J Sci Food Agric 1994, **64**, 249–256

Amino Acid and Energy Digestibility in Peas (*Pisum sativum*) from White-Flowered Spring Cultivars for Growing Pigs

Ming Z Fan, Willem C Sauer*

Department of Animal Science, University of Alberta, Edmonton, Alberta, Canada, T6G 2P5

and Sam Jaikaran

Alberta Agriculture, Edmonton, Alberta, Canada, T6H 4P2

(Received 15 April 1993; revised version received 25 August 1993; accepted 18 October 1993)

Abstract: Six barrows, average initial weight 35 kg, fitted with a simple T-cannula at the distal ileum, were used to determine the apparent ileal digestibilities of amino acids (AA) and the digestibility of energy in six diets according to a 6 × 6 Latin square design. The pigs were fed six corn starch-based diets formulated to contain 165 g CP per kg from six different white-flowered spring pea cultivars. Chromic oxide was used as the digestibility marker. The pigs were fed twice daily, at 08:00 and 20:00 h. Each experimental period lasted 9 days. Faeces were collected from 08:00 on day 6 to 08:00 h on day 8; ileal digesta from 08:00 on day 7 to 08:00 h on day 9. Of the indispensable (+semi-) AA, there were differences ($P < 0.05$) in the AA digestibilities of arginine, methionine, phenylalanine and tyrosine between the cultivars. In the same order for these AA, the digestibilities ranged from 81·3 to 89·0%, 67·8 to 75·1%, 68·0 to 74·6% and 66·1 to 74·8%, respectively. Within each cultivar, the digestibilities of cysteine and threonine were relatively low, ranging from 58·5 to 65·9% and from 59·6 to 67·4%, respectively. The digestibility of lysine was relatively high, ranging from 80·3 to 84·0%. The energy digestibilities in the pea cultivars ranged from 87·4 to 90·2% ($P < 0.05$); the digestible energy content from 14·0 to 14·4 MJ kg^{-1} DM. There was considerable disappearance of energy in the large intestine, ranging from 4·4 to 6·2 MJ kg^{-1} DM intake from peas. In conclusion, when measured with the ileal analysis method, there were differences ($P < 0.05$) in the digestibilities of some of the indispensable AA between the pea samples. Furthermore, the relatively low digestibilities of methionine and cysteine further accentuate the limitation of the sulphur-containing AA in protein from peas.

Key words: pigs, peas (*pisum sativum*), amino acids, energy, digestibility

B4

B4

B4

B4

B4

B4

B4

B4

From:	Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To:	Jones, Jennifer L; Palmer, Lee Anne; Queen, Jackie L; Hodges, April; Norris, Anne; Carey, Lauren; Glover, Mark
Sent:	4/4/2018 2:19:21 PM
Subject:	FYI -lentils--deficient in sulfur containing amino acids--methionine, tryptophan, and cysteine

Lentil protein, like other pulse proteins, is a good source of the essential amino acids, particularly leucine, lysine, threonine, and phenylalanine, but is deficient in the sulfur-containing essential amino acids methionine and cysteine

https://www.sciencedirect.com/science/article/pii/B9780123979353000013

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

Ko and Fascetti *Journal of Animal Science and Technology* (2016) 58:29
DOI 10.1186/s40781-016-0112-6

Journal of Animal Science and Technology

RESEARCH Open Access

Dietary beet pulp decreases taurine status in dogs fed low protein diet

Kwang Suk Ko[1,2*] and Andrea J. Fascetti[2]

Abstract

Background: It is known that large dogs who are fed lamb and rice diets are at increased risk to develop taurine-deficiency-induced dilated cardiomyopathy. Since dogs obligatorily conjugate bile acids (BA) with taurine, we determined whether rice bran (RB) or other fibers (cellulose; CL, beet pulp; BP) would affect BA excretion and/or the taurine status of dogs.

Results: Eighteen medium/large mixed-breed dogs were given purified diets containing CL, BP, or RB for 12 weeks. Taurine concentrations in plasma and whole blood were significantly decreased at week 12. The BP group, compared to the CL or RB groups, showed significantly lower taurine concentrations in plasma (6.5 ± 0.5 vs 20.4 ± 3.9 and 13.1 ± 2.0 μmol/L, respectively, $P < 0.01$, mean ± SEM) and in whole blood (79 ± 10 vs 143 ± 14 and 127 ± 14 μmol/L, respectively, $P < 0.01$), lower apparent protein digestibility (81.9 ± 0.6 vs 88.8 ± 0.6 and 88.1 ± 1.2 %, respectively, $P < 0.01$), and higher BA excretions (5.6 ± 0.1 vs 3.4 ± 0.5 and 3.4 ± 0.4 μmol/g feces, respectively, $P < 0.05$) at week 12.

Conclusions: These results do not support the hypothesis that RB is likely to be a primary cause of lamb meal and rice diets, increasing the risk of taurine deficiency in large dogs. However these indicate that BP may contribute to a decrease taurine status in dogs by increasing excretion of fecal BA and decreasing protein digestibility, thus decreasing the bioavailability of sulfur amino acids, the precursors of taurine.

Keywords: Taurine deficiency, Bile acid excretion, Fiber, Dogs, Dilated cardiomyopathy

Background

It is known that dogs, under normal dietary conditions, synthesize taurine via the activities of two key enzymes, cysteine dioxygenase and cysteine sulfinic acid decarboxylase [1]. Taurine is synthesized from its precursor cysteine, resulting in sufficient quantities to meet their metabolic needs. However in recent years there were several reports that dogs may develop taurine deficiency-induced dilated cardiomyopathy (DCM). This has become more common in large dogs fed certain diets [2] and/or belonging to certain breeds [3, 4]. The main ingredients in the dog food fed to the taurine deficient dogs were lamb meal and rice, including rice bran [5]. Lamb meal has been reported to have a particularly low bioavailability of cysteine in dogs [6]. In a study where cats were fed a diet containing full fat stabilized rice bran, the cats had a lower blood taurine concentration compared to cats fed the same diet with cornstarch substituted for the rice bran [7]. Therefore, rice bran, in addition to lamb meal, may play a role in the development of taurine deficiency in dogs.

Various investigators have reported that the consumption of diets containing full fat rice bran results in reducing cholesterol concentrations in both liver and blood of several species; eg, in rats [8, 9], hamsters [10], and humans [11, 12]. One of the possible mechanisms for this effect is the high fermentability of rice bran, resulting in enhanced bile acid (BA) excretion and/or degradation (by increased microflora activity in the gut). According to the report of Gestel et al. [13], full fat rice bran fed to rats increased both BA excretion and bacterial activity, compared to controls fed a starch-based diet. Supporting evidence for the role of gut microflora in taurine loss has been reported for other species. Kim et al. [14, 15] reported a significant decrease in fecal cholyltaurine hydrolase activity (an enzyme produced by intestinal bacteria), and total fecal BA excretion with the addition of dietary

* Correspondence: kko@ewha.ac.kr
[1]Department of Nutritional Science and Food Management, Collage of Science & Industry Convergence, Ewha Womans University, 52 Ewhayeodae-gil, Seodaemun-gu, Seoul 120-750, Korea
[2]Department of Molecular Biosciences, School of Veterinary Medicine, University of California Davis, One Shield Ave, Davis, CA 95616, USA

antibiotics in cats. The administration of antibiotics resulted in the repletion of taurine in taurine-deficient cats within 3 weeks of treatment. It has been reported that dogs fed a lamb meal and rice diet showed higher urinary taurine excretion when antibiotics were added to their diet [16]. This suggests that highly populated microflora in the gut interferes with normal entero-hepatic re-utilization of taurine (taurocholic acid), which in turn prevents the maintenance of taurine homeostasis and decreases the quantity of taurine available for other metabolic functions and for renal excretion.

We postulate that dietary full-fat rice bran binds BA in the small intestine in dogs and thereby increases BA excretion, interfering with the entero-hepatic recycling of taurine-conjugated bile salts and lowering total body taurine status in dogs.

In the present study, the effects of dietary full fat rice bran on taurine status and BA excretion in dogs fed a diet near-limiting in sulfur amino acids were compared to those of dogs fed beet pulp, another common fiber source in dog food. Cellulose was used as the control fiber. Since an excess of dietary sulfur amino acids in dogs may mask the effects of marginally limiting sulfur amino acid metabolites such as taurine and glutathione, dogs were restricted in the amount of protein intake to 20–25 % above their minimum maintenance requirement described in National Research Council [17].

Methods

Animals and diets

The husbandry and treatments of the animals for the study were approved by the Animal Use and Care Administrative Advisory Committee at the University of California at Davis and the dogs in this study were taken care of in compliance with the National Research Council [18] guidance for laboratory animals. Eighteen intact male, mixed-breed dogs (Covance Stock and Broodstock Colony, Kalamazoo, MI, USA) were used for the study. Mean body weight (BW) of the 1–6 years old dogs at the initiation of the study was 29.1 ± 0.7 Kg (mean ± SEM). Six animals were assigned to each of the three experimental groups: cellulose (CL), beet pulp (BP) and rice bran (RB), based on similar BW of the dogs. The dogs were housed individually in indoor wire-mesh enclosures with coated rod-bottom floors at commercial facilities (Covance Research Products, Kalamazoo, MI, USA), providing a 12 h dark-light cycle and temperature control at 18–29 °C. Observations for general health and appearance were done three times a day at the discretion of the veterinarians and daily monitoring for food consumption was provided throughout the study. Weekly BW and body condition score (BCS, 9 point scale) were measured for each dog [19]. Food for all of the dogs for the study was provided once a day between 7 AM and 9 AM and water was given *ad-libitum* throughout the experiment.

Four complete, balanced diets were provided by a commercial laboratory animal food company (TestDiet®/LabDiet®, Purina, St. Louis, MI, USA). The ingredients and chemical compositions of the diets for the study are shown in Table 1. For the adaptation period, a pre-feeding (PF) diet, a complete and balanced dry expanded diet with 29.5 % protein containing 0.58 % methionine and 0.46 % cyst(e)ine (as-fed basis) was prepared to maintain an excess production of taurine for the maintenance of taurine homeostasis in these dogs. For the experimental period, three purified diets with the three different fiber sources, CL, BP and RB, were prepared, which, by design, included 12 % protein containing 0.23 % methionine and 0.12 % cyst(e)ine (as-fed basis). This prevented an excess of substrates for taurine synthesis that might overwhelm the effects of fibers on taurine metabolism studied. Twelve percent protein is higher than the minimum requirement of protein for maintenance of dogs described in National Research Council [17] and 0.35 % of sulfur amino acid concentration in the diets is within the range of total sulfur amino acid requirement (0.2–0.4 % of diets) for maintenance of adult dogs as determined by short-term nitrogen balance experiments [20–22]. Ten percent full-fat RB was used for the RB diet and the amounts of the fibers used in the other two diets were formulated, by calculation, to have the same amount of total dietary fiber (TDF) as that in the RB diet. Chromium oxide (0.02 %) was added to the experimental diets to use in determining apparent protein digestibility. The leftover and spilled food was collected daily and used to calculate food intake of each dog. The amounts of the food provided were adjusted weekly, based on changes of BW and BCS to aim toward an ideal BCS (5 out of 9 on the 9 point scale).

Design and treatments

During the adaptation period the dogs were given the PF diet for 8 weeks to ensure that they were not taurine deficient. The last two weeks of the adaptation period were included for sample collections as week 0, which was the initiation of the measurements. Then, dogs were assigned to one of three experimental groups (CL, BP, or RB group, respectively) to establish similar mean BW among the experimental groups. During the experimental period (from week 2 to week 12), the three different experimental diets were given to the designated groups. Throughout the experiment, including the last two weeks of the adaptation period, blood was collected on the last day of each 2 week-period, urine was collected biweekly on a day before blood collection, and feces were collected during the last 5 days of each 2 week-period. Plasma (PL) taurine, whole blood (WB)

Table 1 Chemical composition and ingredients of the diets for the experiment[b,c]

	Units	PF Diet[a,d]	CL Diet[a]	BP Diet[a]	RB Diet[a]
Protein	%	29.5	11.8	11.7	11.7
Methionine + Cystine	%	1.04	0.35	0.35	0.34
Taurine	%	0.04	-	-	-
Fat	%	18.5	20.3	20.3	20.3
Fibers	%	2.0[e]	2.51[f]	1.98[f]	2.68[f]
Insoluble dietary fibers[f]	%	-	1.83	1.98	1.81
Soluble dietary fibers[f]	%	-	0.68	0.00	0.87
Metabolizable Energy[c]	kJ/g	15.0	19.2	18.7	17.5
Casein - vitamin free	%	-	5.00	6.7	3.00
Soy protein isolate	%	-	7.90	5.62	8.38
Corn starch	%	-	37.61	35.55	33.76
Sucrose	%	-	20.00	20.00	20.00
Lard	%	-	20.18	20.16	18.18
Cellulose – powdered[g]	%	-	2.15	-	-
Beet pulp– dried[g]	%	-	-	4.70	-
Rice bran – full fat[g]	%	-	-	-	10.00
Mineral/Vitamin[h]	%	-	6.84	6.94	6.36
Chromium oxide	%	-	0.02	0.02	0.02
Choline chloride	%	-	0.30	0.30	0.30
Total	%	-	100.00	100.00	100.00

Notes: [a]*PF* Pre-feeding, *CL* Cellulose, *BD* Beet pulp, *RB* Rice bran. [b]The values were based on as-fed basis and provided from Purina Mills, LLC (St. Louis, MO) except where otherwise mentioned. All diets were formulated by the manufacturer to meet or exceed AAFCO (Association of American Feed Control Officials) requirements for macro and micronutrients for dogs. [c]The values were calculated, based on the latest (as of March 2005) ingredient analysis information by Purina Mills, LLC (St. Louis, MO) except where otherwise mentioned. Since nutrient composition of natural ingredients varies, analysis will differ accordingly. [d]PF diet; ingredients: ground corn, ground brown rice, poultry by-product meal, poultry meal, corn gluten meal, dehulled soybean meal, animal fat preserved with BHA (butylated hydroxyanisole), poultry fat preserved with ethoxyquin, wheat middlings, poultry digest, calcium carbonate, dried whole eggs, dried beet pulp, brewers dried yeast, soybean oil, dicalcium phosphate, salt, lecithin, pyridoxine hydrochloride, choline chloride, potassium chloride, menadione dimethylpyrimidinol bisulfate, biotin, cholecalciferol, vitamin A acetate, di-alpha tocopheryl acetate, inositol, DL-methionine, folic acid, calcium pantothenate, thiamin mononitrate, ethoxyquin, nicotinic acid, riboflavin, cyanocobalamin, manganous oxide, ferrous sulfate, cobalt carbonate, copper sulfate, zinc oxide, sodium selenite. [e]Crude fiber. [f]Total dietary fibers (TDF), dry-matter basis, analyzed by Dr. George C. Fahey Jr. in the Department of Animal Sciences, University of Illinois, Urbana, IL 61801. [g]Amount of the ingredients was decided by calculation based on the amount of TDF equal to the amount of TDF in the rice bran diet with 10 % full fat rice bran. [h]Provided the following amounts of minerals and vitamins/kg diet: calcium 10 g, phosphorous 6.6 g, potassium 7 g, magnesium 0.5 g, sodium 4.6 g, chloride 6.7 g, fluoride 48 mg, iron 365 mg, manganese 55 mg, copper 12 mg, cobalt 0.4 mg, iodine 1.5 mg, chromium 2.3 mg, molybdenum 1.23 mg, selenium 0.46 mg, vitamin A 10,900 IU, vitamin D-3 2,200 IU, vitamin E 44 IU, menadione 0.68 mg, thiamin hydrochloride 10.9 mg, riboflavin 4.9 mg, niacin 64 mg, pantothenic acid 20 mg, folic acid 4.0 mg, pyridoxine 12.4 mg, biotin 0.2 mg, vitamin B-12 28 μg, choline chloride 2.1 g

taurine, urine taurine, BA excretion, apparent protein digestibility, blood thiols and PL complete amino acid profiles (CAAP) were measured. To assure the health conditions of the dogs, blood chemistries and complete blood cell counts were performed on the samples taken on the last day of the adaptation period (IDEXX Preclinical Research Services, Westbrook, ME, USA) and the concentrations of total protein and albumin of PL were done from the PL drawn on the last day of the experimental periods (Veterinary Medicine Teaching Hospital of the School of Veterinary Medicine, University of California, CA, USA).

Sample collections and measurements

Blood (approximately 6 mL) was taken at the end of each 2 week-period to measure taurine, thiols, and amino acids. Every blood drawing was performed prior to feeding through cephalic vein by venipuncture using heparinized syringes (20 μL of sodium heparin solution, 1000 USP units/mL). Urine for assays of taurine and creatinine concentrations was collected, biweekly, for 14 h in an individual metabolic cage, one day before the blood was collected. The urine was collected in a container held in ice water.

A portion of WB (approximately 2 mL) was stored frozen (−20 °C) for WB taurine assay. Another portion of WB collected (approximately 4 mL) was immediately centrifuged (~1,200 × g for 10 min) to obtain PL. An aliquot of PL or urine (approximately 0.5 mL) was mixed with an equal volume of 0.24 mol/L of 5-sulfosalicylic acid, centrifuged at 15,800 × g for 15 min at 4 °C and the supernatant was collected. The resulting deproteinized PL or urine samples were assayed for taurine and for PL

CAAP. The PL samples remaining were stored at −20 °C for determination of PL thiols. The frozen WB samples were thawed and frozen three times to lyse the blood cells, to release intracellular taurine, then diluted with an equal volume of double deionized water (DDIW) and deproteinized by the same method as described for PL.

Feces were stored at −20 °C. Each feces sample was mixed with DDIW to obtain a slurry homogenate. Approximately 100 g of the homogenate slurry of feces was frozen at −20 °C for BA and protein assay.

Taurine concentrations of deproteinized PL, WB and urine were measured using an amino acid analyzer (Beckman 7300 Analyzer C7 Model, Beckman Instruments, Fullerton, CA, USA). To normalize urinary taurine concentration, urinary creatinine concentrations were determined with a commercial kit (Cold Stable, Pointe Scientific Inc., Canton, MI, USA). Deproteinized PL CAAP was measured using an amino acid analyzer (Biochrom 30, Biochrom Ltd., Cambridge, UK). In order to quantify the concentrations of total cyst(e)ine (free plus that bound to protein), cysteinyl-glycine and homocysteine in PL and the concentrations of total glutathione (GSH + GSSG) in WB, the combined and modified HPLC method of Ubbink et al. [23] and Gilfix et al. [24] was used. All of the volumes of reagents and samples were scaled down to one-fourth to quantify thiol concentrations in PL and WB and, for WB total glutathione concentrations. WB blood was diluted with an equal volume of DDIW before assay. Bile acid concentrations in feces were measured using a commercial kit (Bile Acid Kit No. 450-A, Trinity Biotech USA, Jamestown, NY, USA) and BA in feces was extracted by the method of Porter et al. [25] Apparent digestibility of dietary protein was measured by calculation using dietary and fecal nitrogen concentrations. The concentrations of nitrogen, protein and chromium in the diets and feces were analyzed at Analytical Laboratory at the University of California Davis. Total nitrogen and total crude protein were measured by a nitrogen gas analyzer (LECO FP-528, LECO Corporation, St Joseph, MI, USA). Chromium concentration was determined by Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES).

Statistical analysis

Significance of the data among three experimental groups at each time point for all of the variables was analyzed by mixed regression. Comparison of the variables between two time points in a group was done by paired t-test. All data were analyzed using SAS program [26]. All data in the report were expressed as mean ± SEM unless otherwise mentioned. For all analyses, differences were considered significant at $P < 0.05$. Probability values in the range of $0.05 \leq P < 0.1$ were considered as an indicator of a noteworthy trend.

Results

During the experimental period, one dog in the BP group ingested insufficient food to maintain BW and, therefore, was removed from the experiment at week 10 (BCS was 3 out of 9; BW was 82 % of week 0 at week 3). All of the data from the BP group were obtained from the remaining five dogs after week 10. Except for that dog, all of the dogs maintained BW and had normal blood chemistries and completed blood cell counts at the beginning of the experiment. However, at the end of the experiment, the mean PL albumin concentrations were 29 ± 2, 28 ± 1 and 29 ± 2 g/L for the CL, BP and RB group, respectively, which are below of the lower end of the reference range for PL albumin concentration of normal dogs (30–44 g/L). The mean PL total protein concentrations, at the end of the experiment, were 66 ± 4, 62 ± 5 and 66 ± 3 g/L for the CL, BP and RB group, respectively. These values are within the normal reference range for PL total protein concentration of normal dogs (54–76 g/L). There were no significant differences among the groups in PL albumin and total protein concentrations.

Mean food intakes (FI) of the dogs to maintain a BCS of 5/9 were 515 ± 35, 543 ± 43, and 566 ± 70 g/day for CL, BP and RB groups, respectively during the adaptation period and were 426 ± 11, 443 ± 14, and 425 ± 10 g/day for CL, BP and RB groups, respectively, during the experimental period. No significant differences among the groups were found throughout the study. Mean BW of the dogs at the end of the study were 24.8 ± 0.4, 27.1 ± 1.4 and 28.1 ± 1.3 kg for CL, BP and RB groups, respectively. No statistical differences in BW occurred among the groups during the experiment except that the CL group had lower BW than the RB group from week 9 to week 12 ($P < 0.05$). The BCS of all dogs were maintained between 4 and 6 throughout the study.

Plasma taurine concentrations decreased to under 40 μmol/L for all the groups (Fig. 1a) during the experimental period. The BP group decreased taurine concentrations lower than the other 2 groups from week 4 to the end of the experiment ($P < 0.01$) and the CL group maintained the highest mean PL taurine concentrations from week 6, but was significantly higher than the other two groups only at week 10 ($P < 0.01$). Whole blood taurine concentrations showed a similar pattern as those of PL taurine concentrations but the rates of decrease were slower (Fig. 1b). From week 6, the WB taurine concentration in BP group was lower than the other two groups ($P < 0.01$) with no statistical differences between the CL and RB groups. Urinary taurine excretions were markedly decreased from week 0; 3981 ± 790, 8880 ± 4496 and 5858 ± 910 nmol/ml/mg creatinine to week 12; 85 ± 7, 101 ± 23 and 120 ± 19 nmol/ml/mg creatinine for CL, BP and RB groups, respectively (ie, at week 12, only 2.1, 0.8 and 0.8 %, respectively of the week 0 values).

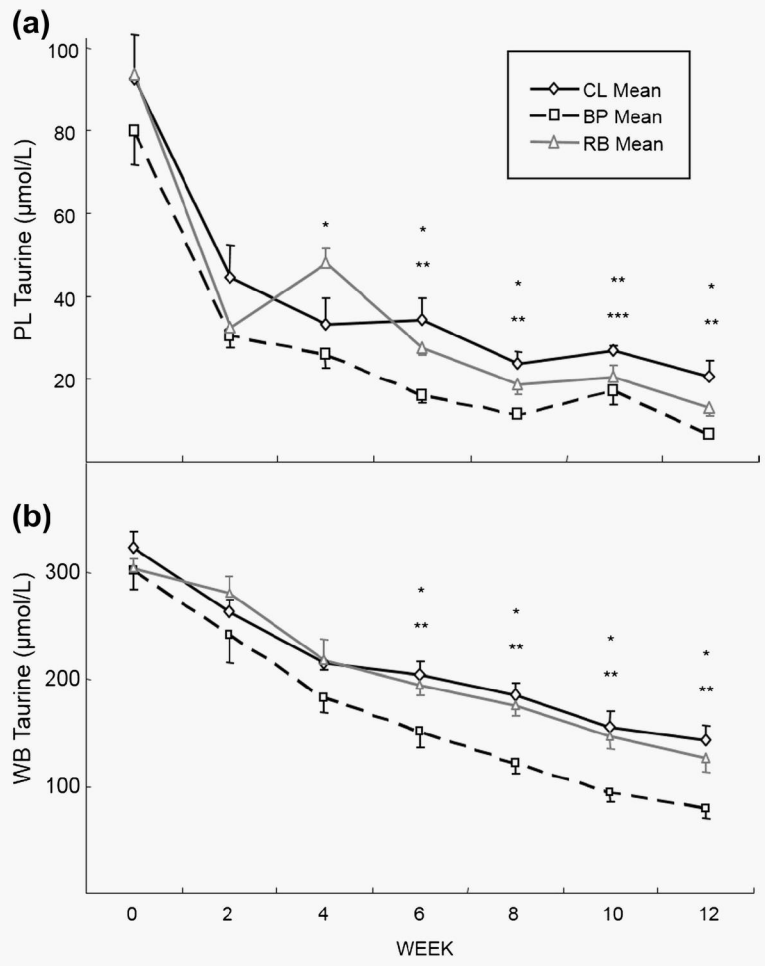


Fig 1 Concentrations of plasma (PL) and whole blood (WB) taurine among groups during 12 weeks of the experiment. **a** and **b** show taurine concentrations in PL and WB of dogs, respectively, fed the purified diets containing different fiber sources. The values are expressed as mean ± SEM. The symbols represent the groups that have significant differences ($P < 0.05$ unless otherwise mentioned in the text) at the time point (*significance between BP and RB, **significance between BP and CL, and ***significance between RB and CL). From week 10, $n = 5$ for the BP group due to omission of one dog for excessive weight loss

However no statistical differences were found among the 3 groups at any time point.

