



Memorandum

April 2, 2004

Date

Veterinary Medical Officer, HFV-222

From

Go Natural Dog and Cat Food Recall

Subject

Barbara Rodgers, Recall Coordinator, (HFV-235)

To Thru: CVM Animal Health Hazard Evaluation Committee (HFV-210 & 220)

Products & Background: Merrick Pet Foods (Hereford, TX) apparently manufactured at least 9 lots of Go Natural Pet Food for Petcurean Pet Nutrition, Inc. beginning in June 2003. Merrick manufactured the product and packaged it in finished form. Petcurean owns the formulation, but did not retain oversight of the manufacturing operations (i.e. they did not review batch records, perform audits, etc.). The formulations for the Go Natural dog and cat foods are provided in Appendix A.

On October 22, 2003, Petcurean Pet Nutrition, Inc. (the firm) initiated a voluntary recall of all Go Natural dog and cat foods manufactured at Merrick Pet Foods (Merrick) since June 2003. This recall was initiated because the firm was aware of 15-18 complaints of pet illness and 7 dog deaths that were associated with these dog and cat foods.

Approximately 30,000 pounds of product in 4, 8, 12 and 30 pound bags were removed from the shelves of over 60 retail stores by Wednesday, October 22, 2003. The retail stores were located in the Denver, Colorado area (Colorado Springs, Longmont, Falcon, Greenwood Village, Greeley, Fort Collins, Pueblo, Lafayette, Wheatridge and Broomfield), in the Seattle, Washington area (Mukilteo, Stanwood, Snohomish, Seattle, Maplevalley, Woodinville, Mill Creek, Monroe, Bellingham, Mt. Vernon and Spanaway), and in southern California (Reseda, Mission Viejo, Sherman Oaks, Chula Vista, Riverside, Los Angeles, Fallbrook, Glendora, San Diego, La Jolla, Vista, Solana Beach, Temecula, Ojai, Fullerton, Manhattan Beach, Rancho Bernardo, Van Nuys and San Marcos). The retail stores in the bay area (San Francisco/Oakland) were not provided to CVM, but the distributor for this area was Pet Food Express in San Leandro, CA. We are not aware of any reports of adverse effects from Go Natural dog or cat food delivered to the Denver or Seattle areas.

Owners and/or veterinarians have reported that dogs were consuming or had recently consumed 5 different lots of Go Natural dog food when adverse effects were noted. The 5 implicated lot numbers (#) include F1332, F1631, F1931, G1631 and H2731. (Note: F1631 indicates this was the first run or batch produced on June 16, 2003; F = 6th month; 16=16th day of month; 3 = 2003; 1 =1st run or batch of day). In at least 4 additional households where adverse effects were noted, the Go Natural lot # was unknown. The FDA collected two samples of dog food from lot # F2031. This lot was manufactured between the implicated lots above, but has not been associated with any adverse effects reported to CVM (Appendix B). The FDA also collected 3 samples of dog food (Garth Merrick's Beef 'n More Brand, n=2; O&M Holistic Puppy Food, n=1) and 1 sample of a custom vitamin/mineral premix during their inspection at Merrick, but these samples were not included in Appendix B.

Lots F1731 and G0931 were fed to 2 cats in the same household. Lot G0931 was only provided to encourage these cats to eat after adverse effects were noted while the owner was feeding lot F1731. Thus, lot G0931 probably should not be considered an implicated lot. The FDA also collected 1 sample of cat food from lot G1731, but this lot has not been associated with any adverse effects reported to CVM (Appendix B).

On October 8, 2003, FDA Consumer Complaint #21315 was received by the Los Angeles District Office of the FDA (LOS-DO). On October 22, Oct. 24, Oct. 27 and Oct. 27 complaints of additional illnesses and deaths in dogs and/or cats were received from [redacted]

[redacted] respectively. On November 12, 2003, Katherine Jacobitz, FDA, LOS-DO provided findings in the report entitled "Follow Up to Complaint #21315" and Andrea Scott (San Francisco DO) faxed data on 2 cases to Dr. Bill Burkholder (CVM).

In addition, FDA has received clinical pathology information on 5 dogs from the [redacted]

[redacted] and on a dog from the [redacted]
CVM has communicated via e-mail with [redacted]

[redacted] about 2 dogs in one household that became ill after consuming the Go Natural dog food. In the collection reports from FDA samples #242471 and #253754, there is limited information about one dog, its owner, and the veterinarian that treated it [redacted]. In the collection reports from FDA samples #254747 and #253748, there is limited information about three dogs in one household and the veterinary that treated them [redacted]. In the collection report from FDA sample #253755, there is limited information about one dog, its owner, and the veterinarian that treated it [redacted]. Andrea P. Scott sent an e-mail to Britt L. Pratt entitled Updated Petcarean chart on Wednesday, October 29, 2003 (5:14 PM). This e-mail provided information (pet, dog/cat, attending vet, referring vet, diagnosis, metal, status, Go! Natural lot, sample location and FDA sample #) on 25 dogs and 3 cats. Finally, FDA has worked with and obtained information from the California Animal Health and Food Safety Laboratory System (CAHFS) on Go Natural-related cases (primarily Drs. Birgit Puschner and Asheesh Tiwary).

The suspect pet food has been analyzed by at least three labs for multiple elements (aluminum, antimony, barium, boron, cadmium, calcium, chromium, cobalt, copper, iron, lead, magnesium, manganese, mercury, molybdenum, phosphorus, potassium, selenium, sodium, sulfur, thallium, uranium, and/or zinc). None of the values in the suspect pet food for copper, iron or zinc were above maximum limits established by the Association of American Feed Control Officials, Inc. (AAFCO) in dog and cat foods (see Official Publication 2004 of AAFCO pages 129 and 134). The AAFCO maximum levels for copper, iron and zinc in dog food on a dry matter basis are 250 mg/kg (parts per million or ppm), 3000 mg/kg, and 1000 mg/kg, respectively. No maximum levels for copper and iron have been established by AAFCO in cat food. The maximum level for zinc in cat food on a dry matter basis is 2000 mg/kg. Copper levels in the Go Natural dog and cat foods ranged from about 30 to 85 mg/kg. Iron levels in the Go Natural dog and cat foods ranged from about 390 to 580 mg/kg. Zinc levels in the Go Natural dog and cat food ranged from about 450 to 930 mg/kg.

None of the non-essential elements that were measured in the Go Natural dog and cat foods were considered to be present at toxic amounts. All of the essential elements that were measured in the Go Natural dog and cat foods appeared to be present within normal ranges (not toxic and not deficient).

Maximum tolerated levels for many elements have been established in Mineral Tolerances of Domestic Animals (National Academy of Sciences/National Research Council, Washington, DC, 1980). CAHFS analyzed the liver and kidneys from 8 dogs that died for copper, iron and zinc. CAHFS analyzed 16 serum samples for copper, iron, and zinc.

Copper values in the liver ranged from 19.3 to 138 mg/kg with a median of 45.3 ppm. Copper values in the kidney ranged from 8.8 to 32.6 mg/kg with a median of 21.0 ppm. Serum copper values ranged from 0.64 to 1.2 ppm with a median of 0.89 ppm.

Iron values in the liver ranged from 199 to 768 mg/kg with a median of 450 mg/kg. Iron values in the kidney ranged from 178 to 849 mg/kg with a median of 528 mg/kg. Serum iron values ranged from 0.72 to 6.71 ppm with a median of 1.86 ppm.

Zinc levels in the liver ranged from 31.4 to 77.9 mg/kg with a median of 38.4 mg/kg. Zinc levels in the kidney ranged from 18.9 to 35.5 mg/kg with a median of 28.7 mg/kg. Serum zinc values ranged from 0.20 to 2.29 ppm with a median of 0.95 ppm.

We believe the best perspective is gained by showing a reference range for values that are considered deficient, normal, adequate, high and/or toxic and the number of dogs within each category. The reference ranges came from Mineral Levels in Animal Health – Diagnostic Data (R. Puls, Sherpa International, 1988).

In this case, the levels of copper, iron and zinc are all within acceptable levels in the dog and cat food. In addition, liver copper, iron and zinc levels were consistently in the normal/adequate range or between the adequate and high ranges. However, 12 of the 16 serum copper values were slightly above the normal range (high and toxic range not defined) and 5 of the 8 kidney copper levels would be considered in the toxic range (4 of these 5 just barely so). Six of the 16 serum iron values were between the adequate and high range and 7 of the 16 values were in the high range (toxic range not defined). Seven of the 8 kidney iron values were above the high range (toxic range not defined).

To establish a copper, iron or zinc toxicosis as a result of consuming the diet, one would expect to find values in the high or toxic ranges in the diet, liver, kidney and serum. Copper, iron and zinc levels in the pet food were all well below the maximum levels set by AAFCO. The liver copper and zinc levels were consistently in the adequate or normal range and most of the liver iron levels were between the adequate and high range. Interestingly, serum iron and copper levels were consistently above the normal/adequate range or in the high range and kidney copper and iron values were above the high range or in the toxic range. Our interpretation of this data is that elevated copper and iron levels in the serum may play a role in the adverse effects noted in these dogs; however, the copper and iron levels in the pet food were within acceptable limits and likely did not directly cause these serum elevations.

