev	0.072	0.042	0.059	0.092	0.143	0.139	0.087	0.093
Q wave amplitude mV	N	5	3	3	5	5	3	3	5
	Mean	-0.37	-0.37	-0.50	-0.48	-0.39	-0.67	-0.69	-0.51
	Sdev	0.168	0.144	0.242	0.181	0.128	0.389	0.160	0.348
R wave amplitude mV	N	5	3	3	5	5	3	3	5
	Mean	1.88	2.99	3.01	2.17	2.45	2.31	2.71	3.00
	Sdev	0.839	0.483	0.449	0.483	0.348	0.829	0.578	1.378
S wave amplitude mV	N	5	3	3	5	5	3	3	5
	Mean	-0.19	-0.14	-0.10	-0.16	-0.31	-0.30	-0.23	-0.12
	Sdev	0.098	0.110	0.058	0.080	0.163	0.167	0.229	0.063
S-T segment deviation mV	N	5	3	3	5	5	3	3	5
	Mean	-0.07	-0.04	-0.10	-0.06	-0.03	-0.04	-0.05	-0.07
	Sdev	0.057	0.059	0.058	0.025	0.062	0.166	0.026	0.060
T wave amplitude mV	N	5	3	3	5	5	3	3	5
	Mean	0.20	0.10	0.17	0.15	0.20	-0.22	0.55	0.05
	Sdev	0.333	0.165	0.225	0.348	0.243	0.411	0.191	0.267

Group 1:Vehicle                      Group 2:50 mg/kg/day                      Group 3:200 mg/kg/day                      Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

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 Table 3  
 Day 24 ECG Examinations  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
Heart rate bpm	N	5	3	3	5	5	3	3	5
	Mean	95.	102.	97.	100.	99.	108.	112.	110.
	Sdev	19.2	38.3	36.7	13.1	20.2	11.6	14.4	32.3
R-R interval ms	N	5	3	3	5	5	3	3	5
	Mean	646.	665.	669.	606.	629.	555.	543.	580.
	Sdev	117.3	316.0	213.1	82.6	143.3	63.9	75.9	169.7
P wave duration ms	N	5	3	3	5	5	3	3	5
	Mean	35.	34.	40.	37.	42.	35.+	40.	38.
	Sdev	3.2	2.3	4.2	3.8	3.5	1.5	1.0	4.2
P-R interval ms	N	5	3	3	5	5	3	3	5
	Mean	81.	82.	90.	86.	83.	89.	87.	86.
	Sdev	8.0	6.4	7.8	5.9	6.6	0.6	2.5	10.0
QRS complex duration ms	N	5	3	3	5	5	3	3	5
	Mean	47.	45.	53.	44.	48.	48.	53.	53.
	Sdev	5.9	3.8	7.6	1.9	5.6	6.1	3.5	7.9
Q-T interval ms	N	5	3	3	5	5	3	3	5
	Mean	189.	187.	196.	197.	186.	184.	192.	192.
	Sdev	9.9	14.0	8.5	8.1	13.5	10.1	7.6	16.5
Q-T interval (Fridericia) ms	N	5	3	3	5	5	3	3	5
	Mean	219.	219.	227.	233.	218.	224.	235.+	231.
	Sdev	5.7	15.4	19.2	12.0	6.7	5.8	8.9	9.7

Group 1: Vehicle

Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test

CONFIDENTIAL  
 Table 3  
 Day 24 ECG Examinations  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
Mean Electrical Axis degree	N	5	3	3	5	5	3	3	5	
	Mean	52.	57.	61.	63.	53.	56.	50.	53.	
	Sdev	43.2	6.7	2.1	23.1	36.3	9.2	19.1	23.7	
P wave amplitude mV	N	5	3	3	5	5	3	3	5	
	Mean	0.35	0.39	0.38	0.41	0.40	0.40	0.48	0.40	
	Sdev	0.059	0.012	0.036	0.086	0.070	0.062	0.167	0.162	
Q wave amplitude mV	N	5	3	3	5	5	3	3	5	
	Mean	-0.32	-0.40	-0.63	-0.55	-0.42	-0.57	-0.68	-0.46	
	Sdev	0.110	0.111	0.460	0.295	0.220	0.240	0.137	0.314	
R wave amplitude mV	N	5	3	3	5	5	3	3	5	
	Mean	2.05	3.17	3.24	2.25	2.62	2.62	3.05	2.88	
	Sdev	0.904	0.706	0.299	0.406	0.443	0.691	0.813	1.182	
S wave amplitude mV	N	5	3	3	5	5	3	3	5	
	Mean	-0.16	-0.13	-0.16	-0.23	-0.26	-0.38	-0.26	-0.12	
	Sdev	0.104	0.026	0.142	0.130	0.236	0.302	0.254	0.076	
S-T segment deviation mV	N	5	3	3	5	5	3	3	5	
	Mean	-0.05	-0.08	-0.10	-0.07	-0.02	-0.02	-0.08	-0.06	
	Sdev	0.028	0.084	0.066	0.077	0.054	0.038	0.025	0.072	
T wave amplitude mV	N	5	3	3	5	5	3	3	5	
	Mean	0.29	-0.20	0.02	-0.14	0.40	0.03	0.46	-0.02+	
	Sdev	0.286	0.168	0.335	0.222	0.209	0.313	0.135	0.218	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test

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 Table 3  
 Day 38 ECG Examinations  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
Heart rate bpm	N	2	0	0	2	2	0	0	2
	Mean	83.	-	-	91.	101.	-	-	102.
	Sdev	15.6	-	-	35.4	35.4	-	-	28.3
R-R interval ms	N	2	0	0	2	2	0	0	2
	Mean	734.	-	-	708.	629.	-	-	609.
	Sdev	137.9	-	-	273.7	219.9	-	-	169.0
P wave duration ms	N	2	0	0	2	2	0	0	2
	Mean	39.	-	-	42.	41.	-	-	40.
	Sdev	4.9	-	-	3.5	4.9	-	-	2.8
P-R interval ms	N	2	0	0	2	2	0	0	2
	Mean	87.	-	-	101.	102.	-	-	90.
	Sdev	9.2	-	-	2.8	19.8	-	-	2.1
QRS complex duration ms	N	2	0	0	2	2	0	0	2
	Mean	51.	-	-	51.	51.	-	-	49.
	Sdev	3.5	-	-	11.3	5.7	-	-	7.8
Q-T interval ms	N	2	0	0	2	2	0	0	2
	Mean	199.	-	-	203.	194.	-	-	204.
	Sdev	7.1	-	-	14.8	10.6	-	-	10.6
Q-T interval (Fridericia) ms	N	2	0	0	2	2	0	0	2
	Mean	222.	-	-	230.	228.	-	-	241.
	Sdev	21.7	-	-	13.2	14.4	-	-	9.8

Group 1: Vehicle

Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

CONFIDENTIAL  
 Table 3  
 Day 38 ECG Examinations  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
Mean Electrical Axis degree	N	2	0	0	2	2	0	0	2
	Mean	19.	-	-	84.	57.	-	-	70.
	Sdev	53.7	-	-	7.8	22.6	-	-	6.4
P wave amplitude mV	N	2	0	0	2	2	0	0	2
	Mean	0.30	-	-	0.39	0.39	-	-	0.36
	Sdev	0.057	-	-	0.078	0.127	-	-	0.141
Q wave amplitude mV	N	2	0	0	2	2	0	0	2
	Mean	-0.26	-	-	-0.34	-0.39	-	-	-0.46
	Sdev	0.141	-	-	0.184	0.014	-	-	0.269
R wave amplitude mV	N	2	0	0	2	2	0	0	2
	Mean	1.61	-	-	2.23	2.64	-	-	2.98
	Sdev	0.997	-	-	0.332	0.403	-	-	1.301
S wave amplitude mV	N	2	0	0	2	2	0	0	2
	Mean	-0.30	-	-	-0.17	-0.36	-	-	-0.09
	Sdev	0.049	-	-	0.014	0.283	-	-	0.042
S-T segment deviation mV	N	2	0	0	2	2	0	0	2
	Mean	-0.03	-	-	-0.07	0.05	-	-	0.00
	Sdev	0.064	-	-	0.014	0.064	-	-	0.071
T wave amplitude mV	N	2	0	0	2	2	0	0	2
	Mean	0.22	-	-	0.27	-0.04	-	-	0.18
	Sdev	0.141	-	-	0.269	0.573	-	-	0.071

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.



***Table 4 Ophthalmoscopic Examination***

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Table 4  
Incidence of Ophthalmoscopic Findings

Fexinidazole

Study Number: 0505-2007

Study Day	Group:	M a l e s					
		1	2	3	4		
-5	NORMAL /Normal (No Abnormal Findings)	5	3	3	5		
24	NORMAL /Normal (No Abnormal Findings)	5	3	3	5		
38	NORMAL /Normal (No Abnormal Findings)	2	0	0	2		
Group 1:Vehicle		Group 2:50 mg/kg/day		Group 3:200 mg/kg/day		Group 4:800 mg/kg/day	

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Table 4

Incidence of Ophthalmoscopic Findings

Fexinidazole

Study Number: 0505-2007

Study Day	Group:	F e m a l e s			
		1	2	3	4
-5	NORMAL /Normal (No Abnormal Findings)	5	3	3	5
24	NORMAL /Normal (No Abnormal Findings)	4	3	3	5
	CORNEA /opacity area/s, monolateral	1	0	0	0
38	NORMAL /Normal (No Abnormal Findings)	1	0	0	2
	CORNEA /opacity area/s, monolateral	1	0	0	0
Group 1:Vehicle		Group 2:50 mg/kg/day		Group 3:200 mg/kg/day	
				Group 4:800 mg/kg/day	

***Table 5 Hematology***

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Table 5  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
RED BLOOD CELLS 10 <sup>6</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	6.55	7.08	6.74	6.57	6.54	7.46*	6.77	6.81	
	Sdev	0.342	0.498	0.662	0.484	0.298	0.427	0.162	0.403	
HEMOGLOBIN g/dL	N	5	3	3	5	5	3	3	5	
	Mean	14.9	16.2	15.3	15.0	14.9	17.2*	15.4	15.5	
	Sdev	0.86	1.10	1.35	0.96	0.79	0.85	0.65	0.73	
HEMATOCRIT %	N	5	3	3	5	5	3	3	5	
	Mean	42.4	46.0	43.8	42.8	43.9	50.5*	45.2	46.1	
	Sdev	2.45	2.97	4.01	2.84	2.10	2.25	1.69	2.44	
MEAN CORPUSCULAR VOLUME fL	N	5	3	3	5	5	3	3	5	
	Mean	64.8	65.0	65.0	65.2	67.1	67.8	66.8	67.6	
	Sdev	1.07	1.42	0.52	0.89	0.49	0.86	0.96	1.36	
MEAN CORPUSCULAR HEMOGLOBIN pg	N	5	3	3	5	5	3	3	5	
	Mean	22.8	22.8	22.7	22.9	22.7	23.1	22.6	22.8	
	Sdev	0.62	0.70	0.20	0.36	0.23	0.20	0.55	0.67	
MEAN CORPUSCULAR HGB CONC. g/dL	N	5	3	3	5	5	3	3	5	
	Mean	35.2	35.1	34.9	35.1	33.8	34.1	33.9	33.7	
	Sdev	0.44	0.35	0.15	0.29	0.37	0.17	0.40	0.35	
RED CELL DISTRIBUTION WIDTH %	N	5	3	3	5	5	3	3	5	
	Mean	13.2	13.1	13.1	13.1	11.2	11.4	11.4	11.2	
	Sdev	0.53	0.23	0.26	0.26	0.48	0.36	0.15	0.31	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day -7 Hematology Data  
 Pretest phase

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
HEMOGLOBIN DISTRIB. WIDTH g/dL	N	5	3	3	5	5	3	3	5
	Mean	1.59	1.65	1.59	1.62	1.70	1.71	1.67	1.68
	Sdev	0.048	0.040	0.085	0.088	0.044	0.021	0.047	0.041
RETICULOCYTES %	N	5	3	3	5	5	3	3	5
	Mean	0.7	1.1	0.7	0.6	0.5	0.8	0.5	0.5
	Sdev	0.27	0.21	0.17	0.26	0.13	0.25	0.14	0.21
RETICULOCYTES ABS 10 <sup>9</sup> /L	N	5	3	3	5	5	3	3	5
	Mean	48.2	76.1	46.2	42.3	30.3	61.5+	33.7	37.1
	Sdev	18.30	10.24	15.60	19.39	7.54	20.22	9.01	15.87
MEAN CORPUSCOLAR VOL. RETIC. fL	N	5	3	3	5	5	3	3	5
	Mean	85.4	87.4	86.0	85.4	85.7	88.0	84.8	85.3
	Sdev	2.57	2.45	3.33	2.68	1.44	3.67	2.87	3.31
MEAN HEMOGLOBIN CONC. RETIC. g/dL	N	5	3	3	5	5	3	3	5
	Mean	30.5	30.0	30.4	30.8	29.0	28.5	28.7	29.1
	Sdev	0.78	0.95	0.59	0.63	0.62	0.83	0.26	0.71
CELLULAR HEMOGLOBIN RETIC. pg	N	5	3	3	5	5	3	3	5
	Mean	25.9	26.2	26.0	26.2	24.6	25.0	24.3	24.5
	Sdev	0.41	0.76	0.92	0.56	0.38	0.35	0.65	0.75
PLATELETS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	332.	229.	322.	300.	341.	321.	348.	294.
	Sdev	100.0	53.6	85.0	88.3	82.3	89.4	69.6	30.1

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

CONFIDENTIAL  
Table 5  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
MEAN PLATELET VOLUME fL	N	5	3	3	5	5	3	3	5	
	Mean	11.1	11.8	11.4	11.0	9.5	10.5	9.4	9.6	
	Sdev	0.91	0.66	1.97	1.62	1.12	1.46	0.99	0.53	
PLATELET DISTRIBUTION WIDTH %	N	5	3	3	5	5	3	3	5	
	Mean	62.4	63.7	60.7	62.7	56.6	59.6	56.9	54.3	
	Sdev	2.51	4.32	4.91	3.24	6.62	1.83	1.92	3.79	
PLATELET HEMATOCRIT %	N	5	3	3	5	5	3	3	5	
	Mean	0.37	0.27	0.36	0.33	0.32	0.33	0.32	0.28	
	Sdev	0.110	0.056	0.040	0.093	0.083	0.066	0.074	0.016	
WHITE BLOOD CELLS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	8.93	8.50	10.34	8.30	10.50	10.82	9.58	8.07+	
	Sdev	1.218	1.792	1.990	1.632	1.667	1.275	1.092	0.493	
NEUTROPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	5.01	4.74	6.31	4.70	6.12	6.53	5.57	4.59	
	Sdev	0.909	1.311	1.067	1.317	1.129	1.184	2.026	0.517	
LYMPHOCYTES ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	3.07	2.89	3.02	2.77	3.47	3.12	2.92	2.63	
	Sdev	0.370	0.480	0.608	0.525	0.655	0.152	0.870	0.263	
MONOCYTES ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	0.43	0.41	0.64	0.42	0.50	0.53	0.42	0.31	
	Sdev	0.105	0.137	0.361	0.095	0.148	0.129	0.078	0.102	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day -7 Hematology Data  
 Pretest phase

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
EOSINOPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	0.28	0.26	0.21	0.28	0.21	0.43	0.46	0.39
	Sdev	0.162	0.139	0.044	0.219	0.131	0.140	0.483	0.357
BASOPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	0.08	0.14	0.11	0.10	0.14	0.15	0.15	0.10
	Sdev	0.037	0.042	0.023	0.029	0.031	0.031	0.091	0.021
LARGE UNSTAINED CELLS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	0.04	0.06	0.06	0.04	0.07	0.05	0.05	0.04
	Sdev	0.016	0.015	0.021	0.021	0.011	0.010	0.040	0.013
NEUTROPHILS %	N	5	3	3	5	5	3	3	5
	Mean	55.9	55.2	61.2	56.2	58.2	60.1	57.2	56.9
	Sdev	4.69	5.03	2.36	7.00	5.12	3.70	13.89	5.46
LYMPHOCITES %	N	5	3	3	5	5	3	3	5
	Mean	34.7	34.5	29.3	33.6	33.1	29.1	31.2	32.7
	Sdev	4.10	5.57	2.67	4.85	4.58	2.45	11.31	3.55
MONOCYTES %	N	5	3	3	5	5	3	3	5
	Mean	4.9	4.8	5.8	5.1	4.7	4.9	4.4	3.8
	Sdev	0.86	1.04	2.46	1.22	0.72	0.98	0.35	1.30
EOSINOPHILS %	N	5	3	3	5	5	3	3	5
	Mean	3.2	2.9	2.1	3.3	2.0	4.0	5.1	4.8
	Sdev	1.69	1.10	0.53	2.59	1.06	1.66	5.72	4.15

Group 1:Vehicle                      Group 2:50 mg/kg/day                      Group 3:200 mg/kg/day                      Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.



CONFIDENTIAL  
 Table 5  
 Day -7 Hematology Data  
 Pretest phase

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
BASOPHILS %	N	5	3	3	5	5	3	3	5	
	Mean	0.9	1.8	1.1	1.2	1.4	1.4	1.6	1.3	
	Sdev	0.40	0.96	0.15	0.33	0.32	0.26	0.98	0.30	
LARGE UNSTAINED CELLS %	N	5	3	3	5	5	3	3	5	
	Mean	0.5	0.7	0.5	0.5	0.6	0.5	0.6	0.5	
	Sdev	0.18	0.36	0.12	0.25	0.15	0.12	0.46	0.16	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

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Table 5  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
RED BLOOD CELLS 10 <sup>6</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	6.09	7.10	6.16	6.06	6.37	6.97	6.27	6.80
	Sdev	0.466	0.492	0.717	0.449	0.611	0.293	0.323	0.496
HEMOGLOBIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	13.3	15.5	13.4	13.3	13.9	15.5	13.7	14.9
	Sdev	0.89	1.31	1.59	1.00	1.41	0.17	0.91	1.12
HEMATOCRIT %	N	5	3	3	5	5	3	3	5
	Mean	40.1	46.6	40.5	39.7	42.6	46.5	41.2	45.0
	Sdev	2.98	4.05	4.63	2.74	4.19	1.32	2.46	3.50
MEAN CORPUSCULAR VOLUME fL	N	5	3	3	5	5	3	3	5
	Mean	65.8	65.6	65.8	65.6	66.8	66.8	65.6	66.1
	Sdev	1.21	1.39	0.68	0.99	0.64	1.23	0.82	1.20
MEAN CORPUSCULAR HEMOGLOBIN pg	N	5	3	3	5	5	3	3	5
	Mean	21.9	21.9	21.8	22.0	21.8	22.3	21.8	21.9
	Sdev	0.61	0.36	0.49	0.15	0.46	0.71	0.59	0.54
MEAN CORPUSCULAR HGB CONC. g/dL	N	5	3	3	5	5	3	3	5
	Mean	33.3	33.4	33.1	33.5	32.6	33.3	33.2	33.1
	Sdev	0.45	0.81	0.32	0.47	0.59	0.61	0.44	0.29
RED CELL DISTRIBUTION WIDTH %	N	5	3	3	5	5	3	3	5
	Mean	12.2	11.6	12.0	11.9	11.7	12.4	11.4	11.4
	Sdev	0.24	0.53	0.40	0.39	0.39	0.49	0.45	0.23

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

CONFIDENTIAL  
Table 5  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
HEMOGLOBIN DISTRIB. WIDTH g/dL	N	5	3	3	5	5	3	3	5
	Mean	1.81	1.75	1.80	1.81	1.75	1.89	1.72	1.79
	Sdev	0.063	0.075	0.055	0.071	0.085	0.103	0.026	0.047
RETICULOCYTES %	N	5	3	3	5	5	3	3	5
	Mean	1.0	0.7	0.5	0.6	0.6	1.3	0.4	0.5
	Sdev	0.35	0.29	0.11	0.24	0.41	0.64	0.15	0.24
RETICULOCYTES ABS 10 <sup>9</sup> /L	N	5	3	3	5	5	3	3	5
	Mean	60.5	47.8	30.9	33.9	38.7	86.8+	23.8	32.4
	Sdev	21.72	21.01	6.64	15.33	21.27	44.03	8.20	18.19
MEAN CORPUSCOLAR VOL. RETIC. fL	N	5	3	3	5	5	3	3	5
	Mean	89.7	89.5	87.3	87.8	87.7	89.8	86.6	88.3
	Sdev	2.47	2.91	2.64	2.59	1.48	2.60	4.00	2.38
MEAN HEMOGLOBIN CONC. RETIC. g/dL	N	5	3	3	5	5	3	3	5
	Mean	27.5	28.0	27.8	28.3	27.8	27.8	27.7	27.9
	Sdev	0.54	0.92	0.15	0.43	0.32	0.76	0.17	0.43
CELLULAR HEMOGLOBIN RETIC. pg	N	5	3	3	5	5	3	3	5
	Mean	24.5	24.9	24.2	24.7	24.3	24.8	23.9	24.5
	Sdev	0.55	0.40	0.90	0.62	0.44	0.31	1.25	0.65
PLATELETS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5
	Mean	370.	242.	384.	273.	424.	387.	363.	291.+
	Sdev	107.6	13.4	190.0	63.2	48.0	17.2	127.2	35.8

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day 28 Hematology Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
MEAN PLATELET VOLUME fL	N	5	3	3	5	5	3	3	5	
	Mean	10.6	10.9	10.4	10.9	9.1	9.5	10.1	10.3+	
	Sdev	0.79	0.93	1.10	1.46	0.60	0.85	0.40	0.66	
PLATELET DISTRIBUTION WIDTH %	N	5	3	3	5	5	3	3	5	
	Mean	58.7	61.5	58.3	64.4+	50.2	55.2	59.1+	57.4+	
	Sdev	3.36	3.09	0.44	3.86	4.25	4.01	3.77	1.44	
PLATELET HEMATOCRIT %	N	5	3	3	5	5	3	3	5	
	Mean	0.39	0.26	0.38	0.30	0.39	0.37	0.36	0.30	
	Sdev	0.117	0.035	0.145	0.071	0.062	0.015	0.115	0.029	
WHITE BLOOD CELLS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	8.95	7.72	7.78	7.84	11.79	11.06	9.99	7.88+	
	Sdev	1.865	1.203	0.972	1.625	2.592	1.892	1.036	0.746	
NEUTROPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	5.51	4.36	5.07	5.19	7.26	7.34	6.57	4.97+	
	Sdev	1.555	0.794	1.117	1.559	1.680	1.758	0.826	0.763	
LYMPHOCYTES ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	2.75	2.81	2.19	2.09+	3.57	2.62	2.65	2.22*	
	Sdev	0.126	0.400	0.263	0.545	0.712	0.060	0.609	0.375	
MONOCYTES ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	0.44	0.23	0.25	0.32	0.60	0.55	0.49	0.30+	
	Sdev	0.277	0.046	0.045	0.090	0.212	0.105	0.123	0.049	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

CONFIDENTIAL  
Table 5  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
EOSINOPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	0.16	0.20	0.19	0.15	0.22	0.44	0.16	0.29	
	Sdev	0.023	0.058	0.055	0.187	0.196	0.436	0.095	0.263	
BASOPHILS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	0.04	0.07*	0.05	0.04	0.06	0.07	0.07	0.04	
	Sdev	0.013	0.015	0.006	0.013	0.021	0.015	0.031	0.007	
LARGE UNSTAINED CELLS ABS 10 <sup>3</sup> /mcL	N	5	3	3	5	5	3	3	5	
	Mean	0.04	0.05	0.05	0.04	0.08	0.05	0.06	0.06	
	Sdev	0.013	0.006	0.010	0.023	0.021	0.010	0.044	0.024	
NEUTROPHILS %	N	5	3	3	5	5	3	3	5	
	Mean	60.8	56.3	64.6	65.5	61.4	65.9	65.8	62.9	
	Sdev	5.33	2.87	6.99	10.31	3.86	5.40	5.77	5.60	
LYMPHOCITES %	N	5	3	3	5	5	3	3	5	
	Mean	31.8	36.6	28.5	27.2	30.6	24.1	26.5	28.2	
	Sdev	6.05	2.54	5.98	7.70	3.54	4.03	5.00	4.28	
MONOCYTES %	N	5	3	3	5	5	3	3	5	
	Mean	4.7	3.0	3.2	4.2	5.1	5.0	4.8	3.8+	
	Sdev	1.91	0.40	0.81	0.98	0.88	0.25	0.72	0.50	
EOSINOPHILS %	N	5	3	3	5	5	3	3	5	
	Mean	1.8	2.5	2.3	2.1	1.8	4.0	1.7	3.8	
	Sdev	0.42	0.40	0.51	2.91	1.21	3.72	1.16	3.62	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day 28 Hematology Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
BASOPHILS %	N	5	3	3	5	5	3	3	5
	Mean	0.4	0.9*	0.6	0.5	0.5	0.6	0.6	0.5
	Sdev	0.10	0.32	0.15	0.20	0.23	0.10	0.32	0.11
LARGE UNSTAINED CELLS %	N	5	3	3	5	5	3	3	5
	Mean	0.5	0.7	0.6	0.6	0.6	0.5	0.6	0.7
	Sdev	0.04	0.17	0.21	0.38	0.15	0.06	0.46	0.34
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day		Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day 42 Hematology Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
RED BLOOD CELLS 10 <sup>6</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	5.95	-	-	6.50	6.80	-	-	6.57
	Sdev	0.092	-	-	0.537	0.085	-	-	0.042
HEMOGLOBIN g/dL	N	2	0	0	2	2	0	0	2
	Mean	13.1	-	-	14.4	15.3	-	-	14.5
	Sdev	0.71	-	-	1.13	0.42	-	-	0.35
HEMATOCRIT %	N	2	0	0	2	2	0	0	2
	Mean	40.0	-	-	43.8	45.2	-	-	43.2
	Sdev	0.57	-	-	3.11	1.34	-	-	1.77
MEAN CORPUSCULAR VOLUME fL	N	2	0	0	2	2	0	0	2
	Mean	67.3	-	-	67.4	66.4	-	-	65.6
	Sdev	0.07	-	-	0.71	1.06	-	-	2.40
MEAN CORPUSCULAR HEMOGLOBIN pg	N	2	0	0	2	2	0	0	2
	Mean	22.1	-	-	22.1	22.5	-	-	22.0
	Sdev	0.78	-	-	0.00	0.28	-	-	0.42
MEAN CORPUSCULAR HGB CONC. g/dL	N	2	0	0	2	2	0	0	2
	Mean	32.8	-	-	32.8	33.9	-	-	33.6
	Sdev	1.27	-	-	0.28	0.14	-	-	0.49
RED CELL DISTRIBUTION WIDTH %	N	2	0	0	2	2	0	0	2
	Mean	12.8	-	-	12.8	11.4	-	-	12.0
	Sdev	0.07	-	-	0.42	0.57	-	-	0.00

Group 1: Vehicle                      Group 2: 50 mg/kg/day                      Group 3: 200 mg/kg/day                      Group 4: 800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

CONFIDENTIAL  
Table 5  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
HEMOGLOBIN DISTRIB. WIDTH g/dL	N	2	0	0	2	2	0	0	2
	Mean	1.78	-	-	1.97	1.65	-	-	1.75
	Sdev	0.021	-	-	0.085	0.092	-	-	0.049
RETICULOCYTES %	N	2	0	0	2	2	0	0	2
	Mean	1.0	-	-	1.2	0.4	-	-	0.7
	Sdev	0.64	-	-	0.29	0.21	-	-	0.23
RETICULOCYTES ABS 10 <sup>9</sup> /L	N	2	0	0	2	2	0	0	2
	Mean	59.5	-	-	77.7	24.4	-	-	43.3
	Sdev	37.69	-	-	12.45	14.42	-	-	14.42
MEAN CORPUSCOLAR VOL. RETIC. fL	N	2	0	0	2	2	0	0	2
	Mean	91.4	-	-	88.3	85.5	-	-	88.1
	Sdev	3.04	-	-	0.21	1.98	-	-	3.25
MEAN HEMOGLOBIN CONC. RETIC. g/dL	N	2	0	0	2	2	0	0	2
	Mean	27.7	-	-	27.9	29.2	-	-	28.7
	Sdev	0.28	-	-	0.28	0.35	-	-	0.42
CELLULAR HEMOGLOBIN RETIC. pg	N	2	0	0	2	2	0	0	2
	Mean	25.3	-	-	24.6	24.8	-	-	25.2
	Sdev	0.64	-	-	0.21	0.28	-	-	1.27
PLATELETS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	421.	-	-	336.	381.	-	-	334.
	Sdev	26.9	-	-	113.8	108.9	-	-	2.1

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.



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Table 5  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
MEAN PLATELET VOLUME fL	N	2	0	0	2	2	0	0	2
	Mean	10.0	-	-	9.7	9.0	-	-	9.0
	Sdev	1.20	-	-	1.70	0.07	-	-	0.07
PLATELET DISTRIBUTION WIDTH %	N	2	0	0	2	2	0	0	2
	Mean	55.8	-	-	59.8	50.9	-	-	55.0
	Sdev	2.19	-	-	1.13	1.13	-	-	0.99
PLATELET HEMATOCRIT %	N	2	0	0	2	2	0	0	2
	Mean	0.42	-	-	0.34	0.34	-	-	0.30
	Sdev	0.021	-	-	0.170	0.099	-	-	0.000
WHITE BLOOD CELLS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	8.72	-	-	6.63	9.51	-	-	7.61
	Sdev	1.103	-	-	1.393	2.220	-	-	0.898
NEUTROPHILS ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	5.12	-	-	3.60	4.87	-	-	4.59
	Sdev	0.990	-	-	1.287	1.513	-	-	0.403
LYMPHOCYTES ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	2.98	-	-	2.58	3.47	-	-	2.44
	Sdev	0.014	-	-	0.163	0.219	-	-	0.410
MONOCYTES ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	0.42	-	-	0.28	0.60	-	-	0.29
	Sdev	0.049	-	-	0.021	0.134	-	-	0.014

Group 1: Vehicle

Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

CONFIDENTIAL  
Table 5  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
EOSINOPHILS ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	0.15	-	-	0.08	0.44	-	-	0.17
	Sdev	0.113	-	-	0.021	0.318	-	-	0.042
BASOPHILS ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	0.03	-	-	0.06	0.08	-	-	0.07
	Sdev	0.021	-	-	0.014	0.014	-	-	0.007
LARGE UNSTAINED CELLS ABS 10 <sup>3</sup> /mcL	N	2	0	0	2	2	0	0	2
	Mean	0.04	-	-	0.04	0.07	-	-	0.06
	Sdev	0.014	-	-	0.007	0.028	-	-	0.014
NEUTROPHILS % %	N	2	0	0	2	2	0	0	2
	Mean	58.4	-	-	53.5	50.7	-	-	60.4
	Sdev	3.96	-	-	8.20	4.10	-	-	1.84
LYMPHOCITES % %	N	2	0	0	2	2	0	0	2
	Mean	34.5	-	-	39.5	37.2	-	-	32.0
	Sdev	4.45	-	-	5.87	6.43	-	-	1.70
MONOCYTES % %	N	2	0	0	2	2	0	0	2
	Mean	4.7	-	-	4.4	6.3	-	-	3.8*
	Sdev	0.00	-	-	1.20	0.00	-	-	0.28
EOSINOPHILS % %	N	2	0	0	2	2	0	0	2
	Mean	1.6	-	-	1.2	4.3	-	-	2.3
	Sdev	1.13	-	-	0.57	2.40	-	-	0.21

Group 1: Vehicle

Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

CONFIDENTIAL  
 Table 5  
 Day 42 Hematology Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
BASOPHILS %	N	2	0	0	2	2	0	0	2	
	Mean	0.3	-	-	1.0	0.9	-	-	0.9	
	Sdev	0.28	-	-	0.35	0.07	-	-	0.07	
LARGE UNSTAINED CELLS %	N	2	0	0	2	2	0	0	2	
	Mean	0.5	-	-	0.6	0.8	-	-	0.8	
	Sdev	0.28	-	-	0.28	0.07	-	-	0.07	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

***Table 6 Coagulation***

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Table 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
PROTHROMBIN TIME sec	N	5	3	3	5	5	3	3	5	
	Mean	7.2	7.6	7.2	7.4	7.8	7.7	7.2	7.8	
	Sdev	0.46	0.36	0.31	0.46	0.99	0.99	0.15	0.75	
PROTHROMBIN TIME RATIO ratio	N	5	3	3	5	5	3	3	5	
	Mean	1.0	1.0	1.0	1.0	1.1	1.1	1.0	1.1	
	Sdev	0.06	0.05	0.04	0.06	0.14	0.14	0.02	0.10	
ACT. PAR. THROMB. TIME sec	N	5	3	3	5	5	3	3	5	
	Mean	12.5	12.8	12.7	12.6	24.2	12.6	12.8	12.9	
	Sdev	0.23	0.31	0.18	0.37	25.44	0.31	0.24	0.47	
ACT. PAR. THROMB. TIME RATIO ratio	N	5	3	3	5	5	3	3	5	
	Mean	1.0	1.0	1.0	1.0	1.9	1.0	1.0	1.0	
	Sdev	0.02	0.03	0.01	0.03	2.01	0.02	0.02	0.04	
FIBRINOGEN mg/dL	N	5	3	3	5	5	3	3	5	
	Mean	209.	171.	196.	209.	183.	188.	215.	166.	
	Sdev	17.3	14.8	45.2	29.2	22.0	50.2	43.0	23.5	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

CONFIDENTIAL  
Table 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
PROTHROMBIN TIME sec	N	5	3	3	5	5	3	3	5
	Mean	7.2	8.0	7.4	7.7	7.4	7.4	7.2	7.6
	Sdev	0.29	0.34	0.87	0.56	0.34	0.49	0.31	0.52
PROTHROMBIN TIME RATIO ratio	N	5	3	3	5	5	3	3	5
	Mean	1.0	1.1	1.0	1.1	1.0	1.0	1.0	1.0
	Sdev	0.04	0.05	0.12	0.08	0.05	0.07	0.04	0.07
ACT. PAR. THROMB. TIME sec	N	5	3	3	5	5	3	3	5
	Mean	12.4	13.1+	12.7	12.6	12.9	12.5	12.5	12.7
	Sdev	0.19	0.40	0.29	0.32	0.52	0.10	0.06	0.10
ACT.PAR.THROMB.TIME RATIO ratio	N	5	3	3	5	5	3	3	5
	Mean	1.0	1.0+	1.0	1.0	1.0	1.0	1.0	1.0
	Sdev	0.01	0.03	0.03	0.03	0.04	0.01	0.01	0.01
FIBRINOGEN mg/dL	N	5	3	3	5	5	3	3	5
	Mean	220.	164.+	216.	173.+	188.	194.	213.	184.
	Sdev	14.3	9.3	57.0	17.9	26.8	15.3	60.8	25.9

Group 1:Vehicle                      Group 2:50 mg/kg/day                      Group 3:200 mg/kg/day                      Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.  
+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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 Table 6  
 Day 42 Hematology Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
PROTHROMBIN TIME sec	N	2	0	0	2	2	0	0	2
	Mean	7.8	-	-	7.9	7.5	-	-	7.6
	Sdev	0.74	-	-	0.05	0.17	-	-	0.59
PROTHROMBIN TIME RATIO ratio	N	2	0	0	2	2	0	0	2
	Mean	1.1	-	-	1.1	1.0	-	-	1.0
	Sdev	0.10	-	-	0.01	0.03	-	-	0.08
ACT. PAR. THROMB. TIME sec	N	2	0	0	2	2	0	0	2
	Mean	12.6	-	-	12.4	12.4	-	-	12.3
	Sdev	0.28	-	-	0.28	0.06	-	-	0.24
ACT.PAR.THROMB.TIME RATIO ratio	N	2	0	0	2	2	0	0	2
	Mean	1.0	-	-	1.0	1.0	-	-	1.0
	Sdev	0.02	-	-	0.03	0.00	-	-	0.02
FIBRINOGEN mg/dL	N	2	0	0	2	2	0	0	2
	Mean	215.	-	-	190.	167.	-	-	188.
	Sdev	11.0	-	-	35.6	0.4	-	-	19.6

Group 1:Vehicle                      Group 2:50 mg/kg/day                      Group 3:200 mg/kg/day                      Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

***Table 7 Clinical Chemistry***



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Table 7  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
UREA mg/dL	N	5	3	3	5	5	3	3	5
	Mean	30.	21.+	23.	24.	26.	31.	28.	31.
	Sdev	5.4	2.6	1.7	3.1	2.8	5.6	4.7	8.6
CREATININE mg/dL	N	5	3	3	5	5	3	3	5
	Mean	0.91	0.87	0.86	0.87	0.82	0.84	0.77	0.89
	Sdev	0.067	0.065	0.042	0.049	0.113	0.047	0.035	0.084
ASPARTATE AMINO TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	39.	33.	35.	38.	41.	37.	36.	34.
	Sdev	8.4	5.5	10.5	8.0	7.8	4.6	7.0	5.1
ALANINE AMINO TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	33.	30.	31.	32.	29.	29.	23.	30.
	Sdev	8.5	0.6	8.1	6.1	2.5	9.0	2.1	7.0
ALKALINE PHOSPHATASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	78.	78.	78.	73.	57.	70.	68.	62.
	Sdev	23.0	10.1	23.5	16.8	16.7	13.6	14.8	21.0
GAMMA GLUTAMYL TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	6.	8.	8.	7.	8.	10.	7.	8.
	Sdev	1.1	1.5	3.0	1.8	1.9	1.5	0.6	0.4
TOTAL BILIRUBIN mg/dL	N	5	3	3	5	5	3	3	5
	Mean	0.10	0.12	0.15	0.09	0.14	0.14	0.12	0.16
	Sdev	0.020	0.023	0.078	0.005	0.060	0.061	0.006	0.041
Group 1:Vehicle	Group 2:50 mg/kg/day	Group 3:200 mg/kg/day			Group 4:800 mg/kg/day				

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
TOTAL PROTEIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	5.9	5.8	6.1	6.2	5.8	5.8	5.9	5.9
	Sdev	0.22	0.25	0.00	0.30	0.24	0.00	0.21	0.21
ALBUMIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	2.80	2.95	2.84	2.95	2.87	2.88	2.92	2.90
	Sdev	0.152	0.104	0.254	0.125	0.175	0.268	0.156	0.127
GLOBULIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	3.1	2.9	3.3	3.2	2.9	2.9	3.0	3.0
	Sdev	0.23	0.17	0.25	0.20	0.30	0.27	0.16	0.30
GLUCOSE mg/dL	N	5	3	3	5	5	3	3	5
	Mean	87.	91.	92.	94.	96.	88.	98.	100.
	Sdev	1.9	5.0	3.0	9.4	14.6	19.6	11.9	6.3
TRIGLYCERIDES mg/dL	N	5	3	3	5	5	3	3	5
	Mean	18.	22.	18.	14.	14.	30.+	22.	21.
	Sdev	5.8	13.6	4.0	5.2	3.7	10.6	5.6	7.3
TOTAL CHOLESTEROL mg/dL	N	5	3	3	5	5	3	3	5
	Mean	124.	125.	122.	117.	112.	136.	131.+	135.
	Sdev	20.9	25.2	12.5	20.8	10.6	29.6	2.3	21.8
CALCIUM mg/dL	N	5	3	3	5	5	3	3	5
	Mean	10.8	10.6	10.8	10.7	10.4	10.7	10.6	10.9+
	Sdev	0.45	0.40	0.67	0.36	0.22	0.00	0.32	0.23

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
PHOSPHOROUS mg/dL	N	5	3	3	5	5	3	3	5	
	Mean	5.0	4.8	4.2+	4.7	4.4	4.9	4.6	4.5	
	Sdev	0.37	0.32	0.38	0.42	0.59	0.15	0.17	0.84	
ALBUMIN/GLOBULIN	N	5	3	3	5	5	3	3	5	
	Mean	0.9	1.0	0.9	0.9	1.0	1.0	1.0	1.0	
	Sdev	0.09	0.04	0.15	0.04	0.14	0.18	0.08	0.14	
SODIUM mEq/L	N	5	3	3	5	5	3	3	5	
	Mean	141.2	142.3	141.7	141.4	141.8	142.7	142.0	143.0	
	Sdev	1.30	0.58	2.31	0.89	1.79	1.15	2.00	1.00	
POTASSIUM mEq/L	N	5	3	3	5	5	3	3	5	
	Mean	4.7	4.7	4.6	4.6	4.3	4.7	4.4	4.4	
	Sdev	0.18	0.25	0.08	0.14	0.20	0.10	0.27	0.16	
CHLORIDE mEq/L	N	5	3	3	5	5	3	3	5	
	Mean	109.2	109.0	110.0	109.8	108.0	106.0	108.0	106.4	
	Sdev	1.48	1.00	3.46	2.17	1.58	1.00	1.00	3.05	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
UREA mg/dL	N	5	3	3	5	5	3	3	5
	Mean	30.	24.+	27.	33.	23.	27.	27.	32.
	Sdev	1.5	1.7	6.2	6.7	1.9	4.6	4.0	11.1
CREATININE mg/dL	N	5	3	3	5	5	3	3	5
	Mean	0.90	0.87	0.85	0.93	0.89	0.89	0.84	0.93
	Sdev	0.058	0.015	0.104	0.107	0.070	0.012	0.035	0.079
ASPARTATE AMINO TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	37.	33.	31.	31.	35.	34.	40.	29.
	Sdev	6.6	2.0	7.5	6.4	6.2	4.6	6.5	4.3
ALANINE AMINO TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	41.	34.	30.	36.	35.	34.	29.	39.
	Sdev	12.8	7.2	2.5	9.0	1.9	8.1	6.0	17.4
ALKALINE PHOSPHATASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	68.	76.	82.	100.	65.	75.	78.	74.
	Sdev	8.7	12.1	19.2	33.8	17.2	17.0	18.0	17.6
GAMMA GLUTAMYL TRANSFERASE IU/L	N	5	3	3	5	5	3	3	5
	Mean	4.	5.	6.	8.*	4.	6.	7.+	7.*
	Sdev	1.8	0.6	0.6	2.5	1.0	1.5	1.0	1.1
TOTAL BILIRUBIN mg/dL	N	5	3	3	5	5	3	3	5
	Mean	0.25	0.25	0.24	0.27	0.13	0.14	0.11	0.18
	Sdev	0.034	0.036	0.021	0.051	0.053	0.064	0.006	0.088

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

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Table 7  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
TOTAL PROTEIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	5.4	5.4	5.3	5.4	5.6	5.5	5.4	5.6
	Sdev	0.28	0.17	0.31	0.15	0.25	0.26	0.12	0.34
ALBUMIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	2.74	2.95	2.75	2.88	2.85	2.89	2.86	2.96
	Sdev	0.205	0.095	0.361	0.157	0.187	0.193	0.125	0.124
GLOBULIN g/dL	N	5	3	3	5	5	3	3	5
	Mean	2.6	2.5	2.6	2.5	2.7	2.6	2.6	2.7
	Sdev	0.13	0.11	0.21	0.10	0.32	0.08	0.02	0.29
GLUCOSE mg/dL	N	5	3	3	5	5	3	3	5
	Mean	92.	95.	99.	93.	92.	92.	99.	106.
	Sdev	6.1	2.6	7.0	8.5	10.0	18.0	13.1	7.6
TRIGLYCERIDES mg/dL	N	5	3	3	5	5	3	3	5
	Mean	23.	26.	27.	28.	21.	36.	39.+	33.
	Sdev	5.4	11.4	4.0	4.8	2.9	13.9	4.4	8.6
TOTAL CHOLESTEROL mg/dL	N	5	3	3	5	5	3	3	5
	Mean	117.	126.	141.	155.	111.	141.	143.	180.+
	Sdev	18.2	12.5	12.4	33.0	18.5	40.8	33.2	40.5
CALCIUM mg/dL	N	5	3	3	5	5	3	3	5
	Mean	10.3	10.3	10.3	10.2	10.3	10.7	10.3	10.9
	Sdev	0.57	0.10	0.71	0.48	0.53	0.38	0.46	0.38

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
PHOSPHOROUS mg/dL	N	5	3	3	5	5	3	3	5
	Mean	4.3	4.4	3.9	4.3	4.0	4.3	3.9	3.9
	Sdev	0.42	0.06	0.60	0.56	0.41	0.15	0.80	0.32
ALBUMIN/GLOBULIN	N	5	3	3	5	5	3	3	5
	Mean	1.0	1.2	1.1	1.2	1.1	1.1	1.1	1.1
	Sdev	0.08	0.05	0.21	0.09	0.18	0.05	0.05	0.12
SODIUM mEq/L	N	5	3	3	5	5	3	3	5
	Mean	141.2	142.3	142.3	142.2	142.0	142.3	143.0	144.2+
	Sdev	0.45	0.58	1.53	1.30	0.71	1.15	1.00	1.64
POTASSIUM mEq/L	N	5	3	3	5	5	3	3	5
	Mean	4.5	4.3	4.4	4.4	4.5	4.3	4.4	4.3
	Sdev	0.12	0.16	0.21	0.19	0.24	0.14	0.27	0.18
CHLORIDE mEq/L	N	5	3	3	5	5	3	3	5
	Mean	110.2	110.3	111.3	111.6	110.6	109.7	111.7	109.8
	Sdev	2.59	0.58	4.04	2.19	2.07	1.15	1.53	3.90

Group 1:Vehicle                      Group 2:50 mg/kg/day                      Group 3:200 mg/kg/day                      Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.  
+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day 42 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
UREA mg/dL	N	2	0	0	2	2	0	0	2
	Mean	37.	-	-	25.	26.	-	-	28.
	Sdev	7.1	-	-	0.7	4.9	-	-	4.2
CREATININE mg/dL	N	2	0	0	2	2	0	0	2
	Mean	0.88	-	-	0.77	0.96	-	-	0.91
	Sdev	0.042	-	-	0.057	0.035	-	-	0.049
ASPARTATE AMINO TRANSFERASE IU/L	N	2	0	0	2	2	0	0	2
	Mean	38.	-	-	40.	36.	-	-	24.+
	Sdev	9.2	-	-	5.7	3.5	-	-	2.1
ALANINE AMINO TRANSFERASE IU/L	N	2	0	0	2	2	0	0	2
	Mean	32.	-	-	43.	31.	-	-	34.
	Sdev	12.7	-	-	21.9	7.1	-	-	6.4
ALKALINE PHOSPHATASE IU/L	N	2	0	0	2	2	0	0	2
	Mean	59.	-	-	71.	80.	-	-	69.
	Sdev	3.5	-	-	10.6	37.5	-	-	9.2
GAMMA GLUTAMYL TRANSFERASE IU/L	N	2	0	0	2	2	0	0	2
	Mean	7.	-	-	10.	7.	-	-	8.
	Sdev	2.1	-	-	4.2	0.7	-	-	0.7
TOTAL BILIRUBIN mg/dL	N	2	0	0	2	2	0	0	2
	Mean	0.08	-	-	0.08	0.08	-	-	0.08
	Sdev	0.007	-	-	0.014	0.007	-	-	0.014

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

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Table 7  
Day 42 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
TOTAL PROTEIN g/dL	N	2	0	0	2	2	0	0	2
	Mean	5.7	-	-	6.2+	5.9	-	-	5.8
	Sdev	0.14	-	-	0.07	0.21	-	-	0.07
ALBUMIN g/dL	N	2	0	0	2	2	0	0	2
	Mean	2.56	-	-	2.92*	2.89	-	-	2.92
	Sdev	0.014	-	-	0.035	0.028	-	-	0.021
GLOBULIN g/dL	N	2	0	0	2	2	0	0	2
	Mean	3.1	-	-	3.2	3.0	-	-	2.8
	Sdev	0.13	-	-	0.04	0.18	-	-	0.05
GLUCOSE mg/dL	N	2	0	0	2	2	0	0	2
	Mean	99.	-	-	91.	97.	-	-	105.
	Sdev	8.5	-	-	12.7	5.7	-	-	14.8
TRIGLYCERIDES mg/dL	N	2	0	0	2	2	0	0	2
	Mean	29.	-	-	23.	33.	-	-	29.
	Sdev	6.4	-	-	6.4	7.8	-	-	12.0
TOTAL CHOLESTEROL mg/dL	N	2	0	0	2	2	0	0	2
	Mean	117.	-	-	116.	123.	-	-	159.
	Sdev	44.5	-	-	35.4	17.0	-	-	40.3
CALCIUM mg/dL	N	2	0	0	2	2	0	0	2
	Mean	10.3	-	-	10.7	11.0	-	-	10.9
	Sdev	0.99	-	-	0.28	0.21	-	-	0.35

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance



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Table 7

Day 42 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
PHOSPHOROUS mg/dL	N	2	0	0	2	2	0	0	2	
	Mean	4.8	-	-	4.4	4.7	-	-	4.5	
	Sdev	0.35	-	-	0.49	0.07	-	-	0.21	
ALBUMIN/GLOBULIN	N	2	0	0	2	2	0	0	2	
	Mean	0.8	-	-	0.9+	1.0	-	-	1.0	
	Sdev	0.03	-	-	0.00	0.05	-	-	0.01	
SODIUM mEq/L	N	2	0	0	2	2	0	0	2	
	Mean	141.5	-	-	142.0	141.0	-	-	140.0	
	Sdev	0.71	-	-	0.00	1.41	-	-	0.00	
POTASSIUM mEq/L	N	2	0	0	2	2	0	0	2	
	Mean	4.5	-	-	4.5	4.4	-	-	4.5	
	Sdev	0.11	-	-	0.17	0.12	-	-	0.03	
CHLORIDE mEq/L	N	2	0	0	2	2	0	0	2	
	Mean	111.5	-	-	108.5	111.0	-	-	109.5	
	Sdev	3.54	-	-	0.71	1.41	-	-	2.12	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

+ The group mean was significantly different from the control at p=0.05 with Dunnett's test of significance

***Table 8 Urinalysis Quantitative***

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Table 8  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
URINARY VOLUME mL	N	5	3	3	5	5	3	3	5
	Mean	242.8	163.7	192.7	414.0	196.2	146.3	164.7	179.6
	Sdev	71.83	88.27	174.46	258.63	110.68	97.30	108.85	112.61
PH UNITS	N	5	3	3	5	5	3	3	5
	Mean	7.2	7.5	7.0	7.0	6.9	7.0	6.8	7.1
	Sdev	0.45	0.87	2.00	0.00	0.22	0.00	0.29	0.55
SPECIFIC GRAVITY	N	5	3	3	5	5	3	3	5
	Mean	1.017	1.021	1.020	1.023	1.027	1.019	1.023	1.021
	Sdev	0.0016	0.0064	0.0136	0.0118	0.0084	0.0038	0.0125	0.0067
Group 1:Vehicle	Group 2:50 mg/kg/day	Group 3:200 mg/kg/day		Group 4:800 mg/kg/day					

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

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Table 8  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
URINARY VOLUME mL	N	5	3	3	5	5	3	3	5	
	Mean	148.6	224.7	309.0	355.6	216.2	165.0	167.3	190.8	
	Sdev	96.44	291.43	126.53	170.55	155.53	16.46	91.59	115.38	
PH UNITS	N	5	3	3	5	5	3	3	5	
	Mean	7.0	7.0	6.7*	7.0	7.6	7.0	7.7	7.1	
	Sdev	0.00	0.00	0.29	0.00	0.89	0.00	0.58	0.55	
SPECIFIC GRAVITY	N	5	3	3	5	5	3	3	5	
	Mean	1.023	1.026	1.020	1.019	1.028	1.015	1.026	1.021	
	Sdev	0.0049	0.0095	0.0035	0.0037	0.0073	0.0104	0.0074	0.0081	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

\* The group mean was significantly different from the control at p=0.01 with Dunnett's test of significance

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Table 8  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
URINARY VOLUME mL	N	2	0	0	2	2	0	0	2	
	Mean	416.0	-	-	130.0	196.0	-	-	236.5	
	Sdev	313.96	-	-	25.46	62.23	-	-	125.16	
PH UNITS	N	2	0	0	2	2	0	0	2	
	Mean	6.8	-	-	7.5	8.5	-	-	8.0	
	Sdev	0.35	-	-	0.71	0.71	-	-	1.41	
SPECIFIC GRAVITY	N	2	0	0	2	2	0	0	2	
	Mean	1.020	-	-	1.031	1.026	-	-	1.020	
	Sdev	0.0078	-	-	0.0078	0.0021	-	-	0.0064	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

Group means without footnotes were not statistically different from the control at p=0.05 or p=0.01.

***Table 9 Urinalysis Semi-quantitative***

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Table 9  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
WHITE BLOOD CELLS SCORE	N	5	3	3	5	5	3	3	5
	Mean	1.	1.	1.	1.	0.	0.	0.	0.
	Sdev	0.7	1.0	1.2	0.9	0.0	0.0	0.0	0.4
NITRITES SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.4	0.0	0.0	0.4	0.0	0.0	0.0	0.5
PROTEINS SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	1.
	Sdev	0.4	0.6	0.6	0.5	0.0	0.0	0.0	0.9
GLUCOSE SCORE	N	5	3	3	5	5	3	3	5
	Mean	1.	0.	1.	0.	0.	0.	0.	1.
	Sdev	1.3	0.0	1.2	0.0	0.0	0.0	0.0	1.8
KETONE BODIES SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4
UROBILINOGEN SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
BILIRUBIN SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
HEMOGLOBIN/RED BLOOD CE/+ SCORE	N	5	3	3	5	5	3	3	5
	Mean	1.	0.	1.	1.	0.	0.	0.	1.
	Sdev	0.9	0.6	0.6	0.5	0.0	0.0	0.0	1.4

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 9  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s			
		1	2	3	4	1	2	3	4
WHITE BLOOD CELLS SCORE	N	5	3	3	5	5	3	3	5
	Mean	2.	2.	1.	2.	0.	1.	1.	0.
	Sdev	0.5	0.0	1.0	0.4	0.5	1.2	1.2	0.9
NITRITES SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	1.	0.
	Sdev	0.5	0.6	0.6	0.4	0.0	0.6	0.6	0.5
PROTEINS SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	1.	0.	0.	0.	0.	0.	1.
	Sdev	0.4	0.6	0.6	0.4	0.4	0.6	0.6	0.9
GLUCOSE SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	1.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3
KETONE BODIES SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4
UROBILINOGEN SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
BILIRUBIN SCORE	N	5	3	3	5	5	3	3	5
	Mean	0.	0.	0.	0.	0.	0.	0.	0.
	Sdev	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
HEMOGLOBIN/RED BLOOD CE/+ SCORE	N	5	3	3	5	5	3	3	5
	Mean	1.	0.	1.	0.	0.	1.	0.	1.
	Sdev	0.8	0.6	0.6	0.4	0.4	1.2	0.6	1.1

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day



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Table 9  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

Parameter	Group Number:	M a l e s				F e m a l e s				
		1	2	3	4	1	2	3	4	
WHITE BLOOD CELLS SCORE	N	2	0	0	2	2	0	0	2	
	Mean	2.	-	-	1.	2.	-	-	0.	
	Sdev	0.0	-	-	1.4	0.7	-	-	0.0	
NITRITES SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	1.	0.	-	-	0.	
	Sdev	0.0	-	-	0.7	0.0	-	-	0.0	
PROTEINS SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	1.	0.	-	-	0.	
	Sdev	0.0	-	-	0.7	0.0	-	-	0.0	
GLUCOSE SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	0.	0.	-	-	0.	
	Sdev	0.0	-	-	0.0	0.0	-	-	0.0	
KETONE BODIES SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	1.	0.	-	-	0.	
	Sdev	0.0	-	-	0.7	0.0	-	-	0.0	
UROBILINOGEN SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	0.	0.	-	-	0.	
	Sdev	0.0	-	-	0.0	0.0	-	-	0.0	
BILIRUBIN SCORE	N	2	0	0	2	2	0	0	2	
	Mean	0.	-	-	0.	0.	-	-	0.	
	Sdev	0.0	-	-	0.0	0.0	-	-	0.0	
HEMOGLOBIN/RED BLOOD CE/+ SCORE	N	2	0	0	2	2	0	0	2	
	Mean	1.	-	-	1.	1.	-	-	0.	
	Sdev	0.7	-	-	1.4	1.4	-	-	0.0	
Group 1:Vehicle		Group 2:50 mg/kg/day			Group 3:200 mg/kg/day			Group 4:800 mg/kg/day		

***Table 10 Absolute Organ Weights***

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s							
1	Vehicle						
	N	3	3	3	3	3	3
	Mean	8.47	21.83	5.063	39.29	284.38	1.260
	Sdev	0.366	3.340	3.2756	4.728	40.574	0.1323
2	50 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	8.21	23.94	3.000	41.86	254.01	1.233
	Sdev	1.077	3.770	0.9299	6.169	11.157	0.0757
3	200 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	8.10	18.64	1.483	36.33	280.82	1.420
	Sdev	0.504	5.496	0.2954	0.820	40.392	0.3874
4	800 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	7.97	19.22	2.487	38.62	320.11	1.460
	Sdev	1.249	7.269	0.8406	3.819	25.000	0.1442

Note: Data collected using grace days.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	8.47	62.57	75.61	12.26	3.44
	Sdev	0.366	3.057	10.097	1.036	0.990
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	8.21	67.97	70.33	12.93	4.66
	Sdev	1.077	5.713	3.451	2.840	0.814
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	8.10	63.46	72.85	10.94	3.58
	Sdev	0.504	5.660	4.945	4.583	1.230
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.97	60.41	66.60	11.12	3.57
	Sdev	1.249	1.059	11.516	5.596	1.981

Note: Data collected using grace days.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	6.61	16.89	1.567	31.87	248.47
	Sdev	0.276	3.199	0.7504	1.010	12.579
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.52	24.23	3.203	33.48	248.92
	Sdev	0.907	7.486	1.5864	2.945	46.166
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.25	19.89	2.247	36.31	282.12
	Sdev	0.688	8.765	1.4275	2.933	30.857
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	6.62	16.72	1.323	29.80	249.56
	Sdev	0.889	3.666	0.3320	2.819	29.715

Note: Data collected using grace days.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	6.61	1.287	56.76	74.08	0.787
	Sdev	0.276	0.1365	1.687	2.305	0.1718
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.52	1.140	59.45	69.02	1.894+
	Sdev	0.907	0.0964	2.395	4.286	0.2362
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.25	1.290	60.32	75.30	1.667
	Sdev	0.688	0.2307	10.318	1.752	0.4140
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	6.62	1.213	53.86	66.86	1.654
	Sdev	0.889	0.0839	8.825	8.293	0.7240

Note: Data collected using grace days.

+ The group mean was significantly different from the control at p=0.05.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s							
1	Vehicle						
	N	2	2	2	2	2	2
	Mean	7.62	18.91	2.580	32.32	246.77	1.140
	Sdev	0.351	1.563	1.4849	1.520	10.769	0.0424
4	800 mg/kg/day						
	N	2	2	2	2	2	2
	Mean	7.60	17.27	1.380	39.86	245.12	1.110
	Sdev	1.323	4.313	0.3111	8.273	51.237	0.0849

Note: Data collected using grace days.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	7.62	70.02	69.58	13.63	2.38
	Sdev	0.351	2.616	6.152	1.266	1.796
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.60	67.03	69.37	10.22	2.08
	Sdev	1.323	6.145	8.429	0.198	1.817

Note: Data collected using grace days.



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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	8.33	25.41	3.045	35.25	270.76
	Sdev	0.310	4.830	0.4313	0.247	7.905
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.07	20.57	2.035	31.80*	263.59
	Sdev	0.348	0.148	0.7566	0.205	11.003

Note: Data collected using grace days.

\* The group mean was significantly different from the control at p=0.01.

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Table 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	8.33	1.035	63.75	68.02	1.981
	Sdev	0.310	0.2333	4.822	4.773	0.4171
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.07	1.150	51.97	68.59	1.583
	Sdev	0.348	0.0283	7.333	0.417	0.0591

Note: Data collected using grace days.

***Table 11 Organ/Terminal Body Weight Ratios***

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s							
1	Vehicle						
	N	3	3	3	3	3	3
	Mean	8.47	0.26	0.060	0.46	3.36	0.015
	Sdev	0.366	0.028	0.0390	0.039	0.511	0.0011
2	50 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	8.21	0.29	0.037	0.51	3.12	0.015
	Sdev	1.077	0.056	0.0127	0.013	0.324	0.0025
3	200 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	8.10	0.23	0.018	0.45	3.47	0.017
	Sdev	0.504	0.060	0.0033	0.031	0.483	0.0045
4	800 mg/kg/day						
	N	3	3	3	3	3	3
	Mean	7.97	0.24	0.031	0.49	4.07	0.019
	Sdev	1.249	0.079	0.0066	0.027	0.642	0.0043

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	8.47	0.74	0.89	0.14	0.04
	Sdev	0.366	0.012	0.088	0.007	0.011
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	8.21	0.83	0.87	0.16	0.06
	Sdev	1.077	0.051	0.139	0.021	0.009
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	8.10	0.78	0.90	0.14	0.04
	Sdev	0.504	0.021	0.063	0.062	0.018
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.97	0.77	0.85	0.13	0.04
	Sdev	1.249	0.112	0.183	0.054	0.020

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	6.61	0.25	0.024	0.48	3.77
	Sdev	0.276	0.039	0.0120	0.020	0.347
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.52	0.32	0.041	0.45	3.29
	Sdev	0.907	0.065	0.0159	0.021	0.222
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.25	0.27	0.031	0.50	3.90
	Sdev	0.688	0.092	0.0199	0.020	0.331
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	6.62	0.25	0.020	0.45	3.79
	Sdev	0.889	0.028	0.0046	0.034	0.374

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s						
1	Vehicle					
	N	3	3	3	3	3
	Mean	6.61	0.019	0.86	1.12	0.012
	Sdev	0.276	0.0021	0.059	0.042	0.0028
2	50 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.52	0.015	0.80	0.93	0.025
	Sdev	0.907	0.0027	0.078	0.144	0.0015
3	200 mg/kg/day					
	N	3	3	3	3	3
	Mean	7.25	0.018	0.83	1.04	0.023
	Sdev	0.688	0.0043	0.070	0.100	0.0035
4	800 mg/kg/day					
	N	3	3	3	3	3
	Mean	6.62	0.019	0.81	1.01	0.024
	Sdev	0.889	0.0032	0.038	0.024	0.0072

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s							
1	Vehicle						
	N	2	2	2	2	2	2
	Mean	7.62	0.25	0.033	0.42	3.24	0.015
	Sdev	0.351	0.009	0.0179	0.000	0.008	0.0012
4	800 mg/kg/day						
	N	2	2	2	2	2	2
	Mean	7.60	0.23	0.018	0.52	3.22	0.015
	Sdev	1.323	0.017	0.0009	0.018	0.114	0.0037

Note: Data collected using grace days.



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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	7.62	0.92	0.92	0.18	0.03
	Sdev	0.351	0.008	0.123	0.025	0.022
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.60	0.89	0.92	0.14	0.03
	Sdev	1.323	0.074	0.049	0.021	0.019

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	8.33	0.30	0.037	0.42	3.25
	Sdev	0.310	0.047	0.0065	0.019	0.026
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.07	0.29	0.029	0.45	3.73
	Sdev	0.348	0.016	0.0093	0.019	0.028

Note: Data collected using grace days.

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Table 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number	Dose Level	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s						
1	Vehicle					
	N	2	2	2	2	2
	Mean	8.33	0.012	0.77	0.82	0.024
	Sdev	0.310	0.0023	0.087	0.088	0.0059
4	800 mg/kg/day					
	N	2	2	2	2	2
	Mean	7.07	0.016	0.73	0.97	0.022
	Sdev	0.348	0.0004	0.068	0.042	0.0003

Note: Data collected using grace days.

***Table 12 Gross Pathology***

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Table 12  
Incidence Summary for Gross Necropsy Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Group Number:	M a l e s				F e m a l e s			
	1	2	3	4	1	2	3	4
Number in Group:	3	3	3	3	3	3	3	3
<hr/>								
GENER. CONDITION								
GOOD .....	3	3	2	2	2	3	2	3
FAIRLY GOOD .....	0	0	1	1	1	0	1	0
LYMPH NODES								
ENLARGED .....	0	0	1	0	0	0	0	0
PERITONEAL CAV.								
CLEAR LIQUID CONTENT .....	0	0	1	0	2	0	1	0
PROSTATE								
SMALL .....	0	0	0	1	0	0	0	0
TESTES								
SMALL, BILATERALLY .....	0	0	1	1	0	0	0	0
FLACCID .....	0	0	1	1	0	0	0	0
THYMUS								
SMALL .....	0	0	0	0	1	0	1	0

Note: The necropsy was conducted over multiple days.  
Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 12  
Incidence Summary for Gross Necropsy Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

	M a l e s				F e m a l e s			
	1	2	3	4	1	2	3	4
Group Number:	1	2	3	4	1	2	3	4
Number in Group:	2	0	0	2	2	0	0	2
<b>GENER. CONDITION</b>								
GOOD .....	2	0	0	1	2	0	0	2
FAIRLY GOOD .....	0	0	0	1	0	0	0	0
<b>PROSTATE</b>								
SMALL .....	1	0	0	1	0	0	0	0

Note: The necropsy was conducted over multiple days.