Mean apparent protein digestibilities of the diets for the dogs were 88.8 ± 0.6, 81.9 ± 0.6 and 88.1 ± 1.2 % for CL, BP and RB groups, respectively. The BP group had the lowest protein digestibility from week 2 to week 12 ($P < 0.001$) and the RB group had a protein digestibility lower than the CL group but higher than the BP group at week 2, 4 and 8 ($P < 0.05$).

The concentrations of thiols in PL or WB of the 3 groups are shown in Fig. 2. Plasma total cyst(e)ine concentrations (Fig. 2a) for RB group appeared to be maintained better than the other two groups which decreased during the experimental period. At week 8, the PL total cyst(e)ine concentration was significantly higher in the RB group than the BP group; at week 10, higher in the RB group than the BP and the CL group; and at week12, higher in the RB than the CL group ($P < 0.05$). Total glutathione (GSH + GSSG) in WB (Fig. 2b) did not show any significant differences among the groups. However, the mean concentrations of total glutathione in WB at week 12 of the CL, BP and RB groups increased by 46, 65, and 49 % from those at week 2 ($P < 0.01$). Plasma cysteinyl-glycine (Fig. 2c) and homocysteine (Fig. 2d) had similar patterns. The concentrations decreased between week 2 and week 4 and remained low until the end of the experiment. Only PL cysteinyl-glycine concentrations at weeks 10 and 12 between BP and RB, developed statistical differences ($P < 0.05$). The PL cysteinyl-glycine concentrations at week 12 were approximately 45, 47, and 45 % of those at week 2 ($P < 0.01$) and in PL homocysteine concentrations at week 12 were approximately 50, 37, and

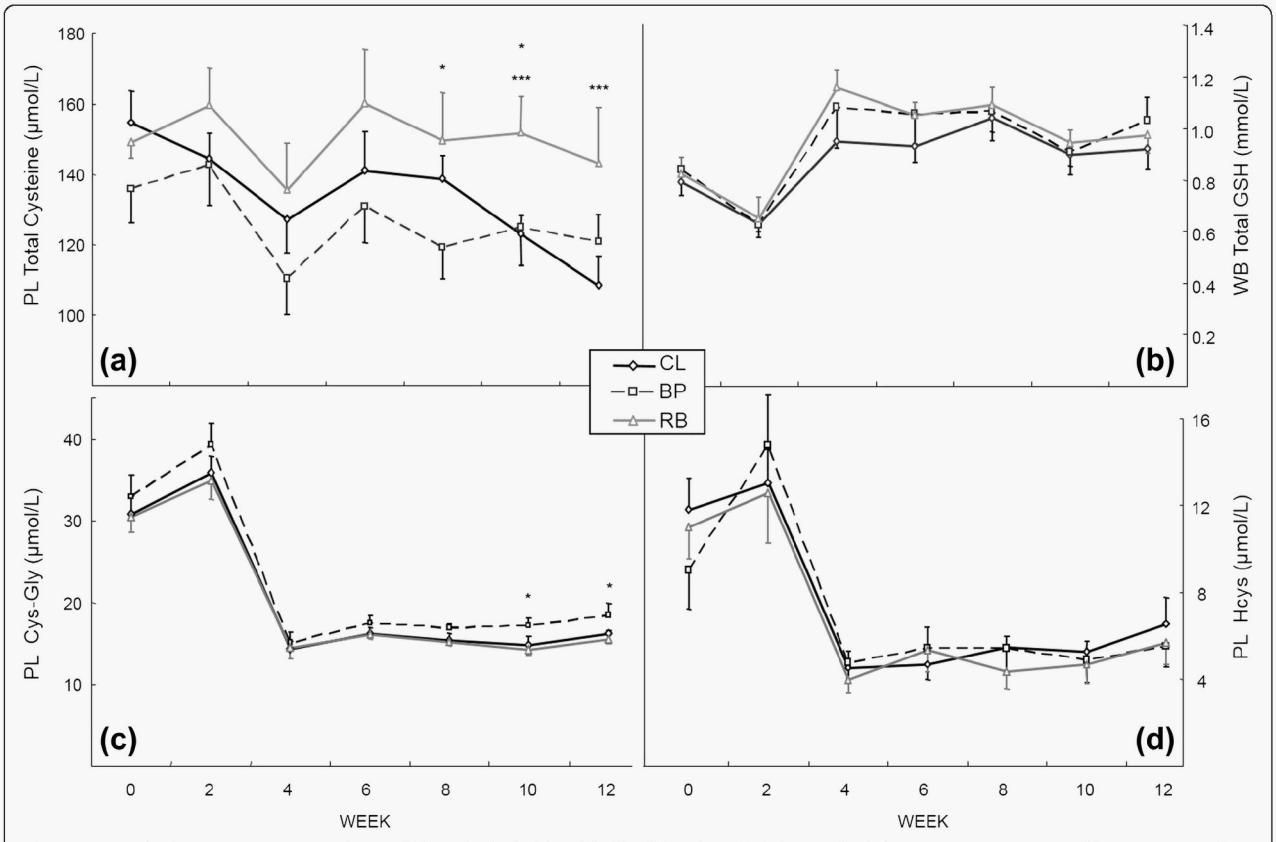


Fig 2 Various thiol concentrations in plasma (PL) and whole blood (WB) of the dogs fed the purified diets containing various fiber sources. **a** PL total cysteine (free + bound); **b** WB total glutathione (GSH + GSSG); **c** PL cysteinyl-glycine; **d** PL homocysteine. The values are expressed as mean ± SEM. The symbols represent the groups that have significant different ($P < 0.05$ unless otherwise mentioned in the text) at the time point (*significance between BP and RB and ***significance between RB and CL). From week 10, $n = 5$ for the BP group due to omission of one dog for excessive weight loss

45 % of those at week 2 ($P < 0.01$) for the CL, BP and RB group, respectively.

Plasma free cysteine (not including that bound to plasma proteins) and methionine concentrations were determined with the PL CAAP. At week 2, PL free cysteine in the BP group was significantly lower than the RB group ($P < 0.05$) with a noteworthy trend lower than the CL group ($p = 0.08$, 34 ± 3, 26 ± 4 and 36 ± 3 μmol/L for CL, BP and RB groups, respectively). However, at week 12, PL free cysteine concentrations among the two groups did not show any significant differences (23 ± 1, 25 ± 4 and 28 ± 5 μmol/L for CL, BP and RB groups, respectively). Plasma methionine concentrations did not show any significant differences among groups or with time. The mean PL methionine concentrations for CL, BP and RB group at week 0 were 53 ± 4, 56 ± 6 and 64 ± 7 μmol/L, respectively and at week 12 were 60 ± 2, 56 ± 2 and 51 ± 6 μmol/L, respectively.

Bile acid excretions of the dogs for the study are shown in Table 2. Throughout the study, the BP group had higher BA excretion than those of CL and RB regardless of the method of expression ($P < 0.01$).

Discussion

Food intake of the dogs decreased when the diets were changed from the PF diet to the experimental purified diets. Average FI of the dogs for the last two weeks of the adaptation period for the PF diet was 26 % higher than that for the experimental period for the purified diets. Decrease of FI after changing diets was mainly due to the characteristic differences of the diets. Purified diets have higher digestible energy as compared to the diets consisting of natural food ingredients. In this study, the energy (Table 1) of the PF diet (15.0 kJ/g diet) was about 20–25 % lower than those of the three purified diets (19.2 kJ/g diet, 18.7 kJ/g diet and 17.5 kJ/g diet for CL, BP and RB diet, respectively). However, the dogs throughout the study maintained BCS levels between 4 and 6. Food intake and protein intake throughout the study appeared to be adequate to maintain BW, even though the protein content of the purified diets was limited to about 12 % of their diets. However, the decrease in PL albumin below the normal reference range for all of three groups indicates that either total protein or an

Table 2 Bile acid excretion in dogs fed the purified diets containing various fiber sources[c]

	μmol/g feces (DM[e]-basis)			μmol/5 day		
Time	CL[e]	BP[e]	RB[e]	CL[e]	BP[e]	RB[e]
Week 0	5.17 ± 0.64[a]	7.03 ± 0.71[b]	5.76 ± 0.38[ab]	1123 ± 155	869 ± 120	1008 ± 67
Week 2	5.27 ± 0.62	6.56 ± 0.48	5.96 ± 0.21	944 ± 165	1145 ± 104	1047 ± 237
Week 4	4.53 ± 0.51[a]	7.40 ± 0.27[b]	5.17 ± 1.12[ab]	597 ± 119[a]	1053 ± 104[b]	721 ± 97[a]
Week 6	4.21 ± 0.63	4.18 ± 0.89	2.96 ± 0.39	684 ± 80	948 ± 241	514 ± 71
Week 8	2.69 ± 0.33[a]	5.34 ± 0.65[b]	4.93 ± 0.75[b]	487 ± 95[a]	868 ± 141[b]	693 ± 71[ab]
Week 10	3.32 ± 0.32[ab]	4.63 ± 0.84[a]	2.62 ± 0.34[b]	562 ± 92[ab]	[d]737 ± 146[a]	401 ± 52[b]
Week 12	3.43 ± 0.54[a]	5.60 ± 0.14[b]	3.42 ± 0.35[a]	513 ± 111[a]	[d]946 ± 177[b]	555 ± 64[a]

Notes: [ab]The letters superscripted represent significant differences between groups ($P < 0.05$). [c]The values are expressed as mean ± SEM, $n = 6$ for each group. [d]$n = 5$ due to omission of one dog for excessive weight loss. [e]*DM* Dry matter, *CL* Cellulose, *BP* Beet pulp, *RB* Rice bran

essential amino acid may have been slightly limiting for normal albumin homeostasis. Except for branched chain amino acids, none of the concentrations of essential amino acids in the PL during the experimental period were lower than those at week 0 (data not shown) and all were within the normal range for dogs [27]. The branched chain amino acids for weeks 8 and 12 were about 64–69 % of the concentrations found at week 0 (for PF diet) which were about at the first quartile of normal concentrations for dogs [27]. It would therefore appear that cyst(e)ine (60 % of the first quartile of the normal cyst(e)ine concentration) was the most limiting amino acid for protein synthesis as well as for taurine synthesis.

Mean taurine concentrations (Fig. 1) of the dogs at week 12 were 20.4 ± 3.9, 6.7 ± 0.5 and 13.1 ± 1.0 μmol/L for PL and 143 ± 14, 79 ± 10 and 127 ± 14 μmol/L for WB for the CL, BP and RB groups, respectively. Since the lower limits for PL and WB taurine concentration for preventing a risk for DCM in dogs are 40 μmol/L and 180 μmol/L, respectively [3], all of dogs that were participating in this study were taurine deficient by study's end. There appears to be three reasons for the taurine deficiency in this study.

The first is protein digestibility (sulfur amino acid bioavailability). The BP group showed the lowest protein digestibility throughout the study among the three experimental groups and, therefore it would be predicted that less sulfur amino acids were available for taurine synthesis. The digestibility of protein in animals fed diets containing BP has been reported by various researchers. Several have reported no effect of BP on protein digestibility in horses [28], cats [29], and even in dogs [30]. In contrast, reports in pigs [31] and in chickens [32], indicate that protein digestibility was decreased when fed BP. It is known that taurine is a non-essential amino acid that is synthesized in most mammals from cyst(e)ine [33]. Our results indicate that when protein, and thus sulfur amino acids, are low yet sufficient for nitrogen balance and glutathione homeostasis, taurine synthesis is inadequate and that a decrease in protein digestibility may be a part of this process. Therefore, the key to a diet providing adequate taurine synthesis in dogs would be an adequate quantity of "bio-available" sulfur amino acids. That quantity appears to be more than we had in the diets of the present experiment.

The second possible reason is the effects of fibers that would interfere with the entero-hepatic recycling of BA, the recycling route for the major taurine metabolite to maintain taurine status. Fibers have various physiological effects on the metabolism of animals, including satiety, slowing gastric emptying, thus delaying or interfering with nutrient absorption that, in turn, results in improvement of glucose tolerance and lowering serum cholesterol [34]. There are several hypotheses regarding the cholesterol-lowering effect of fiber, which include increasing BA excretion through feces. Since most dogs diagnosed with DCM had been fed lamb and rice (including RB) diets, we postulated that RB may contribute to the low taurine status of these dogs [5]. In general, BAs are synthesized in liver from cholesterol and conjugated with glycine or taurine to make these strong detergents, glycocholic acid or taurocholic acid. These detergents play an important role in the small intestine to emulsify various kinds of lipids to enhance their absorption by forming water soluble micelles. After functioning, the bile salts are recycled via passive diffusion in the small intestine and via receptor-mediated transport in the lower ileum with approximately 99 % of recycling efficiency [33]. Dogs, like cats, obligatorily conjugate BA with taurine, ie, the liver enzyme responsible for conjugation, cholyl-CoA:*N-acyltransferase*, is specific for taurine in dogs [34]. An interference with entero-hepatic recycling of bile salts would result in the depletion of the taurine pool of dogs if a limited quantity of taurine or its precursors are available. Therefore, fecal BA excretion was determined as an indicator of the efficiency of entero-hepatic recycling of bile salts of the dogs fed the various fibers. Fecal BA excretions, on a dry matter basis, gradually decreased in all 3 groups ($P < 0.01$), apparently the result of switching from commercial diet to the purified diets. However, the

excretion of BA/5 days by week 12 for the BP group was nearly twice that of the CL or RB group. Possible reason for decrease of fecal BA excretion with time may be the limited amount of protein in the diets. The synthesis and secretion of BA are reported to be enhanced by the hormonal stimulation of cholecystokinin whose release is evoked by fats and amino acids in the digestive tracks of the animals [35]. That is, the lower consumption of protein by the dogs may have led to less release of cholecystokinin and, in turn, less BA production and secretion. However, it is clear that the BP group had the highest BA excretion regardless of the method of expression. Even though the initial fecal BA excretion of the BP group on a dry matter basis was the highest, the BA excretions at week 12 were 64, 80, and 59 % of the BA excretions at week 0 for CL, BP and RB groups, respectively, showing that the BP group had the lowest percentage decrease. By analyses, the TDF of the CL, BP and RB diets (Table 1) were 2.51, 1.98, and 2.68 %, respectively, demonstrating that the BP fiber effect was not the result of more dietary fiber. Moreover, all had about the same percentage of insoluble dietary fiber, 1.83, 1.98 and 1.81 % for CL, BP and RB diets, respectively and all had about 1 % crude fiber. Thus, it does not appear that it is the quantity of the various fibers, but the nature of the fiber that is contributing to the different response of the BP on BA excretion and taurine depletion.

The third possible reason for the decrease in taurine status in the present study is the interaction of fiber with the small intestinal microbes. Thus, the difference between the overall effects of the three dietary treatments on taurine status may reside in the difference in fermentability of the fibers by the small intestinal microbes. If an increased microbial fermentation occurs as the result of an increased consumption of BP fiber as compared to the fiber in CL or RB, then it would be expected that more taurine would be destroyed, similar to the increase catabolism of taurine that occurs in cats that have more microbial fermentation [13–15, 36]. Sunvold et al. [37] have reported that BP supports a greater rate of fermentation than CL, and even if BP has no soluble fiber (ie, 100 % insoluble finer), it is still considerably more fermentable than CL. Thus, although we could not rule out some microbial fermentation by the CL or RB groups because we had no control diet without fiber, the results still support the idea that BP, not RB, fiber may contribute to a significant loss of endogenous taurine in dogs.

With the possible exception of free and total PL cyst(e)ine, there is no indication that there was an effect of fiber on body thiol status (Fig. 2). Although total PL cyst(e)ine (free + bound) was somewhat lower in the BP group at 4 of the time points, it was never significantly lower than the CL group, suggesting that it was not a decrease in PL cyst(e)ine alone that was the cause of the lower PL taurine in the BP group, even though it is apparent that there was not enough dietary sulfur amino acids (more specifically, hepatic cysteine) for any group to synthesize adequate taurine. Plasma free cysteine (cysteine not bound to protein) concentrations in the current experiment were already depleted in the BP group (26 ± 4 μmol/L) at week 2 and were maintained until the end of the study (25 ± 4 μmol/L), whereas the other 2 groups, although decreasing at week 2 (34 ± 3 μmol/L and 36 ± 3 μmol/L for CL and RB group, respectively), were not as depleted as the BP group until week 12 (23 ± 1 μmol/L and 28 ± 5 μmol/L for CL and RB group, respectively) supporting the idea that dietary BP decreases the bioavailability of cysteine in the diet, thus contributing to the depletion of taurine in dogs.

Whole blood was chosen for total glutathione assay since red blood cells contain the higher concentration of glutathione. Although glutathione is known as a reservoir for cysteine [38], it is interesting that in the present experiment glutathione did not decrease after feeding the low protein diets but actually increased about 20 % in all groups. According to Stipanuk et al. [38] glutathione concentration is regulated by the activity of glutamate-cysteine ligase (known as γ-glutamyl-cysteine synthetase) whose activity is regulated by the cellular concentration of cysteine. When cellular cysteine is decreased, glutamate-cysteine ligase is up-regulated to increase synthesis of glutathione and when cellular cysteine is in excess, cysteine dioxygenase is up-regulated to catabolize excess cysteine to maintain a narrow range of tissue cysteine concentrations. In this study, the concentrations of total cysteine in PL at week 12 were approximately 75, 85 and 90 % of those of week 2 for CL, BP and RB group, respectively. Free cysteine concentrations in PL at the end of the study were 62, 49, and 46 % of those of week 0 for CL, BP and RB group, respectively, perhaps indicating that free cyst(e)ine is a better indicator of cysteine availability for metabolic needs (including taurine synthesis) than total cyst(e)ine (free plus that bound to protein via sulfhydryl bonding).

It is interesting that metabolic regulation conserves glutathione rather than taurine, perhaps simply because the dietary excess of sulfur amino acids goes through the liver first where the majority of the enzymes involved are located and because of the *Km*s of the enzymes involved. That is, the priority for the use of cysteine in dogs in our experiment appears to be first for glutathione, second for general protein synthesis and finally for taurine synthesis. The apparent anomaly (ie, of glutathione being a reservoir for cyst(e)ine) here is that there appeared to be insufficient albumin synthesis or increased albumin breakdown under the conditions of our experiment, even though the dogs appeared to be in nitrogen balance (ie, maintaining BW) and WB total glutathione actually increased.

Conclusion

In summary, rather than RB, dietary BP showed the most significant effect in lowering PL and WB taurine concentrations, in part, by decreasing the protein digestibility (sulfur amino acid bioavailability), by enhancing fecal excretion of BA and possibly, by enhancing degradation of taurine by gut microflora in dogs. These effects may result from the greater effect of BP fiber than RB or CL on intestinal bacterial fermentation that cleaves taurocholic acid and destroys the taurine released. In conclusion, since CL was the control fiber, and RB caused similar responses as CL, we conclude that RB is unlikely the cause of the increased risk of taurine deficiency in dogs fed lamb and rice diets.

Acknowledgement

The research was supported by, the Center for Companion Animal Health at the School of Veterinary Medicine, University of California Davis; Margery Reibold Sommer Memorial Endowment, Department of Molecular Biosciences, University of California Davis and Purina TestDiet®/LabDiet®, Richmond, IN.

The authors thank to Dr Quinton Roger who provided fundermental ideas and guidance for the research, the staffs of Covance Research Product Inc. (Kalamazoo, MI) for their technical work in collecting the samples and Zengshou Yu at the Department of Molecular Biosciences at UC Davis (Davis, CA) for taurine and amino acid analyses.

Funding

Not applicable.

Availability of data and materials

All data and materials to generate this manuscript are available with authors.

Authors' contributions

KS KO designed and performed the major part of experiments and wrote the manuscript. AJF cooperated in analyes and writing the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interest.

Consent for publication

All authors agree for this manuscript to be published.

Ethics approval and consent to participate

The husbandry and treatments of the animals for the study were approved by the Animal Use and Care Administrative Advisory Committee at the University of California, Davis and the dogs in this study were taken care of in compliance with the National Research Council [18] guidance for laboratory animals.

Received: 8 July 2016 Accepted: 22 July 2016
Published online: 02 August 2016

References

1. Hayes KC. Taurine nutrition. Nutr Res Rev. 1998;1:99–113.
2. Torres CL. The effects of dietary ingredients, bacterial degradation in the gut and amount of food consumed on taurine status of dogs of different body sizes (dissertation). CA, USA: University of California Davis; 2003.
3. Backus RC, Cohen G, Pion PD, et al. Taurine deficiency in Newfoundlands fed commercially available complete and balanced diets. J Am Vet Med Assoc. 2003;223:1130–6.
4. Backus RC, Ko KS, Fascetti AJ, et al. Low plasma taurine concentrations in Newfoundland dogs is associated with low plasma methionine and cyst(e)ine concentrations and low taurine synthesis. J Nutr. 2006;136:2525–33.
5. Fascetti AJ, Reed JR, Rogers QR, et al. Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997-2001). J Am Vet Med Assoc. 2003;223:1137–41.
6. Johnson ML, Parsons CM, Fahey GC, et al. Effects of species raw material source, ash content, and processing temperature on amino acid digestibility of animal by-product meals by cecectomized roosters and ileallycannulated dogs. J Anim Sci. 1998;76:1112–22.
7. Stratton-Phelps M, Backus RC, Rogers QR, et al. Dietary rice bran decreases plasma and whole-blood taurine in cats. J Nutr. 2002;132:1745s–7s.
8. Topping DL, Illman RJ, Roach PD, et al. Modulation of the hypolipidemic effect of fish oils by dietary fiber in rats: studies with rice and wheat bran. J Nutr. 1990;120:325–30.
9. Hundemer JK, Nabar SP, Shriver BJ, et al. Dietary fiber sources lower blood cholesterol in C57BL/6 mice. J Nutr. ´991;121:1360–5.
10. Kahlon TS, Chow FI, Sayre RN, et al. Cholesterol-lowering in hamsters fed rice bran at various levels, defatted rice bran and rice bran oil. J Nutr. 1992;122:513–9.
11. Tomlin J, Read NW. Comparison of the effects on colonic function caused by feeding rice bran and wheat bran. Eur J Clin Nutr. 1998;42:857–61.
12. Gerhardt AL, Gallo NB. Full-fat rice bran and oat bran similarly reduce hypercholesterolemia in humans. J Nutr. 1998;128:865–9.
13. Gestel G, Besancon P, Rouanet JM. Comparative evaluation of the effects of two different forms of dietary fibre (rice bran vs. wheat bran) on rat colonic mucosa and faecalmicroflora. Ann Nutr Metab. 1994;38:249–56.
14. Kim SW, Rogers QR, Morris JG. Dietary antibiotics decrease taurine loss in cats fed a canned heat-processed diet. J Nutr. 1996;126:509–15.
15. Kim SW, Rogers QR, Morris JG. Maillard reaction products in purified diets induce taurine depletion in cats which is reversed by antibiotics. J Nutr. 1996;126:195–201.
16. Torres CL, Backus RC, Fascetti AJ, et al. Taurine status in normal dogs fed a commercial diet associated with taurine deficiency and dilated cardiomyopathy. J Anim Physiol Anim Nutr. 2003;87:359–72.
17. National Research Council. Nutrient requirements of dogs and cats, Rev. Washington D.C: National Academy Press; 2006.
18. National Research Council. Guide for the care and use of laboratory animals. Washington D.C: National Academy Press; 1996.
19. Mawby DI, Bartges JW, Laflamme DP, et al. Comparison of various methods for estimating body fat in dogs. J Am Anim Hosp Assoc. 2004;40:109–14.
20. Allison JB, Anderson JA, Seeley RD. Some effects of methionine on the utilization of nitrogen in the adult dog. J Nutr. 1947;33:361–70.
21. Kade CF, Phillips JH, Phillips WA. The determination of the minimum nitrogen requirement of the adult dog for maintenance of nitrogen balance. J Nutr. 1948;36:109–21.
22. Arnold A, Schad JS. Nitrogen balance studies with dogs on casein or methionine-supplemented casein. J Nutr. 1954;53:265–73.
23. Ubbink JB, Hayward Vermaak WJ, Bissbort S. Rapid high-performance liquid chromatographic assay for total homocysteine levels in human serum. J Chromatogr. 1991;565:441–6.
24. Gilfix BM, Blank DW, Rosenblatt DS. Novel reductant for determination of total plasma homocysteine. Clin Chem. 1997;43:687–8.
25. Porter JL, Fordtran JS, Santa Ana CA, et al. Accurate enzymatic measurement of fecal bile acids in patients with malabsorption. J Lab Clin Med. 2003;141:411–8.
26. Institute SAS. SAS system for windows, release 8.2. Cary: SAS Institute; 2001.
27. Delaney SJ, Kass PH, Rogers QR, et al. Plasma and whole blood taurine in normal dogs of varying size fed commercially prepared food. J Anim Physiol Anim Nutr. 2003;87:236–44.
28. Olsmanm AF, Huurdeman CM, Jansen WL, et al. Macronutrient digestibility, nitrogen balance, plasma indicators of protein metabolism and mineral absorption in horses fed a ration rich in sugar beet pulp. J Anim Physiol Anim Nutr. 2004;88:321–31.
29. Fekete SG, Hullar I, Andrasofszky E, et al. Effect of different fibre types on the digestibility of nutrients in cats. J Anim Physiol Anim Nutr. 2004;88:138–42.
30. Cole JT, Fahey Jr GC, Merchen NR, et al. Soybean hulls as a dietary fiber source for dogs. J Anim Sci. 1999;77:917–24.
31. Graham H, Hesselman K, Aman P. The influence of wheat bran and sugar-beet pulp on the digestibility of dietary components in a cereal-based pig diet. J Nutr. 1986;116:242–51.
32. Pettersson D, Razdan A. Effects of increasing levels of sugar-beet pulp in broiler chicken diets on nutrient digestion and serum lipids. Br J Nutr. 1993;70:127–37.