LIVER COPPER

	Reference Range (ppm wet wt.)	# of dogs
Deficient	< 20	1
Normal	30 – 100	6
	[101 – 399]	1
Toxic	400 – 3000	0

KIDNEY COPPER

	Reference Range (ppm wet wt.)	# of dogs
Deficient	<5.0	0
Normal	5.0 – 15.0	3
Toxic	>20	4
	[20.0 – 25.0]	4
	[32.6]	1

SERUM COPPER

	Range (ppm)	# of dogs
Deficient	<0.20	0
Normal	0.20 – 0.80	4
	[0.81 – 1.20]	12
Toxic	not defined	

LIVER IRON

	Reference Range (ppm wet wt.)	# of dogs
Deficient	20 – 60	0
Adequate	100 – 300	1
	[301 – 499]	5
High	500 – 1125	2
Toxic	not defined	

KIDNEY IRON

	Reference Range (ppm wet wt.)	# of dogs
Deficient	30	0
Adequate	75 – 260	1
High	120 - 270	0
	[271 – 550]	5
	[750 – 850]	2
Toxic	not defined	

SERUM IRON

	Range (ppm wet)	# of dogs
Deficient	<0.95	1
Adequate	0.94 – 1.22	2
	[1.23 – 2.00]	6
High	>2.00	6
	[2.01 – 3.00]	6
	[6.71]	1
Toxic	not defined	

LIVER ZINC

	Reference Range (ppm wet wt.)	# of dogs
Deficient	< 15	0
Adequate	30 – 70 [71 – 80]	7 1
Toxic	369	0

KIDNEY ZINC

	Reference Range (ppm wet wt.)	# of dogs
Deficient	< 8	0
Adequate	16 – 30 [31 – 40]	6 2
Toxic	295	0

SERUM ZINC

	Range (ppm)	# of dogs
Deficient	[<] 0.20 [0.20 – 0.69]	0 3
Adequate	0.70 – 2.00 [2.01 – 2.30]	12 1
Toxic	10.0 – 32.0	0

CAHFS, the FDA and/or private labs have also analyzed various samples for mycotoxins (aflatoxins, sterigmatocystin), non-steroidal anti-inflammatory drugs, anticoagulant rodenticides, anti-oxidants (BHA, BHT, ethoxyquin, and Ionox-100), fat-soluble vitamins (A, D and E), organophosphate and organochlorine pesticides, equine DNA, and percentage of fat. Samples have also been analyzed by a GC/MS screen, examined by a feed microscopist, and cultured for Salmonella, aerobic bacteria, and anaerobic bacteria. The only two findings of interest were elevated levels of BHA (butylated hydroxyanisole) in four lots of Go Natural dog food and the culturing of a few colonies of *Pseudomonas aeruginosa* from a liver biopsy in 1 dog.

BHA is generally recognized as safe for use in food when the total content of antioxidants is not over 0.02 percent of fat or oil content, including essential (volatile) oil content of the food, provided the substance is used in accordance with good manufacturing practice (21 CFR 582.3169; Title 21 of the Code of Federal Regulations, Section 582, part 3169). Go Natural lot #F1631 contained about 12.2% fat and about 250 ppm of BHA. Thus, BHA was overformulated about 10X in this lot. Go Natural lot #G1631 contained about 13.9% fat and about 365 ppm of BHA. Thus, BHA was overformulated about 13X in this lot. Go Natural lot #H2731 contained about 12.9% fat and about 312 ppm of BHA. Thus, BHA was overformulated by about 12X in this lot. Go Natural lot #F1931 contained about 12.9% fat and about 104 ppm of BHA and was overformulated by about 4X. BHA and fat levels in Go Natural lots #F2031 (dog food) and #G1731 (cat food) ranged from non-detect to 24 ppm and from 16.3 to 21.1%, respectively. The BHA levels in these two lots were within the concentrations approved in 21 CFR 582.3169 (Appendix B).

It is worth noting that the 4 lots of dog food that were overformulated 4-13X with BHA (F1631, G1631, H2731, and F1931) were also implicated by the owners and/or veterinarians in complaints to the FDA. Lot G1731 was a cat food sample that was collected at the request of the Dallas District Office (DAL-DO) and has not been implicated by an owner or veterinarian. Lot F2031 was a dog food sample that was also collected at the request of the DAL-DO. This lot, which has not been implicated by an owner or veterinarian, was selected because the lot code is between other lot codes that are in question in relation to dog illnesses. Despite the overformulation of BHA in 4 implicated lots (and no overformulation of BHA in 2 non-implicated lots), a preliminary review of the toxicity of BHA in dogs indicated that no adverse effects would be expected even at these elevated (4-13X) levels (Food Antioxidants – Technological, Toxicological, and Health Perspectives; edited by D. L. Madhavi, S. S. Deshpande, and D. K. Salunkhe; Marcel Dekker, Inc., 1996; chapter 5).

The second interesting finding came from one dog that had a fine needle aspirate of the liver taken on 9/23/03 and a liver biopsy taken on 9/26/03. An aerobic culture of the fine needle aspirate by [redacted] showed no growth on direct plating media and broth culture in 72 hours. An aerobic culture of the biopsy showed a few colonies of gram negative organisms on the third day and a few colonies of *Pseudomonas aeruginosa* were identified on the fourth day. To our knowledge, this is the only positive culture finding in tissues and may be due to contamination during sample collection, during sample transport, or during culturing.

Despite extensive testing by CAHFS, the FDA and private laboratories, a definitive cause of the ill effects in the dogs and cats has not been determined. The clinical pathology, clinical signs, histology, urinalysis, ultrasound, radiograph, and gross necropsy findings were provided on 1 to 25 dogs by the sources described above. These results are summarized below.

Age, Gender and Breed of Dogs

There did not appear to be an age, breed or gender predilection, although in at least 5 households (and likely six) multiple dogs were affected.

2 month old, male, Golden Retriever
2 month old, male, Golden Retriever
2 month old, female, Golden Retriever
2 ½ year old, female, Golden Retriever
1 year old, female, Golden Retriever
1 year old, male, Golden Retriever
1 year old, male, Golden Retriever
7 month old, female, Golden Retriever

3 month old, female, Golden Retriever
5 year old, female, Golden Retriever
Age not provided, male, Golden Retriever
3 year old, male, Golden Retriever
2 year old, male, Golden Retriever
< 6 month old, gender and breed not provided
9 month old, male, Golden Retriever

Age, gender and breed not provided

Age, gender and breed not provided

Age, gender and breed not provided

2 ½ year old, male neutered, Labrador Retriever

1 year old, male, Labrador Retriever

Age not provided, male Weimaraner

Age and breed not provided, female

10 month old, male neutered, Cocker Spaniel

10 month old, female spayed, Cocker Spaniel

4 year old, female spayed, Cocker Spaniel

1 year old, male neutered, Cockapoo

3 year old, male, English Springer Spaniel

3 year old, female spayed, Staffordshire Bull Terrier

15 month old, male

2 year old, female spayed, Boxer

8 ½ mo old, female, Australian Shepherd/Border Collie mix

10 year old, female, Australian Shepherd

Age, gender and breed not provided

Age, gender and breed not provided

Age, gender, breed and name not provided.

Age, gender and name not provided; breed American Staffordshire

In addition, 12 dogs

from 6 different attending veterinarians

were mentioned in the 10/29/03 e-mail from Andrea Scott. [Note: No age, gender, breed or owner information was available on these 12 dogs.]

Clinical Pathology

Clinical pathology results were available from 25 dogs. There was evidence of cholestasis, liver dysfunction, anemia, and/or hemolysis in all animals. These results are presented in Appendix C.

Appendix C (page 1) shows the results in what appears to be the most seriously affected dogs. These 6 dogs all have clinical pathology findings suggestive of

cholestasis (increased alkaline phosphatase [ALP],

liver dysfunction (increased alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]) (decreased total protein, albumin, globulin, and/or cholesterol),

anemia (decreased red blood cell count [RBC], hemoglobin [Hg] and/or hematocrit [Hct]), and

hemolysis (increased total bilirubin, direct bilirubin and/or indirect bilirubin).

Appendix C (page 2) shows the results in 6 dogs with evidence of hemolysis, cholestasis, and/or liver dysfunction, but where generally no information was provided about whether an anemia was present.

Appendix C (page 3) presents data on 4 dogs. In 2 dogs there is no bilirubin data. In the other 2 dogs, there is evidence of anemia and cholestasis, but no evidence of hemolysis and only minimal to slight evidence of liver dysfunction.

Appendix C (page 4) shows the results in 6 dogs where the RBC, Hg and Hct values are at the very low end of normal. These dogs show evidence of cholestasis, only minimal to slight evidence of liver dysfunction, and no evidence of hemolysis.

