FREEDOM OF INFORMATION SUMMARY
GASTROGARD™ (omeprazole)

I. GENERAL INFORMATION

NADA Number: 141-123

Sponsor: Merial Limited
2100 Ronson Road
Iselin, New Jersey 08830-3077

Generic Name: Omeprazole

Trade Name: GASTROGARD™

Marketing Status: Rx; For use by or on the order of a licensed veterinarian.

II. INDICATIONS FOR USE:

Gastrogard (omeprazole) is indicated for the treatment and prevention of recurrence of gastric ulcers in horses and foals four weeks of age and older.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, RECOMMENDED DOSAGE:

A. Dosage Form: GASTROGARD is an oral paste containing 2.28 g of omeprazole per syringe

B. Route of Administration: For oral administration only.

C. Recommended Dosage: GASTROGARD should be administered once-a-day for 28 days at the recommended dosage of 1.8 mg omeprazole/lb body weight (4 mg/kg). The recommended dosage for prevention of recurrence of ulcers after treatment is 0.9 mg omeprazole/lb body weight (2 mg/kg) for 30 days.

IV. EFFECTIVENESS:

A. Dose Justification:

Omeprazole is a proton pump inhibitor that affects the secretion of gastric acid into the stomach. This inhibition of acid secretion is the result of specific binding of omeprazole to the H^+/K^+ ATPase of the parietal cells in the gastric mucosa. Because this enzyme is involved in the final step in the acid secretion cycle, omeprazole will inhibit acid secretion in response to any stimulus.

The utility of omeprazole in ulcer therapy is based upon the ability of the drug to inhibit acid secretion. Therefore, a dosage of omeprazole that is at or near the dosage which maximally inhibits acid secretion in horses should maximize ulcer therapy. Based on this reasoning, dose selection for omeprazole for use in horses was established based on its effects in a pharmacodynamic model in which acid secretion was stimulated by pentagastrin infusion.

Preliminary pharmacodynamic studies in cannulated horses showed that acid suppression was incomplete when omeprazole was administered at a dosage of 3 mg/kg, and maximal acid suppression was demonstrated at a dosage of 5 mg/kg. Similarly, preliminary efficacy studies conducted in horses with gastric ulcers indicated that an improved response could be expected at dosages higher than 3 mg/kg. On this basis, dosages of 4 mg/kg and 5 mg/kg were used in a definitive dose selection study described below. From preliminary studies, ulcer healing rate was determined to increase as horses remained on omeprazole. This was confirmed in the dose confirmation studies in which ulcer healing and ulcer improvement increased from two weeks, through three weeks, to four weeks, reaching a maximum of 92% at four weeks.

Pharmacodynamic study (ASR 14646)

Purpose: To evaluate the effect of omeprazole in suppressing gastric acid when omeprazole is administered at 4 and 5 mg/kg/day to horses treated with pentagastrin

Investigators: J.E. Holste DVM, A. Merritt DVM and F. M. Andrews DVM

Study Locations: Three sites were used: Branchburg Farm, Somerville, NJ; Cherokee Farm, Knoxville, TN; and the University of Florida, Gainesville, FL

Animals: 13 horses (8 females, 5 males) with a gastric cannula, and ranging in age from 7 to 20 years

Study Design: A two-period crossover design was used. There was a ten-day washout period between periods. Pentagastrin-stimulated acid output was measured at three time points (6-8 hours, 14-16 hours, and 22-24 hours after administration) during each period.

Dosage Form: Paste, final market formulation

Route of Administration: Oral

Dosage and Frequency of Treatment: Each dosage - 4 mg/kg and 5 mg/kg - was administered to each horse daily for 15 days.

Controls: A gastric acid baseline was established for each horse prior to treatment.

Duration of Study: 42 days.

Data Analysis: Percent inhibition of acid output was analyzed by a mixed model analysis of variance to compare the effects of treatment at 4 mg/kg vs 5 mg/kg.

Results:

Table 1: Percent inhibition of pentagastrin-stimulated acid secretion (least squares mean ± standard deviation)

Dosage	**8 h**	**16 h**	**24 h**
4 mg/kg/d	98.9 ± 1.5	95.0 ± 7.7	90.3 ± 6.5
5 mg/kg/d	99.5 ± 0.7	97.7 ± 2.5	92.3 ± 5.5

Conclusions: Omeprazole at 4 mg/kg/day was selected as a dose that would effectively inhibit gastric acid secretion for 24 hours.