33. Tso P, Crissinger K. Overview of digestion and absorption, in Biochemical and physiological aspects of human nutritio. PA, USA: W. B. Saunders Company; 2003.
34. Czuba B, Vessey DA. Identification of a unique mammalian species of cholyl-CoA: amino acid N-acyltransferase. Biochim Biophys Acta. 1981;665:612–4.
35. Jones PJH, Stanley K. Lipid, sterols, and their metabolites, in Modern nutrition in health and disease. 9th ed. PA, USA: Lippincott Williams & Wilkins; 1999.
36. Hickman MA, Rogers QR, Morris JG. Effect of processing on fate of dietary [^{14}C]taurine in cats. J Nutr. 1990;120:995–1000.
37. Sunvold GD, Fahey Jr GC, Titgemeyer EC, et al. Dietary fiber for dogs: IV. In vitro fermentation of selected fiber sources by dog fecal inoculum and in vivo digestion and metabolism of fiber-supplemented diets. J Anim Sci. 1995;73:1099–109.
38. Stipanuk MH, Dominy Jr JE, Lee JI, et al. Mammalian cysteine metabolism: new insights into regulation of cysteine metabolism. J Nutr. 2006;136:1652S–9S.

Asian-Aust. J. Anim. Sci.
Vol. 21, No. 3 : 434 - 442
March 2008

www.ajas.info

The Optimum Methionine to Methionine Plus Cystine Ratio for Growing Pigs Determined Using Plasma Urea Nitrogen and Nitrogen Balance

Shiyan Qiao, Xiangshu Piao, Zhanyu Feng, Yuhua Ding*, Longyao Yue and P. A. Thacker
Ministry of Agriculture Feed Industry Center, China Agricultural University
No. 2 Yuanmingyuan West Road, Beijing 100094, China

ABSTRACT : The objective of this study was to determine the optimum ratio of methionine to methionine plus cystine for growing pigs. A nitrogen balance trial was conducted using a total of 21 barrows (Large White×Landrace) over two replicates. The initial body weight was 20.36±1.22 kg (mean±SD) in the first replicate and 23.54±1.02 kg (mean±SD) in the second. For each replicate, the 21 pigs were randomly assigned to one of seven dietary treatments with three observations per treatment. The diets included a methionine and cystine-deficient basal diet with all other essential nutrients meeting nutrient requirements and six diets formulated with graded levels of DL-methionine (0.00, 0.03, 0.06, 0.10, 0.13, 0.16%) and L-Cystine·HCl·H_2O (0.19, 0.15, 0.11, 0.07, 0.04, 0.00%). This resulted in ratios of methionine to methionine plus cystine of 41.3, 29.6, 35.3, 41.2, 46.0, 51.6 and 57.5%. Each experimental period lasted 12 days consisting of a seven-day adaptation period followed by a five-day total collection of urine and feces. During the collection period, pigs were fed 900 g/day for the first replicate and 1,200 g/day for the second replicate. The feed was provided in three equal portions at 0800, 1500, and 2200 h daily. Pigs had *ad libitum* access to water after feeding. There was a linear ($p<0.01$) and quadratic ($p<0.01$) effect on daily gain and feed conversion as the ratio of methionine to methionine plus cystine increased. Pigs receiving the diets providing a methionine to methionine plus cystine ratio of 51.6% had the best daily gain and feed conversion. Plasma urea nitrogen was also lowest for this treatment. Nitrogen retention increased ($p<0.01$) as the relative proportion of methionine increased up to 51.6% and then a downward trend occurred at 57.5%. The quadratic regression model, as well as one- and two- slope regression line models, were used to determine the optimum ratio of methionine to methionine plus cystine. Eliminating the 35.3% methionine to methionine plus cystine treatment resulted in R^2 values in excess of 0.92. The optimal ratio of methionine to methionine plus cystine was estimated to be 54.15% for nitrogen retention and 56.72% for plasma urea nitrogen. (**Key Words :** Pigs, Methionine, Cystine, Ratio, Nitrogen Retention, Plasma Urea Nitrogen)

INTRODUCTION

The sulfur containing amino acids methionine and cystine are often the third or fourth limiting amino acids in practical diets fed to growing pigs (Russell et al., 1983). Methionine is essential for normal growth as it cannot be synthesized in the body, but cystine can be converted from methionine as needed, hence it is considered dispensable. As a result, the amount of methionine needed in the diet depends on the amount of cystine also present (Chung and Baker, 1992; Yang et al., 1997; Zimmermann et al., 2005). The absolute amounts of methionine and cystine are important but so is the ratio between methionine and cystine. Therefore, nutritionists need to consider not only methionine but also methionine plus cystine requirements when formulating pig diets.

Previous studies with growing pigs have shown that the minimum methionine to methionine plus cystine ratio ranged between 30 and 70% (Wang and Fuller, 1989; Fuller et al., 1989). Part of this variability is due to differences in response criteria (i.e., nitrogen balance vs. growth performance), the bioavailability of the amino acids in the basal diet, and weight of pigs used in the experiments. In a nitrogen balance study with growing gilts (40-80 kg) fed varying ratios of methionine to cystine diets, Reijmers et al. (2002) found the minimum methionine to methionine plus cystine ratio at which protein deposition was maximized was 55%. This value is within the range of values reported in the literature (NRC 1998, Roth and Kirchgessner, 1989).

There is very limited data about the required methionine to methionine plus cystine ratio for maximal protein

* Corresponding Author: Yuhua Ding. Tel: +86-10-6273-3588, Fax: +86-10-6273-3688, E-mail: Dingyh@mafic.ac.cn
Received August 9, 2006; Accepted January 3, 2007

Table 1. Ingredient composition of experimental diets formulated to determine the effects of various methionine to methionine plus cystine ratios on pig performance and nitrogen balance (% as fed)

Ingredients	Methionine to methionine plus cystine ratio						
	41.3	29.6	35.3	41.2	46.0	51.6	57.5
Corn	39.90	39.90	39.90	39.90	39.90	39.90	39.90
Field peas	24.79	24.79	24.79	24.79	24.79	24.79	24.79
Peanut meal	10.00	10.00	10.00	10.00	10.00	10.00	10.00
Corn starch	8.90	8.71	8.72	8.73	8.73	8.73	8.74
Wheat barn	7.00	7.00	7.00	7.00	7.00	7.00	7.00
Sucrose	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Dicalcium phosphate	1.28	1.28	1.28	1.28	1.28	1.28	1.28
Limestone	0.83	0.83	0.83	0.83	0.83	0.83	0.83
Vitamin and mineral premix[a]	0.50	0.50	0.50	0.50	0.50	0.50	0.50
NaCl	0.41	0.41	0.41	0.41	0.41	0.41	0.41
Choline chloride (50%)	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Soybean oil	0.20	0.20	0.20	0.20	0.20	0.20	0.20
L-lysine HCl (98.5%)	0.49	0.49	0.49	0.49	0.49	0.49	0.49
L-threonine (99%)	0.23	0.23	0.23	0.23	0.23	0.23	0.23
L-valine (99.5%)	0.14	0.14	0.14	0.14	0.14	0.14	0.14
L-isoleucine (99%)	0.14	0.14	0.14	0.14	0.14	0.14	0.14
L-tryptophan (98%)	0.09	0.09	0.09	0.09	0.09	0.09	0.09
DL-methionine (99%)	-	-	0.03	0.06	0.10	0.13	0.16
L-cystine·HCl·H_2O[b] (99.1%)	-	0.19	0.15	0.11	0.07	0.04	-

[a] Provided per kilogram of complete feed: vitamin A, 5,512 IU; vitamin D_3, 2,200 IU; vitamin E, 66.1 IU; riboflavin, 5.5 mg; D-pantothenic acid, 13.8 mg; niacin, 30.3 mg; vitamin B_{12}, 27.6 μg; Mn, 100 mg; Fe, 100 mg; Cu, 234 mg; Zn, 100 mg; I, 0.3 mg; Se, 0.3 mg; Co, 1.0 mg.

[b] 1 kg of L-cystine·HCl·H2O (99.1%) contained 0.851 kg of L-cystine.

deposition in 20 to 30 kg growing pigs. Therefore, the objective of the current study was to establish the optimum dietary ratio of methionine to methionine plus cystine for growing pigs using the nitrogen balance technique and plasma urea nitrogen.

MATERIALS AND METHODS

Animals and diets

A nitrogen balance trial was conducted in the Metabolism Laboratory of the Animal Science and Technology College located on the campus of China Agriculture University (Beijing, China). The trial, conducted in two replicates, utilized 21 barrows (Large White×Landrace) obtained from the Haudu Group (Beijing, China). The initial bodyweight of the pigs averaged 20.36±1.22 kg in the first replicate and 23.54±1.02 kg in the second replicate. In each replicate, the 21 pigs were randomly allocated to one of seven different dietary treatments with three observations per treatment. The basal diet was formulated to meet the requirements for all amino acids except methionine and cystine (NRC, 1998). All other nutrients were formulated to meet or exceed requirements (NRC, 1998). Batches of each feed ingredient were obtained before the start of the study, sampled and analyzed in order to adjust the nutrient composition of the diets.

The content of methionine and cystine in the basal diet was determined to be 0.19 and 0.27%, respectively. Crystalline DL-methionine (0.0, 0.03, 0.06, 0.10, 0.13 and 0.16%) and L-Cystine·HCl·H_2O (0.19, 0.15, 0.11, 0.07, 0.04 and 0.0%) were added to the basal diet by replacing corn starch resulting in seven treatments with ratios of methionine to methionine plus cystine ranging from 29.6 to 57.5% (41.3, 29.6, 35.3, 41.2, 46.0, 51.6 and 57.55%). The ingredient composition of all the diets is presented in Table 1.

For all experimental diets, the vitamin-trace mineral mix and synthetic amino acids were premixed with 10 kg corn before addition to the mixer. A basal mix was manufactured and aliquots of this mix were used to manufacture the final feed.

Experimental procedures

Each replicate consisted of a seven day adjustment period followed by a five day total collection of feces and urine. The pigs were kept in individual metabolic crates and separate collection of feces and urine was accomplished by fitting adhesive feces collection bags onto the back of pigs (Van Kleef et al., 1994). Each stainless steel crate (0.6×0.3 ×0.5 m) was equipped with plastic slotted flooring and contained a 0.25 m^3 round bottom single feeder at the front. The temperature and humidity of the room were controlled within the range of 22 to 25°C and 55 to 70%, using the environmental control system.

The daily ration was divided into three feedings per day, with approximately one third of the ration being fed at

Table 2. Chemical analysis for experimental diets formulated to determine the effects of various methionine to methionine plus cystine ratios on pig performance and nitrogen balance (% as fed)[a]

	Methionine to methionine plus cystine ratio						
	41.3	29.6	35.3	41.2	46.0	51.6	57.5
Chemical analysis							
Dry matter	89.62	90.10	88.98	88.28	89.20	88.94	90.12
Ash	4.83	4.93	5.01	4.81	5.01	4.81	47.56
Crude protein	14.92	15.02	14.82	14.71	15.01	14.68	14.08
Crude fibre	2.28	2.51	2.36	2.29	2.37	2.89	2.40
Ether extract	3.45	3.68	3.81	3.69	3.76	3.72	3.68
Analyzed amino acids							
Arginine	1.18	1.21	1.17	1.11	1.15	1.17	1.18
Cystine	0.27	0.45	0.42	0.37	0.34	0.30	0.27
Histidine	0.34	0.36	0.36	0.35	0.37	0.35	0.36
Isoleucine	0.63	0.62	0.65	0.63	0.63	0.62	0.63
Leucine	1.07	1.11	1.10	1.08	1.09	1.09	1.11
Lysine	1.03	1.10	1.07	1.10	1.02	1.06	1.06
Methionine	0.19	0.19	0.23	0.26	0.29	0.32	0.38
Phenylalanine	0.68	0.67	0.69	0.68	0.66	0.67	0.68
Threonine	0.68	0.68	0.69	0.68	0.70	0.70	0.65
Tryptophan	0.23	0.26	0.20	0.22	0.22	0.23	0.21
Valine	0.82	0.78	0.78	0.76	0.74	0.73	0.79

8,000, 1,500 and 2,200 h. The daily feed allowance of the experimental animals was adjusted according to the feed intake observed in the last three days of the acclimation period. This was the amount of feed that pigs could consume within 20 minutes based on our observations.

From d 4 until the end of the 12-d experimental period, the same amount of feed was fed which exceeded 2.6 times the pig's maintenance energy requirements. This energy intake has been shown not to limit protein deposition (Möhn et al., 2000; De Lange et al., 2001). The feeding rate ranged from 4% to 5.5% of body weight (900 g/d/pig for the first replicate and 1,200 g/d/pig for the second replicate). In the collection period, the wasted feed for each pig was collected, dried and recorded on a dry matter basis.

The animals were weighed at the start of every quantitative feeding period and again at the termination of the trial. Weighing was conduced at 0800 to 0900 h with no feed available. After feeding, water was provided *ad libitum* in the feeding trough.

Sample collection

Feces were collected in the morning, afternoon and evening for five consecutive days taking care to avoid contamination with urine. The total weight of the raw feces for each pig was recorded daily. After collection, feces were placed into labeled plastic bags and frozen at approximately -20°C. At the end of each trial, each pig's daily samples were combined into a single composite sample. From that, a 5% sub-sample was preserved for laboratory analysis. Sub-samples were dried to a constant weight in a forced-air oven at 65°C, equilibrated at room temperature for 24 h, and ground through a 0.45 mm mesh screen.

The urine of individual pigs was collected in plastic containers containing 50 ml of 6 N HCl to maintain the pH of the urine below 3. The total amount of urine excreted by each pig was measured once a day at approximately 1,530 h and recorded on a daily basis. After being filtered through glass wool, a fixed proportion of the urine from each pig was preserved in screw-capped polyethylene containers and frozen at approximately -20°C. When the collection for all five days was completed, each pig's daily samples were thawed and combined into a single sample. A 100 ml composite sample was obtained and then frozen until needed for nitrogen analysis.

At the end of each replicate, 7 ml of blood was collected from the jugular vein of each pig using heparinized vacutainer tubes (Greiner Bio-One Company), approximately 1 h after feeding. All blood samples were chilled and then centrifuged at 3,000×g for 15 min at 4°C within 1 h after collection (Ciji 800 Model Centrifuge, Surgical Instrument Factory, Shanghai, China). An aliquot of plasma was stored at -20°C until analyzed for plasma urea nitrogen.

Chemical analysis

Samples of the feed ingredients were collected before the diets were manufactured, while samples of complete feeds were collected at the start of the trial for analyses. The chemical composition and the amino acid content of all ingredients was analyzed in duplicate in the laboratory of the Ministry of Feed Industry Center (Beijing, China). Moisture, crude protein, crude fiber, ether extract and ash were determined following standard methods (AOAC, 1995).

Table 3. Performance and plasma urea nitrogen for growing pigs fed varying ratios of methionine to methionine plus cystine

	Methionine to methionine plus cystine ratio							SEM[a]	Linear	Quadratic
	41.3	29.6	35.3	41.2	46.0	51.6	57.5			
Weight gain (g/day)	368	375	375	397	395	422	422	36.92	0.01	0.01
Feed intake (g/day)	924	923	923	927	925	924	927	59.36	0.96	0.99
Feed conversion	2.56	2.47	2.51	2.33	2.39	2.20	2.22	0.27	0.01	0.01
Plasma urea nitrogen (mg/dl)	12.50	12.33	12.67	11.83	10.17	9.33	10.17	1.96	0.14	0.33

[a] SEM = Standard error of the mean.

Table 4. Nitrogen balance response for growing pigs fed varying ratios of methionine to methionine plus cystine

	Methionine to methionine plus cystine ratio							SEM[a]	Linear	Quadratic
	41.3	29.6	35.3	41.2	46.0	51.6	57.5			
Nitrogen intake (g/day)	24.79	24.73	26.11	25.60	26.14	26.16	26.07	1.65	0.58	0.80
Fecal nitrogen (g/day)	3.12	3.56	3.54	3.43	3.00	3.19	2.81	0.48	0.18	0.41
Urinary nitrogen (g/day)	9.62	8.85	10.49	7.88	7.66	6.91	7.88	1.29	0.17	0.37
Retained nitrogen (g/day)	12.05	12.32	12.09	14.29	15.49	16.05	15.38	1.23	0.01	0.01
Nitrogen retained (%)	48.61	51.07	46.64	56.61	60.00	62.05	59.57	4.53	0.02	0.05
Nitrogen digestibility (%)	88.74	86.01	86.62	86.76	88.48	88.09	89.30	1.38	0.04	0.13

[a] SEM = Standard error of the mean.

The amino acid content of the diets was determined by High Performance Liquid Chromatography (Hitachi L-8800 Amino Acid Analyzer, Tokyo, Japan). All samples were hydrolyzed for 24 h at 110°C with 6 N HCl prior to analysis. Sulfur-containing amino acids were analyzed after cold formic acid oxidation for 16 h before acid hydrolysis. Tryptophan was determined after alkaline hydrolysis (4 N NaOH) for 22 h at 110°C. The chemical composition of the diets is listed in Table 2.

Plasma urea nitrogen was determined on a fully automatic Biochemical Analyzer (Technicon RA 1000) and by enzymatic UV test (Ureaza method/GLDH) based on the report of Kerschner and Ziegenhorn (1985). A urea kit produced by Zhong Sheng Beikong Bio-technology and Science Inc. (Beijing, China) was used for this analysis. Fecal and urinary nitrogen were analyzed with a semi-automatic analyzer (Kjeltec^{TM} 2100 Distillation Unit) by the Kjeldahl method (AOAC, 1990).

Statistical analysis

Data from the two replicates were analyzed using the General Linear Model (GLM) procedure of the SAS statistical package (SAS, 2002) using the pig as the experimental unit. The experimental data were subjected to analysis of variance using a model that included the effect of diet and the two replicates. The results were considered significant if $p<0.05$.

The optimal ratio between methionine and methionine plus cystine of the growing pigs was estimated with a quadratic regression model as well as one- and two- slope regression line models (Coma et al., 1995a) using nitrogen retention and plasma urea nitrogen as the dependent variables regressed against dietary level of methionine to methionine plus cystine ratio. The appropriate GLM and NLIN procedures of SAS (2002) were used for these estimates. The applied quadratic model was:

$$Y = b_0+b_1X+b_{11}X^2$$

Where Y = the response parameter (nitrogen retention, plasma urea nitrogen) and X_1 = the ratio of methionine to methionine plus cystine b_0, b_1, b_{11} = the coefficients of the equation. The ratio at which the response reached 95% of the maximum response was estimated as the optimal value.

The regression of the one-slope and two-slope models used in the present experiment are described as follows:

$$Y = L+U\ (R-X_{LR});$$

$$Y = L+U\ (R-X_{LR})+V(X_{GR}-R)$$

Where L = the ordinate; R = the abscissa of the breakpoint (the estimated requirement). X_{LR} means X less than R; X_{GR} means X greater than R. U = the slope of the line at X<R, and V = the slope of the line at X>R. By definition, $(R-X_{LR})$ is zero when X greater than R, and $(X_{GR}-R)$ is zero when X less than R. The ratio at which the breakpoint was achieved was estimated as the optimal value (Robbins et al., 1979; Coma et al., 1995a). The mean square error (MSE) and the coefficient of determination (R^2) were used to assess the goodness of fit for the different models (Coma et al., 1995a).

RESULTS

The results showed no significant replicate×treatment interaction ($p>0.05$) for any of the studied variables. Therefore, data from the two replicates were pooled for analysis.

Since the level of feed intake was controlled, feed intake

Table 5. Asymptotic characteristics of plasma urea nitrogen and nitrogen retention responses to relative proportions of methionine to methionine plus cystine

Variable	Model	Requirement	R^2	MSE
Nitrogen retention	Quadratic	54.15	0.99	0.095
	One-slope broken line	51.24	0.96	0.192
	Two-slope broken line	53.96	0.98	0.159
Plasma urea nitrogen	Quadratic	56.17	0.92	0.563
	One-slope broken line	53.94	0.94	0.233
	Two-slope broken line	56.72	0.99	0.113

was similar among all dietary treatments. As the relative proportion of methionine to methionine plus cystine increased from 29.6 to 57.5%, average daily gain and feed conversion improved linearly ($p = 0.01$) and quadratically ($p = 0.01$). The poorest weight gain and feed utilization was observed for pigs fed the basal diet. The best daily gain and feed conversion was observed for pigs fed the diet in which the methionine to methionine plus cystine ratio was 51.6%. For plasma urea nitrogen, the lowest and highest values occurred for pigs fed the 51.6 and 35.3% methionine to methionine plus cystine ratio diets (Table 3).

Increasing the relative proportion of methionine to methionine plus cystine resulted in a significant linear ($p = 0.02$) and quadratic ($p = 0.05$) increase in nitrogen retention (Table 4). Nitrogen digestibility increased linearly ($p = 0.04$) with increased proportions of methionine to methionine plus cystine.

Three statistical models were fitted to the nitrogen retention and plasma urea nitrogen data (Tables 3 and 4). Based on the nitrogen retention response to the ratio of methionine to methionine plus cystine, three regression equations were obtained using the quadratic regression, one- and two- slope regression models, respectively:

$$Y = -18.19+1.20X-0.011X^2$$

$$Y = 15.72-0.26\times(51.24-X_{LR})$$

$$Y = 16.42-0.26\times(53.96-X_{LR})-0.10\times(X_{GR} - 53.96)$$

Based on the corresponding equations, the optimal ratios of methionine to methionine plus cystine were determined to be 54.15, 51.24 and 53.96%, respectively.

When plasma urea nitrogen was considered as the dependent variable, the optimal ratios of methionine to methionine plus cystine were estimated to be 56.17, 53.94 and 56.72%. The corresponding regression equations were listed as followed:

$$Y = 33.951-0.816\ X-0.0069\ X^2$$

$$Y = 9.75+0.19\times(53.94-X_{LR})$$

$$Y = 9.22+0.19\times(56.72-X_{LR})-0.13\times(X_{GR}-56.72)$$

DISCUSSION

In the present study, the optimal ratio of methionine to methionine plus cystine was estimated in 20 to 30 kg growing pigs using the nitrogen balance technique. Based on our design, the six test diets contained varying levels of methionine and cystine but the total content of methionine plus cystine was similar across treatments and was close to the value recommended by the NRC (1998). Moreover, all other essential nutrients, especially energy and other amino acids were designed to be at or above requirement (NRC, 1998).

For growing animals, amino acids are basically used for protein accretion and maintenance and deposited protein relies on the level of the first limiting amino acid. Assuming our dietary formulation was accurate and the methionine plus cystine content of the test diets did not exceed the requirements of growing pigs, whole-body protein synthesis should theoretically occur at a level determined by the optimal ratio of methionine to cystine. If the dietary ratio of methionine to cystine is below the optimal value, more cystine and less methionine will be consumed. Protein synthesis will be determined by the level of dietary methionine, which leads to less protein deposition. When the ratio in the test diets is above the value, methionine will be in relative excess and cystine will be in relative deficiency. However, the deficiency in cystine can be overcome by conversion from methionine via the trans-sulfuration pathway. In fact, cysteine (1/2 cystine) is the genuine element used to incorporate into protein. Cystine (the dimmer form of cysteine), is produced when cysteine is in solution (Lewis, 2003). Because of the molecular weight difference between methionine and cysteine, the efficiency of methionine in meeting the biological need for cysteine on a weight basis is 80% (Chung and Baker, 1992). Thus, an excess of methionine is not sufficient to make up for a deficiency in cystine in this condition. Protein synthesis will also be reduced due to the low cystine intake. From this, it can be concluded that increasing the relative proportion of methionine will result in greater protein synthesis until the optimal ratio of methionine to cystine is attained, and subsequently, when the relative proportion of methionine is above its optimal value, protein synthesis will be reduced with further increases in methionine intake.

