

Approval Date: July 31, 1989

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 139-879

B. Sponsor

Wildlife Laboratories
1401 Duff Drive, Suite 600
Fort Collins, CO 80524

C. Proprietary Name

Spartrix

D. Established Name

carnidazole

E. Dosage Form

Tablet (Each tablet contains 10 mg of Carnidazole).

F. Dispensing Status

OTC

G. Dosage Regimen

One (10 mg) tablet per adult pigeon. One half tablet (5 mg) per newly weaned pigeon.

H. Route of Administration

Oral

I. Indication

Spartrix (Carnidazole) is indicated for oral treatment of trichomoniasis (canker) in ornamental and homing (non-food) pigeons.

II. EFFECTIVENESS

A. Pivotal Studies

1. Dose Titration Study

i. Name and Address of Investigator:

Dr. D. Thienpont
Dept. of Chemotherapy
Janssen Pharmaceutica

Beerse, Belgium

ii. General Design of the Investigation:

1. Purpose: Determine the effective dose level of Carnidazole in pigeons with artificially induced infections
2. Test Animals:

Species: *Columba livia*
3. Type of Control: Saline treated placebo
4. Diagnosis: Artificial infections were induced by gastric lavage with approximately 100,000 *Trichomonas columbae* organisms. After an incubation period of one week, throat swabs were examined microscopically to confirm infection.
5. Dosage Form: Pure active Carnidazole in gelatin capsules.
6. Route of Administration: Oral
7. All birds received treatments for only one day.

Dosage Used:	Number of Birds / Group
(a) 2.5 mg/kg	(3 birds)
(b) 5 mg/kg	(11 birds)
(c) 10 mg/kg	(23 birds)
(d) 10 mg/kg twice same day	(6 birds)
(e) 20 mg/kg single dose	(20 birds)
(f) Saline controls	(19 birds)

8. Test Duration: Fourteen days
9. Pertinent Parameters Measured:
Presence or absence of trichomonads in throat swabs on days 9 and 14, after treatment

iii. Results:

Dosage Used:	Number of negative birds per group
2.5 mg/kg	0/3
5 mg/kg	7/11
10 mg/kg	21/23
10 mg/kg twice same day	6/6
20 mg/kg single dose	20/20
Saline controls	0/19

These dose range studies indicated that a single oral dose of 10 mg per pigeon resulted in a 100% effectiveness in all treated birds.

iv. Conclusions Drawn from the Study:

The lowest effective dose rate that resulted in 100% efficacy in all treated pigeons was a single oral dose of 10 mg/adult bird (20 mg/kg).

2. Validation Study

i. Type of Study: Validation of the Artificial Infection Model Used for Dose Titration.

ii. Name and Address of Investigator:

Dr. Charles Hibler
Department of Parasitology
College of Veterinary Medicine
Colorado State University
Fort Collins, Colorado

iii. General Design of the Investigation:

1. Purpose: To validate that exposure of a pigeon to approximately 100,000 trichomonad (*Trichomonas columbae*) will establish an infection.
2. Test Animals:
 - a. Species: *Columba livia*
 - b. Number per group: 9
 - c. Number of groups: 2
3. Type of Control: Negative
4. Method of Infection:
 - a. All birds selected for this study were negative for *Trichomonas columbae* organisms in crop mucus samples pretreatment.
 - b. Pigeons with active lesions of trichomoniasis supplied the inoculum for this study.
 - c. Pigeons in the treatment group were drenched with physiological saline suspension containing 100,000 active trichomonad. The number of organisms in the drench was determined by the Stole dilution technique.
5. Route of Exposure: Oral
6. Test Duration: Fourteen days

7. Diagnosis or Confirmation of Infection: Presence of pathognomonic lesions and/or microscopic examination of crop mucus for *Trichomonas columbae* organisms.
8. Pertinent Parameters Measured: Development of positive mucus samples containing *Trichomonas columbae* and/or active lesions. Mucus examinations were made on days 3, 7 and 14.

iv. Results:

All birds exposed to the infective material were scored as having trichomonad present in the crop by microscopic examination on day 14 of the trial, but were free of clinical lesions. Eight of nine controls (88%) were free of trichomoniasis and did not have clinical lesions.

v. Conclusions Drawn from the Study:

The results of this trial confirm that exposure of non-infected pigeons to approximately 100,000 trichomonas organisms will produce an infection. These results validate the model used for generation of safety and efficacy data by Janssen Pharmaceutica, Beerse, Belgium.