Group 1:Vehicle

Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

***Table 13 Microscopic Pathology***

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
ADRENALS	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
AORTA-THORACIC	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ECTOPIC THYROID		Nad>	3	0	0	2	3	0	0	2
		Present>	0	0	0	1	0	0	0	1
BONE MARROW	. . . . .	.NUMBER EXAMINED:	3	3	3	3	3	0	0	3
REDUCED CELLULARITY		Nad>	3	3	2	2	3	0	0	3
		Minimal>	0	0	1	0	0	0	0	0
		Moderate>	0	0	0	1	0	0	0	0
ATROPHY OF ADIPOSE TISSUE IN STERNAL AND FEMORAL MARROW		Nad>	3	3	3	2	3	0	0	3
		Moderate>	0	0	0	1	0	0	0	0
BRAIN	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CECUM	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
COLON	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS		Nad>	1	0	0	3	3	0	0	3
		Minimal>	2	0	0	0	0	0	0	0
DIAPHRAGM	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
DUODENUM	. . . . .	.NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ECTOPIC PANCREATIC TISSUE IN SUBMUCOSA		Nad>	3	0	0	3	3	0	0	3

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day



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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole		Study Number: 0505-2007								
CONTROLS FROM GROUP(S): 1		ANIMAL SEX:	M a l e s				F e m a l e s			
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
DUODENUM	(Continued)	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS		Nad>	2	0	0	3	3	0	0	1
		Minimal>	0	0	0	0	0	0	0	2
		Slight>	1	0	0	0	0	0	0	0
EPIDIDYMIDES		NUMBER EXAMINED:	3	0	0	3	0	0	0	0
IMMATURE		Nad>	3	0	0	2	0	0	0	0
		Present>	0	0	0	1	0	0	0	0
LUMENAL GERM CELLS/DEBRIS		Nad>	3	0	0	2	0	0	0	0
		Minimal>	0	0	0	1	0	0	0	0
ESOPHAGUS		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACUTE INFLAMMATION		Nad>	3	0	0	2	3	0	0	3
		Minimal>	0	0	0	1	0	0	0	0
CHRONIC INFLAMMATION		Nad>	3	0	0	3	2	0	0	2
		Minimal>	0	0	0	0	1	0	0	1
EYES		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
FEMUR HEAD		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
GALL BLADDER		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
LYMPHOCYTIC INFILTRATION		Nad>	1	0	0	0	0	0	0	0
		Minimal>	2	0	0	2	2	0	0	2
		Slight>	0	0	0	1	1	0	0	1
HEART		NUMBER EXAMINED:	3	0	0	3	3	0	0	3

Nad = No abnormalities detected      NOS = Not otherwise specified  
 Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
HEART (Continued)	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACUTE INFLAMMATION		Nad>	3	0	0	2	3	0	0	3
		Minimal>	0	0	0	1	0	0	0	0
MESOTHELIAL HYPERPLASIA, ATRIAL		Nad>	1	0	0	3	2	0	0	2
		Minimal>	1	0	0	0	0	0	0	0
		Slight>	1	0	0	0	1	0	0	1
ARTERIAL MEDIAL HYPERTROPHY		Nad>	3	0	0	3	3	0	0	2
		Minimal>	0	0	0	0	0	0	0	1
ILEUM	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
JEJUNUM	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
KIDNEYS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CHRONIC INFLAMMATION		Nad>	3	0	0	3	2	0	0	3
		Minimal>	0	0	0	0	1	0	0	0
PAPILLARY MINERALIZATION		Nad>	0	0	0	1	0	0	0	1
		Minimal>	3	0	0	2	3	0	0	2
CORTICAL TUBULAR DILATION		Nad>	3	0	0	3	3	0	0	3
CORTICAL FIBROSIS		Nad>	3	0	0	3	3	0	0	3
CORTICAL TUBULAR REGENERATIVE BASOPHILIA		Nad>	3	0	0	3	3	0	0	3
ATROPHY OF ADJACENT ADIPOSE TISSUE		Nad>	3	0	0	2	3	0	0	3
		Slight>	0	0	0	1	0	0	0	0
LACRIMAL GLANDS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole		Study Number: 0505-2007								
CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
LACRIMAL GLANDS (Continued)	NUMBER EXAMINED:	3	0	0	3	3	0	0	3	
ONLY ONE GLAND AVAILABLE FOR EXAMINATION										
	Nad>	2	0	0	2	2	0	0	2	
	Present>	1	0	0	1	1	0	0	1	
LIVER	NUMBER EXAMINED:	3	0	0	3	3	0	0	3	
CHRONIC INFLAMMATION										
	Nad>	1	0	0	2	3	0	0	0	
	Minimal>	2	0	0	1	0	0	0	3	
GLYCOGEN DEPLETION										
	Nad>	3	0	0	2	3	0	0	3	
	Slight>	0	0	0	1	0	0	0	0	
HEPATOCELLULAR VACUOLATION										
	Nad>	3	0	0	3	2	0	0	3	
	Slight>	0	0	0	0	1	0	0	0	
EXTRAMEDULLARY HEMATOPOIESIS										
	Nad>	2	0	0	3	2	0	0	3	
	Minimal>	1	0	0	0	1	0	0	0	
MANDIBULAR L.N.	NUMBER EXAMINED:	3	0	1	3	3	0	0	3	
SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS										
	Nad>	3	0	1	3	2	0	0	3	
	Minimal>	0	0	0	0	1	0	0	0	
MESENTERIC L.N.	NUMBER EXAMINED:	3	0	1	3	3	0	0	3	
SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS										
	Nad>	1	0	1	2	0	0	0	1	
	Minimal>	1	0	0	1	3	0	0	2	
	Slight>	1	0	0	0	0	0	0	0	
LUNG	NUMBER EXAMINED:	3	0	0	3	3	0	0	3	

Nad = No abnormalities detected      NOS = Not otherwise specified  
 Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
LUNG (Continued)	NUMBER EXAMINED:	3	0	0	3	3	0	0	3	3
ALVEOLAR HEMORRHAGE	Nad>	3	0	0	3	3	0	0	3	3
ACUTE INFLAMMATION	Nad>	3	0	0	3	1	0	0	2	2
	Minimal>	0	0	0	0	2	0	0	1	1
CHRONIC INFLAMMATION	Nad>	2	0	0	3	2	0	0	3	3
	Minimal>	0	0	0	0	1	0	0	0	0
	Slight>	1	0	0	0	0	0	0	0	0
ALVEOLAR MACROPHAGE INFILTRATION	Nad>	1	0	0	1	0	0	0	0	0
	Minimal>	2	0	0	2	3	0	0	2	2
	Slight>	0	0	0	0	0	0	0	1	1
BRONCHOPNEUMONIA	Nad>	3	0	0	3	3	0	0	2	2
	Slight>	0	0	0	0	0	0	0	1	1
CAPILLARY ANGIOMATOSIS	Nad>	3	0	0	3	3	0	0	3	3
MAMMARY GLAND	NUMBER EXAMINED:	3	0	0	3	3	3	3	3	3
NO MAMMARY TISSUE IN THE SECTION	Nad>	0	0	0	0	0	3	3	3	3
	Present>	3	0	0	3	3	0	0	0	0
IMMATURE	Nad>	3	0	0	3	3	2	3	3	3
	Present>	0	0	0	0	0	1	0	0	0
EDEMA	Nad>	3	0	0	3	3	1	0	1	1
	Minimal>	0	0	0	0	0	1	1	0	0
	Slight>	0	0	0	0	0	1	1	2	2
	Moderate>	0	0	0	0	0	0	1	0	0

Nad = No abnormalities detected  
Group 1: Vehicle

NOS = Not otherwise specified  
Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole		Study Number: 0505-2007								
CONTROLS FROM GROUP(S): 1		ANIMAL SEX:	M a l e s				F e m a l e s			
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
MAMMARY GLAND (Continued)	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	3	3	3
STROMAL PROLIFERATION		Nad>	3	0	0	3	3	1	0	1
		Minimal>	0	0	0	0	0	1	0	0
		Slight>	0	0	0	0	0	0	2	2
		Moderate>	0	0	0	0	0	1	1	0
DUCTAL-ALVEOLAR HYPERPLASIA		Nad>	3	0	0	3	3	1	0	1
		Minimal>	0	0	0	0	0	1	1	1
		Slight>	0	0	0	0	0	1	1	1
		Moderate>	0	0	0	0	0	0	1	0
LOBULAR HYPERPLASIA		Nad>	3	0	0	3	3	3	3	2
		Slight>	0	0	0	0	0	0	0	1
SECRETORY ACTIVITY		Nad>	3	0	0	3	3	3	3	2
		Slight>	0	0	0	0	0	0	0	1
SKELETAL MUSCLE	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CHRONIC INFLAMMATION		Nad>	3	0	0	3	3	0	0	3
SCIATIC NERVE	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
OPTIC NERVES	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
OVARIES	. . . . .	NUMBER EXAMINED:	0	0	0	0	3	3	3	3
IMMATURE		Nad>	0	0	0	0	0	3	3	3
		Present>	0	0	0	0	3	0	0	0
CORPORA LUTEA		Nad>	0	0	0	0	3	1	0	0
		Present>	0	0	0	0	0	2	3	3

Nad = No abnormalities detected      NOS = Not otherwise specified  
 Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
OVARIES (Continued)	. . . . .	NUMBER EXAMINED:	0	0	0	0	3	3	3	3
CYSTS		Nad>	0	0	0	0	3	3	3	3
PANCREAS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACINAR DEGRANULATION		Nad>	3	0	0	2	3	0	0	3
		Minimal>	0	0	0	1	0	0	0	0
ACINAR APOPTOSIS		Nad>	3	0	0	3	3	0	0	3
PITUITARY	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CYSTS, PARS DISTALIS		Nad>	1	0	0	3	2	0	0	3
		Minimal>	0	0	0	0	1	0	0	0
		Slight>	2	0	0	0	0	0	0	0
CRANIOPHARINGEAL CYSTS		Nad>	3	0	0	3	3	0	0	3
PROSTATE	. . . . .	NUMBER EXAMINED:	3	0	0	3	0	0	0	0
IMMATURE		Nad>	3	0	0	2	0	0	0	0
		Present>	0	0	0	1	0	0	0	0
PARATHYROIDS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION		Nad>	1	0	0	2	0	0	0	0
		Present>	2	0	0	1	3	0	0	3
CYSTS		Nad>	3	0	0	2	2	0	0	2
		Minimal>	0	0	0	1	1	0	0	1
SPINAL CORD-CERV.	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
STAGE OF ESTRUS	. . . . .	NUMBER EXAMINED:	0	0	0	0	3	3	3	3

Nad = No abnormalities detected      NOS = Not otherwise specified  
Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
STAGE OF ESTRUS (Continued)	. . . . .	NUMBER EXAMINED:	0	0	0	0	3	3	3	3
IMMATURE		Nad>	0	0	0	0	0	3	3	3
		Present>	0	0	0	0	3	0	0	0
PROESTRUS		Nad>	0	0	0	0	3	3	3	3
ESTRUS		Nad>	0	0	0	0	3	2	3	3
		Present>	0	0	0	0	0	1	0	0
METESTRUS		Nad>	0	0	0	0	3	3	3	2
		Present>	0	0	0	0	0	0	0	1
DIESTRUS		Nad>	0	0	0	0	3	1	0	1
		Present>	0	0	0	0	0	2	3	2
ANESTRUS		Nad>	0	0	0	0	3	3	3	3
MANDIBULAR S.G.	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
LYMPHOCYTIC INFILTRATION		Nad>	3	0	0	3	2	0	0	2
		Minimal>	0	0	0	0	1	0	0	0
		Slight>	0	0	0	0	0	0	0	1
PAROTIDS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
LYMPHOCYTIC INFILTRATION		Nad>	3	0	0	3	3	0	0	2
		Minimal>	0	0	0	0	0	0	0	1
ACINAR ATROPHY		Nad>	2	0	0	1	1	0	0	3
		Minimal>	1	0	0	2	2	0	0	0
SKIN	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
SKIN (Continued)	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CHRONIC INFLAMMATION		Nad>	2	0	0	3	3	0	0	3
		Minimal>	1	0	0	0	0	0	0	0
SPLEEN	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
EXTRAMEDULLARY HEMATOPOIESIS		Nad>	3	0	0	3	3	0	0	3
STOMACH	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACUTE INFLAMMATION		Nad>	3	0	0	3	3	0	0	3
GASTRITIS		Nad>	3	0	0	3	3	0	0	3
STERNUM	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
TESTES	. . . . .	NUMBER EXAMINED:	3	0	1	3	0	0	0	0
IMMATURE		Nad>	3	0	0	2	0	0	0	0
		Present>	0	0	1	1	0	0	0	0
SEGMENTAL HYPOPLASIA		Nad>	2	0	1	2	0	0	0	0
		Minimal>	0	0	0	1	0	0	0	0
		Slight>	1	0	0	0	0	0	0	0
THYROIDS	. . . . .	NUMBER EXAMINED:	3	0	0	3	3	0	0	3
CYSTIC FOLLICLES		Nad>	3	0	0	3	3	0	0	3
THYMUS	. . . . .	NUMBER EXAMINED:	3	0	0	2	3	0	0	3

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day



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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
THYMUS	(Continued)	NUMBER EXAMINED:	3	0	0	2	3	0	0	3
CYSTS		Nad>	2	0	0	1	2	0	0	2
		Minimal>	1	0	0	0	1	0	0	0
		Slight>	0	0	0	1	0	0	0	1
INVOLUTION		Nad>	1	0	0	0	0	0	0	0
		Slight>	2	0	0	1	0	0	0	0
		Moderate>	0	0	0	0	2	0	0	0
		Marked>	0	0	0	0	1	0	0	3
		Severe>	0	0	0	1	0	0	0	0
TONGUE		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACUTE INFLAMMATION		Nad>	3	0	0	2	3	0	0	3
		Minimal>	0	0	0	1	0	0	0	0
CHRONIC INFLAMMATION		Nad>	3	0	0	3	2	0	0	3
		Minimal>	0	0	0	0	1	0	0	0
TRACHEA		NUMBER EXAMINED:	3	0	0	3	3	0	0	3
ACUTE INFLAMMATION		Nad>	3	0	0	3	2	0	0	3
		Minimal>	0	0	0	0	1	0	0	0
URINARY BLADDER		NUMBER EXAMINED:	3	0	0	3	3	0	0	2
MINERALIZATION IN MUSCULARIS/SUBSEROSA		Nad>	2	0	0	3	3	0	0	2
		Slight>	1	0	0	0	0	0	0	0
UTERUS		NUMBER EXAMINED:	0	0	0	0	3	3	3	3
IMMATURE		Nad>	0	0	0	0	1	3	3	3
		Present>	0	0	0	0	2	0	0	0

Nad = No abnormalities detected  
Group 1: Vehicle

NOS = Not otherwise specified  
Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX:	M a l e s				F e m a l e s			
T I S S U E S    W I T H    D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	3	3	3	3	3	3	3	3
UTERUS	(Continued)	NUMBER EXAMINED:	0	0	0	0	3	3	3	3
ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA		Nad>	0	0	0	0	3	0	1	1
		Minimal>	0	0	0	0	0	2	0	0
		Slight>	0	0	0	0	0	0	1	1
		Moderate>	0	0	0	0	0	1	1	1
EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN		Nad>	0	0	0	0	3	2	1	2
		Minimal>	0	0	0	0	0	1	2	0
		Slight>	0	0	0	0	0	0	0	1
VAGINA		NUMBER EXAMINED:	0	0	0	0	3	3	1	3

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
ADRENALS	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
AORTA-THORACIC	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ECTOPIC THYROID		Nad>	2	0	0	2	2	0	0	2
BONE MARROW	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
REDUCED CELLULARITY		Nad>	2	0	0	2	2	0	0	2
ATROPHY OF ADIPOSE TISSUE IN STERNAL AND FEMORAL MARROW		Nad>	2	0	0	2	2	0	0	2
BRAIN	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CECUM	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
COLON	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS		Nad>	2	0	0	2	2	0	0	2
DIAPHRAGM	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
DUODENUM	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ECTOPIC PANCREATIC TISSUE IN SUBMUCOSA		Nad>	2	0	0	2	2	0	0	1
		Present>	0	0	0	0	0	0	0	1
CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS		Nad>	1	0	0	1	2	0	0	2
		Minimal>	1	0	0	1	0	0	0	0
EPIDIDYMIDES	. . . . .	.NUMBER EXAMINED:	2	0	0	2	0	0	0	0
IMMATURE		Nad>	2	0	0	2	0	0	0	0

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
EPIDIDYMIDES (Continued)	. . . . .	NUMBER EXAMINED:	2	0	0	2	0	0	0	0
LUMENAL GERM CELLS/DEBRIS		Nad>	2	0	0	2	0	0	0	0
ESOPHAGUS	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ACUTE INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
CHRONIC INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
EYES	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
FEMUR HEAD	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
GALL BLADDER	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Lymphocytic Infiltration		Nad>	0	0	0	0	0	0	0	1
		Minimal>	2	0	0	2	1	0	0	1
		Slight>	0	0	0	0	1	0	0	0
HEART	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ACUTE INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
Mesothelial Hyperplasia, Atrial		Nad>	1	0	0	2	2	0	0	1
		Minimal>	1	0	0	0	0	0	0	1
Arterial Medial Hypertrophy		Nad>	2	0	0	2	2	0	0	2
ILEUM	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
JEJUNUM	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
KIDNEYS	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2

Nad = No abnormalities detected  
Group 1: Vehicle

NOS = Not otherwise specified  
Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
KIDNEYS (Continued)	NUMBER EXAMINED:	2	0	0	2	2	0	0	2	
CHRONIC INFLAMMATION	Nad>	1	0	0	2	1	0	0	1	
	Minimal>	0	0	0	0	1	0	0	1	
	Slight>	1	0	0	0	0	0	0	0	
PAPILLARY MINERALIZATION	Nad>	0	0	0	1	0	0	0	0	
	Minimal>	2	0	0	1	2	0	0	2	
CORTICAL TUBULAR DILATION	Nad>	1	0	0	2	1	0	0	2	
	Minimal>	0	0	0	0	1	0	0	0	
	Moderate>	1	0	0	0	0	0	0	0	
CORTICAL FIBROSIS	Nad>	2	0	0	2	1	0	0	2	
	Minimal>	0	0	0	0	1	0	0	0	
CORTICAL TUBULAR REGENERATIVE BASOPHILIA	Nad>	0	0	0	1	1	0	0	2	
	Minimal>	1	0	0	1	0	0	0	0	
	Slight>	1	0	0	0	1	0	0	0	
ATROPHY OF ADJACENT ADIPOSE TISSUE	Nad>	2	0	0	2	2	0	0	2	
LACRIMAL GLANDS . . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2	
ONLY ONE GLAND AVAILABLE FOR EXAMINATION	Nad>	2	0	0	2	2	0	0	2	
LIVER . . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2	
CHRONIC INFLAMMATION	Nad>	2	0	0	2	2	0	0	2	
GLYCOGEN DEPLETION	Nad>	2	0	0	2	2	0	0	2	

Nad = No abnormalities detected      NOS = Not otherwise specified  
Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX:	M a l e s				F e m a l e s			
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
LIVER (Continued)	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
HEPATOCELLULAR VACUOLATION		Nad>	2	0	0	2	2	0	0	2
EXTRAMEDULLARY HEMATOPOIESIS		Nad>	0	0	0	2	1	0	0	2
		Minimal>	2	0	0	0	1	0	0	0
MANDIBULAR L.N.	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS		Nad>	1	0	0	2	2	0	0	2
		Minimal>	1	0	0	0	0	0	0	0
MESENTERIC L.N.	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS		Nad>	0	0	0	1	0	0	0	0
		Minimal>	1	0	0	1	2	0	0	2
		Slight>	1	0	0	0	0	0	0	0
LUNG	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ALVEOLAR HEMORRHAGE		Nad>	1	0	0	2	1	0	0	2
		Minimal>	0	0	0	0	1	0	0	0
		Slight>	1	0	0	0	0	0	0	0
ACUTE INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
CHRONIC INFLAMMATION		Nad>	2	0	0	2	1	0	0	2
		Minimal>	0	0	0	0	1	0	0	0
ALVEOLAR MACROPHAGE INFILTRATION		Nad>	1	0	0	1	0	0	0	1
		Minimal>	1	0	0	1	1	0	0	1
		Slight>	0	0	0	0	1	0	0	0

Nad = No abnormalities detected      NOS = Not otherwise specified  
Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
LUNG (Continued)	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
BRONCHOPNEUMONIA		Nad>	2	0	0	2	2	0	0	2
CAPILLARY ANGIOMATOSIS		Nad>	1	0	0	2	2	0	0	2
		Slight>	1	0	0	0	0	0	0	0
MAMMARY GLAND	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
NO MAMMARY TISSUE IN THE SECTION		Nad>	0	0	0	0	2	0	0	2
		Present>	2	0	0	2	0	0	0	0
IMMATURE		Nad>	2	0	0	2	2	0	0	2
EDEMA		Nad>	2	0	0	2	0	0	0	0
		Minimal>	0	0	0	0	1	0	0	0
		Slight>	0	0	0	0	1	0	0	1
		Moderate>	0	0	0	0	0	0	0	1
STROMAL PROLIFERATION		Nad>	2	0	0	2	0	0	0	0
		Minimal>	0	0	0	0	1	0	0	0
		Moderate>	0	0	0	0	1	0	0	2
DUCTAL-ALVEOLAR HYPERPLASIA		Nad>	2	0	0	2	0	0	0	0
		Minimal>	0	0	0	0	1	0	0	0
		Moderate>	0	0	0	0	1	0	0	2
LOBULAR HYPERPLASIA		Nad>	2	0	0	2	2	0	0	2
SECRETORY ACTIVITY		Nad>	2	0	0	2	2	0	0	2
SKELETAL MUSCLE	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2

Nad = No abnormalities detected      NOS = Not otherwise specified  
Group 1:Vehicle      Group 2:50 mg/kg/day      Group 3:200 mg/kg/day      Group 4:800 mg/kg/day

CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
SKELETAL MUSCLE (Continued)		.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CHRONIC INFLAMMATION		Nad>	2	0	0	2	2	0	0	1
		Minimal>	0	0	0	0	0	0	0	1
SCIATIC NERVE		.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
OPTIC NERVES		.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
OVARIES		.NUMBER EXAMINED:	0	0	0	0	2	0	0	2
IMMATURE		Nad>	0	0	0	0	2	0	0	2
CORPORA LUTEA		Present>	0	0	0	0	2	0	0	2
CYSTS		Nad>	0	0	0	0	2	0	0	1
		Slight>	0	0	0	0	0	0	0	1
PANCREAS		.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ACINAR DEGRANULATION		Nad>	2	0	0	2	2	0	0	2
ACINAR APOPTOSIS		Nad>	2	0	0	2	1	0	0	1
		Minimal>	0	0	0	0	1	0	0	1
PITUITARY		.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CYSTS, PARS DISTALIS		Nad>	2	0	0	1	1	0	0	2
		Slight>	0	0	0	1	1	0	0	0
CRANIOPHARINGEAL CYSTS		Nad>	2	0	0	2	2	0	0	1
		Moderate>	0	0	0	0	0	0	0	1
PROSTATE		.NUMBER EXAMINED:	2	0	0	2	0	0	0	0

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day



CONFIDENTIAL

Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
PROSTATE (Continued)	. . . . .	NUMBER EXAMINED:	2	0	0	2	0	0	0	0
IMMATURE		Nad>	1	0	0	1	0	0	0	0
		Present>	1	0	0	1	0	0	0	0
PARATHYROIDS	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION		Nad>	1	0	0	1	0	0	0	0
		Present>	1	0	0	1	2	0	0	2
CYSTS		Nad>	2	0	0	1	2	0	0	2
		Minimal>	0	0	0	1	0	0	0	0
SPINAL CORD-CERV.	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2
STAGE OF ESTRUS	. . . . .	NUMBER EXAMINED:	0	0	0	0	2	0	0	2
IMMATURE		Nad>	0	0	0	0	2	0	0	2
PROESTRUS		Nad>	0	0	0	0	2	0	0	2
ESTRUS		Nad>	0	0	0	0	2	0	0	2
METESTRUS		Nad>	0	0	0	0	2	0	0	2
DIESTRUS		Present>	0	0	0	0	2	0	0	2
ANESTRUS		Nad>	0	0	0	0	2	0	0	2
MANDIBULAR S.G.	. . . . .	NUMBER EXAMINED:	2	0	0	2	2	0	0	2

Nad = No abnormalities detected  
Group 1: Vehicle

NOS = Not otherwise specified  
Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
MANDIBULAR S.G. (Continued)		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Lymphocytic Infiltration		Nad>	1	0	0	2	1	0	0	1
		Minimal>	1	0	0	0	1	0	0	0
		Slight>	0	0	0	0	0	0	0	1
PAROTIDS		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Lymphocytic Infiltration		Nad>	2	0	0	2	2	0	0	2
ACINAR ATROPHY		Nad>	0	0	0	1	1	0	0	1
		Minimal>	2	0	0	0	1	0	0	1
		Slight>	0	0	0	1	0	0	0	0
SKIN		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Chronic Inflammation		Nad>	2	0	0	1	2	0	0	2
		Minimal>	0	0	0	1	0	0	0	0
SPLEEN		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Extramedullary Hematopoiesis		Nad>	2	0	0	2	1	0	0	1
		Minimal>	0	0	0	0	1	0	0	1
STOMACH		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
Acute Inflammation		Nad>	2	0	0	2	2	0	0	0
		Minimal>	0	0	0	0	0	0	0	2
GASTRITIS		Nad>	2	0	0	2	0	0	0	2
		Minimal>	0	0	0	0	1	0	0	0
		Slight>	0	0	0	0	1	0	0	0
STERNUM		NUMBER EXAMINED:	2	0	0	2	2	0	0	2

Nad = No abnormalities detected  
Group 1: Vehicle

NOS = Not otherwise specified  
Group 2: 50 mg/kg/day

Group 3: 200 mg/kg/day

Group 4: 800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX:	M a l e s				F e m a l e s			
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
TESTES	. . . . .	.NUMBER EXAMINED:	2	0	0	2	0	0	0	0
IMMATURE		Nad>	2	0	0	2	0	0	0	0
SEGMENTAL HYPOPLASIA		Nad>	2	0	0	2	0	0	0	0
THYROIDS	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CYSTIC FOLLICLES		Nad>	1	0	0	1	2	0	0	2
		Slight>	1	0	0	1	0	0	0	0
THYMUS	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
CYSTS		Nad>	1	0	0	1	2	0	0	1
		Minimal>	1	0	0	1	0	0	0	1
INVOLUTION		Minimal>	0	0	0	0	2	0	0	1
		Slight>	1	0	0	0	0	0	0	0
		Moderate>	1	0	0	0	0	0	0	1
		Marked>	0	0	0	2	0	0	0	0
TONGUE	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ACUTE INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
CHRONIC INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
TRACHEA	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2
ACUTE INFLAMMATION		Nad>	2	0	0	2	2	0	0	2
URINARY BLADDER	. . . . .	.NUMBER EXAMINED:	2	0	0	2	2	0	0	2

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

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Table 13  
Expanded Incidence Summary for Microscopic Observations  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

CONTROLS FROM GROUP(S): 1		ANIMAL SEX: M a l e s				F e m a l e s				
T I S S U E S W I T H D I A G N O S E S		DOSAGE GROUP:	1	2	3	4	1	2	3	4
		NO. IN GROUP:	2	0	0	2	2	0	0	2
URINARY BLADDER (Continued)		NUMBER EXAMINED:	2	0	0	2	2	0	0	2
MINERALIZATION IN MUSCULARIS/SUBSEROSA		Nad>	2	0	0	2	2	0	0	2
UTERUS		NUMBER EXAMINED:	0	0	0	0	2	0	0	2
IMMATURE		Nad>	0	0	0	0	2	0	0	2
ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA		Minimal>	0	0	0	0	0	0	0	2
		Slight>	0	0	0	0	2	0	0	0
EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN		Nad>	0	0	0	0	2	0	0	0
		Minimal>	0	0	0	0	0	0	0	2
VAGINA		NUMBER EXAMINED:	0	0	0	0	2	0	0	2

Nad = No abnormalities detected  
Group 1:Vehicle

NOS = Not otherwise specified  
Group 2:50 mg/kg/day

Group 3:200 mg/kg/day

Group 4:800 mg/kg/day

***Table 14 Histological changes in ovaries***

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Table 14  
Histological Changes in Ovaries  
Test period

Fexinidazole

Study No. 0505-2007

Dates of necropsy	End of treatment		27-28 february 2008									
	Recovery		12 march 2008									
<b>END OF TREATMENT - Day 29</b>												
Test group	1			2			3			4		
Dose (mg/kg/day)	0	0	0	50	50	50	200	200	200	800	800	800
Female No.	2560	2568	2572	2562	2563	2576	2561	2570	2567	2564	2565	2569
IMMATURE	P	P	P	-	-	-	-	-	-	-	-	-
CORPORA LUTEA	-	-	-	P	-	P	P	P	P	P	P	P
<b>RECOVERY - Day 43</b>												
Test group	1							4				
Dose (mg/kg/day)	0	0						800	800			
Female No.	2575	2577						2571	2573			
IMMATURE	-	-						-	-			
CORPORA LUTEA	P	P						P	P			

<b>Non gradable findings</b>
- = finding absent P = present

***Table 15 Stage of Estrus Evaluation***

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Table 15  
Stage of Estrus Evaluation  
Test period

Fexinidazole

Study No. 0505-2007

Dates of necropsy	End of treatment		27-28 february 2008									
	Recovery		12 march 2008									
END OF TREATMENT												
27-28 february 2008												
Test group	1			2			3			4		
Dose (mg/kg/day)	0	0	0	50	50	50	200	200	200	800	800	800
Female No.	2560	2568	2572	2562	2563	2576	2561	2570	2567	2564	2565	2569
Date of birth	03-5-07	09-5-07	11-5-07	05-5-07	05-5-07	16-5-07	05-5-07	11-5-07	06-5-07	05-5-07	05-5-07	11-5-07
IMMATURE	P	P	P	-	-	-	-	-	-	-	-	-
PROESTRUS	-	-	-	-	-	-	-	-	-	-	-	-
ESTRUS	-	-	-	-	P	-	-	-	-	-	-	-
METESTRUS	-	-	-	-	-	-	-	-	-	-	-	P
DIESTRUS	-	-	-	P	-	P	P	P	P	P	P	-
ANESTRUS	-	-	-	-	-	-	-	-	-	-	-	-
RECOVERY												
12 march 2008												
Test group	1								4			
Dose (mg/kg/day)	0	0							800	800		
Female No.	2575	2577							2571	2573		
Date of birth	16-5-07	17-5-07							11-5-07	13-5-07		
Date of birth												
IMMATURE	-	-							-	-		
PROESTRUS	-	-							-	-		
ESTRUS	-	-							-	-		
METESTRUS	-	-							-	-		
DIESTRUS	P	P							P	P		
ANESTRUS	-	-							-	-		

Length of estrus stages:  
Proestrus + Estrus + Metestrus = 18 days  
Diestrus = 2-3 month  
Anestrus = 3-5 month



## APPENDICES

## ***Appendix 1 QA Statement***

## ***Appendix 2 Clinical Signs***

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2516	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	36	Pretest phase -8--2
		DIARRHEA, MODERATE	1	Test period 1-29
		SOFT STOOL, SLIGHT	4	Test period 9
		SOFT STOOL, MODERATE	5	Test period 2,8,22-23
				Pretest phase -1
2518	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	34	Test period 10,13-14,18
		DIARRHEA, SLIGHT	1	Pretest phase -8--6,-3--2
		DIARRHEA, MODERATE	2	Test period 1-29
		DIARRHEA, MARKED	2	Test period 6
		SOFT STOOL, SLIGHT	6	Pretest phase -4,-1
		SOFT STOOL, MODERATE	3	Test period 14-15
		REDUCED FOOD INTAKE, SLIGHT	1	Pretest phase -5
2520	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	38	Test period 2-3,8,12-13
		SOFT STOOL, SLIGHT	5	Test period 7,11,16
		SOFT STOOL, MODERATE	3	Test period 12
2527	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	48	Pretest phase -8--1
		SOFT STOOL, SLIGHT	2	Test period 1-30
		SOFT STOOL, MODERATE	2	Test period 10-13,16
		REDUCED FOOD INTAKE, SLIGHT	1	Test period 3-4,21
2533	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	49	Pretest phase -8--5,-2--1
		DIARRHEA, SLIGHT	1	Test period 1-36,38-43
		SOFT STOOL, SLIGHT	5	Test period 22,37
			1	Pretest phase -4--3
			1	Test period 4
			1	Pretest phase -8--4,-2--1
			1	Test period 1-34,36-43
			1	Test period 6
			5	Test period 2-3,10,17,28

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2533	Vehicle	SOFT STOOL, MODERATE	4	Pretest phase -3 Test period 9,15,35
2514	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS SOFT STOOL, SLIGHT	37 1	Pretest phase -8--1 Test period 1-29 Test period 12
2521	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS REDUCED FOOD INTAKE, SLIGHT	37 6	Pretest phase -8--1 Test period 1-29 Test period 2,4-6,8,10
2529	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS DIARRHEA, SLIGHT DIARRHEA, MODERATE DIARRHEA, MARKED SOFT STOOL, SLIGHT SOFT STOOL, MODERATE	35 2 2 1 11 3	Pretest phase -8--4,-2 Test period 1-29 Test period 22-23 Test period 15,30 Test period 29 Pretest phase -3,-1 Test period 2-3,7-8,10,13,16-17,26 Test period 11,14,21
2515	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS SOFT STOOL, MODERATE	36 1	Pretest phase -8,-6--1 Test period 1-29 Pretest phase -7
2523	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS SOFT STOOL, SLIGHT SOFT STOOL, MODERATE	36 1 3	Pretest phase -8--4,-2--1 Test period 1-29 Pretest phase -3 Test period 11,14-15
2526	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS SOFT STOOL, MODERATE	36 2	Pretest phase -8,-6--2 Test period 1-30 Pretest phase -7,-1

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2526	200 mg/kg/day	REDUCED FOOD INTAKE, SLIGHT	2	Test period 5,15
		REDUCED FOOD INTAKE, MODERATE	1	Test period 16
2517	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	37	Pretest phase -8--1
		DIARRHEA, SLIGHT	1	Test period 1-29
		SOFT STOOL, SLIGHT	3	Test period 22
		SOFT STOOL, MODERATE	3	Test period 2-4 Test period 7-8,12
2519	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	35	Pretest phase -8--6,-3--1
		SOFT STOOL, SLIGHT	3	Test period 1-29
		SOFT STOOL, MODERATE	3	Test period 2,8,22
		REDUCED FOOD INTAKE, MODERATE	1	Pretest phase -5--4 Test period 16 Test period 5
2525	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	38	Pretest phase -8--1
		DIARRHEA, MODERATE	1	Test period 1-30
		SOFT STOOL, SLIGHT	3	Test period 5 Test period 3,8,12
2528	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	51	Pretest phase -8--1
		DIARRHEA, MODERATE	1	Test period 1-43
		SOFT STOOL, SLIGHT	3	Test period 4
		SOFT STOOL, MODERATE	1	Test period 5-6,28 Test period 13
2530	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	49	Pretest phase -8--4,-2--1
		DIARRHEA, SLIGHT	1	Test period 1-41,43
		DIARRHEA, MODERATE	2	Test period 6
		SOFT STOOL, SLIGHT	2	Test period 9,42 Test period 5,22

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

M a l e s

<u>Animal Number</u>	<u>Dose</u>	<u>Clinical Signs</u>	<u>Days Present</u>	<u>Study Day(s) Noted</u>
2530	800 mg/kg/day	SOFT STOOL, MODERATE	2	Pretest phase -3 Test period 16

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2560	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	35	Pretest phase -8--6,-4--1
		DIARRHEA, SLIGHT	2	Test period 1-28
		DIARRHEA, MARKED	1	Test period 5,14
		SOFT STOOL, SLIGHT	2	Test period 28
		SOFT STOOL, MODERATE	6	Test period 19,22
				Pretest phase -5
				Test period 4,11,13,15,29
2568	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	38	Pretest phase -8--1
		SOFT STOOL, SLIGHT	2	Test period 1-30
		REDUCED FOOD INTAKE, SLIGHT	1	Test period 14,21
				Test period 4
2572	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	38	Pretest phase -8--1
		DIARRHEA, SLIGHT	1	Test period 1-30
		SOFT STOOL, SLIGHT	1	Test period 5
				Test period 11
2575	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	50	Pretest phase -8--1
		SOFT STOOL, MODERATE	2	Test period 1-36,38-43
				Test period 8,37
2577	Vehicle	NORMAL/NO SIGNIFICANT SIGNS	50	Pretest phase -8--1
		DIARRHEA, SLIGHT	2	Test period 1-35,37-43
		DIARRHEA, MODERATE	1	Test period 10,17
		SOFT STOOL, SLIGHT	2	Test period 16
		SOFT STOOL, MODERATE	1	Test period 3,36
				Test period 8
2562	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	37	Pretest phase -8--1
		SOFT STOOL, SLIGHT	2	Test period 1-29
				Test period 15,21



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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2563	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	35	Pretest phase -8--4,-1
		SOFT STOOL, SLIGHT	3	Test period 2-30
		SOFT STOOL, MODERATE, 2-4h AFTER DOSING	1	Pretest phase -3--2 Test period 16 Test period 1
2576	50 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	38	Pretest phase -8--1
		REDUCED FOOD INTAKE, SLIGHT	1	Test period 1-30 Test period 4
2561	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	36	Pretest phase -8--5,-3--1
		SOFT STOOL, SLIGHT	1	Test period 1-29
		REDUCED FOOD INTAKE, SLIGHT	1	Pretest phase -4 Test period 28
2570	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	38	Pretest phase -8--1
		DIARRHEA, SLIGHT	4	Test period 1-30
		SOFT STOOL, SLIGHT	2	Test period 5,12,25-26
		SOFT STOOL, MODERATE	3	Test period 14,21 Test period 8,15,23
2567	200 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	34	Pretest phase -8--5,-3
		SOFT STOOL, SLIGHT	5	Test period 1-25,27-30
		SOFT STOOL, MODERATE	3	Pretest phase -4,-2--1
		REDUCED FOOD INTAKE, SLIGHT	3	Test period 14-15
		REDUCED FOOD INTAKE, MODERATE	1	Test period 6,25-26 Test period 4,8,20 Test period 16
2564	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	37	Pretest phase -8--1
		SOFT STOOL, SLIGHT	1	Test period 1-29 Test period 16

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Appendix 2  
Individual Animal Clinical Signs

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Days Present	Study Day(s) Noted
2564	800 mg/kg/day	REDUCED FOOD INTAKE, SLIGHT	2	Test period 8,19
		REDUCED FOOD INTAKE, MODERATE	9	Test period 2-4,6-7,11,14-15,18
		REDUCED FOOD INTAKE, MARKED	1	Test period 5
2565	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	37	Pretest phase -8--2
		DIARRHEA, MARKED	1	Test period 1-30
		SOFT STOOL, SLIGHT	1	Test period 28
		REDUCED FOOD INTAKE, SLIGHT	7	Pretest phase -1
		REDUCED FOOD INTAKE, MODERATE	8	Test period 8,13-16,19-20
2569	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	38	Test period 2-7,11,18
		REDUCED FOOD INTAKE, SLIGHT	2	Pretest phase -8--1
				Test period 1-30
2571	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	50	Test period 22,28
		SOFT STOOL, SLIGHT	2	Pretest phase -8--1
		REDUCED FOOD INTAKE, SLIGHT	8	Test period 1-30,32-43
		REDUCED FOOD INTAKE, MODERATE	6	Test period 21,31
		REDUCED FOOD INTAKE, MARKED	1	Test period 2,8,10-11,14-15,19,23
2573	800 mg/kg/day	NORMAL/NO SIGNIFICANT SIGNS	47	Test period 3-5,7,18,28
		DIARRHEA, SLIGHT	1	Test period 6
		EMESIS OF FOOD, MODERATE	1	Pretest phase -8--5,-3--1
		SOFT STOOL, MODERATE	2	Test period 1-28,32-43
		REDUCED FOOD INTAKE, SLIGHT	16	Test period 29
				Test period 18
				Test period 30-31
REDUCED FOOD INTAKE, MODERATE	5	Pretest phase -4		
		Test period 3,6,9-10,13-17,19,22		
		Test period 23,25-26,28		
		Test period 2,4-5,8,11		

### ***Appendix 3 Body Weights***

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Appendix 3  
Body Weights (kg)

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Study Day	M a l e s							-8"	1#	8	14	22	28	35	40
Vehicle																		
	2516	1/1		8.19	8.45	8.36	8.48	8.63	8.30	Dead								
	2518	1/1		8.90	9.04	8.74	8.87	8.94	8.59	Dead								
	2520	1/1		7.94	8.08	8.01	8.11	8.29	8.11	Dead								
	2527	1/1		7.72	7.90	7.77	7.82	7.90	8.02	7.75		7.82						
	2533	1/1		8.26	8.34	7.79	7.98	7.84	7.48	7.41		7.60						
		N		5	5	5	5	5	5	2		2						
		Mean		8.20	8.36	8.14	8.25	8.32	8.10	7.58		7.71						
		Sdev		0.444	0.436	0.410	0.423	0.472	0.411	0.240		0.153						
50 mg/kg/day																		
	2514	2/1		9.61	9.78	9.54	9.68	9.92	9.43	Dead								
	2521	2/1		8.03	8.08	7.67	7.85	7.80	7.50	Dead								
	2529	2/1		7.35	7.56	7.40	7.54	7.65	7.63	Dead								
		N		3	3	3	3	3	3	0		0						
		Mean		8.33	8.47	8.20	8.36	8.46	8.19	-		-						
		Sdev		1.160	1.163	1.165	1.155	1.271	1.081	-		-						
200 mg/kg/day																		
	2515	3/1		8.93	8.87	8.76	8.84	8.73	8.33	Dead								
	2523	3/1		8.66	8.70	8.32	8.41	8.32	7.79	Dead								
	2526	3/1		7.62	7.96	7.49	7.88	7.67	7.67	Dead								
		N		3	3	3	3	3	3	0		0						
		Mean		8.40	8.51	8.19	8.37	8.24	7.93	-		-						
		Sdev		0.691	0.482	0.642	0.479	0.531	0.351	-		-						
800 mg/kg/day																		
	2517	4/1		8.00	7.85	7.36	7.31	7.12	6.76	Dead								
	2519	4/1		8.18	8.27	7.81	7.97	8.01	8.07	Dead								
	2525	4/1		9.40	9.87	9.48	9.70	9.44	9.25	Dead								
	2528	4/1		8.84	9.11	8.62	8.70	8.62	8.65	8.35		8.49						
	2530	4/1		7.53	7.54	7.03	7.18	7.08	6.77	6.75		7.02						
		N		5	5	5	5	5	5	2		2						
		Mean		8.39	8.53	8.06	8.17	8.05	7.90	7.55		7.75						
		Sdev		0.734	0.954	0.993	1.049	1.010	1.117	1.131		1.039						

Note: " = Pretest phase; # = Test period

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Appendix 3  
Body Weights (kg)

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Study Day	F e m a l e s								
				-8"	1#	8	14	22	28	35	40	
Vehicle												
	2560	1/1		6.85	6.83	6.72	6.46	6.50	6.27	Dead		
	2568	1/1		7.22	7.38	7.11	6.98	7.09	6.92	Dead		
	2572	1/1		7.07	7.23	6.76	6.75	6.70	6.44	Dead		
	2575	1/1		7.82	7.76	7.75	7.64	7.79	7.84	7.74	7.91	
	2577	1/1		7.92	8.39	8.12	8.29	8.38	8.70	8.37	8.51	
		N		5	5	5	5	5	5	2	2	
		Mean		7.37	7.52	7.29	7.22	7.29	7.23	8.06	8.21	
		Sdev		0.471	0.592	0.621	0.737	0.783	1.020	0.445	0.426	
50 mg/kg/day												
	2562	2/1		6.96	6.91	6.96	6.84	7.00	6.65	Dead		
	2563	2/1		7.55	7.56	7.53	7.53	7.82	7.56	Dead		
	2576	2/1		8.30	8.64	8.47	8.53	8.57	8.26	Dead		
		N		3	3	3	3	3	3	0	0	
		Mean		7.60	7.70	7.65	7.63	7.80	7.49	-	-	
		Sdev		0.674	0.872	0.762	0.847	0.784	0.803	-	-	
200 mg/kg/day												
	2561	3/1		7.32	7.41	7.31	7.23	7.53	7.03	Dead		
	2570	3/1		6.90	6.95	6.77	6.76	6.75	6.38	Dead		
	2567	3/1		8.73	8.52	8.36	8.43	8.29	7.99	Dead		
		N		3	3	3	3	3	3	0	0	
		Mean		7.65	7.63	7.48	7.48	7.52	7.13	-	-	
		Sdev		0.960	0.807	0.808	0.862	0.770	0.809	-	-	
800 mg/kg/day												
	2564	4/1		7.53	7.57	6.96	6.58	6.51	6.43	Dead		
	2565	4/1		7.17	6.83	6.15	6.53	6.39	6.01	Dead		
	2569	4/1		7.87	7.96	7.81	8.01	7.96	7.70	Dead		
	2571	4/1		7.66	7.86	7.13	7.27	7.21	6.84	7.23	7.37	
	2573	4/1		6.90	6.85	6.31	6.43	6.45	6.27	6.38	6.54	
		N		5	5	5	5	5	5	2	2	
		Mean		7.42	7.41	6.87	6.96	6.90	6.65	6.81	6.95	
		Sdev		0.391	0.546	0.670	0.671	0.677	0.659	0.601	0.592	

Note: " = Pretest phase; # = Test period

## ***Appendix 4 ECG Examinations***

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Appendix 4  
Individual Animal ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2516	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2518	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2520	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2527	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24,38
2533	Vehicle	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24 Test period 38
2514	50mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 24 Pretest phase -5
2521	50mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 24 Pretest phase -5
2529	50mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 24 Pretest phase -5
2515	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2523	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2526	200mg/kg/day	No ECG abnormalities detected	Test period 24

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Appendix 4  
Individual Animal ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2526	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -5
2517	800mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2519	800mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2525	800mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -5 Test period 24
2528	800mg/kg/day	No ECG abnormalities detected	Pretest phase -5 Test period 24,38
2530	800mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 24 Pretest phase -5 Test period 38



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Appendix 4  
Individual Animal ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2560	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2568	Vehicle	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2572	Vehicle	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2575	Vehicle	No ECG abnormalities detected	Pretest phase -6 Test period 24,37
2577	Vehicle	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 37 Pretest phase -6 Test period 24
2562	50mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2563	50mg/kg/day	No ECG abnormalities detected Respiratory Sinus Arrhythmia	Test period 24 Pretest phase -6
2576	50mg/kg/day	No ECG abnormalities detected	Pretest phase -6 Test period 24
2561	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2570	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2567	200mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -6

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Appendix 4  
Individual Animal ECG Rhythm and Morphology Findings

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2567	200mg/kg/day	Respiratory Sinus Arrhythmia	Test period 24
2564	800mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24
2565	800mg/kg/day	No ECG abnormalities detected	Pretest phase -6 Test period 24
2569	800mg/kg/day	No ECG abnormalities detected	Pretest phase -6 Test period 24
2571	800mg/kg/day	No ECG abnormalities detected	Pretest phase -6 Test period 24,37
2573	800mg/kg/day	Respiratory Sinus Arrhythmia	Pretest phase -6 Test period 24,37

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.	-5"	24#	38
Dosage		Day:	S 1	S 1	S 1
mg/kg : 0.		Session:			
HR	bpm	2516	97.	89.	
		2518	94.	103.	
		2520	87.	80.	
		2527	101.	125.	94.
		2533	87.	79.	72.
		Mean	93.	95.	83.
		SD	6.2	19.2	15.6
	N	5	5	2	
RR	ms	2516	613.	673.	
		2518	634.	579.	
		2520	688.	749.	
		2527	594.	478.	636.
		2533	683.	751.	831.
		Mean	642.	646.	734.
		SD	41.8	117.3	137.9
	N	5	5	2	
Pdur	ms	2516	39.	33.	
		2518	37.	33.	
		2520	37.	38.	
		2527	37.	31.	35.
		2533	41.	38.	42.
		Mean	38.	35.	39.
		SD	1.8	3.2	4.9
	N	5	5	2	
PR	ms	2516	83.	84.	
		2518	88.	85.	
		2520	87.	74.	
		2527	81.	72.	80.
		2533	96.	91.	93.
		Mean	87.	81.	87.
		SD	5.8	8.0	9.2
	N	5	5	2	

Note: " = Pretest phase; # = Test period

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ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.	Day:	24#	38
Dosage		mg/kg :	0.	S 1	S 1
QRS	ms	2516	68.	56.	
		2518	43.	40.	
		2520	42.	47.	
		2527	43.	45.	48.
		2533	40.	45.	53.
		Mean	47.	47.	51.
		SD	11.7	5.9	3.5
		N	5	5	2
QT	ms	2516	180.	197.	
		2518	178.	179.	
		2520	177.	196.	
		2527	181.	177.	204.
		2533	181.	195.	194.
		Mean	179.	189.	199.
		SD	1.8	9.9	7.1
		N	5	5	2
QTcF	ms	2516	212.	225.	
		2518	207.	214.	
		2520	200.	216.	
		2527	215.	226.	237.
		2533	205.	214.	206.
		Mean	208.	219.	222.
		SD	5.7	5.7	21.7
		N	5	5	2
MEA	degree	2516	34.	39.	
		2518	-21.	1.	
		2520	26.	54.	
		2527	44.	44.	57.
		2533	143.	120.	-19.
		Mean	45.	52.	19.
		SD	60.1	43.2	53.7
		N	5	5	2

Note: " = Pretest phase; # = Test period

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ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
Pamp	mV	2516	0.32	0.38	
		2518	0.32	0.40	
		2520	0.22	0.37	
		2527	0.24	0.25	0.26
		2533	0.40	0.34	0.34
		Mean	0.30	0.35	0.30
		SD	0.072	0.059	0.057
	N	5	5	2	
Qamp	mV	2516	-0.15	-0.20	
		2518	-0.54	-0.46	
		2520	-0.53	-0.41	
		2527	-0.33	-0.28	-0.36
		2533	-0.28	-0.25	-0.16
		Mean	-0.37	-0.32	-0.26
		SD	0.168	0.110	0.141
	N	5	5	2	
Ramp	mV	2516	2.68	3.13	
		2518	1.37	1.38	
		2520	2.46	2.73	
		2527	2.22	2.06	2.31
		2533	0.67	0.96	0.90
		Mean	1.88	2.05	1.61
		SD	0.839	0.904	0.997
	N	5	5	2	
Samp	mV	2516	-0.11	-0.06	
		2518	-0.26	-0.13	
		2520	-0.07	-0.09	
		2527	-0.21	-0.20	-0.26
		2533	-0.30	-0.32	-0.33
		Mean	-0.19	-0.16	-0.30
		SD	0.098	0.104	0.049
	N	5	5	2	

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
STd	mV	2516	-0.10	-0.08	
		2518	-0.07	-0.01	
		2520	-0.04	-0.04	
		2527	-0.15	-0.07	-0.07
		2533	0.00	-0.04	0.02
		Mean	-0.07	-0.05	-0.03
		SD	0.057	0.028	0.064
		N	5	5	2
Tamp	mV	2516	-0.16	-0.15	
		2518	0.68	0.62	
		2520	-0.07	0.24	
		2527	0.27	0.44	0.12
		2533	0.28	0.28	0.32
		Mean	0.20	0.29	0.22
		SD	0.333	0.286	0.141
		N	5	5	2

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
HR	bpm	2560	63.	70.	
		2568	94.	123.	
		2572	116.	106.	
		2575	87.	88.	76.
		2577	113.	106.	126.
		Mean	95.	99.	101.
		SD	21.5	20.2	35.4
		N	5	5	2
RR	ms	2560	952.	853.	
		2568	634.	484.	
		2572	515.	565.	
		2575	688.	679.	784.
		2577	530.	563.	473.
		Mean	664.	629.	629.
		SD	176.5	143.3	219.9
		N	5	5	2
Pdur	ms	2560	47.	47.	
		2568	41.	39.	
		2572	40.	44.	
		2575	38.	41.	44.
		2577	40.	39.	37.
		Mean	41.	42.	41.
		SD	3.4	3.5	4.9
		N	5	5	2
PR	ms	2560	79.	79.	
		2568	75.	77.	
		2572	87.	82.	
		2575	108.	94.	116.
		2577	89.	83.	88.
		Mean	88.	83.	102.
		SD	12.8	6.6	19.8
		N	5	5	2

Note: " = Pretest phase; # = Test period

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ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
QRS	ms	2560	42.	44.	
		2568	40.	43.	
		2572	45.	46.	
		2575	45.	49.	47.
		2577	58.	57.	55.
		Mean	46.	48.	51.
		SD	7.0	5.6	5.7
		N	5	5	2
QT	ms	2560	189.	206.	
		2568	182.	169.	
		2572	175.	181.	
		2575	191.	185.	201.
		2577	188.	189.	186.
		Mean	185.	186.	194.
		SD	6.5	13.5	10.6
		N	5	5	2
QTcF	ms	2560	192.	217.	
		2568	212.	215.	
		2572	218.	219.	
		2575	216.	210.	218.
		2577	232.	228.	238.
		Mean	214.	218.	228.
		SD	14.3	6.7	14.4
		N	5	5	2
MEA	degree	2560	101.	114.	
		2568	41.	53.	
		2572	34.	18.	
		2575	37.	44.	41.
		2577	17.	37.	73.
		Mean	46.	53.	57.
		SD	32.1	36.3	22.6
		N	5	5	2

Note: " = Pretest phase; # = Test period



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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
Pamp	mV	2560	0.36	0.39	
		2568	0.44	0.44	
		2572	0.33	0.50	
		2575	0.08	0.32	0.30
		2577	0.41	0.36	0.48
	Mean		0.32	0.40	0.39
	SD		0.143	0.070	0.127
	N		5	5	2
Qamp	mV	2560	-0.57	-0.81	
		2568	-0.22	-0.29	
		2572	-0.37	-0.30	
		2575	-0.34	-0.35	-0.40
		2577	-0.43	-0.35	-0.38
	Mean		-0.39	-0.42	-0.39
	SD		0.128	0.220	0.014
	N		5	5	2
Ramp	mV	2560	2.22	2.27	
		2568	2.37	2.64	
		2572	2.99	2.82	
		2575	2.56	3.23	2.92
		2577	2.10	2.12	2.35
	Mean		2.45	2.62	2.64
	SD		0.348	0.443	0.403
	N		5	5	2
Samp	mV	2560	-0.19	-0.17	
		2568	-0.19	-0.16	
		2572	-0.20	-0.61	
		2575	-0.48	0.00	-0.16
		2577	-0.50	-0.38	-0.56
	Mean		-0.31	-0.26	-0.36
	SD		0.163	0.236	0.283
	N		5	5	2

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 0.	Session:	S 1	S 1	S 1
STd	mV	2560	-0.05	-0.05	
		2568	0.00	-0.06	
		2572	-0.09	-0.05	
		2575	-0.08	-0.03	0.00
		2577	0.06	0.07	0.09
	Mean		-0.03	-0.02	0.05
	SD		0.062	0.054	0.064
	N		5	5	2
Tamp	mV	2560	0.33	0.46	
		2568	0.53	0.61	
		2572	0.19	0.45	
		2575	0.04	0.44	0.36
		2577	-0.09	0.05	-0.45
	Mean		0.20	0.40	-0.04
	SD		0.243	0.209	0.573
	N		5	5	2

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 50.		Session:	S 1	S 1	S 1
HR	bpm	2514	67.	120.	
		2521	64.	58.	
		2529	114.	128.	
		Mean	82.	102.	-
	SD	28.0	38.3	-	
	N	3	3	0	
RR	ms	2514	885.	499.	
		2521	929.	1029.	
		2529	525.	466.	
		Mean	780.	665.	-
	SD	221.6	316.0	-	
	N	3	3	0	
Pdur	ms	2514	37.	37.	
		2521	38.	33.	
		2529	35.	33.	
		Mean	37.	34.	-
	SD	1.5	2.3	-	
	N	3	3	0	
PR	ms	2514	99.	85.	
		2521	81.	75.	
		2529	86.	87.	
		Mean	89.	82.	-
	SD	9.3	6.4	-	
	N	3	3	0	
QRS	ms	2514	49.	47.	
		2521	45.	48.	
		2529	44.	41.	
		Mean	46.	45.	-
	SD	2.6	3.8	-	
	N	3	3	0	
QT	ms	2514	193.	181.	
		2521	193.	203.	
		2529	173.	177.	

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 50.		Session:	S 1	S 1	S 1
		Mean	186.	187.	-
		SD	11.5	14.0	-
		N	3	3	0
QTcF	ms	2514	201.	228.	
		2521	198.	201.	
		2529	214.	228.	
		Mean	204.	219.	-
		SD	8.6	15.4	-
		N	3	3	0
MEA	degree	2514	54.	59.	
		2521	62.	63.	
		2529	38.	50.	
		Mean	51.	57.	-
		SD	12.2	6.7	-
		N	3	3	0
Pamp	mV	2514	0.35	0.40	
		2521	0.33	0.40	
		2529	0.41	0.38	
		Mean	0.36	0.39	-
		SD	0.042	0.012	-
		N	3	3	0
Qamp	mV	2514	-0.25	-0.30	
		2521	-0.33	-0.39	
		2529	-0.53	-0.52	
		Mean	-0.37	-0.40	-
		SD	0.144	0.111	-
		N	3	3	0
Ramp	mV	2514	2.84	3.00	
		2521	3.53	3.95	
		2529	2.60	2.57	
		Mean	2.99	3.17	-
		SD	0.483	0.706	-
		N	3	3	0

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 50.	Session:	S 1	S 1	S 1
Samp	mV	2514	-0.05	-0.10	
		2521	-0.26	-0.15	
		2529	-0.10	-0.14	
	Mean		-0.14	-0.13	-
	SD		0.110	0.026	-
	N		3	3	0
STd	mV	2514	0.00	0.02	
		2521	-0.02	-0.13	
		2529	-0.11	-0.12	
	Mean		-0.04	-0.08	-
	SD		0.059	0.084	-
	N		3	3	0
Tamp	mV	2514	0.26	-0.05	
		2521	-0.07	-0.16	
		2529	0.10	-0.38	
	Mean		0.10	-0.20	-
	SD		0.165	0.168	-
	N		3	3	0

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.	Day:	24#	38
Dosage			-5"		
mg/kg : 50.		Session:	S 1	S 1	S 1
HR	bpm	2562	113.	95.	
		2563	101.	114.	
		2576	133.	116.	
		Mean	116.	108.	-
	SD	16.2	11.6	-	
	N	3	3	0	
RR	ms	2562	531.	629.	
		2563	589.	522.	
		2576	448.	515.	
		Mean	523.	555.	-
	SD	70.9	63.9	-	
	N	3	3	0	
Pdur	ms	2562	35.	35.	
		2563	39.	37.	
		2576	36.	34.	
		Mean	37.	35.	-
	SD	2.1	1.5	-	
	N	3	3	0	
PR	ms	2562	83.	89.	
		2563	85.	88.	
		2576	80.	89.	
		Mean	83.	89.	-
	SD	2.5	0.6	-	
	N	3	3	0	
QRS	ms	2562	49.	49.	
		2563	45.	53.	
		2576	59.	41.	
		Mean	51.	48.	-
	SD	7.2	6.1	-	
	N	3	3	0	
QT	ms	2562	179.	195.	
		2563	181.	175.	
		2576	181.	182.	

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 50.	Session:	S 1	S 1	S 1
		Mean	180.	184.	-
		SD	1.2	10.1	-
		N	3	3	0
QTcF	ms	2562	221.	227.	
		2563	216.	217.	
		2576	236.	227.	
		Mean	224.	224.	-
		SD	10.6	5.8	-
		N	3	3	0
MEA	degree	2562	55.	45.	
		2563	40.	61.	
		2576	36.	61.	
		Mean	44.	56.	-
		SD	10.0	9.2	-
		N	3	3	0
Pamp	mV	2562	0.30	0.35	
		2563	0.32	0.38	
		2576	0.55	0.47	
		Mean	0.39	0.40	-
		SD	0.139	0.062	-
		N	3	3	0
Qamp	mV	2562	-1.10	-0.83	
		2563	-0.58	-0.51	
		2576	-0.34	-0.36	
		Mean	-0.67	-0.57	-
		SD	0.389	0.240	-
		N	3	3	0
Ramp	mV	2562	3.21	2.76	
		2563	1.58	1.87	
		2576	2.13	3.23	
		Mean	2.31	2.62	-
		SD	0.829	0.691	-
		N	3	3	0

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 50.	Session:	S 1	S 1	S 1
Samp	mV	2562	-0.15	-0.03	
		2563	-0.27	-0.58	
		2576	-0.48	-0.52	
	Mean		-0.30	-0.38	-
	SD		0.167	0.302	-
	N		3	3	0
STd	mV	2562	-0.19	-0.05	
		2563	-0.06	0.02	
		2576	0.14	-0.04	
	Mean		-0.04	-0.02	-
	SD		0.166	0.038	-
	N		3	3	0
Tamp	mV	2562	-0.58	-0.30	
		2563	-0.30	0.32	
		2576	0.23	0.08	
	Mean		-0.22	0.03	-
	SD		0.411	0.313	-
	N		3	3	0

Note: " = Pretest phase; # = Test period



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ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.	Day:	24#	38
Dosage			-5"		
mg/kg : 200.		Session:	S 1	S 1	S 1
HR	bpm	2515	63.	71.	
		2523	77.	81.	
		2526	102.	139.	
		Mean	81.	97.	-
		SD	19.8	36.7	-
		N	3	3	0
RR	ms	2515	951.	839.	
		2523	773.	738.	
		2526	583.	430.	
		Mean	769.	669.	-
		SD	184.0	213.1	-
		N	3	3	0
Pdur	ms	2515	35.	35.	
		2523	42.	41.	
		2526	34.	43.	
		Mean	37.	40.	-
		SD	4.4	4.2	-
		N	3	3	0
PR	ms	2515	95.	88.	
		2523	98.	84.	
		2526	99.	99.	
		Mean	97.	90.	-
		SD	2.1	7.8	-
		N	3	3	0
QRS	ms	2515	60.	51.	
		2523	61.	61.	
		2526	45.	46.	
		Mean	55.	53.	-
		SD	9.0	7.6	-
		N	3	3	0
QT	ms	2515	195.	197.	
		2523	201.	204.	
		2526	175.	187.	

Note: " = Pretest phase; # = Test period

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Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 200.		Session:	S 1	S 1	S 1
		Mean	190.	196.	-
		SD	13.6	8.5	-
		N	3	3	0
QTcF	ms	2515	198.	209.	
		2523	219.	226.	
		2526	209.	247.	
		Mean	209.	227.	-
		SD	10.3	19.2	-
		N	3	3	0
MEA	degree	2515	46.	59.	
		2523	70.	63.	
		2526	62.	62.	
		Mean	59.	61.	-
		SD	12.2	2.1	-
		N	3	3	0
Pamp	mV	2515	0.37	0.34	
		2523	0.39	0.41	
		2526	0.28	0.39	
		Mean	0.35	0.38	-
		SD	0.059	0.036	-
		N	3	3	0
Qamp	mV	2515	-0.76	-0.55	
		2523	-0.47	-1.12	
		2526	-0.28	-0.21	
		Mean	-0.50	-0.63	-
		SD	0.242	0.460	-
		N	3	3	0
Ramp	mV	2515	3.42	3.58	
		2523	2.53	3.10	
		2526	3.08	3.03	
		Mean	3.01	3.24	-
		SD	0.449	0.299	-
		N	3	3	0

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 200.	Session:	S 1	S 1	S 1
Samp	mV	2515	-0.07	-0.08	
		2523	-0.07	-0.07	
		2526	-0.17	-0.32	
	Mean		-0.10	-0.16	-
	SD		0.058	0.142	-
	N		3	3	0
STd	mV	2515	-0.07	-0.09	
		2523	-0.07	-0.04	
		2526	-0.17	-0.17	
	Mean		-0.10	-0.10	-
	SD		0.058	0.066	-
	N		3	3	0
Tamp	mV	2515	0.22	-0.13	
		2523	0.36	0.40	
		2526	-0.08	-0.22	
	Mean		0.17	0.02	-
	SD		0.225	0.335	-
	N		3	3	0

Note: " = Pretest phase; # = Test period

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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.	Day:	24#	38
Dosage			-5"		
mg/kg : 200.		Session:	S 1	S 1	S 1
HR	bpm	2561	83.	95.	
		2570	116.	120.	
		2567	81.	120.	
		Mean	93.	112.	-
	SD	19.7	14.4	-	
	N	3	3	0	
RR	ms	2561	719.	631.	
		2570	515.	499.	
		2567	741.	500.	
		Mean	658.	543.	-
	SD	124.6	75.9	-	
	N	3	3	0	
Pdur	ms	2561	37.	39.	
		2570	40.	41.	
		2567	37.	40.	
		Mean	38.	40.	-
	SD	1.7	1.0	-	
	N	3	3	0	
PR	ms	2561	85.	84.	
		2570	95.	87.	
		2567	95.	89.	
		Mean	92.	87.	-
	SD	5.8	2.5	-	
	N	3	3	0	
QRS	ms	2561	46.	49.	
		2570	45.	53.	
		2567	55.	56.	
		Mean	49.	53.	-
	SD	5.5	3.5	-	
	N	3	3	0	
QT	ms	2561	189.	197.	
		2570	171.	183.	
		2567	188.	195.	