Appendix C (page 5) shows the results in 3 dogs where the only abnormal value was a slight increase in alkaline phosphatase (suggestive of cholestasis).

Finally, in 2 dogs that died, blood/serum samples were collected over several days and they provided clinical pathology changes over time (Appendix C, page 6). A few days to hours before death there was a marked drop in hematocrit and a sharp increase in total bilirubin in both animals. This suggests that hemolysis of red blood cells and the resulting anemia played a major role in their deaths.

[Note: Alkaline phosphatase is one of the most sensitive indicators of cholestasis and increases in serum activities precede the onset of hyperbilirubinemia or bilirubinuria. Hyperbilirubinemia (increased total bilirubin) only occurs if hemolysis is of sufficient duration for bilirubin to be formed and bilirubin formation is of sufficient magnitude to exceed the capacity of the liver to conjugate it.]

Clinical Signs

Clinical signs were well characterized in 13 dogs. The specific clinical sign and the number of dogs (out of 13) in which the clinical sign was reported are presented below:

Clinical Sign	# of Dogs
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Anorexia/Not Eating/Inappetence	11
Icterus	10
Lethargy/Depression/Dull/Decreased Activity	9
Diarrhea/Loose Stool	7
Discolored Urine (orange/chocolate/tea-colored & hematuria)	7
Vomiting	7

Inappropriate Urination/Urinating on Bed Spread or Floor	4
Seizure	3 (1 was glucose responsive)
Polyuria/Polydipsia	3
Resents (painful) abdomen on palpation	2
Melena	2
Fever	2
Weight Loss/Thin	2
Weakness	2
Systolic murmur (II/VI and 0 - 1/2/VI)	2

Clinical signs reported in only 1 dog included hypersalivation, ascites, pale and tacky mucous membranes, and trouble breathing.

[Note: It appears that at least fourteen dogs and 2 unnamed dogs associated with this recall have died or were euthanized. It appears these 14 dogs came from at least 10 different owners.]

Histology

Eight dogs had liver biopsies taken for histology. Hepatitis was noted in 7 dogs and was described as:

mild, diffuse, pleocellular (n=2),
mild-moderate, multifocal, random, pleocellular (n=1),
mild, portal and parenchymal, pleocellular (n=1),
chronic, mild, plasmacytic, lymphocytic, periportal (n=1),
moderate, chronic, active, portal (n=1), and
hepatocellular inflammation (not otherwise specified) (n=1).

Individual or single cell hepatocyte necrosis was found in 6 dogs. Cholestasis was reported in 2 dogs. Hepatocellular pigment accumulation was noted in 2 dogs. Mild copper accumulation was noted in 2 dogs with special staining. In one dog, this mild copper accumulation was described as occurring in clusters of hepatocytes that were primarily (but not always) in periportal locations. Excessive iron deposits, primarily in the sinusoidal macrophage population, were seen with special stains in 1 dog. Other findings reported in only 1 dog were extramedullary hematopoiesis, lobular atrophy, mild bridging fibrosis, mild widespread hepatic lipidosis, diffuse marked vacuolar hepatopathy, and vascular dysplasia.

The CAHFS reported histologic findings from 5 dogs that were presented for necropsy (Appendix D). The lesion pattern in the liver was diffuse (n=4) or periacinar (n=1) in these 5 dogs at death compared to periportal (n=3), diffuse (n=2), multifocal, random (n=1) or not specified (n=1) in the 7 biopsy samples in the live dogs reported above. One interpretation of this data is that the lesion pattern in the liver may change from mostly periportal in live dogs to primarily diffuse at death.

Ultrasound

Ultrasound results were reported on 8 dogs. The liver was described as normal sized in 3 animals and slightly enlarged in 1 dog. Liver echogenicity was decreased (hypoechoic) in 3 dogs and normal in 1 dog. There was marked periportal echogenicity in 1 dog and prominent visualization of portal vasculature in another. The echogenicity of the gall bladder was mildly increased (hyperechoic) in 2 dogs. In 1 dog there was a mild peritoneal effusion and the gall bladder wall was echogenic and thickened. The pancreas was diffusely enlarged in 1 dog, thickened and homogeneously hypoechoic in another, and diffusely thickened and edematous (hypoechoic) in a third.

Urinalysis

Urinalysis results were reported on 8 dogs. Six dogs had bilirubin present (2+, 3+, 3+, 3+, 4+, increased nos). Protein was noted in the urine in 4 dogs (1+, 2+, 3+ and increased nos). Isothenuria or specific gravity of 1.006-1.008 was reported in 4 dogs. Blood (or occult blood) was noted in 3 dogs (3+, 3+ and increased nos). Urobilinogen was found in the urine of 2 dogs (both 12). Findings in only 1 dog included ketone (3+), bile pigment (2+), bilirubin crystals, chocolate-brown color, and orange color. In one dog, every parameter measured was within normal limits.

Radiographs

Radiographs were taken of 4 dogs. Two dogs had gas distention of the GI tract and two had a plump or prominent spleen. One dog had a distended stomach with fluid.

Gross Necropsy

Gross necropsy findings were reported in 1 dog and included icterus, ascites, thickened gall bladder, an enlarged greenish tan liver, serous atrophy of thymic fat, and ~200 ml of a yellow transudate in the thoracic cavity.

Time Course

Few specifics were provided about the number of days a dog was fed a suspect lot of Go Natural before the onset of adverse effects.

One owner indicated to the attending veterinarian that 'He stopped eating the diet a few weeks back.'

Another owner indicates "We began feeding it to our dogs in late February 2003. Sometime in July or August, the dogs appeared to be losing their appetites. We thought this reduced appetite was due to the heat, since it was not uncommon for a dog to eat less in the summer. In August 2003, we weaned a litter of puppies to the food go! NATURAL. The puppies were sent home on August 28. On September 1, we were notified that one of these puppies was sick. We took the puppy to the veterinarian on September 2, and within an hour we received a call that a second pup was sick. The symptoms of both pups were the same. They were lethargic and not eating. On September 3, another puppy still in our possession became sick and was also taken to the vet."

From the records provided, it appears that a litter of Golden Retriever puppies was born on July 7, 2003. These puppies were apparently vaccinated for DMPP (likely distemper, measles, parainfluenza and parvo) on August 18 and for parvo on August 28. Two puppies were sent to their adoptive homes on August 28 and each new owner purchased a bag of Go Natural dog food (lot #G1631) from the original owner. One new owner indicated that the puppy "did not eat anything at all for the first few days." The attending veterinarian indicates the following in the records on September 2, 2003: acquired 8/28—ate only = 1 cup food on day 3—other days minimally.

Based on this information, it seems that the 2 adopted puppies consumed very little of the Go Natural dog food (lot #G1631 which their new owners purchased on 8/28/03) before adverse effects were noted. This begs 2 questions.

First, did the small amount of Go Natural dog food (lot #G1631) consumed between August 28 and September 2 produce the profound clinical pathology changes?

We do not know, but on 9/2/03 both adopted puppies were anemic (Hct 24-31%) and had low albumin levels (1.9-2.0 mg/dL) and increased alkaline phosphatase (931 - 1,029 IU/dL) and alanine aminotransferase activities (309 - 555 IU/dL). Total bilirubin was increased (2.3 mg/dL) in the one puppy in which this parameter was measured.

Second, were the puppies just starting to get sick at the time they were adopted?

We do not know, but we believe the dog food fed to the puppies from the time they were weaned (likely around August 18 at 6 weeks of age) until they were adopted is just as suspect as the dog food given to the adoptive owners. It seems likely these puppies were fed Go Natural dog food from the day they were weaned until they were adopted, but this information was not provided in the records.

Treatments and Outcomes

Treatment of the affected dogs was at least partially described in 12 cases. Although no definitive conclusions can be made, it is worth noting that several animals either did not improve or seemed to get worse for several days after being placed on a beta-lactam antibiotic (amoxicillin, ampicillin) alone or in combination with enrofloxacin (Baytril) and/or other drugs. One record indicates that the dog was on amoxicillin or something similar and developed diarrhea. The veterinarian switched to Flagyl (metronidazole) and the dog did well. Appendix E provides the treatments and outcomes (page 1 shows 9 cases that were given a beta-lactam antibiotic; page 2 shows 3 cases that were not).

Conclusions for Dogs: After reviewing the clinical signs and the results from clinical pathology, histology, urinalysis, ultrasound, radiographs, gross necropsy and time course, we believe hemolysis of red blood cells will be at least a major contributing factor, if not the primary factor, in many of the adverse effects noted in these dogs. The degree and rate of hemolysis may determine whether the animal dies or has only a slight increase in alkaline phosphatase activity with no clinical signs.