3. Field Efficacy Study

i. Type of Study: Clinical Field Efficacy Study

ii. Names and Addresses of Investigators:

Dr. Thomas Angel
7640 Burington Pike
Florence, Kentucky 41042

Dr. David Marx
111 North Mercedes Road
Norman, Oklahoma 73069

Dr. John Esposito
Dog, Cat & Bird Hospital
3233 North Mesa
El Paso, Texas 78802

Dr. Daniel S. Dohl
1220 North Julia
Spokane, Washington 99202

Dr. R.A. Van Ryswyk
455 West Dickman Road
Battle Creek, Michigan 49015

Dr. Mel Sowell
647 South Horizon
El Paso, Texas 79927

Dr. W.R. Lance
Wildlife Laboratories, Inc.
1401 Duff Drive, Suite 600
Fort Collins, Colorado 80524

iii. General Design of the Investigation:

1. Purpose: To demonstrate the efficacy of a single 10 mg Carnidazole tablet for the treatment of trichomoniasis in pigeons with natural infections.
2. Test Animals: Species - Columba livia
3. Type of Control: Placebo
4. Diagnosis: Microscopic examination of throat swab
5. Dosage Form: Tablets
6. Route of Administration: Oral
7. Dosage Used: A single 10 mg tablet per bird
8. Test Duration: Seven days
9. Parameters Measured: Presence or absence of trichomonad in throat swabs obtained 7 days after treatment.

iv. Results:

Summary of Data From Multicenter Study Showing the Efficacy of Carnidazole In Naturally Infected Pigeons and Spontaneous Cure Rate In Placebo Treated Pigeons.

	Treated			Placebo	
Investigator	Treated	Cured	Failure	Treated	Spontaneous Cured
Lance	5	5	0	5	0
Marx	5	4	1	5	0
Esposito	5	3	2	5	0
Dohl	4	3	1	5	0
Angel	5	3	2	5	1
Van Ryswyk	4	2	2	3	0
Sowell	5	5	0	4	2
Total	33	25	8	32	3

Efficacy = 75%³⁷;
Spontaneous Cure Rate = 9.3%³⁷;

As shown above a total of 33 birds were treated with Carnidazole resulting in a cure rate of 75%. An equal number (32) of birds were

included under placebo treatment. The spontaneous cure rate for untreated birds was less than 10%, which supports the conclusion that a single 10 mg Carnidazole oral dose for adult pigeons is efficacious against *Trichomonas columbae* infections.

Conclusions Drawn from the Study: A single Spartrix (Carnidazole) table was shown to have a 75% cure rate against *Trichomonas columbae* infections.

v. Conclusions Drawn from the Study:

A single Spartrix (Carnidazole) table was shown to have a 75% cure rate against *Trichomonas columbae* infections.

vi. Adverse Reactions: None

vii. Special Issues: None

B. Corroborative Studies

1. Clinical Field Efficacy Study

i. Type of Study: Clinical

ii. Name and Address of Investigator:

Dr. Marcel Rogiers
Janssen Pharmaceutica
Trunhoutseweg 30
B-2340 Beerse
Belgium 41042

iii. Test Animals:

Species - *Columba livia*
Number - 147 adult pigeons in 9 separate lofts.

iv. Type of Control: None

v. Dosage Used: Single 10 mg tablet of Carnidazole

vi. Other Information:

Infection was determined by direct microscopic examination of throat swabs. During the experiment, the owners of the loft were requested to clean all the drinking vessels daily. One owner did not take these precautions in one loft of six pigeons.

vii. Results and Conclusions:

Administration of a single oral dose of 10 mg tablet of Carnidazole resulted in a 98% cure rate when all pigeons in the loft were treated

under hygienic precautions. The data from one loft of six pigeons were not included in calculating the cure rate, since the owner did not follow the protocol and therefore his data were considered irrelevant.

2. Clinical Field Efficacy Study

i. Name and Address of Investigator:

Dr. Marcel Rogiers
Janssen Pharmaceutica
Turnhoutseweg 30
B-2340 Beerse
Belgium 41042

ii. Test Animals:

Species - *Columba livia*
Number - 120 breeding couples, 80 of them couples with young ones.

iii. Controls: None

iv. Dosage:

Single 10 mg tablet of Spartrix (Carnidazole) for adult and young unweaned pigeons older than 23 days and half (1/2) a tablet for young unweaned pigeons 14 to 22 days old.

v. Study Design:

All adult pigeons, weaned and unweaned pigeons 14 to 22 days old were treated with a single oral dose of Spartrix (Carnidazole) as mentioned above. Young pigeons less than 14 days old were left untreated. This group of untreated young pigeons got the medication from their mother's crop milk.