Note: " = Pretest phase; # = Test period

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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.	Day:	24#	38
Dosage		mg/kg	200.	S 1	S 1
		Mean	183.	192.	-
		SD	10.1	7.6	-
		N	3	3	0
QTcF	ms	2561	211.	229.	
		2570	213.	230.	
		2567	208.	245.	
		Mean	210.	235.	-
		SD	2.7	8.9	-
		N	3	3	0
MEA	degree	2561	63.	60.	
		2570	54.	62.	
		2567	10.	28.	
		Mean	42.	50.	-
		SD	28.4	19.1	-
		N	3	3	0
Pamp	mV	2561	0.39	0.30	
		2570	0.54	0.63	
		2567	0.39	0.51	
		Mean	0.44	0.48	-
		SD	0.087	0.167	-
		N	3	3	0
Qamp	mV	2561	-0.85	-0.71	
		2570	-0.70	-0.80	
		2567	-0.53	-0.53	
		Mean	-0.69	-0.68	-
		SD	0.160	0.137	-
		N	3	3	0
Ramp	mV	2561	2.92	2.72	
		2570	3.16	3.98	
		2567	2.06	2.46	
		Mean	2.71	3.05	-
		SD	0.578	0.813	-
		N	3	3	0

Note: " = Pretest phase; # = Test period

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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 200.	Session:	S 1	S 1	S 1
Samp	mV	2561	-0.18	-0.18	
		2570	-0.03	-0.05	
		2567	-0.48	-0.54	
	Mean		-0.23	-0.26	-
	SD		0.229	0.254	-
	N		3	3	0
STd	mV	2561	-0.08	-0.08	
		2570	-0.04	-0.06	
		2567	-0.03	-0.11	
	Mean		-0.05	-0.08	-
	SD		0.026	0.025	-
	N		3	3	0
Tamp	mV	2561	0.34	0.32	
		2570	0.61	0.47	
		2567	0.71	0.59	
	Mean		0.55	0.46	-
	SD		0.191	0.135	-
	N		3	3	0

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.							
Dosage		Day:		24#		38			
mg/kg : 800.		Session:		S 1		S 1			
HR	bpm	2517	126.	88.					
		2519	80.	85.					
		2525	60.	104.					
		2528	108.	116.		116.			
		2530	101.	107.		66.			
		Mean	95.	100.		91.			
		SD	25.6	13.1		35.4			
		N	5	5		2			
		RR	ms	2517	474.	680.			
				2519	749.	706.			
2525	991.			575.					
2528	551.			514.		514.			
2530	593.			557.		901.			
Mean	672.			606.		708.			
SD	204.8			82.6		273.7			
N	5			5		2			
Pdur	ms			2517	42.	39.			
				2519	37.	34.			
		2525	36.	35.					
		2528	43.	43.		44.			
		2530	39.	35.		39.			
		Mean	39.	37.		42.			
		SD	3.0	3.8		3.5			
		N	5	5		2			
		PR	ms	2517	81.	90.			
				2519	75.	77.			
2525	90.			83.					
2528	89.			90.		99.			
2530	97.			90.		103.			
Mean	86.			86.		101.			
SD	8.5			5.9		2.8			
N	5			5		2			

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 800.		Session:	S 1	S 1	S 1
QRS	ms	2517	44.	44.	
		2519	43.	46.	
		2525	43.	41.	
		2528	45.	44.	43.
		2530	46.	45.	59.
		Mean	44.	44.	51.
		SD	1.3	1.9	11.3
	N	5	5	2	
QT	ms	2517	175.	204.	
		2519	179.	201.	
		2525	181.	185.	
		2528	189.	203.	192.
		2530	171.	193.	213.
		Mean	179.	197.	203.
		SD	6.8	8.1	14.8
	N	5	5	2	
QTcF	ms	2517	224.	232.	
		2519	197.	225.	
		2525	182.	222.	
		2528	230.	253.	239.
		2530	203.	234.	220.
		Mean	207.	233.	230.
		SD	19.9	12.0	13.2
	N	5	5	2	
MEA	degree	2517	30.	41.	
		2519	34.	57.	
		2525	58.	47.	
		2528	40.	71.	78.
		2530	30.	99.	89.
		Mean	38.	63.	84.
		SD	11.7	23.1	7.8
	N	5	5	2	

Note: " = Pretest phase; # = Test period



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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 800.		Session:	S 1	S 1	S 1
Pamp	mV	2517	0.53	0.54	
		2519	0.46	0.45	
		2525	0.36	0.38	
		2528	0.42	0.33	0.44
		2530	0.29	0.35	0.33
		Mean	0.41	0.41	0.39
		SD	0.092	0.086	0.078
	N	5	5	2	
Qamp	mV	2517	-0.24	-0.16	
		2519	-0.47	-0.44	
		2525	-0.73	-0.64	
		2528	-0.41	-0.55	-0.21
		2530	-0.56	-0.97	-0.47
		Mean	-0.48	-0.55	-0.34
		SD	0.181	0.295	0.184
	N	5	5	2	
Ramp	mV	2517	1.97	1.97	
		2519	2.41	2.64	
		2525	2.86	2.75	
		2528	2.02	1.95	2.46
		2530	1.59	1.95	1.99
		Mean	2.17	2.25	2.23
		SD	0.483	0.406	0.332
	N	5	5	2	
Samp	mV	2517	-0.30	-0.43	
		2519	-0.15	-0.27	
		2525	-0.13	-0.09	
		2528	-0.12	-0.18	-0.18
		2530	-0.10	-0.17	-0.16
		Mean	-0.16	-0.23	-0.17
		SD	0.080	0.130	0.014
	N	5	5	2	

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

M a l e s		Animal No.					
Dosage		Day:	-5"	24#	38		
mg/kg	: 800.	Session:	S 1	S 1	S 1		
<hr/>							
STd	mV	2517	-0.05	0.00			
		2519	-0.04	-0.08			
		2525	-0.04	0.00			
		2528	-0.10	-0.18	-0.06		
		2530	-0.07	-0.11	-0.08		
		Mean	-0.06	-0.07	-0.07		
		SD	0.025	0.077	0.014		
		N	5	5	2		
		Tamp	mV	2517	0.29	0.20	
				2519	0.34	-0.27	
2525	-0.47			-0.09			
2528	0.33			-0.13	0.46		
2530	0.26			-0.39	0.08		
Mean	0.15			-0.14	0.27		
SD	0.348			0.222	0.269		
N	5			5	2		

Note: " = Pretest phase; # = Test period

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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 800.	Session:	S 1	S 1	S 1
HR	bpm	2564	89.	107.	
		2565	87.	84.	
		2569	108.	151.	
		2571	136.	134.	122.
		2573	92.	75.	82.
		Mean	102.	110.	102.
		SD	20.5	32.3	28.3
		N	5	5	2
RR	ms	2564	667.	558.	
		2565	687.	706.	
		2569	552.	395.	
		2571	441.	446.	489.
		2573	648.	796.	728.
		Mean	599.	580.	609.
		SD	102.4	169.7	169.0
		N	5	5	2
Pdur	ms	2564	33.	39.	
		2565	37.	36.	
		2569	35.	45.	
		2571	35.	35.	38.
		2573	39.	35.	42.
		Mean	36.	38.	40.
		SD	2.3	4.2	2.8
		N	5	5	2
PR	ms	2564	105.	103.	
		2565	89.	83.	
		2569	77.	85.	
		2571	88.	79.	91.
		2573	78.	79.	88.
		Mean	87.	86.	90.
		SD	11.3	10.0	2.1
		N	5	5	2

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.	Day:	24#	38
Dosage	: 800.	Session:	-5" S 1	S 1	S 1
QRS	ms	2564	49.	49.	
		2565	39.	44.	
		2569	59.	59.	
		2571	62.	63.	54.
		2573	40.	49.	43.
		Mean	50.	53.	49.
		SD	10.6	7.9	7.8
QT	ms	2564	180.	191.	
		2565	177.	196.	
		2569	182.	168.	
		2571	166.	189.	196.
		2573	180.	214.	211.
		Mean	177.	192.	204.
		SD	6.4	16.5	10.6
QTcF	ms	2564	206.	232.	
		2565	200.	220.	
		2569	221.	228.	
		2571	217.	247.	248.
		2573	208.	231.	234.
		Mean	211.	231.	241.
		SD	8.7	9.7	9.8
MEA	degree	2564	56.	57.	
		2565	7.	12.	
		2569	59.	64.	
		2571	57.	63.	65.
		2573	71.	71.	74.
		Mean	50.	53.	70.
		SD	24.8	23.7	6.4
	N	5	5	2	

Note: " = Pretest phase; # = Test period

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Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg : 800.		Session:	S 1	S 1	S 1
Pamp	mV	2564	0.30	0.20	
		2565	0.32	0.46	
		2569	0.50	0.64	
		2571	0.43	0.37	0.46
		2573	0.29	0.35	0.26
		Mean	0.37	0.40	0.36
		SD	0.093	0.162	0.141
	N	5	5	2	
Qamp	mV	2564	-0.20	-0.06	
		2565	-0.38	-0.48	
		2569	-0.76	-0.60	
		2571	-0.99	-0.89	-0.65
		2573	-0.23	-0.29	-0.27
		Mean	-0.51	-0.46	-0.46
		SD	0.348	0.314	0.269
	N	5	5	2	
Ramp	mV	2564	2.63	2.23	
		2565	1.52	1.62	
		2569	4.36	3.98	
		2571	4.53	4.30	3.90
		2573	1.96	2.29	2.06
		Mean	3.00	2.88	2.98
		SD	1.378	1.182	1.301
	N	5	5	2	
Samp	mV	2564	-0.13	0.00	
		2565	-0.17	-0.19	
		2569	-0.05	-0.18	
		2571	-0.19	-0.11	-0.06
		2573	-0.06	-0.13	-0.12
		Mean	-0.12	-0.12	-0.09
		SD	0.063	0.076	0.042
	N	5	5	2	

Note: " = Pretest phase; # = Test period

CONFIDENTIAL  
Appendix 4  
ECG Examinations Data

Fexinidazole

Study Number: 0505-2007

F e m a l e s		Animal No.			
Dosage		Day:	-5"	24#	38
mg/kg	: 800.	Session:	S 1	S 1	S 1
<hr/>					
STd	mV	2564	-0.13	0.06	
		2565	-0.13	-0.11	
		2569	-0.04	-0.12	
		2571	-0.06	-0.07	-0.05
		2573	0.01	-0.06	0.05
	Mean		-0.07	-0.06	0.00
	SD		0.060	0.072	0.071
	N		5	5	2
Tamp	mV	2564	-0.35	0.11	
		2565	0.32	-0.07	
		2569	-0.04	-0.29	
		2571	0.26	0.27	0.23
		2573	0.04	-0.14	0.13
	Mean		0.05	-0.02	0.18
	SD		0.267	0.218	0.071
	N		5	5	2

Note: " = Pretest phase; # = Test period

## ***Appendix 5 Ophthalmoscopic Examination***

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Appendix 5  
Individual Animal Ophthalmoscopic Observations

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2516	Vehicle	NORMAL	Pretest phase -5 Test period 24
2518	Vehicle	NORMAL	Pretest phase -5 Test period 24
2520	Vehicle	NORMAL	Pretest phase -5 Test period 24
2527	Vehicle	NORMAL	Pretest phase -5 Test period 24,38
2533	Vehicle	NORMAL	Pretest phase -5 Test period 24,38
2514	50mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2521	50mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2529	50mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2515	200mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2523	200mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2526	200mg/kg/day	NORMAL	Pretest phase -5 Test period 24



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Appendix 5  
Individual Animal Ophthalmoscopic Observations

Fexinidazole

Study Number: 0505-2007

M a l e s

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2517	800mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2519	800mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2525	800mg/kg/day	NORMAL	Pretest phase -5 Test period 24
2528	800mg/kg/day	NORMAL	Pretest phase -5 Test period 24,38
2530	800mg/kg/day	NORMAL	Pretest phase -5 Test period 24,38

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Appendix 5  
Individual Animal Ophthalmoscopic Observations

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2560	Vehicle	NORMAL	Pretest phase -6 Test period 24
2568	Vehicle	NORMAL	Pretest phase -6 Test period 24
2572	Vehicle	NORMAL	Pretest phase -6 Test period 24
2575	Vehicle	NORMAL opacity area/s, monolateral	Pretest phase -6 Test period 24,37
2577	Vehicle	NORMAL	Pretest phase -6 Test period 24,37
2562	50mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2563	50mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2576	50mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2561	200mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2570	200mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2567	200mg/kg/day	NORMAL	Pretest phase -6 Test period 24

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Appendix 5  
Individual Animal Ophthalmoscopic Observations

Fexinidazole

Study Number: 0505-2007

F e m a l e

Animal Number	Dose	Clinical Signs	Study Day(s) Noted
2564	800mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2565	800mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2569	800mg/kg/day	NORMAL	Pretest phase -6 Test period 24
2571	800mg/kg/day	NORMAL	Pretest phase -6 Test period 24,37
2573	800mg/kg/day	NORMAL	Pretest phase -6 Test period 24,37

## ***Appendix 6 Hematology***

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Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2516	1/1	-7	6.94	15.7	45.1	65.0	22.6	34.7	12.8	1.58
	2518	1/1	-7	6.55	15.5	43.4	66.2	23.6	35.7	13.1	1.54
	2520	1/1	-7	6.38	14.0	40.3	63.2	21.9	34.7	13.0	1.60
	2527	1/1	-7	6.79	15.5	43.9	64.6	22.8	35.3	14.1	1.67
	2533	1/1	-7	6.07	14.0	39.4	64.9	23.0	35.4	12.9	1.58
			N	5	5	5	5	5	5	5	5
			Mean	6.55	14.9	42.4	64.8	22.8	35.2	13.2	1.59
			Sdev	0.342	0.86	2.45	1.07	0.62	0.44	0.53	0.048
50 mg/kg/day											
	2514	2/1	-7	6.51	15.1	42.9	65.9	23.1	35.1	13.0	1.69
	2521	2/1	-7	7.41	17.3	48.8	65.8	23.3	35.4	13.4	1.66
	2529	2/1	-7	7.33	16.1	46.4	63.4	22.0	34.7	13.0	1.61
			N	3	3	3	3	3	3	3	3
			Mean	7.08	16.2	46.0	65.0	22.8	35.1	13.1	1.65
			Sdev	0.498	1.10	2.97	1.42	0.70	0.35	0.23	0.040
200 mg/kg/day											
	2515	3/1	-7	7.30	16.4	47.0	64.4	22.5	34.9	13.2	1.68
	2523	3/1	-7	6.01	13.8	39.3	65.3	22.9	35.1	12.8	1.59
	2526	3/1	-7	6.91	15.7	45.1	65.3	22.7	34.8	13.3	1.51
			N	3	3	3	3	3	3	3	3
			Mean	6.74	15.3	43.8	65.0	22.7	34.9	13.1	1.59
			Sdev	0.662	1.35	4.01	0.52	0.20	0.15	0.26	0.085
800 mg/kg/day											
	2517	4/1	-7	6.32	14.6	41.0	64.9	23.0	35.5	13.2	1.74
	2519	4/1	-7	6.96	15.8	45.1	64.8	22.8	35.2	12.7	1.52
	2525	4/1	-7	7.06	16.1	46.1	65.4	22.9	35.0	13.0	1.66
	2528	4/1	-7	6.65	14.9	42.8	64.4	22.4	34.7	13.4	1.55
	2530	4/1	-7	5.88	13.7	39.2	66.7	23.4	35.0	13.0	1.63
			N	5	5	5	5	5	5	5	5
			Mean	6.57	15.0	42.8	65.2	22.9	35.1	13.1	1.62
			Sdev	0.484	0.96	2.84	0.89	0.36	0.29	0.26	0.088

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

CONFIDENTIAL

Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2516	1/1	-7	1.1	74.2	86.3	30.0	25.7	213.	12.0	61.1
	2518	1/1	-7	0.6	38.5	86.3	30.8	26.5	244.	10.6	58.9
	2520	1/1	-7	0.9	54.6	84.8	30.3	25.6	450.	10.9	65.4
	2527	1/1	-7	0.7	48.5	88.3	29.7	26.2	387.	12.0	63.8
	2533	1/1	-7	0.4	25.2	81.4	31.7	25.6	366.	9.9	63.0
			N	5	5	5	5	5	5	5	5
			Mean	0.7	48.2	85.4	30.5	25.9	332.	11.1	62.4
			Sdev	0.27	18.30	2.57	0.78	0.41	100.0	0.91	2.51
50 mg/kg/day											
	2514	2/1	-7	1.3	87.8	89.8	29.0	26.0	205.	12.5	58.7
	2521	2/1	-7	0.9	68.9	87.6	30.9	27.0	191.	11.7	66.5
	2529	2/1	-7	1.0	71.5	84.9	30.1	25.5	290.	11.2	65.8
			N	3	3	3	3	3	3	3	3
			Mean	1.1	76.1	87.4	30.0	26.2	229.	11.8	63.7
			Sdev	0.21	10.24	2.45	0.95	0.76	53.6	0.66	4.32
200 mg/kg/day											
	2515	3/1	-7	0.9	64.0	87.2	29.7	25.8	246.	12.7	62.5
	2523	3/1	-7	0.6	34.9	82.2	30.8	25.2	414.	9.1	55.1
	2526	3/1	-7	0.6	39.7	88.5	30.6	27.0	307.	12.3	64.4
			N	3	3	3	3	3	3	3	3
			Mean	0.7	46.2	86.0	30.4	26.0	322.	11.4	60.7
			Sdev	0.17	15.60	3.33	0.59	0.92	85.0	1.97	4.91
800 mg/kg/day											
	2517	4/1	-7	0.9	56.2	84.4	30.7	25.9	409.	9.5	58.2
	2519	4/1	-7	0.5	36.3	82.5	30.8	25.4	212.	10.9	66.1
	2525	4/1	-7	0.9	66.0	87.6	30.6	26.7	239.	13.3	65.0
	2528	4/1	-7	0.6	36.6	88.8	30.2	26.7	260.	9.5	63.4
	2530	4/1	-7	0.3	16.2	83.7	31.9	26.4	379.	11.8	60.6
			N	5	5	5	5	5	5	5	5
			Mean	0.6	42.3	85.4	30.8	26.2	300.	11.0	62.7
			Sdev	0.26	19.39	2.68	0.63	0.56	88.3	1.62	3.24

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCULAR VOL. RETIC.  
PLT - PLATELETS

CONFIDENTIAL

Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL	
Vehicle											
	2516	1/1	-7	0.26	9.51	5.14	3.36	0.36	0.55	0.07	
	2518	1/1	-7	0.26	8.84	5.47	2.57	0.43	0.15	0.14	
	2520	1/1	-7	0.49	6.92	3.42	2.81	0.35	0.26	0.05	
	2527	1/1	-7	0.47	10.14	5.65	3.44	0.61	0.29	0.09	
	2533	1/1	-7	0.36	9.22	5.38	3.17	0.42	0.16	0.05	
			N	5	5	5	5	5	5	5	
			Mean	0.37	8.93	5.01	3.07	0.43	0.28	0.08	
			Sdev	0.110	1.218	0.909	0.370	0.105	0.162	0.037	
50 mg/kg/day											
	2514	2/1	-7	0.26	9.85	5.49	3.44	0.39	0.38	0.11	
	2521	2/1	-7	0.22	9.19	5.51	2.64	0.56	0.30	0.13	
	2529	2/1	-7	0.33	6.47	3.23	2.58	0.29	0.11	0.19	
			N	3	3	3	3	3	3	3	
			Mean	0.27	8.50	4.74	2.89	0.41	0.26	0.14	
			Sdev	0.056	1.792	1.311	0.480	0.137	0.139	0.042	
200 mg/kg/day											
	2515	3/1	-7	0.31	8.35	5.14	2.62	0.26	0.19	0.10	
	2523	3/1	-7	0.38	10.34	6.56	2.72	0.67	0.26	0.10	
	2526	3/1	-7	0.38	12.33	7.23	3.72	0.98	0.18	0.14	
			N	3	3	3	3	3	3	3	
			Mean	0.36	10.34	6.31	3.02	0.64	0.21	0.11	
			Sdev	0.040	1.990	1.067	0.608	0.361	0.044	0.023	
800 mg/kg/day											
	2517	4/1	-7	0.39	6.48	3.87	2.07	0.37	0.07	0.07	
	2519	4/1	-7	0.23	7.99	4.06	2.64	0.54	0.58	0.14	
	2525	4/1	-7	0.32	10.19	6.82	2.75	0.35	0.18	0.08	
	2528	4/1	-7	0.25	9.78	5.12	3.54	0.51	0.45	0.11	
	2530	4/1	-7	0.45	7.08	3.62	2.83	0.34	0.14	0.08	
			N	5	5	5	5	5	5	5	
			Mean	0.33	8.30	4.70	2.77	0.42	0.28	0.10	
			Sdev	0.093	1.632	1.317	0.525	0.095	0.219	0.029	

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

CONFIDENTIAL

Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2516	1/1	-7	0.03	54.0	35.3	3.7	5.8	0.7	0.4
	2518	1/1	-7	0.07	61.9	29.1	4.9	1.7	1.6	0.8
	2520	1/1	-7	0.03	49.4	40.6	5.0	3.8	0.8	0.4
	2527	1/1	-7	0.04	55.8	34.0	6.1	2.9	0.9	0.4
	2533	1/1	-7	0.04	58.4	34.3	4.6	1.8	0.6	0.4
			N	5	5	5	5	5	5	5
			Mean	0.04	55.9	34.7	4.9	3.2	0.9	0.5
			Sdev	0.016	4.69	4.10	0.86	1.69	0.40	0.18
50 mg/kg/day										
	2514	2/1	-7	0.04	55.8	35.0	4.0	3.8	1.1	0.4
	2521	2/1	-7	0.06	59.9	28.7	6.0	3.3	1.4	0.6
	2529	2/1	-7	0.07	49.9	39.8	4.5	1.7	2.9	1.1
			N	3	3	3	3	3	3	3
			Mean	0.06	55.2	34.5	4.8	2.9	1.8	0.7
			Sdev	0.015	5.03	5.57	1.04	1.10	0.96	0.36
200 mg/kg/day										
	2515	3/1	-7	0.05	61.5	31.4	3.1	2.3	1.2	0.6
	2523	3/1	-7	0.04	63.4	26.3	6.4	2.5	0.9	0.4
	2526	3/1	-7	0.08	58.7	30.2	7.9	1.5	1.1	0.6
			N	3	3	3	3	3	3	3
			Mean	0.06	61.2	29.3	5.8	2.1	1.1	0.5
			Sdev	0.021	2.36	2.67	2.46	0.53	0.15	0.12
800 mg/kg/day										
	2517	4/1	-7	0.02	59.8	32.0	5.7	1.1	1.1	0.4
	2519	4/1	-7	0.04	50.8	33.0	6.7	7.3	1.7	0.5
	2525	4/1	-7	0.02	66.9	27.0	3.4	1.7	0.8	0.2
	2528	4/1	-7	0.05	52.4	36.2	5.2	4.6	1.1	0.5
	2530	4/1	-7	0.07	51.2	40.0	4.7	2.0	1.1	0.9
			N	5	5	5	5	5	5	5
			Mean	0.04	56.2	33.6	5.1	3.3	1.2	0.5
			Sdev	0.021	7.00	4.85	1.22	2.59	0.33	0.25

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %



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Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2560	1/1	-7	6.45	14.8	43.3	67.1	22.9	34.1	11.0	1.65
	2568	1/1	-7	6.54	14.7	44.2	67.5	22.5	33.2	11.1	1.65
	2572	1/1	-7	6.16	13.9	41.4	67.1	22.6	33.7	11.9	1.72
	2575	1/1	-7	6.99	16.1	47.2	67.5	23.0	34.1	10.6	1.71
	2577	1/1	-7	6.57	14.8	43.6	66.3	22.5	33.9	11.4	1.75
			N	5	5	5	5	5	5	5	5
			Mean	6.54	14.9	43.9	67.1	22.7	33.8	11.2	1.70
			Sdev	0.298	0.79	2.10	0.49	0.23	0.37	0.48	0.044
50 mg/kg/day											
	2562	2/1	-7	7.94	18.2	53.1	66.9	22.9	34.3	11.7	1.73
	2563	2/1	-7	7.13	16.6	48.9	68.6	23.3	34.0	11.5	1.69
	2576	2/1	-7	7.30	16.9	49.6	68.0	23.1	34.0	11.0	1.70
			N	3	3	3	3	3	3	3	3
			Mean	7.46	17.2	50.5	67.8	23.1	34.1	11.4	1.71
			Sdev	0.427	0.85	2.25	0.86	0.20	0.17	0.36	0.021
200 mg/kg/day											
	2561	3/1	-7	6.96	16.0	47.1	67.7	23.0	34.0	11.6	1.63
	2570	3/1	-7	6.67	14.7	43.8	65.8	22.0	33.5	11.4	1.72
	2567	3/1	-7	6.69	15.4	44.8	67.0	22.9	34.3	11.3	1.65
			N	3	3	3	3	3	3	3	3
			Mean	6.77	15.4	45.2	66.8	22.6	33.9	11.4	1.67
			Sdev	0.162	0.65	1.69	0.96	0.55	0.40	0.15	0.047
800 mg/kg/day											
	2564	4/1	-7	6.45	15.0	44.1	68.4	23.3	34.0	10.7	1.63
	2565	4/1	-7	7.13	16.6	49.1	68.9	23.2	33.7	11.5	1.67
	2569	4/1	-7	7.20	15.9	47.8	66.3	22.1	33.3	11.0	1.73
	2571	4/1	-7	6.97	15.4	46.0	66.0	22.0	33.4	11.3	1.71
	2573	4/1	-7	6.32	14.8	43.3	68.5	23.3	34.1	11.3	1.65
			N	5	5	5	5	5	5	5	5
			Mean	6.81	15.5	46.1	67.6	22.8	33.7	11.2	1.68
			Sdev	0.403	0.73	2.44	1.36	0.67	0.35	0.31	0.041

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

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Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2560	1/1	-7	0.6	39.1	84.1	29.0	24.2	317.	11.4	66.5
	2568	1/1	-7	0.5	30.1	87.6	28.5	24.8	301.	8.6	49.6
	2572	1/1	-7	0.6	34.9	86.7	28.2	24.3	467.	9.3	55.7
	2575	1/1	-7	0.4	28.5	85.0	29.7	25.1	368.	8.8	52.0
	2577	1/1	-7	0.3	19.1	84.9	29.4	24.8	250.	9.2	59.1
			N	5	5	5	5	5	5	5	5
			Mean	0.5	30.3	85.7	29.0	24.6	341.	9.5	56.6
			Sdev	0.13	7.54	1.44	0.62	0.38	82.3	1.12	6.62
50 mg/kg/day											
	2562	2/1	-7	1.0	76.6	87.2	28.8	25.0	261.	10.0	58.2
	2563	2/1	-7	1.0	69.3	92.0	27.6	25.3	279.	12.1	61.7
	2576	2/1	-7	0.5	38.5	84.8	29.2	24.6	424.	9.3	59.0
			N	3	3	3	3	3	3	3	3
			Mean	0.8	61.5	88.0	28.5	25.0	321.	10.5	59.6
			Sdev	0.25	20.22	3.67	0.83	0.35	89.4	1.46	1.83
200 mg/kg/day											
	2561	3/1	-7	0.5	34.1	85.2	28.6	24.3	365.	10.5	58.6
	2570	3/1	-7	0.6	42.5	81.8	29.0	23.6	407.	8.7	54.8
	2567	3/1	-7	0.4	24.5	87.5	28.5	24.9	271.	8.9	57.2
			N	3	3	3	3	3	3	3	3
			Mean	0.5	33.7	84.8	28.7	24.3	348.	9.4	56.9
			Sdev	0.14	9.01	2.87	0.26	0.65	69.6	0.99	1.92
800 mg/kg/day											
	2564	4/1	-7	0.3	18.2	87.0	29.2	25.1	287.	9.5	52.9
	2565	4/1	-7	0.7	50.5	90.2	28.3	25.4	281.	10.0	52.8
	2569	4/1	-7	0.7	47.8	82.1	29.0	23.6	324.	9.0	50.8
	2571	4/1	-7	0.7	47.7	84.1	28.7	24.0	324.	9.3	54.3
	2573	4/1	-7	0.3	21.5	83.0	30.2	24.6	254.	10.3	60.7
			N	5	5	5	5	5	5	5	5
			Mean	0.5	37.1	85.3	29.1	24.5	294.	9.6	54.3
			Sdev	0.21	15.87	3.31	0.71	0.75	30.1	0.53	3.79

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCULAR VOL. RETIC.  
PLT - PLATELETS

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Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL
Vehicle										
	2560	1/1	-7	0.36	12.60	7.58	4.01	0.70	0.09	0.15
	2568	1/1	-7	0.26	10.13	5.71	3.64	0.42	0.21	0.09
	2572	1/1	-7	0.44	9.83	6.50	2.53	0.38	0.18	0.16
	2575	1/1	-7	0.32	11.65	6.30	4.07	0.62	0.43	0.17
	2577	1/1	-7	0.23	8.31	4.50	3.08	0.39	0.14	0.14
			N	5	5	5	5	5	5	5
			Mean	0.32	10.50	6.12	3.47	0.50	0.21	0.14
			Sdev	0.083	1.667	1.129	0.655	0.148	0.131	0.031
50 mg/kg/day										
	2562	2/1	-7	0.26	12.29	7.89	3.26	0.64	0.29	0.16
	2563	2/1	-7	0.34	10.02	5.71	3.15	0.57	0.42	0.12
	2576	2/1	-7	0.39	10.15	6.00	2.96	0.39	0.57	0.18
			N	3	3	3	3	3	3	3
			Mean	0.33	10.82	6.53	3.12	0.53	0.43	0.15
			Sdev	0.066	1.275	1.184	0.152	0.129	0.140	0.031
200 mg/kg/day										
	2561	3/1	-7	0.38	9.18	4.50	3.81	0.37	0.15	0.25
	2570	3/1	-7	0.35	10.82	7.91	2.07	0.51	0.22	0.08
	2567	3/1	-7	0.24	8.75	4.31	2.89	0.38	1.02	0.11
			N	3	3	3	3	3	3	3
			Mean	0.32	9.58	5.57	2.92	0.42	0.46	0.15
			Sdev	0.074	1.092	2.026	0.870	0.078	0.483	0.091
800 mg/kg/day										
	2564	4/1	-7	0.27	7.83	3.77	2.90	0.48	0.50	0.12
	2565	4/1	-7	0.28	8.55	4.81	2.36	0.30	0.97	0.07
	2569	4/1	-7	0.29	8.65	5.12	2.88	0.30	0.19	0.12
	2571	4/1	-7	0.30	7.70	4.44	2.65	0.26	0.23	0.10
	2573	4/1	-7	0.26	7.61	4.80	2.37	0.21	0.08	0.11
			N	5	5	5	5	5	5	5
			Mean	0.28	8.07	4.59	2.63	0.31	0.39	0.10
			Sdev	0.016	0.493	0.517	0.263	0.102	0.357	0.021

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

CONFIDENTIAL

Appendix 6  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2560	1/1	-7	0.06	60.2	31.9	5.5	0.8	1.2	0.5
	2568	1/1	-7	0.05	56.4	36.0	4.2	2.1	0.9	0.5
	2572	1/1	-7	0.08	66.2	25.7	3.8	1.8	1.6	0.8
	2575	1/1	-7	0.07	54.1	34.9	5.3	3.7	1.4	0.6
	2577	1/1	-7	0.07	54.1	37.1	4.6	1.7	1.7	0.8
			N	5	5	5	5	5	5	5
			Mean	0.07	58.2	33.1	4.7	2.0	1.4	0.6
			Sdev	0.011	5.12	4.58	0.72	1.06	0.32	0.15
50 mg/kg/day										
	2562	2/1	-7	0.05	64.2	26.6	5.2	2.3	1.3	0.4
	2563	2/1	-7	0.04	57.0	31.5	5.7	4.2	1.2	0.4
	2576	2/1	-7	0.06	59.1	29.2	3.8	5.6	1.7	0.6
			N	3	3	3	3	3	3	3
			Mean	0.05	60.1	29.1	4.9	4.0	1.4	0.5
			Sdev	0.010	3.70	2.45	0.98	1.66	0.26	0.12
200 mg/kg/day										
	2561	3/1	-7	0.10	49.0	41.5	4.0	1.6	2.7	1.1
	2570	3/1	-7	0.03	73.2	19.1	4.7	2.0	0.8	0.3
	2567	3/1	-7	0.03	49.3	33.0	4.4	11.7	1.3	0.3
			N	3	3	3	3	3	3	3
			Mean	0.05	57.2	31.2	4.4	5.1	1.6	0.6
			Sdev	0.040	13.89	11.31	0.35	5.72	0.98	0.46
800 mg/kg/day										
	2564	4/1	-7	0.05	48.2	37.0	6.1	6.4	1.6	0.7
	2565	4/1	-7	0.03	56.3	27.6	3.5	11.3	0.8	0.4
	2569	4/1	-7	0.05	59.2	33.3	3.4	2.1	1.4	0.6
	2571	4/1	-7	0.02	57.7	34.4	3.3	3.0	1.3	0.3
	2573	4/1	-7	0.04	63.0	31.1	2.8	1.1	1.4	0.6
			N	5	5	5	5	5	5	5
			Mean	0.04	56.9	32.7	3.8	4.8	1.3	0.5
			Sdev	0.013	5.46	3.55	1.30	4.15	0.30	0.16

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %

CONFIDENTIAL

Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2516	1/1	28	6.46	14.1	43.0	66.6	21.9	32.9	12.1	1.76
	2518	1/1	28	6.11	13.8	41.1	67.2	22.6	33.6	12.5	1.91
	2520	1/1	28	6.62	13.9	42.4	64.0	21.0	32.9	11.9	1.80
	2527	1/1	28	5.77	12.8	37.9	65.7	22.3	33.9	12.4	1.75
	2533	1/1	28	5.50	12.0	36.1	65.6	21.7	33.1	12.3	1.81
			N	5	5	5	5	5	5	5	5
			Mean	6.09	13.3	40.1	65.8	21.9	33.3	12.2	1.81
			Sdev	0.466	0.89	2.98	1.21	0.61	0.45	0.24	0.063
50 mg/kg/day											
	2514	2/1	28	7.00	15.1	46.5	66.4	21.6	32.5	12.0	1.82
	2521	2/1	28	7.63	17.0	50.7	66.4	22.3	33.5	11.8	1.75
	2529	2/1	28	6.66	14.5	42.6	64.0	21.8	34.1	11.0	1.67
			N	3	3	3	3	3	3	3	3
			Mean	7.10	15.5	46.6	65.6	21.9	33.4	11.6	1.75
			Sdev	0.492	1.31	4.05	1.39	0.36	0.81	0.53	0.075
200 mg/kg/day											
	2515	3/1	28	6.81	14.6	44.4	65.3	21.5	33.0	12.0	1.80
	2523	3/1	28	5.39	11.6	35.4	65.6	21.6	32.9	11.6	1.86
	2526	3/1	28	6.27	14.0	41.8	66.6	22.4	33.5	12.4	1.75
			N	3	3	3	3	3	3	3	3
			Mean	6.16	13.4	40.5	65.8	21.8	33.1	12.0	1.80
			Sdev	0.717	1.59	4.63	0.68	0.49	0.32	0.40	0.055
800 mg/kg/day											
	2517	4/1	28	5.72	12.6	37.2	65.1	22.0	33.7	11.4	1.82
	2519	4/1	28	6.41	14.0	41.1	64.1	21.8	34.1	11.5	1.76
	2525	4/1	28	6.64	14.7	43.7	65.8	22.2	33.8	12.3	1.83
	2528	4/1	28	5.95	13.0	39.4	66.2	21.9	33.1	12.0	1.74
	2530	4/1	28	5.59	12.3	37.3	66.6	22.0	33.0	12.1	1.92
			N	5	5	5	5	5	5	5	5
			Mean	6.06	13.3	39.7	65.6	22.0	33.5	11.9	1.81
			Sdev	0.449	1.00	2.74	0.99	0.15	0.47	0.39	0.071

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

CONFIDENTIAL

Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2516	1/1	28	1.3	82.6	90.9	26.8	24.3	221.	11.5	57.7
	2518	1/1	28	1.2	73.0	91.2	27.9	25.3	302.	10.3	58.2
	2520	1/1	28	0.8	52.0	87.1	27.6	23.9	493.	11.2	64.5
	2527	1/1	28	0.5	27.1	92.4	27.0	24.9	418.	10.7	57.1
	2533	1/1	28	1.2	67.9	87.1	28.0	24.3	415.	9.5	55.9
			N	5	5	5	5	5	5	5	5
			Mean	1.0	60.5	89.7	27.5	24.5	370.	10.6	58.7
			Sdev	0.35	21.72	2.47	0.54	0.55	107.6	0.79	3.36
50 mg/kg/day											
	2514	2/1	28	1.0	66.4	92.8	27.0	25.0	252.	12.0	58.9
	2521	2/1	28	0.7	51.9	88.2	28.8	25.3	227.	10.3	60.6
	2529	2/1	28	0.4	25.0	87.4	28.2	24.5	248.	10.5	64.9
			N	3	3	3	3	3	3	3	3
			Mean	0.7	47.8	89.5	28.0	24.9	242.	10.9	61.5
			Sdev	0.29	21.01	2.91	0.92	0.40	13.4	0.93	3.09
200 mg/kg/day											
	2515	3/1	28	0.5	36.8	86.0	27.8	23.7	263.	11.1	58.1
	2523	3/1	28	0.6	32.1	85.5	27.7	23.6	603.	9.1	58.0
	2526	3/1	28	0.4	23.7	90.3	28.0	25.2	286.	10.9	58.8
			N	3	3	3	3	3	3	3	3
			Mean	0.5	30.9	87.3	27.8	24.2	384.	10.4	58.3
			Sdev	0.11	6.64	2.64	0.15	0.90	190.0	1.10	0.44
800 mg/kg/day											
	2517	4/1	28	0.4	22.5	83.6	28.5	23.7	374.	9.8	58.6
	2519	4/1	28	0.3	19.9	87.8	28.9	25.2	271.	11.0	64.5
	2525	4/1	28	0.8	50.1	90.6	28.0	25.2	254.	12.8	67.8
	2528	4/1	28	0.9	51.0	89.0	27.9	24.8	200.	9.2	68.0
	2530	4/1	28	0.5	26.2	87.9	28.0	24.5	265.	11.8	63.2
			N	5	5	5	5	5	5	5	5
			Mean	0.6	33.9	87.8	28.3	24.7	273.	10.9	64.4
			Sdev	0.24	15.33	2.59	0.43	0.62	63.2	1.46	3.86

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCULAR VOL. RETIC.  
PLT - PLATELETS

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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL	
Vehicle											
	2516	1/1	28	0.25	9.38	5.93	2.91	0.28	0.15	0.05	
	2518	1/1	28	0.31	9.08	5.82	2.63	0.37	0.17	0.05	
	2520	1/1	28	0.55	6.49	3.41	2.62	0.27	0.13	0.02	
	2527	1/1	28	0.45	11.61	7.62	2.82	0.93	0.15	0.04	
	2533	1/1	28	0.39	8.19	4.78	2.79	0.36	0.19	0.03	
			N	5	5	5	5	5	5	5	
			Mean	0.39	8.95	5.51	2.75	0.44	0.16	0.04	
			Sdev	0.117	1.865	1.555	0.126	0.277	0.023	0.013	
50 mg/kg/day											
	2514	2/1	28	0.30	8.79	4.91	3.26	0.28	0.23	0.06	
	2521	2/1	28	0.23	7.96	4.72	2.69	0.20	0.23	0.07	
	2529	2/1	28	0.26	6.42	3.45	2.49	0.20	0.13	0.09	
			N	3	3	3	3	3	3	3	
			Mean	0.26	7.72	4.36	2.81	0.23	0.20	0.07	
			Sdev	0.035	1.203	0.794	0.400	0.046	0.058	0.015	
200 mg/kg/day											
	2515	3/1	28	0.29	8.49	6.14	1.89	0.20	0.19	0.05	
	2523	3/1	28	0.55	8.17	5.15	2.39	0.29	0.24	0.04	
	2526	3/1	28	0.31	6.67	3.91	2.28	0.25	0.13	0.05	
			N	3	3	3	3	3	3	3	
			Mean	0.38	7.78	5.07	2.19	0.25	0.19	0.05	
			Sdev	0.145	0.972	1.117	0.263	0.045	0.055	0.006	
800 mg/kg/day											
	2517	4/1	28	0.37	6.83	5.32	1.13	0.30	0.03	0.02	
	2519	4/1	28	0.30	6.52	3.43	2.22	0.31	0.48	0.05	
	2525	4/1	28	0.33	9.91	7.18	2.31	0.26	0.10	0.03	
	2528	4/1	28	0.18	9.28	6.14	2.47	0.48	0.11	0.04	
	2530	4/1	28	0.31	6.64	3.87	2.33	0.27	0.04	0.05	
			N	5	5	5	5	5	5	5	
			Mean	0.30	7.84	5.19	2.09	0.32	0.15	0.04	
			Sdev	0.071	1.625	1.559	0.545	0.090	0.187	0.013	

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2516	1/1	28	0.05	63.3	31.0	3.0	1.6	0.5	0.5
	2518	1/1	28	0.05	64.1	28.9	4.1	1.9	0.5	0.5
	2520	1/1	28	0.03	52.6	40.5	4.1	2.0	0.3	0.5
	2527	1/1	28	0.06	65.6	24.3	8.0	1.3	0.3	0.5
	2533	1/1	28	0.03	58.3	34.1	4.4	2.4	0.4	0.4
			N	5	5	5	5	5	5	5
			Mean	0.04	60.8	31.8	4.7	1.8	0.4	0.5
			Sdev	0.013	5.33	6.05	1.91	0.42	0.10	0.04
50 mg/kg/day										
	2514	2/1	28	0.05	55.9	37.1	3.2	2.6	0.7	0.6
	2521	2/1	28	0.05	59.4	33.8	2.5	2.9	0.8	0.6
	2529	2/1	28	0.06	53.7	38.8	3.2	2.1	1.3	0.9
			N	3	3	3	3	3	3	3
			Mean	0.05	56.3	36.6	3.0	2.5	0.9	0.7
			Sdev	0.006	2.87	2.54	0.40	0.40	0.32	0.17
200 mg/kg/day										
	2515	3/1	28	0.04	72.3	22.2	2.3	2.2	0.6	0.4
	2523	3/1	28	0.06	63.0	29.2	3.6	2.9	0.5	0.7
	2526	3/1	28	0.05	58.6	34.1	3.8	1.9	0.8	0.8
			N	3	3	3	3	3	3	3
			Mean	0.05	64.6	28.5	3.2	2.3	0.6	0.6
			Sdev	0.010	6.99	5.98	0.81	0.51	0.15	0.21
800 mg/kg/day										
	2517	4/1	28	0.02	78.0	16.6	4.3	0.5	0.3	0.3
	2519	4/1	28	0.04	52.5	34.1	4.7	7.3	0.7	0.6
	2525	4/1	28	0.03	72.4	23.4	2.6	1.0	0.3	0.3
	2528	4/1	28	0.04	66.1	26.6	5.2	1.2	0.4	0.4
	2530	4/1	28	0.08	58.3	35.1	4.1	0.6	0.7	1.2
			N	5	5	5	5	5	5	5
			Mean	0.04	65.5	27.2	4.2	2.1	0.5	0.6
			Sdev	0.023	10.31	7.70	0.98	2.91	0.20	0.38

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %



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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2560	1/1	28	5.57	12.3	37.2	66.8	22.0	33.0	11.7	1.75
	2568	1/1	28	6.57	13.9	44.0	67.0	21.2	31.7	11.7	1.76
	2572	1/1	28	5.91	12.7	39.2	66.2	21.4	32.3	12.1	1.74
	2575	1/1	28	6.82	15.2	46.2	67.8	22.3	32.9	11.1	1.64
	2577	1/1	28	7.00	15.4	46.4	66.3	22.0	33.1	12.0	1.88
			N	5	5	5	5	5	5	5	5
			Mean	6.37	13.9	42.6	66.8	21.8	32.6	11.7	1.75
			Sdev	0.611	1.41	4.19	0.64	0.46	0.59	0.39	0.085
50 mg/kg/day											
	2562	2/1	28	7.29	15.7	47.7	65.4	21.5	32.9	12.2	1.86
	2563	2/1	28	6.89	15.4	46.8	67.8	22.4	33.0	13.0	2.00
	2576	2/1	28	6.72	15.4	45.1	67.1	22.9	34.0	12.1	1.80
			N	3	3	3	3	3	3	3	3
			Mean	6.97	15.5	46.5	66.8	22.3	33.3	12.4	1.89
			Sdev	0.293	0.17	1.32	1.23	0.71	0.61	0.49	0.103
200 mg/kg/day											
	2561	3/1	28	6.01	13.3	39.6	65.8	22.0	33.5	11.8	1.70
	2570	3/1	28	6.16	13.0	39.9	64.7	21.1	32.7	10.9	1.75
	2567	3/1	28	6.63	14.7	44.0	66.3	22.2	33.4	11.4	1.71
			N	3	3	3	3	3	3	3	3
			Mean	6.27	13.7	41.2	65.6	21.8	33.2	11.4	1.72
			Sdev	0.323	0.91	2.46	0.82	0.59	0.44	0.45	0.026
800 mg/kg/day											
	2564	4/1	28	6.04	13.5	40.3	66.7	22.4	33.6	11.2	1.77
	2565	4/1	28	7.32	16.3	49.2	67.2	22.2	33.1	11.8	1.86
	2569	4/1	28	7.11	15.3	46.5	65.4	21.6	33.0	11.5	1.79
	2571	4/1	28	6.63	14.0	42.7	64.4	21.1	32.8	11.4	1.79
	2573	4/1	28	6.91	15.3	46.3	67.0	22.2	33.1	11.3	1.73
			N	5	5	5	5	5	5	5	5
			Mean	6.80	14.9	45.0	66.1	21.9	33.1	11.4	1.79
			Sdev	0.496	1.12	3.50	1.20	0.54	0.29	0.23	0.047

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2560	1/1	28	1.3	73.6	85.8	28.0	24.0	446.	10.0	57.4
	2568	1/1	28	0.6	41.6	88.8	27.8	24.6	358.	8.4	47.3
	2572	1/1	28	0.5	29.0	89.4	27.6	24.6	461.	9.4	50.3
	2575	1/1	28	0.5	31.8	88.0	28.2	24.7	466.	8.9	48.7
	2577	1/1	28	0.3	17.7	86.7	27.4	23.7	389.	9.0	47.1
			N	5	5	5	5	5	5	5	5
			Mean	0.6	38.7	87.7	27.8	24.3	424.	9.1	50.2
			Sdev	0.41	21.27	1.48	0.32	0.44	48.0	0.60	4.25
50 mg/kg/day											
	2562	2/1	28	0.9	65.4	87.1	28.3	24.5	381.	9.6	59.7
	2563	2/1	28	2.0	137.4	92.3	26.9	24.7	373.	10.3	53.7
	2576	2/1	28	0.9	57.5	89.9	28.1	25.1	406.	8.6	52.1
			N	3	3	3	3	3	3	3	3
			Mean	1.3	86.8	89.8	27.8	24.8	387.	9.5	55.2
			Sdev	0.64	44.03	2.60	0.76	0.31	17.2	0.85	4.01
200 mg/kg/day											
	2561	3/1	28	0.4	23.9	90.5	27.9	25.2	355.	10.2	59.6
	2570	3/1	28	0.5	31.9	82.5	27.6	22.7	494.	9.7	55.1
	2567	3/1	28	0.2	15.5	86.7	27.6	23.8	240.	10.5	62.6
			N	3	3	3	3	3	3	3	3
			Mean	0.4	23.8	86.6	27.7	23.9	363.	10.1	59.1
			Sdev	0.15	8.20	4.00	0.17	1.25	127.2	0.40	3.77
800 mg/kg/day											
	2564	4/1	28	0.5	29.4	88.8	27.6	24.5	303.	10.2	55.3
	2565	4/1	28	0.9	62.4	91.0	27.3	24.7	239.	11.3	57.4
	2569	4/1	28	0.5	32.1	85.8	28.1	24.1	338.	10.1	56.7
	2571	4/1	28	0.4	24.4	85.8	27.9	23.8	283.	9.5	58.5
	2573	4/1	28	0.2	13.7	89.9	28.4	25.5	290.	10.5	58.9
			N	5	5	5	5	5	5	5	5
			Mean	0.5	32.4	88.3	27.9	24.5	291.	10.3	57.4
			Sdev	0.24	18.19	2.38	0.43	0.65	35.8	0.66	1.44

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCULAR VOL. RETIC.  
PLT - PLATELETS

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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL
Vehicle										
	2560	1/1	28	0.45	13.22	8.04	4.35	0.56	0.12	0.07
	2568	1/1	28	0.30	11.94	7.67	3.45	0.56	0.16	0.04
	2572	1/1	28	0.43	10.45	6.86	2.84	0.46	0.10	0.09
	2575	1/1	28	0.41	15.06	9.10	4.27	0.97	0.57	0.06
	2577	1/1	28	0.35	8.28	4.62	2.95	0.46	0.16	0.04
			N	5	5	5	5	5	5	5
			Mean	0.39	11.79	7.26	3.57	0.60	0.22	0.06
			Sdev	0.062	2.592	1.680	0.712	0.212	0.196	0.021
50 mg/kg/day										
	2562	2/1	28	0.37	8.98	5.64	2.56	0.45	0.24	0.05
	2563	2/1	28	0.38	12.68	9.15	2.61	0.66	0.14	0.07
	2576	2/1	28	0.35	11.52	7.22	2.68	0.54	0.94	0.08
			N	3	3	3	3	3	3	3
			Mean	0.37	11.06	7.34	2.62	0.55	0.44	0.07
			Sdev	0.015	1.892	1.758	0.060	0.105	0.436	0.015
200 mg/kg/day										
	2561	3/1	28	0.36	11.00	7.51	2.73	0.59	0.07	0.06
	2570	3/1	28	0.48	8.93	6.24	2.01	0.35	0.26	0.04
	2567	3/1	28	0.25	10.05	5.96	3.22	0.52	0.15	0.10
			N	3	3	3	3	3	3	3
			Mean	0.36	9.99	6.57	2.65	0.49	0.16	0.07
			Sdev	0.115	1.036	0.826	0.609	0.123	0.095	0.031
800 mg/kg/day										
	2564	4/1	28	0.31	7.64	4.06	2.52	0.33	0.59	0.04
	2565	4/1	28	0.27	7.32	4.82	1.59	0.26	0.57	0.04
	2569	4/1	28	0.34	9.19	6.18	2.46	0.36	0.09	0.04
	2571	4/1	28	0.27	7.64	4.87	2.35	0.24	0.12	0.03
	2573	4/1	28	0.30	7.60	4.90	2.18	0.31	0.09	0.05
			N	5	5	5	5	5	5	5
			Mean	0.30	7.88	4.97	2.22	0.30	0.29	0.04
			Sdev	0.029	0.746	0.763	0.375	0.049	0.263	0.007

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

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Appendix 6  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2560	1/1	28	0.08	60.8	32.9	4.3	0.9	0.5	0.6
	2568	1/1	28	0.06	64.3	28.9	4.7	1.3	0.3	0.5
	2572	1/1	28	0.10	65.7	27.1	4.4	0.9	0.9	0.9
	2575	1/1	28	0.09	60.4	28.4	6.4	3.8	0.4	0.6
	2577	1/1	28	0.05	55.8	35.6	5.5	1.9	0.5	0.6
			N	5	5	5	5	5	5	5
			Mean	0.08	61.4	30.6	5.1	1.8	0.5	0.6
			Sdev	0.021	3.86	3.54	0.88	1.21	0.23	0.15
50 mg/kg/day										
	2562	2/1	28	0.04	62.8	28.5	5.0	2.7	0.6	0.5
	2563	2/1	28	0.05	72.1	20.6	5.2	1.1	0.5	0.4
	2576	2/1	28	0.06	62.7	23.2	4.7	8.2	0.7	0.5
			N	3	3	3	3	3	3	3
			Mean	0.05	65.9	24.1	5.0	4.0	0.6	0.5
			Sdev	0.010	5.40	4.03	0.25	3.72	0.10	0.06
200 mg/kg/day										
	2561	3/1	28	0.04	68.3	24.9	5.3	0.6	0.5	0.3
	2570	3/1	28	0.03	69.9	22.5	4.0	2.9	0.4	0.3
	2567	3/1	28	0.11	59.2	32.1	5.2	1.5	1.0	1.1
			N	3	3	3	3	3	3	3
			Mean	0.06	65.8	26.5	4.8	1.7	0.6	0.6
			Sdev	0.044	5.77	5.00	0.72	1.16	0.32	0.46
800 mg/kg/day										
	2564	4/1	28	0.09	53.2	33.0	4.4	7.8	0.5	1.2
	2565	4/1	28	0.04	65.8	21.8	3.5	7.8	0.6	0.5
	2569	4/1	28	0.06	67.3	26.7	3.9	0.9	0.5	0.6
	2571	4/1	28	0.03	63.8	30.8	3.1	1.5	0.4	0.4
	2573	4/1	28	0.07	64.5	28.7	4.0	1.2	0.7	1.0
			N	5	5	5	5	5	5	5
			Mean	0.06	62.9	28.2	3.8	3.8	0.5	0.7
			Sdev	0.024	5.60	4.28	0.50	3.62	0.11	0.34

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %

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Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2527	1/1	42	6.01	13.6	40.4	67.2	22.6	33.7	12.8	1.76
	2533	1/1	42	5.88	12.6	39.6	67.3	21.5	31.9	12.7	1.79
			N	2	2	2	2	2	2	2	2
			Mean	5.95	13.1	40.0	67.3	22.1	32.8	12.8	1.78
			Sdev	0.092	0.71	0.57	0.07	0.78	1.27	0.07	0.021
800 mg/kg/day											
	2528	4/1	42	6.88	15.2	46.0	66.9	22.1	33.0	12.5	1.91
	2530	4/1	42	6.12	13.6	41.6	67.9	22.1	32.6	13.1	2.03
			N	2	2	2	2	2	2	2	2
			Mean	6.50	14.4	43.8	67.4	22.1	32.8	12.8	1.97
			Sdev	0.537	1.13	3.11	0.71	0.00	0.28	0.42	0.085

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

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Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2527	1/1	42	0.6	32.8	93.5	27.5	25.7	402.	10.8	57.3
	2533	1/1	42	1.5	86.1	89.2	27.9	24.8	440.	9.1	54.2
			N	2	2	2	2	2	2	2	2
			Mean	1.0	59.5	91.4	27.7	25.3	421.	10.0	55.8
			Sdev	0.64	37.69	3.04	0.28	0.64	26.9	1.20	2.19
800 mg/kg/day											
	2528	4/1	42	1.0	68.9	88.1	27.7	24.4	255.	8.5	59.0
	2530	4/1	42	1.4	86.5	88.4	28.1	24.7	416.	10.9	60.6
			N	2	2	2	2	2	2	2	2
			Mean	1.2	77.7	88.3	27.9	24.6	336.	9.7	59.8
			Sdev	0.29	12.45	0.21	0.28	0.21	113.8	1.70	1.13

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCULAR VOL. RETIC.  
PLT - PLATELETS

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Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
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Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL	
Vehicle											
	2527	1/1	42	0.43	9.50	5.82	2.97	0.45	0.23	0.01	
	2533	1/1	42	0.40	7.94	4.42	2.99	0.38	0.07	0.04	
			N	2	2	2	2	2	2	2	
			Mean	0.42	8.72	5.12	2.98	0.42	0.15	0.03	
			Sdev	0.021	1.103	0.990	0.014	0.049	0.113	0.021	
800 mg/kg/day											
	2528	4/1	42	0.22	5.64	2.69	2.46	0.29	0.09	0.07	
	2530	4/1	42	0.46	7.61	4.51	2.69	0.26	0.06	0.05	
			N	2	2	2	2	2	2	2	
			Mean	0.34	6.63	3.60	2.58	0.28	0.08	0.06	
			Sdev	0.170	1.393	1.287	0.163	0.021	0.021	0.014	

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

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Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2527	1/1	42	0.03	61.2	31.3	4.7	2.4	0.1	0.3
	2533	1/1	42	0.05	55.6	37.6	4.7	0.8	0.5	0.7
			N	2	2	2	2	2	2	2
			Mean	0.04	58.4	34.5	4.7	1.6	0.3	0.5
			Sdev	0.014	3.96	4.45	0.00	1.13	0.28	0.28
800 mg/kg/day										
	2528	4/1	42	0.04	47.7	43.6	5.2	1.6	1.2	0.8
	2530	4/1	42	0.03	59.3	35.3	3.5	0.8	0.7	0.4
			N	2	2	2	2	2	2	2
			Mean	0.04	53.5	39.5	4.4	1.2	1.0	0.6
			Sdev	0.007	8.20	5.87	1.20	0.57	0.35	0.28

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %



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Appendix 6  
Day 42 Hematology Data  
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Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	RBC 10 <sup>6</sup> /mcL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	HDW g/dL
Vehicle											
	2575	1/1	42	6.86	15.6	46.1	67.1	22.7	33.8	11.0	1.58
	2577	1/1	42	6.74	15.0	44.2	65.6	22.3	34.0	11.8	1.71
			N	2	2	2	2	2	2	2	2
			Mean	6.80	15.3	45.2	66.4	22.5	33.9	11.4	1.65
			Sdev	0.085	0.42	1.34	1.06	0.28	0.14	0.57	0.092
800 mg/kg/day											
	2571	4/1	42	6.54	14.2	41.9	63.9	21.7	33.9	12.0	1.78
	2573	4/1	42	6.60	14.7	44.4	67.3	22.3	33.2	12.0	1.71
			N	2	2	2	2	2	2	2	2
			Mean	6.57	14.5	43.2	65.6	22.0	33.6	12.0	1.75
			Sdev	0.042	0.35	1.77	2.40	0.42	0.49	0.00	0.049

RBC - RED BLOOD CELLS  
MCV - MEAN CORPUSCULAR VOLUME  
RDW - RED CELL DISTRIBUTION WIDTH

HGB - HEMOGLOBIN  
MCH - MEAN CORPUSCULAR HEMOGLOBIN  
HDW - HEMOGLOBIN DISTRIB. WIDTH

HCT - HEMATOCRIT  
MCHC - MEAN CORPUSCULAR HGB CONC.

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Appendix 6  
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Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	R %	RAB 10 <sup>9</sup> /L	MCVr fL	CHCM g/dL	CHr pg	PLT 10 <sup>3</sup> /mcL	MPV fL	PDW %
Vehicle											
	2575	1/1	42	0.5	34.6	84.1	29.4	24.6	458.	9.0	51.7
	2577	1/1	42	0.2	14.2	86.9	28.9	25.0	304.	8.9	50.1
			N	2	2	2	2	2	2	2	2
			Mean	0.4	24.4	85.5	29.2	24.8	381.	9.0	50.9
			Sdev	0.21	14.42	1.98	0.35	0.28	108.9	0.07	1.13
800 mg/kg/day											
	2571	4/1	42	0.8	53.5	85.8	28.4	24.3	335.	8.9	54.3
	2573	4/1	42	0.5	33.1	90.4	29.0	26.1	332.	9.0	55.7
			N	2	2	2	2	2	2	2	2
			Mean	0.7	43.3	88.1	28.7	25.2	334.	9.0	55.0
			Sdev	0.23	14.42	3.25	0.42	1.27	2.1	0.07	0.99

R - RETICULOCYTES  
CHCM - MEAN HEMOGLOBIN CONC. RETIC.  
MPV - MEAN PLATELET VOLUME

RAB - RETICULOCYTES ABS  
CHr - CELLULAR HEMOGLOBIN RETIC.  
PDW - PLATELET DISTRIBUTION WIDTH

MCVr - MEAN CORPUSCOLAR VOL. RETIC.  
PLT - PLATELETS

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Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/ Subgroup	Study Day	PCT %	WBC 10 <sup>3</sup> /mcL	NAB 10 <sup>3</sup> /mcL	LYAB 10 <sup>3</sup> /mcL	MAB 10 <sup>3</sup> /mcL	EAB 10 <sup>3</sup> /mcL	BAB 10 <sup>3</sup> /mcL
Vehicle										
	2575	1/1	42	0.41	11.08	5.94	3.62	0.69	0.66	0.09
	2577	1/1	42	0.27	7.94	3.80	3.31	0.50	0.21	0.07
			N	2	2	2	2	2	2	2
			Mean	0.34	9.51	4.87	3.47	0.60	0.44	0.08
			Sdev	0.099	2.220	1.513	0.219	0.134	0.318	0.014
800 mg/kg/day										
	2571	4/1	42	0.30	6.97	4.30	2.15	0.28	0.14	0.06
	2573	4/1	42	0.30	8.24	4.87	2.73	0.30	0.20	0.07
			N	2	2	2	2	2	2	2
			Mean	0.30	7.61	4.59	2.44	0.29	0.17	0.07
			Sdev	0.000	0.898	0.403	0.410	0.014	0.042	0.007

PCT - PLATELET HEMATOCRIT  
LYAB - LYMPHOCYTES ABS  
BAB - BASOPHILS ABS

WBC - WHITE BLOOD CELLS  
MAB - MONOCYTES ABS

NAB - NEUTROPHILS ABS  
EAB - EOSINOPHILS ABS

CONFIDENTIAL

Appendix 6  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	LUAB 10 <sup>3</sup> /mcL	N %	LY %	M %	E %	B %	LU %
Vehicle										
	2575	1/1	42	0.09	53.6	32.6	6.3	6.0	0.8	0.8
	2577	1/1	42	0.05	47.8	41.7	6.3	2.6	0.9	0.7
			N	2	2	2	2	2	2	2
			Mean	0.07	50.7	37.2	6.3	4.3	0.9	0.8
			Sdev	0.028	4.10	6.43	0.00	2.40	0.07	0.07
800 mg/kg/day										
	2571	4/1	42	0.05	61.7	30.8	4.0	2.1	0.8	0.7
	2573	4/1	42	0.07	59.1	33.2	3.6	2.4	0.9	0.8
			N	2	2	2	2	2	2	2
			Mean	0.06	60.4	32.0	3.8	2.3	0.9	0.8
			Sdev	0.014	1.84	1.70	0.28	0.21	0.07	0.07

LUAB - LARGE UNSTAINED CELLS ABS  
M - MONOCYTES %  
LU - LARGE UNSTAINED CELLS %

N - NEUTROPHILS %  
E - EOSINOPHILS %

LY - LYMPHOCITES %  
B - BASOPHILS %

## ***Appendix 7 Coagulation***

CONFIDENTIAL

Appendix 7  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	PT sec	PTr ratio	PTT sec	PTTr ratio	FIB mg/dL	
Vehicle									
	2516	1/1	-7	7.3	1.0	12.7	1.0	213.	
	2518	1/1	-7	6.9	1.0	12.4	1.0	222.	
	2520	1/1	-7	6.9	1.0	12.4	1.0	216.	
	2527	1/1	-7	7.0	1.0	12.7	1.0	215.	
	2533	1/1	-7	8.0	1.1	12.2	1.0	179.	
			N	5	5	5	5	5	
			Mean	7.2	1.0	12.5	1.0	209.	
			Sdev	0.46	0.06	0.23	0.02	17.3	
50 mg/kg/day									
	2514	2/1	-7	7.7	1.1	12.4	1.0	164.	
	2521	2/1	-7	7.2	1.0	12.9	1.0	188.	
	2529	2/1	-7	8.0	1.1	13.0	1.0	161.	
			N	3	3	3	3	3	
			Mean	7.6	1.0	12.8	1.0	171.	
			Sdev	0.36	0.05	0.31	0.03	14.8	
200 mg/kg/day									
	2515	3/1	-7	7.4	1.0	12.7	1.0	176.	
	2523	3/1	-7	6.9	0.9	12.6	1.0	248.	
	2526	3/1	-7	7.5	1.0	12.9	1.0	165.	
			N	3	3	3	3	3	
			Mean	7.2	1.0	12.7	1.0	196.	
			Sdev	0.31	0.04	0.18	0.01	45.2	
800 mg/kg/day									
	2517	4/1	-7	7.4	1.0	13.1	1.0	205.	
	2519	4/1	-7	6.8	0.9	12.2	1.0	250.	
	2525	4/1	-7	8.0	1.1	12.5	1.0	175.	
	2528	4/1	-7	7.1	1.0	13.0	1.0	226.	
	2530	4/1	-7	7.5	1.0	12.4	1.0	191.	
			N	5	5	5	5	5	
			Mean	7.4	1.0	12.6	1.0	209.	
			Sdev	0.46	0.06	0.37	0.03	29.2	

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

PTr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME

CONFIDENTIAL

Appendix 7  
Day -7 Hematology Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s								
Dose Level	Animal Number	Group/ Subgroup	Study Day	PT sec	PTr ratio	PTT sec	PTTr ratio	FIB mg/dL
Vehicle								
	2560	1/1	-7	7.0	1.0	12.9	1.0	217.
	2568	1/1	-7	9.5	1.3	69.7	5.5	163.
	2572	1/1	-7	7.1	1.0	12.8	1.0	189.
	2575	1/1	-7	7.6	1.0	12.6	1.0	179.
	2577	1/1	-7	7.8	1.1	12.8	1.0	166.
			N	5	5	5	5	5
			Mean	7.8	1.1	24.2	1.9	183.
			Sdev	0.99	0.14	25.44	2.01	22.0
50 mg/kg/day								
	2562	2/1	-7	8.7	1.2	12.9	1.0	166.
	2563	2/1	-7	6.8	0.9	12.4	1.0	246.
	2576	2/1	-7	7.5	1.0	12.5	1.0	154.
			N	3	3	3	3	3
			Mean	7.7	1.1	12.6	1.0	188.
			Sdev	0.99	0.14	0.31	0.02	50.2
200 mg/kg/day								
	2561	3/1	-7	7.0	1.0	13.0	1.0	264.
	2570	3/1	-7	7.2	1.0	12.6	1.0	199.
	2567	3/1	-7	7.3	1.0	12.9	1.0	182.
			N	3	3	3	3	3
			Mean	7.2	1.0	12.8	1.0	215.
			Sdev	0.15	0.02	0.24	0.02	43.0
800 mg/kg/day								
	2564	4/1	-7	7.3	1.0	12.3	1.0	172.
	2565	4/1	-7	7.1	1.0	12.7	1.0	202.
	2569	4/1	-7	8.0	1.1	13.0	1.0	164.
	2571	4/1	-7	7.4	1.0	13.1	1.0	150.
	2573	4/1	-7	8.9	1.2	13.6	1.1	141.
			N	5	5	5	5	5
			Mean	7.8	1.1	12.9	1.0	166.
			Sdev	0.75	0.10	0.47	0.04	23.5

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

PTr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME

CONFIDENTIAL

Appendix 7  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s								
Dose Level	Animal Number	Group/ Subgroup	Study Day	PT sec	PTr ratio	PTT sec	PTTr ratio	FIB mg/dL
Vehicle								
	2516	1/1	28	7.4	1.0	12.4	1.0	197.
	2518	1/1	28	7.0	1.0	12.2	1.0	224.
	2520	1/1	28	6.9	1.0	12.5	1.0	227.
	2527	1/1	28	7.2	1.0	12.7	1.0	216.
	2533	1/1	28	7.7	1.1	12.4	1.0	235.
			N	5	5	5	5	5
			Mean	7.2	1.0	12.4	1.0	220.
			Sdev	0.29	0.04	0.19	0.01	14.3
50 mg/kg/day								
	2514	2/1	28	8.0	1.1	12.6	1.0	174.
	2521	2/1	28	7.7	1.1	13.2	1.0	161.
	2529	2/1	28	8.4	1.2	13.4	1.1	156.
			N	3	3	3	3	3
			Mean	8.0	1.1	13.1	1.0	164.
			Sdev	0.34	0.05	0.40	0.03	9.3
200 mg/kg/day								
	2515	3/1	28	7.0	1.0	12.4	1.0	262.
	2523	3/1	28	6.9	1.0	12.6	1.0	235.
	2526	3/1	28	8.4	1.2	13.0	1.0	152.
			N	3	3	3	3	3
			Mean	7.4	1.0	12.7	1.0	216.
			Sdev	0.87	0.12	0.29	0.03	57.0
800 mg/kg/day								
	2517	4/1	28	7.5	1.0	13.0	1.0	175.
	2519	4/1	28	7.4	1.0	12.4	1.0	170.
	2525	4/1	28	8.6	1.2	13.0	1.0	162.
	2528	4/1	28	7.2	1.0	12.3	1.0	203.
	2530	4/1	28	8.0	1.1	12.4	1.0	158.
			N	5	5	5	5	5
			Mean	7.7	1.1	12.6	1.0	173.
			Sdev	0.56	0.08	0.32	0.03	17.9