Observations: No adverse reaction was reported.

B. Dose Confirmation

Four well-controlled, blinded, dose confirmation trials were conducted under a single protocol.

Purposes: To confirm the effectiveness of omeprazole at 4 mg/kg/day for treatment of gastric ulcers in horses, and to determine the dosage of omeprazole required to prevent recurrence of gastric ulcers after the treatment regimen was completed.

Study Designations, Investigators and Study Locations:

Study	Investigator	Location
ASR 15212	F. M. Andrews, DVM	Poindexter Farms, Denison, TX 72020
ASR 15215	F. Hughes, DVM	Sharon Biamonte Training Center, Morriston, FL 32668
ASR 15235	R. L. Sifferman, DVM	Poindexter Farms, Denison, TX 72020
ASR 15238	W. Bernard, DVM	The Kentucky Horse Center, Lexington, KY 40511

Animals: 100 clinically healthy, adult, Thoroughbred racehorses in training ranging in age from 2 to 11 years. Horses were diagnosed with gastric ulcers using gastric endoscopy.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: For the first 28 days of the studies, omeprazole was administered daily at 4 mg/kg. For the next 30 days, daily omeprazole dosages of 2 and 4 mg/kg were tested.

Controls: Control horses were sham dosed.

Duration of Study: 58 days

Study Design: Twenty-five horses were assigned to the control group and seventy-five horses to the treatment group, which consisted of daily administration of omeprazole at 4

mg/kg. In the first part of the study, severity of ulcers was confirmed at baseline and reassessed after 14, 21, and 28 days. Ulcer severity was assessed using gastric endoscopic examinations and a uniform scoring system as follows:

Ulcer scoring system: A score for the worst stomach lesion was recorded for each horse.
0= intact mucosal epithelium (can have reddening/hyperkeratosis)
1=small single or small multifocal lesions
2=large single or large multifocal lesions
3=extensive lesions with areas of deep ulceration
The presence of reddening or hyperkeratosis was also recorded.

In the second part of the study, 75 horses that had received omeprazole at 4 mg/kg for 28 days were reassigned either to continue on a daily dosage of 4 mg/kg for an additional 30 days, or to a reduced daily dosage of 2 mg/kg, or to sham dosing with an empty syringe (25 horses/group). The original 25 horses assigned to sham dosing in part one of the study were continued on sham treatment. Ulcers were reassessed in all groups at the end of the 30 days.

Data Analysis: The pooled data on change in ulcer score for animals in all four trials were analyzed non-parametrically using a Cochran-Mantel-Haenszel procedure to assess differences between omeprazole and control in the first 28 days, and to assess differences between dosages in the next 30 days, and to compare ulcer status of horses maintained on omeprazole vs. those discontinued from treatment.

Results: Horses treated with omeprazole for 28 days had significantly ($p<0.01$) greater improvement in ulcer score than the controls. Ulcer scores were improved (lower gastric score at day 28 vs. pretreatment score) in 92% of omeprazole treated horses after 28 days of treatment compared to only 32% of control horses. Of the omeprazole treated horses, 77% had complete ulcer healing (lesion score of 0) vs. 4% of the control horses had completely healed.

For the second part of the study, prevention of recurrence was represented by the % of horses with gastric lesion scores at day 57 that were healed, improved from the day 27 score, or did not change from the day 27 score for each treatment group. There was a significant difference ($p<0.01$) in prevention of recurrence between the horses removed from omeprazole treatment vs. those continuing on omeprazole at either the 2 or 4 mg/kg dose of omeprazole. However; there was no significant difference between the effects of omeprazole at dosages of 2 and 4 mg/kg in prevention of recurrence of ulcers.

Of those horses treated with placebo for the second part of the study, 8% of the controls were healed (See Table 2) at the end of 57 days. None of the horses in this group

improved from their day 27 scores, 8% maintained the same score, and 84% worsened compared to their day 27 scores.

Of those horses treated at 2 mg/kg for the second part of the study, 76% of the horses had healed gastric ulcers, no horses improved from their day 27 scores, 8% maintained the same score and 16% worsened as compared to their day 27 scores.

Of those horses treated at 4 mg/kg for the second part of the study, 84% were healed, 4% improved over their day 27 scores, none of the horses maintained the same score and 12% worsened as compared to their day 27 scores.