It is not clear if minimal oral exposure to lot #G1631 for 4 or 5 days produced the marked clinical pathology changes noted in 2 adopted puppies or if dogs must consume the suspect dog food for about 10-14 days before clinical signs are noted. Vaccination histories of all affected dogs (not just from the 1 litter of puppies described above) would have been useful in this evaluation as hemolytic anemias have been associated with vaccinations (see Merck Veterinary Manual below). Finally, although no definitive conclusions can be made from the treatment/outcome data, there did not appear to be many initial beneficial responses from the use of beta-lactam antibiotics (amoxicillin, ampicillin) when used alone or in combination with enrofloxacin and/or other drugs.

CATS.

CVM has received detailed information on only 4 cats, 2 of which came from the same household. Unfortunately, one of these cats had a large fibrous foreign body in the stomach upon presentation to the veterinarian. This cat underwent surgery (gastrotomy) to remove the foreign body. The veterinarian felt that the foreign body ingestion and the slow recovery from surgery may have been related to the Go Natural exposure. While this could certainly be the case, all data collected on this cat were not included in the summary information provided below because one cannot readily differentiate whether the adverse effects were related to the foreign body in the stomach or to the Go Natural exposure.

Another cat had repeated problems with a feeding tube. When the cat died, there was a dissecting mediastinitis around the feeding tube. We will only present the data on this cat that was apparently collected prior to use of the feeding tube.

Clinical Signs

The clinical signs reported below came from the 3 cats where detailed information was obtained. The specific clinical sign and the number of cats (out of 3) in which the clinical sign was reported are as follows:

Clinical Sign	# of Cats
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Anorexia/Not Eating/Inappetence	2
Weight Loss	2
Icterus	2 (very slight in 1 case)
Vomiting	1
Poor Skin Turgor/10% Dehydration	1

In addition, the [] indicated the following in a facsimile entitled Cat Cases of Go Natural and sent to Dr. Birgit Puschner on November 15, 2003:

“We received 6 reports of cats that would not touch the food after new bags were opened although they had been eating Go Natural for months. I did not check labwork on these cats unless they were not eating. Affected cats ate some of the food and then wouldn’t eat for a more prolong time.”

Clinical Pathology

Three cats had clinical pathology data and the results are presented in Appendix F. There are several similarities with the changes noted in dogs.

Histology

Two cats had liver biopsies taken for histology and the results are provided below:

Moderate to marked hepatic lipidosis (n=2),
Biliary hyperplasia (n=1)
Suppurative and lymphoplasmacytic hepatitis (n=1),
Mild periportal fibrosis (n=1),
Special stain for copper inclusion particles was negative (n=1).

Radiographs

Radiographs were taken on 1 cat and they revealed no evidence of constipation or GI obstruction. The liver appeared slightly enlarged.

Feeding History

The feeding history in one household indicates the following:

“Owner reported that she had been feeding Go Natural Diet for a number of months. When she opened the current bag (lot F1731...) she noted that the kibbles looked very different. They were much smaller than the previous bags of this diet, and the color had uneven dark streaks. Some kibbles were entirely black. There were also 2 larger pieces of food (rounded—not triangular like the other kibbles) that looked more like dog food than cat kibble. The cats did not appear to eat the food readily, and gradually became more anorectic over the course of a few weeks. The owner tried to add in a different bag of Go Natural (lot G01931) [note: likely meant G0931] to encourage the cats to eat, but they were both relatively unwilling to eat the food...”

Conclusions for Cats: All the adverse effects noted in cats appear to have come from owners/veterinarians in the bay area of California (San Francisco, Oakland, etc.). While there are several similarities between the adverse effects noted in dogs and cats, the data in the cats is not as robust and the number of cats with detailed information is much lower. Only 1 cat owner was able to provide lot numbers from the bags of Go Natural. Based on this extremely limited data, the possibility that the adverse effects in cats are due to carryover of dog food into lot F1731 and that this lot was distributed almost exclusively to the bay area of California deserves consideration.

THE MERCK VETERINARY MANUAL.

The following statements come from The Merck Veterinary Manual (8th edition, page 14):

Excessive Destruction

Hemolytic anemias may be extravascular or intravascular. Extravascular hemolysis occurs when the reticuloendothelial system phagocytizes RBC. Hgb (hemoglobin) is converted into bilirubin, resulting in icterus and bilirubinuria. When intravascular hemolysis occurs, RBC release

Hgb into the blood vascular system, resulting in hemoglobinemia, hemoglobinuria, and later, icterus...

Immune-mediated Hemolytic Anemia (IHA): Immune-mediated hemolytic anemia is the accelerated destruction of RBC coated with antibody or antigen-antibody complexes adhered to the RBC surface. It is characterized by a regenerative anemia, spherocytosis (in dogs), and often the presence of autoantibodies against the RBC (positive Coombs' test). Primary (idiopathic) IHA involves only the RBC themselves and accounts for 60-70% of cases in dogs. High concentrations of serum antibody to viral antigens in dogs with primary IHA suggest that idiopathic disease may follow viral infection. One study has provided clinical evidence for a temporal relationship of vaccine-associated IHA in dogs. Secondary IHA is associated with a wide variety of underlying conditions. These include immune-mediated thrombocytopenia, systemic lupus erythematosus, viral disease, severe bacterial infection, granulomatous disease, lymphosarcoma, lymphocytic leukemia, and drug administration. Drugs associated with IHA include trimethoprim sulfa and ormetoprim sulfa in dogs and methimazole and propylthiouracil in cats.

Clinical signs vary with the type of hemolysis and the onset of disease. In cases of complement-mediated intravascular hemolysis, the animal may present with a peracute onset of anemia, hemoglobinemia, hemoglobinuria, sudden weakness, collapse and shock. Animals with acute or chronic disease involving extravascular hemolysis may present with weakness, fever, anemia, and possibly jaundice. Many animals have splenomegaly because the spleen is usually primarily involved in the RBC destruction.

Laboratory findings also vary with the severity and type of RBC destruction. In peracute cases, there is a lack of reticulocytosis. Later, a marked reticulocytosis is seen. Simultaneous bone marrow stimulation commonly results in a neutrophilic leukocytosis with a significant left shift. Serum bilirubin levels vary, as does the presence of hemoglobinuria and bilirubinuria..."

Conclusion: This health hazard evaluation will be written from the perspective that a hemolytic anemia likely played at least a major contributing factor in many of the adverse effects noted in the dogs and possibly played the same role in the cats. The exact cause of the adverse effects in these dogs and cats may never be known as hemolytic anemias have been associated with a wide variety of underlying conditions; however, the ingestion of Go Natural dog or cat foods was the only common factor identified in these cases to date. In addition, no additional cases [adverse effects first noted by an owner] have been reported to CVM within two weeks after the voluntary recall was initiated.

Recalling Firm:

Petcurean Pet Nutrition Inc.
2650 Progressive Way Unit 5
Abbotsford, British Columbia, Canada
FEI #3004062804

Manufacturer:

Merrick Pet Foods
1977 E US Highway 60
Hereford, Texas 79045-3631
FEI Unknown

The CVM/AHHE Committee has considered the information available relative to the referenced proposed recall and offers the following animal health hazard evaluation, based on information available to us at this time.

A. Factors for Consideration [21 CFR 7.41(a) and RPM 5-00-20(h)].

1. Death, illnesses or injuries which have already occurred, from the use of these products.

Death, illness or injury have been reported in at least 48 dogs from over 25 households. These adverse effects were associated with the consumption of at least 5 different lots of the Go Natural dog food. Death, illness or injury have been reported in up to 10 cats. While there are several similarities between the adverse effects noted in dogs and cats, the data in the cats is not as robust and the number of cats with detailed information is much lower than in the dogs.

2. Existing conditions which might contribute to a clinical situation which could expose an animal(s) to a health hazard.

On October 22, 2003, Petcurean Pet Nutrition, Inc. initiated a voluntary recall of all Go Natural dog and cat foods manufactured at Merrick since June 2003. Approximately 30,000 pounds of product in 4, 8, 12 and 30 pound bags were removed from the shelves of over 60 retail stores by Wednesday, October 22, 2003. No additional cases [adverse effects first noted by an owner] have been reported to CVM within two weeks after the voluntary recall was initiated. Since a definitive cause of these adverse effects has not been established, one cannot say with certainty that there are no existing conditions which might contribute to a clinical situation that could expose an animal to a health hazard. All we can say is there have not been any reported problems shortly after this voluntary recall was initiated and Petcurean moved their manufacturing of the Go Natural dog and cat foods from Texas back to Canada.

3. Assessment of the animal population at greatest risk.

Dogs exposed to 5 lots of the Go Natural dog food.(F1332, F1631, F1931, G1631, H2731) appear to be the animals at greatest risk. Cats exposed to lot F1731 also may be at increased risk. Additional lots of the Go Natural dog and cat food may also be problematic, but were not identified. Several owners had already discarded the bag of dog/cat food when they noticed their pet was sick and were not able to provide the lot number(s).

4. Assessment of degree of seriousness of the health hazard to animal population at greatest risk.

Life Threatening. It appears that at least 14 dogs from at least 10 different households have died (or were euthanized) and the only common factor noted to date is that they were or had been consuming various lots of the Go Natural dog food. Many dogs and cats were sick for several days. A few dogs, although markedly improved, still may not have fully recovered.