Because of conversion from methionine, a deficiency of cystine will lead to relatively less of a change in protein synthesis than a deficiency of methionine in the presence of a constant methionine plus cystine content. This has been confirmed by Roth and Kirchgessner (1989). In a similar experiment for 30 to 60 and 60 to 90 kg pigs, they found that pigs with a predominant proportion of methionine obtained higher performance than those with a predominant proportion of cystine. Here, the parameters of performance reflect the status of protein synthesis. According to the current experimental design and statistical analysis, when the optimal ratio of methionine to cystine is fed, maximal protein synthesis occurs.

The status of protein synthesis can be measured using biological response criteria such as growth, nitrogen retention and plasma urea. In fact, an inherent relationship exists between several criteria. Nitrogen retention is a direct indicator of protein synthesis. Here, protein deposition (synthesis) can be calculated as nitrogen retained×100/16 (Möhn et al., 2000). For young pigs with minimal fat deposition, growth is almost directly proportional to lean tissue deposition which primarily relies on protein deposition.

When protein synthesis is limited due to an unsuitable ratio of methionine to cystine, excess amino acids (including methionine or cystine) are catabolized to their metabolic end-products which for all amino acids include bicarbonate and ammonia. Ammonia enters the nitrogen pool of the body and is excreted primarily as urea in mammals. The status of urea in the body is therefore reflected by plasma urea. The measurement of these excreta provides an indirect and inverse measurement of changes in protein synthesis. As the relative proportion of methionine increases towards its optimal value, more protein is synthesized which leads to increased nitrogen retention, improved animal performance and decreased plasma urea. The inverse changes of nitrogen retention, animal performance and plasma urea occur when there is a continuous increase in the relative proportion of methionine from its optimal value. The inverse relationship between plasma urea (nitrogen) and lean growth (growth for young pigs) was also detected in previous reports published by Coma et al. (1995b).

So, based on maximal nitrogen retention or minimal plasma urea, the optimal ratio of methionine to cystine can be determined for the growing pigs in the present study. This estimation can be conducted by applying suitable statistical modeling techniques to the chosen biological response. We observed nitrogen retention and plasma urea nitrogen exhibited an anticipative change tendency from 35.3 to 57.5% methionine to methionine plus cystine (Tables 3 and 4). However, nitrogen retention and plasma urea nitrogen in the 29.6% treatment were superior to those in the 35.3% methionine to methionine plus cystine treatments, which meant that an increase in the relative proportion of methionine towards its optimal value caused a decrease in those variables. The reason for this is not known.

The quadratic and broken-line regression analyses were used to determine the relation between methionine and cystine in our study. For nitrogen retention and plasma urea nitrogen, when the values generated from the treatment for 29.6% of methionine to methionine plus cystine were removed, those models fitted the data very well.

Using the quadratic regression, as well as the one- and two- slope broken-line regression models, the required ratios of methionine to methionine plus cystine were estimated to be 54.15, 51.24 and 53.96% for nitrogen retention. However, when considering the plasma urea nitrogen variable, using the corresponding statistical models, the required ratios of methionine to methionine plus cystine were estimated to be 56.17, 53.94 and 56.72%. Obviously, the plasma urea nitrogen assay resulted in higher values than the nitrogen retention assay using the corresponding statistical models.

These differences may be attributed to an imbalance of electrolytes in the diets, where the chloride existing in the crystalline cystine (L-Cystine·HCl·H_2O) would tend to decrease the cation:anion ratio. Several reports in pigs have indicated that a diet with excess anion or chloride resulted in markedly lower plasma urea nitrogen concentrations (Slagle and Zimmerman, 1979; Honeyfield et al., 1985). However, total nitrogen excretion in pigs was found to be constant, although the excess cation intake resulted in significantly greater urea excretion (Cai et al. 1992). This was explained by Welbourne et al. (1986) who suggested that with the maintenance of acid-base balance in the body, urea was isochronously synthesized with ammonia production so that nitrogen excretion remained constant. Thus, the addition of various levels of L-Cystine-HC1 in the test diets influenced plasma urea nitrogen but not nitrogen retention, which may have produced the difference between the estimated results from the two variables. So the result from the nitrogen retention assay is more reasonable and acceptable.

For the nitrogen retention response, we found that the quadratic regression model had lower MSE and higher R^2 than either of the broken-line regression models (Figures 1-3). So the nitrogen retention response is better described by the quadratic regression model than by the broken-line regression models. Therefore, the determined value 54.15% is considered to be the estimated required ratio methionine to methionine plus cystine according to the nitrogen retention response. Similarly, for the plasma urea nitrogen response, we observed that the two-slope broken-line regression model tended to fit the data better than the other two regression models. The determined value 56.72% is

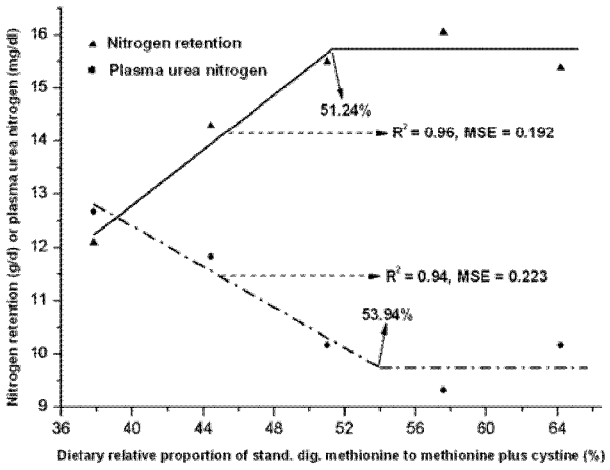


Figure 1. Use of the one-slope, broken-line regression model to describe the responses of nitrogen retention and plasma urea nitrogen to the proportion of methionine to methionine plus cystine in 20-50 kg growing pigs.

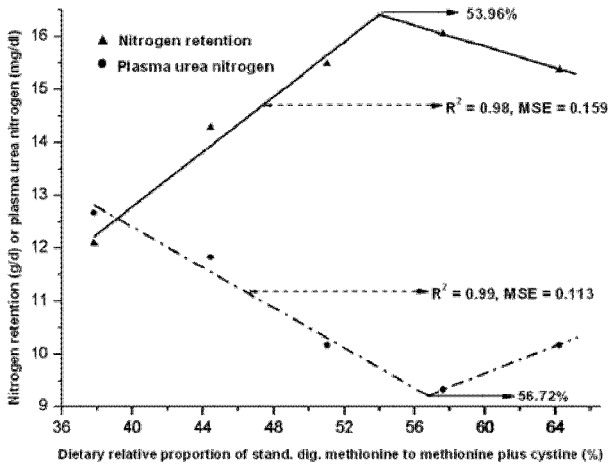


Figure 2. Use of the two-slope, broken-line regression model to describe the responses of nitrogen retention and plasma urea nitrogen to the relative proportion of methionine to methionine plus cystine in 20-50 kg growing pigs.

considered to be the estimated required ratio when the plasma urea nitrogen response was considered (Figures 1-3).

Referring to the dietary amino acid requirements for 20 to 50 kg growing pigs (NRC 1998), the recommended methionine and methionine plus cystine levels are 0.25% and 0.54%, respectively. Therefore, the ratio of methionine to methionine plus cystine is 46.29%. Obviously, our determined value is higher than this value. However, in a recent nitrogen balance experiment for 40 to 80 kg growing gilts, Reijmers et al. (2002) found the ratio of digestible methionine to methionine plus cystine for maximal body protein deposition was 55%. This value is very close to our evaluation of 54.15% based on maximal nitrogen retention.

These results agree with the studies conducted by

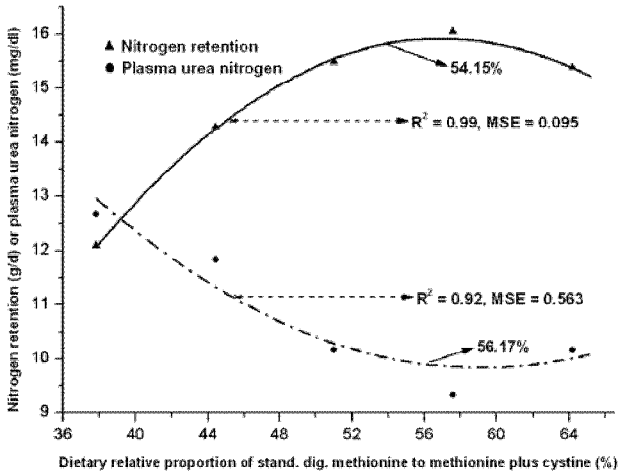


Figure 3. Use of the quadratic model to describe the responses of nitrogen retention and plasma urea nitrogen to the relative proportion of methionine to methionine plus cystine in 20-50 kg growing pigs.

Schutte et al. (1991) and Chung and Baker (1992), who indicated in growing pigs (respectively 20 to 50 kg and 10 to 20 kg) that methionine should contribute more than 50% of the total methionine and cystine requirement. In a previous growth assay for 30 to 60 kg and 60 to 90 kg pigs, Roth and Kirchgessner (1989) found that the ratio of methionine to methionine plus cystine, at maximal weight gain or feed efficiency, was more than 55%. This is somewhat higher than either of our estimated values. Several factors may have contributed to the differences in the relative proportion of methionine to methionine plus cystine estimates of growing pigs in the above studies including: 1) use of a different experimental design, i.e. nitrogen balance vs. growth assay, 2) use of different response criteria, i.e., nitrogen retention, plasma urea nitrogen or performance, 3) differing methionine plus cystine content employed in the diets, In addition, young animals use more amino acids for protein accretion than for maintenance compared with older ones. Protein accretion in pigs requires a greater proportion of methionine (Fuller et al., 1989; Mahan and Shields, 1998), while maintenance in pigs requires a greater proportion of cystine (Fuller et al., 1989; NRC, 1998). So the estimated result may also be influenced by age of pig.

For the present experiment, there are some additional factors which may have affected our results. In our design, the test diets were provided with constant levels of methionine plus cystine and varying levels of methionine and cystine. Lewis (2003) indicated that the molecular weight of methionine (149) is greater than that of cysteine (121), and equal weights of these two amino acids provide only 81% as many moles of methionine as cysteine (121/149 = 0.81). Thus, on a weight basis, increasing the

methionine to cystine ratio provides a decreasing number of moles of sulfur containing amino acids. In our study, the content of methionine plus cystine was not constant when expressed on a molar basis, which possibly influenced the results to some extent. However, we found that previous experiments also ignored this effect (Roth and Kirchgessner, 1989; Reijmers et al., 2002).

In practical swine diets containing sufficient amounts of the sulfur amino acids, generally cystine is more in excess than methionine. A high cystine intake increased the requirement of methionine plus cystine in pigs, but there was no evidence that excess cystine interferes with methionine (Lewis, 2003). When low protein diets are used in young pigs, perhaps methionine will be lacking. In this case, methionine should be added to meet its requirement, even though methionine plus cystine may appear to be adequate.

CONCLUSION

In the present nitrogen balance trial with an equal feed intake, nitrogen retention and plasma urea nitrogen variables were used to determine the optimum methionine to methionine plus cystine ratio. The data from the two variables were analyzed to fit a quadratic regression, as well as one- and two- slope regression models. By comparing the estimated results from three regression models, the two most precise values, 54.15 and 56.72%, were concluded to be the optimal relative proportion of methionine for nitrogen retention and plasma urea nitrogen responses, respectively. Due to the influence of added crystalline cystine on plasma urea nitrogen, the value 54.15% estimated by nitrogen retention assay, was considered to be the more reasonable result.

REFERENCES

AOAC. 1995. Official Methods of Analysis, 16th ed. Association of Official Analysis Chemists, Washington, DC.

Cai, Y. J., R. C. Ewan and D. R. Zimmerman. 1992. Effects of dietary energy, protein and potassium levels on plasma urea nitrogen and free amino acids in finishing pigs. J. Anim. Sci. 70(Suppl. 1):236(Abstr.).

Chung, T. K. and D. H. Baker. 1992. Maximal portion of the young pig's sulfur amino acid requirement that can be furnished by cystine. J. Anim. Sci. 70:1182-1187.

Coma, J., D. Carrion and D. R. Zimmerman. 1995a. Use of plasma urea nitrogen as a rapid response criterion to determine the lysine requirement of pigs. J. Anim. Sci. 73:472-481.

Coma, J., D. R. Zimmerman and D. Carrion. 1995b. Relationship of rate of lean tissue growth and other factors to concentration of urea in plasma of pigs. J. Anim. Sci. 73: 3649-3656.

De Lange, C. F. M., A. M. Gillis and G. J. Simpson. 2001. Influence of threonine intake on whole-body protein deposition and threonine utilization in growing pigs fed purified diets. J. Anim. Sci. 79:3087-3095.

Fuller, M. F., R. McWilliam, T. C. Wang and L. R. Giles. 1989. The optimum dietary amino acid pattern for growing pigs. 2. Requirements for maintenance and for tissue protein accretion. Br. J. Nutr. 64:255-267.

Honeyfield, D. C., J. A. Froseth and R. J. Barke. 1985. Dietary sodium and chloride levels for growing-finishing pigs. J. Anim. Sci. 60:691-698.

Kerschner, L. and J. Ziegenhorn. 1985. Urea. In: Methods in Enzymatic Analysis. 3rd edn. (Ed. H. U. Bergmeyer). Vol. 8, Verlag Chemie, Weinheim, pp. 444-453.

Lewis, A. J. 2003. Methionine-cystine relationships in pig nutrition. In: Amino Acids in Animal Nutrition., 2nd edn. (Ed. J. P. F. D'Mello) vol. 8, CAB International, Wallingford, UK pp. 143-155.

Mahan, D. C. and R. G. Jr. Shields. 1998. Essential and nonessential amino acid composition of pigs from birth to 145 kilograms of body weight, and comparison to other studies. J. Anim. Sci. 76:513-521.

Möhn, S., A. M. Gillis, P. J. Moughan and C. F. M. de Lange. 2000. Influence of dietary lysine and energy intakes on body protein deposition and lysine utilization in the growing pig. J. Anim. Sci. 78:1510-1519.

NRC. 1998. Nutrient Requirements of Swine, 10th ed. National Academic Press, Washington, DC.

Reijmers, A. T. H., A. M. Gillis and C. F. M. de Lang. 2002. Optimum dietary methionine to methionine+cystine ratio for growing pigs. In: Amino Acids in Animal Nutrition (Ed. M. Pack, J. Ficklen, M. Rademachen, A. Lemme, S. Mack, D. Hohlen, J. Fonlaine and A. Petoi), CORAL SANIVET, Bucharest pp. 453-457.

Robbins, K. B., H. W. Norton and D. H. Baker. 1979. Estimation of nutrient requirements from growth data. J. Nutr. 109:1710-1714.

Roth, F. X. and M. Kirchgesser. 1989. Influence of the methionine:cysteine relationship in the feed on the performance of growing pigs. J. Anim. Physiol. Anim. Nutr. 61:265-274.

Russell, L. E., G. L. Cromwell and T. S. Stahly. 1983. Tryptophan, threonine, isoleucine and methionine supplementation of a 12% protein, lysine-supplemented, corn-soybean meal diet for growing pigs. J. Anim. Sci. 56:1115-1123.

SAS. 2002. SAS/STAT at User's Guide (Release 9.2.0.1.0 Ed.). SAS Inst. Inc., Cary, NC.

Schutte, J. B., M. W. Bosch, J. de Jong, E. J. van Weerden and F. Koch. 1991. Factors affecting the requirement of dietary sulphur-containing amino acids of young pigs. Netherland J. Agric. Sci. 39:91-101.

Slagle, S. P. and D. R. Zimmerman. 1979. Evaluation of a yeast single cell protein with young pigs. J. Anim. Sci. 49:1252-1260.

Van Kleef, D. J., K. Deuring and P. van Leeuwen. 1994. A new method of faeces collection in the pig. Lab. Anim. 28:78-79.

Wang, T. C. and M. F. Fuller. 1989. The optimum dietary amino acid pattern for growing pigs. 1. Experiments by amino acid deletion. Br. J. Nutr. 62:77-89.

Welbourne, T. C., V. Phromphetcharat, G. Givens and S. Joshi. 1986. Regulation of interorganal glutamine flow in metabolic acidosis. Am. J. Physiol. 250(4 Pt 1):E457-E463.

Yang, C. J., D. W. Lee, I. B. Chung, Y. M. Cho, I. S. Shin, B. J. Chae, J. H. Kim and In K. Han. 1997. Developing model equation to subdivide methionine+cystine requirements into requirement for growth and maintenance in pigs. Asian-Aust. J. Anim. Sci. 10(1):86-97.

Zimmermann, B., R. Mosenthin, M. Rademacher, P. B. Lynch and E. Esteve-Garcia. 2005. Comparative studies on the relative efficacy of DL-methionine and liquid mechionine hydroxy analogue in growing pigs. Asian-Aust. J. Anim. Sci. 18(7):1003-1010.

NUTRITION RESEARCH, Vol. 11, pp. 355-363,1991
0271-5317/91 $3.00 + .00 Printed in the USA.

DIETARY CYSTEINE/METHIONINE RATIOS AND TAURINE SUPPLEMENTATION: EFFECTS ON RAT GROWTH, AMINO ACIDS AND BILE ACIDS

G. Sarwar, Ph.D., R.W. Peace, M.Sc and H.G. Botting
Bureau of Nutritional Sciences, Food Directorate,
Health Protection Branch, Health and Welfare Canada
Tunney's Pasture, Ottawa, Ontario, Canada K1A 0L2

ABSTRACT

Diets containing 15% protein (casein plus arginine, threonine and tryptophan), 20% fat (soybean-coconut oil) and adequate amounts of minerals and vitamins were supplemented with methionine and/or cysteine to provide cysteine/methionine ratios of 0.2, 1.0 and 2.0 simulating those in various dietary proteins, human milk and infant formulas. The dietary cysteine/methionine ratios had significant ($P < 0.05$) effects on 2-wk weight gain and levels of blood serum urea nitrogen (BUN) and taurine-conjugated bile acids in bile of weanling rats, indicating an inferior nutritional quality of the low cysteine/methionine diet (0.2) compared to the medium (1.0) or high (2.0) cysteine/methionine diet. Taurine supplementation increased levels of taurine in liver, serum and urine of rats fed all three cysteine/methionine diets. Taurine supplementation also increased levels of taurine-conjugated bile acids in the bile of rats fed the low cysteine/methionine diet but produced fatty livers in those fed the high cysteine/methionine diet.

KEY WORDS: cysteine/methionine ratio, taurine supplementation, rat growth, protein quality, bile acids, fatty livers

B4

B4

B4

B4

B4

B4

B4

B4

B4

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Jones, Jennifer L
Sent: 3/23/2019 3:42:44 PM
Subject: Cobalt

Hi Jen,
In the Feb, 2019 Vet-LIRN report, it states that cobalt was tested in the diets and was within normal nutrient ranges recommended by AAFCO. B5

B5

Thanks,
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Board Certified Veterinary Nutritionist™
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: 'Andrea Fascetti'
Sent: 9/18/2018 11:23:41 AM
Subject: control dog Taurine-urine

Good morning Andrea,

B5, B6

Thank you for the collaborative opportunity!

B6

Take care,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From:	Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To:	Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David
Sent:	12/4/2018 10:01:57 PM
Subject:	DCM 12/4/2018 1656
Attachments:	Acana Lamb and Apple singles: Lisa Freeman - EON-372606; Blue Buffalo Wilderness Large Breed Grain free dry: Lisa Freeman - EON-372652; Loyall Professional All Life Stages dry: Lisa Freeman - EON-372653; Rachel Ray Nutrish Zero Grain: B6 - EON-372718

Not as many reports.. **B5**

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/3/2018 2:36:39 PM

Subject: Acana Lamb and Apple singles: Lisa Freeman - EON-372606

Attachments: 2059540-report.pdf; 2059540-attachments.zip

A PFR Report has been received and PFR Event [EON-372606] has been created in the EON System.

A "PDF" report by name "2059540-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2059540-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-372606
ICSR #: 2059540
EON Title: PFR Event created for Acana Lamb and Apple singles; 2059540

AE Date	11/08/2018	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Irish Wolfhound		
Age	3 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2059540
Product Group: Pet Food
Product Name: Acana Lamb and Apple singles
Description: Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable

Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Acana Lamb and Apple singles		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6
USA

To view this PFR Event, please click the link below:
B6

To view the PFR Event Report, please click the link below:
B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-372606

ICSR:	2059540		
Type Of Submission:	Initial		
Report Version:	FPSR.FDA.PETF.V.V1		
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)		
Reporting Type:	Voluntary		
Report Submission Date:	2018-12-03 09:27:13 EST		
Reported Problem:	**Problem Description:**	Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months	
	Date Problem Started:	11/08/2018	
	Concurrent Medical Problem:	Yes	
	Pre Existing Conditions:	Chronic diarrhea Hx of anaplasmosis	
	Outcome to Date:	Stable	
Product Information:	**Product Name:**	Acana Lamb and Apple singles	
	Product Type:	Pet Food	
	Lot Number:		
	Package Type:	BAG	
	Product Use Information:	**Description:**	Fed since 2016
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
Animal Information:	**Name:**	**B6**	
	Type Of Species:	Dog	
	Type Of Breed:	Irish Wolfhound	
	Gender:	Male	
	Reproductive Status:	Intact	
	Weight:	82.7 Kilogram	
	Age:	3 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:	**Owner Information provided:**	Yes
		Contact:	**Name:** **B6**
			Phone:
			Email:
		Address:	**B6** United States
	Healthcare Professional Information:	**Practice Name:**	Tufts Cummings School of Veterinary Medicine
		Contact:	**Name:** Lisa Freeman
			Phone: (508) 887-4523

		Email:	lisa.freeman@tufts.edu
		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States

Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	

Additional Documents:		
	Attachment:	**B6** compiled records.pdf
	Description:	Medical records
	Type:	Medical Records

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/3/2018 7:48:38 PM

Subject: Blue Buffalo Wilderness Large Breed Grain free dry: Lisa Freeman - EON-372652

Attachments: 2059566-report.pdf; 2059566-attachments.zip

A PFR Report has been received and PFR Event [EON-372652] has been created in the EON System.

A "PDF" report by name "2059566-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2059566-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-372652
ICSR #: 2059566
EON Title: PFR Event created for Blue Buffalo Wilderness Large Breed Grain free dry; 2059566

AE Date	09/18/2018	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Great Dane		
Age	6 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2059566
Product Group: Pet Food
Product Name: Blue Buffalo Wilderness Large Breed Grain free dry
Description: Evaluated for exercise intolerance; identified ventricular arrhythmia and mildly reduced contractile function. Plasma taurine 174 (WB not evaluated). We will be rechecking dog in a 3-4 months. Was eating BEG diet (Blue Buffalo) at time of diagnosis then switched to Fromm Lg Breed after diagnosis but now transitioning to Pro Plan Weight Management
Submission Type: Initial

Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Blue Buffalo Wilderness Large Breed Grain free dry		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6
USA

To view this PFR Event, please click the link below:
B6

To view the PFR Event Report, please click the link below:
B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-372652

ICSR:	2059566	
Type Of Submission:	Initial	
Report Version:	FPSR.FDA.PETF.V.V1	
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)	
Reporting Type:	Voluntary	
Report Submission Date:	2018-12-03 14:40:10 EST	
Reported Problem:	**Problem Description:**	Evaluated for exercise intolerance; identified ventricular arrhythmia and mildly reduced contractile function. Plasma taurine 174 (WB not evaluated). We will be rechecking dog in a 3-4 months. Was eating BEG diet (Blue Buffalo) at time of diagnosis then switched to Fromm Lg Breed after diagnosis but now transitioning to Pro Plan Weight Management
	Date Problem Started:	09/18/2018
	Concurrent Medical Problem:	No
	Outcome to Date:	Stable
Product Information:	**Product Name:**	Blue Buffalo Wilderness Large Breed Grain free dry
	Product Type:	Pet Food
	Lot Number:	
	Package Type:	BAG
	Product Use Information:	
	Manufacturer /Distributor Information:	
	Purchase Location Information:	
Animal Information:	**Name:**	B6
	Type Of Species:	Dog
	Type Of Breed:	Great Dane
	Gender:	Male
	Reproductive Status:	Neutered
	Weight:	97.8 Kilogram
	Age:	6 Years
	Assessment of Prior Health:	Excellent
	Number of Animals Given the Product:	1
	Number of Animals Reacted:	1
	Owner Information:	**Owner Information provided:** Yes
		Contact: **Name:** B6
		Phone:
		Email:
		Address: B6
		United States
	Healthcare Professional Information:	**Practice Name:** Tufts Cummings School of Veterinary Medicine
		Contact: **Name:** Lisa Freeman
		Phone: (508) 887-4523

		Email:	lisa.freeman@tufts.edu
		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States

Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	

Additional Documents:		
	Attachment:	records B6 pdf
	Description:	Records
	Type:	Medical Records

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

All Medical Records

Client:
Address: B6

Patient: B6
Breed: Great Dane
DOB: B6

Species: Canine
Sex: Male (Neutered)

Home Phone:
Work Phone:
Cell Phone: B6

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Emergency

SOAP Text B6 **8:22PM -** B6

B6 is a 6 y/o MN Great Dane presenting for a history of exercise intolerance and labored breathing over 6 months that has worsened in the last week.