Table 2. Day 57 results of study for horses in each treatment group (0 = placebo, 2 mg omeprazole/kg, 4 mg omeprazole/kg) represented as percent healed, improved, no change and worsened as compared to the day 27 gastric lesion score.

Day 57	0	2 mg/kg	4 mg/kg
% healed*	8	76	72
% improved from day 27 score*	0	0	4
% no change from day 27 score*	8	8	0
% worsend from day 27 score	84	16	12

*prevention of recurrence is represented by the percent of horses healed, improved or no change from the day 27 gastric lesion score, i.e., for the 2 mg/kg treatment group 76 + 0 + 8 = 84%

Conclusions: The omeprazole paste formulation, administered daily at 4 mg/kg for 28 days, is effective for treatment of gastric ulcers in horses. Continuation of treatment for 30 days at a dosage of 2 mg/kg/day effectively prevents recurrence of gastric ulcers while being treated.

Observations: No adverse reactions were reported.

C. Clinical Field Trial

A multi-center well-controlled, blinded, clinical field trial was conducted under a single protocol. Six sites included clinically healthy horses and foals with gastric ulcers. Ulcers were diagnosed by gastric endoscopic examination.

Clinical Field Trial in Horses with Gastric Ulcers

Purpose: To confirm the safety, efficacy and acceptability of omeprazole at 4 mg/kg/day under field conditions.

Investigators and Trial Locations:

Study	Investigator	Location
ASR 15244	S. McClure, DVM, PhD	Wea Valley Ranch, Lafayette, IN 47905
ASR 15245	G. W. White, DVM	Blue Ribbon Downs, Sallisaw, OK 74955
ASR 15247	C. G. MacAllister, DVM	Equine Research Park, Stillwater, OK 74075
ASR 15250	R. L. Sifferman, DVM	Los Alamitos Race Track, Los Alamitos, CA 90720
ASR 15264	R. L. Sifferman, DVM	Richard Wise Farm, Monett, MO 65708 Shawn Corcoran Farm, Edwardsville, IL 62025 A. B. Twisdale Farm, Mason, TN 38049 Paul Nelms Farm, Lewisburg, TN 37091
ASR 15266	N. J. Vatistas, BVSc, PhD	Peninsula Equine, Inc., Menlo Park, CA 94026

Animals: 139 clinically healthy horses ranging in age from 4 weeks to 28 years. A total of 26 foals between 4 and 7 weeks old were included. Breeds included: Standardbreds, Thoroughbreds, Quarterhorses, Appaloosas, Paints, Tennessee Walking Horses, Arabians, Holsteiner, Hanoverian, Swedish, Danish and Dutch Warmbloods, ponies, Trakehner cross, Warmblood crosses and Quarterhorse crosses.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: Omeprazole was administered daily at 4 mg/kg for 28 days.

Controls: Control horses were sham dosed daily.

Duration of Study: 28 days

Study Design: Using gastric endoscopic examinations and the standardized scoring system used in the dose confirmation trials, severity of ulcers was confirmed at baseline and reassessed after 28 days of daily treatment with omeprazole at 4 mg/kg. Each horse was examined clinically by a veterinarian before treatment began and again after approximately 14 and 28 days on trial. Ulcer severity was assessed using gastric endoscopic examinations and a uniform scoring system as follows:

Ulcer scoring system: A score for the worst stomach lesion was recorded for each horse.
0= intact mucosal epithelium (can have reddening/hyperkeratosis)
1=small single or small multifocal lesions
2=large single or large multifocal lesions
3=extensive lesions with areas of deep ulceration
The presence of reddening or hyperkeratosis was also recorded.

Data Analysis: The pooled data on change in ulcer score from the six sites were analyzed non-parametrically using a Cochran-Mantel-Haenszel procedure to assess differences between omeprazole and control after 28 days. Incidences of observations on health condition were analyzed by a Mantel-Haenszel test.

Results: Horses treated with omeprazole had significantly ($p<0.01$) greater improvement in ulcer score than the controls. Improvement is defined as a lower gastric lesion score at day 28 compared to pretreatment score. Ulcers scores were improved in 99.0% of omeprazole treated horses compared to 32.4% of control horses. Ulcers were healed (gastric score of 0) in 86.7% of omeprazole treated horses compared to 8.8% of control horses.