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

PTr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME



CONFIDENTIAL

Appendix 7  
Day 28 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s								
Dose Level	Animal Number	Group/Subgroup	Study Day	PT sec	PTr ratio	PTT sec	PTTr ratio	FIB mg/dL
Vehicle								
	2560	1/1	28	7.2	1.0	13.0	1.0	209.
	2568	1/1	28	7.8	1.1	12.5	1.0	157.
	2572	1/1	28	7.2	1.0	13.1	1.0	210.
	2575	1/1	28	7.2	1.0	12.4	1.0	202.
	2577	1/1	28	7.8	1.1	13.7	1.1	160.
			N	5	5	5	5	5
			Mean	7.4	1.0	12.9	1.0	188.
			Sdev	0.34	0.05	0.52	0.04	26.8
50 mg/kg/day								
	2562	2/1	28	8.0	1.1	12.4	1.0	176.
	2563	2/1	28	7.0	1.0	12.6	1.0	204.
	2576	2/1	28	7.3	1.0	12.5	1.0	202.
			N	3	3	3	3	3
			Mean	7.4	1.0	12.5	1.0	194.
			Sdev	0.49	0.07	0.10	0.01	15.3
200 mg/kg/day								
	2561	3/1	28	7.5	1.0	12.5	1.0	175.
	2570	3/1	28	7.3	1.0	12.5	1.0	181.
	2567	3/1	28	6.9	0.9	12.4	1.0	283.
			N	3	3	3	3	3
			Mean	7.2	1.0	12.5	1.0	213.
			Sdev	0.31	0.04	0.06	0.01	60.8
800 mg/kg/day								
	2564	4/1	28	7.3	1.0	12.7	1.0	206.
	2565	4/1	28	7.1	1.0	12.9	1.0	218.
	2569	4/1	28	8.4	1.2	12.6	1.0	162.
	2571	4/1	28	7.4	1.0	12.8	1.0	170.
	2573	4/1	28	7.8	1.1	12.6	1.0	165.
			N	5	5	5	5	5
			Mean	7.6	1.0	12.7	1.0	184.
			Sdev	0.52	0.07	0.10	0.01	25.9

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

PTr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME

CONFIDENTIAL

Appendix 7  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	PT sec	Ptr ratio	PTT sec	PTTr ratio	FIB mg/dL	
Vehicle									
	2527	1/1	42	7.3	1.0	12.8	1.0	223.	
	2533	1/1	42	8.3	1.1	12.4	1.0	207.	
			N	2	2	2	2	2	
			Mean	7.8	1.1	12.6	1.0	215.	
			Sdev	0.74	0.10	0.28	0.02	11.0	
800 mg/kg/day									
	2528	4/1	42	7.9	1.1	12.6	1.0	165.	
	2530	4/1	42	8.0	1.1	12.2	1.0	215.	
			N	2	2	2	2	2	
			Mean	7.9	1.1	12.4	1.0	190.	
			Sdev	0.05	0.01	0.28	0.03	35.6	

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

Ptr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME

CONFIDENTIAL

Appendix 7  
Day 42 Hematology Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	PT sec	PTr ratio	PTT sec	PTTr ratio	FIB mg/dL	
Vehicle									
	2575	1/1	42	7.4	1.0	12.5	1.0	167.	
	2577	1/1	42	7.6	1.1	12.4	1.0	167.	
			N	2	2	2	2	2	
			Mean	7.5	1.0	12.4	1.0	167.	
			Sdev	0.17	0.03	0.06	0.00	0.4	
800 mg/kg/day									
	2571	4/1	42	7.1	1.0	12.2	1.0	201.	
	2573	4/1	42	8.0	1.1	12.5	1.0	174.	
			N	2	2	2	2	2	
			Mean	7.6	1.0	12.3	1.0	188.	
			Sdev	0.59	0.08	0.24	0.02	19.6	

PT - PROTHROMBIN TIME  
PTTr - ACT. PAR. THROMB. TIME RATIO

PTr - PROTHROMBIN TIME RATIO  
FIB - FIBRINOGEN

PTT - ACT. PAR. THROMB. TIME

## ***Appendix 8 Clinical Chemistry***

CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2516	1/1	-7	24.	0.86	35.	39.	84.	6.	0.09
	2518	1/1	-7	26.	0.92	38.	39.	114.	5.	0.13
	2520	1/1	-7	29.	0.83	28.	21.	55.	6.	0.08
	2527	1/1	-7	38.	0.94	44.	26.	72.	7.	0.09
	2533	1/1	-7	31.	1.00	50.	38.	63.	8.	0.11
			N	5	5	5	5	5	5	5
			Mean	30.	0.91	39.	33.	78.	6.	0.10
			Sdev	5.4	0.067	8.4	8.5	23.0	1.1	0.020
50 mg/kg/day										
	2514	2/1	-7	18.	0.94	28.	31.	79.	8.	0.09
	2521	2/1	-7	23.	0.81	33.	30.	67.	7.	0.13
	2529	2/1	-7	22.	0.87	39.	30.	87.	10.	0.13
			N	3	3	3	3	3	3	3
			Mean	21.	0.87	33.	30.	78.	8.	0.12
			Sdev	2.6	0.065	5.5	0.6	10.1	1.5	0.023
200 mg/kg/day										
	2515	3/1	-7	22.	0.91	34.	36.	89.	11.	0.10
	2523	3/1	-7	25.	0.85	46.	36.	51.	8.	0.24
	2526	3/1	-7	22.	0.83	25.	22.	94.	5.	0.11
			N	3	3	3	3	3	3	3
			Mean	23.	0.86	35.	31.	78.	8.	0.15
			Sdev	1.7	0.042	10.5	8.1	23.5	3.0	0.078
800 mg/kg/day										
	2517	4/1	-7	26.	0.80	30.	36.	67.	9.	0.09
	2519	4/1	-7	23.	0.92	33.	24.	93.	6.	0.10
	2525	4/1	-7	23.	0.90	34.	26.	84.	8.	0.09
	2528	4/1	-7	28.	0.85	45.	35.	74.	9.	0.10
	2530	4/1	-7	20.	0.90	48.	37.	49.	5.	0.09
			N	5	5	5	5	5	5	5
			Mean	24.	0.87	38.	32.	73.	7.	0.09
			Sdev	3.1	0.049	8.0	6.1	16.8	1.8	0.005

UREA - UREA  
ALT - ALANINE AMINO TRANSFERASE  
TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
GGT - GAMMA GLUTAMYL TRANSFERASE

CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL	
Vehicle										
	2516	1/1	-7	5.6	2.74	2.9	85.	19.	112.	
	2518	1/1	-7	6.1	3.03	3.1	90.	17.	146.	
	2520	1/1	-7	6.0	2.85	3.2	88.	9.	101.	
	2527	1/1	-7	6.1	2.62	3.5	86.	23.	147.	
	2533	1/1	-7	5.8	2.77	3.0	88.	23.	116.	
			N	5	5	5	5	5	5	
			Mean	5.9	2.80	3.1	87.	18.	124.	
			Sdev	0.22	0.152	0.23	1.9	5.8	20.9	
50 mg/kg/day										
	2514	2/1	-7	5.6	2.90	2.7	90.	8.	98.	
	2521	2/1	-7	5.8	2.88	2.9	86.	35.	148.	
	2529	2/1	-7	6.1	3.07	3.0	96.	24.	128.	
			N	3	3	3	3	3	3	
			Mean	5.8	2.95	2.9	91.	22.	125.	
			Sdev	0.25	0.104	0.17	5.0	13.6	25.2	
200 mg/kg/day										
	2515	3/1	-7	6.1	3.12	3.0	89.	17.	134.	
	2523	3/1	-7	6.1	2.62	3.5	95.	22.	109.	
	2526	3/1	-7	6.1	2.79	3.3	92.	14.	123.	
			N	3	3	3	3	3	3	
			Mean	6.1	2.84	3.3	92.	18.	122.	
			Sdev	0.00	0.254	0.25	3.0	4.0	12.5	
800 mg/kg/day										
	2517	4/1	-7	6.4	3.10	3.3	88.	8.	141.	
	2519	4/1	-7	6.5	2.99	3.5	90.	12.	108.	
	2525	4/1	-7	6.2	3.00	3.2	93.	20.	137.	
	2528	4/1	-7	5.8	2.79	3.0	90.	18.	105.	
	2530	4/1	-7	5.9	2.85	3.1	111.	10.	94.	
			N	5	5	5	5	5	5	
			Mean	6.2	2.95	3.2	94.	14.	117.	
			Sdev	0.30	0.125	0.20	9.4	5.2	20.8	

TPRO - TOTAL PROTEIN  
GLUC - GLUCOSE

ALB - ALBUMIN  
TG - TRIGLYCERIDES

GLOB - GLOBULIN  
TCHO - TOTAL CHOLESTEROL

CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L	
Vehicle										
	2516	1/1	-7	10.6	5.5	1.0	140.0	5.0	109.0	
	2518	1/1	-7	10.9	4.7	1.0	142.0	4.5	110.0	
	2520	1/1	-7	11.0	4.6	0.9	140.0	4.6	109.0	
	2527	1/1	-7	11.4	5.2	0.8	141.0	4.6	107.0	
	2533	1/1	-7	10.2	5.0	0.9	143.0	4.6	111.0	
			N	5	5	5	5	5	5	
			Mean	10.8	5.0	0.9	141.2	4.7	109.2	
			Sdev	0.45	0.37	0.09	1.30	0.18	1.48	
50 mg/kg/day										
	2514	2/1	-7	11.0	4.9	1.1	143.0	4.8	110.0	
	2521	2/1	-7	10.7	5.0	1.0	142.0	4.4	108.0	
	2529	2/1	-7	10.2	4.4	1.0	142.0	4.8	109.0	
			N	3	3	3	3	3	3	
			Mean	10.6	4.8	1.0	142.3	4.7	109.0	
			Sdev	0.40	0.32	0.04	0.58	0.25	1.00	
200 mg/kg/day										
	2515	3/1	-7	11.4	4.5	1.0	143.0	4.6	108.0	
	2523	3/1	-7	10.1	3.8	0.8	143.0	4.7	114.0	
	2526	3/1	-7	11.0	4.4	0.8	139.0	4.6	108.0	
			N	3	3	3	3	3	3	
			Mean	10.8	4.2	0.9	141.7	4.6	110.0	
			Sdev	0.67	0.38	0.15	2.31	0.08	3.46	
800 mg/kg/day										
	2517	4/1	-7	10.9	4.2	0.9	142.0	4.8	108.0	
	2519	4/1	-7	11.0	5.2	0.9	142.0	4.5	109.0	
	2525	4/1	-7	11.1	5.1	0.9	140.0	4.6	108.0	
	2528	4/1	-7	10.4	4.7	0.9	141.0	4.7	111.0	
	2530	4/1	-7	10.3	4.5	0.9	142.0	4.5	113.0	
			N	5	5	5	5	5	5	
			Mean	10.7	4.7	0.9	141.4	4.6	109.8	
			Sdev	0.36	0.42	0.04	0.89	0.14	2.17	

CA - CALCIUM  
NA - SODIUM

PHOS - PHOSPHOROUS  
K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
CL - CHLORIDE

CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2560	1/1	-7	26.	0.78	39.	28.	46.	11.	0.10
	2568	1/1	-7	29.	0.79	54.	31.	53.	6.	0.25
	2572	1/1	-7	24.	0.81	39.	25.	51.	8.	0.12
	2575	1/1	-7	29.	0.71	37.	28.	87.	9.	0.13
	2577	1/1	-7	23.	1.01	34.	31.	50.	7.	0.12
			N	5	5	5	5	5	5	5
			Mean	26.	0.82	41.	29.	57.	8.	0.14
			Sdev	2.8	0.113	7.8	2.5	16.7	1.9	0.060
50 mg/kg/day										
	2562	2/1	-7	30.	0.79	38.	30.	77.	11.	0.21
	2563	2/1	-7	26.	0.86	32.	20.	54.	10.	0.11
	2576	2/1	-7	37.	0.88	41.	38.	78.	8.	0.10
			N	3	3	3	3	3	3	3
			Mean	31.	0.84	37.	29.	70.	10.	0.14
			Sdev	5.6	0.047	4.6	9.0	13.6	1.5	0.061
200 mg/kg/day										
	2561	3/1	-7	32.	0.73	28.	21.	52.	7.	0.12
	2570	3/1	-7	30.	0.79	41.	25.	72.	7.	0.12
	2567	3/1	-7	23.	0.79	39.	24.	81.	8.	0.13
			N	3	3	3	3	3	3	3
			Mean	28.	0.77	36.	23.	68.	7.	0.12
			Sdev	4.7	0.035	7.0	2.1	14.8	0.6	0.006
800 mg/kg/day										
	2564	4/1	-7	28.	0.92	38.	28.	47.	8.	0.13
	2565	4/1	-7	46.	0.84	29.	23.	51.	8.	0.21
	2569	4/1	-7	30.	1.02	39.	36.	74.	7.	0.12
	2571	4/1	-7	28.	0.88	35.	39.	94.	8.	0.15
	2573	4/1	-7	24.	0.80	28.	25.	46.	8.	0.20
			N	5	5	5	5	5	5	5
			Mean	31.	0.89	34.	30.	62.	8.	0.16
			Sdev	8.6	0.084	5.1	7.0	21.0	0.4	0.041

UREA - UREA  
ALT - ALANINE AMINO TRANSFERASE  
TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
GGT - GAMMA GLUTAMYL TRANSFERASE



CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL	
Vehicle										
	2560	1/1	-7	5.8	2.57	3.2	79.	16.	109.	
	2568	1/1	-7	5.9	3.03	2.9	96.	11.	108.	
	2572	1/1	-7	5.6	2.95	2.7	104.	14.	111.	
	2575	1/1	-7	6.1	2.89	3.2	86.	19.	130.	
	2577	1/1	-7	5.5	2.89	2.6	116.	10.	102.	
			N	5	5	5	5	5	5	
			Mean	5.8	2.87	2.9	96.	14.	112.	
			Sdev	0.24	0.175	0.30	14.6	3.7	10.6	
50 mg/kg/day										
	2562	2/1	-7	5.8	3.09	2.7	66.	34.	116.	
	2563	2/1	-7	5.8	2.58	3.2	104.	38.	170.	
	2576	2/1	-7	5.8	2.98	2.8	93.	18.	122.	
			N	3	3	3	3	3	3	
			Mean	5.8	2.88	2.9	88.	30.	136.	
			Sdev	0.00	0.268	0.27	19.6	10.6	29.6	
200 mg/kg/day										
	2561	3/1	-7	6.1	2.90	3.2	90.	28.	128.	
	2570	3/1	-7	6.0	3.08	2.9	112.	17.	132.	
	2567	3/1	-7	5.7	2.77	2.9	93.	21.	132.	
			N	3	3	3	3	3	3	
			Mean	5.9	2.92	3.0	98.	22.	131.	
			Sdev	0.21	0.156	0.16	11.9	5.6	2.3	
800 mg/kg/day										
	2564	4/1	-7	5.9	2.74	3.2	106.	18.	148.	
	2565	4/1	-7	6.1	2.79	3.3	99.	20.	156.	
	2569	4/1	-7	5.6	2.99	2.6	108.	12.	104.	
	2571	4/1	-7	5.7	3.01	2.7	95.	32.	145.	
	2573	4/1	-7	6.0	2.98	3.0	94.	22.	120.	
			N	5	5	5	5	5	5	
			Mean	5.9	2.90	3.0	100.	21.	135.	
			Sdev	0.21	0.127	0.30	6.3	7.3	21.8	

TPRO - TOTAL PROTEIN  
GLUC - GLUCOSE

ALB - ALBUMIN  
TG - TRIGLYCERIDES

GLOB - GLOBULIN  
TCHO - TOTAL CHOLESTEROL

CONFIDENTIAL

Appendix 8  
Day -7 Clinical Chemistry Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L	
Vehicle										
	2560	1/1	-7	10.1	4.2	0.8	140.0	4.5	110.0	
	2568	1/1	-7	10.7	4.9	1.1	140.0	4.2	109.0	
	2572	1/1	-7	10.4	3.6	1.1	143.0	4.3	108.0	
	2575	1/1	-7	10.5	5.1	0.9	142.0	4.6	106.0	
	2577	1/1	-7	10.5	4.4	1.1	144.0	4.1	107.0	
			N	5	5	5	5	5	5	
			Mean	10.4	4.4	1.0	141.8	4.3	108.0	
			Sdev	0.22	0.59	0.14	1.79	0.20	1.58	
50 mg/kg/day										
	2562	2/1	-7	10.7	5.0	1.1	142.0	4.7	106.0	
	2563	2/1	-7	10.7	4.9	0.8	142.0	4.7	105.0	
	2576	2/1	-7	10.7	4.7	1.1	144.0	4.6	107.0	
			N	3	3	3	3	3	3	
			Mean	10.7	4.9	1.0	142.7	4.7	106.0	
			Sdev	0.00	0.15	0.18	1.15	0.10	1.00	
200 mg/kg/day										
	2561	3/1	-7	10.7	4.7	0.9	142.0	4.7	108.0	
	2570	3/1	-7	10.8	4.7	1.1	144.0	4.3	109.0	
	2567	3/1	-7	10.2	4.4	0.9	140.0	4.1	107.0	
			N	3	3	3	3	3	3	
			Mean	10.6	4.6	1.0	142.0	4.4	108.0	
			Sdev	0.32	0.17	0.08	2.00	0.27	1.00	
800 mg/kg/day										
	2564	4/1	-7	10.9	5.5	0.9	143.0	4.4	107.0	
	2565	4/1	-7	11.3	5.1	0.8	144.0	4.1	102.0	
	2569	4/1	-7	10.7	3.6	1.1	142.0	4.4	110.0	
	2571	4/1	-7	10.8	3.7	1.1	144.0	4.6	108.0	
	2573	4/1	-7	10.8	4.7	1.0	142.0	4.4	105.0	
			N	5	5	5	5	5	5	
			Mean	10.9	4.5	1.0	143.0	4.4	106.4	
			Sdev	0.23	0.84	0.14	1.00	0.16	3.05	

CA - CALCIUM  
NA - SODIUM

PHOS - PHOSPHOROUS  
K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
CL - CHLORIDE

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2516	1/1	28	28.	0.90	33.	50.	72.	3.	0.30
	2518	1/1	28	31.	0.81	46.	57.	80.	6.	0.24
	2520	1/1	28	30.	0.95	29.	26.	57.	2.	0.27
	2527	1/1	28	28.	0.88	37.	32.	66.	2.	0.21
	2533	1/1	28	31.	0.95	41.	38.	64.	5.	0.24
			N	5	5	5	5	5	5	5
			Mean	30.	0.90	37.	41.	68.	4.	0.25
			Sdev	1.5	0.058	6.6	12.8	8.7	1.8	0.034
50 mg/kg/day										
	2514	2/1	28	23.	0.87	35.	39.	83.	6.	0.21
	2521	2/1	28	26.	0.89	31.	38.	62.	5.	0.28
	2529	2/1	28	23.	0.86	33.	26.	83.	5.	0.26
			N	3	3	3	3	3	3	3
			Mean	24.	0.87	33.	34.	76.	5.	0.25
			Sdev	1.7	0.015	2.0	7.2	12.1	0.6	0.036
200 mg/kg/day										
	2515	3/1	28	25.	0.97	31.	32.	99.	5.	0.23
	2523	3/1	28	34.	0.78	39.	30.	61.	6.	0.22
	2526	3/1	28	22.	0.80	24.	27.	85.	6.	0.26
			N	3	3	3	3	3	3	3
			Mean	27.	0.85	31.	30.	82.	6.	0.24
			Sdev	6.2	0.104	7.5	2.5	19.2	0.6	0.021
800 mg/kg/day										
	2517	4/1	28	43.	0.78	31.	49.	87.	9.	0.32
	2519	4/1	28	34.	0.94	23.	25.	116.	6.	0.20
	2525	4/1	28	32.	1.03	30.	35.	151.	7.	0.28
	2528	4/1	28	29.	1.03	31.	32.	80.	12.	0.25
	2530	4/1	28	25.	0.87	41.	40.	66.	6.	0.32
			N	5	5	5	5	5	5	5
			Mean	33.	0.93	31.	36.	100.	8.	0.27
			Sdev	6.7	0.107	6.4	9.0	33.8	2.5	0.051

UREA - UREA  
ALT - ALANINE AMINO TRANSFERASE  
TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
GGT - GAMMA GLUTAMYL TRANSFERASE

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL	
Vehicle										
	2516	1/1	28	5.3	2.82	2.5	97.	21.	112.	
	2518	1/1	28	5.6	2.92	2.7	90.	28.	132.	
	2520	1/1	28	5.7	2.92	2.8	85.	16.	110.	
	2527	1/1	28	5.3	2.57	2.7	99.	22.	137.	
	2533	1/1	28	5.0	2.48	2.5	87.	29.	92.	
			N	5	5	5	5	5	5	
			Mean	5.4	2.74	2.6	92.	23.	117.	
			Sdev	0.28	0.205	0.13	6.1	5.4	18.2	
50 mg/kg/day										
	2514	2/1	28	5.5	3.05	2.5	98.	21.	113.	
	2521	2/1	28	5.5	2.94	2.6	94.	39.	138.	
	2529	2/1	28	5.2	2.86	2.3	93.	18.	127.	
			N	3	3	3	3	3	3	
			Mean	5.4	2.95	2.5	95.	26.	126.	
			Sdev	0.17	0.095	0.11	2.6	11.4	12.5	
200 mg/kg/day										
	2515	3/1	28	5.4	3.05	2.4	92.	31.	155.	
	2523	3/1	28	5.0	2.35	2.7	98.	23.	133.	
	2526	3/1	28	5.6	2.85	2.8	106.	26.	134.	
			N	3	3	3	3	3	3	
			Mean	5.3	2.75	2.6	99.	27.	141.	
			Sdev	0.31	0.361	0.21	7.0	4.0	12.4	
800 mg/kg/day										
	2517	4/1	28	5.2	2.87	2.3	88.	25.	169.	
	2519	4/1	28	5.4	2.79	2.6	86.	22.	125.	
	2525	4/1	28	5.6	3.15	2.5	89.	28.	172.	
	2528	4/1	28	5.3	2.76	2.5	95.	35.	193.	
	2530	4/1	28	5.3	2.82	2.5	107.	28.	116.	
			N	5	5	5	5	5	5	
			Mean	5.4	2.88	2.5	93.	28.	155.	
			Sdev	0.15	0.157	0.10	8.5	4.8	33.0	

TPRO - TOTAL PROTEIN  
GLUC - GLUCOSE

ALB - ALBUMIN  
TG - TRIGLYCERIDES

GLOB - GLOBULIN  
TCHO - TOTAL CHOLESTEROL

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L	
Vehicle										
	2516	1/1	28	10.5	4.6	1.1	142.0	4.6	112.0	
	2518	1/1	28	10.5	4.9	1.1	141.0	4.6	111.0	
	2520	1/1	28	10.7	3.9	1.1	141.0	4.5	108.0	
	2527	1/1	28	10.5	4.3	0.9	141.0	4.3	107.0	
	2533	1/1	28	9.3	4.0	1.0	141.0	4.6	113.0	
			N	5	5	5	5	5	5	
			Mean	10.3	4.3	1.0	141.2	4.5	110.2	
			Sdev	0.57	0.42	0.08	0.45	0.12	2.59	
50 mg/kg/day										
	2514	2/1	28	10.4	4.3	1.2	143.0	4.5	111.0	
	2521	2/1	28	10.3	4.4	1.1	142.0	4.4	110.0	
	2529	2/1	28	10.2	4.4	1.2	142.0	4.2	110.0	
			N	3	3	3	3	3	3	
			Mean	10.3	4.4	1.2	142.3	4.3	110.3	
			Sdev	0.10	0.06	0.05	0.58	0.16	0.58	
200 mg/kg/day										
	2515	3/1	28	10.4	3.9	1.3	144.0	4.4	112.0	
	2523	3/1	28	9.5	3.3	0.9	142.0	4.6	115.0	
	2526	3/1	28	10.9	4.5	1.0	141.0	4.2	107.0	
			N	3	3	3	3	3	3	
			Mean	10.3	3.9	1.1	142.3	4.4	111.3	
			Sdev	0.71	0.60	0.21	1.53	0.21	4.04	
800 mg/kg/day										
	2517	4/1	28	9.4	3.9	1.2	141.0	4.5	111.0	
	2519	4/1	28	10.4	4.2	1.1	143.0	4.1	109.0	
	2525	4/1	28	10.7	5.2	1.3	144.0	4.6	111.0	
	2528	4/1	28	10.2	4.4	1.1	142.0	4.3	115.0	
	2530	4/1	28	10.1	3.8	1.1	141.0	4.5	112.0	
			N	5	5	5	5	5	5	
			Mean	10.2	4.3	1.2	142.2	4.4	111.6	
			Sdev	0.48	0.56	0.09	1.30	0.19	2.19	

CA - CALCIUM  
NA - SODIUM

PHOS - PHOSPHOROUS  
K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
CL - CHLORIDE

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2560	1/1	28	21.	0.79	45.	36.	48.	3.	0.22
	2568	1/1	28	26.	0.91	34.	38.	55.	5.	0.12
	2572	1/1	28	23.	0.86	29.	35.	66.	4.	0.09
	2575	1/1	28	22.	0.91	31.	33.	93.	5.	0.10
	2577	1/1	28	22.	0.98	35.	34.	62.	3.	0.11
			N	5	5	5	5	5	5	5
			Mean	23.	0.89	35.	35.	65.	4.	0.13
			Sdev	1.9	0.070	6.2	1.9	17.2	1.0	0.053
50 mg/kg/day										
	2562	2/1	28	31.	0.88	30.	38.	92.	6.	0.10
	2563	2/1	28	22.	0.88	33.	25.	58.	4.	0.10
	2576	2/1	28	28.	0.90	39.	40.	76.	7.	0.21
			N	3	3	3	3	3	3	3
			Mean	27.	0.89	34.	34.	75.	6.	0.14
			Sdev	4.6	0.012	4.6	8.1	17.0	1.5	0.064
200 mg/kg/day										
	2561	3/1	28	31.	0.84	47.	30.	60.	8.	0.11
	2570	3/1	28	26.	0.81	34.	35.	77.	6.	0.11
	2567	3/1	28	23.	0.88	40.	23.	96.	7.	0.10
			N	3	3	3	3	3	3	3
			Mean	27.	0.84	40.	29.	78.	7.	0.11
			Sdev	4.0	0.035	6.5	6.0	18.0	1.0	0.006
800 mg/kg/day										
	2564	4/1	28	23.	0.83	31.	26.	66.	8.	0.12
	2565	4/1	28	51.	0.92	25.	28.	58.	7.	0.32
	2569	4/1	28	30.	1.03	33.	57.	101.	9.	0.20
	2571	4/1	28	29.	0.98	31.	59.	81.	7.	0.12
	2573	4/1	28	26.	0.88	23.	25.	62.	6.	0.12
			N	5	5	5	5	5	5	5
			Mean	32.	0.93	29.	39.	74.	7.	0.18
			Sdev	11.1	0.079	4.3	17.4	17.6	1.1	0.088

UREA - UREA  
ALT - ALANINE AMINO TRANSFERASE  
TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
GGT - GAMMA GLUTAMYL TRANSFERASE

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL	
Vehicle										
	2560	1/1	28	5.6	2.52	3.1	87.	20.	97.	
	2568	1/1	28	5.3	2.94	2.4	79.	23.	93.	
	2572	1/1	28	5.3	2.91	2.4	101.	17.	113.	
	2575	1/1	28	5.8	2.87	2.9	91.	23.	140.	
	2577	1/1	28	5.8	2.99	2.8	103.	24.	111.	
			N	5	5	5	5	5	5	
			Mean	5.6	2.85	2.7	92.	21.	111.	
			Sdev	0.25	0.187	0.32	10.0	2.9	18.5	
50 mg/kg/day										
	2562	2/1	28	5.6	3.00	2.6	75.	43.	107.	
	2563	2/1	28	5.2	2.67	2.5	111.	45.	186.	
	2576	2/1	28	5.7	3.01	2.7	91.	20.	129.	
			N	3	3	3	3	3	3	
			Mean	5.5	2.89	2.6	92.	36.	141.	
			Sdev	0.26	0.193	0.08	18.0	13.9	40.8	
200 mg/kg/day										
	2561	3/1	28	5.5	2.92	2.6	108.	37.	181.	
	2570	3/1	28	5.5	2.95	2.6	105.	44.	128.	
	2567	3/1	28	5.3	2.72	2.6	84.	36.	120.	
			N	3	3	3	3	3	3	
			Mean	5.4	2.86	2.6	99.	39.	143.	
			Sdev	0.12	0.125	0.02	13.1	4.4	33.2	
800 mg/kg/day										
	2564	4/1	28	5.4	2.74	2.7	106.	25.	232.	
	2565	4/1	28	5.9	3.01	2.9	104.	38.	200.	
	2569	4/1	28	5.4	3.00	2.4	118.	45.	122.	
	2571	4/1	28	5.4	2.99	2.4	105.	34.	177.	
	2573	4/1	28	6.1	3.05	3.1	97.	25.	171.	
			N	5	5	5	5	5	5	
			Mean	5.6	2.96	2.7	106.	33.	180.	
			Sdev	0.34	0.124	0.29	7.6	8.6	40.5	

TPRO - TOTAL PROTEIN  
GLUC - GLUCOSE

ALB - ALBUMIN  
TG - TRIGLYCERIDES

GLOB - GLOBULIN  
TCHO - TOTAL CHOLESTEROL

CONFIDENTIAL

Appendix 8  
Day 28 Clinical Chemistry Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L	
Vehicle										
	2560	1/1	28	9.6	3.8	0.8	141.0	4.6	113.0	
	2568	1/1	28	10.6	4.6	1.2	142.0	4.8	109.0	
	2572	1/1	28	10.1	3.5	1.2	142.0	4.3	112.0	
	2575	1/1	28	10.3	4.0	1.0	142.0	4.4	111.0	
	2577	1/1	28	11.0	4.1	1.1	143.0	4.2	108.0	
			N	5	5	5	5	5	5	
			Mean	10.3	4.0	1.1	142.0	4.5	110.6	
			Sdev	0.53	0.41	0.18	0.71	0.24	2.07	
50 mg/kg/day										
	2562	2/1	28	10.5	4.3	1.2	141.0	4.4	109.0	
	2563	2/1	28	10.4	4.2	1.1	143.0	4.2	109.0	
	2576	2/1	28	11.1	4.5	1.1	143.0	4.4	111.0	
			N	3	3	3	3	3	3	
			Mean	10.7	4.3	1.1	142.3	4.3	109.7	
			Sdev	0.38	0.15	0.05	1.15	0.14	1.15	
200 mg/kg/day										
	2561	3/1	28	10.8	3.1	1.1	144.0	4.2	112.0	
	2570	3/1	28	9.9	4.7	1.2	143.0	4.7	113.0	
	2567	3/1	28	10.2	3.9	1.1	142.0	4.2	110.0	
			N	3	3	3	3	3	3	
			Mean	10.3	3.9	1.1	143.0	4.4	111.7	
			Sdev	0.46	0.80	0.05	1.00	0.27	1.53	
800 mg/kg/day										
	2564	4/1	28	10.6	3.9	1.0	145.0	4.2	112.0	
	2565	4/1	28	11.5	4.4	1.0	146.0	4.0	104.0	
	2569	4/1	28	10.6	3.7	1.3	145.0	4.4	114.0	
	2571	4/1	28	10.9	3.6	1.2	142.0	4.3	111.0	
	2573	4/1	28	10.7	4.1	1.0	143.0	4.4	108.0	
			N	5	5	5	5	5	5	
			Mean	10.9	3.9	1.1	144.2	4.3	109.8	
			Sdev	0.38	0.32	0.12	1.64	0.18	3.90	

CA - CALCIUM  
NA - SODIUM

PHOS - PHOSPHOROUS  
K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
CL - CHLORIDE



CONFIDENTIAL

Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2527	1/1	42	42.	0.91	31.	23.	56.	5.	0.07
	2533	1/1	42	32.	0.85	44.	41.	61.	8.	0.08
			N	2	2	2	2	2	2	2
			Mean	37.	0.88	38.	32.	59.	7.	0.08
			Sdev	7.1	0.042	9.2	12.7	3.5	2.1	0.007
800 mg/kg/day										
	2528	4/1	42	24.	0.81	36.	58.	78.	13.	0.09
	2530	4/1	42	25.	0.73	44.	27.	63.	7.	0.07
			N	2	2	2	2	2	2	2
			Mean	25.	0.77	40.	43.	71.	10.	0.08
			Sdev	0.7	0.057	5.7	21.9	10.6	4.2	0.014

UREA - UREA  
 ALT - ALANINE AMINO TRANSFERASE  
 TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
 AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
 GGT - GAMMA GLUTAMYL TRANSFERASE

CONFIDENTIAL

Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

M a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL
Vehicle									
	2527	1/1	42	5.8	2.57	3.2	105.	33.	148.
	2533	1/1	42	5.6	2.55	3.1	93.	24.	85.
			N	2	2	2	2	2	2
			Mean	5.7	2.56	3.1	99.	29.	117.
			Sdev	0.14	0.014	0.13	8.5	6.4	44.5
800 mg/kg/day									
	2528	4/1	42	6.1	2.89	3.2	82.	27.	141.
	2530	4/1	42	6.2	2.94	3.3	100.	18.	91.
			N	2	2	2	2	2	2
			Mean	6.2	2.92	3.2	91.	23.	116.
			Sdev	0.07	0.035	0.04	12.7	6.4	35.4

TPRO - TOTAL PROTEIN  
 GLUC - GLUCOSE

ALB - ALBUMIN  
 TG - TRIGLYCERIDES

GLOB - GLOBULIN  
 TCHO - TOTAL CHOLESTEROL

CONFIDENTIAL

Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

M a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L
Vehicle									
	2527	1/1	42	11.0	5.0	0.8	142.0	4.4	109.0
	2533	1/1	42	9.6	4.5	0.8	141.0	4.6	114.0
			N	2	2	2	2	2	2
			Mean	10.3	4.8	0.8	141.5	4.5	111.5
			Sdev	0.99	0.35	0.03	0.71	0.11	3.54
800 mg/kg/day									
	2528	4/1	42	10.9	4.0	0.9	142.0	4.6	108.0
	2530	4/1	42	10.5	4.7	0.9	142.0	4.3	109.0
			N	2	2	2	2	2	2
			Mean	10.7	4.4	0.9	142.0	4.5	108.5
			Sdev	0.28	0.49	0.00	0.00	0.17	0.71

CA - CALCIUM  
 NA - SODIUM

PHOS - PHOSPHOROUS  
 K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
 CL - CHLORIDE

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Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UREA mg/dL	CREA mg/dL	AST IU/L	ALT IU/L	AP IU/L	GGT IU/L	TBIL mg/dL
Vehicle										
	2575	1/1	42	22.	0.93	33.	26.	106.	7.	0.07
	2577	1/1	42	29.	0.98	38.	36.	53.	6.	0.08
			N	2	2	2	2	2	2	2
			Mean	26.	0.96	36.	31.	80.	7.	0.08
			Sdev	4.9	0.035	3.5	7.1	37.5	0.7	0.007
800 mg/kg/day										
	2571	4/1	42	31.	0.94	22.	38.	75.	8.	0.07
	2573	4/1	42	25.	0.87	25.	29.	62.	7.	0.09
			N	2	2	2	2	2	2	2
			Mean	28.	0.91	24.	34.	69.	8.	0.08
			Sdev	4.2	0.049	2.1	6.4	9.2	0.7	0.014

UREA - UREA  
 ALT - ALANINE AMINO TRANSFERASE  
 TBIL - TOTAL BILIRUBIN

CREA - CREATININE  
 AP - ALKALINE PHOSPHATASE

AST - ASPARTATE AMINO TRANSFERASE  
 GGT - GAMMA GLUTAMYL TRANSFERASE

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Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

F e m a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	TPRO g/dL	ALB g/dL	GLOB g/dL	GLUC mg/dL	TG mg/dL	TCHO mg/dL
Vehicle									
	2575	1/1	42	6.0	2.91	3.1	93.	27.	135.
	2577	1/1	42	5.7	2.87	2.8	101.	38.	111.
			N	2	2	2	2	2	2
			Mean	5.9	2.89	3.0	97.	33.	123.
			Sdev	0.21	0.028	0.18	5.7	7.8	17.0
800 mg/kg/day									
	2571	4/1	42	5.8	2.93	2.9	115.	37.	187.
	2573	4/1	42	5.7	2.90	2.8	94.	20.	130.
			N	2	2	2	2	2	2
			Mean	5.8	2.92	2.8	105.	29.	159.
			Sdev	0.07	0.021	0.05	14.8	12.0	40.3

TPRO - TOTAL PROTEIN  
 GLUC - GLUCOSE

ALB - ALBUMIN  
 TG - TRIGLYCERIDES

GLOB - GLOBULIN  
 TCHO - TOTAL CHOLESTEROL

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Appendix 8  
 Day 42 Clinical Chemistry Data  
 Test period

Session 1 (Scheduled)  
 Fexinidazole

Study Number: 0505-2007

F e m a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	CA mg/dL	PHOS mg/dL	AG	NA mEq/L	K mEq/L	CL mEq/L
Vehicle									
	2575	1/1	42	10.8	4.6	0.9	140.0	4.5	112.0
	2577	1/1	42	11.1	4.7	1.0	142.0	4.3	110.0
			N	2	2	2	2	2	2
			Mean	11.0	4.7	1.0	141.0	4.4	111.0
			Sdev	0.21	0.07	0.05	1.41	0.12	1.41
800 mg/kg/day									
	2571	4/1	42	11.1	4.3	1.0	140.0	4.5	111.0
	2573	4/1	42	10.6	4.6	1.0	140.0	4.6	108.0
			N	2	2	2	2	2	2
			Mean	10.9	4.5	1.0	140.0	4.5	109.5
			Sdev	0.35	0.21	0.01	0.00	0.03	2.12

CA - CALCIUM  
 NA - SODIUM

PHOS - PHOSPHOROUS  
 K - POTASSIUM

AG - ALBUMIN/GLOBULIN  
 CL - CHLORIDE

## ***Appendix 9 Urinalysis***

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Appendix 9  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE
Vehicle										
	2516	1/1	-7	246.0	7.0	1.	0.	0.	0.	0.
	2518	1/1	-7	364.0	7.0	2.	0.	0.	0.	0.
	2520	1/1	-7	192.0	8.0	1.	0.	0.	0.	0.
	2527	1/1	-7	188.0	7.0	1.	0.	0.	0.	0.
	2533	1/1	-7	224.0	7.0	0.	1.	1.	3.	0.
			N	5	5	5	5	5	5	5
			Mean	242.8	7.2	1.	0.	0.	1.	0.
			Sdev	71.83	0.45	0.7	0.4	0.4	1.3	0.0
50 mg/kg/day										
	2514	2/1	-7	240.0	8.0	0.	0.	0.	0.	0.
	2521	2/1	-7	67.0	8.0	1.	0.	0.	0.	0.
	2529	2/1	-7	184.0	6.5	2.	0.	1.	0.	0.
			N	3	3	3	3	3	3	3
			Mean	163.7	7.5	1.	0.	0.	0.	0.
			Sdev	88.27	0.87	1.0	0.0	0.6	0.0	0.0
200 mg/kg/day										
	2515	3/1	-7	98.0	9.0	2.	0.	1.	0.	0.
	2523	3/1	-7	394.0	7.0	2.	0.	0.	0.	0.
	2526	3/1	-7	86.0	5.0	0.	0.	0.	2.	0.
			N	3	3	3	3	3	3	3
			Mean	192.7	7.0	1.	0.	0.	1.	0.
			Sdev	174.46	2.00	1.2	0.0	0.6	1.2	0.0
800 mg/kg/day										
	2517	4/1	-7	690.0	7.0	0.	0.	0.	0.	0.
	2519	4/1	-7	191.0	7.0	1.	1.	1.	0.	0.
	2525	4/1	-7	383.0	7.0	0.	0.	0.	0.	0.
	2528	4/1	-7	138.0	7.0	0.	0.	1.	0.	0.
	2530	4/1	-7	668.0	7.0	2.	0.	0.	0.	0.
			N	5	5	5	5	5	5	5
			Mean	414.0	7.0	1.	0.	0.	0.	0.
			Sdev	258.63	0.00	0.9	0.4	0.5	0.0	0.0

VOL - URINARY VOLUME  
NIT - NITRITES  
KET - KETONE BODIES

PH - PH  
PRO - PROTEINS

WBC - WHITE BLOOD CELLS  
GLU - GLUCOSE



CONFIDENTIAL

Appendix 9  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP	
Vehicle										
	2516	1/1	-7	0.	0.	0.	1.017	A	L	
	2518	1/1	-7	0.	0.	1.	1.018	Y	T	
	2520	1/1	-7	0.	0.	0.	1.014	Y	L	
	2527	1/1	-7	0.	0.	0.	1.018	Y	L	
	2533	1/1	-7	0.	0.	2.	1.017	A	LT	
			N	5	5	5	5	0	0	
			Mean	0.	0.	1.	1.017	-	-	
			Sdev	0.0	0.0	0.9	0.0016	-	-	
50 mg/kg/day										
	2514	2/1	-7	0.	0.	0.	1.026	A	L	
	2521	2/1	-7	0.	0.	0.	1.014	W	L	
	2529	2/1	-7	0.	0.	1.	1.024	A	L	
			N	3	3	3	3	0	0	
			Mean	0.	0.	0.	1.021	-	-	
			Sdev	0.0	0.0	0.6	0.0064	-	-	
200 mg/kg/day										
	2515	3/1	-7	0.	0.	0.	1.034	B	LT	
	2523	3/1	-7	0.	0.	1.	1.018	Y	L	
	2526	3/1	-7	0.	0.	1.	1.007	W	L	
			N	3	3	3	3	0	0	
			Mean	0.	0.	1.	1.020	-	-	
			Sdev	0.0	0.0	0.6	0.0136	-	-	
800 mg/kg/day										
	2517	4/1	-7	0.	0.	0.	1.011	Y	L	
	2519	4/1	-7	0.	0.	1.	1.029	A	T	
	2525	4/1	-7	0.	0.	0.	1.020	A	L	
	2528	4/1	-7	0.	0.	1.	1.040	B	T	
	2530	4/1	-7	0.	0.	1.	1.014	Y	T	
			N	5	5	5	5	0	0	
			Mean	0.	0.	1.	1.023	-	-	
			Sdev	0.0	0.0	0.5	0.0118	-	-	

UBG - UROBILINOGEN  
SG - SPECIFIC GRAVITY

BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

CONFIDENTIAL

Appendix 9  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE
Vehicle										
	2560	1/1	-7	121.0	7.0	0.	0.	0.	0.	0.
	2568	1/1	-7	113.0	7.0	0.	0.	0.	0.	0.
	2572	1/1	-7	381.0	7.0	0.	0.	0.	0.	0.
	2575	1/1	-7	152.0	6.5	0.	0.	0.	0.	0.
	2577	1/1	-7	214.0	7.0	0.	0.	0.	0.	0.
			N	5	5	5	5	5	5	5
			Mean	196.2	6.9	0.	0.	0.	0.	0.
			Sdev	110.68	0.22	0.0	0.0	0.0	0.0	0.0
50 mg/kg/day										
	2562	2/1	-7	34.0	7.0	0.	0.	0.	0.	0.
	2563	2/1	-7	201.0	7.0	0.	0.	0.	0.	0.
	2576	2/1	-7	204.0	7.0	0.	0.	0.	0.	0.
			N	3	3	3	3	3	3	3
			Mean	146.3	7.0	0.	0.	0.	0.	0.
			Sdev	97.30	0.00	0.0	0.0	0.0	0.0	0.0
200 mg/kg/day										
	2561	3/1	-7	82.0	7.0	0.	0.	0.	0.	0.
	2570	3/1	-7	288.0	7.0	0.	0.	0.	0.	0.
	2567	3/1	-7	124.0	6.5	0.	0.	0.	0.	0.
			N	3	3	3	3	3	3	3
			Mean	164.7	6.8	0.	0.	0.	0.	0.
			Sdev	108.85	0.29	0.0	0.0	0.0	0.0	0.0
800 mg/kg/day										
	2564	4/1	-7	159.0	8.0	0.	0.	0.	0.	0.
	2565	4/1	-7	50.0	6.5	0.	1.	2.	4.	1.
	2569	4/1	-7	275.0	7.0	1.	1.	1.	0.	0.
	2571	4/1	-7	314.0	7.0	0.	0.	0.	0.	0.
	2573	4/1	-7	100.0	7.0	0.	0.	0.	0.	0.
			N	5	5	5	5	5	5	5
			Mean	179.6	7.1	0.	0.	1.	1.	0.
			Sdev	112.61	0.55	0.4	0.5	0.9	1.8	0.4

VOL - URINARY VOLUME  
NIT - NITRITES  
KET - KETONE BODIES

PH - PH  
PRO - PROTEINS

WBC - WHITE BLOOD CELLS  
GLU - GLUCOSE

CONFIDENTIAL

Appendix 9  
Day -7 Urine Data  
Pretest phase

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP	
Vehicle										
	2560	1/1	-7	0.	0.	0.	1.034	A	LT	
	2568	1/1	-7	0.	0.	0.	1.035	A	LT	
	2572	1/1	-7	0.	0.	0.	1.016	Y	L	
	2575	1/1	-7	0.	0.	0.	1.028	Y	L	
	2577	1/1	-7	0.	0.	0.	1.020	Y	L	
			N	5	5	5	5	0	0	
			Mean	0.	0.	0.	1.027	-	-	
			Sdev	0.0	0.0	0.0	0.0084	-	-	
50 mg/kg/day										
	2562	2/1	-7	0.	0.	0.	1.021	Y	L	
	2563	2/1	-7	0.	0.	0.	1.015	Y	L	
	2576	2/1	-7	0.	0.	0.	1.022	Y	L	
			N	3	3	3	3	0	0	
			Mean	0.	0.	0.	1.019	-	-	
			Sdev	0.0	0.0	0.0	0.0038	-	-	
200 mg/kg/day										
	2561	3/1	-7	0.	0.	0.	1.011	W	L	
	2570	3/1	-7	0.	0.	0.	1.022	A	L	
	2567	3/1	-7	0.	0.	0.	1.036	A	LT	
			N	3	3	3	3	0	0	
			Mean	0.	0.	0.	1.023	-	-	
			Sdev	0.0	0.0	0.0	0.0125	-	-	
800 mg/kg/day										
	2564	4/1	-7	0.	0.	0.	1.020	Y	L	
	2565	4/1	-7	0.	0.	3.	1.026	A	T	
	2569	4/1	-7	0.	0.	2.	1.019	Y	T	
	2571	4/1	-7	0.	0.	0.	1.011	Y	L	
	2573	4/1	-7	0.	0.	0.	1.028	Y	LT	
			N	5	5	5	5	0	0	
			Mean	0.	0.	1.	1.021	-	-	
			Sdev	0.0	0.0	1.4	0.0067	-	-	

UBG - UROBILINOGEN  
SG - SPECIFIC GRAVITY

BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

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Appendix 9  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE	
Vehicle											
	2516	1/1	28	212.0	7.0	2.	0.	0.	0.	0.	
	2518	1/1	28	144.0	7.0	2.	1.	0.	0.	0.	
	2520	1/1	28	52.0	7.0	2.	0.	0.	0.	0.	
	2527	1/1	28	275.0	7.0	1.	0.	0.	0.	0.	
	2533	1/1	28	60.0	7.0	1.	1.	1.	0.	0.	
			N	5	5	5	5	5	5	5	
			Mean	148.6	7.0	2.	0.	0.	0.	0.	
			Sdev	96.44	0.00	0.5	0.5	0.4	0.0	0.0	
50 mg/kg/day											
	2514	2/1	28	558.0	7.0	2.	0.	0.	0.	0.	
	2521	2/1	28	18.0	7.0	2.	1.	1.	0.	0.	
	2529	2/1	28	98.0	7.0	2.	0.	1.	0.	0.	
			N	3	3	3	3	3	3	3	
			Mean	224.7	7.0	2.	0.	1.	0.	0.	
			Sdev	291.43	0.00	0.0	0.6	0.6	0.0	0.0	
200 mg/kg/day											
	2515	3/1	28	221.0	6.5	2.	1.	1.	0.	0.	
	2523	3/1	28	454.0	6.5	1.	0.	0.	0.	0.	
	2526	3/1	28	252.0	7.0	0.	0.	0.	0.	0.	
			N	3	3	3	3	3	3	3	
			Mean	309.0	6.7	1.	0.	0.	0.	0.	
			Sdev	126.53	0.29	1.0	0.6	0.6	0.0	0.0	
800 mg/kg/day											
	2517	4/1	28	197.0	7.0	1.	0.	0.	0.	0.	
	2519	4/1	28	149.0	7.0	2.	0.	0.	0.	0.	
	2525	4/1	28	478.0	7.0	2.	0.	0.	0.	0.	
	2528	4/1	28	432.0	7.0	2.	1.	1.	0.	0.	
	2530	4/1	28	522.0	7.0	2.	0.	0.	0.	0.	
			N	5	5	5	5	5	5	5	
			Mean	355.6	7.0	2.	0.	0.	0.	0.	
			Sdev	170.55	0.00	0.4	0.4	0.4	0.0	0.0	

VOL - URINARY VOLUME  
NIT - NITRITES  
KET - KETONE BODIES

PH - PH  
PRO - PROTEINS

WBC - WHITE BLOOD CELLS  
GLU - GLUCOSE

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Appendix 9  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP	
Vehicle										
	2516	1/1	28	0.	0.	0.	1.018	A	L	
	2518	1/1	28	0.	0.	1.	1.026	Y	T	
	2520	1/1	28	0.	0.	1.	1.018	A	L	
	2527	1/1	28	0.	0.	0.	1.022	Y	L	
	2533	1/1	28	0.	0.	2.	1.029	A	T	
			N	5	5	5	5	0	0	
			Mean	0.	0.	1.	1.023	-	-	
			Sdev	0.0	0.0	0.8	0.0049	-	-	
50 mg/kg/day										
	2514	2/1	28	0.	0.	1.	1.019	A	T	
	2521	2/1	28	0.	0.	0.	1.023	B	LT	
	2529	2/1	28	0.	0.	0.	1.037	B	LT	
			N	3	3	3	3	0	0	
			Mean	0.	0.	0.	1.026	-	-	
			Sdev	0.0	0.0	0.6	0.0095	-	-	
200 mg/kg/day										
	2515	3/1	28	0.	0.	1.	1.024	A	T	
	2523	3/1	28	0.	0.	1.	1.017	Y	L	
	2526	3/1	28	0.	0.	0.	1.020	A	L	
			N	3	3	3	3	0	0	
			Mean	0.	0.	1.	1.020	-	-	
			Sdev	0.0	0.0	0.6	0.0035	-	-	
800 mg/kg/day										
	2517	4/1	28	0.	0.	1.	1.017	Y	LT	
	2519	4/1	28	0.	0.	0.	1.023	Y	L	
	2525	4/1	28	0.	0.	0.	1.018	A	L	
	2528	4/1	28	0.	0.	0.	1.022	A	T	
	2530	4/1	28	0.	0.	0.	1.014	Y	L	
			N	5	5	5	5	0	0	
			Mean	0.	0.	0.	1.019	-	-	
			Sdev	0.0	0.0	0.4	0.0037	-	-	

UBG - UROBILINOGEN  
SG - SPECIFIC GRAVITY

BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

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Appendix 9  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE
Vehicle										
	2560	1/1	28	90.0	9.0	1.	0.	1.	0.	0.
	2568	1/1	28	98.0	7.0	1.	0.	0.	0.	0.
	2572	1/1	28	474.0	7.0	0.	0.	0.	0.	0.
	2575	1/1	28	222.0	7.0	0.	0.	0.	0.	0.
	2577	1/1	28	197.0	8.0	0.	0.	0.	0.	0.
			N	5	5	5	5	5	5	5
			Mean	216.2	7.6	0.	0.	0.	0.	0.
			Sdev	155.53	0.89	0.5	0.0	0.4	0.0	0.0
50 mg/kg/day										
	2562	2/1	28	174.0	7.0	0.	0.	0.	0.	0.
	2563	2/1	28	146.0	7.0	0.	0.	0.	0.	0.
	2576	2/1	28	175.0	7.0	2.	1.	1.	0.	0.
			N	3	3	3	3	3	3	3
			Mean	165.0	7.0	1.	0.	0.	0.	0.
			Sdev	16.46	0.00	1.2	0.6	0.6	0.0	0.0
200 mg/kg/day										
	2561	3/1	28	138.0	7.0	0.	1.	0.	0.	0.
	2570	3/1	28	94.0	8.0	2.	1.	1.	0.	0.
	2567	3/1	28	270.0	8.0	0.	0.	0.	0.	0.
			N	3	3	3	3	3	3	3
			Mean	167.3	7.7	1.	1.	0.	0.	0.
			Sdev	91.59	0.58	1.2	0.6	0.6	0.0	0.0
800 mg/kg/day										
	2564	4/1	28	290.0	7.0	0.	0.	0.	0.	0.
	2565	4/1	28	16.0	6.5	0.	1.	2.	3.	1.
	2569	4/1	28	233.0	7.0	2.	1.	1.	0.	0.
	2571	4/1	28	280.0	7.0	0.	0.	0.	0.	0.
	2573	4/1	28	135.0	8.0	0.	0.	0.	0.	0.
			N	5	5	5	5	5	5	5
			Mean	190.8	7.1	0.	0.	1.	1.	0.
			Sdev	115.38	0.55	0.9	0.5	0.9	1.3	0.4

VOL - URINARY VOLUME  
NIT - NITRITES  
KET - KETONE BODIES

PH - PH  
PRO - PROTEINS

WBC - WHITE BLOOD CELLS  
GLU - GLUCOSE

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Appendix 9  
Day 28 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s										
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP	
Vehicle										
	2560	1/1	28	0.	0.	1.	1.035	A	T	
	2568	1/1	28	0.	0.	0.	1.022	Y	L	
	2572	1/1	28	0.	0.	0.	1.019	Y	LT	
	2575	1/1	28	0.	0.	0.	1.035	A	LT	
	2577	1/1	28	0.	0.	0.	1.028	Y	L	
			N	5	5	5	5	0	0	
			Mean	0.	0.	0.	1.028	-	-	
			Sdev	0.0	0.0	0.4	0.0073	-	-	
50 mg/kg/day										
	2562	2/1	28	0.	0.	0.	1.010	W	L	
	2563	2/1	28	0.	0.	2.	1.008	W	L	
	2576	2/1	28	0.	0.	2.	1.027	A	T	
			N	3	3	3	3	0	0	
			Mean	0.	0.	1.	1.015	-	-	
			Sdev	0.0	0.0	1.2	0.0104	-	-	
200 mg/kg/day										
	2561	3/1	28	0.	0.	0.	1.032	A	L	
	2570	3/1	28	0.	0.	1.	1.029	A	T	
	2567	3/1	28	0.	0.	0.	1.018	Y	L	
			N	3	3	3	3	0	0	
			Mean	0.	0.	0.	1.026	-	-	
			Sdev	0.0	0.0	0.6	0.0074	-	-	
800 mg/kg/day										
	2564	4/1	28	0.	0.	0.	1.015	Y	L	
	2565	4/1	28	0.	0.	2.	1.035	Y	T	
	2569	4/1	28	0.	0.	2.	1.019	A	T	
	2571	4/1	28	0.	0.	0.	1.016	Y	L	
	2573	4/1	28	0.	0.	0.	1.022	Y	L	
			N	5	5	5	5	0	0	
			Mean	0.	0.	1.	1.021	-	-	
			Sdev	0.0	0.0	1.1	0.0081	-	-	

UBG - UROBILINOGEN  
SG - SPECIFIC GRAVITY

BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

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Appendix 9  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s											
Dose Level	Animal Number	Group/ Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE	
Vehicle											
	2527	1/1	42	194.0	6.5	2.	0.	0.	0.	0.	
	2533	1/1	42	638.0	7.0	2.	0.	0.	0.	0.	
			N	2	2	2	2	2	2	2	
			Mean	416.0	6.8	2.	0.	0.	0.	0.	
			Sdev	313.96	0.35	0.0	0.0	0.0	0.0	0.0	
800 mg/kg/day											
	2528	4/1	42	148.0	7.0	0.	0.	0.	0.	0.	
	2530	4/1	42	112.0	8.0	2.	1.	1.	0.	1.	
			N	2	2	2	2	2	2	2	
			Mean	130.0	7.5	1.	1.	1.	0.	1.	
			Sdev	25.46	0.71	1.4	0.7	0.7	0.0	0.7	

VOL - URINARY VOLUME  
NIT - NITRITES  
KET - KETONE BODIES

PH - PH  
PRO - PROTEINS

WBC - WHITE BLOOD CELLS  
GLU - GLUCOSE



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Appendix 9  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

M a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP
Vehicle									
	2527	1/1	42	0.	0.	0.	1.025	Y	L
	2533	1/1	42	0.	0.	1.	1.014	Y	T
			N	2	2	2	2	0	0
			Mean	0.	0.	1.	1.020	-	-
			Sdev	0.0	0.0	0.7	0.0078	-	-
800 mg/kg/day									
	2528	4/1	42	0.	0.	0.	1.036	A	LT
	2530	4/1	42	0.	0.	2.	1.025	A	T
			N	2	2	2	2	0	0
			Mean	0.	0.	1.	1.031	-	-
			Sdev	0.0	0.0	1.4	0.0078	-	-

UBG - UROBILINOGEN  
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BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

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Appendix 9  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s

Dose Level	Animal Number	Group/ Subgroup	Study Day	VOL mL	PH UNITS	WBC SCORE	NIT SCORE	PRO SCORE	GLU SCORE	KET SCORE
Vehicle										
	2575	1/1	42	152.0	9.0	1.	0.	0.	0.	0.
	2577	1/1	42	240.0	8.0	2.	0.	0.	0.	0.
			N	2	2	2	2	2	2	2
			Mean	196.0	8.5	2.	0.	0.	0.	0.
			Sdev	62.23	0.71	0.7	0.0	0.0	0.0	0.0
800 mg/kg/day										
	2571	4/1	42	325.0	7.0	0.	0.	0.	0.	0.
	2573	4/1	42	148.0	9.0	0.	0.	0.	0.	0.
			N	2	2	2	2	2	2	2
			Mean	236.5	8.0	0.	0.	0.	0.	0.
			Sdev	125.16	1.41	0.0	0.0	0.0	0.0	0.0

VOL - URINARY VOLUME  
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Appendix 9  
Day 42 Urine Data  
Test period

Session 1 (Scheduled)  
Fexinidazole

Study Number: 0505-2007

F e m a l e s									
Dose Level	Animal Number	Group/ Subgroup	Study Day	UBG SCORE	BIL SCORE	RBC SCORE	SG	COL	APP
Vehicle									
	2575	1/1	42	0.	0.	2.	1.027	A	T
	2577	1/1	42	0.	0.	0.	1.024	Y	L
			N	2	2	2	2	0	0
			Mean	0.	0.	1.	1.026	-	-
			Sdev	0.0	0.0	1.4	0.0021	-	-
800 mg/kg/day									
	2571	4/1	42	0.	0.	0.	1.015	Y	L
	2573	4/1	42	0.	0.	0.	1.024	Y	L
			N	2	2	2	2	0	0
			Mean	0.	0.	0.	1.020	-	-
			Sdev	0.0	0.0	0.0	0.0064	-	-

UBG - UROBILINOGEN  
SG - SPECIFIC GRAVITY

BIL - BILIRUBIN  
COL - COLOUR

RBC - HEMOGLOBIN/RED BLOOD CELLS  
APP - APPEARANCE

## ***Appendix 10 Absolute Organ Weights***

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s								
Vehicle	2516	1/1	8.41	21.81	8.690	40.50	238.06	1.160
	2518	1/1	8.86	25.18	4.180	43.29	301.45	1.410
	2520	1/1	8.14	18.50	2.320	34.07	313.63	1.210
		N	3	3	3	3	3	3
		Mean	8.47	21.83	5.063	39.29	284.38	1.260
		Sdev	0.366	3.340	3.2756	4.728	40.574	0.1323
50 mg/kg/day	2514	2/1	9.45	24.80	3.110	48.91	262.00	1.180
	2521	2/1	7.58	27.20	3.870	37.44	258.76	1.320
	2529	2/1	7.59	19.81	2.020	39.24	241.26	1.200
		N	3	3	3	3	3	3
		Mean	8.21	23.94	3.000	41.86	254.01	1.233
		Sdev	1.077	3.770	0.9299	6.169	11.157	0.0757
200 mg/kg/day	2515	3/1	8.60	24.19	1.770	35.71	269.07	1.370
	2523	3/1	8.10	13.20	1.180	37.26	325.78	1.830
	2526	3/1	7.60	18.52	1.500	36.02	247.60	1.060
		N	3	3	3	3	3	3
		Mean	8.10	18.64	1.483	36.33	280.82	1.420
		Sdev	0.504	5.496	0.2954	0.820	40.392	0.3874
800 mg/kg/day	2517	4/1	6.87	10.92	1.580	35.25	330.48	1.620
	2519	4/1	7.71	24.45	2.640	37.85	291.59	1.340
	2525	4/1	9.33	22.29	3.240	42.77	338.25	1.420
		N	3	3	3	3	3	3
		Mean	7.97	19.22	2.487	38.62	320.11	1.460
		Sdev	1.249	7.269	0.8406	3.819	25.000	0.1442

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s							
Vehicle							
	2516	1/1	8.41	63.18	67.65	12.63	4.44
	2518	1/1	8.86	65.27	86.97	13.06	3.42
	2520	1/1	8.14	59.25	72.22	11.09	2.46
		N	3	3	3	3	3
		Mean	8.47	62.57	75.61	12.26	3.44
		Sdev	0.366	3.057	10.097	1.036	0.990
50 mg/kg/day							
	2514	2/1	9.45	74.02	67.20	15.74	5.19
	2521	2/1	7.58	62.67	69.75	12.99	3.72
	2529	2/1	7.59	67.21	74.03	10.06	5.06
		N	3	3	3	3	3
		Mean	8.21	67.97	70.33	12.93	4.66
		Sdev	1.077	5.713	3.451	2.840	0.814
200 mg/kg/day							
	2515	3/1	8.60	69.10	72.18	11.97	3.33
	2523	3/1	8.10	63.49	78.10	5.93	2.50
	2526	3/1	7.60	57.78	68.28	14.92	4.92
		N	3	3	3	3	3
		Mean	8.10	63.46	72.85	10.94	3.58
		Sdev	0.504	5.660	4.945	4.583	1.230
800 mg/kg/day							
	2517	4/1	6.87	60.61	72.09	5.06	1.41
	2519	4/1	7.71	59.27	53.37	12.22	4.01
	2525	4/1	9.33	61.36	74.35	16.09	5.30
		N	3	3	3	3	3
		Mean	7.97	60.41	66.60	11.12	3.57
		Sdev	1.249	1.059	11.516	5.596	1.981

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s							
Vehicle							
	2560	1/1	6.35	15.28	2.260	32.03	261.69
	2568	1/1	6.90	20.57	1.670	32.79	236.65
	2572	1/1	6.60	14.81	0.770	30.79	247.06
		N	3	3	3	3	3
		Mean	6.61	16.89	1.567	31.87	248.47
		Sdev	0.276	3.199	0.7504	1.010	12.579
50 mg/kg/day							
	2562	2/1	6.57	19.48	1.960	30.90	200.63
	2563	2/1	7.61	20.35	2.660	32.86	253.51
	2576	2/1	8.38	32.86	4.990	36.69	292.62
		N	3	3	3	3	3
		Mean	7.52	24.23	3.203	33.48	248.92
		Sdev	0.907	7.486	1.5864	2.945	46.166
200 mg/kg/day							
	2561	3/1	7.10	16.59	3.720	34.40	252.23
	2570	3/1	6.65	13.26	0.870	34.85	280.27
	2567	3/1	8.00	29.83	2.150	39.69	313.86
		N	3	3	3	3	3
		Mean	7.25	19.89	2.247	36.31	282.12
		Sdev	0.688	8.765	1.4275	2.933	30.857
800 mg/kg/day							
	2564	4/1	6.10	16.09	0.940	26.90	216.61
	2565	4/1	6.11	13.41	1.510	29.96	257.76
	2569	4/1	7.65	20.66	1.520	32.53	274.32
		N	3	3	3	3	3
		Mean	6.62	16.72	1.323	29.80	249.56
		Sdev	0.889	3.666	0.3320	2.819	29.715

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s							
Vehicle							
	2560	1/1	6.35	1.350	58.70	71.76	0.917
	2568	1/1	6.90	1.380	55.94	74.11	0.852
	2572	1/1	6.60	1.130	55.64	76.37	0.592
		N	3	3	3	3	3
		Mean	6.61	1.287	56.76	74.08	0.787
		Sdev	0.276	0.1365	1.687	2.305	0.1718
50 mg/kg/day							
	2562	2/1	6.57	1.210	56.94	71.89	1.725
	2563	2/1	7.61	1.030	61.71	64.09	1.793
	2576	2/1	8.38	1.180	59.70	71.07	2.164
		N	3	3	3	3	3
		Mean	7.52	1.140	59.45	69.02	1.894
		Sdev	0.907	0.0964	2.395	4.286	0.2362
200 mg/kg/day							
	2561	3/1	7.10	1.510	54.28	77.32	1.458
	2570	3/1	6.65	1.310	54.44	74.16	1.400
	2567	3/1	8.00	1.050	72.23	74.43	2.144
		N	3	3	3	3	3
		Mean	7.25	1.290	60.32	75.30	1.667
		Sdev	0.688	0.2307	10.318	1.752	0.4140
800 mg/kg/day							
	2564	4/1	6.10	1.170	50.79	63.38	1.127
	2565	4/1	6.11	1.310	46.98	60.88	1.355
	2569	4/1	7.65	1.160	63.81	76.33	2.479
		N	3	3	3	3	3
		Mean	6.62	1.213	53.86	66.86	1.654
		Sdev	0.889	0.0839	8.825	8.293	0.7240

Note: Data collected using grace days.