Subjective
NEW VISIT (ER)

Doctor: B6
Presenting complaint: labored breathing/exercise intolerance for past 6 months, worse for 1 week
Referral visit? no
Diagnostics completed prior to visit

HISTORY:

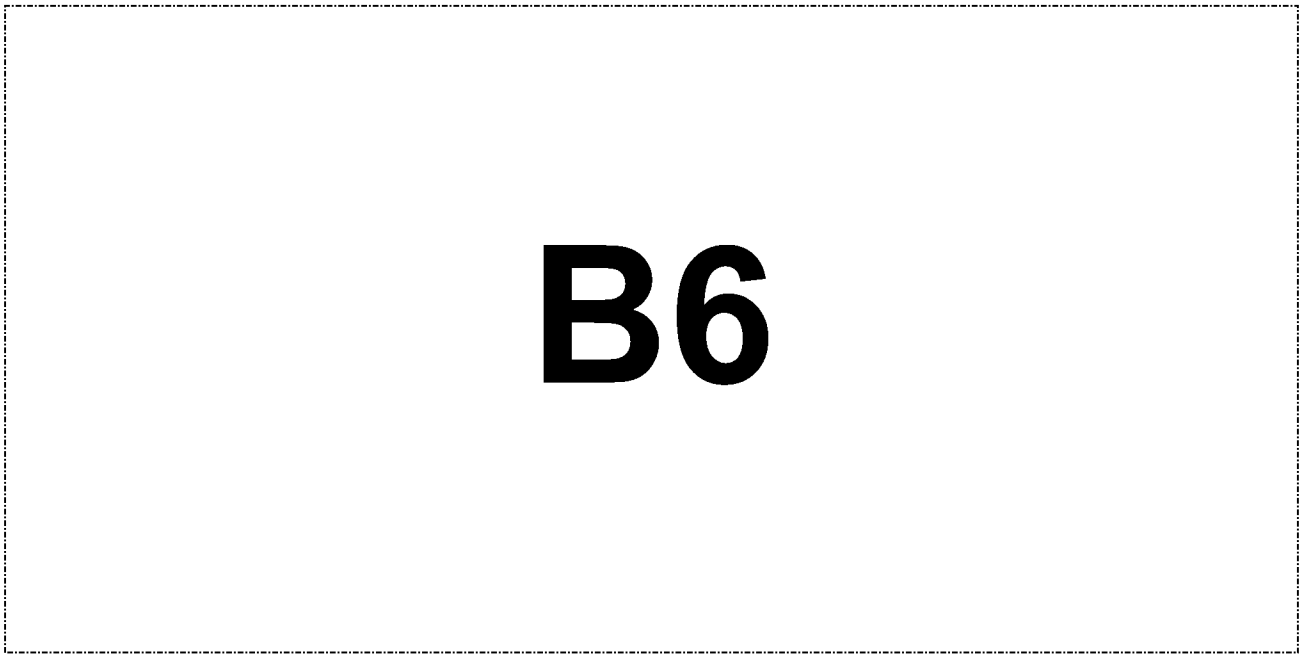
Signalment: 6 yo MN Great Dane
Current history: For about a week, O started noticing labored breathing and dog seemed uncomfortable and restless. O concerned that he doesnt seem like himself, restless at night, slowed down. Exercise intolerance since spring (gradually) and got much worse past 1 week. O concerned with how he is exhaling. More discharge from his nose. O believes he has some muscle wasting. O indicated that they called cardio liason who indicated to bring him to ER and will be transfered to cardiology. No v/d/c/s. Eating/drinking normally. Urinating/defecating normally.

Prior medical history: Gastroplexy surgery when he was 18 months; Doesn't clot well according to owner

Client: B6
Patient:

Current medications: no meds
Diet: Blue Wilderness Giant breed - 2 cups twice a day, then 1 cup of chicken twice a day
Vaccination status/flea & tick preventative use: UTD on vaccines, Ivermectin
Travel history: None

EXAM:



ASSESSMENT:
A1: exercise intolerance/labored breathing r/o cardiac disease (DCM vs other) vs primary respiratory disease

PLAN:

Diagnostics completed:
Big 4: lac 1.0, gluc 102, PCV/TS 55%/8.0
TFAST: difficult to assess heart due to deep chest, no obvious B lines

Diagnostics pending:

Client communication:

Client: B6
Patient:

B6

SOAP approved (DVM to sign): B6

SOAP Text B6 **8:13AM** - B6

B6 is a 6 y/o MN Great Dane presenting for a history of exercise intolerance and labored breathing over 6 months that has worsened in the last week.

Subjective

Exam, cardiology

B6

Overall impression since arrival or since last exam: Seems stable since last exam on arrival, possibly mildly dehydrated but was not on arrival.

B6

Client: B6
Patient:

B6

SOAP completed by: B6
SOAP reviewed by: B6

Initial Complaint:
Recheck - B6

Disposition/Recommendations

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Great Dane
Sex:	Male (Neutered)
Age:	B6 ears Old

Lab Results Report

CBC, Comprehensive, Sm Animal B6 9:50:13 PM B6

Test	Results	Reference Range	Units
WBC (ADVIA)	B6	4.4 - 15.1	K/uL
RBC(ADVIA)		5.8 - 8.5	M/uL
HGB(ADVIA)		13.3 - 20.5	g/dL
HCT(ADVIA)		39 - 55	%
MCV(ADVIA)		64.5 - 77.5	fL
MCH(ADVIA)		21.3 - 25.9	pg
MCHC(ADVIA)		31.9 - 34.3	g/dL
RDW (ADVIA)		11.9 - 15.2	
PLT(ADVIA)		173 - 486	K/uL
MPV (ADVIA)		8.29 - 13.2	fl
PLTCRT		0.129 - 0.403	%
RETIC(ADVIA)		0.2 - 1.6	%
RETICS (ABS) ADVIA		14.7 - 113.7	K/uL
COMMENTS (HEMATOLOGY)		0 - 0	

CBC, Comprehensive, Sm Animal B6 9:50:27 PM B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL

MAGNESIUM 2+		1.8 - 3	mEq/L
T. PROTEIN		5.5 - 7.8	g/dL
ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
POTASSIUM		3.7 - 5.4	mEq/L
tCO2 (BICARB)		14 - 28	mEq/L
AGAP	B6	8 - 19	
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
D.BILIRUBIN		0 - 0.1	mg/dL
I BILIRUBIN		0 - 0.2	mg/dL
ALK PHOS		12 - 127	U/L
GGT		0 - 10	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CK		22 - 422	U/L
CHOLESTEROL		82 - 355	mg/dL
TRIGLYCERIDES		30 - 338	mg/dl
AMYLASE		409 - 1250	U/L
OSMOLALITY (CALCULATED)		291 - 315	mmol/L

CBC, Comprehensive, Sm Animal B6 9:50:10 PM B6

Test	Results	Reference Range	Units
SEGS%		43 - 86	%
LYMPHS%		7 - 47	%
MONOS%		1 - 15	%
EOS%		0 - 16	%
NRBC	B6	0 - 1	/100 WBC
SEGS (AB)ADVIA		2.8 - 11.5	K/ul
LYMPHS (ABS)ADVIA		1 - 4.8	K/uL
MONOS (ABS)ADVIA		0.1 - 1.5	K/uL
EOS (ABS)ADVIA		0 - 1.4	K/uL
WBC MORPHOLOGY		0 - 0	
No Morphologic Abnormalities			
POIKILOCYTOSIS		0 - 0	

CBC, Comprehensive, Sm Animal B6 10:44:58 PM B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dL

Client:
Patient: B6

Lactate (FHSA) *	B6	0 - 0	mmol/L
BG (FHSA)		0 - 0	g/dL
TS (FHSA)		0 - 0	g/dL
PCV		0 - 0	%

CBC, Comprehensive, Sm Animal B6 **12:45:25 PM** B6

Test	Results	Reference Range	Units
SO2%		94 - 100	%
HCT (POC)		38 - 48	%
HB (POC)		12.6 - 16	g/dL
NA (POC)		140 - 154	mmol/L
K (POC)		3.6 - 4.8	mmol/L
CL(POC)		109 - 120	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
MG (POC)		0.1 - 0.4	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
CREAT (POC)		0.2 - 2.1	mg/dL
TCO2 (POC)	B6	0 - 0	mmol/L
nCA		0 - 0	mmol/L
nMG		0 - 0	mmol/L
GAP		0 - 0	mmol/L
CA/MG		0 - 0	mol/mol
BEecf		0 - 0	mmol/L
BEb		0 - 0	mmol/L
Λ		0 - 0	mmHg
NOVA SAMPLE		0 - 0	
FiO2		0 - 0	%
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

CBC, Comprehensive, Sm Animal B6 **12:45:00 PM** B6

Test	Results	Reference Range	Units
TAURINE P	B6	60 - 120	nmol/mL

B6

Sample Submission Form

B6

UNIVERSITY OF CALIFORNIA, DAVIS

B6

Lab Results University of California Amino Acid Lab B6

B6

B6

UCDAVIS VETERINARY MEDICINE

CARDIOLOGY SERVICE UPDATES: DOG FOOD & DILATED CARDIOMYOPATHY

B6

Client:
Patient: B6

Vitals Results

	9:53:54 PM	Notes
	11:12:57 PM	Respiratory Rate
	11:13:23 PM	Eliminations
	11:16:17 PM	Amount eaten
	11:16:39 PM	Heart Rate (/min)
	2:31:29 AM	Cardiac rhythm
	2:31:30 AM	Heart Rate (/min)
	2:33:04 AM	Lasix treatment note
	4:06:19 AM	Cardiac rhythm
	4:06:20 AM	Heart Rate (/min)
	4:06:34 AM	Respiratory Rate
	4:59:57 AM	Cardiac rhythm
	4:59:58 AM	Heart Rate (/min)
	5:44:28 AM	Eliminations
	5:50:00 AM	Cardiac rhythm
	5:50:01 AM	Heart Rate (/min)
	6:36:32 AM	Cardiac rhythm
	6:36:33 AM	Heart Rate (/min)
	7:50:51 AM	Cardiac rhythm
B6	7:50:52 AM	Heart Rate (/min)
	8:02:12 AM	Temperature (F)
	8:02:28 AM	Weight (kg)
	8:02:40 AM	Respiratory Rate
	8:02:54 AM	Amount eaten
	8:13:29 AM	Weight (kg)
	8:13:30 AM	Respiratory Rate
	8:13:31 AM	Heart Rate (/min)
	8:13:32 AM	Temperature (F)
	8:13:33 AM	Body Condition Score (BCS)
	8:13:34 AM	Muscle Condition Score (MCS)
	8:13:35 AM	Pain assessment
	8:58:16 AM	Cardiac rhythm
	8:58:17 AM	Heart Rate (/min)
	9:33:17 AM	Cardiac rhythm
	9:33:18 AM	Heart Rate (/min)
	11:50:48 AM	Cardiac rhythm
	11:50:49 AM	Heart Rate (/min)
	11:52:18 AM	Heart Rate (/min)
	11:52:29 AM	Respiratory Rate

B6

Client:
Patient: B6

Vitals Results

B6

1:53:50 AM	Amount eaten	
:31:04 PM	Cardiac rhythm	
:31:05 PM	Heart Rate (/min)	
:27:13 PM	Eliminations	
:27:24 PM	Cardiac rhythm	
:27:25 PM	Heart Rate (/min)	
:28:19 PM	Respiratory Rate	
:37:13 PM	Quantify IV fluids (mls)	
:37:14 PM	Catheter Assessment	
:14:37 PM	Cardiac rhythm	
:14:38 PM	Heart Rate (/min)	
:42:51 PM	Heart Rate (/min)	
:42:59 PM	Cardiac rhythm	
:43:00 PM	Heart Rate (/min)	
1:02:07 PM	Weight (kg)	

B6

ECG from cardio

ECG from cardio

ECG from Cardio

Client: B6
Patient:

ECG from Cardio

ECG from Cardio

Client: B6
Patient:

Patient History

B6

06:52 PM	UserForm
06:53 PM	UserForm
08:43 PM	UserForm
09:49 PM	Purchase
09:49 PM	Purchase
09:53 PM	Purchase
09:53 PM	Vitals
09:54 PM	Purchase
10:45 PM	Labwork
10:47 PM	Purchase
10:47 PM	Purchase
11:07 PM	Treatment
11:12 PM	Treatment
11:12 PM	Vitals
11:13 PM	Treatment
11:13 PM	Vitals
11:16 PM	Treatment
11:16 PM	Vitals
11:16 PM	Treatment
11:16 PM	Treatment
11:16 PM	Vitals
02:31 AM	Treatment
02:31 AM	Vitals
02:31 AM	Vitals
02:33 AM	Vitals
02:33 AM	Treatment
04:06 AM	Treatment
04:06 AM	Vitals
04:06 AM	Vitals
04:06 AM	Treatment
04:06 AM	Vitals
04:59 AM	Treatment
04:59 AM	Vitals
04:59 AM	Vitals
05:44 AM	Treatment
05:44 AM	Vitals
05:50 AM	Treatment
05:50 AM	Vitals
05:50 AM	Vitals
06:36 AM	Treatment

B6

Client: B6
Patient:

Patient History

	06:36 AM	Vitals
	06:36 AM	Vitals
	07:50 AM	Treatment
	07:50 AM	Vitals
	07:50 AM	Vitals
	07:50 AM	Vitals
	07:51 AM	Treatment
	08:02 AM	Treatment
	08:02 AM	Vitals
	08:02 AM	Treatment
	08:02 AM	Vitals
	08:02 AM	Treatment
	08:02 AM	Vitals
	08:02 AM	Treatment
	08:02 AM	Vitals
	08:02 AM	Vitals
	08:12 AM	Purchase
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:13 AM	Vitals
	08:58 AM	Treatment
	08:58 AM	Vitals
	08:58 AM	Vitals
	09:33 AM	Treatment
	09:33 AM	Vitals
	09:33 AM	Vitals
	09:35 AM	UserForm
	09:35 AM	Purchase
	09:36 AM	Purchase
	10:00 AM	Treatment
	10:08 AM	Purchase
	10:42 AM	Purchase
	10:51 AM	Purchase
	11:16 AM	Prescription
	11:50 AM	Treatment
	11:50 AM	Vitals

B6

B6

Client: B6
Patient:

Patient History

B6

11:50 AM	Vitals
11:52 AM	Treatment
11:52 AM	Treatment
11:52 AM	Vitals
11:52 AM	Treatment
11:52 AM	Vitals
11:53 AM	Treatment
11:53 AM	Vitals
12:30 PM	Treatment
12:39 PM	Purchase
12:40 PM	Purchase
12:40 PM	Purchase
12:46 PM	Purchase
12:58 PM	UserForm
01:04 PM	Treatment
01:04 PM	Treatment
01:31 PM	Treatment
01:31 PM	Vitals
01:31 PM	Vitals
01:58 PM	Purchase
01:59 PM	Treatment
03:27 PM	Treatment
03:27 PM	Vitals
03:27 PM	Treatment
03:27 PM	Vitals
03:27 PM	Vitals
03:27 PM	Treatment
03:28 PM	Treatment
03:28 PM	Vitals
03:37 PM	Treatment
03:37 PM	Vitals
03:37 PM	Vitals
04:14 PM	Treatment
04:14 PM	Vitals
04:14 PM	Vitals
05:20 PM	UserForm
05:42 PM	Treatment
05:42 PM	Vitals
05:42 PM	Treatment
05:42 PM	Vitals

B6

Client: B6
Patient:

Patient History

B6

05:42 PM	Vitals
06:29 PM	Prescription
06:31 PM	Purchase
07:50 AM	Deleted Reason
07:50 AM	Deleted Reason
09:38 AM	Appointment
04:05 PM	Appointment
11:58 AM	UserForm
12:10 PM	Treatment
12:25 PM	UserForm
12:31 PM	Purchase
12:48 PM	Purchase
01:02 PM	Vitals
01:07 PM	Prescription
01:13 PM	Purchase
01:51 PM	Email
02:07 PM	Appointment

B6

Appears this way on original

Appears this way on original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Notice of Patient Admit

Date: B6 5:43:39 PM

B6

B6

Dear B6

B6

Thank you for your referral to our Emergency Service.

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/3/2018 7:49:11 PM

Subject: Loyall Professional All Life Stages dry: Lisa Freeman - EON-372653

Attachments: 2059567-report.pdf; 2059567-attachments.zip

A PFR Report has been received and PFR Event [EON-372653] has been created in the EON System.

A "PDF" report by name "2059567-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2059567-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-372653
ICSR #: 2059567
EON Title: PFR Event created for Loyall Professional All Life Stages dry; 2059567

AE Date	11/20/2018	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Pointing Dog - German Short-haired		
Age	10.5 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2059567
Product Group: Pet Food
Product Name: Loyall Professional All Life Stages dry
Description: Collapsing episodes began soon before diagnosis DCM and CHF diagnosed. Taurine pending One other dog in household that we will evaluate soon (asymptomatic)
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 2

Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Loyall Professional All Life Stages dry		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6
USA

To view this PFR Event, please click the link below:
B6

To view the PFR Event Report, please click the link below:
B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-372653

ICSR:	2059567		
Type Of Submission:	Initial		
Report Version:	FPSR.FDA.PETF.V.V1		
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)		
Reporting Type:	Voluntary		
Report Submission Date:	2018-12-03 14:40:53 EST		
Reported Problem:	**Problem Description:**	Collapsing episodes began soon before diagnosis DCM and CHF diagnosed. Taurine pending One other dog in household that we will evaluate soon (asymptomatic)	
	Date Problem Started:	11/20/2018	
	Concurrent Medical Problem:	No	
	Outcome to Date:	Stable	
Product Information:	**Product Name:**	Loyall Professional All Life Stages dry	
	Product Type:	Pet Food	
	Lot Number:		
	Package Type:	BAG	
	Product Use Information:	**Description:**	Fed since May 2018 Before that, fed Native Food Performance dry for many years
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
Animal Information:	**Name:**	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Pointing Dog - German Short-haired	
	Gender:	Male	
	Reproductive Status:	Intact	
	Weight:	26.7 Kilogram	
	Age:	B6 Years	
	Assessment of Prior Health:	Excellent	
	Number of Animals Given the Product:	2	
	Number of Animals Reacted:	1	
	Owner Information:	**Owner Information provided:**	Yes
		Contact:	**Name:** B6
			Phone:
			Email:
		Address:	B6 United States
	Healthcare Professional Information:	**Practice Name:**	Tufts Cummings School of Veterinary Medicine
		Contact:	**Name:** Lisa Freeman
			Phone: (508) 887-4523
			Email: lisa.freeman@tufts.edu

		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States
Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
Additional Documents:			
	Attachment:	compiled medical record **B6** pdf	
	Description:	Medical records	
	Type:	Medical Records	

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

All Medical Records

Client:
Address: B6

Patient: B6
Breed: German Shorthair Pointer
DOB: B6

Species: Canine
Sex: Male

Home Phone:
Work Phone:
Cell Phone: B6

Referring Information

B6

Initial Complaint:

Initial Complaint:
cut on paw, recheck stiches done in B6

SOAP Text Nov 3 2014 1:23PM B6

11-3-14

B6 is a 6.5 yo intact German Short haired Pointer. He was hunting in B6 10 days ago and came up lame and bleeding on his front left leg. He was taken to a local vet who did a laceration repair. He had internal sutures and skin staples. The owner is hear today for staple removal. B6 has pulled out about half of the staples already.

S: BAR-H

B6

Client: B6
Patient:

B6

Initial Complaint:
Emergency

SOAP Text B6 **8:35AM - Clinician, Unassigned FHSA**

Subjective
NEW VISIT (ER)

Doctor: B6
Student: B6
Presenting complaint: Collapsing episodes
Referral visit? N
Diagnostics completed prior to visit

HISTORY:

Signalment: 10 yo Intact German Shorthair Pointer

Current history:
Between Nov 1-12 was in B6 and B6 hunting. 10-12th wasn't hunting but still in B6 Had a lot of exercise with no issues noted. Evening of the 7th and 8th were cold (in the teens) - was in a dog trailer with six compartments. Morning of the 9th he seemed a little bit stiff and had less interest in breakfeast but ultimately ate a small amount (unusual for him). On the evening of the 13th, back legs folded under him and he collapsed onto his side in the kitchen (hardwood floor). Didn't cry, just laid there. Was eventually put on his feet by the owner and walked fine. Next night, same thing happened. Took to rDVM on Wednesday (came back with a little bit of a cough after hunting trip) - placed on doxycycline at rDVM. Owner gone 15-18th so dog walker watched at home - was in crate or on carpeted floor the whole time - no exercise/long walks. Sunday night he collapsed again - seemed like his back legs gave out. This morning O's younger dog bumped into him and he fell down again. Owner put on his feet but patient was unable to stand, tried this several times, eventually was able to stand after 2-3 minutes. Later ate his whole meal. Came straight here. O notes collapsing primarily occurs in evenings apart from this AM but is not associated with anything. Was able to jump into truck to get here. No crying, doesn't seem to be in pain. No V/D/S. Little bit of a cough. His breathing has seemed a little ragid to owner recently.

B6

EXAM:
S: BAR

Client: B6
Patient:

B6

B6

ASSESSMENT:
A1: Collapsing episodes (cardiogenic (DCM vs DMVD) vs neurologic)

PLAN:

B6

Diagnostics completed:
NOVA: Mg 0.5 (H), Lactate 3.3 (H)
AFAST/TFAST: Dilated cardiac compartments, thinned walls, poor contractility, no FF in either cavity, few B lines
EKG-- consistent with A fib
Radiographs: Generalized cardiomegaly, caudodorsal interstitial infiltrates - final report pending
Cardio Consult: Dilated cardiomyopathy, mitral valve degeneration - final report pending

Diagnostics pending:
None

Client communication:

B6

Client: B6
Patient:

B6

SOAP approved (DVM to sign): B6

SOAP Text B6 6:51AM - B6

History:

B6 is a 10 year old male german shorthaired pointer pesenting for recurrent episodes of collapse, mild cough and mild labored breathing starting 11/13.

He was diagnosed with DCM, active CHF, and atrial fibrillation yesterday.

Subjective:

B6

Overall impression since arrival or since last exam: B6 has been noted to be in A-fibb for the entire evening (on every 1 hour telemetry reading). He had occasional VPC's on 11/20 at 10pm. His heart rate has ranged from 119-238 overnight. B6 rcvd 3 doses of furosemide 50mg IV on 11/20/18 at 8am, 4pm and 12am (11/21). He has received diltiazem ER at 12pm on 11/20 and 12am on 11/21. He has had no to mild effort overnight with his respiratory rate ranging from 28-36. He urinated frequently overnight. B6 ate well when offered food overnight.

Appetite: Ate 1 cup of proplan dry and 1/2 can proplan wet at 8pm and then ate 2/4 can chicken and barley SD wet.

Objective:

B6

Diagnostics Completed:

B6

Client: B6
Patient:

AFAST/TFAST: Dilated cardiac compartments, thinned walls, poor contractility, no FF in either cavity, few B lines
Radiographs: Generalized cardiomegaly with LAE, diffuse interstitial infiltrates worse on the right, VHS 13.5, consistent with cardiogenic pulmonary edema.
Echocardiogram: Marked cardiac enlargement, atrial fibrillation, and CHF with CHF and arrhythmia both being potential causes for the collapse episodes. TSignificant MR and reduced contractile function so it is difficult to determine whether the disease process is primary mitral valve disease with reduced LV contractile function associated with being a large breed dog and atrial fibrillation or primary DCM with secondary functional MR.
ECG: Atrial fibrillation with rapid ventricular response rate of 240 bpm, rare isolated VPCs.