There was no clinically significant difference between groups in incidences of observations on health condition. The paste was well accepted by horses and foals.

Concomitant medications including anesthetics, anthelmintics, antibiotics, diuretics, steroidal and non-steroidal anti-inflammatory agents, tranquilizers and vaccines were administered during the field trials without adverse effects.

Observations: No adverse reactions were reported.

Conclusions: The omeprazole paste formulation, administered daily at 4 mg/kg for 28 days, is safe, acceptable, and effective for treatment of gastric ulcers in horses and foals four weeks of age and older.

Acceptability Field Trials in Horses Without Gastric Ulcers

These trials followed the same protocol (dosage form, route of administration, dosage and frequency of treatment, use of controls, and duration of study) as the six sites above, but there was no requirement for pre-existing ulcers.

Purpose: To evaluate acceptability of the paste to foals and yearlings.

Investigator and Trial Locations:

Study	Investigator	Location
ASR 15241	M. J. Murray, DVM	Virginia Tech Mare Center, Middleburg, VA 20117
ASR 15242	M. J. Murray, DVM	Virginia Tech Mare Center, Middleburg, VA 20117

Animals: 40 Thoroughbred foals/yearlings, ranging in age from 11 to 16 weeks and from 15 to 17 months. There were 18 female foals and 22 males.

Results: These studies demonstrated that administration of 4 mg omeprazole/kg to weanlings and yearlings was clinically safe and that product acceptability was satisfactory. This study was not designed to evaluate efficacy; however, endoscopic exams were performed pre and post treatment. As a result, it was found that two of the foals in study ASR 15241, which initially did not have ulcers, developed ulcers while on omeprazole (4 mg/kg). Likewise, one of the treated yearlings which was free of ulcers at the start of the trial, also developed ulcers by the end of the study. It appears from these observations, that the 4 mg/kg of omeprazole did not prevent the development of ulcers in these animals.

Conclusion: Omeprazole paste for horses was clinically safe and acceptable when administered to foals and yearlings under field conditions; however, it did not prevent the development of ulcers in several foals.

Observations: No adverse reactions were reported.

V. TARGET ANIMAL SAFETY

Four controlled, GLP safety trials were conducted using exaggerated dosages of the marketed formulation of omeprazole paste for horses. One study was conducted in foals. Two studies were conducted in adult horses of both sexes. One study evaluated reproductive safety in breeding stallions.

A. Safety Trial in Foals (ASR 15237)

Purpose: To evaluate the health effects of omeprazole when administered orally to young horses at 4, 12 and 20 mg/kg (1, 3 and 5X the use level) daily for three months.

Investigator and Trial Location: Raymond Plue DVM
Merial Missouri Research Center
Fulton, MO 65251

Animals: 24 Tennessee Walking Horse foals (12 males, 12 females), ranging in age from 66 to 110 days.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: Foals were dosed daily for 91 days with omeprazole at either 4, 12 or 20 mg/kg (1, 3, or 5X). Each treatment group consisted of 6 foals (3 males, 3 females).

Controls: 6 control foals (3 males, 3 females) were sham dosed daily using empty syringes.

Duration of Study: 91 days

Evaluation: Foals were observed twice daily for clinical signs of toxicity and health problems. Blood chemistry, hematology and physical examinations were conducted on Days -7, 15, 29, 59 and 90 for all foals. Hematology profile included RBC, WBC, platelet count, hemoglobin, PCV, MCV, MCH, MCHC, WBC differential, and RBC morphology. Chemistry profile included calcium, phosphorus, sodium, potassium, chloride, AST, GGT, cholesterol, triglycerides, glucose, total bilirubin, total protein, total globulin, A/G ratio, blood urea nitrogen, creatinine, alkaline phosphatase, sorbitol dehydrogenase, serum iron, and albumin. Physical exams evaluated general appearance, appearance of feces,

respiration rate, temperature, heart rate, auscultation of the GI tract, and appearance of oral and ocular mucous membranes.

Foals were necropsied on Day 91, 92 or 93. Following a gross macroscopic observation, samples were collected and submitted for histopathology from the adrenals, lungs, heart, liver, mesenteric lymph node, lower esophagus, stomach (squamous, fundic, and pyloric), duodenum, jejunum, ileum, cecum, spleen, submandibular lymph node, large colon, rectum, gonads, prostate, uterus, pancreas, kidneys, urinary bladder, thymus, and small colon. Any gross lesion noted was also submitted. A bone marrow smear from each foal was also prepared at necropsy.