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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s								
Vehicle	2527	1/1	7.87	20.01	3.630	33.39	254.38	1.110
	2533	1/1	7.38	17.80	1.530	31.24	239.15	1.170
		N	2	2	2	2	2	2
		Mean	7.62	18.91	2.580	32.32	246.77	1.140
		Sdev	0.351	1.563	1.4849	1.520	10.769	0.0424
800 mg/kg/day	2528	4/1	8.53	20.32	1.600	45.71	281.35	1.050
	2530	4/1	6.66	14.22	1.160	34.01	208.89	1.170
		N	2	2	2	2	2	2
		Mean	7.60	17.27	1.380	39.86	245.12	1.110
		Sdev	1.323	4.313	0.3111	8.273	51.237	0.0849

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s							
Vehicle							
	2527	1/1	7.87	71.87	65.23	12.73	3.65
	2533	1/1	7.38	68.17	73.93	14.52	1.11
		N	2	2	2	2	2
		Mean	7.62	70.02	69.58	13.63	2.38
		Sdev	0.351	2.616	6.152	1.266	1.796
800 mg/kg/day							
	2528	4/1	8.53	71.37	75.33	10.36	3.36
	2530	4/1	6.66	62.68	63.41	10.08	0.79
		N	2	2	2	2	2
		Mean	7.60	67.03	69.37	10.22	2.08
		Sdev	1.323	6.145	8.429	0.198	1.817

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s							
Vehicle							
	2575	1/1	8.11	21.99	3.350	35.42	265.17
	2577	1/1	8.55	28.82	2.740	35.07	276.35
		N	2	2	2	2	2
		Mean	8.33	25.41	3.045	35.25	270.76
		Sdev	0.310	4.830	0.4313	0.247	7.905
800 mg/kg/day							
	2571	4/1	7.32	20.46	2.570	31.94	271.37
	2573	4/1	6.83	20.67	1.500	31.65	255.81
		N	2	2	2	2	2
		Mean	7.07	20.57	2.035	31.80	263.59
		Sdev	0.348	0.148	0.7566	0.205	11.003

Note: Data collected using grace days.

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Appendix 10  
 Absolute Organ Weights (g)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s							
Vehicle	2575	1/1	8.11	0.870	67.16	71.39	2.276
	2577	1/1	8.55	1.200	60.34	64.64	1.686
		N	2	2	2	2	2
		Mean	8.33	1.035	63.75	68.02	1.981
		Sdev	0.310	0.2333	4.822	4.773	0.4171
800 mg/kg/day	2571	4/1	7.32	1.170	57.15	68.88	1.625
	2573	4/1	6.83	1.130	46.78	68.29	1.542
		N	2	2	2	2	2
		Mean	7.07	1.150	51.97	68.59	1.583
		Sdev	0.348	0.0283	7.333	0.417	0.0591

Note: Data collected using grace days.

## ***Appendix 11 Organ/Terminal Body Weight Ratios***

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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s								
Vehicle	2516	1/1	8.41	0.26	0.103	0.48	2.83	0.014
	2518	1/1	8.86	0.28	0.047	0.49	3.40	0.016
	2520	1/1	8.14	0.23	0.029	0.42	3.85	0.015
		N	3	3	3	3	3	3
		Mean	8.47	0.26	0.060	0.46	3.36	0.015
		Sdev	0.366	0.028	0.0390	0.039	0.511	0.0011
50 mg/kg/day	2514	2/1	9.45	0.26	0.033	0.52	2.77	0.012
	2521	2/1	7.58	0.36	0.051	0.49	3.41	0.017
	2529	2/1	7.59	0.26	0.027	0.52	3.18	0.016
		N	3	3	3	3	3	3
		Mean	8.21	0.29	0.037	0.51	3.12	0.015
		Sdev	1.077	0.056	0.0127	0.013	0.324	0.0025
200 mg/kg/day	2515	3/1	8.60	0.28	0.021	0.42	3.13	0.016
	2523	3/1	8.10	0.16	0.015	0.46	4.02	0.023
	2526	3/1	7.60	0.24	0.020	0.47	3.26	0.014
		N	3	3	3	3	3	3
		Mean	8.10	0.23	0.018	0.45	3.47	0.017
		Sdev	0.504	0.060	0.0033	0.031	0.483	0.0045
800 mg/kg/day	2517	4/1	6.87	0.16	0.023	0.51	4.81	0.024
	2519	4/1	7.71	0.32	0.034	0.49	3.78	0.017
	2525	4/1	9.33	0.24	0.035	0.46	3.63	0.015
		N	3	3	3	3	3	3
		Mean	7.97	0.24	0.031	0.49	4.07	0.019
		Sdev	1.249	0.079	0.0066	0.027	0.642	0.0043

Note: Data collected using grace days.

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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s							
Vehicle							
	2516	1/1	8.41	0.75	0.80	0.15	0.05
	2518	1/1	8.86	0.74	0.98	0.15	0.04
	2520	1/1	8.14	0.73	0.89	0.14	0.03
		N	3	3	3	3	3
		Mean	8.47	0.74	0.89	0.14	0.04
		Sdev	0.366	0.012	0.088	0.007	0.011
50 mg/kg/day							
	2514	2/1	9.45	0.78	0.71	0.17	0.05
	2521	2/1	7.58	0.83	0.92	0.17	0.05
	2529	2/1	7.59	0.89	0.98	0.13	0.07
		N	3	3	3	3	3
		Mean	8.21	0.83	0.87	0.16	0.06
		Sdev	1.077	0.051	0.139	0.021	0.009
200 mg/kg/day							
	2515	3/1	8.60	0.80	0.84	0.14	0.04
	2523	3/1	8.10	0.78	0.96	0.07	0.03
	2526	3/1	7.60	0.76	0.90	0.20	0.06
		N	3	3	3	3	3
		Mean	8.10	0.78	0.90	0.14	0.04
		Sdev	0.504	0.021	0.063	0.062	0.018
800 mg/kg/day							
	2517	4/1	6.87	0.88	1.05	0.07	0.02
	2519	4/1	7.71	0.77	0.69	0.16	0.05
	2525	4/1	9.33	0.66	0.80	0.17	0.06
		N	3	3	3	3	3
		Mean	7.97	0.77	0.85	0.13	0.04
		Sdev	1.249	0.112	0.183	0.054	0.020

Note: Data collected using grace days.

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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s							
Vehicle							
	2560	1/1	6.35	0.24	0.036	0.50	4.12
	2568	1/1	6.90	0.30	0.024	0.48	3.43
	2572	1/1	6.60	0.22	0.012	0.47	3.74
		N	3	3	3	3	3
		Mean	6.61	0.25	0.024	0.48	3.77
		Sdev	0.276	0.039	0.0120	0.020	0.347
50 mg/kg/day							
	2562	2/1	6.57	0.30	0.030	0.47	3.05
	2563	2/1	7.61	0.27	0.035	0.43	3.33
	2576	2/1	8.38	0.39	0.060	0.44	3.49
		N	3	3	3	3	3
		Mean	7.52	0.32	0.041	0.45	3.29
		Sdev	0.907	0.065	0.0159	0.021	0.222
200 mg/kg/day							
	2561	3/1	7.10	0.23	0.052	0.48	3.55
	2570	3/1	6.65	0.20	0.013	0.52	4.21
	2567	3/1	8.00	0.37	0.027	0.50	3.92
		N	3	3	3	3	3
		Mean	7.25	0.27	0.031	0.50	3.90
		Sdev	0.688	0.092	0.0199	0.020	0.331
800 mg/kg/day							
	2564	4/1	6.10	0.26	0.015	0.44	3.55
	2565	4/1	6.11	0.22	0.025	0.49	4.22
	2569	4/1	7.65	0.27	0.020	0.43	3.59
		N	3	3	3	3	3
		Mean	6.62	0.25	0.020	0.45	3.79
		Sdev	0.889	0.028	0.0046	0.034	0.374

Note: Data collected using grace days.



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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 29 Interim Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/Subgroup	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s							
Vehicle							
	2560	1/1	6.35	0.021	0.92	1.13	0.014
	2568	1/1	6.90	0.020	0.81	1.07	0.012
	2572	1/1	6.60	0.017	0.84	1.16	0.009
		N	3	3	3	3	3
		Mean	6.61	0.019	0.86	1.12	0.012
		Sdev	0.276	0.0021	0.059	0.042	0.0028
50 mg/kg/day							
	2562	2/1	6.57	0.018	0.87	1.09	0.026
	2563	2/1	7.61	0.014	0.81	0.84	0.024
	2576	2/1	8.38	0.014	0.71	0.85	0.026
		N	3	3	3	3	3
		Mean	7.52	0.015	0.80	0.93	0.025
		Sdev	0.907	0.0027	0.078	0.144	0.0015
200 mg/kg/day							
	2561	3/1	7.10	0.021	0.76	1.09	0.021
	2570	3/1	6.65	0.020	0.82	1.12	0.021
	2567	3/1	8.00	0.013	0.90	0.93	0.027
		N	3	3	3	3	3
		Mean	7.25	0.018	0.83	1.04	0.023
		Sdev	0.688	0.0043	0.070	0.100	0.0035
800 mg/kg/day							
	2564	4/1	6.10	0.019	0.83	1.04	0.018
	2565	4/1	6.11	0.021	0.77	1.00	0.022
	2569	4/1	7.65	0.015	0.83	1.00	0.032
		N	3	3	3	3	3
		Mean	6.62	0.019	0.81	1.01	0.024
		Sdev	0.889	0.0032	0.038	0.024	0.0072

Note: Data collected using grace days.

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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER	ADRENALS
M a l e s								
Vehicle	2527	1/1	7.87	0.25	0.046	0.42	3.23	0.014
	2533	1/1	7.38	0.24	0.021	0.42	3.24	0.016
		N	2	2	2	2	2	2
		Mean	7.62	0.25	0.033	0.42	3.24	0.015
		Sdev	0.351	0.009	0.0179	0.000	0.008	0.0012
800 mg/kg/day	2528	4/1	8.53	0.24	0.019	0.54	3.30	0.012
	2530	4/1	6.66	0.21	0.017	0.51	3.14	0.018
		N	2	2	2	2	2	2
		Mean	7.60	0.23	0.018	0.52	3.22	0.015
		Sdev	1.323	0.017	0.0009	0.018	0.114	0.0037

Note: Data collected using grace days.

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Appendix 11  
 Relative Organ Weights (% Body Weight)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	HEART	BRAIN	TESTES	PROSTATE
M a l e s							
Vehicle							
	2527	1/1	7.87	0.91	0.83	0.16	0.05
	2533	1/1	7.38	0.92	1.00	0.20	0.02
		N	2	2	2	2	2
		Mean	7.62	0.92	0.92	0.18	0.03
		Sdev	0.351	0.008	0.123	0.025	0.022
800 mg/kg/day							
	2528	4/1	8.53	0.84	0.88	0.12	0.04
	2530	4/1	6.66	0.94	0.95	0.15	0.01
		N	2	2	2	2	2
		Mean	7.60	0.89	0.92	0.14	0.03
		Sdev	1.323	0.074	0.049	0.021	0.019

Note: Data collected using grace days.

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Appendix 11  
 Relative Organ Weights (% Body Weight)  
 Test period  
 Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	SPLEEN	THYMUS	KIDNEYS	LIVER
F e m a l e s							
Vehicle	2575	1/1	8.11	0.27	0.041	0.44	3.27
	2577	1/1	8.55	0.34	0.032	0.41	3.23
		N	2	2	2	2	2
		Mean	8.33	0.30	0.037	0.42	3.25
		Sdev	0.310	0.047	0.0065	0.019	0.026
800 mg/kg/day	2571	4/1	7.32	0.28	0.035	0.44	3.71
	2573	4/1	6.83	0.30	0.022	0.46	3.75
		N	2	2	2	2	2
		Mean	7.07	0.29	0.029	0.45	3.73
		Sdev	0.348	0.016	0.0093	0.019	0.028

Note: Data collected using grace days.

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Appendix 11  
Relative Organ Weights (% Body Weight)  
Test period  
Days 43 Final Sacrifice

Fexinidazole

Study Number: 0505-2007

Dose Level	Animal Number	Group/ Subgroup	Terminal Body Wt (kg)	ADRENALS	HEART	BRAIN	OVARIES
F e m a l e s							
Vehicle							
	2575	1/1	8.11	0.011	0.83	0.88	0.028
	2577	1/1	8.55	0.014	0.71	0.76	0.020
		N	2	2	2	2	2
		Mean	8.33	0.012	0.77	0.82	0.024
		Sdev	0.310	0.0023	0.087	0.088	0.0059
800 mg/kg/day							
	2571	4/1	7.32	0.016	0.78	0.94	0.022
	2573	4/1	6.83	0.017	0.69	1.00	0.023
		N	2	2	2	2	2
		Mean	7.07	0.016	0.73	0.97	0.022
		Sdev	0.348	0.0004	0.068	0.042	0.0003

Note: Data collected using grace days.

## ***Appendix 12 Gross And Microscopic Pathology***

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2516                      SEX: Male                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.41

Tissue	Gross observations/comments	Correlated Microscopic Observations
COLON . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
DUODENUM . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Slight, Multifocal.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Minimal, Focal, Unilateral left..
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.  EXTRAMEDULLARY HEMATOPOIESIS, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2516                      SEX: Male                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.41

Tissue	Gross observations/comments	Correlated Microscopic Observations
PITUITARY . . . . .	No gross observations on tissue	CYSTS, PARS DISTALIS, Slight, Focal.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
TESTES . . . . .	No gross observations on tissue	SEGMENTAL HYPOPLASIA, Slight, Multifocal, Unilateral..

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
DIAPHRAGM	EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR HEAD
ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.	LUNG
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	PROSTATE
SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN	SPLEEN	STOMACH
STERNUM	THYROIDS	THYMUS	TONGUE	TRACHEA
URINARY BLADDER				



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2518	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	8.86

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Tissue	Gross observations/comments	Correlated Microscopic Observations
COLON . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Slight, Focal, Unilateral left..
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LACRIMAL GLANDS . . . .	No gross observations on tissue	ONLY ONE GLAND AVAILABLE FOR EXAMINATION, Present.
LUNG . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Slight, Multifocal.  ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
THYMUS . . . . .	No gross observations on tissue	CYSTS, Minimal, Focal.  INVOLUTION, Slight.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2518	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	8.86

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Tissue	Gross observations/comments	Correlated Microscopic Observations
URINARY BLADDER . . . .	No gross observations on tissue	MINERALIZATION IN MUSCULARIS/SUBSEROSA, Slight, Focal. / associated with small vessels and smooth muscle tissue

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	ILEUM	JEJUNUM	LIVER
MANDIBULAR L.N.	MESENTERIC L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PITUITARY	PROSTATE	SPINAL CORD-CERV	MANDIBULAR S.G.
PAROTIDS	SKIN	SPLEEN	STOMACH	STERNUM
TESTES	THYROIDS	TONGUE	TRACHEA	

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2520                      SEX: Male                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.14

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Slight.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PITUITARY . . . . .	No gross observations on tissue	CYSTS, PARS DISTALIS, Slight, Multifocal.
SKIN . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal. / in the dermis perifollicular
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Slight.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2520	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	8.14

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS
EYES	FEMUR HEAD	HEART	ILEUM	JEJUNUM
LACRIMAL GLANDS	MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PROSTATE	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.
PAROTIDS	SPLEEN	STOMACH	STERNUM	TESTES
THYROIDS	TONGUE	TRACHEA	URINARY BLADDER	

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2527                      SEX: Male                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 43 Test period                      STATUS: Final phase sacrifice                      TERMINAL BODY WEIGHT (kg) : 7.87

Tissue	Gross observations/comments	Correlated Microscopic Observations
DUODENUM . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Minimal, Multifocal, Unilateral left..
KIDNEYS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Slight, Multifocal.  PAPILLARY MINERALIZATION, Minimal, Multifocal.  CORTICAL TUBULAR DILATION, Moderate, Multifocal.  CORTICAL TUBULAR REGENERATIVE BASOPHILIA, Slight, Multifocal.
LIVER . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Slight.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2527                      SEX: Male                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 43 Test period                      STATUS: Final phase sacrifice                      TERMINAL BODY WEIGHT (kg) : 7.87

Tissue	Gross observations/comments	Correlated Microscopic Observations
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
MANDIBULAR S.G. . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Focal, Unilateral..
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal.
THYROIDS . . . . .	No gross observations on tissue	CYSTIC FOLLICLES, Slight, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	CYSTS, Minimal, Focal.  INVOLUTION, Slight.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:  
ADRENALS                      AORTA-THORACIC                      BONE MARROW                      BRAIN                      CECUM

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2527	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	7.87

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

COLON	DIAPHRAGM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY
PROSTATE	SPINAL CORD-CERV	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	TONGUE	TRACHEA	URINARY BLADDER

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2533	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	7.38

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.  CORTICAL TUBULAR REGENERATIVE BASOPHILIA, Minimal, Focal, Unilateral left..
LIVER . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal, Multifocal.
MANDIBULAR L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR HEMORRHAGE, Slight, Multifocal.  CAPILLARY ANGIOMATOSIS, Slight, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PROSTATE . . . . .	SMALL	Examined 1 correlation found: IMMATURE, Present.



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2533	SEX: Male	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	7.38

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
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THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Moderate.
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The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS
EYES	FEMUR HEAD	HEART	ILEUM	JEJUNUM
LACRIMAL GLANDS	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN
SPLEEN	STOMACH	STERNUM	TESTES	THYROIDS
TONGUE	TRACHEA	URINARY BLADDER		

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

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ANIMAL: 2514	SEX: Male	GROUP: 2	DOSE LEVEL: 50 mg/kg/day
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	9.45

---

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . . GOOD		No micropathology observations on tissue.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	MAMMARY GLAND	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PITUITARY	PROSTATE	PARATHYROIDS	SPINAL CORD-CERV
MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	THYROIDS	THYMUS	TONGUE
TRACHEA	URINARY BLADDER			

The following tissues have no gross observations and were marked as unremarkable microscopically:  
BONE MARROW



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Individual Animal Microscopic vs. Gross Observations

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ANIMAL: 2529	SEX: Male	GROUP: 2	DOSE LEVEL: 50 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	7.59

---

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . . GOOD		No micropathology observations on tissue.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	MAMMARY GLAND	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PITUITARY	PROSTATE	PARATHYROIDS	SPINAL CORD-CERV
MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	THYROIDS	THYMUS	TONGUE
TRACHEA	URINARY BLADDER			

The following tissues have no gross observations and were marked as unremarkable microscopically:  
BONE MARROW

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Individual Animal Microscopic vs. Gross Observations

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ANIMAL: 2515	SEX: Male	GROUP: 3	DOSE LEVEL: 200 mg/kg/day
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	8.60

---

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.

---

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	MAMMARY GLAND	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PITUITARY	PROSTATE	PARATHYROIDS	SPINAL CORD-CERV
MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	THYROIDS	THYMUS	TONGUE
TRACHEA	URINARY BLADDER			

The following tissues have no gross observations and were marked as unremarkable microscopically:  
BONE MARROW

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2523                      SEX: Male                      GROUP: 3                      DOSE LEVEL: 200 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.10

Tissue	Gross observations/comments	Correlated Microscopic Observations
BONE MARROW . . . . .	No gross observations on tissue	REDUCED CELLULARITY, Minimal.
GENER. CONDITION . . . . .	FAIRLY GOOD	No micropathology observations on tissue.
LYMPH NODES . . . . .	ENLARGED/ all lymph nodes.	No micropathology observations on tissue.
PERITONEAL CAV. . . . .	CLEAR LIQUID CONTENT	No micropathology observations on tissue.
TESTES . . . . .	SMALL, BILATERALLY	Examined 1 correlation found: IMMATURE, Present.
	FLACCID	Examined 1 correlation found: IMMATURE, Present.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EPIDIDYIMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	LUNG	MAMMARY GLAND
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY
PROSTATE	PARATHYROID	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROID
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	

The following tissues have no gross observations and were marked as unremarkable microscopically:

MANDIBULAR L.N.    MESENTERIC L.N.

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

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ANIMAL: 2526	SEX: Male	GROUP: 3	DOSE LEVEL: 200 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	7.60

---

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . . GOOD		No micropathology observations on tissue.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	MAMMARY GLAND	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PITUITARY	PROSTATE	PARATHYROIDS	SPINAL CORD-CERV
MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	THYROIDS	THYMUS	TONGUE
TRACHEA	URINARY BLADDER			

The following tissues have no gross observations and were marked as unremarkable microscopically:  
BONE MARROW

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

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ANIMAL: 2517	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.87

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Tissue	Gross observations/comments	Correlated Microscopic Observations
BONE MARROW . . . . .	No gross observations on tissue	REDUCED CELLULARITY, Moderate.  ATROPHY OF ADIPOSE TISSUE IN STERNAL AND FEMORAL MARROW, Moderate, Diffuse.
EPIDIDYMIDES . . . . .	No gross observations on tissue	IMMATURE, Present.  LUMENAL GERM CELLS/DEBRIS, Minimal.
ESOPHAGUS . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal. / associated with submucosal glands
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	FAIRLY GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal, Unilateral left..  ATROPHY OF ADJACENT ADIPOSE TISSUE, Slight, Diffuse.
LIVER . . . . .	No gross observations on tissue	GLYCOGEN DEPLETION, Slight.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.



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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2517                      SEX: Male                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.87

Tissue	Gross observations/comments	Correlated Microscopic Observations
PROSTATE . . . . .	SMALL	Examined 1 correlation found: IMMATURE, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
TESTES . . . . .	SMALL, BILATERALLY	Examined 1 correlation found: IMMATURE, Present.
	FLACCID	Examined 1 correlation found: IMMATURE, Present.
THYMUS . . . . .	No gross observations on tissue	CYSTS, Slight, Multifocal.  INVOLUTION, Severe.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EYES	FEMUR HEAD	HEART
ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN
SPLEEN	STOMACH	STERNUM	THYROIDS	TONGUE
TRACHEA	URINARY BLADDER			

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2519                      SEX: Male                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 7.71

Tissue	Gross observations/comments	Correlated Microscopic Observations
AORTA-THORACIC . . . .	No gross observations on tissue	ECTOPIC THYROID, Present.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LACRIMAL GLANDS . . . .	No gross observations on tissue	ONLY ONE GLAND AVAILABLE FOR EXAMINATION, Present.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PANCREAS . . . . .	No gross observations on tissue	ACINAR DEGRANULATION, Minimal, Multifocal.
PARATHYROIDS . . . . .	No gross observations on tissue	CYSTS, Minimal, Multifocal, Unilateral..
TESTES . . . . .	No gross observations on tissue	SEGMENTAL HYPOPLASIA, Minimal, Focal, Unilateral..



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2525	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	9.33

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Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Focal. / in the septum
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Slight.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2525	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	9.33

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	EPIDIDYMIDES	ESOPHAGUS
EYES	FEMUR HEAD	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE
OPTIC NERVES	PANCREAS	PITUITARY	PROSTATE	SPINAL CORD-CERV
MANDIBULAR S.G.	SKIN	SPLEEN	STOMACH	STERNUM
TESTES	THYROIDS	TONGUE	TRACHEA	URINARY BLADDER

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2528	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.53

Tissue	Gross observations/comments	Correlated Microscopic Observations
DUODENUM . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PITUITARY . . . . .	No gross observations on tissue	CYSTS, PARS DISTALIS, Slight, Focal.
PARATHYROIDS . . . . .	No gross observations on tissue	CYSTS, Minimal, Focal, Unilateral..
SKIN . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal, Granulomatous. / periadnexal in the dermis

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2528	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.53

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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THYROIDS . . . . .	No gross observations on tissue	CYSTIC FOLLICLES, Slight, Focal, Unilateral..
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THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Marked.
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The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	EPIDIDYMIDES	ESOPHAGUS	EYES
FEMUR HEAD	HEART	ILEUM	JEJUNUM	LACRIMAL GLANDS
LIVER	MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
PANCREAS	PROSTATE	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SPLEEN	STOMACH	STERNUM	TESTES	TONGUE
TRACHEA	URINARY BLADDER			

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2530                      SEX: Male                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 43 Test period                      STATUS: Final phase sacrifice                      TERMINAL BODY WEIGHT (kg) : 6.66

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Focal.
GENER. CONDITION . . . . .	FAIRLY GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	CORTICAL TUBULAR REGENERATIVE BASOPHILIA, Minimal, Focal, Unilateral right..
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
PROSTATE . . . . .	SMALL	Examined 1 correlation found: IMMATURE, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Slight, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	CYSTS, Minimal, Multifocal. INVOLUTION, Marked.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:  
ADRENALS                      AORTA-THORACIC                      BONE MARROW                      BRAIN                      CECUM



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2530	SEX: Male	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	6.66

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

COLON	DIAPHRAGM	DUODENUM	EPIDIDYIMIDES	ESOPHAGUS
EYES	FEMUR HEAD	HEART	ILEUM	JEJUNUM
LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.	LUNG
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY
SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN	SPLEEN	STOMACH
STERNUM	TESTES	THYROIDS	TONGUE	TRACHEA
URINARY BLADDER				

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2560	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.35

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Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Slight, Multifocal, Unilateral left..
KIDNEYS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal, Unilateral right..  PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	HEPATOCELLULAR VACUOLATION, Slight, Multifocal.
MANDIBULAR L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal, Unilateral..
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal.  CHRONIC INFLAMMATION, Minimal, Multifocal.  ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2560                      SEX: Female                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.35

Tissue	Gross observations/comments	Correlated Microscopic Observations
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
OVARIES . . . . .	No gross observations on tissue	IMMATURE, Present.
PERITONEAL CAV. . . . .	CLEAR LIQUID CONTENT	No micropathology observations on tissue.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	IMMATURE, Present.
MANDIBULAR S.G. . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Moderate.
TONGUE . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
UTERUS . . . . .	No gross observations on tissue	IMMATURE, Present.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:  
ADRENALS                      AORTA-THORACIC                      BONE MARROW                      BRAIN                      CECUM

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2560	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.35

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	ILEUM	JEJUNUM	LACRIMAL GLANDS	SKELETAL MUSCLE
SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY	SPINAL CORD-CERV
PAROTIDS	SKIN	SPLEEN	STOMACH	STERNUM
THYROIDS	TRACHEA	URINARY BLADDER	VAGINA	

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2568	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.90

Tissue	Gross observations/comments	Correlated Microscopic Observations
ESOPHAGUS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal. / in submucosa
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
OVARIES . . . . .	No gross observations on tissue	IMMATURE, Present.
PITUITARY . . . . .	No gross observations on tissue	CYSTS, PARS DISTALIS, Minimal, Focal.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2568                      SEX: Female                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.90

Tissue	Gross observations/comments	Correlated Microscopic Observations
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.  CYSTS, Minimal, Multifocal.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	IMMATURE, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Marked.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	EYES	FEMUR HEAD
HEART	ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	SPINAL CORD-CERV
MANDIBULAR S.G.	SKIN	SPLEEN	STOMACH	STERNUM
THYROIDS	TONGUE	TRACHEA	URINARY BLADDER	UTERUS
VAGINA				

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2572                      SEX: Female                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.60

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Focal.
GENER. CONDITION . . . . .	FAIRLY GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LACRIMAL GLANDS . . . . .	No gross observations on tissue	ONLY ONE GLAND AVAILABLE FOR EXAMINATION, Present.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal.  ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	NO MAMMARY TISSUE IN THE SECTION, Present.
OVARIES . . . . .	No gross observations on tissue	IMMATURE, Present.
PERITONEAL CAV. . . . .	CLEAR LIQUID CONTENT	No micropathology observations on tissue.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2572                      SEX: Female                      GROUP: 1                      DOSE LEVEL: Vehicle  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.60

Tissue	Gross observations/comments	Correlated Microscopic Observations
STAGE OF ESTRUS . . . .	No gross observations on tissue	IMMATURE, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal, Unilateral..
THYMUS . . . . .	SMALL	Examined 1 correlation found: INVOLUTION, Moderate.  CYSTS, Minimal, Focal.
TRACHEA . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal.
UTERUS . . . . .	No gross observations on tissue	IMMATURE, Present.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	HEART	ILEUM	JEJUNUM	LIVER
MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN	SPLEEN
STOMACH	STERNUM	THYROIDS	TONGUE	URINARY BLADDER
VAGINA				



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2575	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.11

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal, Unilateral right..  PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.  ALVEOLAR MACROPHAGE INFILTRATION, Slight, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Minimal.  STROMAL PROLIFERATION, Minimal.  DUCTAL-ALVEOLAR HYPERPLASIA, Minimal.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2575	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.11

Tissue	Gross observations/comments	Correlated Microscopic Observations
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
MANDIBULAR S.G. . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Focal, Unilateral..
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Multifocal, Unilateral..
SPLEEN . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal.
STOMACH . . . . .	No gross observations on tissue	GASTRITIS, Slight, Multifocal, Chronic active. / in the pyloric region
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Minimal.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Slight, Diffuse.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2575	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.11

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	HEART	ILEUM	JEJUNUM	LACRIMAL GLANDS
MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	SPINAL CORD-CERV	SKIN	STERNUM	THYROIDS
TONGUE	TRACHEA	URINARY BLADDER	VAGINA	

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2577	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.55

Tissue	Gross observations/comments	Correlated Microscopic Observations
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.  CORTICAL TUBULAR DILATION, Minimal, Multifocal.  CORTICAL FIBROSIS, Minimal, Multifocal.  CORTICAL TUBULAR REGENERATIVE BASOPHILIA, Slight, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR HEMORRHAGE, Minimal, Multifocal.  ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight.  STROMAL PROLIFERATION, Moderate.  DUCTAL-ALVEOLAR HYPERPLASIA, Moderate.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2577	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.55

Tissue	Gross observations/comments	Correlated Microscopic Observations
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PANCREAS . . . . .	No gross observations on tissue	ACINAR APOPTOSIS, Minimal, Multifocal.
PITUITARY . . . . .	No gross observations on tissue	CYSTS, PARS DISTALIS, Slight, Multifocal.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
STOMACH . . . . .	No gross observations on tissue	GASTRITIS, Minimal, Multifocal, Chronic active. / in the pyloric region
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Minimal.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Slight, Diffuse.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:  
ADRENALS            AORTA-THORACIC        BONE MARROW            BRAIN            CECUM

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2577	SEX: Female	GROUP: 1	DOSE LEVEL: Vehicle
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	8.55

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	HEART	ILEUM	JEJUNUM	LACRIMAL GLANDS
LIVER	MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES
SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN
STERNUM	THYROIDS	TONGUE	TRACHEA	URINARY BLADDER
VAGINA				

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2562                      SEX: Female                      GROUP: 2                      DOSE LEVEL: 50 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.57

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight. STROMAL PROLIFERATION, Moderate. DUCTAL-ALVEOLAR HYPERPLASIA, Slight.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Minimal. EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Minimal.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	

The following tissues have no gross observations and were marked as unremarkable microscopically:

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2563                                      SEX: Female                                      GROUP: 2                                      DOSE LEVEL: 50 mg/kg/day  
DAY OF DEATH: 30 Test period                                      STATUS: Scheduled phase sacrifice # 1                                      TERMINAL BODY WEIGHT (kg) : 7.61

Tissue                                      Gross observations/comments                                      Correlated Microscopic Observations

GENER. CONDITION . . . . . GOOD                                      No micropathology observations on tissue.  
MAMMARY GLAND . . . . . No gross observations on tissue                                      IMMATURE, Present.  
STAGE OF ESTRUS . . . . . No gross observations on tissue                                      ESTRUS, Present.  
UTERUS . . . . . No gross observations on tissue                                      ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA,  
Minimal.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	

The following tissues have no gross observations and were marked as unremarkable microscopically:

OVARIES                                      VAGINA



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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2576                      SEX: Female                      GROUP: 2                      DOSE LEVEL: 50 mg/kg/day  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.38

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Minimal. STROMAL PROLIFERATION, Minimal. DUCTAL-ALVEOLAR HYPERPLASIA, Minimal.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Moderate.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	

The following tissues have no gross observations and were marked as unremarkable microscopically:  
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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2561                      SEX: Female                      GROUP: 3                      DOSE LEVEL: 200 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 7.10

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Minimal. STROMAL PROLIFERATION, Slight. DUCTAL-ALVEOLAR HYPERPLASIA, Moderate.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
UTERUS . . . . .	No gross observations on tissue	EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Minimal.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	

The following tissues have no gross observations and were marked as unremarkable microscopically:  
VAGINA

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2570	SEX: Female	GROUP: 3	DOSE LEVEL: 200 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.65

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Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	FAIRLY GOOD	No micropathology observations on tissue.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Moderate. STROMAL PROLIFERATION, Moderate. DUCTAL-ALVEOLAR HYPERPLASIA, Slight.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PERITONEAL CAV. . . . .	CLEAR LIQUID CONTENT	No micropathology observations on tissue.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
THYMUS . . . . .	SMALL	Tissue is missing.  only adipose tissue detectable in the samples evaluated
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Slight.  EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Minimal.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2570	SEX: Female	GROUP: 3	DOSE LEVEL: 200 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.65

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
TONGUE	TRACHEA	URINARY BLADDER	VAGINA	

The following tissues have no gross observations and were marked as unremarkable microscopically:  
No tissue to list.

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2567                      SEX: Female                      GROUP: 3                      DOSE LEVEL: 200 mg/kg/day  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 8.00

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight. STROMAL PROLIFERATION, Slight. DUCTAL-ALVEOLAR HYPERPLASIA, Minimal.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
STAGE OF ESTRUS . . . .	No gross observations on tissue	DIESTRUS, Present.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Moderate.

The following tissues have no gross observations and were not examined microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL GLANDS	LIVER	MANDIBULAR L.N.	MESENTERIC L.N.
LUNG	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
PITUITARY	PARATHYROIDS	SPINAL CORD-CERV	MANDIBULAR S.G.	PAROTIDS
SKIN	SPLEEN	STOMACH	STERNUM	THYROIDS
THYMUS	TONGUE	TRACHEA	URINARY BLADDER	VAGINA

The following tissues have no gross observations and were marked as unremarkable microscopically:  
No tissue to list.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2564	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 29 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.10

Tissue	Gross observations/comments	Correlated Microscopic Observations
AORTA-THORACIC . . . .	No gross observations on tissue	ECTOPIC THYROID, Present.
ESOPHAGUS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal. / associated with submucosal glands
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Focal.  ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	LOBULAR HYPERPLASIA, Slight.  SECRETORY ACTIVITY, Slight.

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2564                      SEX: Female                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 29 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.10

Tissue	Gross observations/comments	Correlated Microscopic Observations
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
MANDIBULAR S.G. . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Focal, Unilateral..
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Marked.
UTERUS . . . . .	No gross observations on tissue	EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Slight, Diffuse.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	BONE MARROW	BRAIN	CECUM	COLON
DIAPHRAGM	DUODENUM	EYES	FEMUR HEAD	HEART
ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.	SKELETAL MUSCLE
SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY	SPINAL CORD-CERV
PAROTIDS	SKIN	SPLEEN	STOMACH	STERNUM
THYROIDS	TONGUE	TRACHEA	URINARY BLADDER	VAGINA

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2565	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	6.11

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Tissue	Gross observations/comments	Correlated Microscopic Observations
DUODENUM . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Slight, Multifocal, Unilateral right..
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Slight, Multifocal.  BRONCHOPNEUMONIA, Slight, Multifocal, Subacute.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight.  STROMAL PROLIFERATION, Slight.  DUCTAL-ALVEOLAR HYPERPLASIA, Slight.



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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2565                      SEX: Female                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 6.11

Tissue	Gross observations/comments	Correlated Microscopic Observations
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.  CYSTS, Minimal, Focal. / in adjacent tissue
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
PAROTIDS . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Marked.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Moderate, Diffuse.

The following tissues have no gross observations and were not examined microscopically:

URINARY BLADDER

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	ESOPHAGUS	EYES	FEMUR HEAD
ILEUM	JEJUNUM	LACRIMAL GLANDS	MANDIBULAR L.N.	MESENTERIC L.N.
SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY
SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN	SPLEEN	STOMACH
STERNUM	THYROIDS	TONGUE	TRACHEA	VAGINA

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Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2569	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 30 Test period	STATUS: Scheduled phase sacrifice # 1	TERMINAL BODY WEIGHT (kg) :	7.65

Tissue	Gross observations/comments	Correlated Microscopic Observations
DUODENUM . . . . .	No gross observations on tissue	CRYPT DILATATION WITH/WITHOUT LUMENAL NECROTIC DEBRIS, Minimal, Focal.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	ARTERIAL MEDIAL HYPERTROPHY, Minimal, Focal, Unilateral right.. / in the atrium
LACRIMAL GLANDS . . . . .	No gross observations on tissue	ONLY ONE GLAND AVAILABLE FOR EXAMINATION, Present.
LIVER . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight.  STROMAL PROLIFERATION, Slight.  DUCTAL-ALVEOLAR HYPERPLASIA, Minimal.

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2569                      SEX: Female                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 30 Test period                      STATUS: Scheduled phase sacrifice # 1                      TERMINAL BODY WEIGHT (kg) : 7.65

Tissue	Gross observations/comments	Correlated Microscopic Observations
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	METESTRUS, Present.
THYMUS . . . . .	No gross observations on tissue	CYSTS, Slight, Multifocal.  INVOLUTION, Marked.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Slight, Diffuse.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	ESOPHAGUS	EYES	FEMUR HEAD
ILEUM	JEJUNUM	KIDNEYS	MANDIBULAR L.N.	SKELETAL MUSCLE
SCIATIC NERVE	OPTIC NERVES	PANCREAS	PITUITARY	SPINAL CORD-CERV
MANDIBULAR S.G.	PAROTIDS	SKIN	SPLEEN	STOMACH
STERNUM	THYROIDS	TONGUE	TRACHEA	URINARY BLADDER
VAGINA				

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2571	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	7.32

Tissue	Gross observations/comments	Correlated Microscopic Observations
GENER. CONDITION . . .	GOOD	No micropathology observations on tissue.
HEART . . . . .	No gross observations on tissue	MESOTHELIAL HYPERPLASIA, ATRIAL, Minimal, Focal, Unilateral left..
KIDNEYS . . . . .	No gross observations on tissue	PAPILLARY MINERALIZATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Slight. STROMAL PROLIFERATION, Moderate. DUCTAL-ALVEOLAR HYPERPLASIA, Moderate.
SKELETAL MUSCLE . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.
PANCREAS . . . . .	No gross observations on tissue	ACINAR APOPTOSIS, Minimal, Multifocal.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

ANIMAL: 2571                      SEX: Female                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 43 Test period                      STATUS: Final phase sacrifice                      TERMINAL BODY WEIGHT (kg) : 7.32

Tissue	Gross observations/comments	Correlated Microscopic Observations
STAGE OF ESTRUS . . . .	No gross observations on tissue	DIESTRUS, Present.
MANDIBULAR S.G. . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Slight, Focal, Unilateral..
SPLEEN . . . . .	No gross observations on tissue	EXTRAMEDULLARY HEMATOPOIESIS, Minimal.
STOMACH . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal. / in the pyloric region
THYMUS . . . . .	No gross observations on tissue	INVOLUTION, Minimal.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Minimal, Diffuse.  EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Minimal, Multifocal.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:

ADRENALS	AORTA-THORACIC	BONE MARROW	BRAIN	CECUM
COLON	DIAPHRAGM	DUODENUM	ESOPHAGUS	EYES
FEMUR HEAD	GALL BLADDER	ILEUM	JEJUNUM	LACRIMAL GLANDS
LIVER	MANDIBULAR L.N.	LUNG	SCIATIC NERVE	OPTIC NERVES
PITUITARY	SPINAL CORD-CERV	PAROTIDS	SKIN	STERNUM
THYROIDS	TONGUE	TRACHEA	URINARY BLADDER	VAGINA

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Individual Animal Microscopic vs. Gross Observations

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Study Number: 0505-2007

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ANIMAL: 2573	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	6.83

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Tissue	Gross observations/comments	Correlated Microscopic Observations
DUODENUM . . . . .	No gross observations on tissue	ECTOPIC PANCREATIC TISSUE IN SUBMUCOSA, Present.
GALL BLADDER . . . . .	No gross observations on tissue	LYMPHOCYTIC INFILTRATION, Minimal, Multifocal.
GENER. CONDITION . . . . .	GOOD	No micropathology observations on tissue.
KIDNEYS . . . . .	No gross observations on tissue	CHRONIC INFLAMMATION, Minimal, Focal, Unilateral left..  PAPILLARY MINERALIZATION, Minimal, Multifocal.
MESENTERIC L.N. . . . .	No gross observations on tissue	SINUS ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
LUNG . . . . .	No gross observations on tissue	ALVEOLAR MACROPHAGE INFILTRATION, Minimal, Multifocal.
MAMMARY GLAND . . . . .	No gross observations on tissue	EDEMA, Moderate.  STROMAL PROLIFERATION, Moderate.  DUCTAL-ALVEOLAR HYPERPLASIA, Moderate.
OVARIES . . . . .	No gross observations on tissue	CORPORA LUTEA, Present.  CYSTS, Slight, Focal, Unilateral..

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Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

ANIMAL: 2573                      SEX: Female                      GROUP: 4                      DOSE LEVEL: 800 mg/kg/day  
DAY OF DEATH: 43 Test period                      STATUS: Final phase sacrifice                      TERMINAL BODY WEIGHT (kg) : 6.83

Tissue	Gross observations/comments	Correlated Microscopic Observations
PITUITARY . . . . .	No gross observations on tissue	CRANIOPHARINGEAL CYSTS, Moderate, Focal.
PARATHYROIDS . . . . .	No gross observations on tissue	ONLY ONE PARATHYROID AVAILABLE FOR EXAMINATION, Present.
STAGE OF ESTRUS . . . . .	No gross observations on tissue	DIESTRUS, Present.
PAROTIDS . . . . .	No gross observations on tissue	ACINAR ATROPHY, Minimal, Focal.
STOMACH . . . . .	No gross observations on tissue	ACUTE INFLAMMATION, Minimal, Multifocal. / in the pyloric region
THYMUS . . . . .	No gross observations on tissue	CYSTS, Minimal, Multifocal. INVOLUTION, Moderate.
UTERUS . . . . .	No gross observations on tissue	ENDOMETRIAL GLAND HYPERTROPHY/HYPERPLASIA, Minimal, Diffuse. EOSINOPHILIC SECRETORY MATERIAL IN GLANDULAR LUMEN, Minimal, Multifocal.

The following tissues have no gross observations and were not examined microscopically:  
No tissue to list.

The following tissues have no gross observations and were marked as unremarkable microscopically:  
ADRENALS                      AORTA-THORACIC                      BONE MARROW                      BRAIN                      CECUM

CONFIDENTIAL

Appendix 12  
Individual Animal Microscopic vs. Gross Observations

Fexinidazole

Study Number: 0505-2007

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ANIMAL: 2573	SEX: Female	GROUP: 4	DOSE LEVEL: 800 mg/kg/day
DAY OF DEATH: 43 Test period	STATUS: Final phase sacrifice	TERMINAL BODY WEIGHT (kg) :	6.83

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Tissue	Gross observations/comments	Correlated Microscopic Observations
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The following tissues have no gross observations and were marked as unremarkable microscopically:

COLON	DIAPHRAGM	ESOPHAGUS	EYES	FEMUR HEAD
HEART	ILEUM	JEJUNUM	LACRIMAL GLANDS	LIVER
MANDIBULAR L.N.	SKELETAL MUSCLE	SCIATIC NERVE	OPTIC NERVES	PANCREAS
SPINAL CORD-CERV	MANDIBULAR S.G.	SKIN	SPLEEN	STERNUM
THYROIDS	TONGUE	TRACHEA	URINARY BLADDER	VAGINA



## ***Appendix 13 Toxicokinetic Report***

## **TOXICOKINETIC REPORT FOR THE STUDY**

### **Fexinidazole: 28-day Oral Toxicity Study in the Dog**

Nerviano Medical Sciences Study Number: 0505-2007

Study Director:

Status

Final

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## 1. INTRODUCTION AND OBJECTIVE

Fexinidazole is a 5-nitroimidazole derivate, biologically active against Trypanosoma parasites (*T.b.rhodesiense* and *T.b. brucei*) and useful in the treatment of the Human African trypanosomiasis (HAT), known as sleeping sickness.

As part of a GLP toxicity study, the toxicokinetics of Fexinidazole and its sulfone and sulfoxide metabolites were evaluated after the first and repeated oral administrations of Fexinidazole to male and female Beagle dogs.

## 2. STUDY SPONSOR

DNDi – Drugs for Neglected Diseases *Initiative*  
1 Place St Gervais  
CH - 1201 Geneva, Switzerland.

## 3. TEST FACILITY

Accelera

## 4. REGULATORY REQUIREMENTS

This study was conducted in compliance with

- Decreto Legislativo 2 Marzo 2007, No. 50;
- Organization for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP) (as revised in 1997).

The methods employed in this study were those described in the "Standard Operating Procedures" of the laboratories involved.

## 5. ABBREVIATIONS

The following abbreviations are used in this document:

AUC <sub>0-24</sub>	Area under the plasma concentration vs. time curve up to 24 hours post dosing
AUC <sub>0-t(last)</sub>	Area under the plasma concentration vs. time curve up to finite time
C <sub>max</sub>	Maximal plasma concentration
CV	Coefficient of variation of the mean
F	Female
ID	Animal identification code
LC	Liquid chromatography

LLOQ	Lower limit of quantification
M	Male
MS	Mass-spectrometry
QC	Quality control sample
R <sup>2</sup>	Correlation coefficient
RA	Accumulation ratio
SD	Standard deviation of the mean
STD	Standard sample
t <sub>1/2,z</sub>	Terminal half-life
t <sub>max</sub>	Time to peak plasma concentration
ULOQ	Upper limit of quantification

## 6. METHODS

### 6.1. Study Design

The study was conducted according to the study protocol and related amendment [1,2]. Fexinidazole was orally given by gavage once a day for 28 days to male and female Beagle dogs according to the following scheme

Dose (mg/kg/day)	Volume (mL/kg/day)	Dog ID
0	10	M: 2516, 2518, 2520, 2527, 2533; F: 2560, 2568, 2572, 2575, 2577
50	10	M: 2514, 2521, 2529; F: 2562, 2563, 2576
200	10	M: 2515, 2523, 2526; F: 2561, 2567, 2570
800	10	M: 2517, 2519, 2525, 2528, 2530; F: 2564, 2565, 2569, 2571, 2573

Fexinidazole was suspended with 5% Tween 80 in 0.5% Methyl cellulose 400 cP.

### 6.2. Sample Information

Blood samples (about 1 mL/sampling time) were withdrawn from peripheral veins and put in heparinized plastic tubes kept on a ice-water bath, then centrifuged for 10 min at 1200g at +4°C and two aliquots of about 200 µL of plasma were stored in a freezer at -80°C until analysis. Blood was taken on Days 1, 14 from three dogs/gender/dose at pre-dose and 0.5, 1, 2, 4, 8 and 24 hours post dosing; on Day 28, blood was taken from three dogs/gender after 50 and 200 mg/kg/day at pre-dose and 0.5, 1, 2, 4, 8 and 24 hours post dosing and from five dogs/gender after 800 mg/kg/day at pre-dose and 1, 2, 4, 8, 24, 48 (recovery animals, [n=2]) and 72 (recovery animals, [n=2]) hours post dosing. After the administration of the vehicle, the samples were taken from five dogs/gender at all timepoints.

### 6.3. Bioanalytical Method

Dog plasma concentrations of Fexinidazole and its sulfoxide (M1) and sulfone (M2) metabolites were determined by a validated LC/MS/MS method [3,4]. The calibration range for the assay was 5-1000 ng/mL for Fexinidazole and 25-25000 ng/mL for M1 and M2. Study samples containing analytes concentrations above the upper limit of quantification were diluted with blank matrix prior to analysis.

### 6.4. Pharmacokinetic Calculations

Pharmacokinetic calculations were performed using a non-compartmental approach with the aid of Watson package (v. 6.4.0.04, Thermo Fisher Scientific, Waltham, MA, USA) and Excel spreadsheet (Microsoft Inc., Seattle, USA).

In the calculations, the undetectable concentrations between detectable ones were ignored.

After each dose level,  $C_{max}$  and  $t_{max}$  of Fexinidazole and sulfone and sulfoxide metabolites were read from raw data as the coordinates of the highest measured concentration. The area under plasma concentration vs. time curve up to finite time,  $AUC_{0-t(last)}$ , was determined for each compound by the linear trapezoidal rule up to the last detectable concentration. On Day 28, since the blood sampling was performed up to 72 hours post dosing, in addition to  $AUC_{0-t(last)}$ ,  $AUC_{0-24}$  of both metabolites were calculated. The  $AUC_{0-24}$  was calculated in order to compare AUC values after Day 28 to those after Day 1 and Day 14.

On Day 28, in the two animals underwent recovery, the half-life of the terminal phase,  $t_{1/2,z}$ , was determined by linear regression analysis of the natural-log concentration vs. time curve, where  $t_{1/2,z} = \ln(2)/\text{slope}$  of the regression line.

After each dose,  $C_{max}$  and AUC values of each compound were also normalized to 1 mg/kg/day dose level.

Fexinidazole and metabolites accumulation ratios, based on  $C_{max}$  and  $AUC_{0-t(last)}$  ( $AUC_{0-24}$  for Day 28 sulfone and male sulfoxide data) were calculated as the ratio between the parameters obtained on Day 14 and Day 28 to the corresponding one on Day 1.

Descriptive statistics (mean  $\pm$  SD, %CV) were reported for plasma concentrations and pharmacokinetic parameters of each compound sorted by dose, gender and day of administration.

Plasma concentrations and pharmacokinetic parameters of Fexinidazole and both metabolites were reported to three significant figures.

## 7. RESULTS

### 7.1. Tables and Figures

Mean  $C_{max}$ ,  $t_{max}$  and  $AUC_{0-t(last)}$  parameters of each compound are reported in Tables 1 - 3, whilst individual and mean parameters of each compound are reported in Tables 4 - 57. Individual and mean ( $\pm$ SD, CV%) plasma concentrations of Fexinidazole and metabolites

are reported in Tables 1A1 - 21A1 of Appendix 1. Individual plasma concentrations of Fexinidazole and both metabolites are plot in Figures 1 - 15, whilst the mean concentrations are plot in Figures 16 - 21. Mean normalized  $C_{max}$  and  $AUC_{0-t(last)}$  values of Fexinidazole and metabolites vs. dose are plot in Figures 22 - 27.

In-study bioanalytical validation data are reported in Appendix 2. All analytical batches met acceptance criteria as described in PCD-M-BPK-001-01 SOP [5]. Bioanalytical data are stored in Watson LIMS (v. 6.4.0.04, Thermo Fisher Scientific, Waltham, MA, USA) under Project ID: 348-Fexinidazole and Study ID 0505-2007. Certificates of analysis are reported in Appendix 3.

## 7.2. Pharmacokinetic Results

Control plasma samples were analysed only at pre-dose and 2 hours post dosing. No detectable concentration of each compound was measured in the control samples.

### Day 1

Mean  $\pm$ SD systemic exposure to Fexinidazole is reported in the following table

Dose mg/kg	Male			Female		
	$C_{max}$ ng/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ ng-hour/mL	$C_{max}$ ng/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ ng-hour/mL
50 (n=3)	31.2 $\pm$ 12.4	0.5 $\pm$ 0	140 $\pm$ 147	42.4 $\pm$ 10.6	1 $\pm$ 0.87	237 $\pm$ 105
200 (n=3)	54.9 $\pm$ 10.8	1 $\pm$ 0.87	419 $\pm$ 61.4	84.1 $\pm$ 36.7	1 $\pm$ 0	454 $\pm$ 119
800 (n=5)	100 $\pm$ 21.2	1.1 $\pm$ 0.55	776 $\pm$ 182	184 $\pm$ 75.6	1.2 $\pm$ 0.45	895 $\pm$ 437

At each dose, no relevant gender difference was observed in terms of both  $C_{max}$  and  $AUC_{0-t(last)}$  values. The maximal plasma concentrations of Fexinidazole were promptly achieved, on average at 1 hour post dosing.  $AUC_{0-t(last)}$  values of Fexinidazole increased with the dose (Figures 22 - 23).

Mean  $\pm$ SD systemic exposure to the sulfone metabolite is reported in the following table

Dose mg/kg	Male			Female		
	$C_{max}$ $\mu$ g/mL	$t_{max}$ Hour	$AUC_{0-t(last)}$ $\mu$ g-hour/mL	$C_{max}$ $\mu$ g/mL	$t_{max}$ hour	$AUC_{0-t(last)}$ $\mu$ g-hour/mL
50 (n=3)	7.17 $\pm$ 1.74	8 $\pm$ 0	126 $\pm$ 28.1	10 $\pm$ 1.6	6.67 $\pm$ 2.31	170 $\pm$ 37.8
200 (n=3)	17.2 $\pm$ 1.69	13.3 $\pm$ 9.24	338 $\pm$ 50.8	18.1 $\pm$ 3.42	12 $\pm$ 10.6	358 $\pm$ 85.7
800 (n=5)	38.6 $\pm$ 2.83	17.6 $\pm$ 8.76	705 $\pm$ 94.9	33.6 $\pm$ 10.9	11.2 $\pm$ 7.16	614 $\pm$ 216

At each dose, the levels of the metabolite were similar in males and females.  $T_{max}$  values of the metabolite were achieved later than the corresponding ones of the parent compound. The systemic exposure to the metabolite increased with the dose (Figures 24 - 25). The systemic exposure to the sulfone metabolite was definitely higher than that to the parent compound.

Mean  $\pm$ SD systemic exposure to the sulfoxide metabolite is reported in the following table

Dose mg/kg	Male			Female		
	C <sub>max</sub> $\mu$ g/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> $\mu$ g·hour/mL	C <sub>max</sub> $\mu$ g/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> $\mu$ g·hour/mL
50 (n=3)	3.55 $\pm$ 1.3	1 $\pm$ 0	19.2 $\pm$ 5.82	3.97 $\pm$ 0.74	1.33 $\pm$ 0.58	20 $\pm$ 6.81
200 (n=3)	7.55 $\pm$ 1.03	1.67 $\pm$ 0.58	50.7 $\pm$ 8.61	8.7 $\pm$ 3.95	0.83 $\pm$ 0.29	52.1 $\pm$ 20.6
800 (n=5)	13.4 $\pm$ 3.22	1.5 $\pm$ 0.71	104 $\pm$ 11.3	15.6 $\pm$ 4.64	1.6 $\pm$ 0.55	121 $\pm$ 44.4

At each dose, the levels of the metabolite were similar in males and females. The maximal plasma concentrations of the sulfoxide metabolite were rapidly achieved, on average 1 - 2 hours post dosing.

The systemic exposure to the metabolite increased with the dose (Figures 26 - 27).

The systemic exposure to the metabolite was definitely higher than that to the parent compound.

#### Repeated dosing

Day 14 and Day 28 mean  $\pm$ SD systemic exposure to Fexinidazole is reported in the following table

Dose mg/kg/day	Male			Female		
	C <sub>max</sub> ng/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> ng·hour/mL	C <sub>max</sub> ng/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> ng·hour/mL
Day 14						
50 (n=3)	26.5 $\pm$ 13	0.5 $\pm$ 0	52.1 $\pm$ 29.4	41.9 $\pm$ 2.2	1.67 $\pm$ 0.58	246 $\pm$ 117
200 (n=3)	78.1 $\pm$ 23.5	1 $\pm$ 0.87	452 $\pm$ 41.1	77.7 $\pm$ 50.8	2 $\pm$ 0	443 $\pm$ 217
800 (n=5)	128 $\pm$ 56.9	1 $\pm$ 0	929 $\pm$ 268	152 $\pm$ 44	1.4 $\pm$ 0.55	1170 $\pm$ 309
Day 28						
50 (n=3)	20.3 $\pm$ 7.89	1 $\pm$ 0	124 $\pm$ 67	36.3 $\pm$ 15.1	1 $\pm$ 0	87.1 $\pm$ 38.1
200 (n=3)	57.9 $\pm$ 12.5	1 $\pm$ 0	395 $\pm$ 15.8	73 $\pm$ 12	1 $\pm$ 0	377 $\pm$ 83.5
800 (n=5)	86.2 $\pm$ 38.5	1.2 $\pm$ 0.4	736 $\pm$ 141	101 $\pm$ 47.1	1 $\pm$ 0	956 $\pm$ 378

At each dose, the levels of Fexinidazole were similar in both genders after Day 14 and Day 28 administrations. The maximal plasma concentrations of Fexinidazole were achieved, on average, 1 - 2 hours post dosing. The systemic exposure to Fexinidazole increased with the dose (Figures 22 - 23). C<sub>max</sub> and AUC<sub>0-t(last)</sub> accumulation ratios were about 1.

Day 14 and Day 28 mean  $\pm$ SD systemic exposure to the sulfone metabolite is reported in the following table

Dose mg/kg/day	Male			Female		
	C <sub>max</sub> $\mu$ g/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> $\mu$ g·hour/mL	C <sub>max</sub> $\mu$ g/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> $\mu$ g·hour/mL
Day 14						
50 (n=3)	5.57 $\pm$ 2.19	4 $\pm$ 0	78 $\pm$ 35.3	9.98 $\pm$ 1.25	6.67 $\pm$ 2.31	173 $\pm$ 26.9
200 (n=3)	22 $\pm$ 5.59	5.33 $\pm$ 2.31	387 $\pm$ 49.5	21.5 $\pm$ 2.42	5.33 $\pm$ 2.31	381 $\pm$ 61.2



800 (n=5)	34.6±7.42	5.6±2.19	640±163	38.6±4.73	8±0	667±67.8
Day 28						
50 (n=3)	7.11±1.21	8±0	121±19.1	6.79±0.56	3.33±1.15	107±22.5
200 (n=3)	14±3.31	4±4	258±48	15.4±2.66	11.7±10.1	277±29.9
800 (n=5)	20.8±4.14	12.4±9.81	388±68.2 <sup>(1)</sup>	26±7.7	7.2±1.79	477±145 <sup>(1)</sup>
			601±29 <sup>(2)</sup>			693±351 <sup>(2)</sup>
<sup>(1)</sup> AUC <sub>0-24</sub> ; <sup>(2)</sup> n=2						

At each dose, the levels of the metabolite were similar in both genders. T<sub>max</sub> values of the metabolite were achieved later than the corresponding ones of the parent compound. On Day 28 after 800 mg/kg/day, mean ±SD apparent terminal half-lives were 6.7 ±0.7 and 7.8 ±0.7 (n=2) hours in males and females, respectively. After the three doses, systemic exposure to the metabolite increased with the dose (Figures 24 - 25). Accumulation ratios, in terms of both C<sub>max</sub> and AUC<sub>0-t(last)</sub>, were about 1.

The systemic exposure to the metabolite was remarkably higher than that to the parent compound.

Day 14 and Day 28 mean ±SD systemic exposure to the sulfoxide metabolite is reported in the following table

Dose mg/kg/day	Male			Female		
	C <sub>max</sub> µg/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> µg·hour/mL	C <sub>max</sub> µg/mL	t <sub>max</sub> hour	AUC <sub>0-t(last)</sub> µg·hour/mL
Day 14						
50 (n=3)	2.24±0.45	1±0	8.51±2.53	3.73±0.73	1.67±0.58	18.8±2.06
200 (n=3)	8.96±2.53	2±0	56.1±9.96	9.02±3.69	2±0	57.2±24.3
800 (n=5)	12.5±2.85	1.2±0.45	113±39.9	14.8±5.1	2±1.22	144±37.1
Day 28						
50 (n=3)	1.83±0.57	1.67±0.58	14.2±2.72	2.72±0.73	1±0	9.88±2.72
200 (n=3)	5.76±1.17	1.33±0.58	42.2±6.46	5.43±0.34	1±0	33.8±1.65
800 (n=5)	9.35±3.55	1.6±0.55	74.3±14.4 <sup>(1)</sup>	9.48±3.38	1.4±0.55	89±45.2
			121±33 <sup>(2)</sup>			
<sup>(1)</sup> AUC <sub>0-24</sub> ; <sup>(2)</sup> n=2						

At each dose, the levels of the metabolite were similar in both genders. The maximal plasma concentrations of the sulfoxide metabolite were promptly achieved, on average, 1 - 2 hours post dosing. On Day 28 after 800 mg/kg/day, mean ±SD apparent terminal half-lives were 9.4 ±5.4 (n=2) hours in males. After the three doses, the systemic exposure to the metabolite increased with the dose (Figures 26 - 27). Accumulation ratios, in terms of both C<sub>max</sub> and AUC<sub>0-t(last)</sub>, were about 1.

The systemic exposure to the metabolite was remarkably higher than that to the parent compound.

## 8. CONCLUSIONS

After the first and repeated administrations of the three dose levels, no relevant gender difference in the systemic exposure to Fexinidazole was observed. AUCs of Fexinidazole increased less than expected assuming dose proportionality in the dose range investigated. No accumulation of Fexinidazole was observed.

Fexinidazole was extensively metabolized to the sulfone and sulfoxide derivatives. No accumulation of both metabolites was observed.

## 9. CONTRIBUTORS

## 10. ARCHIVING

Raw data and pharmacokinetic analysis produced at the Test Facility were filed in the Archives of Accelera, Nerviano Medical Sciences S.r.l., Nerviano (Italy) for the period of time agreed with the Sponsor (at least 3 years) after which the Sponsor will be contacted for instructions regarding dispatch or disposal of the material.

A copy of the protocol, the report with original signatures, a reserve sample and all relevant original documentation of the test item were filed by the Sponsor.

## 11. REFERENCES

1. Fexinidazole: 28-day Oral Toxicity Study in the Dog. Nerviano Medical Sciences Study Protocol 0505-2007-P, January 23, 2008.
2. Amendment no. 1 to Fexinidazole: 28-day Oral Toxicity Study in the Dog. February 21, 2008.
3. Analytical Procedure for the Determination of Fexinidazole and its Metabolites Fexinidazole Sulphoxide (M1) and Fexinidazole Sulphone (M2) in Dog Plasma by LC-MS-MS Following Plasma Protein Precipitation. Analytical Procedure Number: NMS/FEXINIDAZOLE/02.0. NervianoMS Reference Number: 0291-2007-AP. February 27, 2008.
4. Validation of an Analytical Method for the Determination of Fexinidazole and its Metabolites M1 and M2 in Dog Plasma by LC-MS-MS. Document Number: 0291-2007-R.
5. SOP: PCD-M-BPK-001-01: "Bioanalytical Run Acceptance". 13 December 2006.

## **TABLES AND FIGURES**

**Table 1.** Mean ( $\pm$ SD, n) systemic exposure parameters of Fexinidazole after single (Day 1) and repeated (Days 14 and 28) oral administrations of Fexinidazole to male and female Beagle dogs.

Gender	Day	Dose mg/kg/day	C <sub>max</sub> ng/mL			t <sub>max</sub> hour			AUC <sub>0-t(last)</sub> ng·hour/mL		
			Mean	SD	n	Mean	SD	n	Mean	SD	n
M	1	50	31.2	12.4	3	0.5	0	3	140	147	3
		200	54.9	10.8	3	1	0.866	3	419	61.4	3
		800	100	21.2	5	1.1	0.548	5	776	182	5
	14	50	26.5	13.0	3	0.5	0	3	52.1	29.4	3
		200	78.1	23.5	3	1	0.866	3	452	41.1	3
		800	128	56.9	5	1	0	5	929	268	5
	28	50	20.3	7.89	3	1	0	3	124	67	3
		200	57.9	12.5	3	1	0	3	395	15.8	3
		800	86.2	38.5	5	1.2	0.447	5	736	141	5
F	1	50	42.4	10.6	3	1	0.866	3	237	105	3
		200	84.1	36.7	3	1	0	3	454	119	3
		800	184	75.6	5	1.2	0.447	5	895	437	5
	14	50	41.9	2.20	3	1.67	0.577	3	246	117	3
		200	77.7	50.8	3	2	0	3	443	217	3
		800	152	44.0	5	1.4	0.548	5	1170	309	5
	28	50	36.3	15.1	3	1	0	3	87.1	38.1	3
		200	73	12	3	1	0	3	377	83.5	3
		800	101	47.1	5	1	0	5	956	378	5
M + F	1	50	36.8	12.0	6	0.75	0.612	6	188	126	6
		200	69.5	29.0	6	1	0.548	6	437	86.5	6
		800	142	68.3	10	1.15	0.474	10	836	322	10
	14	50	34.2	11.8	6	1.08	0.736	6	149	131	6
		200	77.9	35.4	6	1.5	0.775	6	447	140	6
		800	140	49.6	10	1.2	0.422	10	1050	301	10
	28	50	28.3	13.9	6	1	0	6	106	52.8	6
		200	65.4	13.7	6	1	0	6	386	54.7	6
		800	93.5	41.3	10	1.1	0.316	10	846	293	10

**Table 2.** Mean ( $\pm$ SD, n) systemic exposure parameters of the sulfone metabolite after single (Day 1) and repeated (Days 14 and 28) oral administrations of Fexinidazole to male and female Beagle dogs.

Gender	Day	Dose mg/kg/day	C <sub>max</sub> µg/mL			t <sub>max</sub> hour			AUC <sub>0-t(last)</sub> µg·hour/mL		
			Mean	SD	n	Mean	SD	n	Mean	SD	n
M	1	50	7.17	1.74	3	8	0	3	126	28.1	3
		200	17.2	1.69	3	13.3	9.24	3	338	50.8	3
		800	38.6	2.83	5	17.6	8.76	5	705	94.9	5
	14	50	5.57	2.19	3	4	0	3	78.0	35.3	3
		200	22.0	5.59	3	5.33	2.31	3	387	49.5	3
		800	34.6	7.42	5	5.6	2.19	5	640	163	5
	28	50	7.11	1.21	3	8	0	3	121	19.1	3
		200	14	3.31	3	4	4	3	258	48	3
		800	20.8	4.14	5	12.4	9.81	5	388*	68.2	5
F	1	50	10.0	1.60	3	6.67	2.31	3	170	37.8	3
		200	18.1	3.42	3	12.0	10.6	3	358	85.7	3
		800	33.6	10.9	5	11.2	7.16	5	614	216	5
	14	50	9.98	1.25	3	6.67	2.31	3	173	26.9	3
		200	21.5	2.42	3	5.33	2.31	3	381	61.2	3
		800	38.6	4.73	5	8	0	5	667	67.8	5
	28	50	6.79	0.555	3	3.33	1.15	3	107	22.5	3
		200	15.4	2.66	3	11.7	10.1	3	277	29.9	3
		800	26	7.7	5	7.2	1.79	5	477*	145	5
M + F	1	50	8.59	2.15	6	7.33	1.63	6	148	38.3	6
		200	17.6	2.46	6	12.7	8.91	6	348	63.9	6
		800	36.1	7.94	10	14.4	8.26	10	660	164	10
	14	50	7.78	2.89	6	5.33	2.07	6	126	59.1	6
		200	21.8	3.86	6	5.33	2.07	6	384	49.9	6
		800	36.6	6.24	10	6.80	1.93	10	653	118	10
	28	50	6.95	0.862	6	5.67	2.66	6	114	20.1	6
		200	14.7	2.79	6	7.86	8.08	6	267	37.2	6
		800	23.4	6.43	10	9.8	7.19	10	432*	117	10

\* AUC<sub>0-24</sub>

**Table 3.** Mean ( $\pm$ SD, n) systemic exposure parameters of the sulfoxide metabolite after single (Day 1) and repeated (Days 14 and 28) oral administrations of Fexinidazole to male and female Beagle dogs.