Assessments:
A1: DCM and mitral regurgitation - either primary DCM with secondary mitral valve disease or DCM secondary to mitral valve disease
A2: Diffuse pulmonary infiltrates, enlarged cardiac silhouette with LAE, history of cough - pulmonary edema secondary to CHF
A3: Atrial fibrillation with rapid ventricular response rate and occasional VPC's - secondary to DCM
A4: Collapsing episodes r/o secondary to CHF or arrythmia

Plan:

B6

SOAP completed by
SOAP reviewed by: B6

Disposition/Recommendations

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

Client: B6
Veterinarian:
Patient ID: B6
Visit ID:

Patient:	B6
Species:	Canine
Breed:	German Shorthair Pointer
Sex:	Male
Age:	B6 Years Old

Lab Results Report

Nova Full Panel-ICU B6 8:42:25 AM B6

Test	Results	Reference Range	Units
SO2%	B6	94 - 100	%
HCT (POC)		38 - 48	%
HB (POC)		12.6 - 16	g/dL
NA (POC)		140 - 154	mmol/L
K (POC)		3.6 - 4.8	mmol/L
CL(POC)		109 - 120	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
MG (POC)		0.1 - 0.4	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
CREAT (POC)		0.2 - 2.1	mg/dL
TCO2 (POC)		0 - 0	mmol/L
nCA		0 - 0	mmol/L
nMG		0 - 0	mmol/L
GAP		0 - 0	mmol/L
CA/MG		0 - 0	mol/mol
BEecf		0 - 0	mmol/L
BEb		0 - 0	mmol/L
A		0 - 0	mmHg
NOVA SAMPLE		0 - 0	

Client:
Patient: B6

FiO2	B6	0 - 0	%
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

Nova Full Panel-ICU B6 :48:24 AM B6

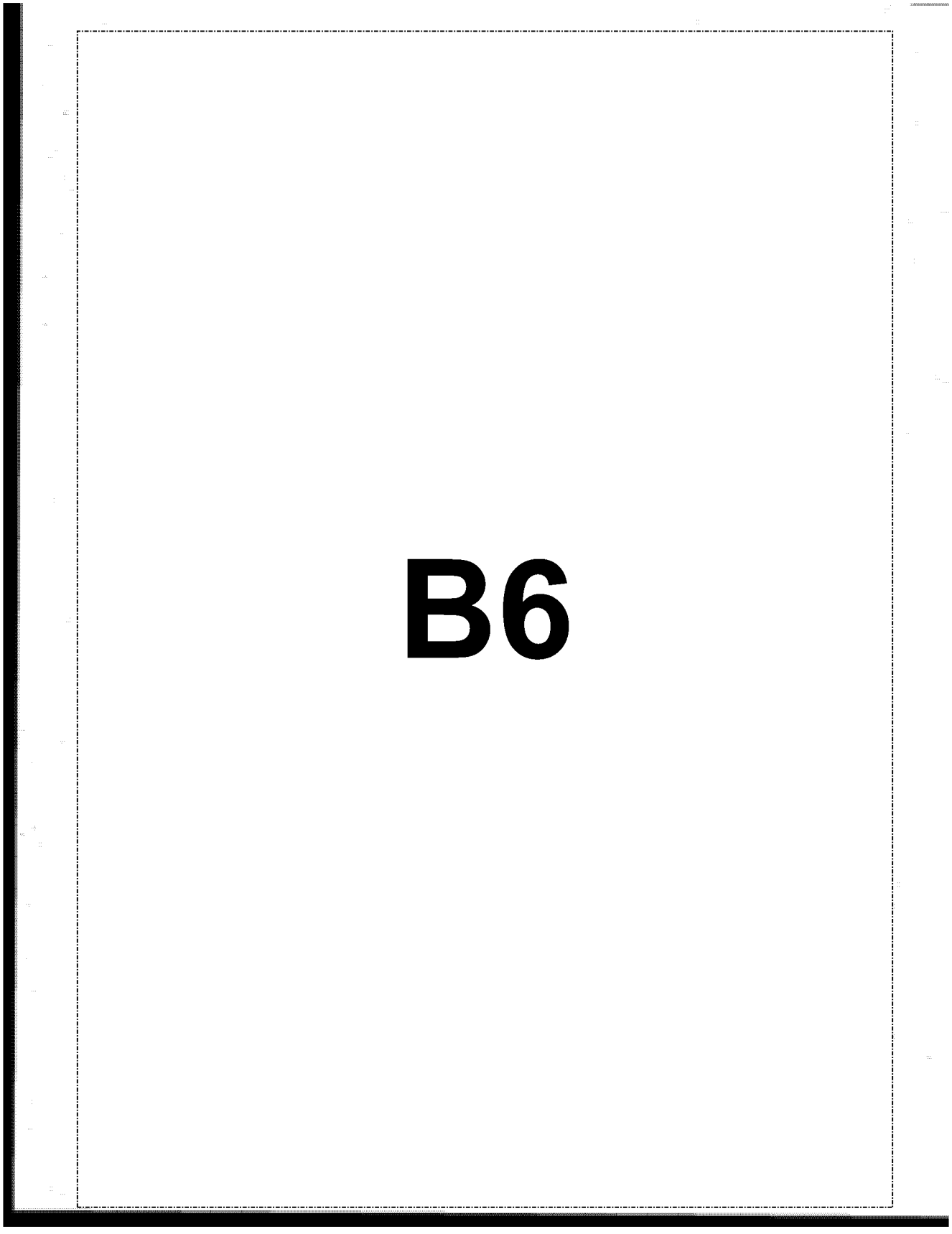
Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

Nova Full Panel-ICU B6 :15:53 PM B6

Test	Results	Reference Range	Units
Troponin I Research - FHSA	B6	0 - 0.08	mg/dl

Nova Full Panel-ICU B6 1:32:21 PM B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
T. PROTEIN		5.5 - 7.8	g/dL
ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
POTASSIUM		3.7 - 5.4	mEq/L
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
D.BILIRUBIN		0 - 0.1	mg/dL
I BILIRUBIN		0 - 0.2	mg/dL
ALK PHOS		12 - 127	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CHOLESTEROL		82 - 355	mg/dL
OSMOLALITY (CALCULATED)		291 - 315	mmol/L
COMMENTS (CHEMISTRY)		0 - 0	
Slight lipemia Slight hemolysis			



B6

B6

B6

B6

B6

B6

IDEXX BNP - 11/21/2018

B6

B6

B6

Client: B6
Patient:

Vitals Results

B6

	9:32:14 AM	Heart Rate (/min)
	9:32:15 AM	Respiratory Rate
	9:32:16 AM	Temperature (F)
	9:32:17 AM	Weight (kg)
	10:43:05 AM	Nursing note
	10:46:20 AM	Cardiac rhythm
	10:46:21 AM	Heart Rate (/min)
	10:46:41 AM	Respiratory Rate
	11:09:38 AM	Cardiac rhythm
	11:09:39 AM	Heart Rate (/min)
	11:36:36 AM	Eliminations
	12:00:19 PM	Cardiac rhythm
	12:00:20 PM	Heart Rate (/min)
	12:01:51 PM	Respiratory Rate
	1:30:26 PM	Cardiac rhythm
	1:30:27 PM	Heart Rate (/min)
	1:30:48 PM	Respiratory Rate
	1:31:11 PM	Cardiac rhythm
	1:31:12 PM	Heart Rate (/min)
	3:34:08 PM	Cardiac rhythm
	3:34:09 PM	Heart Rate (/min)
	4:01:56 PM	Cardiac rhythm
	4:01:57 PM	Heart Rate (/min)
	4:02:06 PM	Respiratory Rate
	4:07:23 PM	Lasix treatment note
	5:13:50 PM	Cardiac rhythm
	5:13:51 PM	Heart Rate (/min)
	5:14:02 PM	Eliminations
	6:10:01 PM	Cardiac rhythm
	6:10:02 PM	Heart Rate (/min)
	6:10:13 PM	Respiratory Rate
	6:33:47 PM	Eliminations
	6:54:42 PM	Cardiac rhythm
	6:54:43 PM	Heart Rate (/min)
	8:22:20 PM	Cardiac rhythm
	8:22:21 PM	Heart Rate (/min)
	8:22:41 PM	Respiratory Rate
	8:26:31 PM	Amount eaten
	8:26:56 PM	Weight (kg)
	8:27:02 PM	Temperature (F)

B6

Client: B6
Patient:

Vitals Results

B6

9:08:09 PM	Cardiac rhythm
9:08:10 PM	Heart Rate (/min)
10:00:15 PM	Cardiac rhythm
10:00:16 PM	Heart Rate (/min)
10:01:20 PM	Respiratory Rate
10:55:05 PM	Cardiac rhythm
10:55:06 PM	Heart Rate (/min)
11:58:52 PM	Cardiac rhythm
11:58:53 PM	Heart Rate (/min)
11:59:28 PM	Respiratory Rate
12:20:21 AM	Eliminations
12:46:44 AM	Lasix treatment note
12:56:50 AM	Cardiac rhythm
12:56:51 AM	Heart Rate (/min)
1:53:38 AM	Cardiac rhythm
1:53:39 AM	Heart Rate (/min)
1:53:55 AM	Respiratory Rate
2:57:07 AM	Cardiac rhythm
2:57:08 AM	Heart Rate (/min)
3:31:02 AM	Eliminations
3:31:21 AM	Amount eaten
3:58:44 AM	Cardiac rhythm
3:58:45 AM	Heart Rate (/min)
3:59:11 AM	Respiratory Rate
4:53:54 AM	Cardiac rhythm
4:53:55 AM	Heart Rate (/min)
6:05:40 AM	Cardiac rhythm
6:05:41 AM	Heart Rate (/min)
6:05:52 AM	Respiratory Rate
6:26:43 AM	Cardiac rhythm
6:26:44 AM	Heart Rate (/min)
7:18:29 AM	Weight (kg)
7:18:38 AM	Temperature (F)
7:18:53 AM	Respiratory Rate
7:22:20 AM	Eliminations
8:29:28 AM	Cardiac rhythm
8:29:29 AM	Heart Rate (/min)
9:05:04 AM	Cardiac rhythm
9:05:05 AM	Heart Rate (/min)
9:46:31 AM	Cardiac rhythm
9:46:32 AM	Heart Rate (/min)

B6

Client:
Patient: B6

Vitals Results

B6

	9:47:40 AM	Respiratory Rate
	10:26:23 AM	Nursing note
	10:31:09 AM	Amount eaten
	10:44:02 AM	Eliminations
	10:46:48 AM	Cardiac rhythm
	10:46:49 AM	Heart Rate (/min)
	10:47:58 AM	Respiratory Rate
	11:51:53 AM	Cardiac rhythm
	11:51:54 AM	Heart Rate (/min)
	11:56:14 AM	Respiratory Rate
	12:59:54 PM	Cardiac rhythm
	12:59:55 PM	Heart Rate (/min)
	1:01:14 PM	Respiratory Rate
	1:03:22 PM	Respiratory Rate
	1:06:27 PM	Eliminations
	1:07:30 PM	Catheter Assessment
	1:48:44 PM	Cardiac rhythm
	1:48:45 PM	Heart Rate (/min)
	3:33:29 PM	Cardiac rhythm
	3:33:30 PM	Heart Rate (/min)
	3:35:21 PM	Respiratory Rate
	3:53:21 PM	Cardiac rhythm
	3:53:22 PM	Heart Rate (/min)
	3:57:55 PM	Respiratory Rate
	4:01:46 PM	Lasix treatment note
	4:08:16 PM	Eliminations
	5:13:51 PM	Eliminations

B6

ECG from Cardio

B6

B6

ECG from Cardio

B6

B6

ECG from Cardio

B6

B6

Patient History

10/29/2014 08:22 AM	Appointment
11/03/2014 01:31 PM	UserForm
11/03/2014 02:06 PM	Purchase
11/19/2018 09:38 AM	Appointment
11/20/2018 08:42 AM	Purchase
11/20/2018 08:48 AM	Labwork
11/20/2018 09:07 AM	UserForm
11/20/2018 09:07 AM	UserForm
11/20/2018 09:16 AM	UserForm
11/20/2018 09:32 AM	Vitals
11/20/2018 09:32 AM	Vitals
11/20/2018 09:32 AM	Vitals
11/20/2018 09:32 AM	Vitals
11/20/2018 09:50 AM	Purchase
11/20/2018 09:50 AM	Purchase
11/20/2018 09:51 AM	Purchase
11/20/2018 09:51 AM	Purchase
11/20/2018 09:51 AM	Purchase
11/20/2018 10:18 AM	Treatment
11/20/2018 10:42 AM	Purchase
11/20/2018 10:42 AM	Treatment
11/20/2018 10:42 AM	Purchase
11/20/2018 10:43 AM	Vitals
11/20/2018 10:46 AM	Treatment
11/20/2018 10:46 AM	Vitals
11/20/2018 10:46 AM	Vitals
11/20/2018 10:46 AM	Treatment
11/20/2018 10:46 AM	Treatment
11/20/2018 10:46 AM	Vitals
11/20/2018 11:09 AM	Treatment
11/20/2018 11:09 AM	Vitals
11/20/2018 11:09 AM	Vitals
11/20/2018 11:36 AM	Treatment
11/20/2018 11:36 AM	Vitals
11/20/2018 11:44 AM	Prescription
11/20/2018 11:59 AM	Prescription
11/20/2018 11:59 AM	Prescription
11/20/2018 12:00 PM	Treatment

B6

Client: B6
Patient:

Patient History

	12:00 PM	Vitals
	12:00 PM	Vitals
	12:01 PM	Treatment
	12:01 PM	Vitals
	12:22 PM	Purchase
	12:22 PM	Purchase
	12:34 PM	Treatment
	12:34 PM	Treatment
	12:35 PM	Treatment
	01:30 PM	Treatment
	01:30 PM	Vitals
	01:30 PM	Vitals
	01:30 PM	Treatment
	01:30 PM	Vitals
	01:31 PM	Treatment
	01:31 PM	Vitals
	01:31 PM	Vitals
	02:16 PM	Treatment
	03:34 PM	Treatment
B6	03:34 PM	Vitals
	03:34 PM	Vitals
	04:01 PM	Treatment
	04:01 PM	Vitals
	04:01 PM	Vitals
	04:02 PM	Treatment
	04:02 PM	Vitals
	04:07 PM	Vitals
	04:07 PM	Treatment
	05:13 PM	Treatment
	05:13 PM	Vitals
	05:13 PM	Vitals
	05:14 PM	Treatment
	05:14 PM	Vitals
	06:10 PM	Treatment
	06:10 PM	Vitals
	06:10 PM	Vitals
	06:10 PM	Treatment
	06:10 PM	Vitals
	06:33 PM	Vitals
	06:54 PM	Treatment
	06:54 PM	Vitals

B6

Client: B6
Patient:

Patient History

B6

06:54 PM	Vitals
08:22 PM	Treatment
08:22 PM	Vitals
08:22 PM	Vitals
08:22 PM	Treatment
08:22 PM	Vitals
08:22 PM	Treatment
08:26 PM	Treatment
08:26 PM	Treatment
08:26 PM	Vitals
08:26 PM	Treatment
08:26 PM	Vitals
08:27 PM	Treatment
08:27 PM	Vitals
09:08 PM	Vitals
09:08 PM	Vitals
09:13 PM	Purchase
09:48 PM	Treatment
10:00 PM	Treatment
10:00 PM	Vitals
10:00 PM	Vitals
10:01 PM	Treatment
10:01 PM	Vitals
10:55 PM	Treatment
10:55 PM	Vitals
10:55 PM	Vitals
11:13 PM	Treatment
11:17 PM	Treatment
11:17 PM	Treatment
11:58 PM	Treatment
11:58 PM	Vitals
11:58 PM	Vitals
11:59 PM	Treatment
11:59 PM	Vitals
12:20 AM	Vitals
12:46 AM	Vitals
12:46 AM	Treatment
12:56 AM	Treatment
12:56 AM	Vitals
12:56 AM	Vitals
01:53 AM	Treatment

B6

Client: B6
Patient:

Patient History

B6

01:53 AM	Vitals
01:53 AM	Vitals
01:53 AM	Treatment
01:53 AM	Vitals
02:57 AM	Treatment
02:57 AM	Vitals
02:57 AM	Vitals
03:16 AM	Treatment
03:30 AM	Treatment
03:31 AM	Treatment
03:31 AM	Vitals
03:31 AM	Treatment
03:31 AM	Vitals
03:58 AM	Treatment
03:58 AM	Vitals
03:58 AM	Vitals
03:59 AM	Treatment
03:59 AM	Vitals
04:53 AM	Treatment
04:53 AM	Vitals
04:53 AM	Vitals
06:05 AM	Treatment
06:05 AM	Vitals
06:05 AM	Vitals
06:05 AM	Treatment
06:05 AM	Vitals
06:26 AM	Treatment
06:26 AM	Vitals
06:26 AM	Vitals
07:12 AM	Treatment
07:18 AM	Treatment
07:18 AM	Vitals
07:18 AM	Treatment
07:18 AM	Vitals
07:18 AM	Treatment
07:18 AM	Vitals
07:22 AM	Vitals
08:29 AM	Treatment
08:29 AM	Vitals
08:29 AM	Vitals
09:05 AM	Treatment

B6

Client:
Patient: B6

Patient History

B6

09:05 AM	Vitals
09:05 AM	Vitals
09:11 AM	Purchase
09:11 AM	Purchase
09:43 AM	Purchase
09:46 AM	Treatment
09:46 AM	Vitals
09:46 AM	Vitals
09:47 AM	Treatment
09:47 AM	Vitals
10:16 AM	Treatment
10:26 AM	Vitals
10:31 AM	Treatment
10:31 AM	Treatment
10:31 AM	Vitals
10:44 AM	Vitals
10:46 AM	Treatment
10:46 AM	Vitals
10:46 AM	Vitals
10:47 AM	Treatment
10:47 AM	Vitals
11:51 AM	Treatment
11:51 AM	Vitals
11:51 AM	Vitals
11:56 AM	Treatment
11:56 AM	Treatment
11:56 AM	Vitals
12:07 PM	UserForm
12:59 PM	Treatment
12:59 PM	Vitals
12:59 PM	Vitals
01:01 PM	Treatment
01:01 PM	Vitals
01:03 PM	Treatment
01:03 PM	Vitals
01:06 PM	Treatment
01:06 PM	Vitals
01:07 PM	Treatment
01:07 PM	Vitals
01:16 PM	Labwork
01:16 PM	Purchase

B6

Client: B6
Patient:

Patient History

B6

1:32 PM	Purchase
1:48 PM	Treatment
1:48 PM	Vitals
1:48 PM	Vitals
3:33 PM	Treatment
3:33 PM	Vitals
3:33 PM	Vitals
3:35 PM	Treatment
3:35 PM	Vitals
3:53 PM	Treatment
3:53 PM	Vitals
3:53 PM	Vitals
3:57 PM	Treatment
3:57 PM	Vitals
4:01 PM	Vitals
4:01 PM	Treatment
4:08 PM	Vitals
4:49 PM	Prescription
4:54 PM	Prescription
4:55 PM	Prescription
4:56 PM	Prescription
5:02 PM	Purchase
5:13 PM	Treatment
5:13 PM	Vitals
6:42 PM	Appointment
0:14 AM	Treatment
0:54 AM	Patient Merge

B6

Appears this Way on Original

Appears this Way on Original

Tufts UNIVERSITY | Cummings School of Veterinary Medicine

Healing Animals. Helping Humans. Transforming Global Health

B6

B6

B6

B6

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

B6

FDA-CVM-FOIA-2019-1704-002453

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/4/2018 3:08:27 PM

Subject: Rachel Ray Nutrish Zero Grain B6 EON-372718

Attachments: 2059592-report.pdf; 2059592-attachments.zip

A PFR Report has been received and PFR Event [EON-372718] has been created in the EON System.

A "PDF" report by name "2059592-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2059592-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-372718
ICSR #: 2059592
EON Title: PFR Event created for Rachel Ray Nutrish Zero Grain; 2059592

AE Date	B6	**Number Fed/Exposed**	3
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Other
Breed	Retriever - Golden		
Age	4 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2059592
Product Group: Pet Food
Product Name: Rachel Ray Nutrish Zero Grain
Description: I was working from home. B6 sleeps next to me while I work. The doorbell rang. B6 jumped up and ran to the window. I got up and looked out the same window to see who it was because we weren't expecting anyone. I didnt know who it was so I did not answer the door. As soon as I said to B6 it's okay...he instantly fell to the ground and had a heart attack. Died in mid air. He was dead before he hit the ground. Devestated, screaming etc. It was horrible. I called 911, called the emergency vet hospital etc. The family came over to say their good byes. When he was taken to the Vet by our town dog service, the director told us she

believes this is due to feeding him GF food. Apparently GF food is fatal to Golden retrievers. It causes widow makers. There is research done on this - not really advertised like it should be and it needs to be on the labels of GF dry dog food that this is potentially harmful to feed golden retrievers. Can be fatal. In our case it was. A perfectly healthy dog. Dead. Our family will never be the same. He was the best dog in the world and he is gone. BECAUSE of GF Food. If it cannot be taken off the shelf then it needs to be on the labels that it can be harmful to golden retrievers and other breeds. It causes dilated cardiomyopathy. It lowers certain levels in the dog and causes heart attacks.
Submission Type: Initial
Report Type: Both
Outcome of reaction/event at the time of last observation: Died Other
Number of Animals Treated With Product: 3
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Rachel Ray Nutrish Zero Grain		

Sender information

B6

USA

B6

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated

through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-372718

ICSR:	2059592
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Both
Reporting Type:	Voluntary
Report Submission Date:	2018-12-04 10:00:58 EST
Reporter is the Animal Owner:	Yes

Reported Problem:

Problem Description:	I was working from home. B6 sleeps next to me while I work. The doorbell rang. B6 jumped up and ran to the window. I got up and looked out the same window to see who it was because we weren't expecting anyone. I didnt know who it was so I did not answer the door. As soon as I said to B6 it's okay...he instantly fell to the ground and had a heart attack. Died in mid air. He was dead before he hit the ground. Devestated, screaming etc. It was horrible. I called 911, called the emergency vet hospital etc. The family came over to say their good byes. When he was taken to the Vet by our town dog service, the director told us she believes this is due to feeding him GF food. Apparently GF food is fatal to Golden retrievers. It causes widow makers. There is research done on this - not really advertised like it should be and it needs to be on the labels of GF dry dog food that this is potentially harmful to feed golden retrievers. Can be fatal. In our case it was. A perfectly healthy dog. Dead. Our family will never be the same. He was the best dog in the world and he is gone. BECAUSE of GF Food. If it cannot be taken off the shelf then it needs to be on the labels that it can be harmful to golden retrievers and other breeds. It causes dilated cardiomyopathy. It lowers certain levels in the dog and causes heart attacks.
Date Problem Started:	B6
Concurrent Medical Problem:	No
Outcome to Date:	Died Other
Date of Death:	B6

Product Information:

Product Name:	Rachel Ray Nutrish Zero Grain
Product Type:	Pet Food
Lot Number:	
Package Type:	BAG
Purchase Date:	08/06/2018
Number Purchased:	1
Possess Unopened Product:	No
Possess Opened Product:	No
Storage Conditions:	Product is stored in a closed container in the cupbaord like a normal person would do for their dog.

Product Use Information:

Description:	My dog ate breakfast and ate dinner each day our of his dog bowl like a normal dog does.
Last Exposure Date:	B6
Time Interval between Product Use and Adverse Event:	4 Years
Product Use Stopped After the Onset of the Adverse Event:	Yes
Adverse Event Abate After Product Stop:	Not Applicable

		Product Use Started Again:	No
		Perceived Relatedness to Adverse Event:	Definitely related
		Other Foods or Products Given to the Animal During This Time Period:	No
	Manufacturer /Distributor Information:		
	Purchase Location Information:	**Name:**	WEGMANS
		Address:	B6 United States
Animal Information:	**Name:**	B6 Golden Retriever	
	Type Of Species:	Dog	
	Type Of Breed:	Retriever - Golden	
	Gender:	Male	
	Reproductive Status:	Neutered	
	Weight:	108 Pound	
	Age:	4 Years	
	Assessment of Prior Health:	Excellent	
	Number of Animals Given the Product:	3	
	Number of Animals Reacted:	1	
	Owner Information:		
	Healthcare Professional Information:	**Practice Name:**	B6
		Contact:	**Name:** **Phone:** **Email:** B6
		Address:	B6 United States
		Type of Veterinarian:	Primary/regular veterinarian
		Date First Seen:	B6
		Permission to Release Records to FDA:	Yes
Sender Information:	**Name:**		
	Address:	B6 United States	
	Contact:	**Phone:** **Email:**	B6

	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Phone
	Reported to Other Parties:	Other
Additional Documents:		

Attachment:	TaurineDef.Goldens.pdf
Description:	GF dry dog food -The condition is linked to a taurine deficiency. The recent cases included Golden and Labrador retrievers 2018 ,
Type:	Investigation Report

Attachment:	FDA Report GF Food linked to retrievers.pdf
Description:	FDA Investigating Potential Connection Between Diet and Cases of Canine Heart Disease
Type:	Investigation Report

July 12, 2018

The U.S. Food and Drug Administration is alerting pet owners and veterinary professionals about reports of canine dilated cardiomyopathy (DCM) in dogs eating certain pet foods containing peas, lentils, other legume seeds, or potatoes as main ingredients. These reports are unusual because DCM is occurring in breeds not typically genetically prone to the disease. The FDA's Center for Veterinary Medicine and the Veterinary Laboratory Investigation and Response Network, a collaboration of government and veterinary diagnostic laboratories, are investigating this potential association.

Canine DCM is a disease of a dog's heart muscle and results in an enlarged heart. As the heart and its chambers become dilated, it becomes harder for the heart to pump, and heart valves may leak, leading to a buildup of fluids in the chest and abdomen. DCM often results in congestive heart failure. Heart function may improve in cases that are not linked to genetics with appropriate veterinary treatment and dietary modification, if caught early.