Results: GGT levels were significantly elevated in the 20 mg/kg dosage group (p= 0.0689). Necropsy results showed no evidence of hepatic disease.

Mean stomach to body weight ratio was higher for foals in the 3X and 5X groups than for controls. No abnormalities of the stomach were evident on histological examination, and this was considered to be of no clinical relevance.

Statistically significant differences among treatment groups were found for albumin, albumin/globulin (females), globulin, cholesterol, SDH, sodium, total protein, calcium, chloride, hematocrit, hemoglobin, lymphocytes, and monocytes (females). However, these changes were not clinically significant.

No statistically significant treatment effects were found for alkaline phosphatase, AST, BUN, creatinine, glucose, serum iron, phosphorus, potassium, total bilirubin, triglycerides, albumin/globulin (males), MCH, MCV, RBC, RDW, WBC, neutrophils, or eosinophils.

Conclusion: No treatment related adverse effects were seen following administration of omeprazole to young horses orally at a dose of 4 mg/kg (1X) once daily for 91 days. Omeprazole administered to young horses at doses of 20 mg/kg for 91 days resulted in elevations of GGT levels. Doses of 12 mg/kg and 20 mg/kg may result in increased stomach weights. Neither of these findings were considered clinically significant, since histopathology of the liver and stomach was considered normal.

B. Safety Trial in Adult Horses (ASR 15205)

Purpose: To determine the occurrence of any adverse health effects of omeprazole when administered orally at 20 mg/kg (5X the use level) daily for 3 months.

Investigator and Trial Location: Raymond Plue DVM
Merial Missouri Research Center

Fulton, MO 65251

Animals: 18 adult Thoroughbred horses (9 males, 9 females), ranging in age from 4 to 20 years.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: Twelve horses were dosed daily for 3 months with omeprazole at 20 mg/kg (5X). One group of 6 horses (3 male, 3 female) was necropsied after 3 months. The other group (3 male, 3 female) was discontinued from treatment at the end of 3 months and kept under observation for an additional 82 days to determine the reversibility of any adverse reactions that may have been apparent after necropsy of the first treatment group.

Controls: 6 control horses (3 male, 3 female) were sham dosed daily using empty syringes. These horses were necropsied after 3 months.

Duration of Study: 3-6 months

Evaluation: Horses were observed twice daily for clinical signs of toxicity and health problems. Blood chemistry, hematology and physical examinations were conducted before treatment and on Days 14, 29, 61 and 90. Necropsies were conducted on Day 91 or 92.

Results: There were no clinical, hematological, blood chemistry, gross or microscopic pathological abnormalities related to treatment in any of the groups. Gastric ulcers were present in each of the 6 control horses and in none of the 6 omeprazole-treated horses that were necropsied ($p<0.01$). Because no treatment-related adverse effects were observed in the horses necropsied at 3 months, the remaining six horses were not necropsied.

Conclusion: There were no treatment related adverse effects observed in adult horses after treatment with omeprazole orally at a dose of 20 mg/kg (5X) daily for 3 months.

C. 10X Tolerance Trial in Adult Horses (ASR 15251)

Purpose: To evaluate the safety of omeprazole when administered orally at 40 mg/kg (10X the use level) daily for 21 days.

Investigator and Trial Location: Raymond Plue DVM
Merial Missouri Research Center
Fulton, MO 65251

Animals: 6 adult Thoroughbred horses (3 males, 3 females), ranging in age from 3 to 17 years

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: Horses were dosed daily for 21 days with omeprazole at 40 mg/kg (10X). Two males and two females received this dosage.

Controls: 2 control horses (1 male, 1 female) were sham dosed daily using empty syringes.

Duration of Study: 3 weeks

Evaluation: Horses were observed for general health at least twice daily. Physical examinations were conducted on Day -1 and on Days 2, 9 and 21. Blood samples were drawn for serum chemistry and hematology evaluation at these times. Physical examination included observations of general appearance, appearance of feces, respiration rate, temperature, heart rate, auscultation of the gastrointestinal tract, and appearance of oral and ocular mucous membranes.