5. Assessment of likelihood of occurrence of the health hazard.

Probable. Despite not knowing the exact cause of the adverse effects, we believe additional complaints would have been noted if Petcurean had not initiated their voluntary recall.

6. Assessment of immediate or long-range consequences of occurrence of the hazard(s) to animals.

Immediate Consequences are probable. Despite not knowing the exact cause of the adverse effects, we believe that immediate (within two weeks to a month) adverse consequences would probably be noted in several animals if the implicated lots of dog foods were fed in a controlled setting. These immediate consequences would likely be cholestasis, anemia, hemolysis, liver dysfunction and/or liver lesions.

Long Range Consequences are possible, but difficult to predict when a definitive cause is not known. We believe most affected animals likely recovered from the immediate consequences within a few weeks after the recall was initiated; however, the possibility exists that some dogs and cats may not fully recover their health or may develop long range consequences such as fibrosis in the liver. It is also possible that the kidneys may not function at their previous capacity due to the high levels of iron and copper that may have accumulated during the illness.

B. History of Hazard Evaluation.

The CVM/AHHE Committee has not previously reviewed health hazard evaluations involving Go Natural dog or cat foods.

C. The CVM/AHHE Committee recommends the following:

a) Recall Classification: [21 CFR 7.41(b) and RPM 5-00-20 (j)].

1-Class I	<u>XX</u>
2-Class II	<u> </u>
3-Class III	<u> </u>

b) Depth of Recall: [21 CFR 7.42(b)(1) and RPM 5-00-20(k)].

1-Consumer or User Level	<u>XX</u>
2-Retail Level/Veterinarian	<u> </u>
3-Wholesale Level	<u> </u>

D. Narrative Summary:

On October 22, 2003, Petcurean Pet Nutrition, Inc. initiated a voluntary recall of all Go Natural dog and cat foods manufactured at Merrick Pet Foods since June 2003. This recall was initiated because the firm was aware of 15-18 complaints of pet illness and 7 dog deaths that were associated with these dog and cat foods. Approximately 30,000 pounds of product in 4, 8, 12 and 30 pound bags were removed from the shelves of over 60 retail stores in the Denver and Seattle areas, in southern California, and in the bay area of California.

Despite extensive testing by CAHFS, the FDA and private laboratories, a definitive cause of the ill effects in the dogs and cats has not been determined. Adverse effects noted in the most severely affected dogs included cholestasis, liver dysfunction, anemia and hemolysis. A few days to hours before death there was often a marked drop in hematocrit and a sharp increase in total bilirubin. After reviewing the clinical signs and the results from clinical pathology, histology, urinalysis, ultrasound, radiographs, gross

necropsy and time course, we believe hemolysis of red blood cells (RBC) will be at least a major contributing factor, if not the primary factor, in many of the adverse effects noted in dogs.

Dogs exposed to 5 lots of the Go Natural dog food (F1332, F1631, F1931, G1631, H2731) appear to be the animals at greatest risk. Cats exposed to lot F1731 also may be at increased risk.

Despite not knowing the exact cause of the adverse effects, the degree of seriousness of the health hazard was judged to be life threatening, the assessment of the likelihood of the health hazard was judged to be probable, and immediate consequences were judged to be probable. These assessments were based largely on the fact that ingestion of Go Natural dog or cat foods is the only common factor identified in these cases to date and no additional consumer complaints have been reported to CVM within two weeks after the voluntary recall was initiated. Long range consequences are possible, but difficult to predict.

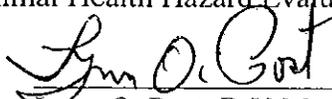
Additional research will likely be needed to definitively establish the exact cause(s) of these adverse effects. Two potential areas of additional research include, but are not limited to, the following:

Dr. Deryck H. Read and Dr. Jenee Odani with CAHFS have reviewed the histology slides and believe there is the potential for an infectious cause of these adverse effects; however, to date no infectious agent has been identified.

Overformulations (4-13X) with BHA were noted in 4 implicated lots of the Go Natural dog food; however, a preliminary review of the toxicity of BHA in dogs indicated that no adverse effects would be expected even at these elevated levels. Consideration needs to be given to analyzing all dog and cat food samples collected by the FDA for BHA.

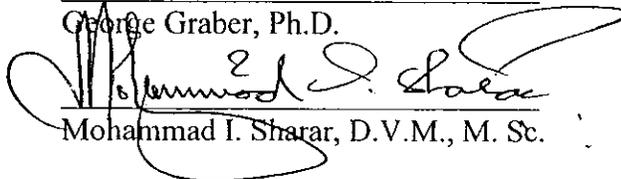
Finally, Dallas DO recommended that recall audit checks will be assigned for each distributor with sub-account recall audit checks of 2%, but not to exceed 3 per distributor. We concur with this recommendation.

Animal Health Hazard Evaluation Committee



Lynn O. Post, D.V.M., Ph.D., Chairman

George Graber, Ph.D.



Mohammad I. Sharar, D.V.M., M. Sc.

Prepared by:



Randall A. Lovell, D.V.M., Ph.D., DABVT

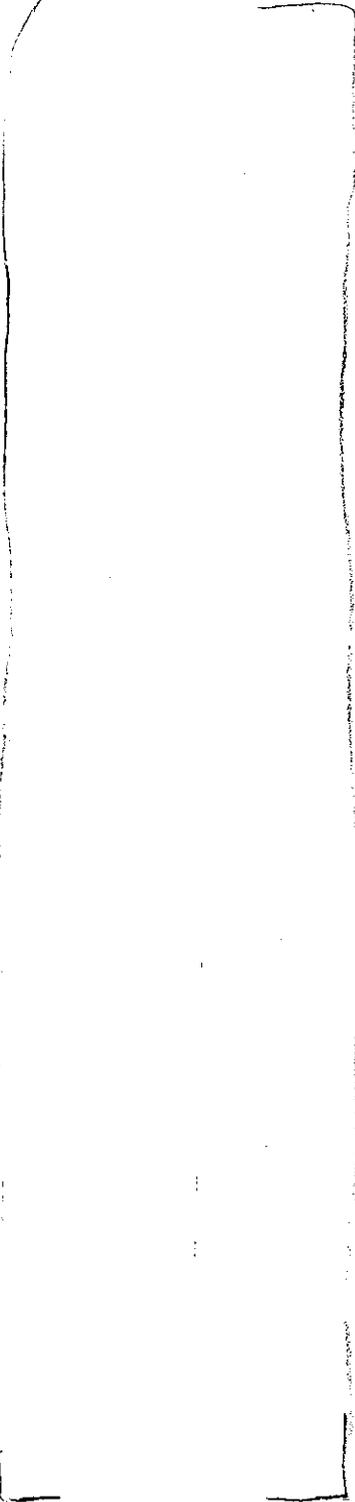
Attachments: Appendices A, B, C, D, E and F.

Appendix A. Formulations of Go Natural Dog and Cat Food.

Ingredients

Go Natural
Dog Food (kg)

Go Natural
Cat Food (kg)



Appendix B. Go Natural Dog and Cat Food Samples Collected by the FDA and their BHA Levels.

FDA Sample #	Manufact. Code	Sample Description with Pet Name, Owner or Veterinarian	BHA Levels in ppm (overformulated)
242466 (dog)	F1332	[redacted]	
253749 (dog)	F1631	Unopened bag that matches a consumer complaint; from Pet Food Express, Inc.	258.6 (10X)
253754 (dog)	F1631	[redacted] Unopened bag collected from owner	241.9 (10X)
242471 (dog)	F1631	[redacted] (zip lock bag collected at vet office-	
253752 (dog)	F1931	Unopened bag from Pet Food Express that matches a lot code # of a sick dog	103.8 (4X)
242468 (dog)	F1931	[redacted]	
253750 (dog)	F2031	Lot code is in between suspected lots; Pet Food Express (San Leandro, CA)	none detected
222293 (dog)	F2031	Bags from returned recall pallet at Western Pet Wholesale	24.0
243886 (dog)	G1631	Golden Retrievers (suspect	365.9 (13X)
243887 (dog)	G1631	same as above, except open bag	442.0 (16X)
222292 (dog)	G1631	Intact bags from returned recall pallet at Western Pet Wholesale	282.5 (10X)
253751 (dog)	H2731	Unopened bag from Pet Food Express that matches lot code # of 3 sick dogs	311.8 (12X)
242469 (dog)	H2731	[redacted]	
242470 (dog)	H2731	[redacted]	
242465 (dog)	unknown	[redacted]	
242467 (dog)	unknown	[redacted]	
253747 (dog)	unknown	[redacted] office at	
253748 (dog)	unknown	Same as above; color variation noted in dog food—this one is much darker	
253755 (dog)	unknown	Dog food provided by owner in 4 separate packages to vet. Vet was unsure why—variation in texture, shape and/or color?	
253753 (cat)	F1731	Unopened bag from Pet Food Express that matches a lot code # of a sick cat	
242464 (cat)	F1731	[redacted]	
242463 (cat)	G0931	[redacted]	
222294 (cat)	G1731	Bags from returned recall pallet at Western Pet Wholesale	13.3