Gender	Day	Dose mg/kg/day	C <sub>max</sub> µg/mL			t <sub>max</sub> hour			AUC <sub>0-t(last)</sub> µg·hour/mL		
			Mean	SD	n	Mean	SD	n	Mean	SD	n
M	1	50	3.55	1.3	3	1	0	3	19.2	5.82	3
		200	7.55	1.03	3	1.67	0.577	3	50.7	8.61	3
		800	13.4	3.22	5	1.50	0.707	5	104	11.3	5
	14	50	2.24	0.454	3	1	0	3	8.51	2.53	3
		200	8.96	2.53	3	2	0	3	56.1	9.96	3
		800	12.5	2.85	5	1.2	0.447	5	113	39.9	5
	28	50	1.83	0.567	3	1.67	0.577	3	14.2	2.72	3
		200	5.76	1.17	3	1.33	0.577	3	42.2	6.46	3
		800	9.35	3.55	5	1.6	0.548	5	74.3*	14.4	5
F	1	50	3.97	0.738	3	1.33	0.577	3	20	6.81	3
		200	8.70	3.95	3	0.833	0.289	3	52.1	20.6	3
		800	15.6	4.64	5	1.60	0.548	5	121	44.4	5
	14	50	3.73	0.725	3	1.67	0.577	3	18.8	2.06	3
		200	9.02	3.69	3	2.00	0.00	3	57.2	24.3	3
		800	14.8	5.10	5	2.00	1.22	5	144	37.1	5
	28	50	2.72	0.729	3	1	0	3	9.88	2.72	3
		200	5.43	0.34	3	1	0	3	33.8	1.65	3
		800	9.48	3.38	5	1.4	0.548	5	89	45.2	5
M + F	1	50	3.76	0.975	6	1.17	0.408	6	19.6	5.68	6
		200	8.12	2.66	6	1.25	0.612	6	51.4	14.1	6
		800	14.5	3.95	10	1.55	0.599	10	112	31.8	10
	14	50	2.99	0.976	6	1.33	0.516	6	13.6	5.99	6
		200	8.99	2.83	6	2	0	6	56.7	16.6	6
		800	13.6	4.09	10	1.60	0.966	10	129	39.8	10
	28	50	2.27	0.76	6	1.33	0.516	6	12.1	3.41	6
		200	5.6	0.792	6	1.17	0.408	6	38	6.26	6
		800	9.41	3.27	10	1.5	0.527	10	81.7*	32.6	10

\* AUC<sub>0-24</sub>

**Table 4.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	ng/mL	45.5	23.1	24.9	31.2	12.4	39.9
t <sub>max</sub>	hour	0.5	0.5	0.5	0.5	0	0
AUC Interval	hour	(0-24)	(0-4)	(0-4)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	309	64.1	45.7	140	147	105.3
C <sub>max</sub> /Dose	ng/mL	0.910	0.462	0.498	0.623	0.249	39.9
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	6.18	1.28	0.914	2.79	2.94	105.3

**Table 5.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	ng/mL	41.4	21.1	17.1	26.5	13	49.1
t <sub>max</sub>	hour	0.5	0.5	0.5	0.5	0	0
AUC Interval	hour	(0-4)	(0-4)	(0-2)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	83.2	48.3	24.8	52.1	29.4	56.4
C <sub>max</sub> /Dose	ng/mL	0.828	0.422	0.342	0.531	0.261	49.1
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.66	0.967	0.496	1.04	0.586	56.2
RA, C <sub>max</sub>		0.91	0.913	0.687	0.84	0.13	15.5
RA, AUC <sub>0-t(last)</sub>		0.269	0.754	0.543	0.522	0.243	46.5

**Table 6.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	ng/mL	29.3	17	14.6	20.3	7.89	38.8
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-8)	(0-24) <sup>(1)</sup>	(0-8)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	104	199	69.6	124	67	54
C <sub>max</sub> /Dose	ng/mL	0.586	0.34	0.292	0.406	0.158	38.8
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	2.08	3.97	1.39	2.48	1.34	53.9
RA, C <sub>max</sub>		0.644	0.736	0.586	0.655	0.0754	0.644
RA, AUC <sub>0-t(last)</sub>		0.337	3.1	1.52	1.65	1.39	0.337

<sup>(1)</sup> Nominal time

**Table 7.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	ng/mL	38.8	54.3	34.1	42.4	10.6	24.9
t <sub>max</sub>	hour	2	0.5	0.5	1.00	0.87	86.6
AUC Interval	hour	(0-24)	(0-4)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	317	118	275	237	105	44.3
C <sub>max</sub> /Dose	ng/mL	0.776	1.09	0.682	0.849	0.214	25.2
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	6.35	2.37	5.50	4.74	2.10	44.2

**Table 8.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	ng/mL	44.4	40.8	40.4	41.9	2.2	5.3
t <sub>max</sub>	hour	1	2	2	1.67	0.577	34.6
AUC Interval	hour	(0-24 )	(0-4 )	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	275	118	346	246	117	47.4
C <sub>max</sub> /Dose	ng/mL	0.888	0.816	0.808	0.837	0.0441	5.3
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	5.51	2.37	6.93	4.94	2.33	47.3
RA,C <sub>max</sub>		1.14	0.751	1.18	1.03	0.239	23.3
RA,AUC <sub>0-t(last)</sub>		0.868	1	1.26	1.04	0.199	19.1

**Table 9.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	ng/mL	23.5	53	32.4	36.3	15.1	41.7
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-4)	(0-4)	(0-4)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	62.9	131	67.5	87.1	38.1	43.7
C <sub>max</sub> /Dose	ng/mL	0.470	1.06	0.648	0.726	0.303	41.7
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.26	2.63	1.35	1.75	0.766	43.9
RA,C <sub>max</sub>		0.606	0.976	0.95	0.844	0.207	24.5
RA,AUC <sub>0-t(last)</sub>		0.198	1.11	0.245	0.518	0.513	99.1



**Table 10.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	ng/mL	46.4	67	51.3	54.9	10.8	19.6
t <sub>max</sub>	hour	0.5	2	0.5	1	0.866	86.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	467	350	441	419	61.4	14.7
C <sub>max</sub> /Dose	ng/mL	0.232	0.335	0.257	0.275	0.0537	19.6
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	2.33	1.75	2.21	2.10	0.306	14.6

**Table 11.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	ng/mL	52.6	82.9	98.8	78.1	23.5	30.1
t <sub>max</sub>	hour	0.5	2	0.5	1	0.866	86.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	491	456	409	452	41.1	9.1
C <sub>max</sub> /Dose	ng/mL	0.263	0.415	0.494	0.391	0.117	30.1
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	2.45	2.28	2.05	2.26	0.201	8.9
RA, C <sub>max</sub>		1.13	1.24	1.93	1.43	0.431	30.1
RA, AUC <sub>0-t(last)</sub>		1.05	1.3	0.927	1.09	0.191	17.5

**Table 12.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	ng/mL	71.2	56.1	46.3	57.9	12.5	21.7
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	399	378	409	395	15.8	4
C <sub>max</sub> /Dose	ng/mL	0.356	0.281	0.232	0.290	0.0625	21.6
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.99	1.89	2.04	1.97	0.0764	3.9
RA, C <sub>max</sub>		1.53	0.837	0.903	1.09	0.385	35.3
RA, AUC <sub>0-t(last)</sub>		0.854	1.08	0.927	0.954	0.115	12.1
<sup>(1)</sup> Nominal time							

**Table 13.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in female Beagle Dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	ng/mL	57.4	126	69	84.1	36.7	43.6
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-24 )	(0-24)	(0-24 )			
AUC <sub>0-t(last)</sub>	ng·hour/mL	357	586	418	454	119	26.1
C <sub>max</sub> /Dose	ng/mL	0.287	0.630	0.345	0.421	0.184	43.6
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.79	2.93	2.09	2.27	0.591	26

**Table 14.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	ng/mL	42.9	136	54.2	77.7	50.8	65.4
t <sub>max</sub>	hour	2	2	2	2	0	0
AUC Interval	hour	(0-8)	(0-8)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	193	588	547	443	217	49.1
C <sub>max</sub> /Dose	ng/mL	0.215	0.680	0.271	0.389	0.254	65.3
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	0.965	2.94	2.73	2.21	1.08	49
RA, C <sub>max</sub>		0.747	1.08	0.786	0.871	0.182	20.9
RA, AUC <sub>0-t(last)</sub>		0.541	1	1.31	0.951	0.387	40.7

**Table 15.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	ng/mL	84	74.7	60.2	73	12	16.4
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-8)	(0-24) <sup>(1)</sup>	(0-24) <sup>(1)</sup>			
AUC <sub>0-t(last)</sub>	ng·hour/mL	286	450	395	377	83.5	22.1
C <sub>max</sub> /Dose	ng/mL	0.420	0.374	0.301	0.365	0.060	16.4
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.43	2.25	1.98	1.89	0.418	22.1
RA, C <sub>max</sub>		1.46	0.593	0.872	0.976	0.444	45.5
RA, AUC <sub>0-t(last)</sub>		0.801	0.768	0.945	0.838	0.094	11.2

<sup>(1)</sup> Nominal time

**Table 16.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	ng/mL	132	108	80.8	98.8	81.5	100	21.2	21.2
t <sub>max</sub>	hour	0.5	1	2	1	1	1.1	0.548	49.8
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	630	623	811	1070	748	776	182	23.5
C <sub>max</sub> /Dose	ng/mL	0.165	0.135	0.101	0.124	0.102	0.125	0.0265	21.1
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	0.787	0.779	1.01	1.34	0.935	0.97	0.229	23.6

**Table 17.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	ng/mL	130	220	75.1	127	86.9	128	56.9	44.5
t <sub>max</sub>	hour	1	1	1	1	1	1	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	1120	663	611	1090	1160	929	268	28.9
C <sub>max</sub> /Dose	ng/mL	0.163	0.275	0.0939	0.159	0.109	0.16	0.0711	44.4
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.4	0.829	0.763	1.36	1.44	1.16	0.333	28.7
RA, C <sub>max</sub>		0.985	2.04	0.929	1.29	1.07	1.26	0.455	36.1
RA, AUC <sub>0-t(last)</sub>		1.78	1.06	0.753	1.02	1.55	1.23	0.419	34

**Table 18.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in male Beagle Dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	ng/mL	141	54.1	107	48.4	80.4	86.2	38.5	44.7
t <sub>max</sub>	hour	1	1	1	2	1	1.2	0.447	37.3
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	938	824	673	605	638	736	141	19.1
C <sub>max</sub> /Dose	ng/mL	0.176	0.0676	0.134	0.0605	0.101	0.108	0.0481	44.6
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.17	1.03	0.842	0.757	0.797	0.919	0.175	19
RA, C <sub>max</sub>		1.07	0.501	1.32	0.49	0.987	0.874	0.367	42
RA, AUC <sub>0-t(last)</sub>		1.49	1.32	0.83	0.565	0.853	1.01	0.381	37.7
<sup>(1)</sup> Nominal time									

**Table 19.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
		293	233	128	135	129	184	75.6	41.2
C <sub>max</sub>	ng/mL	293	233	128	135	129	184	75.6	41.2
t <sub>max</sub>	hour	1	2	1	1	1	1.2	0.447	37.3
AUC Interval	hour	(0-8)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	628	1580	1050	736	479	895	437	48.8
C <sub>max</sub> /Dose	ng/mL	0.366	0.291	0.160	0.169	0.161	0.229	0.0943	41.1
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	0.785	1.97	1.31	0.920	0.599	1.12	0.544	48.7

**Table 20.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
		194	171	182	89.2	124	152	44	29
C <sub>max</sub>	ng/mL	194	171	182	89.2	124	152	44	29
t <sub>max</sub>	hour	1	2	2	1	1	1.4	0.548	39.1
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	1270	1660	1020	869	1030	1170	309	26.4
C <sub>max</sub> /Dose	ng/mL	0.243	0.214	0.228	0.112	0.155	0.19	0.0551	28.9
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	1.59	2.07	1.27	1.09	1.29	1.46	0.384	26.3
RA, C <sub>max</sub>		0.662	0.734	1.42	0.661	0.961	0.888	0.323	36.4
RA, AUC <sub>0-t(last)</sub>		2.02	1.05	0.971	1.18	2.15	1.48	0.565	38.3

**Table 21.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of Fexinidazole after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
		94.7	179	102	69.5	59	101	47.1	46.7
C <sub>max</sub>	ng/mL	94.7	179	102	69.5	59	101	47.1	46.7
t <sub>max</sub>	hour	1	1	1	1	1	1	0	0
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	ng·hour/mL	684	1540	1140	696	720	956	378	39.6
C <sub>max</sub> /Dose	ng/mL	0.118	0.224	0.128	0.0869	0.0738	0.126	0.059	46.8
AUC <sub>0-t(last)</sub> /Dose	ng·hour/mL	0.854	1.93	1.42	0.869	0.900	1.19	0.474	39.7
RA, C <sub>max</sub>		0.323	0.768	0.797	0.515	0.457	0.572	0.205	35.8
RA, AUC <sub>0-t(last)</sub>		1.09	0.975	1.09	0.946	1.5	1.12	0.224	20
<sup>(1)</sup> Nominal time									

**Table 22.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	9.17	6.33	6.02	7.17	1.74	24.2
t <sub>max</sub>	hour	8	8	8	8	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	158	107	112	126	28.1	22.4
C <sub>max</sub> /Dose	µg/mL	0.183	0.127	0.12	0.143	0.035	24.1
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	3.16	2.13	2.25	2.51	0.563	22.4

**Table 23.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	8.09	4.44	4.18	5.57	2.19	39.3
t <sub>max</sub>	hour	4	4	4	4	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	117	68.9	48.1	78	35.3	45.3
C <sub>max</sub> /Dose	µg/mL	0.162	0.0888	0.0836	0.111	0.0438	39.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	2.35	1.38	0.961	1.56	0.712	45.6
RA,C <sub>max</sub>		0.882	0.701	0.694	0.759	0.106	14
RA,AUC <sub>0-t(last)</sub>		0.741	0.644	0.429	0.605	0.159	26.3

**Table 24.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	8.43	6.87	6.04	7.11	1.21	17.1
t <sub>max</sub>	hour	8	8	8	8	0	0
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	139	123	101	121	19.1	15.8
C <sub>max</sub> /Dose	µg/mL	0.169	0.137	0.121	0.142	0.0244	17.2
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	2.77	2.45	2.02	2.41	0.376	15.6
RA,C <sub>max</sub>		0.919	1.09	1	1	0.083	8.3
RA,AUC <sub>0-t(last)</sub>		0.88	1.15	0.902	0.977	0.15	15.3
<sup>(1)</sup> Nominal time							

**Table 25.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	11.5	8.32	10.2	10	1.6	16
t <sub>max</sub>	hour	8	4	8	6.67	2.31	34.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	199	127	183	170	37.8	22.3
C <sub>max</sub> /Dose	µg/mL	0.23	0.166	0.204	0.2	0.0322	16.1
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	3.97	2.54	3.66	3.39	0.752	22.2

**Table 26.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	10.6	8.54	10.8	9.98	1.25	12.5
t <sub>max</sub>	hour	8	8	4	6.67	2.31	34.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	204	157	158	173	26.9	15.5
C <sub>max</sub> /Dose	µg/mL	0.212	0.171	0.216	0.2	0.0249	12.5
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	4.08	3.13	3.16	3.46	0.54	15.6
RA,C <sub>max</sub>		0.922	1.03	1.06	1	0.0717	7.1
RA,AUC <sub>0-t(last)</sub>		1.03	1.24	0.863	1.04	0.187	17.9

**Table 27.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	6.5	7.43	6.44	6.79	0.56	8.2
t <sub>max</sub>	hour	4	4	2	3.33	1.15	34.6
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	83.3	128	110	107	22.5	21
C <sub>max</sub> /Dose	µg/mL	0.13	0.149	0.129	0.136	0.0113	8.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.67	2.56	2.2	2.14	0.448	20.9
RA,C <sub>max</sub>		0.565	0.893	0.631	0.697	0.173	24.9
RA,AUC <sub>0-t(last)</sub>		0.419	1.01	0.601	0.676	0.302	44.6
<sup>(1)</sup> Nominal time							

**Table 28.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	16	16.4	19.1	17.2	1.69	9.8
t <sub>max</sub>	hour	24	8	8	13.3	9.24	69.3
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	295	325	394	338	50.8	15
C <sub>max</sub> /Dose	µg/mL	0.08	0.082	0.0955	0.0858	0.0084	9.8
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.47	1.62	1.97	1.69	0.257	15.2

**Table 29.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	15.6	24.2	26.1	22	5.59	25.5
t <sub>max</sub>	hour	8	4	4	5.33	2.31	43.3
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	336	389	435	387	49.5	12.8
C <sub>max</sub> /Dose	µg/mL	0.078	0.121	0.131	0.11	0.0282	25.6
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.68	1.95	2.17	1.93	0.245	12.7
RA, C <sub>max</sub>		0.975	1.48	1.37	1.27	0.263	20.7
RA, AUC <sub>0-t(last)</sub>		1.14	1.2	1.1	1.15	0.0469	4.1

**Table 30.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	13.3	11.1	17.6	14	3.31	23.6
t <sub>max</sub>	hour	8	4	0	4	4	100
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	256	211	307	258	48	18.6
C <sub>max</sub> /Dose	µg/mL	0.0665	0.0555	0.088	0.07	0.0165	23.6
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.28	1.06	1.53	1.29	0.235	18.2
RA, C <sub>max</sub>		0.831	0.677	0.921	0.81	0.124	15.3
RA, AUC <sub>0-t(last)</sub>		0.868	0.649	0.779	0.765	0.11	14.4
<sup>(1)</sup> Nominal time							

**Table 31.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	15.8	22	16.4	18.1	3.42	18.9
t <sub>max</sub>	hour	24	8	4	12	10.6	88.2
AUC Interval	hour	(0-24)	(0-24)	(0-24 )			
AUC <sub>0-t(last)</sub>	µg·hour/mL	318	456	299	358	85.7	24
C <sub>max</sub> /Dose	µg /mL	0.079	0.11	0.082	0.0903	0.0171	18.9
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.59	2.28	1.5	1.79	0.427	23.8

**Table 32.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	19.3	24.1	21.2	21.5	2.42	11.2
t <sub>max</sub>	hour	4	8	4	5.33	2.31	43.3
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	312	428	404	381	61.2	16.1
C <sub>max</sub> /Dose	µg/mL	0.0965	0.121	0.106	0.108	0.012	11.5
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.56	2.14	2.02	1.91	0.306	16.1
RA,C <sub>max</sub>		1.22	1.1	1.29	1.2	0.1	8.3
RA,AUC <sub>0-t(last)</sub>		0.981	0.939	1.35	1.09	0.227	20.8

**Table 33.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	17.9	12.6	15.6	15.4	2.66	17.3
t <sub>max</sub>	hour	8	4	23.18	11.7	10.1	86.3
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	309	250	271	277	29.9	10.8
C <sub>max</sub> /Dose	µg/mL	0.0895	0.063	0.078	0.0768	0.0133	17.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	1.55	1.25	1.36	1.39	0.152	10.9
RA,C <sub>max</sub>		1.13	0.573	0.951	0.886	0.286	32.3
RA,AUC <sub>0-t(last)</sub>		0.972	0.548	0.906	0.809	0.228	28.2
<sup>(1)</sup> Nominal time							



**Table 34.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
$C_{max}$	$\mu\text{g/mL}$	39.8	37.2	43	36.4	36.5	38.6	2.83	7.3
$t_{max}$	hour	24	8	24	24	8	17.6	8.76	49.8
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	$\mu\text{g}\cdot\text{hour/mL}$	769	544	778	731	703	705	94.9	13.5
$C_{max}/\text{Dose}$	$\mu\text{g/mL}$	0.0498	0.0465	0.0538	0.0455	0.0456	0.048	0.0036	7.4
AUC <sub>0-t(last)</sub> /Dose	$\mu\text{g}\cdot\text{hour/mL}$	0.962	0.68	0.972	0.914	0.878	0.881	0.119	13.5

**Table 35.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
$C_{max}$	$\mu\text{g/mL}$	33.8	25.3	29.8	42.5	41.5	34.6	7.42	21.5
$t_{max}$	hour	4	4	4	8	8	5.6	2.19	39.1
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	$\mu\text{g}\cdot\text{hour/mL}$	675	431	514	807	771	640	163	25.4
$C_{max}/\text{Dose}$	$\mu\text{g/mL}$	0.0423	0.0316	0.0373	0.0531	0.0519	0.043	0.0093	21.4
AUC <sub>0-t(last)</sub> /Dose	$\mu\text{g}\cdot\text{hour/mL}$	0.844	0.539	0.643	1.01	0.964	0.8	0.204	25.4
RA, $C_{max}$		0.849	0.68	0.693	1.17	1.14	0.905	0.235	26
RA,AUC <sub>0-t(last)</sub>		0.878	0.792	0.661	1.1	1.1	0.906	0.193	21.3

**Table 36.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
$C_{max}$	$\mu\text{g/mL}$	21.4	16	20	27.3	19.3	20.8	4.14	19.9
$t_{max}$	hour	23	23	4	8	4	12.4	9.81	79.1
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-72)	(0-72)			
AUC <sub>0-24</sub>	$\mu\text{g}\cdot\text{hour/mL}$	448	282	405	441	362	388	68.2	17.6
AUC <sub>0-t(last)</sub>	$\mu\text{g}\cdot\text{hour/mL}$				580	621	601	29	4.8
$C_{max}/\text{Dose}$	$\mu\text{g/mL}$	0.0268	0.02	0.025	0.0341	0.0241	0.026	0.0052	19.9
AUC <sub>0-24</sub> /Dose	$\mu\text{g}\cdot\text{hour/mL}$	0.561	0.352	0.506	0.551	0.453	0.485	0.0857	17.7
AUC <sub>0-t(last)</sub> /Dose	$\mu\text{g}\cdot\text{hour/mL}$				0.725	0.776	0.751	0.0361	4.8
$t_{1/2,z}$	hour				6.2	7.16	6.68	0.679	10.2
RA, $C_{max}$		0.538	0.43	0.465	0.75	0.529	0.542	0.124	22.9
RA,AUC <sub>0-24</sub>		0.583	0.518	0.521	0.603	0.515	0.548	0.0418	7.6

<sup>(1)</sup> Nominal time**Table 37.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	35	44.9	43.1	23.8	21.1	33.6	10.9	32.4
t <sub>max</sub>	hour	8	8	8	24	8	11.2	7.16	63.9
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	592	848	811	481	340	614	216	35.2
C <sub>max</sub> /Dose	µg/mL	0.0438	0.0561	0.0539	0.0298	0.0264	0.042	0.0136	32.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.74	1.06	1.01	0.601	0.425	0.767	0.269	35.1

**Table 38.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	37.3	47	36.1	37.2	35.6	38.6	4.73	12.2
t <sub>max</sub>	hour	8	8	8	8	8	8	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	696	766	641	586	645	667	67.8	10.2
C <sub>max</sub> /Dose	µg/mL	0.0466	0.0588	0.0451	0.0465	0.0445	0.048	0.0059	12.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.87	0.957	0.802	0.733	0.806	0.834	0.0843	10.1
RA,C <sub>max</sub>		1.07	1.05	0.838	1.56	1.69	1.24	0.365	29.5
RA,AUC <sub>0-t(last)</sub>		1.18	0.903	0.79	1.22	1.9	1.2	0.431	36

**Table 39.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfone metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	18.2	36.2	28.6	28.5	18.3	26	7.7	29.7
t <sub>max</sub>	hour	4	8	8	8	8	7.2	1.79	24.8
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-72)	(0-72)			
AUC <sub>0-24</sub>	µg·hour/mL	353	691	516	493	331	477	145	30.4
AUC <sub>0-t(last)</sub>	µg·hour/mL				941	445	693	351	50.6
C <sub>max</sub> /Dose	µg/mL	0.0228	0.0453	0.0358	0.0356	0.0229	0.033	0.0096	29.6
AUC <sub>0-24</sub> /Dose	µg·hour/mL	0.442	0.863	0.646	0.616	0.414	0.596	0.181	30.4
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL				1.18	0.556	0.868	0.441	50.8
t <sub>1/2,z</sub>	hour				8.24	7.27	7.76	0.686	8.8
RA,C <sub>max</sub>		0.52	0.806	0.664	1.2	0.867	0.811	0.254	31.4
RA,AUC <sub>0-24</sub>		0.596	0.815	0.636	1.02	0.974	0.809	0.193	23.8
<sup>(1)</sup> Nominal time									

**Table 40.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	5.04	2.65	2.95	3.55	1.3	36.7
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	25.7	17.6	14.4	19.2	5.82	30.3
C <sub>max</sub> /Dose	µg/mL	0.101	0.053	0.059	0.071	0.0262	36.8
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.514	0.352	0.287	0.384	0.117	30.4

**Table 41.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	2.76	2.06	1.91	2.24	0.454	20.2
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval	hour	(0-8)	(0-24)	(0-8)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	10.8	8.93	5.79	8.51	2.53	29.8
C <sub>max</sub> /Dose	µg/mL	0.0552	0.0412	0.0382	0.0449	0.00907	20.2
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.217	0.179	0.116	0.171	0.051	29.9
RA,C <sub>max</sub>		0.548	0.777	0.647	0.657	0.115	17.5
RA,AUC <sub>0-t(last)</sub>		0.42	0.507	0.402	0.443	0.0563	12.7

**Table 42.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2514	ID 2521	ID 2529	Mean	SD	%CV
C <sub>max</sub>	µg/mL	2.48	1.44	1.57	1.83	0.567	31
t <sub>max</sub>	hour	2	1	2	1.67	0.577	34.6
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	15.9	15.7	11.1	14.2	2.72	19.1
C <sub>max</sub> /Dose	µg/mL	0.0496	0.0288	0.0314	0.0366	0.0113	31
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.318	0.314	0.221	0.284	0.0549	19.3
RA,C <sub>max</sub>		0.492	0.543	0.532	0.523	0.027	5.2
RA,AUC <sub>0-t(last)</sub>		0.619	0.892	0.771	0.761	0.137	18
<sup>(1)</sup> Nominal time							

**Table 43.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	3.6	4.82	3.49	3.97	0.738	18.6
t <sub>max</sub>	hour	2	1	1	1.33	0.577	43.3
AUC Interval	hour	(0-24)	(0-8)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	26.2	12.7	21	20	6.81	34.1
C <sub>max</sub> /Dose	µg/mL	0.072	0.0964	0.0698	0.0794	0.0148	18.6
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.524	0.255	0.42	0.4	0.136	33.9

**Table 44.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	3.12	3.53	4.53	3.73	0.725	19.5
t <sub>max</sub>	hour	1	2	2	1.67	0.577	34.6
AUC Interval	hour	(0-24)	(0-24)	(0-8)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	21.1	17.2	18	18.8	2.06	11
C <sub>max</sub> /Dose	µg/mL	0.0624	0.0706	0.0906	0.0745	0.0145	19.5
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.421	0.344	0.36	0.375	0.0406	10.8
RA, C <sub>max</sub>		0.867	0.732	1.3	0.966	0.296	30.6
RA, AUC <sub>0-t(last)</sub>		0.805	1.35	0.857	1.01	0.303	30.1

**Table 45.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 50 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2562	ID 2563	ID 2576	Mean	SD	%CV
C <sub>max</sub>	µg/mL	1.91	2.91	3.33	2.72	0.729	26.9
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	6.93	12.3	10.4	9.88	2.72	27.6
C <sub>max</sub> /Dose	µg/mL	0.0382	0.0582	0.0666	0.0543	0.0146	26.9
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.139	0.245	0.207	0.197	0.0537	27.3
RA, C <sub>max</sub>		0.531	0.604	0.954	0.696	0.226	32.5
RA, AUC <sub>0-t(last)</sub>		0.265	0.969	0.495	0.576	0.359	62.3
<sup>(1)</sup> Nominal time							

**Table 46.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	6.37	7.97	8.3	7.55	1.03	13.7
t <sub>max</sub>	hour	1	2	2	1.67	0.58	34.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	44.5	47	60.5	50.7	8.61	17
C <sub>max</sub> /Dose	µg/mL	0.0319	0.0399	0.0415	0.0378	0.0051	13.6
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.223	0.235	0.302	0.253	0.0426	16.8

**Table 47.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	6.97	11.8	8.1	8.96	2.53	28.2
t <sub>max</sub>	hour	2	2	2	2	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	57.4	65.4	45.6	56.1	9.96	17.7
C <sub>max</sub> /Dose	µg/mL	0.0349	0.059	0.0405	0.0448	0.0126	28.2
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.287	0.327	0.228	0.281	0.0498	17.7
RA, C <sub>max</sub>		1.09	1.48	0.976	1.18	0.264	22.3
RA, AUC <sub>0-t(last)</sub>		1.29	1.39	0.754	1.15	0.343	29.9

**Table 48.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	ID 2515	ID 2523	ID 2526	Mean	SD	%CV
C <sub>max</sub>	µg/mL	6.96	5.7	4.62	5.76	1.17	20.3
t <sub>max</sub>	hour	1	2	1	1.33	0.58	43.3
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	44.7	47.1	34.9	42.2	6.46	15.3
C <sub>max</sub> /Dose	µg/mL	0.0348	0.0285	0.0231	0.0288	0.0059	20.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.224	0.235	0.174	0.211	0.0325	15.4
RA, C <sub>max</sub>		1.09	0.715	0.557	0.788	0.275	34.9
RA, AUC <sub>0-t(last)</sub>		1	1	0.577	0.861	0.246	28.6
<sup>(1)</sup> Nominal time							

**Table 49.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	4.92	12.8	8.38	8.7	3.95	45.4
t <sub>max</sub>	hour	0.5	1	1	0.833	0.289	34.6
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	39.4	75.8	41	52.1	20.6	39.5
C <sub>max</sub> /Dose	µg/mL	0.0246	0.064	0.0419	0.0435	0.0197	45.4
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.197	0.379	0.205	0.26	0.103	39.5

**Table 50.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	5.32	12.7	9.03	9.02	3.69	40.9
t <sub>max</sub>	hour	2	2	2	2	0	0
AUC Interval	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	31.7	80.1	59.8	57.2	24.3	42.5
C <sub>max</sub> /Dose	µg/mL	0.0266	0.0635	0.0452	0.0451	0.0185	40.9
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.159	0.401	0.299	0.286	0.121	42.4
RA, C <sub>max</sub>		1.08	0.992	1.08	1.05	0.0504	4.8
RA, AUC <sub>0-t(last)</sub>		0.805	1.06	1.46	1.11	0.33	29.8

**Table 51.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 200 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	ID 2561	ID 2567	ID 2570	Mean	SD	%CV
C <sub>max</sub>	µg/mL	5.41	5.78	5.1	5.43	0.34	6.3
t <sub>max</sub>	hour	1	1	1	1	0	0
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	31.9	34.6	34.9	33.8	1.65	4.9
C <sub>max</sub> /Dose	µg/mL	0.0271	0.0289	0.0255	0.027	0.0017	6.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.16	0.173	0.174	0.169	0.00781	4.6
RA, C <sub>max</sub>		1.1	0.452	0.609	0.72	0.338	47
RA, AUC <sub>0-t(last)</sub>		0.81	0.456	0.851	0.706	0.217	30.7
<sup>(1)</sup> Nominal time							

**Table 52.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	µg/mL	17.5	15.2	9.39	11.1	13.7	13.4	3.22	24.1
t <sub>max</sub>	hour	0.5	2	2	2	1	1.5	0.707	47.1
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	89.7	95	105	114	115	104	11.3	10.9
C <sub>max</sub> /Dose	µg/mL	0.0219	0.019	0.0117	0.0139	0.0171	0.017	0.00404	24.2
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.112	0.119	0.131	0.143	0.144	0.13	0.0142	11

**Table 53.** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	µg/mL	12.8	14.9	7.56	13.9	13.1	12.5	2.85	22.9
t <sub>max</sub>	hour	1	1	1	1	2	1.2	0.4472	37.3
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	116	77.5	69	160	144	113	39.9	35.2
C <sub>max</sub> /Dose	µg/mL	0.016	0.0186	0.00945	0.0174	0.0164	0.016	0.00357	22.9
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.145	0.0969	0.0863	0.200	0.18	0.142	0.0499	35.2
RA, C <sub>max</sub>		0.731	0.98	0.805	1.25	0.956	0.945	0.201	21.2
RA, AUC <sub>0-t(last)</sub>		1.29	0.816	0.657	1.4	1.25	1.08	0.327	30.2

**Table 54.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in male Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2517	2519	2525	2528	2530			
C <sub>max</sub>	µg/mL	15.1	6.19	8.2	7.04	10.2	9.35	3.55	38
t <sub>max</sub>	hour	1	2	1	2	2	1.6	0.548	34.2
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-48)	(0-48)			
AUC <sub>0-24</sub>	µg·hour/mL	87.3	59.8	57.6	84.1	82.8	74.3	14.4	19.3
AUC <sub>0-t(last)</sub>	µg·hour/mL				97.3	144	121	33	27.4
C <sub>max</sub> /Dose		0.0189	0.00774	0.0103	0.0088	0.0128	0.012	0.00445	38
AUC <sub>0-24</sub> /Dose	µg·hour/mL	0.109	0.0747	0.072	0.105	0.104	0.0929	0.018	19.4
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL				0.122	0.18	0.151	0.041	27.2
t <sub>1/2,z</sub>	hour				5.5	13.2	9.35	5.44	58.2
RA, C <sub>max</sub>		0.863	0.407	0.873	0.634	0.745	0.704	0.193	27.3
RA, AUC <sub>0-24</sub>		0.973	0.629	0.549	0.738	0.72	0.722	0.16	22.1

<sup>(1)</sup> Nominal time

**Table 55.** Day 1 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	18.4	21.7	13.8	14.7	9.51	15.6	4.64	29.7
t <sub>max</sub>	hour	2	2	1	1	2	1.6	0.548	34.2
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	135	173	105	136	54	121	44.4	36.8
C <sub>max</sub> /Dose	µg/mL	0.023	0.0271	0.0173	0.0184	0.0119	0.02	0.00578	29.6
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.168	0.216	0.131	0.17	0.0675	0.151	0.0553	36.8

**Table 56** Day 14 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

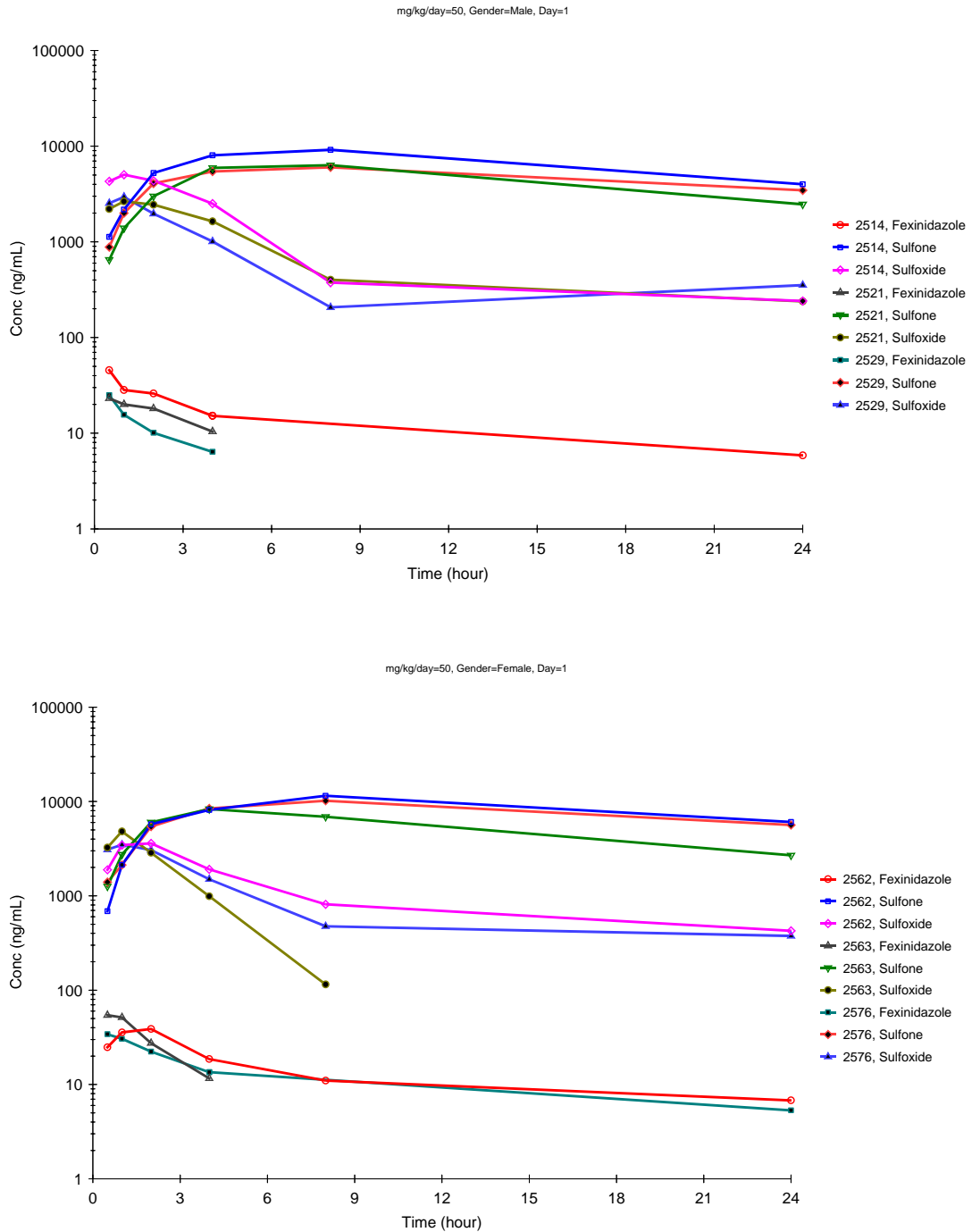
Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	21.7	14.1	18.2	10.5	9.73	14.8	5.1	34.3
t <sub>max</sub>	hour	1	4	2	2	1	2	1.22	61.2
AUC Interval	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	178	190	126	113	113	144	37.1	25.8
C <sub>max</sub> /Dose	µg/mL	0.0271	0.0176	0.0228	0.0131	0.0122	0.019	0.0064	34.3
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.223	0.238	0.157	0.141	0.141	0.18	0.0469	26
RA, C <sub>max</sub>		1.18	0.65	1.32	0.714	1.02	0.977	0.29	29.7
RA, AUC <sub>0-t(last)</sub>		1.32	1.1	1.2	0.831	2.09	1.31	0.474	36.2

**Table 57.** Day 28 individual and mean ( $\pm$ SD, %CV) pharmacokinetic parameters of the sulfoxide metabolite after oral 800 mg/kg/day of Fexinidazole in female Beagle dogs.

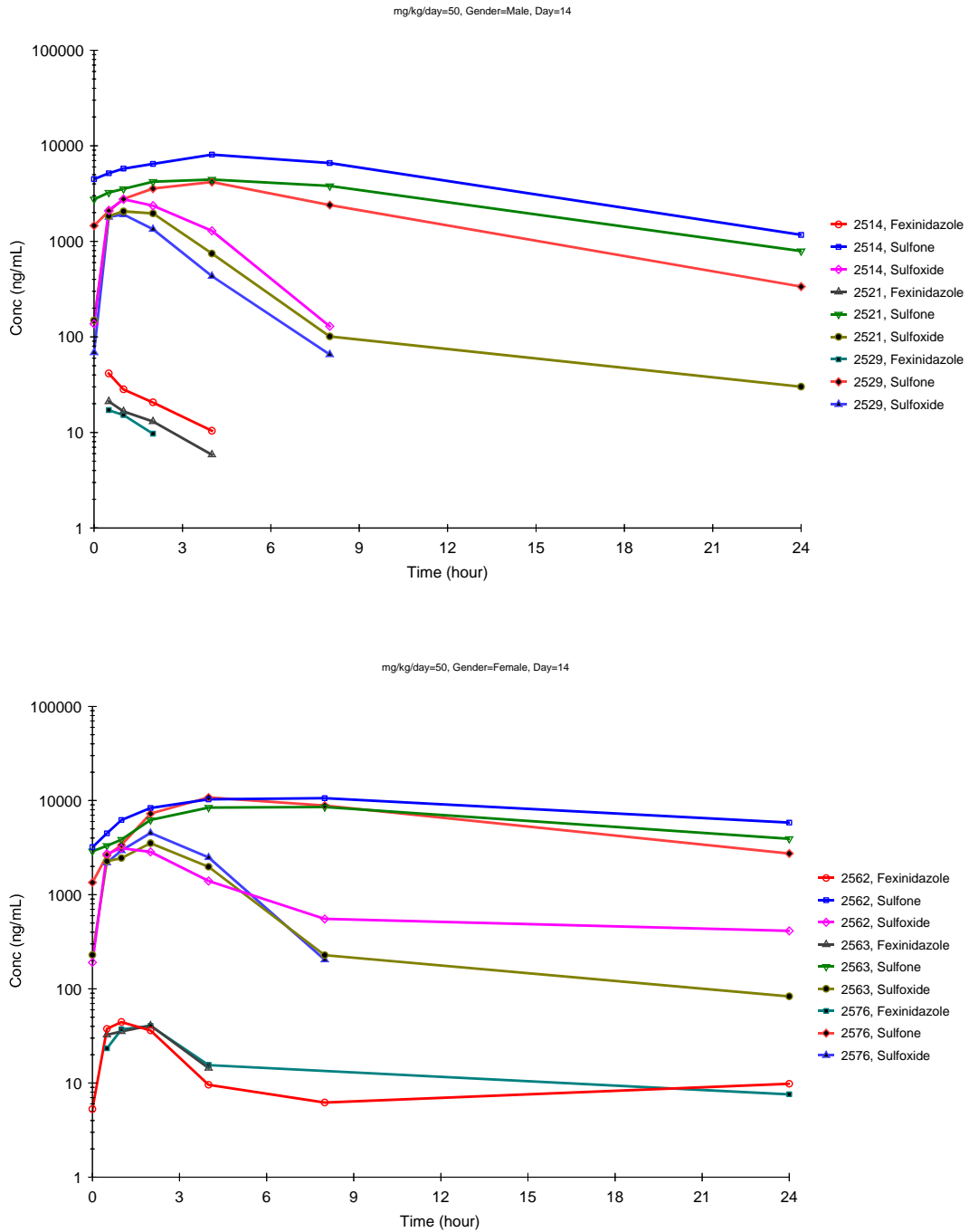
Parameter	Units	Dog ID					Mean	SD	%CV
		2564	2565	2569	2571	2573			
C <sub>max</sub>	µg/mL	11.9	13.2	9.8	7.83	4.66	9.48	3.38	35.7
t <sub>max</sub>	hour	1	2	1	2	1	1.4	0.548	39.1
AUC Interval <sup>(1)</sup>	hour	(0-24)	(0-24)	(0-24)	(0-24)	(0-24)			
AUC <sub>0-t(last)</sub>	µg·hour/mL	66.3	163	73.6	96.7	45.4	89	45.2	50.8
C <sub>max</sub> /Dose	µg/mL	0.0149	0.0165	0.0123	0.00979	0.00583	0.0119	0.00423	35.7
AUC <sub>0-t(last)</sub> /Dose	µg·hour/mL	0.0829	0.203	0.092	0.121	0.0567	0.111	0.0563	50.6
RA, C <sub>max</sub>		0.647	0.608	0.71	0.533	0.49	0.598	0.088	14.7
RA, AUC <sub>0-t(last)</sub>		0.491	0.942	0.701	0.711	0.841	0.737	0.17	23
<sup>(1)</sup> Nominal time									



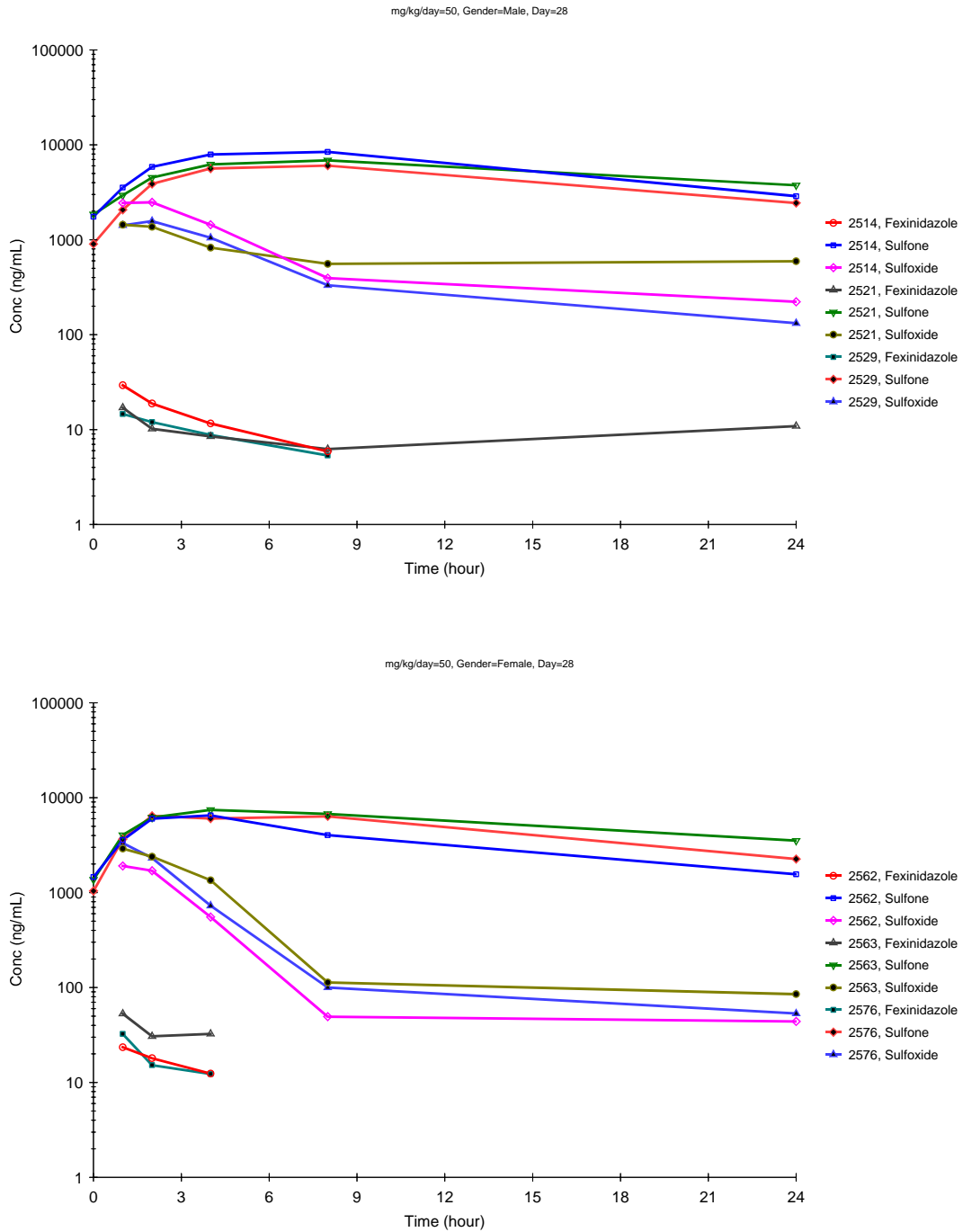
**Figure 1.** Day 1 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 50 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



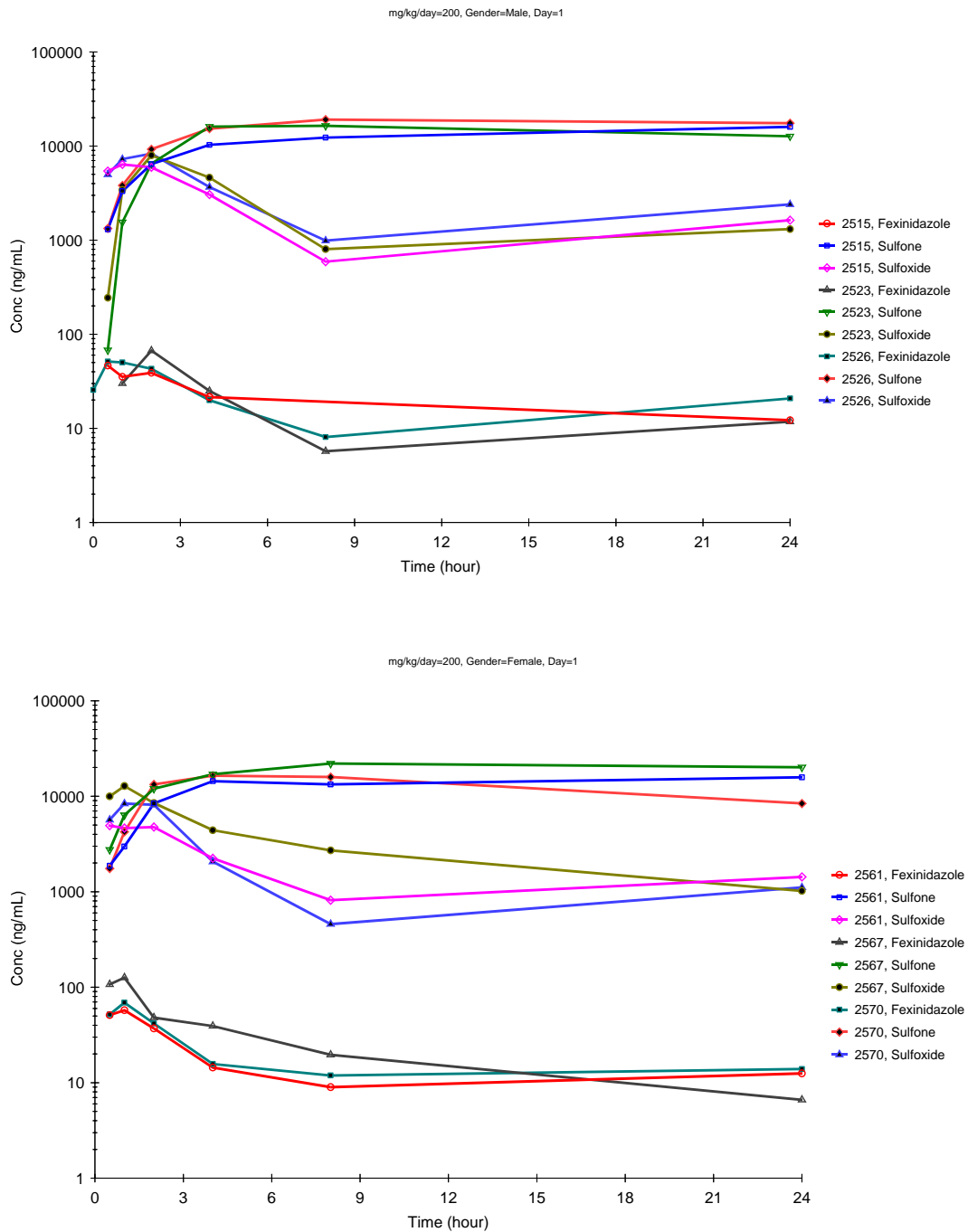
**Figure 2.** Day 14 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 50 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



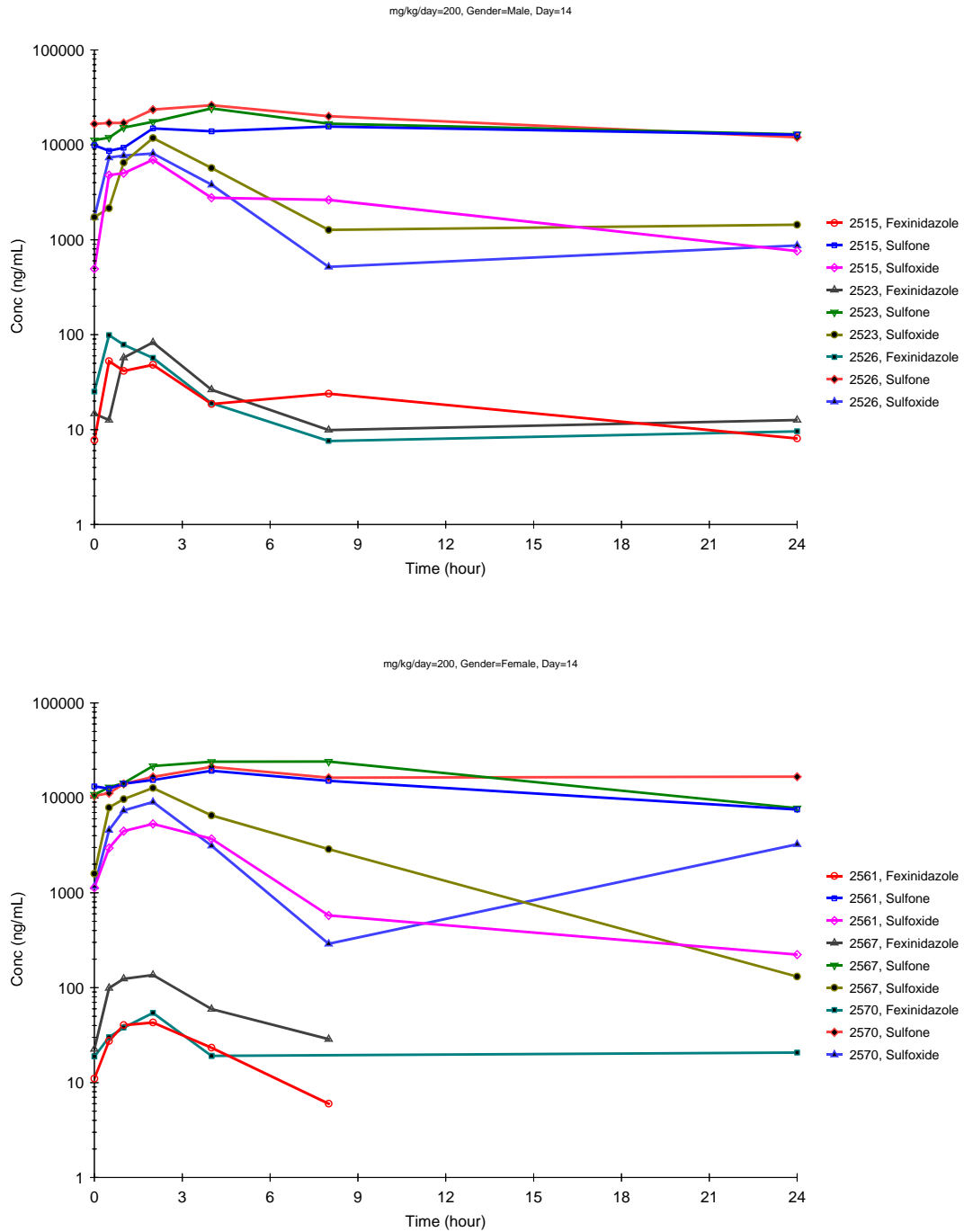
**Figure 3.** Day 28 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 50 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



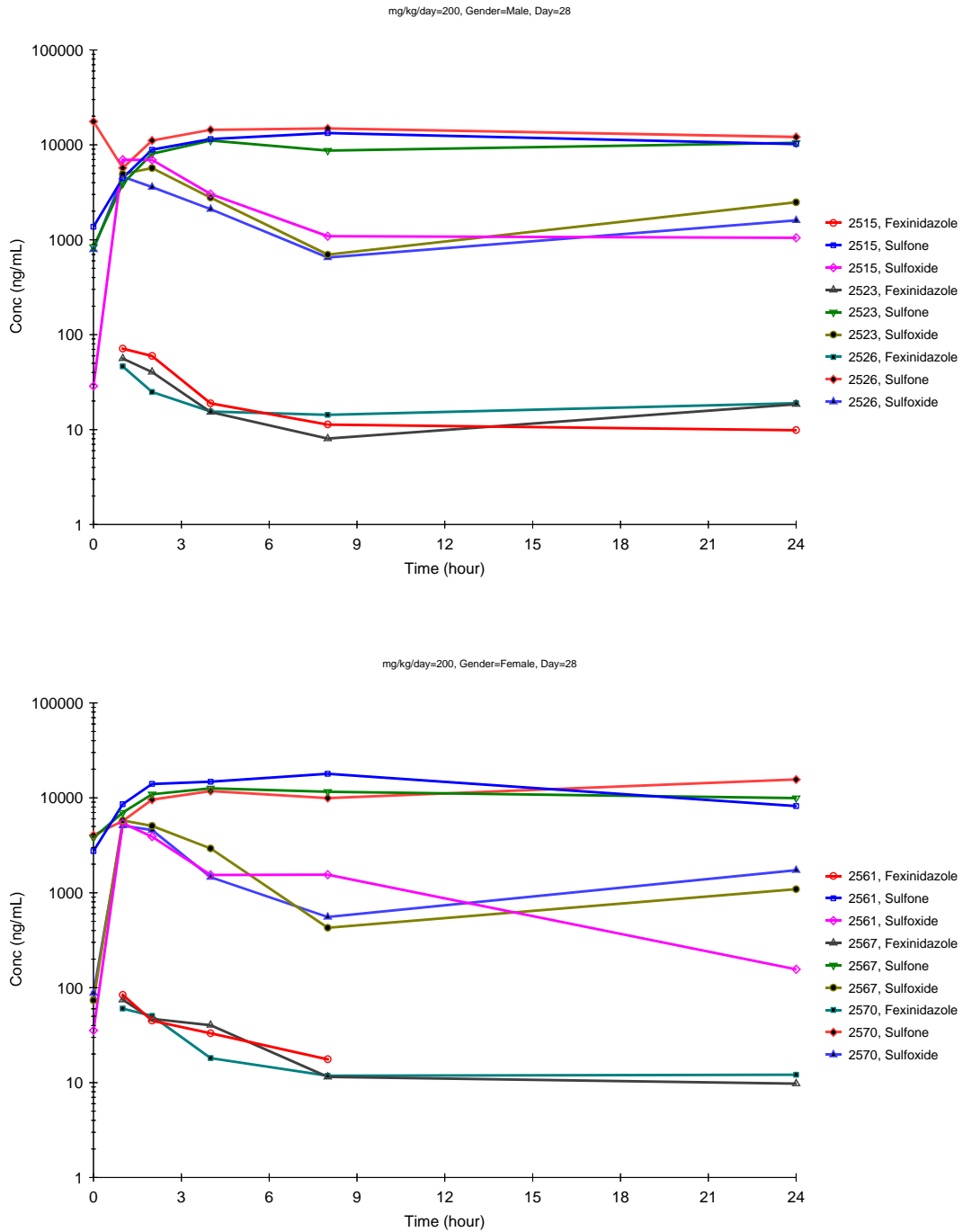
**Figure 4.** Day 1 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 200 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



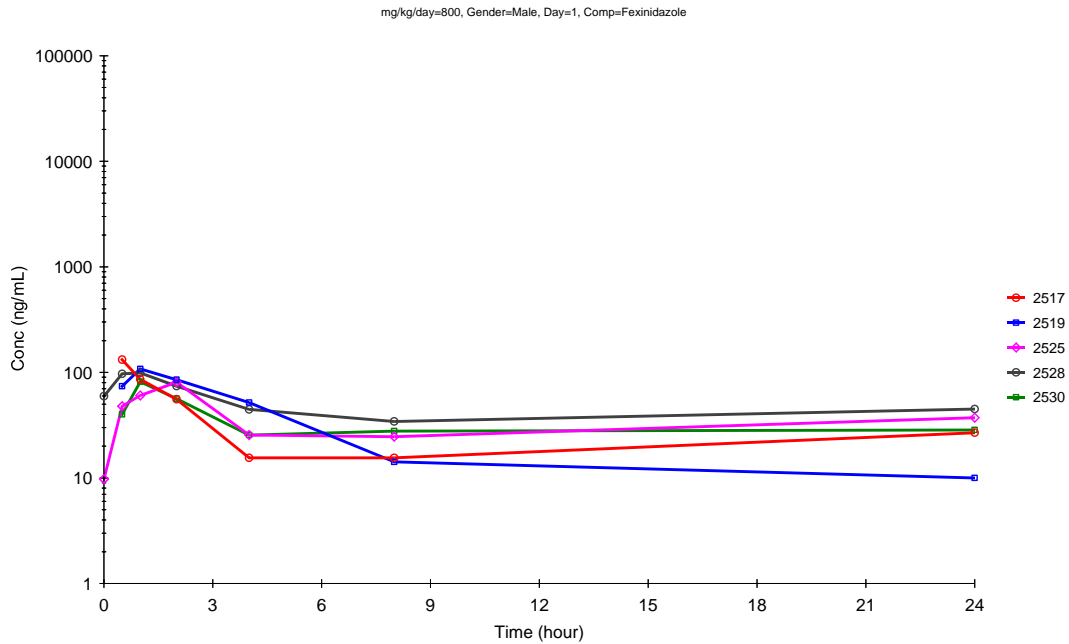
**Figure 5.** Day 14 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 200 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



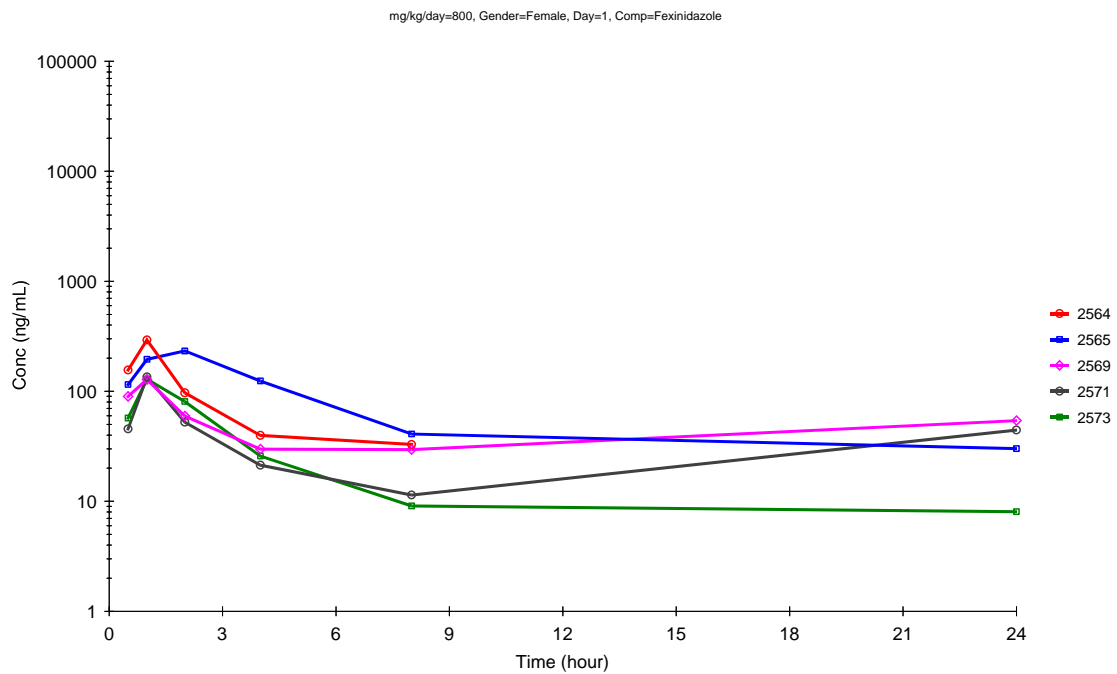
**Figure 6.** Day 28 individual plasma concentrations (ng/mL) of Fexinidazole and metabolites after oral 200 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



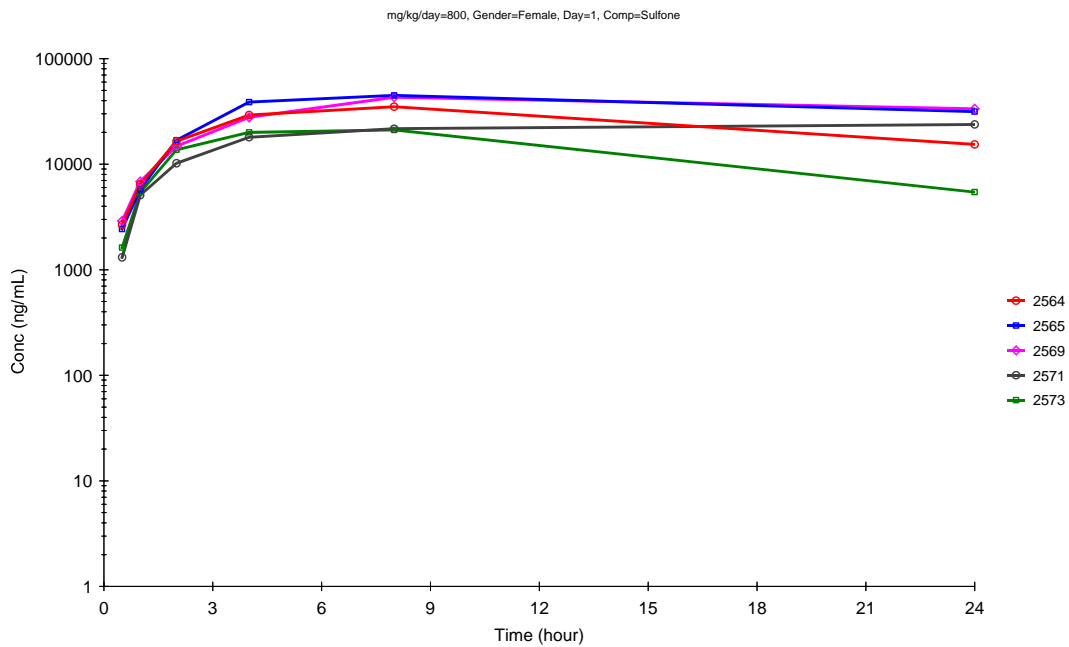
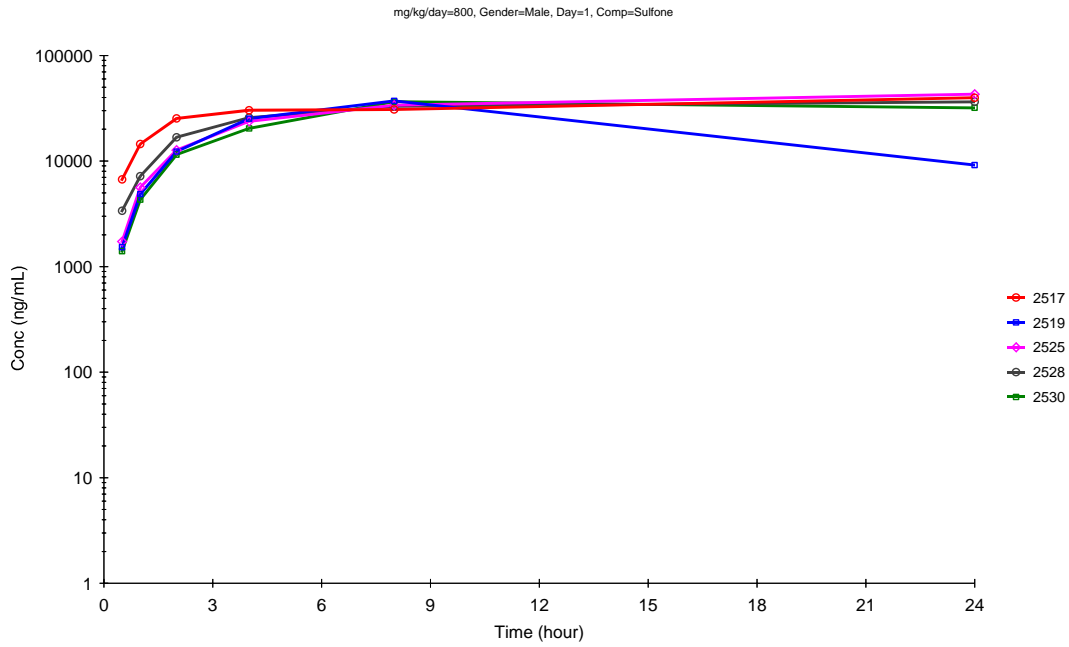
**Figure 7.** Day 1 individual plasma concentrations (ng/mL) of Fexinidazole after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle



dogs.