Hematology profile included RBC, WBC, platelet count, hemoglobin, PCV, MCV, MCH, MCHC, WBC differential, and RBC morphology. Chemistry profile included calcium, phosphorus, sodium, potassium, chloride, AST, GGT, cholesterol, triglycerides, glucose, total bilirubin, total protein, total globulin, A/G ratio, urea nitrogen, creatinine, alkaline phosphatase, sorbitol dehydrogenase, and serum iron. Hematology and chemistry data were not subjected to statistical analysis due to the small sample size.

Horses were necropsied on Day 22. The description of gross lesions, stomach weights, and liver weights were recorded; and gross lesions and tissues were histologically examined.

Results: No adverse effects, gross or histologic lesions attributable to omeprazole were noted during the study. On necropsy, stomach ulcers were identified in one control horse and none of the omeprazole-treated horses.

Conclusion: Omeprazole administered to adult horses at 40 mg/kg (10X) daily for 21 days had no adverse effects on clinical chemistry, hematology, physical examination, and macroscopic or microscopic assessments at necropsy.

D. Safety Trial in Breeding Stallions (ASR 15009)

Investigator and Trial Location: A. Alexander, BVSc (Study Director)
N. Perkins, BVSc, MS, DipACT (Theriogenologist)
Sovereign Lodge Stud Limited
Ohau, New Zealand

Purpose: To determine the effect of omeprazole on reproductive parameters of breeding stallions when administered orally at 12 mg/kg (3X the use level) daily for 10 weeks.

Animals: 20 stallions (Thoroughbred or Standardbred) ranging in age from 3 to 12 years. Stallions were selected based on designated baseline minimum standards for semen parameters (total number of sperm, progressive motility of sperm, sperm morphology, and seminal pH) prior to entering the study. In addition, all stallions were examined and determined to have normal genitalia prior to inclusion in the study.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: 10 stallions were dosed daily for 71 days with omeprazole at 12 mg/kg (3X).

Controls: 10 control stallions were sham dosed daily for 71 days using an empty syringe.

Duration of Study: 10 weeks

Evaluation: Ten pairs of stallions were formed based on a ranking of descending average daily sperm output on Days -11 to -2. In each pair, one stallion was randomly assigned to receive omeprazole and the other to control. Semen was collected from each stallion on Days -16 to -12 and Days 56 to 60 to stabilize extragonadal reserves. Semen was collected for analysis on Days -11 to -2 and Days 61 to 70. Reproductive behavior was evaluated on all days that semen was collected for analysis. Semen was evaluated for the following: volume collected (gel and gel-free), gross appearance, seminal pH, percent progressively motile sperm, sperm concentration, and total number of sperm in the gel-free fraction. Sperm morphology (normal, abnormal head, detached head, proximal droplet, distal droplet, abnormal midpiece, abnormal tail) was determined. The presence of mononuclear cells or other cell types was also noted.

External and internal palpation of the genitals was conducted on Days -21, -19, -18, -17 or -16, and on Day 71. The exam included testis size (length, width, height) and consistency,

and determination of any gross abnormalities of the epididymis and spermatic cord. The prepuce, penis, and scrotum were examined. Internally, the inguinal rings, vesicular gland, ampullae, and prostatic lobes were evaluated.

Results: No treatment-related adverse effects were seen on the variables evaluated.

Conclusion: Omeprazole administered to stallions daily for 71 days at 12 mg/kg/day (3X the recommended dose) had no adverse effects on semen quality or breeding behavior.

VI. HUMAN SAFETY

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. The drug is labeled for use in horses, which are non-food animals. The following Warning statement appears on the product label: "Not for use in horses intended for human consumption."

VII. AGENCY CONCLUSIONS:

The data in support of this NADA comply with the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and Section 514.111 of the implementing regulations. The data demonstrate that Gastrogard™ (omeprazole), when used under labeled conditions, is safe and effective.

The drug is restricted to use by or on the order of a licensed veterinarian because professional expertise is judged to be critical in the diagnosis of gastric ulcer disease in horses.

Under Section 512(c)(2)(F)(i) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for FIVE years of marketing exclusivity beginning on the date of approval because no active ingredient (including any ester or salt of the active ingredient) has been approved in any other application.

Patent Information: US Patent 4255432, Expiration April 5, 2001; US Patent 5708017, Expiration April 4, 2015.

VIII. PRODUCT LABELING

Syringe
Carton
Package Insert