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

	Golden Retriever 3 mo, F 8/29/2003	Pit Bull 5 mo M 10/14/2003	Engl Spr Spaniel 3 yr M 10/20/2003	Cocker Spaniel 10 mo FS 10/9/03 Clin Chem 10/21/03 CBC	Golden Retriever 2 mo F 9/13/2003	Golden Retriever 2 mo M 9/12/2003
AST--IU/L	241 (15 - 66)	NA	304 (15 - 66)	NA	61 (15 - 66)	64 (15 - 66)
ALT--IU/L	168 (12 - 118)	626 (10 - 100)	283 (12 - 118)	866 (8 - 75)	132 (12 - 118)	209 (12 - 118)
Total Bilirubin--mg/dL	5.7 (0.1 - 0.3)	13.53 (0.0 - 0.9)	8.1 (0.1 - 0.3)	1.68 (0.0 - 0.8)	2.0 (0.1 - 0.3)	3.8 (0.1 - 0.3)
Direct Bilirubin--mg/dL	2.2 (0.0 - 0.3)	NA	5.9 (0.0 - 0.3)	NA	0.9 (0.0 - 0.3)	1.8 (0.0 - 0.3)
Indirect Bilirubin--mg/dL	3.5 (0.1 - 0.3)	NA	NA	NA	1.1 (0.1 - 0.3)	2.0 (0.1 - 0.3)
Alkaline Phosphatase--IU/L	1455 (5 - 131)	1298 (23 - 212)	646 (5 - 131)	1777 (46-337)	920 (5 - 131)	919 (5 - 131)
Total Protein--g/dL	4.1 (5.0 - 7.4)	5.57 (5.2 - 8.2)	5.6 (5.0 - 7.4)	4.81 (4.8 - 7.2)	3.1 (5.0 - 7.4)	3.2 (5.0 - 7.4)
Albumin--g/dL	2.0 (2.7 - 4.4)	1.75 (2.7 - 3.8)	2.5 (2.7 - 4.4)	1.72 (2.1 - 3.6)	1.3 (2.7 - 4.4)	1.5 (2.7 - 4.4)
Globulin--g/dL	2.1 (1.6 - 3.6)	3.82 (2.5 - 4.5)	3.1 (1.6 - 3.6)	3.09 (2.3 - 3.8)	1.8 (1.6 - 3.6)	1.7 (1.6 - 3.6)
Cholesterol--mg/dL	58 (92 - 324)	18.8 (110 - 320)	76 (92 - 324)	191.2 (100 - 400)	74 (92 - 324)	67 (92 - 324)
Amylase--IU/L	1790 (290 - 1125)	1477 (500 - 1500)	704 (290 - 1125)	1141 (300 - 1300)	803 (290 - 1125)	912 (290 - 1125)
Lipase--IU/L	910 (77 - 695)	1645 (200 - 1800)	180.4 (77 - 695)	782 (100 - 1500)	232 (77 - 695)	539 (77 - 695)
Red Blood Cell Count--(10 ⁶ /uL)	2.9 (4.8 - 9.3)	4.88 (5.5 - 8.5)	5.39 (5.5 - 8.5)	4.63 (5.5 - 8.5)	3.4 (4.8 - 9.3)	2.9 (4.8 - 9.3)
Hemoglobin--g/dL	6.3 (12.1 - 20.3)	11.6 (12 - 18)	11 (12 - 18)	11.5 (12 - 18)	6.8 (12.1 - 20.3)	5.9 (12.1 - 20.3)
Hematocrit--%	20 (36-60)	32.5 (37 -55)	34.9 (37 - 55)	33.1 (37 - 55)	24 (36 - 60)	21 (36 - 60)
White Blood Cell Count--10 ³ /uL	32.6 (4.0 - 15.5)	10.5 (5.7 - 16.3)	11.18 (6.0 - 17.0)	13.2 (5.7 - 16.3)	27.1 (4.0 - 15.5)	33.1 (4.0 - 15.5)
Neutrophils--/uL	18908 (2060 - 10600)	6405 (3000 - 11500)	3,310 (3000 - 11,800)	8976 (3000 - 11500)	22,764 (2060 - 10,600)	23,501 (2060 - 10,600)
Lymphocytes--/uL	9128 (690 - 4500)	3360 (1000 - 4800)	4,380 (1,000 - 4,800)	3432 (1000 - 4800)	2439 (690 - 4500)	6620 (690 - 4500)
Monocytes--/uL	3260 (0 - 840)	735 (150 - 1350)	3,060 (200 - 2,000)	396 (150 - 1350)	542 (0 - 840)	993 (0 - 840)
Reticulocyte--/mm ³						
Nucleated RBC--/100 wbc	10 (0 - 1)	15 (0 - 2)		263,910 (0 - 60,000)		
Spherocytes	2+			2+		
Prothrombin Time--sec		>100 (6.2 - 8.2)		14.9 (6.2 - 8.2)		
Partial Thromboplastin Time--sec		79.2 (9.0 - 20.0)		18.6 (9.0 - 20.0)		

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

Parameter	Labrador Retriever 31 yr M 10/4/2003	Boxer 22-yr FS 9/7/2008	Staffordshire Bull Terrier, 3 yr FS 10/22/2003	Cocker Spaniel 30 mo NM 10/20/2003	Cockapoo 11 yr NM 10/17/2003	Australian Shepherd 10 yr F 11/4/2003
AST--IU/L	Result NA	Result NA	Result NA	Result NA	Result NA	Result (Ref. Range) NA
ALT--IU/L	1179	1180	increased	996	2544	517 (10 - 100)
Total Bilirubin--mg/dL	2.7	11.7	increased	5.9	3	2.6 (0.0 - 0.9)
Direct Bilirubin--mg/dL	0.8	NA	NA	NA	1.4	NA
Indirect Bilirubin--mg/dL	1.9	NA	NA	NA	1.6	NA
Alkaline Phosphatase--IU/L	894	2440	increased	747	1467	239 (23 - 212)
Total Protein--g/dL	NA	4.6	decreased	NA	NA	7.05 (5.2 - 8.2)
Albumin--g/dL	2.3	2.4	decreased	2.8	NA	2.68 (2.7 - 3.8)
Globulin--g/dL	NA	NA	NA	2.8	NA	4.37 (2.5 - 4.5)
Cholesterol--mg/dL	46	48	decreased	NA	109	345.1 (110 - 320)
Amylase--IU/L	NA	NA	NA	NA	NA	NA
Lipase--IU/L	NA	NA	NA	NA	NA	NA
Red Blood Cell Count--(10 ⁶ /uL)	NA	NA	NA	NA	NA	NA
Hemoglobin--g/dL	NA	NA	NA	NA	NA	15.8 (12-18)
Hematocrit--%	37	NA	NA	NA	NA	45.6 (37-55)
White Blood Cell Count--(10 ³ /uL)	NA	NA	NA	NA	NA	11.3 (6.0 - 16.9)
Neutrophils--/uL	NA	NA	NA	NA	NA	4900 (2800 - 10,500)
Lymphocytes--/uL	NA	NA	NA	NA	NA	NA
Monocytes--/uL	monocytosis	NA	NA	NA	NA	NA

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

	Golden Retriever 28 wk M 9/2/2003	Labrador Retriever 1 1/2 yr NM 7/10/10/03	Puppy < 6 mo 10/2/2003	Golden Retriev. M 9 mo 10/4/2003
AST--IU/L	Result (Ref. Range) NA	Result NA	Result (Ref. Range) NA	Result (Ref. Range) 45 (15 - 66)
ALT--IU/L	309 (12 - 118)	1683	94 (8 - 75)	77 (12 - 118)
Total Bilirubin--mg/dL	NA	NA	<0.1 (0.0 - 0.8)	0.2 (0.1 - 0.3)
Direct Bilirubin--mg/dL	NA	NA	NA	NA
Indirect Bilirubin--mg/dL	NA	NA	NA	NA
Alkaline Phosphatase--IU/L	1029 (5 - 131)	1188	408 (46 - 337)	319 (5 - 131)
Total Protein--g/dL	3.6 (5.0 - 7.4)	NA	4.64 (4.8 - 7.2)	5.0 (5.0 - 7.4)
Albumin--g/dL	1.9 (2.7 - 4.4)	NA	2.0 (2.1 - 3.6)	2.6 (2.7 - 4.4)
Globulin--g/dL	1.7 (1.6 - 3.6)	NA	2.64 (2.3 - 3.8)	2.4 (1.6 - 3.6)
Cholesterol--mg/dL	NA	NA	109.8 (100 - 400)	144 (92 - 324)
Amylase--IU/L	NA	NA	1417 (300 - 1300)	1012 (290 - 1125)
Lipase--IU/L	NA	NA	NA	83 (77 - 695)
Red Blood Cell Count--(10 ⁶ /uL)	3.5 (4.8 - 9.3)	NA	NA	4.3 (4.8 - 9.3)
Hemoglobin--g/dL	7.5 (12.1 - 20.3)	NA	8.8 (12.0 - 18.0)	10.6 (12.1 - 20.3)
Hematocrit--%	24 (36 - 60)	NA	25.7 (37 - 55)	31 (36-60)
White Blood Cell Count--10 ³ /uL)	40.1 (4.0 - 15.5)	NA	18.0 (6.0 - 16.9)	14.6 (4.0 - 15.5)
Neutrophils--/uL	18,847 (2060 - 10,600)	NA	NA	9782 (2060 - 10600)
Lymphocytes--/uL	18,446 (690 - 4500)	NA	NA	3650 (690 - 4500)
Monocytes--/uL	2406 (0 - 840)	NA	NA	1022 (0 - 840)