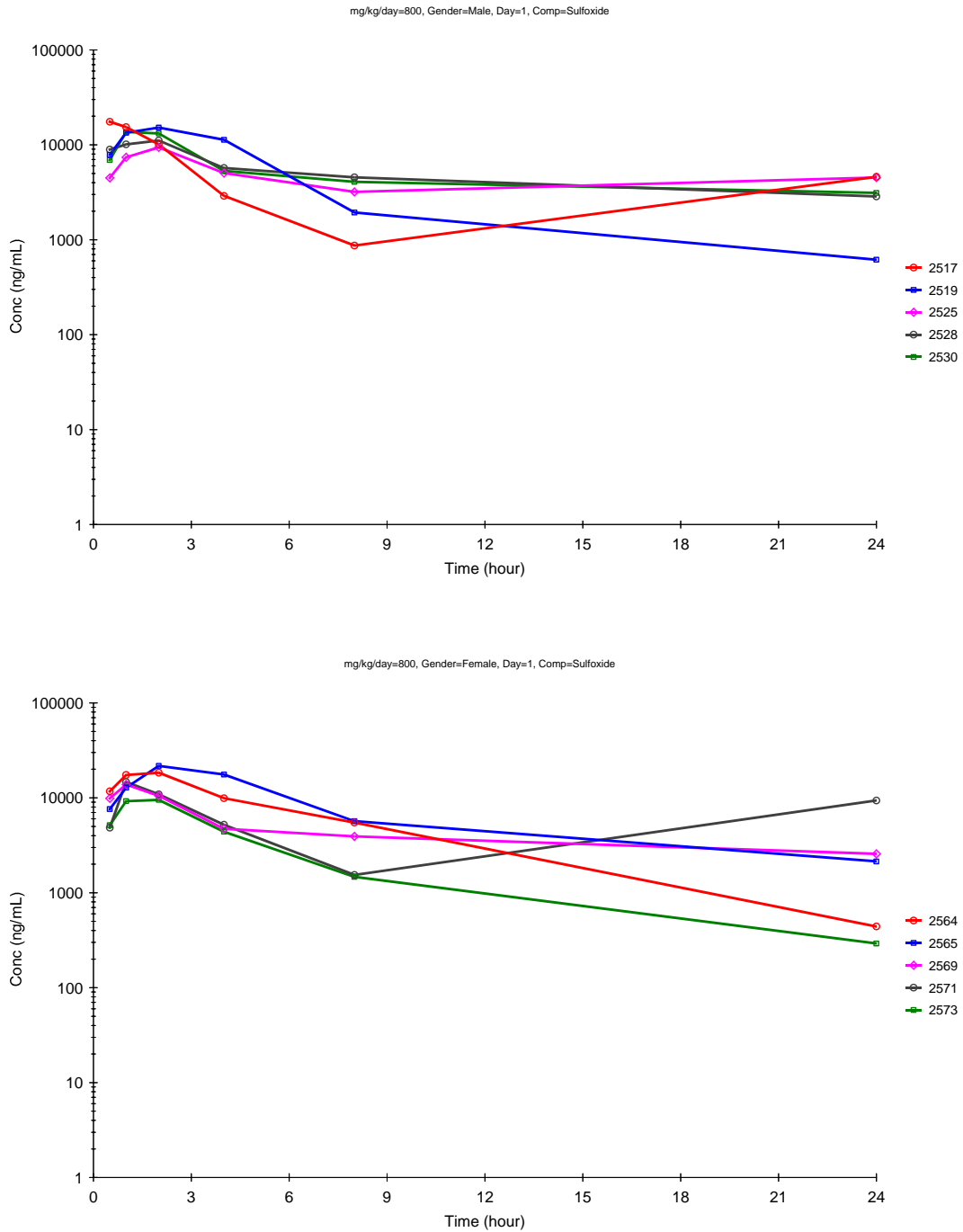


**Figure 8.** Day 1 individual plasma concentrations (ng/mL) of sulfone metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.

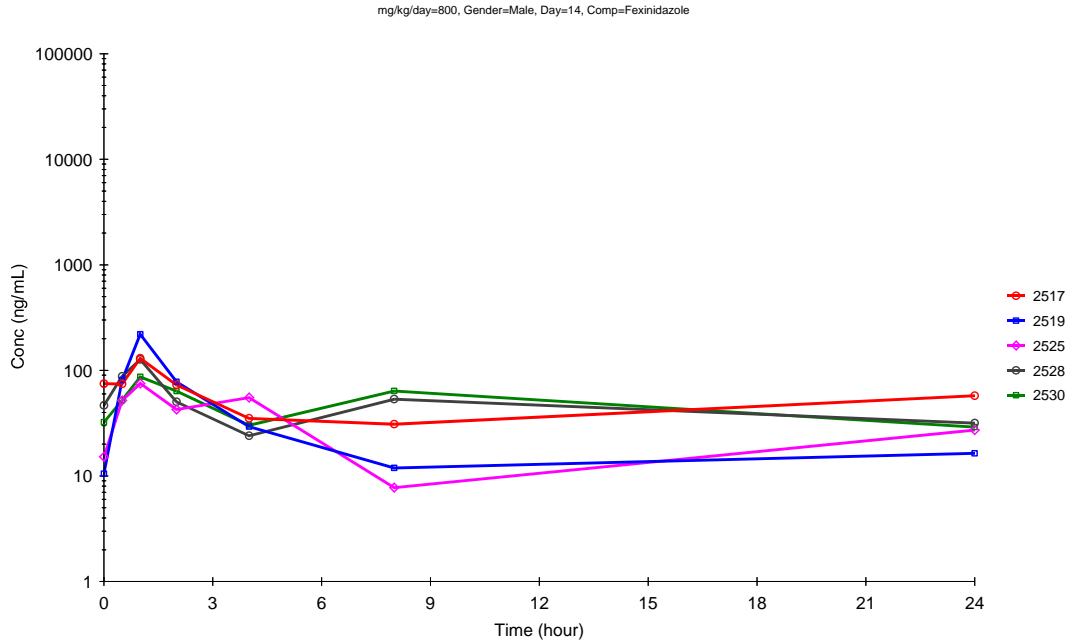




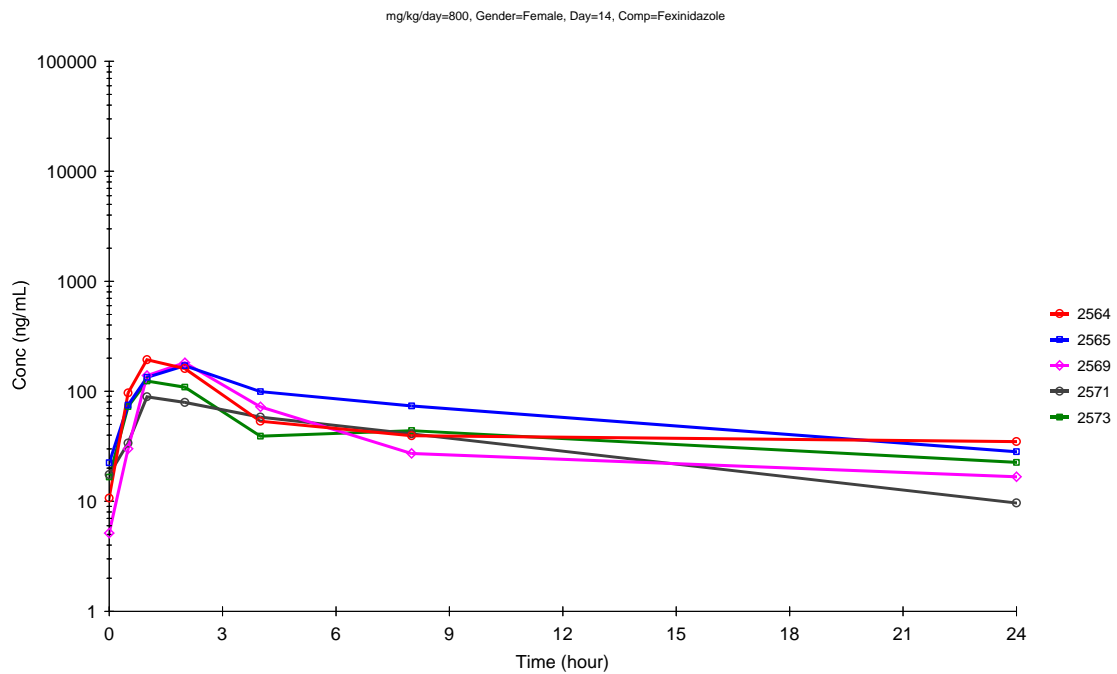
**Figure 9.** Day 1 individual plasma concentrations (ng/mL) of sulfoxide metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



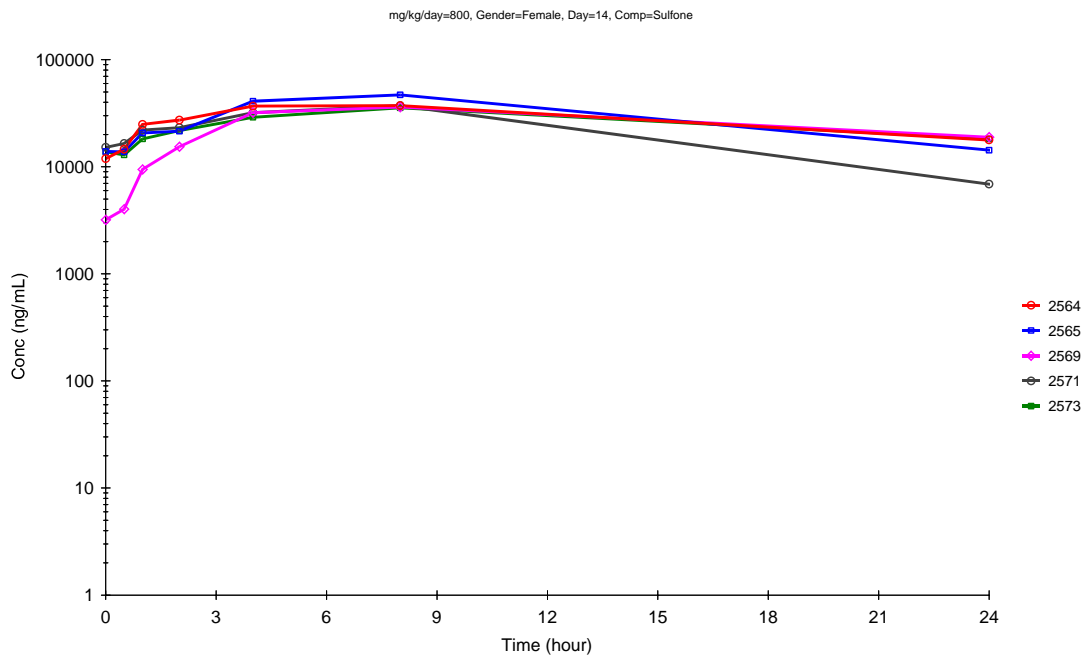
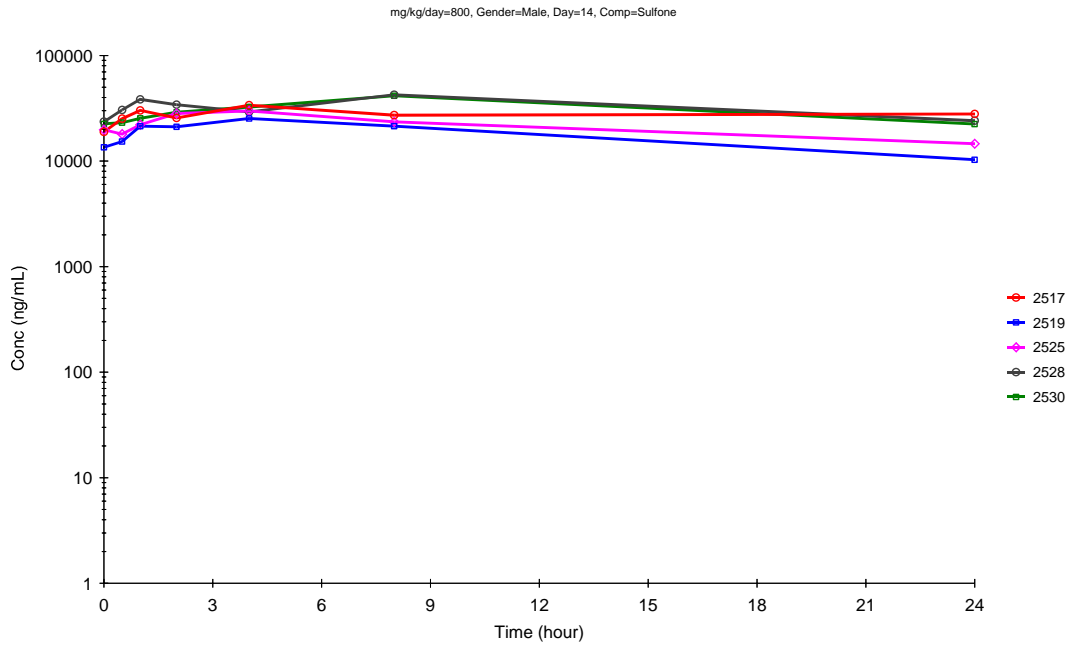
**Figure 10.** Day 14 individual plasma concentrations (ng/mL) of Fexinidazole after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle



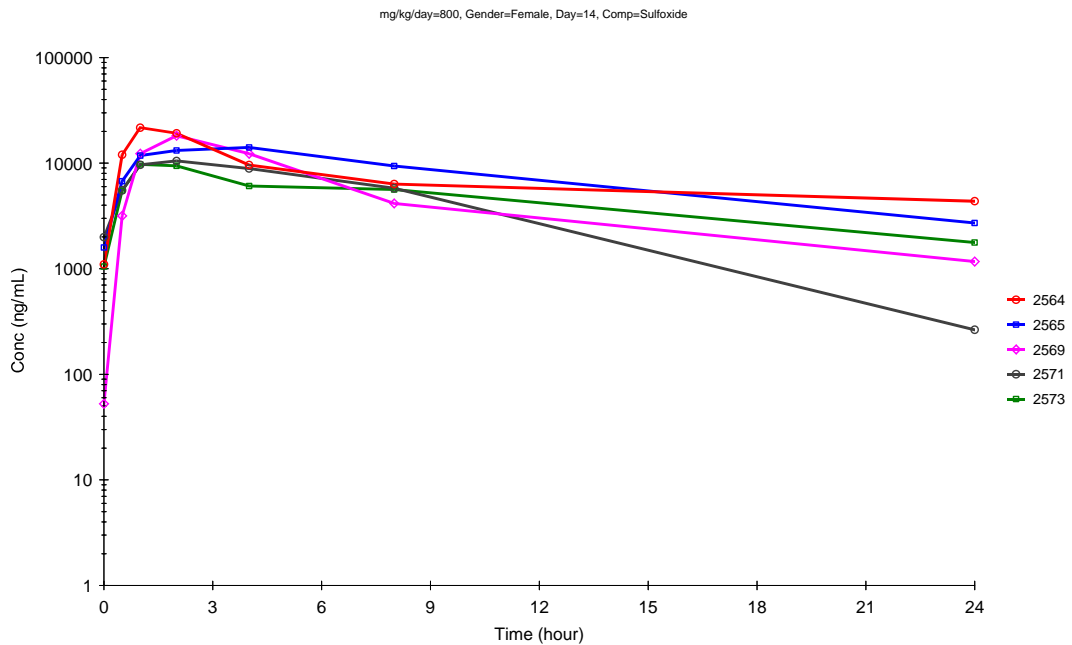
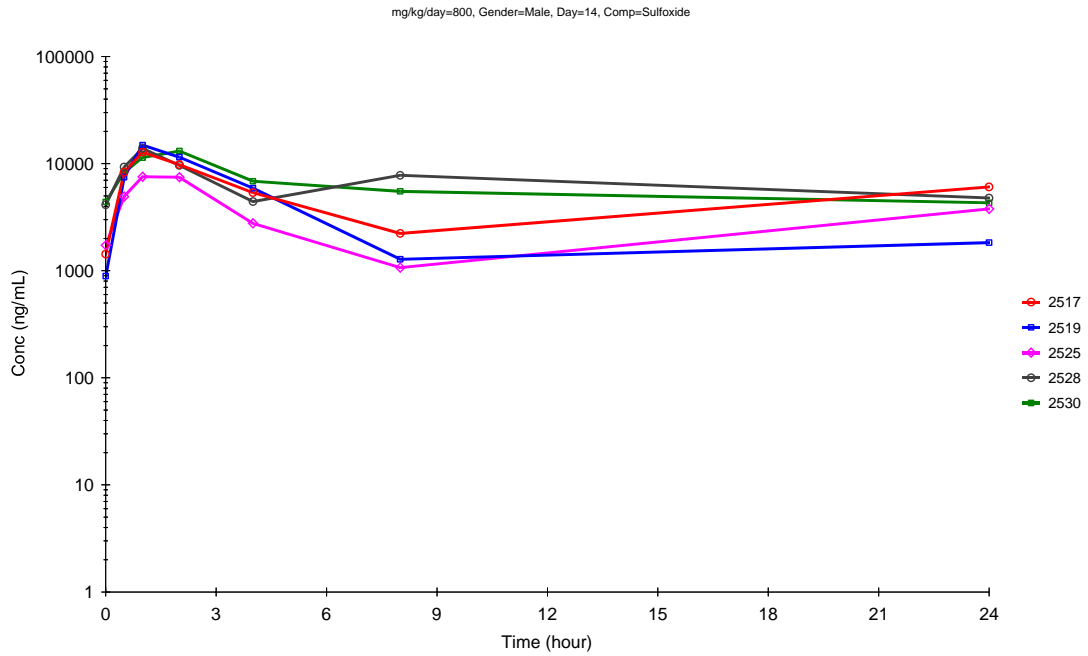
dogs.



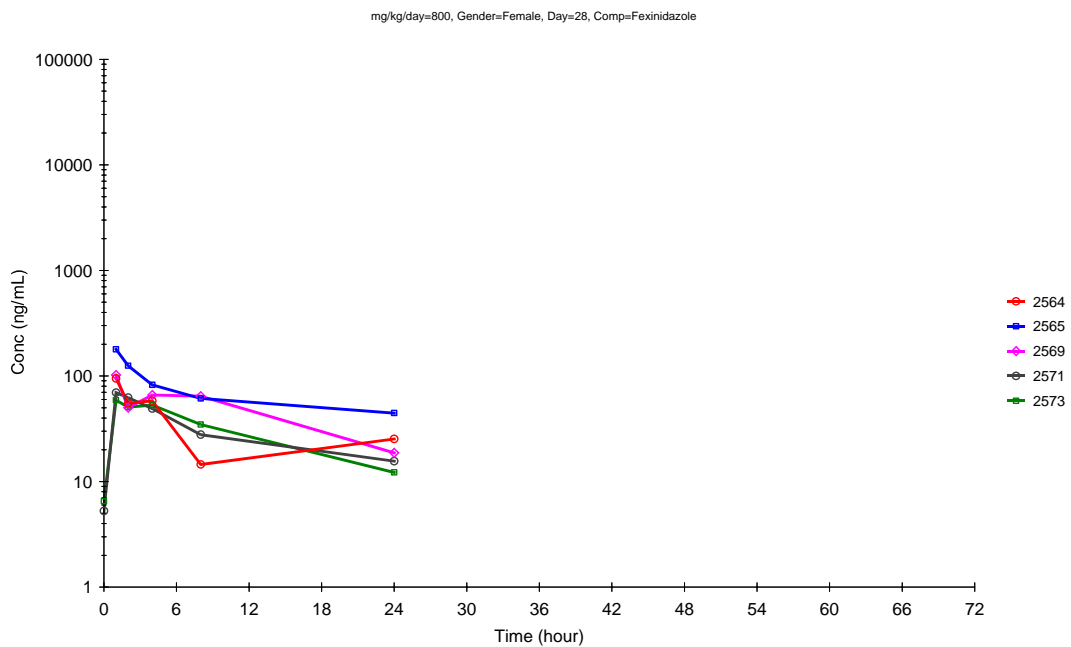
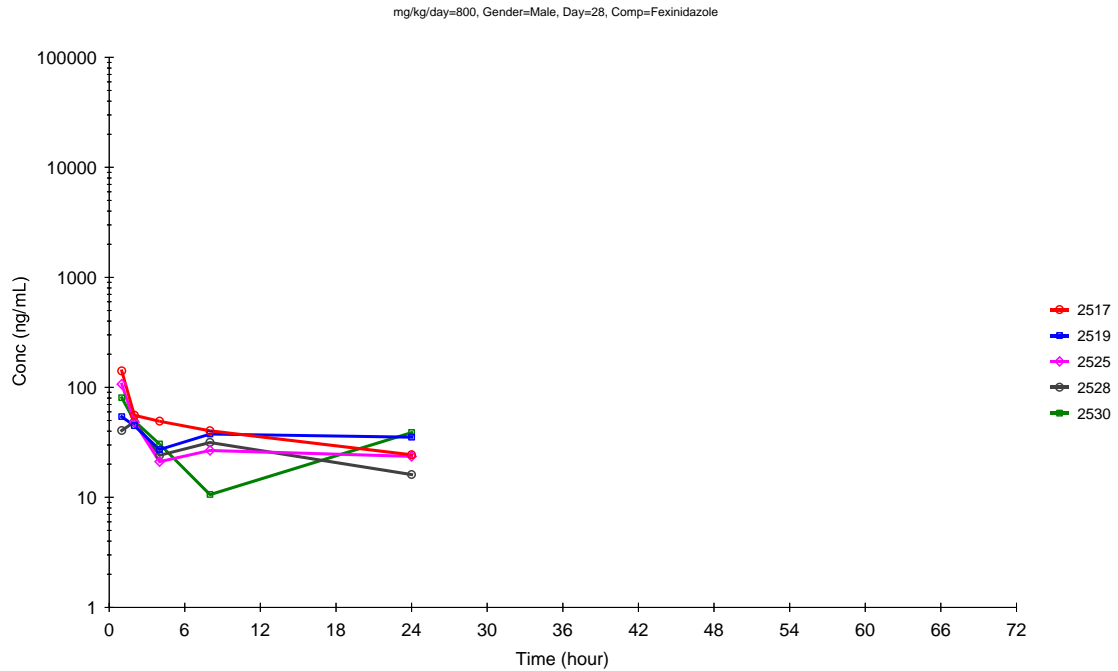
**Figure 11.** Day 14 individual plasma concentrations (ng/mL) of sulfone metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



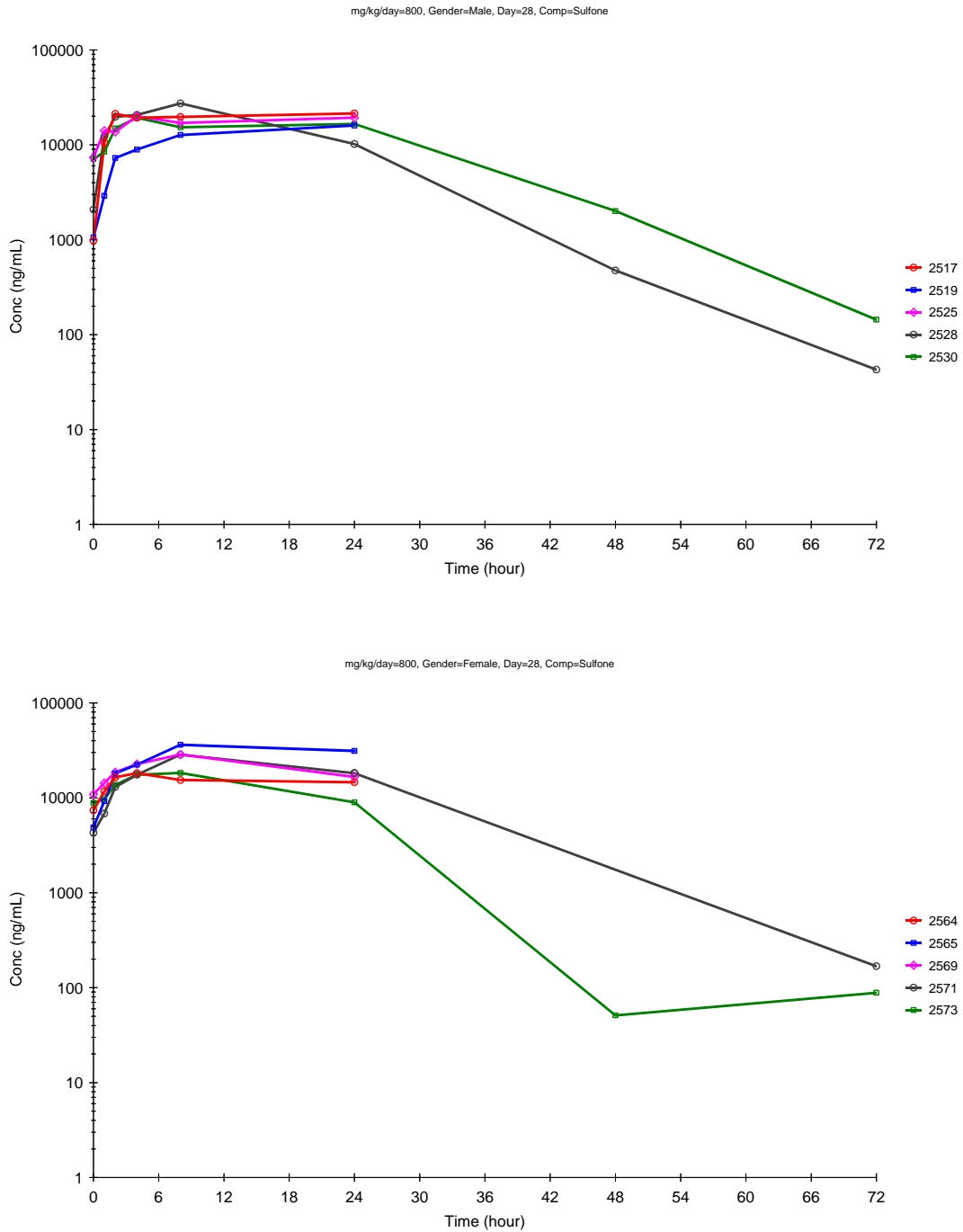
**Figure 12.** Day 14 individual plasma concentrations (ng/mL) of sulfoxide metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



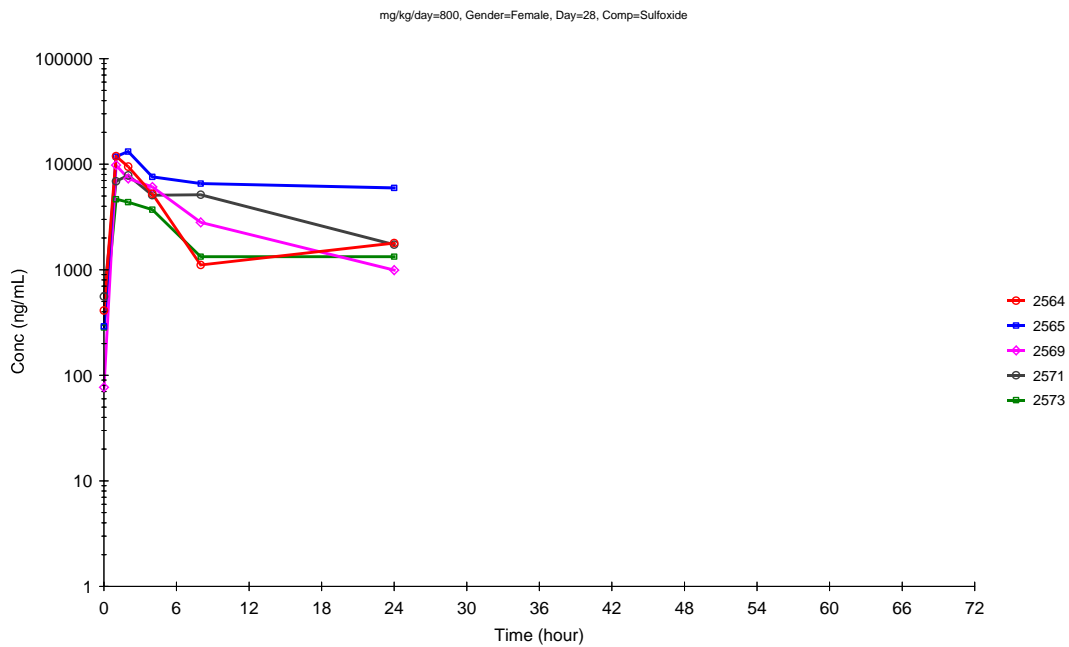
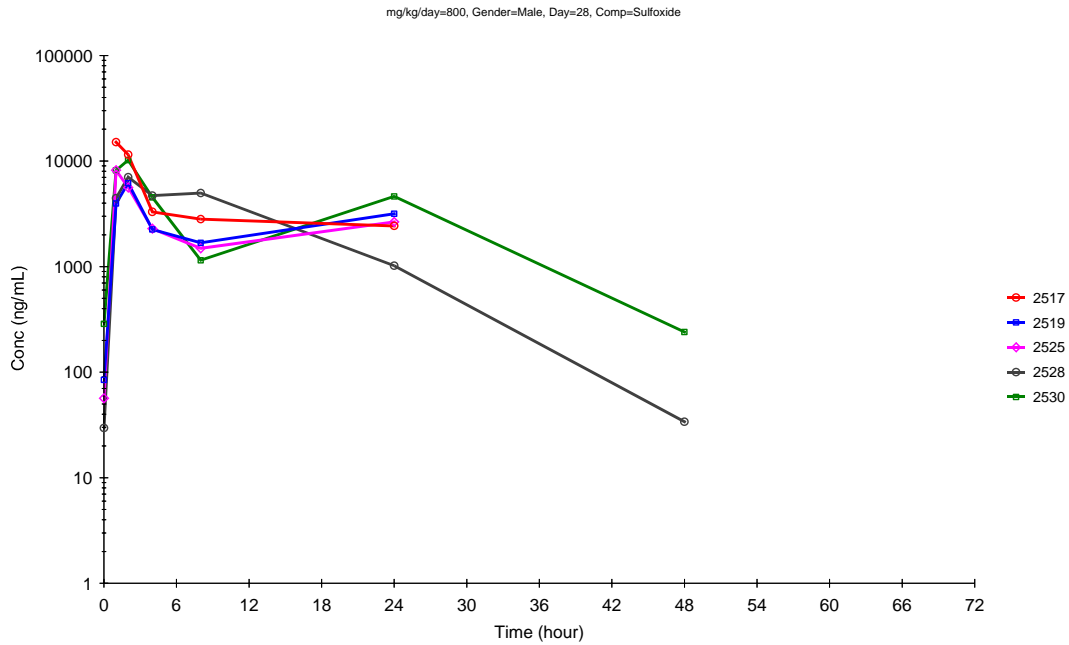
**Figure 13.** Day 28 individual plasma concentrations (ng/mL) of Fexinidazole after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



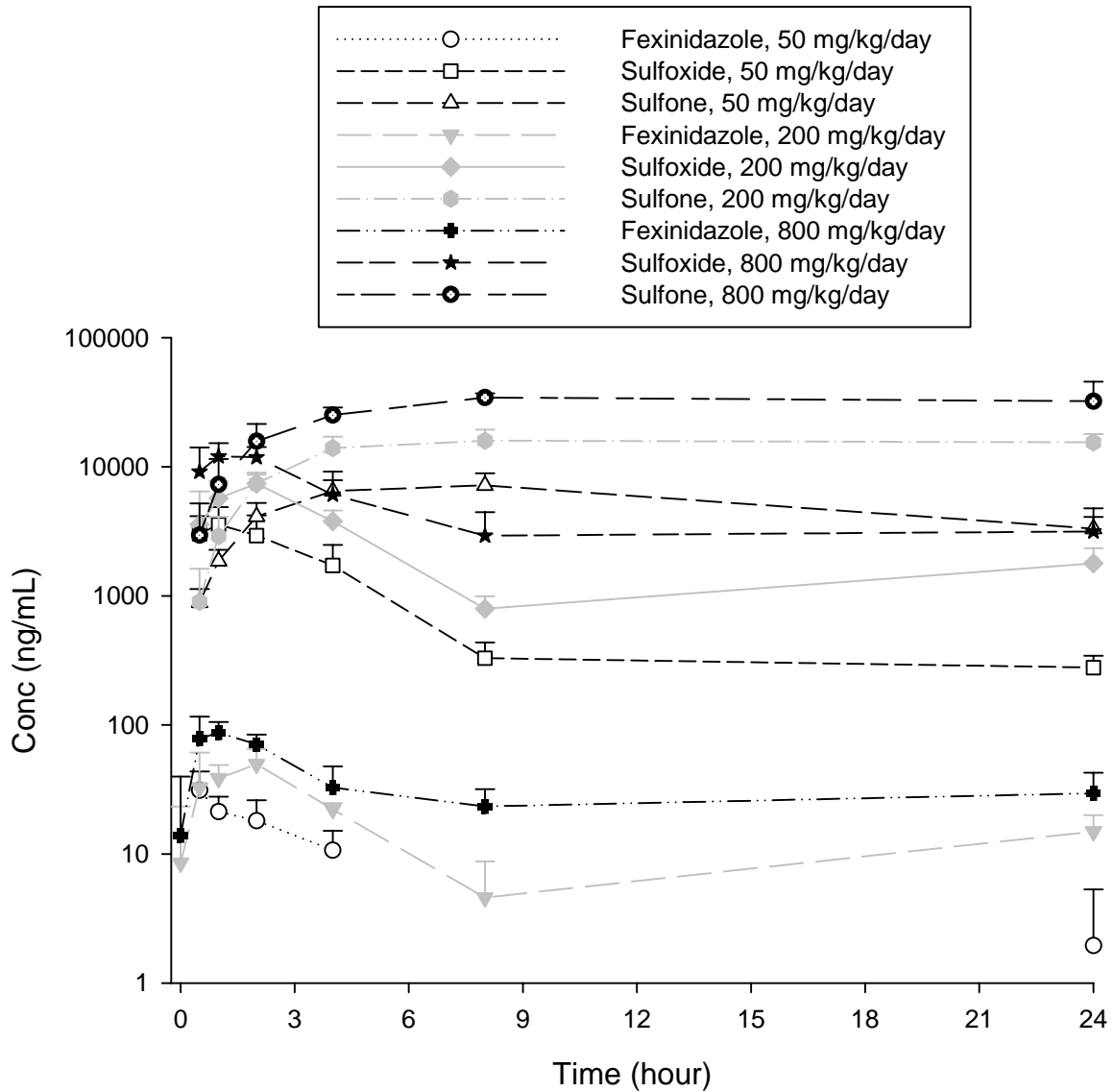
**Figure 14.** Day 28 individual plasma concentrations (ng/mL) of sulfone metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.



**Figure 15.** Day 28 individual plasma concentrations (ng/mL) of sulfoxide metabolite after oral 800 mg/kg/day dose of Fexinidazole in male (upper panel) and female (lower panel) Beagle dogs.

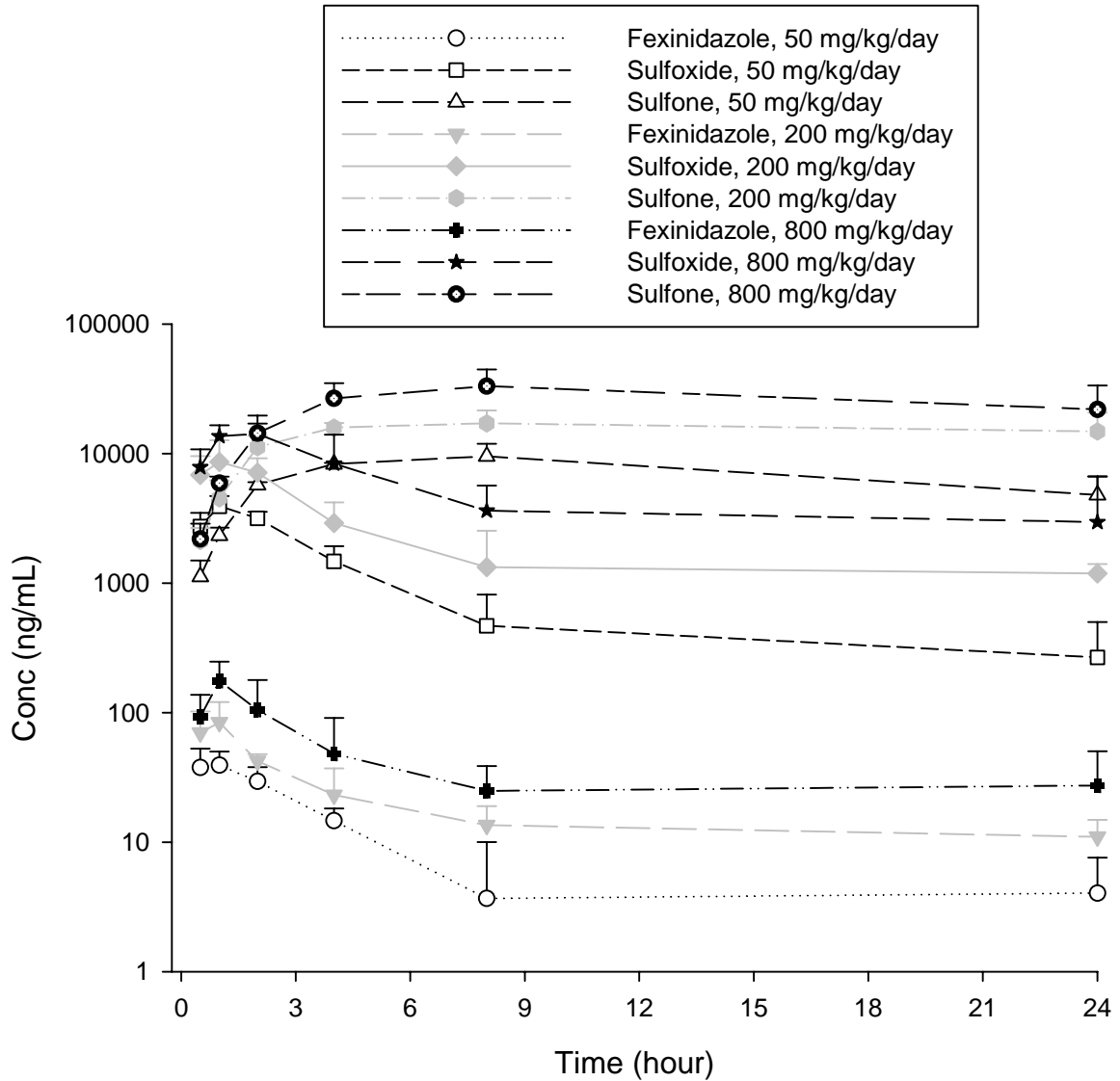


**Figure 16.** Day 1 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.

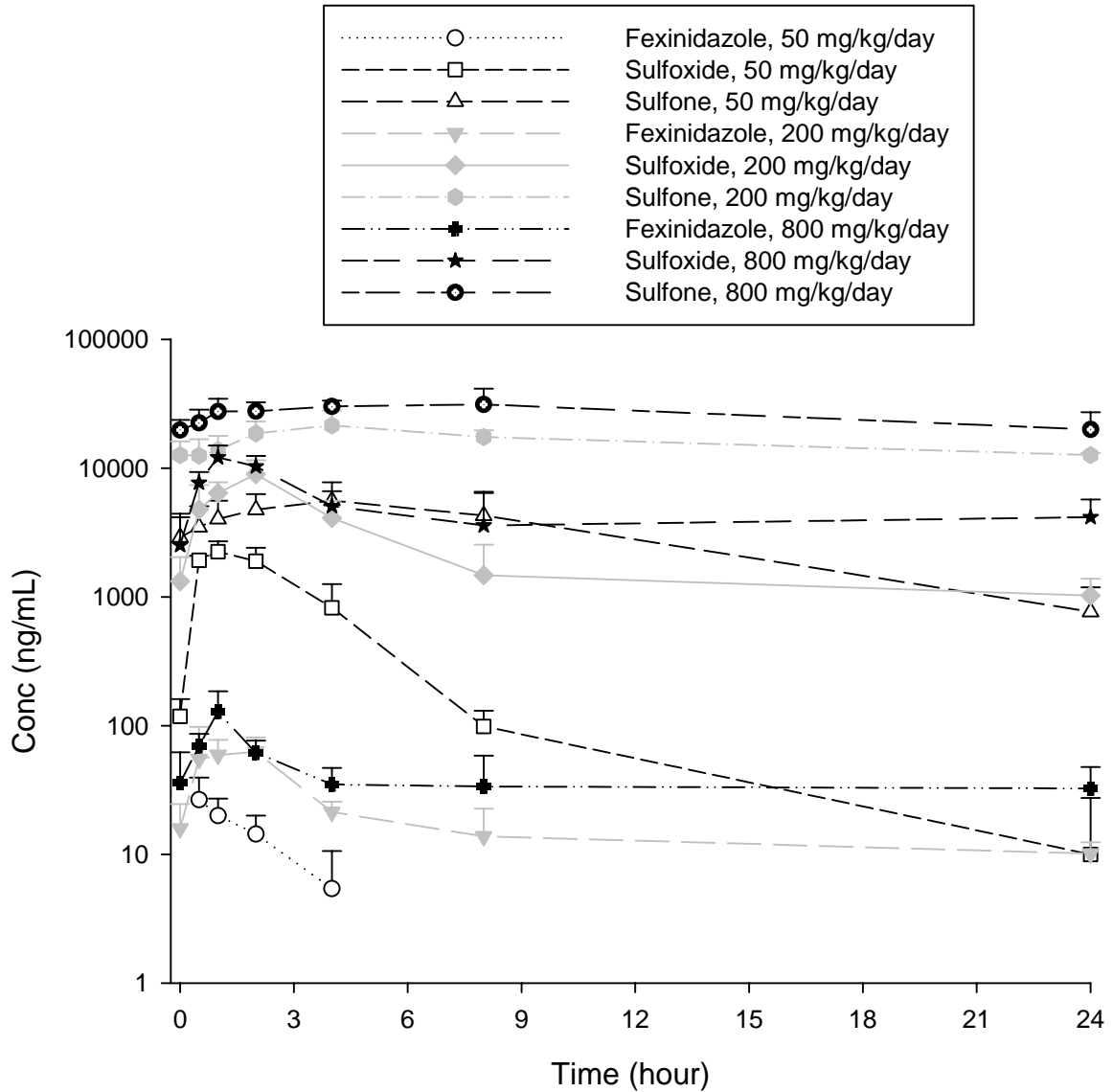




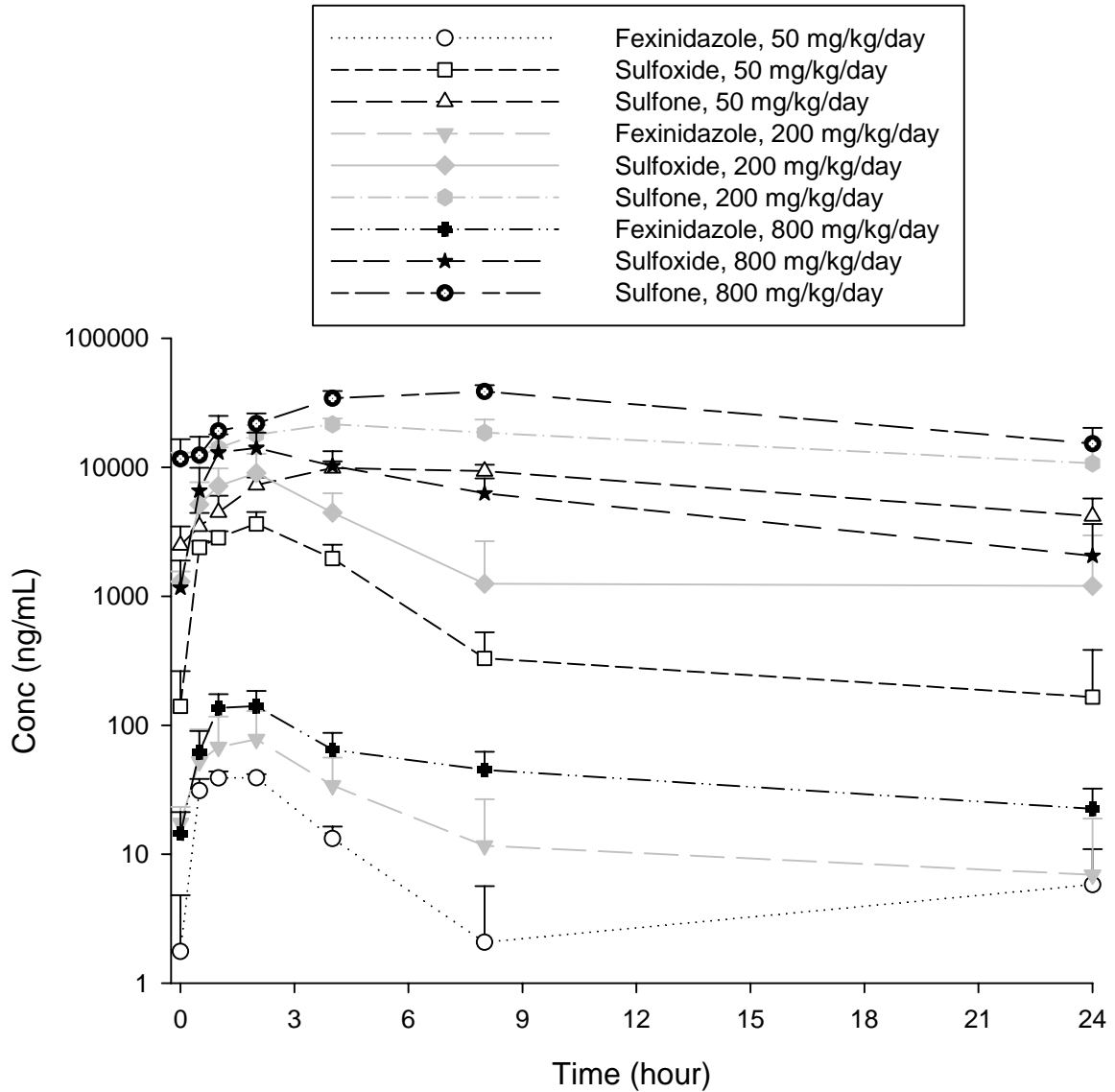
**Figure 17.** Day 1 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.



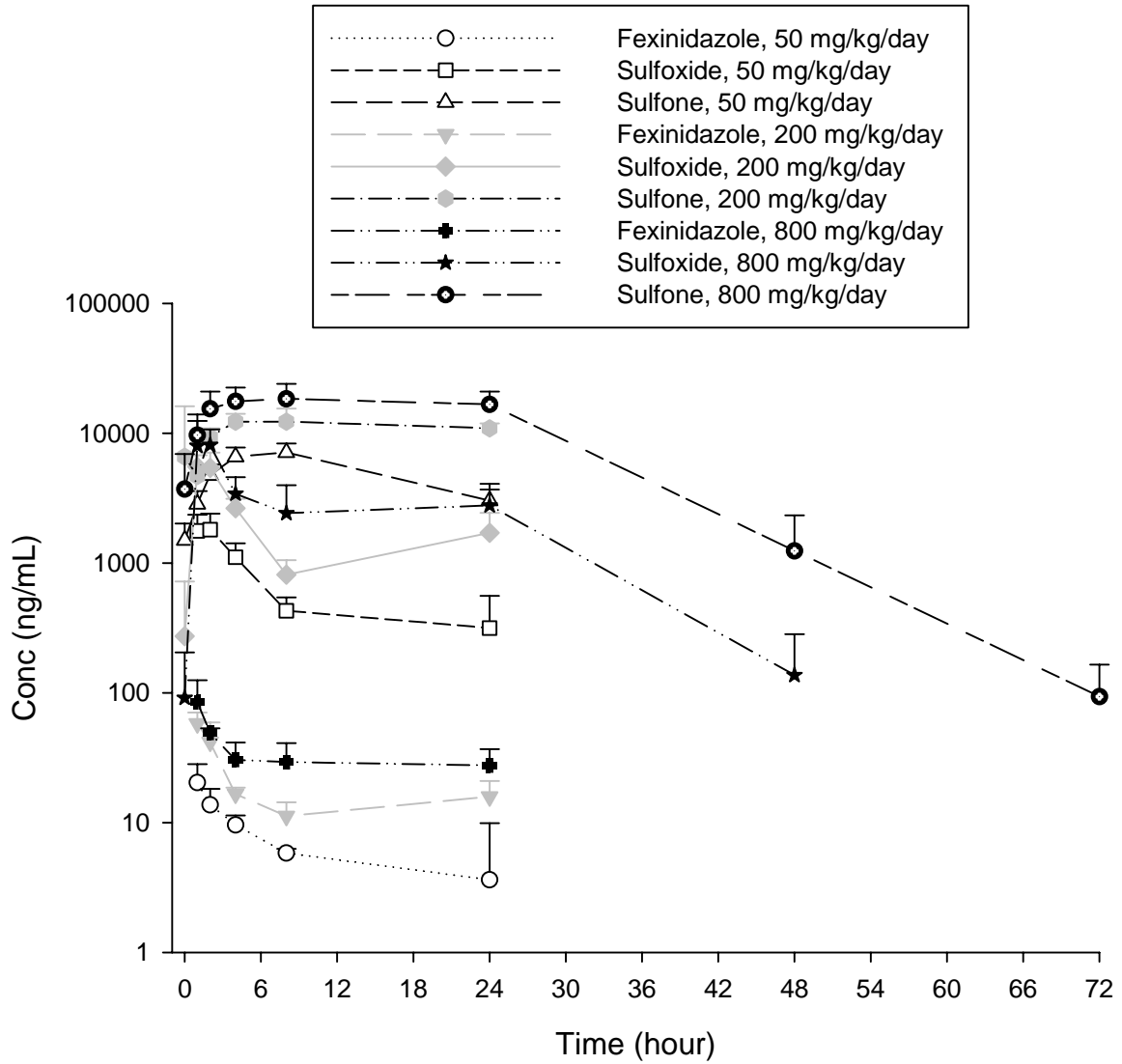
**Figure 18.** Day 14 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.



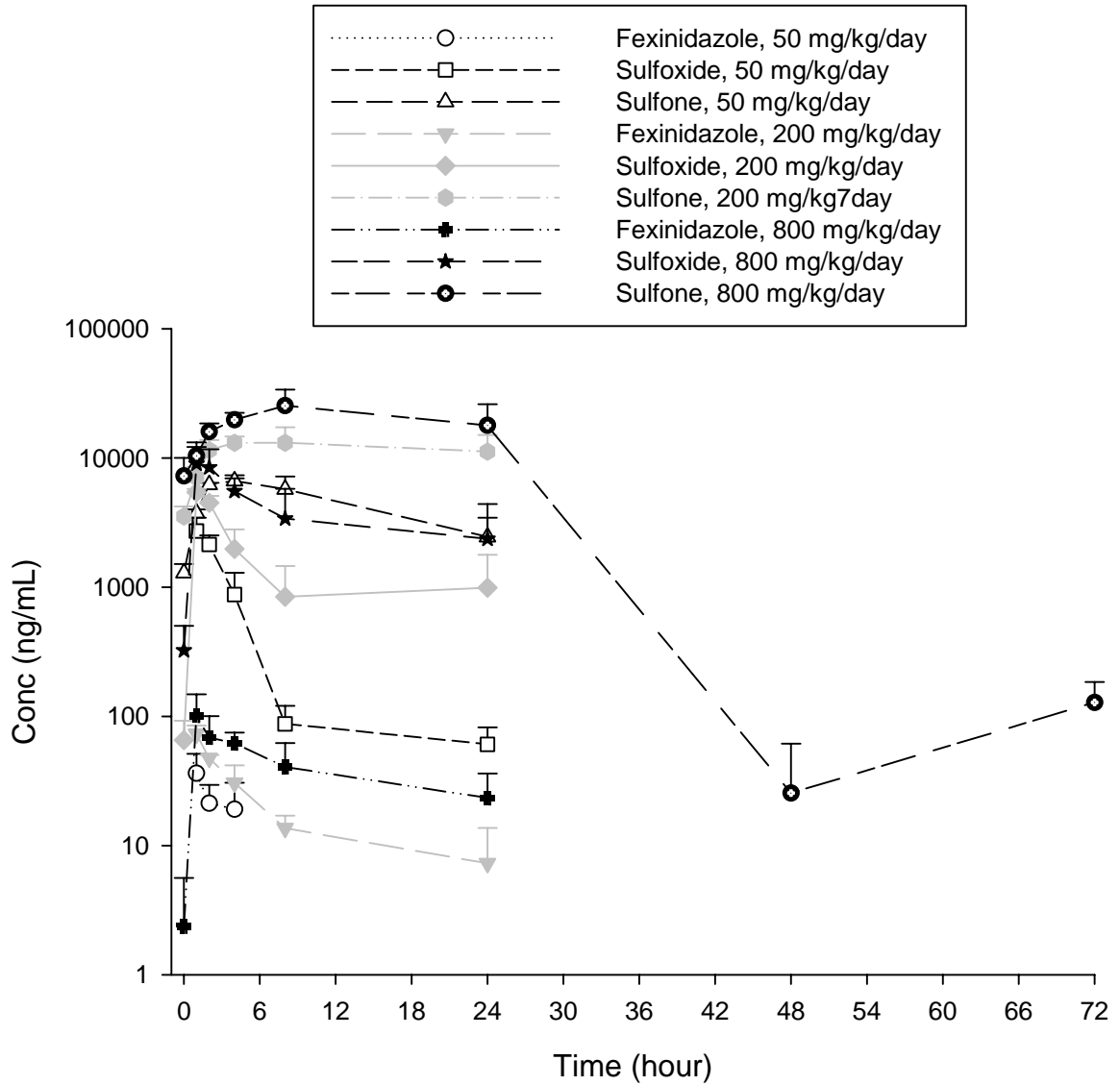
**Figure 19.** Day 14 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.



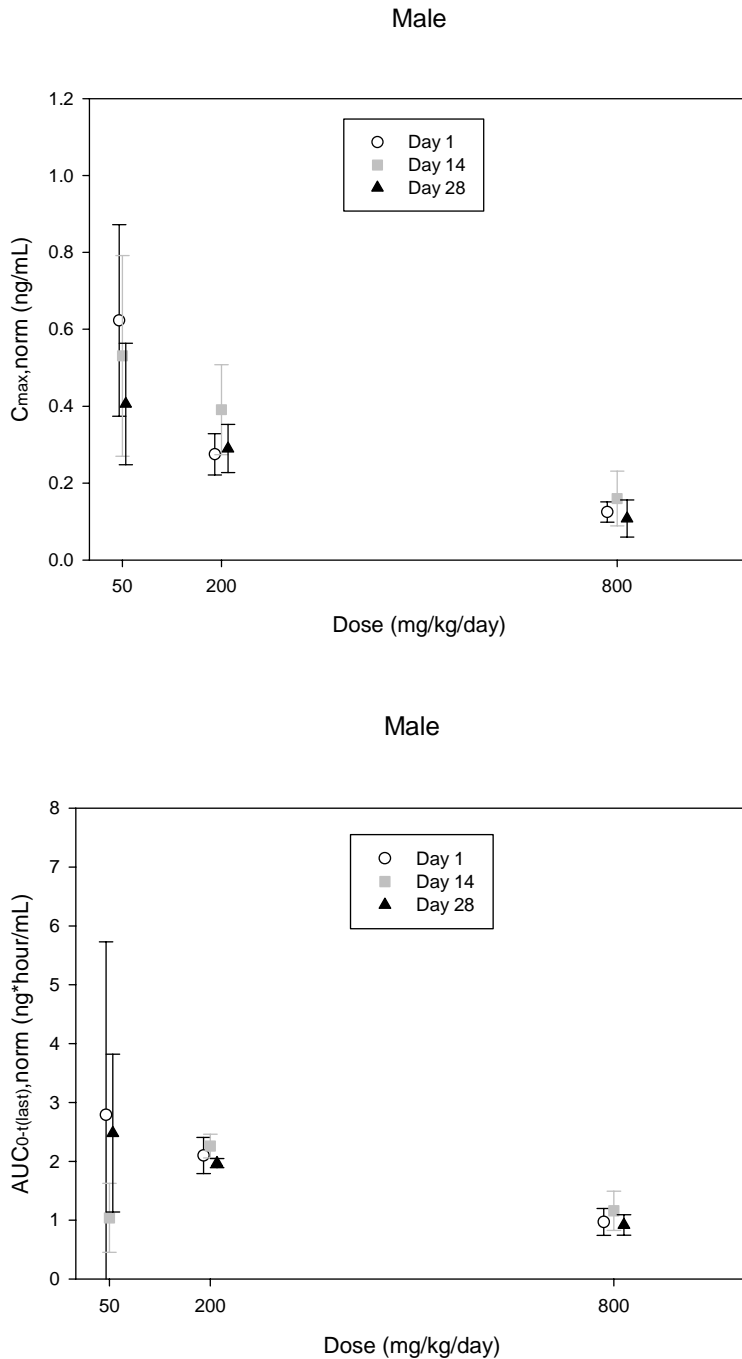
**Figure 20.** Day 28 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.



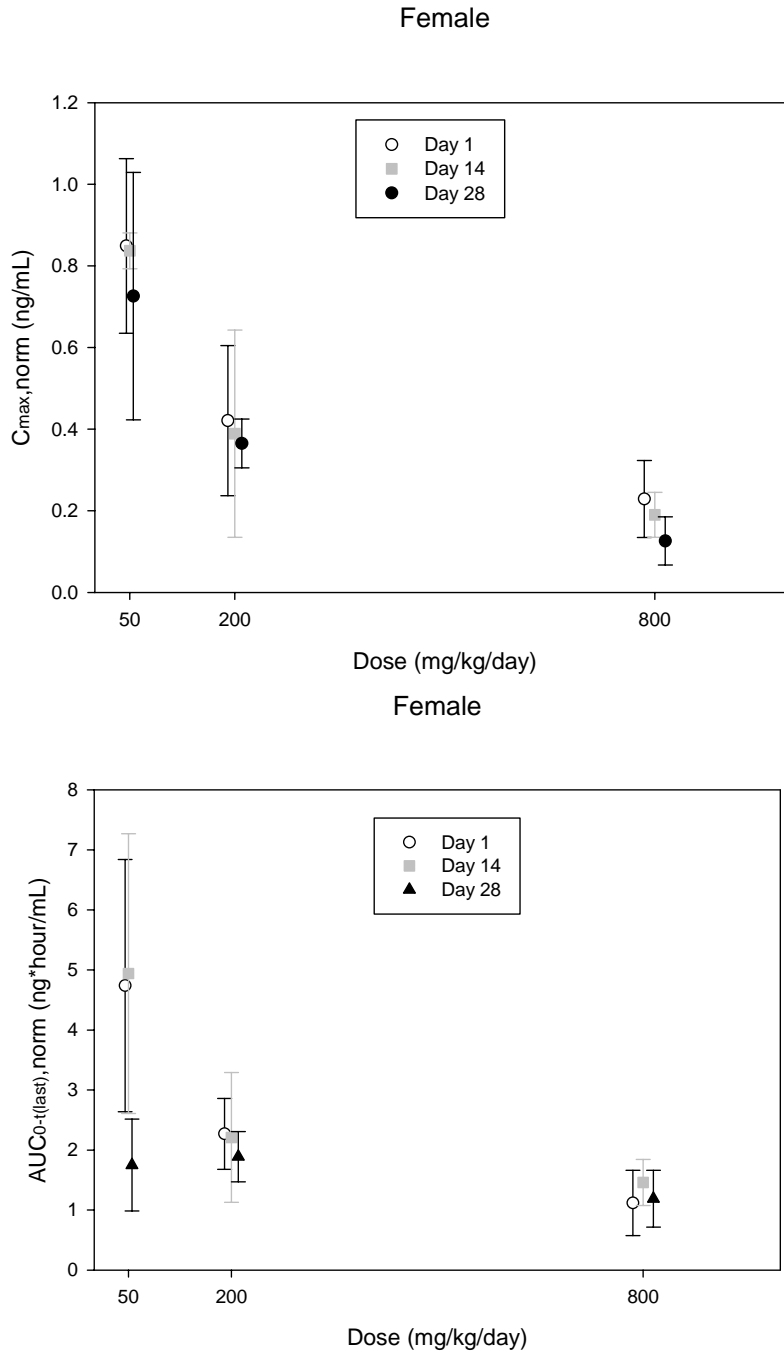
**Figure 21.** Day 28 mean (+SD) plasma concentrations (ng/mL) of Fexinidazole and metabolites after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.



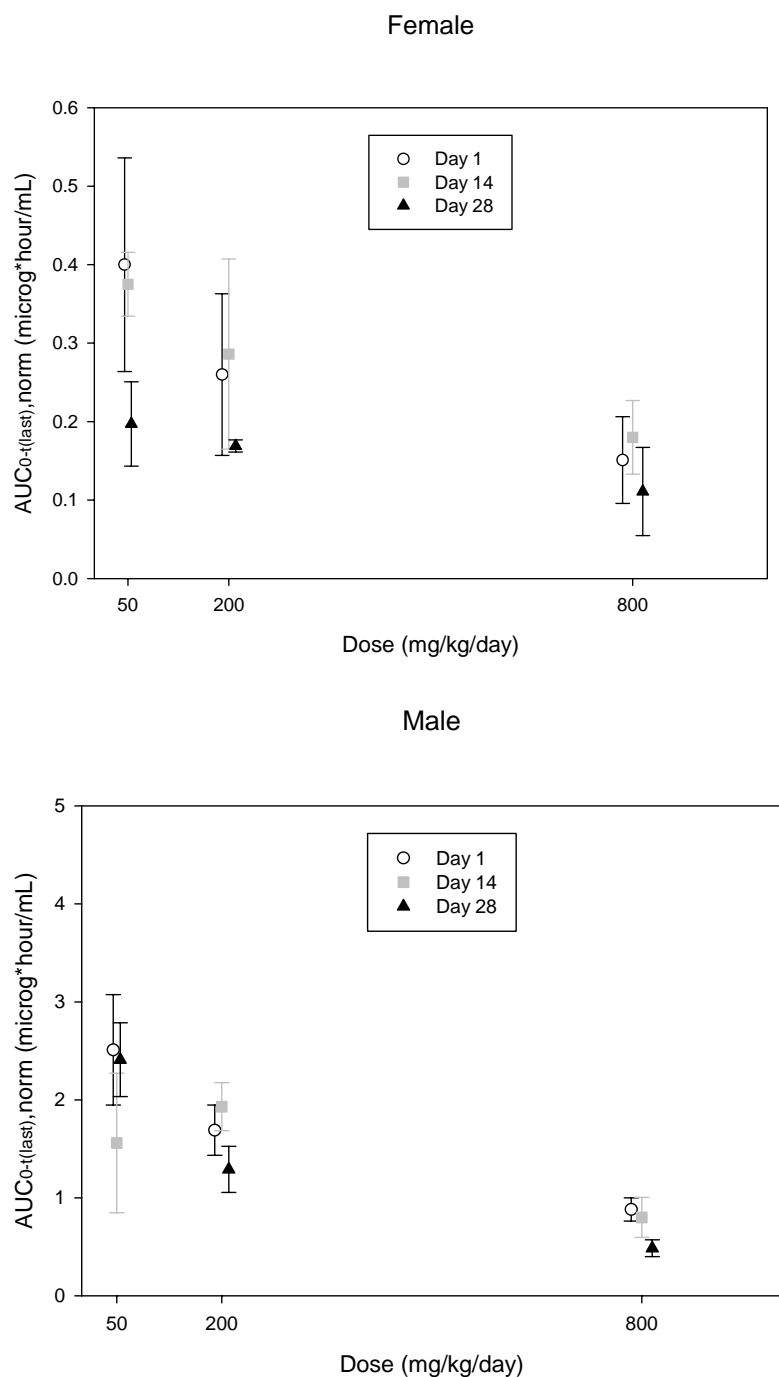
**Figure 22.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of Fexinidazole after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.



**Figure 23.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of Fexinidazole after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.