The underlying cause of DCM is not truly known, but is thought to have a genetic component. Breeds that are typically more frequently affected by DCM include large and giant breed dogs, such as Great Danes, Boxers, Newfoundlands, Irish Wolfhounds, Saint Bernards and Doberman Pinschers. It is less common in small and medium breed dogs, except American and English Cocker Spaniels. However, the cases that have been reported to the FDA have included Golden and Labrador Retrievers, Whippets, a Shih Tzu, a Bulldog and Miniature Schnauzers, as well as mixed breeds.

Diets in cases reported to the FDA frequently list potatoes or multiple legumes such as peas, lentils, other "pulses" (seeds of legumes), and their protein, starch and fiber derivatives early in the ingredient list, indicating that they are main ingredients. Early reports from the veterinary cardiology community indicate that the dogs consistently ate these foods as their primary source of nutrition for time periods ranging from months to years. High levels of legumes or potatoes appear to be more common in diets labeled as "grain-free," but it is not yet known how these ingredients are linked to cases of DCM. Changes in diet, especially for dogs with DCM, should be made in consultation with a licensed veterinarian.

In the reports the FDA has received, some of the dogs showed signs of heart disease, including decreased energy, cough, difficulty breathing and episodes of collapse. Medical records for four atypical DCM cases, three Golden Retrievers and one Labrador Retriever, showthat these dogs had low whole blood levels of the amino acid taurine. Taurine deficiency is well-documented as potentially leading to DCM. The Labrador Retriever with low whole blood taurine levels is recovering with veterinary treatment, including taurine supplementation, and a diet change. Four other cases of DCM in atypical dog breeds, a Miniature Schnauzer, Shih Tzu and two Labrador Retrievers, had normal blood taurine levels. The FDA continues to work with board certified veterinary cardiologists and veterinary nutritionists to better understand the clinical presentation of these dogs. The agency has also been in contact with pet food manufacturers to discuss these reports and to help further the investigation.

The FDA encourages pet owners and veterinary professionals to report cases of DCM in dogs suspected of having a link to diet by using the electronic Safety Reporting Portal or calling their state's FDA Consumer Complaint Coordinators. Please see the link below about "How to Report a Pet Food Complaint" for additional instructions.

VETERINARY CARDIOLOGY SPECIALISTS

Taurine Deficiency Induced Dilated Cardiomyopathy in Golden Retrievers

Taurine Deficiency Induced
Dilated Cardiomyopathy in Golden Retrievers
by Janet Olson, DVM, DACVIM (Cardiology)

Dilated Cardiomyopathy (DCM) is becoming more prevalent in golden retrievers. Dr. Joshua Stern, DVM, PhD, DACVIM (Cardiology) at UC Davis, starting seeing a pattern and recognized that many cases were due to dietary taurine deficiency in golden retrievers fed grain free diets. Here is what we know so far:

Background

Taurine is an amino acid that is found in high concentrations in heart and muscle. Among its many functions, it aids in normal contractile function. Evidence shows that taurine helps mediate calcium channel transports and modulates calcium sensitivity of the myofibrils.

Taurine deficiency as a cause of dilated cardiomyopathy (DCM) is not a new issue. Taurine deficiency in cats was characterized by Pion et al in the late 1980s. Taurine deficiency has since been characterized as a cause of acquired DCM in dogs as well.

Currently identified diets of concern in these golden retrievers

According to Dr. Stern, the majority of cases they are seeing at UC Davis are from grain free diets that are high in legumes, like acana pork and squash singles.

What can we do? Some Guidelines.

- **ASK:** Make sure to ask your clients (whether they own golden retrievers or not) what diets they are currently or previously have fed their dogs
- **INFORM:** Inform your clients of his issue
- **ACT:** If they are currently on, or have been on grain free diets in the past, submit baseline WHOLE blood taurine levels and AFTER submitting the WHOLE blood taurine levels, switch diets if indicated. Temporary taurine supplementation may be necessary. If levels are low, take baseline chest films, if cardiomegaly noted on the radiographs, an echocardiogram is indicated to complete your baseline evaluation. Additional therapy may be indicated.
- **GET MORE INFORMATION:** Dr. Stern has compiled many of the studies in the following links: https://www.dropbox.com/.../AAB1sDvLZe6gE3httPskz9-0a... Taurine Deficient DCM in Dogs

Veterinary Cardiology Specialists, PLLC
612-353-7440
www.vetcardiologist.com <> janet.olson@vetcardiologist.com <> www.facebook.com/vetcardiologist

From:	Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To:	Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David
Sent:	3/22/2019 1:54:08 PM
Subject:	DCM Cases 3/22/2019 1000
Attachments:	Acana Free Run Poultry dry: Lisa Freeman - EON-374786; Acana Free Run Poultry dry: Lisa Freeman - EON-383005; Freshpet select roasted meals chicken flavor: B6 - EON-383014

One related

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/27/2018 3:16:35 PM

Subject: Acana Free Run Poultry dry: Lisa Freeman - EON-374786

Attachments: 2060599-report.pdf; 2060599-attachments.zip

A PFR Report has been received and PFR Event [EON-374786] has been created in the EON System.

A "PDF" report by name "2060599-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2060599-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-374786
ICSR #: 2060599
EON Title: PFR Event created for Acana Free Run Poultry dry; 2060599

AE Date	08/20/2018	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	2
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Doberman Pinscher		
Age	10 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2060599
Product Group: Pet Food
Product Name: Acana Free Run Poultry dry
Description: Housemate was diagnosed with DCM (B6 - previously reported). B6 was asymptomatic but eating same diet (Acana) so was screened 8/20/18 - reduced contractile function. Owner changed diet to Pro Plan Weight Management dry. No improvement on 12/12/18 echo. Will recheck in 3 months WB taurine 328
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)

Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 2
Number of Animals Reacted With Product: 2

Product Name	Lot Number or ID	Best By Date
Acana Free Run Poultry dry		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information

B6

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-374786

ICSR:	2060599			
Type Of Submission:	Initial			
Report Version:	FPSR.FDA.PETF.V.V1			
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)			
Reporting Type:	Voluntary			
Report Submission Date:	2018-12-27 10:09:22 EST			
Reported Problem:	**Problem Description:**	Housemate was diagnosed with DCM (B6 - previously reported). B6 was asymptomatic but eating same diet (Acana) so was screened 8/20/18 - reduced contractile function. Owner changed diet to Pro Plan Weight Management dry. No improvement on 12/12/18 echo. Will recheck in 3 months WB taurine 328		
	Date Problem Started:	08/20/2018		
	Concurrent Medical Problem:	Yes		
	Pre Existing Conditions:	Hypothyroidism, incontinence, history of UTIs/crystalluria		
	Outcome to Date:	Stable		
Product Information:	**Product Name:**	Acana Free Run Poultry dry		
	Product Type:	Pet Food		
	Lot Number:			
	Package Type:	BAG		
	Product Use Information:	**Description:**	Fed since approximately 9/2016 (see diet history form) Changed to Pro Plan Weight Management Aug 2018	
	Manufacturer /Distributor Information:			
	Purchase Location Information:			
Animal Information:	**Name:**	B6		
	Type Of Species:	Dog		
	Type Of Breed:	Doberman Pinscher		
	Gender:	Female		
	Reproductive Status:	Neutered		
	Weight:	38.1 Kilogram		
	Age:	10 Years		
	Assessment of Prior Health:	Excellent		
	Number of Animals Given the Product:	2		
	Number of Animals Reacted:	2		
	Owner Information:	**Owner Information provided:**	Yes	
		Contact:	**Name:** B6	
			Phone:	
			Email:	
		Address:	B6 United States	
	Healthcare Professional Information:	**Practice Name:**	Tufts Cummings School of Veterinary Medicine	
		Contact:	**Name:**	Lisa Freeman

		Phone:	(508) 887-4523
		Email:	lisa.freeman@tufts.edu
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	

Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	

Additional Documents:		
	Attachment:	**B6** medical records.pdf
	Description:	Medical records
	Type:	Medical Records

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

All Medical Records

Client:
Address: B6

Patient: B6
Breed: Doberman
DOB: B6

Species: Canine
Sex: Female (Spayed)

Home Phone: B6
Work Phone: (___) _-____
Cell Phone: B6

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Cardiology Study Appointment

SOAP Text Aug 20 2018 1:58PM - B6

Initial Complaint:
Recheck - B6 - DCM study

SOAP Text Dec 12 2018 12:23PM - B6

Disposition/Recommendations

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Doberman
Sex:	Female (Spayed)
Age:	B6 Years Old

Lab Results Report

Accession ID:

Test	Results	Reference Range	Units

B4

3/28

B6

Printed Thursday, December 27, 2018

Client: B6
Patient:

UCDavis Taurine Level

Best Available Copy

10401

B4

Sample Submission Form

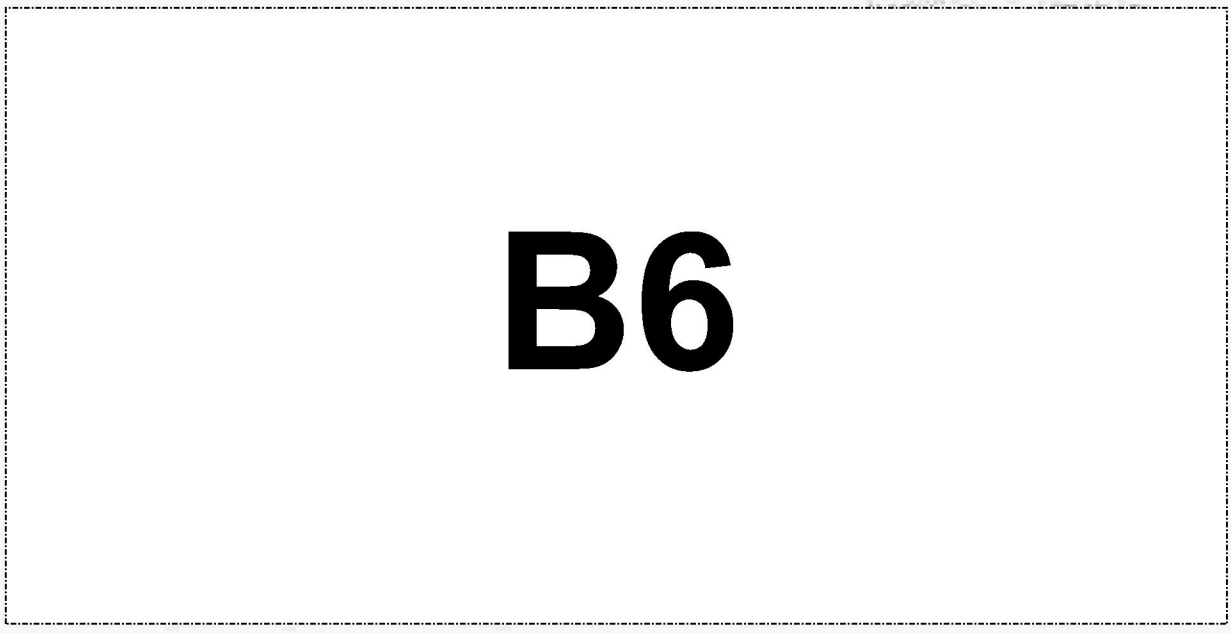
Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
Davis, CA 95616
Tel: (530)752-5058, Fax: [illegible]

[illegible]

B6

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	[illegible]



Client: B6
Patient:

Diet history 12/12/18

Best Available Copy

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 12/12/18

1. How would you assess your pet's appetite? On a scale of 1-10 with 1 being poor and 10 being excellent: 10

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   - [x] Eats about the same amount as usual
   - [ ] Eats less than usual
   - [ ] Eats more than usual
   - [ ] Seems to prefer different foods than usual
   - [ ] Other: [illegible]

3. Over the last few weeks, has your pet (choose one):
   - ( ) Lost weight
   - ( ) Gained weight
   - (x) Stayed about the same weight
   - ( ) Don't know

4. Please list below ALL pet foods, people food, treats, snacks, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what your pet is eating.

Food (include specific product and flavor) Form Amount How often? Fed since
Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free (Chicken, Lentil, & Sweet Potato Adult)	dry	7 ½ cup	2x/day	Jan 2018
85% lean hamburger	[illegible]	[illegible]	1x/week	Jan 2018
[illegible]	treat	[illegible]	1x/day	Aug 2018
[illegible]	treat	[illegible]	1x/week	Dec 2018
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Any additional diet information can be listed at the bottom of this sheet

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? (x) Yes ( ) No If yes, please list which ones and give brands and amounts:

Supplement		Brand/Concentration	Amount per day
Taurine	( ) Yes ( ) No		
Carnitine	( ) Yes ( ) No		
Antioxidants	( ) Yes ( ) No		
Multivitamin	( ) Yes ( ) No		
Fish oil	(x) Yes ( ) No	[illegible]	[illegible]
Coenzyme Q10	( ) Yes ( ) No		
Other (please list):			
Example: Vitamin C		Nature's Bounty	500 mg tablets – 1 per day
[illegible]		[illegible]	[illegible]

6. How do you administer pills to your pet?
   - [ ] I do not give any medications
   - [ ] I put them directly in my pet's mouth without food
   - [ ] I put them in my pet's dog/cat food
   - [ ] I put them in a Pill Pocket or similar product
   - [x] I put them in foods (list foods): [illegible]

Additional diet or supplement information:

Information below to be completed by the veterinarian:

Current body weight: ________ kg Current body condition score (1 to 9): ____/9

Muscle Condition Score: normal muscle ( ) mild muscle loss ( ) moderate muscle loss ( ) severe muscle loss ( )

Client: B6
Patient:

Diet history 8/20/18

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 8/20/18

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: Poor ———————————|——— Excellent
   Poor ——————————————————| Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   - ☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
   - ☐ Seems to prefer different foods than usual ☐ Other ______

3. Over the last few weeks, has your pet (check one)
   ☐ Lost weight ☐ Gained weight ☒ Stayed about the same weight ☐ Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what your pet is eating.

Food (include specific product and flavor) Form Amount How often? Fed since
Examples are shown in the table – please provide enough detail that we could go do the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Acme Grain Free Chicken, Lentil, & Sweet Potato Adult	dry	1 ½ cup	2x/day	Jan 2018
85% lean hamburger	microwaved	3 oz	1x/week	Jan 2018
Pupperoni original beef flavor	treat	½	1x/day	Aug 2015
Rawhide	treat	6 inch twist	1x/week	Dec 2015
Diamond Grain Free Puppy [illegible]		1.5 cups	2x/day	8/[illegible]
Blueberries, [illegible]		[illegible]	[illegible] day	
Apples, organic pumpkin		"	seasonal	
Bananas		½	[illegible] time/week	
organic peanutbutter		[illegible]	[illegible]	
Boiled eggs		1	every other day	
Chicken		½	[illegible] 1 day	[illegible]

*Any additional diet information can be listed on the back of this sheet

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☐ No		
Carnitine	☐ Yes ☐ No		
Antioxidants	☐ Yes ☐ No		
Multivitamin	☐ Yes ☐ No		
Fish oil	☐ Yes ☐ No		
Coenzyme Q10	☐ Yes ☐ No		
Other (please list):			
Example: Vitamin C		Nature's Bounty	500 mg tablets – 1 per day

6. How do you administer pills to your pet?
   - ☐ I do not give any medications
   - ☐ I put them directly in my pet's mouth without food
   - ☐ I put them in my pet's dog/cat food
   - ☐ I put them in a Pill Pocket or similar product
   - ☒ I put them in foods (list foods): in peanutbutter / banana / canned food

Best Available Copy

Client: B6
Patient:

Vitals Results

B6

Client: B6
Patient:

ECG from Cardio

pt: B6

B6

Client: B6
Patient:

ECG from Cardio

B6

B6

Client: B6
Patient

ECG from Cardio

B6

B6

Client: B6
Patient:

Patient History

B6

12:48 PM	UserForm
01:07 PM	Treatment
01:20 PM	UserForm
01:25 PM	Vitals
01:26 PM	Purchase
01:27 PM	Purchase
01:27 PM	Purchase
09:42 AM	Appointment
07:22 PM	Appointment
11:04 AM	UserForm
11:07 AM	Treatment
11:59 AM	Purchase
11:59 AM	Purchase
12:09 PM	UserForm
12:24 PM	Purchase
12:47 PM	Appointment

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

B6

Admit Dat B6 3 PM
Discharge

Diagnoses: Apparently healthy animal

Clinical Findings: On physical exam, her heart rate had mild irregularities called an arrhythmia. Her arrhythmia is called sinus arrhythmia, which happens when the heart rate decreases and increases with respiration. This is a normal finding in dogs. On auscultation, there was no murmur heard at the time. Her physical exam was within normal limits.

Echocardiogram & ECG Findings:
The echocardiogram today found no evidence of Dilated Cardiomyopathy at this time. She does have slightly decreased contractility of the heart, which is something that does not need to be treated at this time; however, it is something to monitor in the future. The ECG showed a sinus arrhythmia, which is consistent with our auscultation.

Medicine at Home:

B6

Diet Suggestions:
We would like to chang B6 s to a low sodium diet. A few diet options would be:

Dry Food:
Royal Canin Early Cardiac diet
Purina Canin Boxer
Purina Pro Plan Adult Weight Management (this does not have low calories in spite of the name of the food)

B6

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

B6

B6

Discharge Instructions

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4096

B6

Patient ID: B6
B6 Canine
B6 ears Old Female Spayed Doberman
Black/Tan

Cardiology Appointment Report

Date: 8/20/2018

Attending Cardiologist:
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

B6

Shortness of breath or difficulty breathing? No
Syncope or collapse? No
Sudden onset lameness? No
Exercise intolerance? No

Current Medications Pertinent to CV System:
Medication: Thyro-Tabs 0.8 mg tablets
Formulation/Tab Size: 1 tab PO BID
Administration Frequency: q 12 hrs
Need refills? No

Cardiac Physical Examination:
General PE:
MM Color and CRT: pink and moist, CRT < 2 seconds.
BCS (1-9): 4/9
BW (kg): 38.1

Heart rate: 104 bpm
Respiratory rate: panting, normal effort
Temp (if possible):

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [ ] Good
- [x] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulses paradoxus
- [ ] Other:

Arrhythmia:
- [ ] None
- [x] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupnea
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

☑ Normal RV sounds

Abdominal exam:

☑ Normal
☐ Hepatomegaly
☐ Abdominal distension
☐ Mild ascites
☐ Marked ascites

Problems:

Apparently healthy animal
Genetic predisposition to DCM

Differential Diagnoses:

DCM

Diagnostic plan:

☑ Echocardiogram
☐ Chemistry profile
☑ ECG
☐ Renal profile
☐ Blood pressure
☐ Dialysis profile
☐ Thoracic radiographs
☑ NT-proBNP
☐ Troponin I
☐ Other tests:

Echocardiogram Findings:

General/2-D findings:

Normal LV wall thicknesses with normal LV cavity size and no LA enlargement. Mild thickening of the MV. Mildly decreased contractile function.

Doppler findings:

WNL

Mitral inflow:

☐ Summated
☑ Normal
☐ Delayed relaxation
☐ Pseudonormal
☐ Restrictive

ECG findings:

sinus arrhythmia

Assessment and recommendations:

Normal cardiac structure, although the contractile function is mildly decreased. This may be indicative of early cardiomyopathy. Taurine levels were submitted for analysis, and the patient will be switched off of the grain-free diet. If contractile function is not improved at the 4 month rechecked despite change in diet, then we should submit a NT-proBNP to help us diagnose if the changes is indicated of primary DCM and not diet related.

Final Diagnosis:

Mild MMVD
R/O diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:

ISACHC Classification:

☑ Ia
☐ IIa

☐ Ib
☐ II
☐ IIb
☐ IIIb

ACVIM Classification:
☐ A
☒ B1
☐ B2
☐ C
☐ D

M-Mode		
IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
%FS		%
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm
M-Mode Normalized	B6	
IVSdN		(0.29 - 0.52)
LVIDdN		(1.35 - 1.73)
LVPWdN		(0.33 - 0.53)
IVSsN		(0.43 - 0.71) !
LVIDsN		(0.79 - 1.14) !
LVPWsN		(0.53 - 0.78) !
Ao Diam N		(0.68 - 0.89)
LA Diam N		(0.64 - 0.90)
2D	B6	
SA LA		cm
Ao Diam		cm
SA LA / Ao Diam		
LVId A4C		cm
LVEDV MOD A4C		ml
LVIs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml
Doppler	B6	
MV E Vel		m/s
MV Dec T		ms
MV A Vel		m/s
MV E/A Ratio		
E'		m/s

A'		m/s
E/E'		
PV Vmax	B6	m/s
PV maxPG		mmHg
AV Vmax		m/s
AV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

B6

B6

Admit Date: 8 4:33 PM
Discharge Da

B6

Diagnoses:
Mild decreased contractile function

B6

B6

Diet Recommendations:
Please continue feeding B6 or Purina Pro Plan Weight Management dry food and Hill's Science Diet adult beef and barley entree. These foods are low in sodium and do not have low calories despite the name.

Exercise Recommendations:
B6 does not need any exercise restriction at this time.

Recommended Medications:
B6 does not need any cardiac medications at this time.

Recheck Visits:
A recheck appointment March 6th 11 am with B6 At the time we will recheck an echocardiogram.

Thank you for entrusting us with B6 care. Please contact our Cardiology liaison at (508)-887-4076 or email us at cardiowt@tufts.edu for scheduling and non-emergent questions or concerns.

Sincerely,
B6

Please visit our HeartSmart website for more information
https://vet.tufts.edu/heartsmart/

B6

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4096

B6

B6 ...an: Old Female (Spayed) Doberman
Black/Tan

Cardiology Appointment Report

Date: 12/12/2018

B6

Presenting Complaint:
Mild MMVD
Mild decreased contractile function R/O diet-related vs. primary DCM related mild decrease in contractile function vs normal variation
DCM Study

B6

B6

Current Medications Pertinent to CV System:
Medication: Thyro-Tabs 0.8 mg tablets
Formulation/Tab Size: 1 tab PO BID
Administration Frequency: q 12 hrs
Need refills? No

Cardiac Physical Examination:
General PE: 2 small SQ masses L axillary region, 1 SQ mass L flank
MM Color and CRT: pink, CRT <2s
BCS (1-9): 4/9
BW (kg): 35.1

Heart rate: 146
Respiratory rate: 110 (panting, NE)
Temp (if possible):

Muscle condition:
- ☑ Normal
- ☐ Mild muscle loss
- ☐ Moderate cachexia
- ☐ Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- ☑ None
- ☐ I/VI
- ☐ II/VI
- ☐ III/VI
- ☐ IV/VI
- ☐ V/VI
- ☐ VI/VI

Jugular vein:
- ☑ Bottom 1/3 of the neck
- ☐ Middle 1/3 of the neck
- ☐ 1/2 way up the neck
- ☐ Top 2/3 of the neck

Arterial pulses:
- ☐ Weak
- ☐ Fair
- ☐ Good
- ☑ Strong
- ☐ Bounding
- ☐ Pulse deficits
- ☐ Pulsus paradoxus
- ☐ Other:

Arrhythmias:
- ☐ None
- ☑ Sinus arrhythmia
- ☐ Premature beats
- ☐ Bradycardia
- ☐ Tachycardia

Gallop:
- ☐ Yes
- ☐ Pronounced

- [x] No
- [ ] Intermittent
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
Mild MMVD
Mildly decreased contractile function r/o diet related vs. primary DCM related mild decrease in contractile function vs normal variation

Diagnostic plan:
- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:

B6

ECG findings:
Sinus rhythm during the echocardiogram.

Assessment and recommendations:

B6

B6

Final Diagnosis:
– Very early DMVD
– Mild decreased contractile function r/o diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:
ISACHC Classification:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

M-Mode

IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm

2D

SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm

LVPWs	B6	cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LVId A4C		cm
LVEDV MOD A4C		ml
LVIs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml

Doppler		
MV E Vel	B6	m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6 Female (Spayed)
Canine: Doberman Black/Tan
426154

8/24/2018

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6 Female (Spayed)
Canine: Doberman Black/Tan
426154

12/19/2018

B6

From: Related PFR Event <pfrsignificantactivitycreation@fda.hhs.gov>

To: Carey, Lauren; Cleary, Michael [B6] [B6]

Sent: 3/21/2019 9:41:00 PM

Subject: Acana Free Run Poultry dry: Lisa Freeman - EON-383005

Attachments: 2064397-report.pdf; 2064397-attachments.zip

A PFR Report has been received and Related PFR Event [EON-383005] has been created in the EON System.