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

Test	Golden Retriever 32.5 yr, F 9/23/2003	Golden Retriever 33 yr, M 10/3 & 10/7/03	Golden Retriever JM, no age 9/29/2003	Golden Retriever 21 yr M 9/26/2003	Golden Retriever 21 yr F 10/2/2003	Australian Shepherd/ Border Collie Cross 38 1/2 mo F 10/28/2003
AST--IU/L	200 (15 - 66)	86 (15 - 66)	26 (15 - 66)	34 (15 - 66)	33 (15 - 66)	50 (5 - 55)
ALT--IU/L	643 (12 - 118)	271 (12 - 188)	20 (12 - 118)	34 (12 - 118)	25 (12 - 118)	236 (5 - 60)
Total Bilirubin--mg/dL	0.3 (0.1 - 0.3)	0.3 (0.1 - 0.3)	0.1 (0.1 - 0.3)	0.1 (0.1 - 0.3)	0.1 (0.1 - 0.3)	0.2 (0.0 - 0.4)
Direct Bilirubin--mg/dL	NA	NA	NA	NA	NA	0.1 (0.0 - 0.1)
Indirect Bilirubin--mg/dL	NA	NA	NA	NA	NA	0.1 (0.0 - 0.3)
Alkaline Phosphatase--IU/L	653 (5 - 131)	757 (5 - 131)	198 (5 - 131)	209 (5 - 131)	229 (5 - 131)	255 (10 - 150)
Total Protein--g/dL	4.9 (5.0 - 7.4)	5.4 (5.0 - 7.4)	4.0 (5.0 - 7.4)	5.5 (5.0 - 7.4)	5.2 (5.0 - 7.4)	4.9 (5.1 - 7.8)
Albumin--g/dL	2.3 (2.7 - 4.4)	2.5 (2.7 - 4.4)	2.8 (2.7 - 4.4)	3.3 (2.7 - 4.4)	2.8 (2.7 - 4.4)	2.4 (2.5 - 3.6)
Globulin--g/dL	2.6 (1.6 - 3.6)	2.9 (1.6 - 3.6)	1.2 (1.6 - 3.6)	2.2 (1.6 - 3.6)	2.4 (1.6 - 3.6)	2.5 (2.8 - 4.5)
Cholesterol--mg/dL	195 (92 - 324)	132 (92 - 324)	267 (92 - 324)	300 (92 - 324)	313 (92 - 324)	169 (112 - 328)
Amylase--IU/L	1393 (290 - 1125)	739 (290 - 1125)	439 (290 - 1125)	961 (290 - 1125)	735 (290 - 1125)	NA
Lipase--IU/L	233 (77 - 695)	212 (77 - 695)	135 (77 - 695)	149 (77 - 695)	122 (77 - 695)	NA
Red Blood Cell Count--(10 ⁹ /uL)	5.0 (4.8 - 9.3)	5.6 (4.8 - 9.3)	5.3 (4.8 - 9.3)	5.2 (4.8 - 9.3)	5.3 (4.8 - 9.3)	5.68 (5.6 - 8.5)
Hemoglobin--g/dL	12.0 (12.1 - 20.3)	12.9 (12.1 - 20.3)	12.7 (12.1 - 20.3)	12.2 (12.1 - 20.3)	13.1 (12.1 - 20.3)	13.4 (12.0 - 18.0)
Hematocrit--%	36 (36 - 60)	38 (36 - 60)	37 (36 - 60)	37 (36 - 60)	39 (36 - 60)	38.6 (37 - 55)
Write Blood Cell Count--(10 ³ /uL)	12.8 (4.0 - 15.5)	15.3 (4.0 - 15.5)	11.2 (4.0 - 15.5)	13.1 (4.0 - 15.5)	15.1 (4.0 - 15.5)	11.4 (5.7 - 16.3)
Neutrophils--/uL	6400 (2060 - 10600)	8262 (2060 - 10600)	5712 (2060 - 10600)	9825 (2060 - 10600)	8003 (2060 - 10600)	5928 (3000 - 11500)
Lymphocytes--/uL	4992 (690 - 4500)	5508 (690 - 4500)	4480 (690 - 4500)	2620 (690 - 4500)	5285 (690 - 4500)	4788 (1000 - 4800)
Monocytes--/uL	1024 (0 - 840)	1224 (0 - 840)	448 (0 - 840)	393 (0 - 840)	1359 (0 - 840)	342 (150 - 1350)

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

	Golden Retriever 31 yr M 10/2/2003	Golden Retriever 35 yr F 10/3/2003	Golden Retriever 31 yr M 9/30/2003
AST--IU/L	Result (Ref. Range) 29 (15 - 66)	Result (Ref. Range) 24 (15 - 66)	Result (Ref. Range) 29 (5 - 55)
ALT--IU/L	62 (12 - 118)	24 (12-118)	32 (5 - 60)
Total Bilirubin--mg/dL	0.1 (0.1 - 0.3)	0.1 (0.1 - 0.3)	0.1 (0.0 - 0.4)
Direct Bilirubin--mg/dL	NA	NA	0.0 (0.0 - 0.1)
Indirect Bilirubin--mg/dL	NA	NA	0.1 (0.0 - 0.3)
Alkaline Phosphatase--IU/L	152 (5 - 131)	195 (5 - 131)	263 (10 - 150)
Total Protein--g/dL	6.3 (5.0 - 7.4)	6.1 (5.0 - 7.4)	5.8 (5.1 - 7.8)
Albumin--g/dL	3.0 (2.7 - 4.4)	3.0 (2.7 - 4.4)	2.8 (2.5 - 3.6)
Globulin--g/dL	3.3 (1.6 - 3.6)	3.1 (1.6 - 3.6)	3 (2.8 - 4.5)
Cholesterol--mg/dL	224 (92 - 324)	262 (92 - 324)	271 (112 - 328)
Amylase--IU/L	645 (290 - 1125)	666 (290 - 1125)	539 (350 - 1050)
Lipase--IU/L	177 (77 - 695)	551 (77 - 695)	286 (100 - 750)
Red Blood Cell Count--(10 ⁶ /uL)	6.7 (4.8 - 9.3)	6.9 (4.8 - 9.3)	7.11 (5.5 - 8.5)
Hemoglobin--g/dL	15.7 (12.1 - 20.3)	16.4 (12.1 - 20.3)	17.3 (12 - 18)
Hematocrit--%	46 (36 - 60)	48 (36 - 60)	50.3 (37 - 55)
White Blood Cell Count--(10 ³ /uL)	9.6 (4.0 - 15.5)	19.0 (4.0 - 15.5)	8.5 (5.7 - 16.3)
Neutrophils--/uL	5184 (2060 - 10,600)	12350 (2060 - 10600)	7480 (3000 - 11500)
Lymphocytes--/uL	3552 (690 - 4500)	3990 (690 - 4500)	510 (1000 - 4800)
Monocytes--/uL	288 (0 - 840)	2280 (0 - 840)	425 (150 - 1350)

Appendix C -- Clinical Pathology Findings in Dogs Associated with the Go Natural Recall

	Labrador Retriever	
	10/4/2003	10/9/2003
ALT--IU/L	1179	NA
Total Bilirubin--mg/dL	2.7	19.9
Direct Bilirubin--mg/dL	0.8	6.9
Indirect Bilirubin--mg/dL	1.9	13
Alkaline Phosphatase--IU/L	894	1324
Albumin--g/dL	2.3	1.8
Hct--%	37	24.6 non regen.