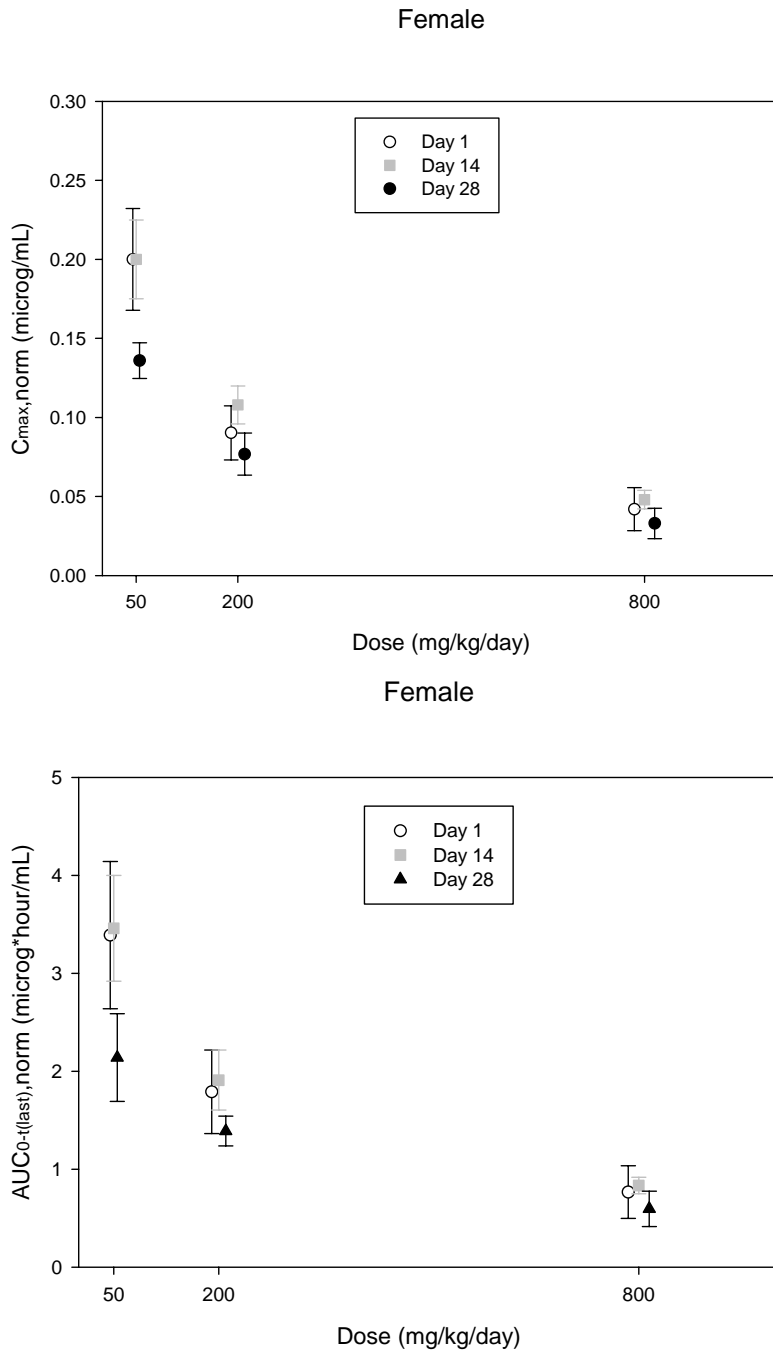


**Figure 24.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of sulfone derivative after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.

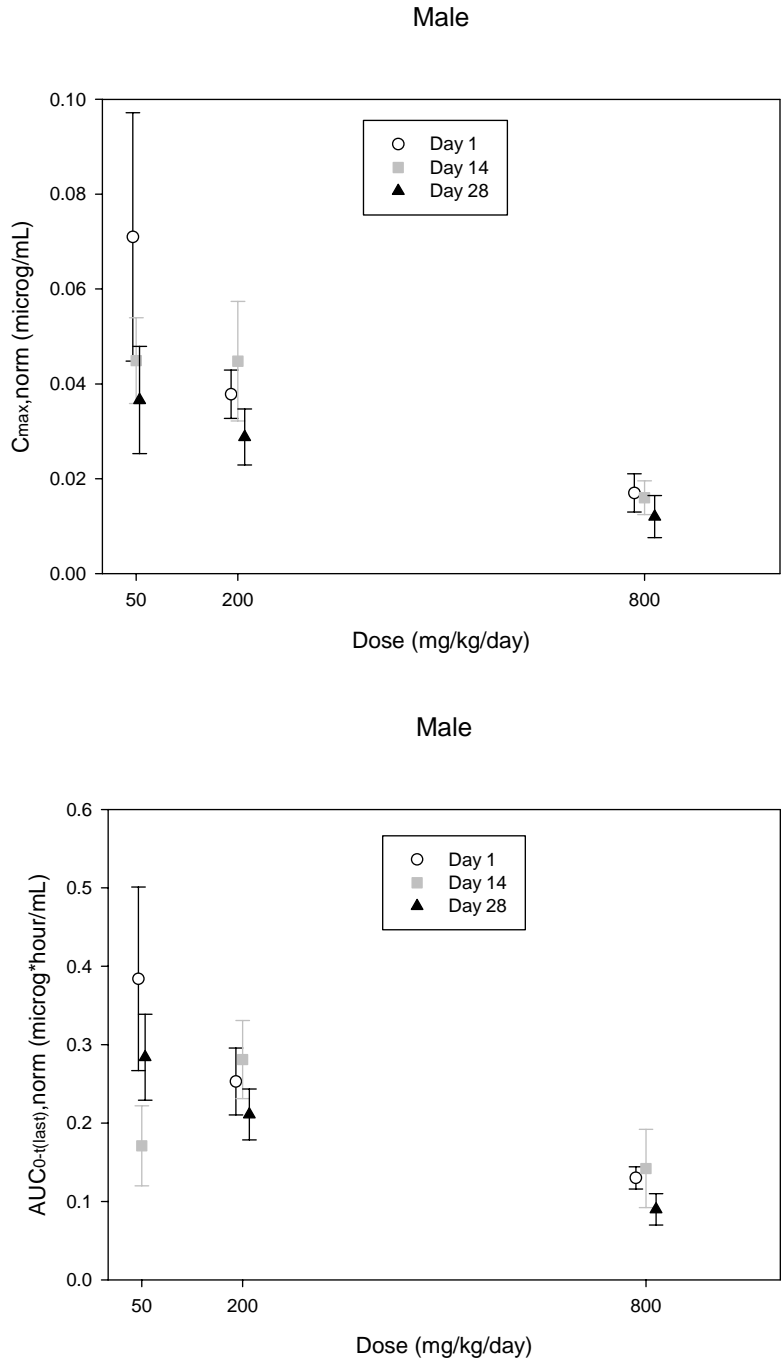




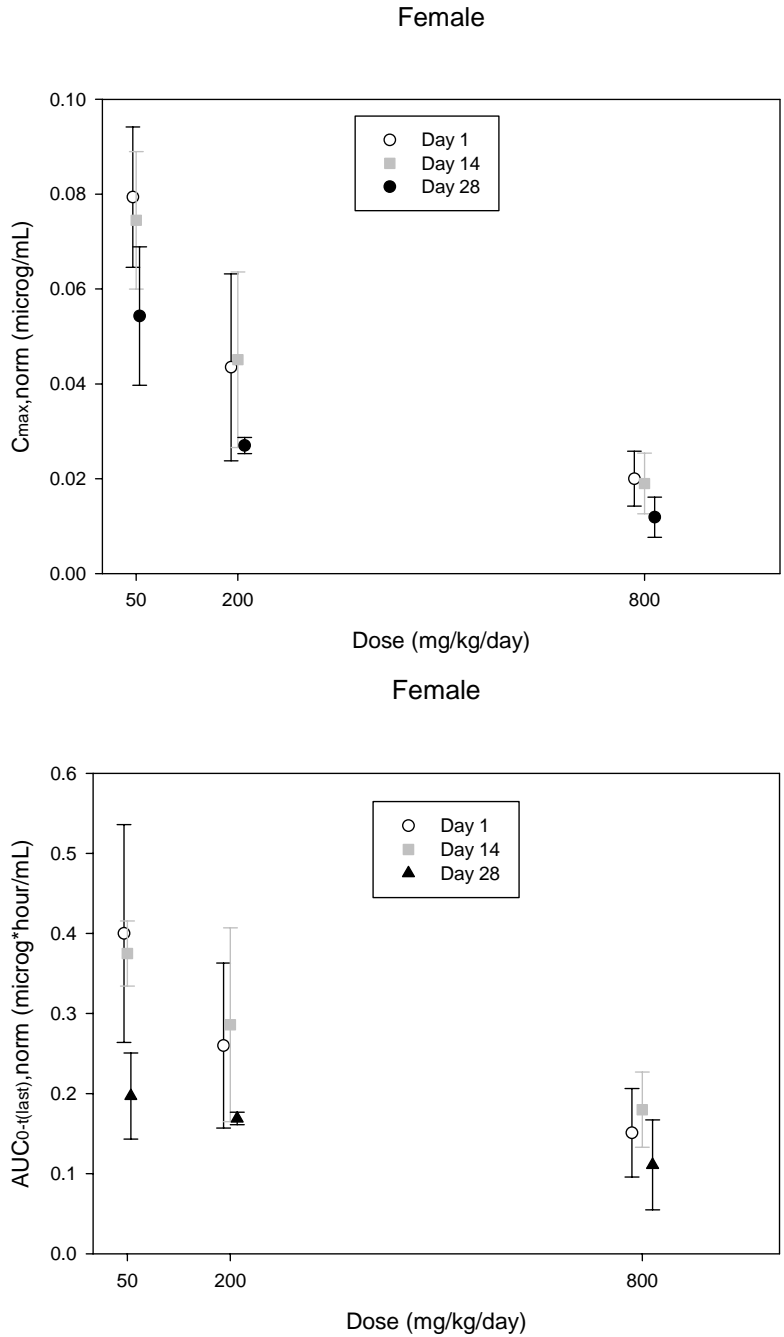
**Figure 25.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of sulfone derivative after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.



**Figure 26.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of sulfoxide derivative after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in male Beagle dogs.



**Figure 27.** Mean ( $\pm$ SD) normalized  $C_{max}$  (upper panel) and  $AUC_{0-t(last)}$  (lower panel) of sulfoxide derivative after single and repeated oral 50, 200 and 800 mg/kg/day of Fexinidazole in female Beagle dogs.



## **APPENDICES**

### **Appendix 1. Individual plasma concentrations**

**Table 1A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of the vehicle of Fexinidazole to male and female Beagle dogs.

Day 1										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5
2	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5

Day 14										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5
2	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5

Day 28										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5
2	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5

**Table 2A1.** Individual plasma concentrations (ng/mL) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of the vehicle of Fexinidazole to male and female Beagle dogs.

Day 1										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

Day 14										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

Day 28										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

**Table 3A1.** Individual plasma concentrations (ng/mL) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of the vehicle of Fexinidazole to male and female Beagle dogs.

Day 1										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

Day 14										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

Day 28										
Time	Dog ID									
(hour)	2516	2518	2520	2527	2533	2560	2568	2572	2575	2577
0	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25

**Table 4A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2514	ID 2521	ID 2529	Mean	SD
Day 1					
0	<5	<5	<5	N/A	N/A
0.5	45.5	23.1	24.9	31.2	12.4
1	28.3	20.0	15.6	21.3	6.45
2	26.0	18.1	10.1	18.1	7.95
4	15.2	10.4	6.38	10.7	4.42
8	<5	<5	<5	N/A	N/A
24	5.86	<5	<5	1.95*	3.38
Day 14					
0	<5	<5	<5	N/A	N/A
0.5	41.4	21.1	17.1	26.5	13.0
1	28.2	16.6	15.2	20.0	7.14
2	20.6	13.0	9.70	14.4	5.59
4	10.4	5.84	<5	5.41	5.21
8	<5	<5	<5	N/A	N/A
24	<5	<5	<5	N/A	N/A
Day 28					
0	<5	<5	<5	N/A	N/A
1	29.3	17.0	14.6	20.3	7.89
2	18.8	10.2	12.0	13.7	4.54
4	11.6	8.47	8.77	9.61	1.73
8	5.89	6.23	5.34	5.82	0.449
24	<5	10.9	<5	3.63*	6.29

Estimates of mean based on approximation that values below LLOQ are equal to zero. For values marked \*, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.

N/A: not applicable.



**Table 5A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2562	ID 2563	ID 2576	Mean	SD
Day 1					
0	<5	<5	<5	N/A	N/A
0.5	24.8	54.3	34.1	37.7	15.1
1	35.7	51.4	30.5	39.2	10.9
2	38.8	27.4	22.3	29.5	8.45
4	18.6	11.6	13.5	14.6	3.62
8	11.0	<5	<5	3.67*	6.35
24	6.79	<5	5.32	4.04	3.57
Day 14					
0	5.28	<5	<5	1.76*	3.05
0.5	37.6	32.5	23.3	31.1	7.25
1	44.4	35.3	37.2	39.0	4.80
2	36.1	40.8	40.4	39.1	2.61
4	9.57	14.4	15.5	13.2	3.15
8	6.20	<5	<5	2.07*	3.58
24	9.81	<5	7.58	5.80	5.14
Day 28					
0	<5	<5	<5	N/A	N/A
1	23.5	53.0	32.4	36.3	15.1
2	18.0	30.6	15.2	21.3	8.20
4	12.4	32.5	12.3	19.1	11.6
8	<5	<5	<5	N/A	N/A
24	<5	<5	<5	N/A	N/A
<p>Estimates of mean based on approximation that values below LLOQ are equal to zero. For values marked *, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.</p> <p>N/A: not applicable.</p>					

**Table 6A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2515	ID 2523	ID 2526	Mean	SD
Day 1					
0	<5	<5	25.6 <sup>(1)</sup>	N/A	N/A
0.5	46.4	<5	51.3	32.6	28.3
1	35.3	30.1	50.2	38.5	10.4
2	38.9	67.0	42.9	49.6	15.2
4	21.5	25.0	19.9	22.1	2.61
8	<5	5.71	8.09	4.60	4.16
24	12.2	11.8	20.8	14.9	5.08
Day 14					
0	7.72	14.7	25.1	15.8	8.75
0.5	52.6	12.6	98.8	54.7	43.1
1	41.5	57.2	78.4	59.0	18.5
2	48.1	82.9	56.9	62.6	18.1
4	18.6	26.3	19.0	21.3	4.33
8	23.9	9.89	7.59	13.8	8.83
24	8.08	12.6	9.57	10.1	2.30
Day 28					
0	<5	<5	<5	N/A	N/A
1	71.2	56.1	46.3	57.9	12.5
2	59.7	40.4	24.9	41.7	17.4
4	18.9	15.3	15.5	16.6	2.02
8	11.3	8.05	14.3	11.2	3.13
24	9.86	18.5	19.0	15.8	5.14

<sup>(1)</sup> Likely due to contamination.

Estimates of mean based on approximation that values below LLOQ are equal to zero.

N/A: not applicable.

**Table 7A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2561	ID 2570	ID 2567	Mean	SD
Day 1					
0	<5	<5	<5	N/A	N/A
0.5	51.0	51.9	107	70.0	32.1
1	57.4	69.0	126	84.1	36.7
2	37.0	41.8	48.0	42.3	5.51
4	14.4	15.7	39.2	23.1	14.0
8	8.98	11.9	19.6	13.5	5.49
24	12.5	13.9	6.61	11.0	3.87
Day 14					
0	11.0	18.8	22.5	17.4	5.87
0.5	27.4	30.1	99.0	52.2	40.6
1	40.3	37.9	124	67.4	49.0
2	42.9	54.2	136	77.7	50.8
4	23.3	19.1	59.5	34.0	22.2
8	5.99	<5	28.7	11.6	15.1
24	<5	20.7	<5	6.90*	12.0
Day 28					
0	<5	<5	<5	N/A	N/A
1	84.0	60.2	74.7	73.0	12.0
2	44.9	50.4	47.0	47.4	2.78
4	33.1	18.1	40.3	30.5	11.3
8	17.6	11.8	11.5	13.6	3.44
24	<5	12.1	9.75	7.28	6.42
<p>Estimates of mean based on approximation that values below LLOQ are equal to zero. For values marked *, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.</p> <p>N/A: not applicable.</p>					

**Table 8A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2517	ID 2519	ID 2525	ID 2528	ID 2530	Mean	SD
Day 1							
0	<5	<5	9.75	59.5	<5	13.9*	25.9
0.5	132	73.8	47.8	97.0	40.0	78.1	37.6
1	86.0	108	60.4	98.8	81.5	86.9	18.2
2	55.6	85.2	80.8	74.1	56.4	70.4	13.7
4	15.5	51.8	25.5	44.6	25.5	32.6	15.0
8	15.5	14.2	24.6	34.3	27.8	23.3	8.46
24	26.8	9.99	37.2	44.9	28.5	29.5	13.1
Day 14							
0	74.9	10.5	15.2	46.6	32.3	35.9	26.1
0.5	74.3	80.9	51.9	87.8	52.1	69.4	16.6
1	130	220	75.1	127	86.9	128	56.9
2	72.8	78.0	42.6	50.3	63.7	61.5	14.9
4	35.1	29.3	55.2	24.0	30.2	34.8	12.1
8	30.9	11.9	7.75	53.4	63.8	33.6	24.8
24	57.5	16.4	27.2	31.7	29.0	32.4	15.2
Day 28							
0	<5	<5	<5	<5	<5	N/A	N/A
1	141	54.1	107	40.5	80.4	84.6	40.5
2	55.7	44.8	48.3	48.4	49.5	49.3	3.97
4	49.2	27.2	21.1	24.1	30.5	30.4	11.1
8	40.3	37.6	26.7	31.5	10.6	29.3	11.7
24	24.4	35.2	23.6	16.1	38.8	27.6	9.24
48				<5	<5	N/A	N/A
72				<5	<5	N/A	N/A
<p>Estimates of mean based on approximation that values below LLOQ are equal to zero. For values marked *, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.</p> <p>N/A: not applicable.</p>							

**Table 9A1.** Individual plasma concentrations (ng/mL) of Fexinidazole after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2564	ID 2565	ID 2569	ID 2571	ID 2573	Mean	SD
Day 1							
0	<5	<5	<5	<5	<5	N/A	N/A
0.5	156	115	89.8	45.5	57.0	92.7	44.8
1	293	195	128	135	129	176	71.1
2	96.9	233	59.6	52.4	80.7	105	73.9
4	39.7	124	29.8	21.3	25.8	48.1	43.0
8	32.9	40.9	29.5	11.4	9.08	24.8	13.9
24	<5	30.1	54.1	44.4	8.04	27.3	23.1
Day 14							
0	10.7	22.4	5.14	17.5	16.6	14.5	6.67
0.5	96.7	74.8	30.0	33.8	72.5	61.6	28.7
1	194	134	139	89.2	124	136	37.8
2	161	171	182	79.2	109	140	44.2
4	53.4	99.3	72.2	58.3	39.1	64.5	22.8
8	39.5	73.5	27.2	41.0	43.9	45.0	17.2
24	34.9	28.2	16.7	9.66	22.6	22.4	9.81
Day 28							
0	<5	<5	<5	5.26	6.52	2.36*	3.26
1	94.7	179	102	69.5	59.0	101	47.1
2	55.2	125	50.1	62.4	50.7	68.7	31.9
4	58.2	82.3	66.0	49.0	53.0	61.7	13.2
8	14.5	61.3	64.4	27.8	34.7	40.5	21.6
24	25.3	44.5	18.7	15.6	12.2	23.3	12.8
48				<5	<5	N/A	N/A
72				<5	<5	N/A	N/A
<p>Estimates of mean based on approximation that values below LLOQ are equal to zero. For values marked *, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.</p> <p>N/A: not applicable.</p>							

**Table 10A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2514	ID 2521	ID 2529	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	1.13	0.650	0.882	0.887	0.240
1	2.18	1.39	2.00	1.86	0.414
2	5.25	3.00	4.08	4.11	1.13
4	8.04	5.93	5.45	6.47	1.38
8	9.17	6.33	6.02	7.17	1.74
24	4.00	2.47	3.46	3.31	0.776
Day 14					
0	4.48	2.75	1.46	2.90	1.52
0.5	5.16	3.24	2.07	3.49	1.56
1	5.77	3.54	2.78	4.03	1.55
2	6.46	4.21	3.57	4.75	1.52
4	8.09	4.44	4.18	5.57	2.19
8	6.60	3.80	2.40	4.27	2.14
24	1.17	0.791	0.336	0.766	0.418
Day 28					
0	1.75	1.85	0.904	1.50	0.520
1	3.55	2.94	2.07	2.85	0.744
2	5.85	4.52	3.88	4.75	1.00
4	7.91	6.22	5.63	6.59	1.18
8	8.43	6.87	6.04	7.11	1.21
24	2.88	3.75	2.44	3.02	0.667
N/A: not applicable.					

**Table 11A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2562	ID 2563	ID 2576	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	0.688	1.26	1.40	1.12	0.377
1	2.13	2.74	2.13	2.33	0.352
2	5.74	6.02	5.43	5.73	0.295
4	8.15	8.32	8.45	8.31	0.150
8	11.5	6.89	10.2	9.53	2.38
24	6.07	2.69	5.64	4.80	1.84
Day 14					
0	3.20	2.89	1.35	2.48	0.991
0.5	4.49	3.31	2.61	3.47	0.950
1	6.22	3.85	3.37	4.48	1.53
2	8.34	6.22	7.27	7.28	1.06
4	10.3	8.43	10.8	9.84	1.25
8	10.6	8.54	8.86	9.33	1.11
24	5.84	3.93	2.74	4.17	1.56
Day 28					
0	1.46	1.37	1.04	1.29	0.221
1	3.58	4.04	3.66	3.76	0.246
2	6.01	6.18	6.44	6.21	0.217
4	6.50	7.43	6.03	6.65	0.712
8	4.04	6.75	6.36	5.72	1.47
24	1.56	3.53	2.26	2.45	0.999

N/A: not applicable.

**Table 12A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2515	ID 2523	ID 2526	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	1.30	0.0676	1.33	0.899	0.720
1	3.32	1.55	3.82	2.90	1.19
2	6.43	6.49	9.25	7.39	1.61
4	10.3	16.1	15.3	13.9	3.14
8	12.3	16.4	19.1	15.9	3.42
24	16.0	12.7	17.5	15.4	2.46
Day 14					
0	9.88	11.2	16.6	12.6	3.56
0.5	8.65	11.9	17.0	12.5	4.21
1	9.32	15.2	17.0	13.8	4.02
2	14.9	17.5	23.5	18.6	4.41
4	13.9	24.2	26.1	21.4	6.56
8	15.6	16.7	20.0	17.4	2.29
24	12.8	12.9	12.0	12.6	0.493
Day 28					
0	1.37	0.840	17.6	6.60	9.53
1	4.47	3.90	5.71	4.69	0.925
2	8.89	8.06	11.1	9.35	1.57
4	11.5	11.1	14.4	12.3	1.80
8	13.3	8.70	14.9	12.3	3.22
24	10.2	10.5	12.1	10.9	1.02
N/A: not applicable.					



**Table 13A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2561	ID 2570	ID 2567	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	1.87	1.75	2.75	2.12	0.546
1	2.98	4.24	6.34	4.52	1.70
2	8.41	13.3	12.0	11.2	2.53
4	14.4	16.4	17.0	15.9	1.36
8	13.3	15.9	22.0	17.1	4.47
24	15.8	8.40	20.1	14.8	5.92
Day 14					
0	13.2	10.5	10.8	11.5	1.48
0.5	12.5	11.2	12.9	12.2	0.889
1	14.1	14.0	14.3	14.1	0.153
2	15.4	16.6	21.6	17.9	3.29
4	19.3	21.2	24.0	21.5	2.36
8	15.1	16.3	24.1	18.5	4.89
24	7.52	16.7	7.79	10.7	5.22
Day 28					
0	2.75	4.04	3.79	3.53	0.684
1	8.58	5.69	7.00	7.09	1.45
2	14.0	9.56	10.9	11.5	2.28
4	14.8	11.8	12.6	13.1	1.55
8	17.9	9.94	11.6	13.1	4.20
24	8.18	15.6	9.94	11.2	3.88
N/A: not applicable.					

**Table 14A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2517	ID 2519	ID 2525	ID 2528	ID 2530	Mean	SD
Day 1							
0	<0.025	<0.025	<0.025	<0.025	<0.025	N/A	N/A
0.5	6.69	1.53	1.73	3.38	1.40	2.95	2.24
1	14.5	4.86	5.62	7.18	4.31	7.29	4.17
2	25.3	12.3	12.7	16.8	11.5	15.7	5.74
4	30.3	25.2	23.8	25.8	20.4	25.1	3.58
8	30.8	37.2	33.8	33.0	36.5	34.3	2.62
24	39.8	9.17	43.0	36.4	31.9	32.1	13.4
Day 14							
0	18.9	13.5	19.8	23.6	22.5	19.7	3.94
0.5	25.2	15.3	18.0	30.5	23.1	22.4	5.99
1	30.2	21.4	22.1	38.4	25.4	27.5	7.02
2	25.6	21.1	28.2	34.2	29.0	27.6	4.80
4	33.8	25.3	29.8	29.2	32.5	30.1	3.29
8	27.2	21.4	23.5	42.5	41.5	31.2	10.1
24	27.9	10.3	14.6	24.1	22.4	19.9	7.21
Day 28							
0	0.978	1.06	7.36	2.08	7.06	3.71	3.23
1	10.6	2.91	14.1	12.2	8.46	9.65	4.30
2	21.2	7.27	13.7	19.7	14.9	15.4	5.51
4	19.3	8.92	20.0	20.7	19.3	17.6	4.91
8	19.7	12.7	17.0	27.3	15.3	18.4	5.59
24	21.4	16.0	19.3	10.2	16.6	16.7	4.23
48				0.475	2.01	1.24	1.09
72				0.0428	0.144	0.0934	0.0716
N/A: not applicable.							

**Table 15A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfone metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2564	ID 2565	ID 2569	ID 2571	ID 2573	Mean	SD
Day 1							
0	<0.025	<0.025	<0.025	<0.025	<0.025	N/A	N/A
0.5	2.67	2.43	2.90	1.31	1.62	2.19	0.688
1	6.45	5.78	6.86	5.09	5.41	5.92	0.730
2	16.5	16.9	14.8	10.2	13.7	14.4	2.69
4	29.2	38.7	27.8	18.0	20.0	26.7	8.25
8	35.0	44.9	43.1	21.7	21.1	33.2	11.4
24	15.4	31.5	33.5	23.8	5.44	21.9	11.7
Day 14							
0	11.9	13.9	3.20	15.2	13.8	11.6	4.84
0.5	14.6	13.8	4.02	16.5	12.9	12.4	4.85
1	24.9	20.7	9.46	22.0	18.2	19.1	5.88
2	27.3	21.5	15.4	23.2	21.8	21.8	4.28
4	36.9	41.0	32.0	32.0	29.0	34.2	4.75
8	37.3	47.0	36.1	37.2	35.6	38.6	4.73
24	17.8	14.3	18.9	6.89	18.2	15.2	4.98
Day 28							
0	7.38	4.88	10.9	4.30	8.83	7.26	2.75
1	11.7	9.22	14.3	6.83	9.70	10.4	2.81
2	16.4	18.1	18.6	13.0	13.7	16.0	2.53
4	18.2	22.4	22.7	17.5	17.5	19.7	2.66
8	15.4	36.2	28.6	28.5	18.3	25.4	8.47
24	14.6	31.2	16.6	18.2	8.97	17.9	8.21
48				<0.025	0.0510	0.0255	0.0361
72				0.168	0.0883	0.128	0.0564
Estimates of mean based on approximation that values below LLOQ (0.025 $\mu\text{g/mL}$ ) are equal to zero.							
N/A: not applicable.							

**Table 16A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2514	ID 2521	ID 2529	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	4.3	2.21	2.54	3.02	1.12
1	5.04	2.65	2.95	3.55	1.3
2	4.36	2.45	1.97	2.93	1.26
4	2.51	1.64	1.01	1.72	0.753
8	0.375	0.402	0.207	0.328	0.106
24	0.241	0.239	0.353	0.278	0.065
Day 14					
0	0.137	0.148	0.0686	0.118	0.043
0.5	2.11	1.84	1.8	1.92	0.169
1	2.76	2.06	1.91	2.24	0.454
2	2.36	1.96	1.34	1.89	0.514
4	1.29	0.745	0.432	0.822	0.434
8	0.129	0.101	0.0654	0.099	0.032
24	<0.025	0.0301	<0.025	0.01*	0.017
Day 28					
0	<0.025	<0.025	<0.025	N/A	N/A
1	2.44	1.44	1.42	1.77	0.58
2	2.48	1.37	1.57	1.81	0.59
4	1.44	0.826	1.05	1.11	0.31
8	0.395	0.557	0.332	0.428	0.12
24	0.222	0.593	0.132	0.316	0.24
<p>Estimates of mean based on approximation that values below LLOQ (0.025 <math>\mu\text{g/mL}</math>) are equal to zero. For values marked *, more than half of the individual levels were below LLOQ; descriptive statistics was reported even if strongly biased.</p> <p>N/A: not applicable.</p>					

**Table 17A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 50 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2562	ID 2563	ID 2576	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	1.89	3.25	3.09	2.74	0.74
1	3.45	4.82	3.49	3.92	0.78
2	3.6	2.86	3.06	3.17	0.38
4	1.91	0.991	1.5	1.47	0.46
8	0.813	0.115	0.476	0.468	0.35
24	0.426	<0.025	0.376	0.267	0.23
Day 14					
0	0.191	0.229	<0.025	0.14	0.12
0.5	2.72	2.27	2.19	2.39	0.29
1	3.12	2.45	2.95	2.84	0.35
2	2.85	3.53	4.53	3.64	0.85
4	1.4	1.98	2.49	1.96	0.55
8	0.554	0.228	0.204	0.329	0.2
24	0.413	0.0831	<0.025	0.165	0.22
Day 28					
0	<0.025	<0.025	<0.025	N/A	N/A
1	1.91	2.91	3.33	2.72	0.729
2	1.7	2.39	2.32	2.14	0.38
4	0.554	1.35	0.728	0.877	0.418
8	0.0493	0.113	0.0999	0.087	0.034
24	0.0439	0.0851	0.0532	0.061	0.022
Estimates of mean based on approximation that values below LLOQ (0.025 $\mu\text{g/mL}$ ) are equal to zero.					
N/A: not applicable.					

**Table 18A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2515	ID 2523	ID 2526	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	5.43	0.244	4.99	3.55	2.88
1	6.37	3.42	7.27	5.69	2.01
2	5.95	7.97	8.3	7.41	1.27
4	3.05	4.62	3.67	3.78	0.79
8	0.591	0.802	0.988	0.794	0.2
24	1.63	1.31	2.4	1.78	0.56
Day 14					
0	0.494	1.73	1.73	1.32	0.71
0.5	4.8	2.15	7.35	4.77	2.6
1	5.03	6.5	7.71	6.41	1.34
2	6.97	11.8	8.1	8.96	2.53
4	2.77	5.71	3.8	4.09	1.49
8	2.63	1.27	0.518	1.47	1.07
24	0.761	1.44	0.871	1.02	0.36
Day 28					
0	0.0287	<0.025	0.79	0.273	0.45
1	6.96	4.93	4.62	5.5	1.27
2	6.94	5.7	3.59	5.41	1.69
4	3.03	2.78	2.1	2.64	0.48
8	1.09	0.698	0.651	0.813	0.24
24	1.05	2.48	1.6	1.71	0.72
Estimates of mean based on approximation that values below LLOQ (0.025 $\mu\text{g/mL}$ ) are equal to zero.					
N/A: not applicable.					

**Table 19A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 200 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2561	ID 2570	ID 2567	Mean	SD
Day 1					
0	<0.025	<0.025	<0.025	N/A	N/A
0.5	4.92	5.67	9.97	6.85	2.73
1	4.64	8.38	12.8	8.61	4.08
2	4.76	8.13	8.5	7.13	2.06
4	2.24	2.07	4.41	2.91	1.3
8	0.816	0.458	2.71	1.33	1.21
24	1.43	1.11	1.02	1.19	0.22
Day 14					
0	1.13	1.17	1.59	1.3	0.26
0.5	2.96	4.57	7.9	5.14	2.52
1	4.46	7.35	9.69	7.17	2.62
2	5.32	9.03	12.7	9.02	3.69
4	3.7	3.13	6.53	4.45	1.82
8	0.577	0.29	2.88	1.25	1.42
24	0.223	3.24	0.131	1.2	1.77
Day 28					
0	0.0354	0.0876	0.0735	0.066	0.027
1	5.41	5.1	5.78	5.43	0.34
2	3.9	4.58	5.06	4.51	0.583
4	1.54	1.46	2.93	1.98	0.827
8	1.55	0.555	0.428	0.844	0.614
24	0.156	1.73	1.09	0.992	0.792
N/A: not applicable.					

**Table 20A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to male Beagle dogs.

Time (hour)	ID 2517	ID 2519	ID 2525	ID 2528	ID 2530	Mean	SD
Day 1							
0	<0.025	<0.025	<0.025	<0.025	<0.025	N/A	N/A
0.5	17.5	7.86	4.49	8.92	6.94	9.14	5
1	15.4	13.4	7.39	10.1	13.7	12	3.2
2	10.1	15.2	9.39	11.1	13.2	11.8	2.4
4	2.9	11.3	5.04	5.7	5.32	6.05	3.1
8	0.869	1.94	3.19	4.54	4.08	2.92	1.5
24	4.61	0.616	4.52	2.86	3.12	3.15	1.6
Day 14							
0	1.43	0.891	1.73	4.14	4.39	2.52	1.6
0.5	8.33	7.49	4.94	9.31	8.29	7.67	1.7
1	12.8	14.9	7.56	13.9	11.4	12.1	2.9
2	9.8	11.5	7.48	9.63	13.1	10.3	2.1
4	5.36	5.9	2.77	4.42	6.86	5.06	1.6
8	2.23	1.28	1.07	7.79	5.51	3.58	3
24	6.06	1.83	3.78	4.78	4.31	4.15	1.6
Day 28							
0	<25	0.0845	0.0566	0.0296	0.287	0.092	0.11
1	15.1	3.96	8.2	4.45	8.16	7.97	4.46
2	11.5	6.19	5.63	7.04	10.2	8.11	2.59
4	3.3	2.25	2.29	4.71	4.53	3.42	1.18
8	2.82	1.68	1.49	4.98	1.15	2.42	1.56
24	2.43	3.17	2.65	1.02	4.63	2.78	1.3
48				0.0339	0.24	0.137	0.15
72				<0.025	<0.025	N/A	N/A
Estimates of mean based on approximation that values below LLOQ (0.025 $\mu\text{g/mL}$ ) are equal to zero.							
N/A: not applicable.							



**Table 21A1.** Individual plasma concentrations ( $\mu\text{g/mL}$ ) of sulfoxide metabolite after single (Day 1) and repeated (Day 14 and Day 28) oral administrations of Fexinidazole at the dose of 800 mg/kg/day to female Beagle dogs.

Time (hour)	ID 2564	ID 2565	ID 2569	ID 2571	ID 2573	Mean	SD
Day 1							
0	<0.025	<0.025	<0.025	<0.025	<0.025	N/A	N/A
0.5	11.7	7.61	9.88	4.85	5.15	7.84	2.97
1	17.4	12.8	13.8	14.7	9.22	13.6	2.98
2	18.4	21.7	10.5	10.9	9.51	14.2	5.49
4	9.91	17.6	4.72	5.20	4.40	8.37	5.63
8	5.49	5.67	3.92	1.54	1.47	3.62	2.05
24	0.441	2.14	2.57	9.37	0.292	2.96	3.72
Day 14							
0	1.10	1.59	0.0525	1.99	1.05	1.16	0.727
0.5	12.0	6.74	3.17	5.52	5.48	6.58	3.29
1	21.7	11.8	12.3	9.64	9.73	13.0	4.99
2	19.2	13.2	18.2	10.5	9.43	14.1	4.43
4	9.61	14.1	12.3	8.90	6.08	10.2	3.11
8	6.34	9.39	4.16	5.78	5.62	6.26	1.93
24	4.36	2.71	1.17	0.264	1.77	2.05	1.57
Day 28							
0	0.411	0.291	0.0769	0.558	0.284	0.324	0.178
1	11.9	11.8	9.80	6.89	4.66	9.01	3.17
2	9.49	13.2	7.32	7.83	4.37	8.44	3.24
4	5.24	7.58	6.09	5.08	3.71	5.54	1.42
8	1.11	6.56	2.81	5.14	1.33	3.39	2.39
24	1.79	5.96	0.992	1.73	1.33	2.36	2.04
48				<0.025	<0.025	N/A	N/A
72				<0.025	<0.025	N/A	N/A
N/A: not applicable.							

**Appendix 2. In-Study Bioanalytical Validation Data****Calibration data**

<b>Table 1A2. Analytical Performance: Back-Calculated Concentrations (ng/mL) of Fexinidazole Calibration Standard in Dog Plasma for Study Protocol 0505-2007.</b>									
<b>Assay Date</b>	<b>Analytical Run Number</b>	<b>STD.1 5.00 ng/mL</b>	<b>STD.2 10.0 ng/mL</b>	<b>STD.3 50.0 ng/mL</b>	<b>STD.4 100 ng/mL</b>	<b>STD.5 250 ng/mL</b>	<b>STD.6 500 ng/mL</b>	<b>STD.7 900 ng/mL</b>	<b>STD.8 1000 ng/mL</b>
12-Mar-2008	1	4.68	10.9	*40.5	99.3	258	479	933	981
		4.94	10.9	44.6	97.7	245	464	970	1040
13-Mar-2008	2	5.45	9.34	50.7	93.6	238	495	897	1000
		4.47	10.8	53.9	102	254	492	868	1040
13-Mar-2008	3	4.5	9.69	46.6	92.5	272	495	869	1060
		5.77	9.4	50.3	97.5	257	499	950	1020
14-Mar-2008	4	4.98	10.4	46.7	89.7	250	480	896	998
		5.03	9.88	44.7	113	264	540	*1100	1030
21-Mar-2008	5	4.92	9.98	52.3	95.5	267	515	901	991
		5.2	9.73	45.8	90.4	250	472	930	1120
26-Mar-2008	6	5.33	10.9	49	94.1	244	524	872	1060
		4.2	11	53.9	96.8	234	509	816	1030
26-Mar-2008	7	5.01	*12.1	46.9	108	*201	497	1000	997
		5.12	9.69	45.4	97.2	256	515	813	1040
27-Mar-2008	8	5	10	44.8	103	257	554	1010	883
		4.76	11	55	87.4	258	457	900	951
27-Mar-2008	9	4.63	9.59	46.1	96.3	267	429	970	912
		5.48	10.2	48.7	97.8	267	515	956	1080
28-Mar-2008	10	4.77	10.6	48.3	101	253	491	963	1030
		5.08	10.1	50.9	90.9	255	508	948	877
29-Mar-2008	11	4.81	10.7	50.9	85.5	260	528	916	1150
		5.23	9.49	45.9	88.4	261	487	852	1070
Mean		4.97	10.2	48.6	96.3	256	498	916	1020
SD		0.365	0.581	3.29	6.63	9.72	28.2	55	67.9
%CV		7.3	5.7	6.8	6.9	3.8	5.7	6	6.7
%Bias		-0.6	2	-2.8	-3.7	2.4	-0.4	1.8	2
n		22	21	21	22	21	22	21	22

\*Accuracy more than 15%; excluded from regression analysis.

<b>Table 2A2. Analytical Performance: Back-Calculated Concentrations (ng/mL) of Sulfone Calibration Standard in Dog Plasma for Study Protocol 0505-2007.</b>									
<b>Assay Date</b>	<b>Analytical Run Number</b>	<b>STD.1 25.0 ng/mL</b>	<b>STD.2 50.0 ng/mL</b>	<b>STD.3 250 ng/mL</b>	<b>STD.4 500 ng/mL</b>	<b>STD.5 2500 ng/mL</b>	<b>STD.6 5000 ng/mL</b>	<b>STD.7 22500 ng/mL</b>	<b>STD.8 25000 ng/mL</b>
12-Mar-2008	1	28.5	*66.6	241	*616	*3130	5630	*27100	25900
		21.9	49	236	511	2630	4830	21300	23700
13-Mar-2008	2	27.1	52.1	266	519	2460	5360	19800	22200
		21.1	52.8	273	538	2690	5110	19700	22600
13-Mar-2008	3	25.1	51.5	237	478	2820	5000	20100	22500
		25.1	46.5	279	524	2810	5220	21400	23200
14-Mar-2008	4	23.2	56.5	236	469	2850	5010	21400	23600
		26	48.8	218	*668	2810	*6060	25000	22500
21-Mar-2008	5	24.9	50.2	267	484	2700	5280	19800	23600
		26.1	44.2	278	488	2610	4990	21000	25400
26-Mar-2008	6	23.7	56.7	269	493	2650	5290	19300	23100
		24.4	*59.3	*301	506	2490	5350	*18300	22400
26-Mar-2008	7	22.2	54.7	239	557	*1990	4970	20400	*20600
		26.1	52.4	240	506	2680	5130	*17600	22100
27-Mar-2008	8	22	50.2	232	539	2730	5640	22100	*19400
		26.6	55.8	*306	470	2730	4860	19500	21400
27-Mar-2008	9	23.5	49.5	236	492	2830	4680	21800	*19700
		26.6	*68.7	260	508	2830	5280	20200	22300
28-Mar-2008	10	25.2	51.2	252	541	2670	5040	20600	21300
		24.4	49.2	269	483	2680	5250	20500	*19300
29-Mar-2008	11	**14.9	*39.1	249	433	2780	5570	20100	25400
		25.9	46.9	248	495	2870	5310	20000	23600
Mean		24.7	51	251	502	2720	5180	20700	23200
SD		1.93	3.47	17.6	29.6	114	258	1310	1320
%CV		7.8	6.8	7	5.9	4.2	5	6.3	5.7
%Bias		-1.2	2	0.4	0.4	8.8	3.6	-8	-7.2
n		21	18	20	20	20	21	19	18
*Accuracy more than 15%; excluded from regression analysis.									
**Accuracy more than 20%; excluded from regression analysis.									

<b>Table 3A2. Analytical Performance: Back-Calculated Concentrations (ng/mL) of Sulfoxide Calibration Standard in Dog Plasma for Study Protocol 0505-2007.</b>									
<b>Assay Date</b>	<b>Analytical Run Number</b>	<b>STD.1 25.0 ng/mL</b>	<b>STD.2 50.0 ng/mL</b>	<b>STD.3 250 ng/mL</b>	<b>STD.4 500 ng/mL</b>	<b>STD.5 2500 ng/mL</b>	<b>STD.6 5000 ng/mL</b>	<b>STD.7 22500 ng/mL</b>	<b>STD.8 25000 ng/mL</b>
12-Mar-2008	1	29.7	*68.8	258	*630	*3130	5580	*27100	26200
		21.4	45.7	240	505	2590	4710	21300	23800
13-Mar-2008	2	26.7	54.4	266	523	2400	5230	20000	22200
		21	52.3	276	558	2620	5030	19800	22900
13-Mar-2008	3	24.4	52.3	224	487	2710	4800	20100	22700
		25.1	48.9	285	539	2750	5230	21800	23600
14-Mar-2008	4	23	57.3	241	483	2760	4850	21300	23800
		25.6	49.7	225	*681	2740	*6040	25200	22300
21-Mar-2008	5	25.5	49.9	265	484	2640	5190	19700	23900
		24.7	48.1	273	495	2590	4960	21300	25600
26-Mar-2008	6	22.8	56.7	261	492	2500	5000	*18800	22600
		25.3	*60.9	*321	552	2540	5480	19200	23500
26-Mar-2008	7	20.9	56.8	243	560	*1930	4870	20200	*20000
		26.6	53.2	240	518	2640	5080	*17500	21700
27-Mar-2008	8	21.7	50.1	237	555	2680	5610	21900	*19300
		27.1	54.6	*303	480	2710	4740	19900	21300
27-Mar-2008	9	22.4	49	235	516	2800	4680	21300	*19500
		27	52.7	269	512	2750	5210	20100	22000
28-Mar-2008	10	25.4	50.9	258	545	2590	4990	20500	21400
		23.6	51.5	267	492	2660	5210	20400	*19200
29-Mar-2008	11	22.6	49.2	263	456	2720	5500	19600	24600
		27.6	49.2	259	507	2790	5270	19500	23200
Mean		24.6	51.6	254	513	2660	5110	20700	23200
SD		2.39	3.15	17.4	30.3	103	283	1360	1360
%CV		9.7	6.1	6.9	5.9	3.9	5.5	6.6	5.9
%Bias		-1.6	3.2	1.6	2.6	6.4	2.2	-8	-7.2
n		22	20	20	20	20	21	19	18

\*Accuracy more than 15%; excluded from regression analysis.

<b>Table 4A2. Calibration Curve Parameters for Fexinidazole Calibration Standards in Dog Plasma for Study Protocol 0505-2007.</b>							
<b>Run Date</b>	<b>Curve Number</b>	<b>Slope</b>	<b>Intercept</b>	<b>R<sup>2</sup></b>	<b>LLOQ ng/mL</b>	<b>ULOQ ng/mL</b>	<b>Regression Footnote(s)</b>
12-Mar-2008	1	0.00403	0.00314	0.9954	5	1000	1
13-Mar-2008	2	0.00415	0.00179	0.9959	5	1000	1
13-Mar-2008	3	0.00598	0.00208	0.9943	5	1000	1
14-Mar-2008	4	0.00552	0.00811	0.9946	5	1000	1
21-Mar-2008	5	0.00599	0.00416	0.9959	5	1000	1
26-Mar-2008	6	0.00536	0.00265	0.9931	5	1000	1
26-Mar-2008	7	0.00562	0.00168	0.9955	5	1000	1
27-Mar-2008	8	0.00515	-0.00008	0.9911	5	1000	1
27-Mar-2008	9	0.00545	-0.00013	0.993	5	1000	1
28-Mar-2008	10	0.00547	-0.00093	0.9965	5	1000	1
29-Mar-2008	11	0.00448	0.00000	0.9922	5	1000	1
Mean		0.00520	0.00204	0.9943			
SD		0.00068	0.00256	0.0017			
%CV		13.2	125.1	0.2			
n		11	11	11			
Regression Footnote(s):							
1) Resp. = Slope * Conc. + Intercept							

<b>Table 5A2. Calibration Curve Parameters for Sulfone Calibration Standards in Dog Plasma for Study Protocol 0505-2007.</b>							
<b>Run Date</b>	<b>Curve Number</b>	<b>Slope</b>	<b>Intercept</b>	<b>R<sup>2</sup></b>	<b>LLOQ ng/mL</b>	<b>ULOQ ng/mL</b>	<b>Regression Footnote(s)</b>
12-Mar-2008	1	0.00433	0.02697	0.9923	25	25000	1
13-Mar-2008	2	0.00425	0.00502	0.9898	25	25000	1
13-Mar-2008	3	0.00614	0.01536	0.9924	25	25000	1
14-Mar-2008	4	0.00543	0.04225	0.9887	25	25000	1
21-Mar-2008	5	0.00655	0.01189	0.9943	25	25000	1
26-Mar-2008	6	0.00485	0.00781	0.9922	25	25000	1
26-Mar-2008	7	0.00543	0.00947	0.992	25	25000	1
27-Mar-2008	8	0.00475	0.01223	0.988	25	25000	1
27-Mar-2008	9	0.00516	0.01442	0.9926	25	25000	1
28-Mar-2008	10	0.00512	0.00214	0.994	25	25000	1
29-Mar-2008	11	0.00398	0.04711	0.9912	25	25000	1
Mean		0.00509	0.01770	0.9916			
SD		0.00078	0.01484	0.002			
%CV		15.4	83.9	0.2			
n		11	11	11			
Regression Footnote(s):							
1) Resp. = Slope * Conc. + Intercept							

<b>Table 6A2. Calibration Curve Parameters for Sulfoxide Calibration Standards in Dog Plasma for Study Protocol 0505-2007.</b>							
<b>Run Date</b>	<b>Curve Number</b>	<b>Slope</b>	<b>Intercept</b>	<b>R<sup>2</sup></b>	<b>LLOQ ng/mL</b>	<b>ULOQ ng/mL</b>	<b>Regression Footnote(s)</b>
12-Mar-2008	1	0.00385	0.01864	0.9894	25	25000	1
13-Mar-2008	2	0.00376	0.01092	0.9895	25	25000	1
13-Mar-2008	3	0.00541	0.01822	0.9927	25	25000	1
14-Mar-2008	4	0.00492	0.04264	0.9905	25	25000	1
21-Mar-2008	5	0.00578	0.00405	0.9964	25	25000	1
26-Mar-2008	6	0.00446	0.01375	0.9915	25	25000	1
26-Mar-2008	7	0.00533	0.00604	0.988	25	25000	1
27-Mar-2008	8	0.00462	0.01543	0.9883	25	25000	1
27-Mar-2008	9	0.00507	0.01603	0.9916	25	25000	1
28-Mar-2008	10	0.00501	0.00873	0.994	25	25000	1
29-Mar-2008	11	0.00407	0.01632	0.991	25	25000	1
Mean		0.00475	0.01553	0.9912			
SD		0.00066	0.01022	0.0025			
%CV		13.9	65.8	0.3			
n		11	11	11			
Regression Footnote(s):							
1) Resp. = Slope * Conc. + Intercept							

**Table 7A2. Analytical Performance of Fexinidazole Quality Control Samples in Dog Plasma for Study Protocol 0505-2007.**

Run Date	Curve Number	QC1 15.0 ng/mL	QC2 75.0 ng/mL	QC3 800 ng/mL	QC3 800 ng/mL Dilution=2	QC4 2000 ng/mL Dilution=5	QC4 2000 ng/mL Dilution=10
12-Mar-2008	1	15.5	83.5	853			
		15.5	81.5	798			
13-Mar-2008	2	14.7	75.9	780			
		15.6	82.4	816			
13-Mar-2008	3	15	83.3	904			
		15.3	~86.5	780			
14-Mar-2008	4	14.2	79.4	822	847		
		15.8	83.7	898	844		
					775		
21-Mar-2008	5	16	80.5	836	757		
		17.8	~89.6	701	912		
					~1120		
26-Mar-2008	6	16.8	71.7	831			2020
		16.7	79.2	784			2220
							2000
26-Mar-2008	7	13.7	77.5	739		1950	
		13.5	80.6	779		1980	
						2020	
27-Mar-2008	8	~36.4	72.6	845		2050	
		17	78.9	838		2170	
						2160	
27-Mar-2008	9	15	76.3	782		1890	
		16.1	80.6	810		2130	
						1900	
28-Mar-2008	10	14.5	74.6	760		2010	
		14.9	77.9	820		1940	
						1980	
29-Mar-2008	11	15.3	68.4	797		2100	
		15.4	80.5	854		2130	
						2220	
Mean		16.4	79.3	810	876	2040	2080
SD		4.59	4.88	47.7	132	104	122
%CV		28	6.2	5.9	15.1	5.1	5.9
%Bias		9.3	5.7	1.3	9.5	2	4
n		22	22	22	6	15	3
~ > 15% Theoretical							



<b>Table 8A2. Analytical Performance of Sulfone Quality Control Samples in Dog Plasma for Study Protocol 0505-2007.</b>							
<b>Run Date</b>	<b>Curve Number</b>	<b>QC1 75.0 ng/mL</b>	<b>QC2 750 ng/mL</b>	<b>QC3 20000 ng/mL</b>	<b>QC3 20000 ng/mL Dilution=2</b>	<b>QC4 50000 ng/mL Dilution=5</b>	<b>QC4 50000 ng/mL Dilution=10</b>
12-Mar-2008	1	~91.4	~931	22200			
		77.2	788	18900			
13-Mar-2008	2	75.5	783	18100			
		82.8	831	18300			
13-Mar-2008	3	69.4	752	19700			
		79	~881	18000			
14-Mar-2008	4	65.6	853	18400	22700		
		84.6	~946	20100	21900		
					21000		
21-Mar-2008	5	78.8	777	19000	18800		
		85.7	~892	~16500	23000		
					~26900		
26-Mar-2008	6	83.5	709	19700			52000
		~92.7	799	17800			~57600
							53100
26-Mar-2008	7	67.7	740	~16000		47400	
		71	789	17400		46000	
						49700	
27-Mar-2008	8	~604	711	19000		52500	
		82.8	821	19100		52600	
						54200	
27-Mar-2008	9	73.4	734	~16900		46100	
		81.6	791	17500		50100	
						45700	
28-Mar-2008	10	72.4	743	~16400		48900	
		80.4	774	18000		46200	
						47600	
29-Mar-2008	11	~244	656	18500		52300	
		84.6	802	22400		56200	
						56000	
Mean		110	796	18500	22400	50100	54200
SD		116	72.2	1630	2680	3670	2970
%CV		105.5	9.1	8.8	12	7.3	5.5
%Bias		46.7	6.1	-7.5	12	0.2	8.4
n		22	22	22	6	15	3

~ &gt; 15% Theoretical

<b>Table 9A2. Analytical Performance of Sulfoxide Quality Control Samples in Dog Plasma for Study Protocol 0505-2007.</b>							
<b>Run Date</b>	<b>Curve Number</b>	<b>QC1 75.0 ng/mL</b>	<b>QC2 750 ng/mL</b>	<b>QC3 20000 ng/mL</b>	<b>QC3 20000 ng/mL Dilution=2</b>	<b>QC4 50000 ng/mL Dilution=5</b>	<b>QC4 50000 ng/mL Dilution=10</b>
12-Mar-2008	1	~92.0	~937	22400			
		83	780	18800			
13-Mar-2008	2	76	772	18500			
		84.1	827	18600			
13-Mar-2008	3	69	754	20100			
		81	~869	18200			
14-Mar-2008	4	65.9	852	18600	22700		
		88.8	~946	20200	21800		
		NA	NA	NA	21100		
21-Mar-2008	5	77.9	769	19100	18600		
		~90.5	844	~16700	23000		
					~27400		
26-Mar-2008	6	77.8	675	19400			50200
		~94.3	858	19100			~61000
							56000
26-Mar-2008	7	69.6	736	~15800		47200	
		69.9	797	17300		46200	
						49300	
27-Mar-2008	8	~613	710	19100		53000	
		84.3	804	19100		53700	
						55200	
27-Mar-2008	9	73.7	729	~16900		46300	
		79.2	788	17500		50000	
						46000	
28-Mar-2008	10	70.3	735	~16500		49300	
		76.4	773	18100		47400	
						47900	
29-Mar-2008	11	83.2	660	17700		51900	
		83.7	808	22100		55500	
						55200	
Mean		104	792	18600	22400	50300	55700
SD		114	73.7	1630	2900	3520	5400
%CV		109.6	9.3	8.8	12.9	7	9.7
%Bias		38.7	5.6	-7	12	0.6	11.4
n		22	22	22	6	15	3
~ > 15% Theoretical							

## ***Appendix 14 Clinical Pathology Methods***

## HEMATOLOGY METHODS

PARAMETERS	CODE	UNIT	METHODS AND INSTRUMENTS
Red blood cells	RBC	$n \times 10^6/\mu\text{L}$	Laser beam method. "ADVIA 120™ System" Bayer
Hemoglobin	HGB	g/dL	Colorimetric method as cyanmethemoglobin. "ADVIA 120™ System" Bayer
Hematocrit	HCT	%	Calculated: Wintrobe formulae "ADVIA 120™ System" Bayer
Mean corpuscular hemoglobin concentration	MCHC	g/dL	Calculated: Wintrobe formulae "ADVIA 120™ System" Bayer
Mean corpuscular volume	MCV	fL	Mean of RBC volume histogram x MCV calibration factor. "ADVIA 120™ System" Bayer
Mean corpuscular hemoglobin	MCH	pg	Calculated: Wintrobe formulae "ADVIA 120™ System" Bayer
Red cell distribution width	RDW	%	Calculated: Standard deviation of RBC volume histogram/MCV (fl) x 100. "ADVIA 120™ System" Bayer
Hemoglobin distribution width	HDW	g/dL	Calculated: Standard deviation of RBC HC histogram. "ADVIA 120™ System" Bayer
Reticulocytes	R	%	Laser beam method with colorimetric reaction for nucleic acids. "ADVIA 120™ System" Bayer
Reticulocytes absolutes	RAB	$n \times 10^9/\text{L}$	Laser beam method with colorimetric reaction for nucleic acids. "ADVIA 120™ System" Bayer
Mean corpuscular volume of reticulocytes	MCVr	fL	Mean of R volume histogram x MCV calibration factor. "ADVIA 120™ System" Bayer
Mean hemoglobin concentration of reticulocytes	CHCM	g/dL	Mean of R hemoglobin histogram "ADVIA 120™ System" Bayer
Cellular hemoglobin of reticulocytes	CHr	pg	Calculated: Wintrobe formulae "ADVIA 120™ System" Bayer
Platelets	PLT	$n \times 10^3/\mu\text{L}$	Laser beam method. "ADVIA 120™ System" Bayer
Mean platelet volume	MPV	fL	Mean platelet volume histogram "ADVIA 120™ System" Bayer
Platelet distribution width	PDW	%	Standard deviation of platelet volume histogram/ MPV (fl) x 100 "ADVIA 120™ System" Bayer
Platelet hematocrit	PCT	%	Mean platelet volume x PLT. "ADVIA 120™ System" Bayer
White blood cells	WBC	$n \times 10^3/\mu\text{L}$	Laser beam method with "Baso/Lobularity method" and Peroxidase reaction. "ADVIA 120™ System" Bayer

HEMATOLOGY METHODS (Cont.)

PARAMETERS	CODE	UNIT	METHODS AND INSTRUMENTS
WBC differential count: Neutrophils Lymphocytes Eosinophils Basophils Monocytes Large unstained cells	N LY E B M LU	%	Peroxidase and Basophil/Lobularity method "ADVIA 120™ System" Bayer
Band Neutrophils Segmented Neutrophils	BANN SEGN		Percentage of Band and Segmented Neutrophils manually calculated on 100 Neutrophils examined at microscopy
WBC differential count: Neutrophils ABS Lymphocytes ABS Eosinophils ABS Basophils ABS Monocytes ABS Large unstained cells ABS	NAB LYAB EAB BAB MAB LUAB	n x 10 <sup>3</sup> /μL	Peroxidase and Basophil/Lobularity method "ADVIA 120™ System" Bayer
Band Neutrophils ABS Segmented Neutrophils ABS	BAAB SEAB		Absolute number of Band and Segmented Neutrophils calculated on percentage of Band and Segmented Neutrophils and value of NAB
Prothrombin Time	PT	Sec	Photometric method. Kit: Dade Behring. Coagulometer "BCS" Dade Behring.
Prothrombin Time Ratio	PTr		Calculated parameter
Fibrinogen	FIBR	mg/dL	Photometric method. Kit: Dade Behring. Coagulometer "BCS" Dade Behring.
Activated Partial Thromboplastin Time	PTT	Sec	Photometric method. Kit: Dade Behring. Coagulometer "BCS" Dade Behring.
Activated Partial Thromboplastin Time Ratio	PTTr		Calculated parameter

## CLINICAL CHEMISTRY METHODS

PARAMETERS	CODE	UNIT	METHODS AND INSTRUMENTS
Urea	UREA	mg/dL	Urease - GLDH": enzymatic UV test. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Creatinine	CREA	mg/dL	Colorimetric complex between the creatinine and the alkaline picrate (Jaffé). Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Aspartate aminotransferase	AST	IU/L	UV-test according to IFCC modified method without pyridoxal phosphate. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Alanine aminotransferase	ALT	IU/L	UV-test according to IFCC modified method without pyridoxal phosphate. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Alkaline phosphatase	AP	IU/L	Kinetic photometric test, according to the IFCC. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
G-Glutamyl transferase	GGT	IU/L	Kinetic photometric test according to Szasz modified. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Total bilirubin	T.BIL	mg/dL	Photometric test using 2,4-dichloroaniline. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Total proteins	TPRO	g/dL	Biuret reaction. End-point method. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Albumin	ALB.	g/dL	Colorimetric determination using bromocresol green. Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Globulin	GLOB	g/dL	Calculated parameter (T.Protein-Albumin) by Xybion.
Glucose	GLUC	mg/dL	Enzymatic determination. (Trinder method). Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Triglycerides	TG	mg/dL	Enzymatic determination Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Total Cholesterol	TCHO	mg/dL	"CHOD-PAP": enzymatic photometric test. (Trinder's reaction). Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Calcium	Ca	mg/dL	Photometric test using ortho-cresolphthalein complexone (OPC). Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Phosphorus	PHOS	mg/dL	UV method using phosphomolybdate Kit: Horiba ABX adapted to the "Pentra 400" analyzer.
Sodium	Na	mEq/L	Direct potentiometry ion selective electrodes. ISE module on the "Pentra 400" analyzer
Chloride	Cl	mEq/L	Direct potentiometry ion selective electrodes. ISE module on the "Pentra 400" analyzer
Potassium	K	mEq/L	Direct potentiometry ion selective electrodes. ISE module on the "Pentra 400" analyzer
Albumin/Globulin	A/G		Calculated parameter by Xybion

URINALYSIS METHODS

PARAMETERS	CODE	UNIT	METHODS AND INSTRUMENTS
Appearance Limpid Turbid Light Turbid	L T LT		Turbidimetric method with Urysis 2400 (Roche).
Colour: Yellow Amber Orange Greenish Reddish Brownish Colorless Other	Y A O G R B W O		Photometric method with Urysis 2400 (Roche).
Volume	VOL	ml/16h	
Specific Gravity	S.G.		Refractometric method with Urysis 2400 (Roche).
pH	pH		
Proteins	PRO	Score 0-4	
Nitrites	NIT	" 0-1	Semi-quantitative determination with Sticks Urysis 2400
Glucose	GLU	" 0-4	Cassette
Ketones	KETO	" 0-3	(Roche).
Urobilinogen	UBG	" 0-3	
Bilirubin	BIL	" 0-2	Photometric method with Urysis 2400 (Roche).
Hemoglobin/Red blood cells	ERY	" 0-3	
White blood cells	WBC	" 0-2	

The scoring system is as follows:

SCORE	PROTEINS mg/dL	NITRITES	GLUCOSE mg/dL	KETONES mg/dL	UROBIL. mg/dL	BILIR. mg/dL	WHITE B.CELLS WBC/ $\mu$ L	HEMOGLOBIN ERYTHROC. RBC/ $\mu$ L
0	Absent	Absent	Absent	Up to 5	Up to 1	Up to 1	Up to 25	Up to 10
1	Up to 25	Present	Up to 50	Up to 15	Up to 4	Up to 3	Up to 100	Up to 50
2	Up to 75	...	Up to 100	Up to 50	Up to 8	Up to 6	Up to 500	Up to 150
3	Up to 150	...	Up to 300	Up to 150	Up to 12	...	...	Up to 250
4	Up to 500	...	Up to 1000	...	...	...	...	...

## ***Appendix 15 Pharmacy Documentation***



## Pharmacy Certification

**STUDY NUMBER** : **0505-2007**  
**TEST ITEM** : **Fexinidazole**  
**NOTEBOOK NUMBER(S)** : **19201/B and 19094/D**

### DOCUMENTATION ENCLOSED IN THE NOTEBOOK:

- A. Analysis certificate dated December 18, 2007 issued by Orgasynth Industries for Fexinidazole test item, raw material, Batch No. 3168-07-01/O
- B. Material safety data sheet issued by Orgasynth Industries for Fexinidazole
- C. Certificate of Analysis issued by Sigma-Aldrich for Methylcellulose 400 cP, raw material, Lot No. 125K0196
- D. Certificate of Analysis issued by Sigma-Aldrich for Tween® 80, raw material, Lot No. 1324202
- E. Label's photocopy of Acqua per preparazioni iniettabili (Bieffe Medital S.p.A.), raw material, Lot No. 07G0201
- F. Label's photocopy of Acqua per preparazioni iniettabili (Bieffe Medital S.p.A.), raw material, Lot No. 07K1503
- G. Copy of request cards of test item

### ANALYTICAL DOCUMENTATION:

Requests and Analytical Results issued by Accelera/ADMET/Preclinical Formulation and Accelera/DMPK&ART/Bioanalysis and Analytical Control

### MATERIALS USED FOR THE STUDY:

1. Fexinidazole test item, raw material, Batch No. 3168-07-01/O
2. Methylcellulose 400 cP, raw material, Lot No. 125K0196
3. Tween® 80, raw material, Lot No. 1324202
4. Acqua per preparazioni iniettabili, raw material, Lot No. 07G0201
5. Acqua per preparazioni iniettabili, raw material, Lot No. 07K1503

### PREPARATIONS:

Prepare suspension of Fexinidazole test item, raw material, Lot No. 3168-07-01/O in the vehicle (5% Tween® 80 in 0.5% Methylcellulose 400 cP solution) at the concentration of 5 mg/mL, 20 mg/mL and 80 mg/mL

**CONCENTRATION CHECKS:****Fexinidazole suspensions:**

		<b>% of L.A.</b>	<b>Preparation date</b>
80 mg/mL	Request No. 200800009 (Top)	95.92%	January 28, 2008
80 mg/mL	Request No. 200800010 (Middle)	97.38%	January 28, 2008
80 mg/mL	Request No. 200800011 (Bottom)	96.87%	January 28, 2008
20 mg/mL	Request No. 200800012 (Top)	104.34%	January 28, 2008
20 mg/mL	Request No. 200800013 (Middle)	99.17%	January 28, 2008
20 mg/mL	Request No. 200800014 (Bottom)	93.68%	January 28, 2008
5 mg/mL	Request No. 200800015 (Top)	95.89%	January 28, 2008
5 mg/mL	Request No. 200800016 (Middle)	107.31%	January 28, 2008
5 mg/mL	Request No. 200800017 (Bottom)	107.93%	January 28, 2008
80 mg/mL	Request No. 200800045 (Top)	97.94%	February 22, 2008
80 mg/mL	Request No. 200800046 (Middle)	105.62%	February 22, 2008
80 mg/mL	Request No. 200800047 (Bottom)	98.53%	February 22, 2008
20 mg/mL	Request No. 200800048 (Top)	95.76%	February 22, 2008
20 mg/mL	Request No. 200800049 (Middle)	98.19%	February 22, 2008
20 mg/mL	Request No. 200800050 (Bottom)	95.13%	February 22, 2008
5 mg/mL	Request No. 200800051 (Top)	108.04%	February 22, 2008
5 mg/mL	Request No. 200800052 (Middle)	105.43%	February 22, 2008
5 mg/mL	Request No. 200800053 (Bottom)	102.30%	February 22, 2008

**STABILITY:****Fexinidazole test item:**

Expire date October 2008 for Fexinidazole, test item, raw material, Lot No. 3168-07-01/O if stored at room temperature protected from light.

**Fexinidazole suspension:**

Stability data indicate that Fexinidazole suspensions in the vehicle (5% Tween® 80 in 0.5% Methylcellulose 400 cP solution) in the range 0.5-100 mg/mL are stable up to 7 days at room temperature and 14 days at +4°C (Nerviano MS 0293-2007-R)

Date: May 20, 2008