Diagnosis of the disease was based on the clinical signs such as listlessness and random mucus samples for isolation and identification of *T. columbae*. Definitive diagnosis of the disease was made by selective autopsies of the birds and postmortem examination of dead pigeons to isolate the pathogen and by identifying the pathognomonic lesions in the throat, crop and liver.

vi. Results:

The study demonstrated the efficacy of Carnidazole in adult and adult with young, under the conditions of use. Sixty nine (69) randomly selected adult pigeons were negative for organism. Six (6) adult pigeons with unweaned young ones were positive for *T. columbae*. Probably, the adults were reinfected while feeding the untreated young. Three (3) weaned five (5) week old young pigeons treated with Carnidazole and three unweaned untreated young pigeons less than

five weeks old were negative for *T. columbae* in the throat, crop and liver, on autopsy.

vii. Conclusions:

The study demonstrated that 10 mg Carnidazole for adults and 5 mg Carnidazole for young unweaned pigeons is efficacious against *T. columbae* infections.

III. ANIMAL SAFETY

A. Pivotal Studies

1. Subacute Toxicity Study

i. Name and Address of Investigator:

Dr. Roger Harlin
7020 S. Shields
Oklahoma City, Oklahoma 73149

ii. General Design of the Study:

1. Purpose of the Study:

To determine subacute toxicity of 10X the recommended dose (5 mg) of Carnidazole (Spartrix) per newly weaned pigeon.

2. Test Animals

- a. Species - *Columba livia* newly weaned
- b. Number per group - 5
- c. Treatment – 5
- d. Control – 5

3. Dosage Form: Tablets

4. Dosage Used: Five 10 mg tablets (100 mg/kg)

5. Route of Administration: Single Oral

6. Test Duration: 5 days

7. Pertinent Parameters Measured:

- a. Clinical signs
- b. Body weight
- c. Hematology

iii. Results:

No mortalities or adverse clinical signs were seen in the treated group. The treated group had a net loss of 17 gms body weight and the

control group had a net loss of 16 gms body weight during the trial period. In the treated group, 3 of 5 birds lost between 2 and 28 gms. One bird had no weight change during the study and one bird gained 22 gms. In the control group, 3 of 5 birds lost between 5 and 14 gms, one bird had no weight change and one gained 14 gms. There was no difference in the hematology results between the treated and control groups.

iv. Conclusions:

Spartrix (Carnidazole) given at 10X the recommended dose (5 mg) in newly weaned pigeons is safe.

2. Acute Toxicity Study

i. Name and Address of Investigator:

Dr. Robert Marsboom
Dept. of Toxicology
Janssen Pharmaceutica
Beerse, Belgium

ii. Test Animals: Species - *Columba livia*

iii. Type of Control:

The study was controlled by the conditions of housing and observations made.

iv. Dosage Used: 40 mg/kg, 160 mg/kg, 320 mg/kg and 640 mg/kg in a single oral dose.

v. Results and Conclusions:

DATA SUMMARY

Dose mg / kg	No. of Animals	Mortality after hours						Observations
		1	3	6	24	72	168	
40	1	0	0	0	0	0	0	None
160	1	0	0	0	0	0	0	None
320	2	0	0	0	0	0	0	None
640	6	0	0	0	0	0	0	Slight vomiting in 4 animals, 3 to 6 hours after dosing

No drug-related adverse reactions were observed in the pigeons treated up to 32 times the recommended therapeutic dose. At 64 times the therapeutic dose, 4 out of 6 birds exhibited slight vomiting. This study supports a 32 fold margin of safety for Carnidazole in adult pigeons.

IV. HUMAN SAFETY

- A. Data on human safety pertaining to consumption of drug residues in food are not required for approval of this NADA. The drug is labeled for use in ornamental and homing (non-food) pigeons only.
- B. The human safety considerations, other than food safety: The labeling contains a statement that, in case of accidental human ingestion, notify the physician immediately and inform him or her that "Spartrix Tablets each contains 10 mg of active Carnidazole. Carnidazole is a member of the 5 nitro-imidazole group."

V. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of Section 512 of the Act and Section 514.111 of the implementing regulations. The data demonstrate that Spartrix (Carnidazole) when used under its approved conditions of use is safe and effective.

This product is OTC (over the counter) because the pigeon fancier has adequate knowledge to accurately diagnose the disease. Pigeon flocks have mature and young pigeons most of the time. Adult birds are asymptomatic carriers and rarely show typical lesions of trichomoniasis, other than unthriftiness. Young pigeons contract the disease while feeding on crop milk and develop pathognomonic lesions in the throat. If untreated, the young birds usually die in one to two days after exhibiting signs whereas older birds may die in one to two weeks. These lesions in young pigeons are easily recognized by pigeon fanciers. OTC distribution will assist the pigeon fancier in controlling the spread of disease by ensuring that the entire loft will be treated when young pigeons show the first signs of disease.

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