	Engl Spr Spaniel			
	10/18/03	10/20/2003	10/21/2003	10/24/2003
AST--IU/L	353 (15 - 66)	304		541
ALT--IU/L	413 (12 - 118)	283		184
Total Bilirubin--mg/dL	4.6 (0.1 - 0.3)	8.1		31
Direct Bilirubin--mg/dL	1.5 (0.0 - 0.3)	5.9		11.4
Indirect Bilirubin--mg/dL	3.1 (0.1 - 0.3)	2.2		19.6
Alkaline Phosphatase--IU/L	821 (5 - 131)	646		719
Total Protein--g/dL	6.2 (5.0 - 7.4)	5.6		3.3
Albumin--g/dL	2.9 (2.7 - 4.4)	2.5		1.7
Globulin--g/dL	3.3 (1.6 - 3.6)	3.1		1.6
Cholesterol--mg/dL	81 (91 - 324)	76		53
RBC--10 ⁶ /uL	7.4 (4.8 - 9.3)	5.39 (5.5 - 8.5)	5.0 (4.8 - 9.3)	2.9
Hemoglobin--g/dL	16.6 (12.1 - 20.3)	11.0 (12.0 - 18.0)	11.2 (12.1 - 20.3)	7
Hematocrit--%	50 (36 - 60)	34.9 (37 - 55)	34 (36 - 60)	20
Reticulocyte Count--%				3.4 (0 - 1)
Absolute Reticulocyte--/uL				98,600 (<60,000)

Appendix D. Go Natural Recall: Pathology Findings in Dogs Examined by CAHFS.

Accession Number	[]	[]	[]	[]	[]
Name of Dog	[]				
Pattern	Diffuse	Diffuse	Diffuse	Periacinar	Diffuse
Sinusoidal Kupffer cell hyperplasia	4	4	0	2	2
Kupffer cell necrosis	4	0	1	0	Unable to interpret**
Single cell necrosis of hepatocytes	1	2	2	2	0
Multifocal hepatocellular loss	0	1	0	0	0
Hepatocellular clear microvacuolation	3	1	3	0	Unable to interpret**
Hepatocellular clear macrovacuolation	0	0	0	4	0
Vacuolation and mononuclear cell infiltration of vascular walls	4	1	2	0	0
Mononuclear cell portal infiltrates	0	1	0	1	0
Multifocal aggregates of mononuclear cells in parenchyma	0	1	1	0	0
Bile stasis (canalicular plugging)	4	4	0	1	2
Bile stasis (green pigment in sinusoidal macrophages)	0	4	0	4	2
Congestion of sinusoids	2	3	4	2	0
Erythrophagocytosis	3	2	2	3	0
Hemosiderin	1	1	1	pending	pending
*likely [] since [] is the owner					
**due to freeze-thaw artifact; 0=none, 1=slight, 2=mild, 3=moderate, 4=marked					

Appendix E. Go Natural Recall: Treatments Administered to Dogs and the Outcomes.

Treatments	Outcomes
<p>Pepcid, carafate, metoclopramide, baytril, ampicillin, fluids, hetastarch, 5% dextrose, normosol, and prednisone. [] 1 yr M Lab. Retriever; []</p>	<p>Euthanasia</p>
<p>Meds at RDVM: amoxicillin, baytril, cimetidine; all given at 4:30 p.m. [] 2 yr FS, Boxer; []</p>	<p>Death</p>
<p>Started treatment on 10/18/03 -- IV catheter and fluids (65 ml/hr); denosyl 225 mg (or ug) sid; food -- Hill's L/D; started amoxicillin and baytril on 10/19/03; started metronidazole 250 mg bid on 10/22/03 [] 3 yr M, English Springer Spaniel; []</p>	<p>Presented on 10/17/03 -- dog continued to become more icteric, depressed every day; diarrhea continued; died on 10/24/03 early morning</p>
<p>On 10/11/03 -- clavarnox 375 mg bid; feed a bland diet On 10/14/03 -- fluids 0.45% NaCl; 2.5% dextrose; supplemented with KCl & B vitamins; baytril inj. 3 cc SQ; polyFlex 600 mg SQ; vit. K inj. 20 mg SQ [] 5 mo M, Blue Pit Bull; []</p>	<p>Presented to [] Presented to [] on 10/14/03; Found dead in AM of 10/15/03</p>
<p>9/10/03 -- the puppies (definitely [] and likely [] rare currently receiving metronidazole and clavarnox; [] Golden Retrievers]</p>	<p>One died on 9/14/03; One was euthanized on 9/26/03;</p>
<p>SQ fluids, metronidazole, amoxicillin, prednisone, Sam-E, milk thistle, 2 inj. of Ca-EDTA, cimetidine [] 3 yr FS Staffordshire Bull Terrier]</p>	<p>Patient progressively worsened with vomiting, diarrhea, melena, fever, and one seizure episode.</p>
<p>10/13/03 discharged on Sam-E, amoxicillin and vit. K by [] acti-gall therapy can be considered; [] 10 mo FS Cocker Spaniel; []</p>	<p>Slow recovery; owners still not certain if [] will survive (March 2004)</p>
<p>On 9/23/03--amoxicillin (750 mg po tid for 7 days) and denosyl SD4 (225 mg tablet po sid for 7 da) [] 2 1/2 yr F, Golden Retriever; []</p>	<p>Hct dropped from 36% on 9/23/03 to 26% on 9/27/03; dog steadily recovered from 10/4/03 (Hct = 31%) to 10/9/03 (Hct = 35%) to 10/16/03 (Hct = 47%).</p>
<p>DMPP given 8/18/03; Parvo 8/28; Recommend begin oral amoxicillin (50 mg bid -- tid) on 9/3/03; [] 2 mo M, Golden Retriever; []</p>	<p>9/23/03 -- On amoxicillin or something similar and developed diarrhea; switched to Flagyl and did well</p>

Appendix E. Go Natural Recall: Treatments Administered to Dogs and the Outcomes.

Treatments	Outcomes
<p>Stop feeding the Go Natural diet. Sam-E 225 mg po sid } 2 ½ yr MN Labrador Retriever;</p>	<p>Doing well per owners at home</p>
<p>Vit. K, Pepcid, metoclopramide and fluid therapy was administered overnight; stop the Go Natural diet; metoclopramide 2.5 mg po bid; famotidine 5 mg po sid; start a bland diet } 1 yr MN Cockapoo; }</p>	<p>Not provided</p>
<p>11/4/03--LRS 1 L (w 1 g cefazolin) iv at 80 ml/hr; metronidazole 1000 mg po; 11/4 thru 11/6/03--denosyl 225 mg po bid; 11/5 thru 11/6/03--fed V/D bid; actigall 300 mg po bid; 11/6/03--received 575 ml of fluids } 10 yr F Aust Shep; }</p>	<p>B.A.R. (bright, alert and responsive) on 11/6/03</p>

Appendix F. Clinical Pathology Findings in Cats Associated with the Go Natural Recall.

	14-yr F/S DSH 10/13/2003	7 yr M Neut. DMH 10/18/2003	7 yr M Neut. DMH 10/21/2003	7 yr M Neut. DMH 10/29/2003	Adult Feline 10/25/2003
AST	NA	NA	87 (5-55)	NA	NA
ALT--IU/L	166	199 (12 - 130)	145 (28 - 76)	296 (12 - 130)	increased
Total Bilirubin--mg/dL	increased	5.99 (0.0 - 0.9)	12.9 (0.0 - 0.4)	4.2 (0.0 - 0.9)	NA
Direct Bilirubin--mg/dL	NA	NA	5.3 (0.0 - 0.1)	NA	NA
Indirect Bilirubin--mg/dL	NA	NA	7.6 (0.0 - 0.3)	NA	NA
Alkaline Phosphatase--IU/L	1779	428 (14 - 111)	734 (0 - 62)	276 (14 - 111)	NA
Total Protein--g/dL	NA	6.75 (5.7 - 8.9)	5.6 (5.9 - 8.5)	6.41 (5.7 - 8.9)	NA
Albumin--g/dL	NA	3.17 (2.6 - 3.9)	2.4 (2.3 - 3.3)	2.83 (2.6 - 3.9)	NA
Globulin--g/dL	NA	3.58 (2.8 - 5.1)	3.2 (3.6 - 5.6)	3.59 (2.8 - 5.1)	NA
Cholesterol--mg/dL	NA	144.1 (65 - 225)	147 (82 - 218)	251.5 (65 - 225)	NA
RBC--10 ⁶ /uL	NA	8.02 (6.0 - 10.0)	6.2 (6.0 - 10.0)	NA	NA
Hemoglobin--g/dL	NA	11.5 (9.5 - 15)	8.8 (9.5 - 15)	6.9 (8.0 - 15.0)	8.6 (8.0 - 15.0)
Hematocrit--%	NA	35.9 (29 - 45)	24 (29 - 45)	21.4 (24 - 45)	27 (24-45)
WBC--10 ³ /uL	NA	6.3 (4.2 - 15.6)	17.9 (4.2 - 15.6)	NA	NA
Neutrophil Seg--/uL	NA	5229 (2500 - 12,500)	16289 (2500 - 12500)	NA	NA
Lymphocytes--/uL	NA	882 (1500 - 7000)	1253 (1500 - 7000)	NA	NA
Monocytes--/uL	NA	126 (0 - 850)	358 (0 - 850)	NA	NA
Blood parasites	NA	No Hemobartonella	No Hemobartonella	NA	NA
Reticulocyte Count	NA	NA	NA	2.1% (NA)	NA
Poikilocytosis	NA	slight	NA	NA	NA