A "PDF" report by name "2064397-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2064397-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-383005
ICSR #: 2064397
EON Title: Related PFR Event created for Acana Free Run Poultry dry; 2064397

AE Date	08/20/2018	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	2
Animal Species	Dog	**Outcome to Date**	Better/Improved/Recovering
Breed	Doberman Pinscher		
Age	10 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2064397
Product Group: Pet Food
Product Name: Acana Free Run Poultry dry
Description: Housemate was diagnosed with DCM ([B6] - previously reported). [B6] was asymptomatic but eating same diet (Acana) so was screened 8/20/18 - reduced contractile function. Owner changed diet to Pro Plan Weight Management dry. No improvement on 12/12/18 echo. Will recheck in 3 months WB taurine 328
Submission Type: Followup

Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Better/Improved/Recovering
Number of Animals Treated With Product: 2
Number of Animals Reacted With Product: 2

Product Name	Lot Number or ID	Best By Date
Acana Free Run Poultry dry		

This report is linked to:
Initial EON Event Key: EON-374786
Initial ICSR: 2060599

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6

To view this Related PFR Event, please click the link below:
B6

To view the Related PFR Event Report, please click the link below:
B6
B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

{

Report Details - EON-383005

ICSR:	2064397
Type Of Submission:	Followup
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-21 17:33:50 EDT
Initial Report Date:	12/27/2018
Parent ICSR:	2060599
Follow-up Report to FDA Request:	Yes

Reported Problem:

Problem Description:	Housemate was diagnosed with DCM (B6 - previously reported). B6 was asymptomatic but eating same diet (Acana) so was screened 8/20/18 - reduced contractile function. Owner changed diet to Pro Plan Weight Management dry. No improvement on 12/12/18 echo. Will recheck in 3 months WB taurine 328
Date Problem Started:	08/20/2018
Concurrent Medical Problem:	Yes
Pre Existing Conditions:	Hypothyroidism, incontinence, history of UTIs/crystalluria
Outcome to Date:	Better/Improved/Recovering

Product Information:

Product Name:	Acana Free Run Poultry dry	
Product Type:	Pet Food	
Lot Number:		
Package Type:	BAG	
Product Use Information:	**Description:**	Fed since approximately 9/2016 (see diet history form) Changed to Pro Plan Weight Management Aug 2018
Manufacturer /Distributor Information:		
Purchase Location Information:		

Animal Information:

Name:	B6
Type Of Species:	Dog
Type Of Breed:	Doberman Pinscher
Gender:	Female
Reproductive Status:	Neutered
Weight:	38.1 Kilogram
Age:	10 Years
Assessment of Prior Health:	Excellent
Number of Animals Given the Product:	2
Number of Animals Reacted:	2

Owner Information:

Owner Information provided:	Yes
Contact:	**Name:** B6
	Phone:
	Email:
Address:	B6

		B6 United States	
	Healthcare Professional Information:	Practice Name:	Tufts Cummings School of Veterinary Medicine
		Contact:	Name: Lisa Freeman
			Phone: (508) 887-4523
			Email: lisa.freeman@tufts.edu
		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States
Sender Information:	Name:	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	Phone:	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
	Reported to Other Parties:	None	
Additional Documents:			
	Attachment:	Medical Record.pdf	
	Description:	Updated diet history, echo, ECG and Holter monitor	
	Type:	Medical Records	

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

All Medical Records

Client:
Address: B6

Patient: B6
Breed: Doberman
DOB: B6

Species: Canine
Sex: Female (Spayed)

Home Phone: B6
Work Phone: ( ) -
Cell Phone: B6

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Cardiology Study Appointment

SOAP Text Aug 20 2018 1:58PM - B6

Initial Complaint:
Recheck - B6 - DCM study

SOAP Text Dec 12 2018 12:23PM - B6

Initial Complaint:
Recheck - B6 - DCM study

Initial Complaint:
PAGE B6 - HOLTER REMOVAL

Disposition/Recommendations

Appears this way on Original

Appears this way on Original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Doberman
Sex:	Female (Spayed)
Age:	B6 Years Old

Lab Results Report

Accession ID:

Test	Results	Reference Range	Units

Client: B6
Patient:

UCDavis Taurine Level

B6

Sample Submission Form

UC CUSTOMERS ONLY:
Non-federal funds ID/Account Number to bill:_____

Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
Davis, CA 95616
Tel: (530)752-5058, Fax: (530)752-4698

http://www.vetmed.ucdavis.edu B6

B6

TAURINE (WHOLE BLOOD)
Lithium Heparin

Vet/Tech Contact: B6
Company Name: Tufts Cummings School of Vet Med - Clinical Pathology Labor
Address: 200 Westboro Road
North Grafton, MA 01536

Email: B6
Tel:

Billing Contact: B6 **TAX ID:**
Email: B6 **Tel:** B6

Patient Name: B6
Species: canine
Owner's Name: B6

Sample Type: ☐ Plasma ☑ Whole Blood ☐ Urine ☐ Food ☐ Other:_____
Test Items: ☑ Taurine ☐ Complete Amino Acid ☐ Other:_____

Taurine Results (nmol/ml)

Plasma:_____ Whole Blood: B6 Urine:_____ Food:_____

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	>150

Client: B6
Patient:

Lab Results B4, B6 **CARDIOPET proBNP 12/12/18**

B4, B6

Client: B6 Patient: B6

B4, B6

Client: B6
Patient: B6
Species: CANINE
Breed: DOBERMAN_PINSCH
Gender: FEMALE SPAYED
Age: 10Y

Date: 12/12/2018
Requisition #: 455387
Accession #: B6
Ordered by: B6

TUFTS UNIVERSITY
200 WESTBORO RD
NORTH GRAFTON, Massachusetts 01536-1828
508-839-5395

Account: B6

CARDIOPET proBNP - CANINE

Test	Result	Reference Range	Low	Normal	High
CARDIOPET proBNP - CANINE	B6	0 - 900 pmol/L	HIGH	B6	

Comments:

B6

Please note: Complete interpretive comments for all concentrations of Cardiopet proBNP are available in the online directory of services. Serum specimens received at room temperature may have decreased NT-proBNP concentrations.

Page 1 of 1

Client: B6
Patient:

Diet history 12/12/18

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 12/12/18

1. How would you assess your pet's appetite? On a scale of 1-10 with 1 being poor and 10 being excellent: 10

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☑ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
   ☐ Seems to prefer different foods than usual ☐ Other Meals divided into 3 daily servings. I'm scarred of bloat. Her brother passed due to bloat 10/15.

3. Over the last few weeks, has your pet (check one)
   ◯ Lost weight ◯ Gained weight ⊗ Stayed about the same weight ◯ Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

Food (include specific product and flavor) Form Amount How often? Fed since

Examples are shown in the table – please provide enough detail that we could go do the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2018*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
Purina Pro Plan Healthy Weight Adult	dry	1.5 cups	2x/day	August 2018
Purina Pro Plan Healthy Weight Adult (1.5 cups 2x/day + 1 cup 1x/day)	dry	1 cup	1x/day	Oct. 2018
Hills Science Diet Beef&Barley | Chicken&Barley | Chicken&Beef	wet	1/4 can	2x/day with 1.5dry	August 2018
Organic salt free, sugar free peanut butter	wet/frozen	1 teaspoon	1x/day or less	since little
Organic pumpkin puree	wet/frozen	1 to 2 teaspoons	1x/day or less	2015?
Banana	mashed	1/2 banana or small	1x/day or less	since little
blue berries or watermelon	organic	a taste	seasonally	since little

***Any additional diet information can be listed at the bottom of this sheet**

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ◉ Yes ◯ No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	◯ Yes ◯ No		
Carnitine	◯ Yes ◯ No		
Antioxidants	◯ Yes ◯ No		
Multivitamin	◯ Yes ◯ No		
Fish oil	◉ Yes ◯ No	CVS Natures Bounty 1200mg 360 omega 3	2 per day but unsure , have questions
Coenzyme Q10	◯ Yes ◯ No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*
Thyrotab		0.8mg	1 tablet twice per day

6. How do you administer pills to your pet?
   ☐ I do not give any medications ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food ☐ I put them in a Pill Pocket or similar product
   ☑ I put them in foods (list foods): I put the thyrotab in a little ball of canned food and she takes it. The fish oil gel tab she'll happily take as is

Additional diet or supplement information:

Information below to be completed by the veterinarian:

Current body weight: _____ kg Current body condition score (1-9): _____/9

Muscle Condition Score: normal muscle ◯ mild muscle loss ◯ moderate muscle loss ◯ severe muscle loss ◯

Client: B6
Patient:

Diet history 8/20/18

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 8/20/18

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: Poor_____ *Excellent*

   Poor_____ Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
   ☐ Seems to prefer different foods than usual ☐ Other_____

3. Over the last few weeks, has your pet (check one)
   ☐ Lost weight ☐ Gained weight ☒ Stayed about the same weight ☐ Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

   Food (include specific product and flavor) Form Amount How often? Fed since

   Examples are shown in the table – please provide enough detail that we could go do the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2018*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
Nutro Food Rich Poultry		1.5 cups	2x/day	9/16?
Blueberries, Applicot mix		handful	throughout day	
Apples, organic pumpkin		"	Seasonal	
Bananas		1/2	few times/week	
organic peanutbutter		1 teaspoon	few times/wk	
Boiled eggs		1	every other day	
Chicken		1/2 cup	1 day	every other

**Any additional diet information can be listed on the back of this sheet*

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☐ No		
Carnitine	☐ Yes ☐ No		
Antioxidants	☐ Yes ☐ No		
Multivitamin	☐ Yes ☐ No		
Fish oil	☐ Yes ☐ No		
Coenzyme Q10	☐ Yes ☐ No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

6. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food
   ☐ I put them in a Pill Pocket or similar product
   ☒ I put them in foods (list foods): in peanutbutter / banana / canned food

Holter Diary

B6

Client: B6
Patient:

Diet Hx 3/6/19

CARDIOLOGY DIET HISTORY FORM
Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: 3/6/19

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: ***Poor*** _____|_____ ***Excellent***

   Poor _____|_____ **Excellent**

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
   ☐ Seems to prefer different foods than usual ☐ Other_____

3. Over the last few weeks, has your pet (check one)
   ☐ Lost weight ☐ Gained weight ☒ Stayed about the same weight ☐ Don't know

1. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats and that you have fed in the last 2 years.

   Please provide enough detail that we could go to the store and buy the exact same food - examples are shown in the table

Food (include specific product and flavor)	Form	Amount	How often?	Dates fed
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2016-present*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*June -Aug 2016*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Sept 2016-present*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2018-present*
Purina Pro Plan weight management	kibble	1.5 cups	3 x /day	
Hills Science Beef Barley canned	canned	⅓ can	2 x /day	
Bananas	fresh	½ banana	few times a week as treat	
organic Peanutbutter (Salt & sugar free)	fresh	teaspoon	1 x /day or less in Kong	
Organic Pumpkin	organic canned	tablespoon	1x /day in Kong	
blueberries	fresh	handful	Seasonally as treat	
watermelon	fresh	handful	"	

**Any additional diet information can be listed on the back of this sheet*

2. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☒ No		
Carnitine	☐ Yes ☒ No		
Antioxidants	☐ Yes ☒ No		
Multivitamin	☐ Yes ☒ No		
Fish oil	☐ Yes ☒ No		
Coenzyme Q10	☐ Yes ☒ No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

3. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☐ I put them in my pet's dog/cat food
   ☐ I put them in a Pill Pocket or similar product
   ☒ I put them in foods (list foods): put them in a little ball of canned food and she takes it like a treat

Client: B6
Patient:

Vitals Results

B6

Client: B6
Patient:

ECG from Cardio

B6 8/20/2018 1:26:13 PM Page 1 of 2

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6

8/20/2018 1:25:05 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6

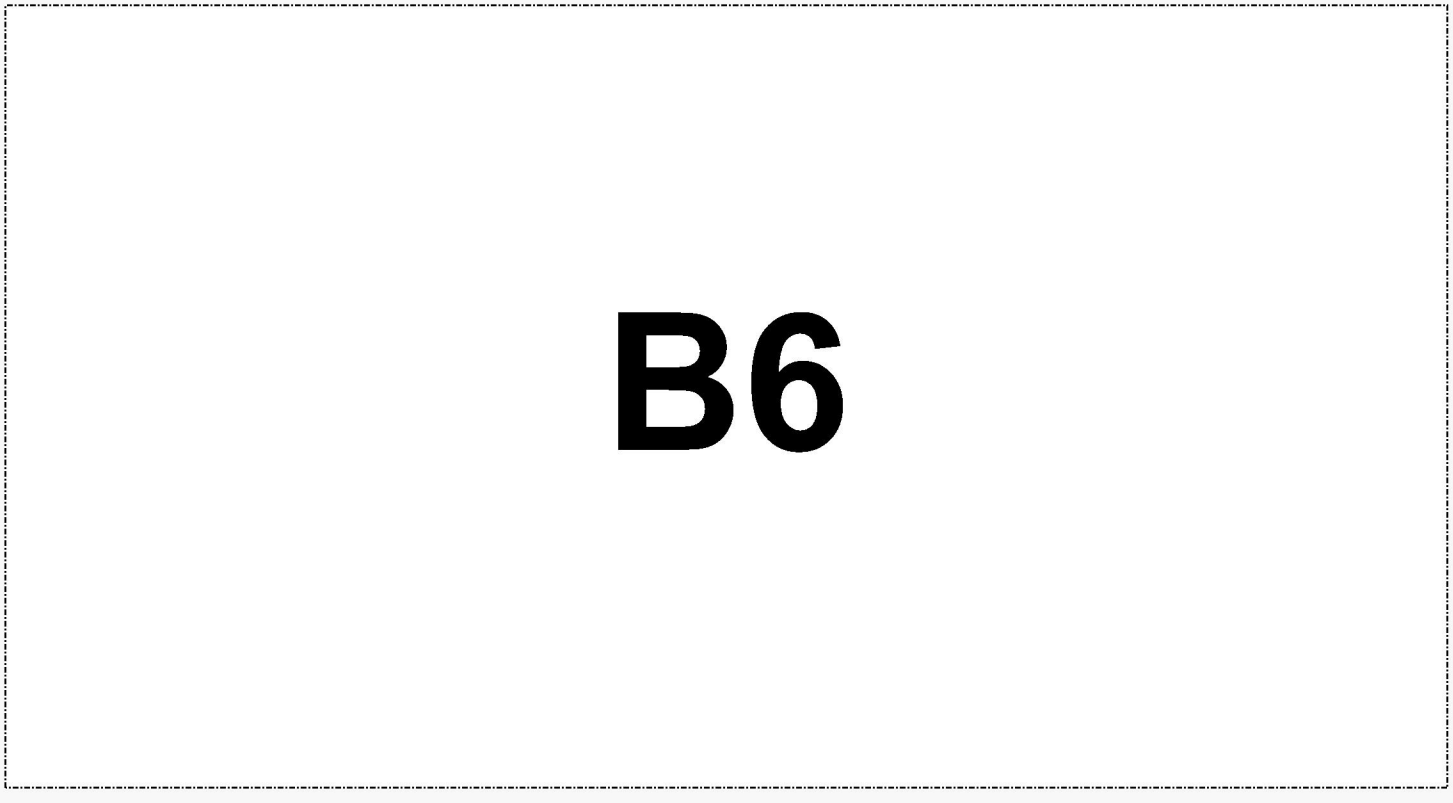
3/6/2019 12:36:12 PM

Tufts University
Tufts Cummings School of Vet Med
Cardiology

B6

Client: B6
Patient:

ECG from Cardio



Client: B6
Patient:

ECG from Cardio

B6 3/6/2019 12:36:17 PM

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

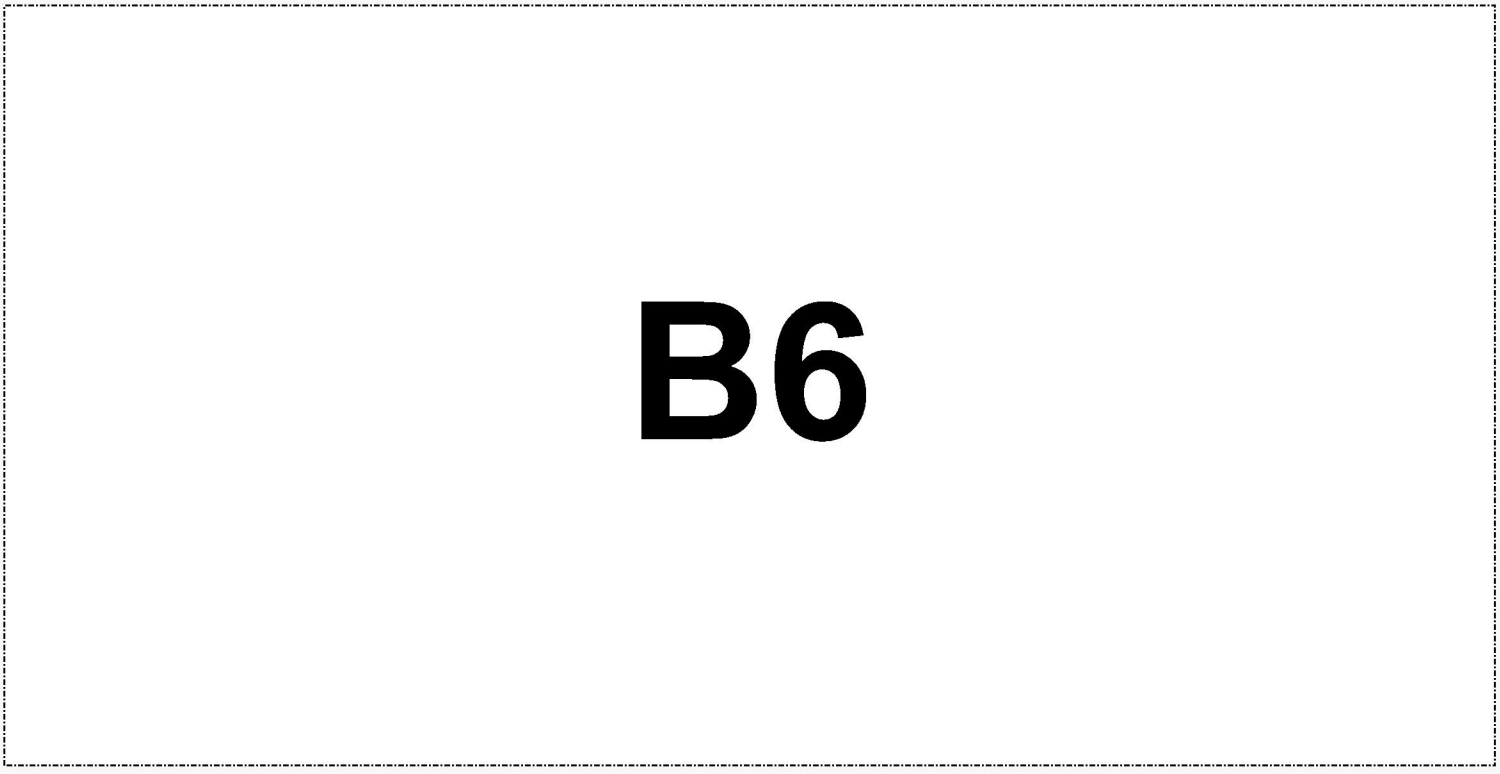
ECG from Cardio

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6 3/6/2019 12:37:14 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology



Client: B6
Patient:

ECG from Cardio

Client: B6
Patient:

Patient History

B6

12:48 PM	UserForm	
01:07 PM	Treatment	
01:20 PM	UserForm	
01:25 PM	Vitals	
01:26 PM	Purchase	
01:27 PM	Purchase	
01:27 PM	Purchase	
09:42 AM	Appointment	
07:22 PM	Appointment	
11:04 AM	UserForm	
11:07 AM	Treatment	
11:59 AM	Purchase	
11:59 AM	Purchase	
12:09 PM	UserForm	
12:24 PM	Purchase	
12:47 PM	Appointment	
11:05 AM	UserForm	
11:30 AM	UserForm	
11:58 AM	Purchase	
11:58 AM	Purchase	
11:58 AM	Purchase	
12:04 PM	Treatment	
12:31 PM	Purchase	
01:10 PM	Appointment	
09:24 AM	Appointment	
02:34 PM	Purchase	

B6

Patient Account History	Description	Qty	price	Extended	Disc	Pmt

Client: B6
Patient:

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Monday, 20 August 2018 13:27	Appointment: Cardiology Study	1.000	B6			

Client:
Patient: B6

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Wednesday, 12 December 2018 11:59	Appointment: Cardiology Study	1.000				

B6

Client: B6
Patient:

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Wednesday, 12 December 2018 12:24	NT Pro BNP Canine B4, B6 2665) - FHSA	1.000		B6		

Client:
Patient: B6

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Wednesday, 06 March 2019 11:57	Appointment: Cardiology Study	1.000	B6			

Client: B6
Patient:

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Wednesday, 06 March 2019 12:31	Alba Holter Monitor	1.000	B6			

Client:
Patient: B6

Patient Account History	Description	Qty	price	Extended	Disc	Pmt
Thursday, 07 March 2019 14:34	Appointment: Cardiology Holter Removal	1.000	B6			

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

Patient
Name: B6
Species: Canine
Black/Tan Female (Spayed) Doberman
Birthdate B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
B6

Cardiology Resident:
B6

Student: B6
Cardiology Technician:
B6

Admit Date: B6 33 PM
Discharge D

Diagnoses: Apparently healthy animal!

Clinical Findings: On physical exam, her heart rate had mild irregularities called an arrhythmia. Her arrhythmia is called sinus arrhythmia, which happens when the heart rate decreases and increases with respiration. This is a normal finding in dogs. On auscultation, there was no murmurs heard at this time. Her physical exam was within normal limits.

Echocardiogram & ECG Findings:
The echocardiogram today found no evidence of Dilated Cardiomyopathy at this time. She does have slightly decreased contractility of the heart, which is something that does not need to be treated at this time; however, it is something to monitor in the future. The ECG showed a sinus arrhythmia, which is consistent with our auscultation.

Monitoring at Home:

B6

Diet Suggestions:
We would like to change B6 diet to a low sodium diet. A few diet options would be:

Dry Food:
Royal Canin Early Cardiac diet
Purina Canin Boxer
Purina Pro Plan Adult Weight Management (this does not have low calories in spite of the name of the food)

Canned Food:
Hills Science diet adult beef and barley entree

Exercise Recommendations:
B6 does not need any exercise restriction at this time.

Recommended Medications:
B6 does not need any cardiac medications at this time. Depending on the results of her bloodwork, taurine supplementation may need to be initiated. We will call you with the bloodwork results when they become available.

Recheck Visits: A recheck visit is scheduled for 4 months. At this visit we will want to check breathing effort and heart function and do a blood test. A recheck echocardiogram is recommended at this time as well to track any progression of structural or functional abnormalities.

Thank you for entrusting us with B6 care. Please contact our Cardiology liaison at (508)-887-4696 or email us at cardiovet@tufts.edu for scheduling and non-emergent questions or concerns.

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:
Please check with your primary veterinarian to purchase the recommended diet(s). If you wish to purchase your food from us, please call 7-10 days in advance (508-887-4629) to ensure the food is in stock. Alternatively, veterinary diets can be ordered from online retailers with a prescription/veterinary approval.

Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

---

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

B6 ID: B6
Canine
ars Old Female (Spayed) Doberman
Black/Tan

Cardiology Appointment Report

Date: 8/20/2018

Attending Cardiologist:
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

Presenting Complaint:
Brother from same litter was unexpectingly diagnosed with DCM with secondary CHF recently

B6

General Medical History:
Acting normally, eating and drinking normally, no changes in bathroom habits, coughing occasionally (randomly), no vomiting, diarrhea, or sneezing noticed.

Diet and Supplements:
Akana Free-Reign Poultry Formulation 1.5-2 cups BID

Cardiovascular History:
Prior CHF diagnosis? No
Prior heart murmur? No
Prior ATE? No
Prior arrhythmia? No
Monitoring respiratory rate and effort at home? Yes, occasionally
Cough? Occasionally, random events

Shortness of breath or difficulty breathing? No
Syncope or collapse? No
Sudden onset lameness? No
Exercise intolerance? No

Current Medications Pertinent to CV System:
Medication: Thyro-Tabs 0.8 mg tablets
Formulation/Tab Size: 1 tab PO BID
Administration Frequency: q 12 hrs
Need refills? No

Cardiac Physical Examination:
General PE:
MM Color and CRT: pink and moist, CRT < 2 seconds
BCS (1-9): 4/9
BW (kg): 38.1

Heart rate: 104 bpm
Respiratory rate: panting, normal effort
Temp (if possible):

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [ ] Good
- [x] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [ ] None
- [x] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

☑ Normal BV sounds

Abdominal exam:

☑ Normal
☐ Hepatomegaly
☐ Abdominal distension
☐ Mild ascites
☐ Marked ascites

Problems:

Apparently healthy animal
Genetic predisposition to DCM

Differential Diagnoses:

DCM

Diagnostic plan:

☑ Echocardiogram
☐ Chemistry profile
☑ ECG
☐ Renal profile
☐ Blood pressure
☐ Dialysis profile
☐ Thoracic radiographs
☑ NT-proBNP
☐ Troponin I
☐ Other tests:

Echocardiogram Findings:

General/2-D findings:

Normal LV wall thicknesses with normal LV cavity size and no LA enlargement. Mild thickening of the MV. Mildly decreased contractile function.

Doppler findings:

WNL

Mitral inflow:

☐ Summated
☑ Normal
☐ Delayed relaxation
☐ Pseudonormal
☐ Restrictive

ECG findings:

sinus arrhythmia

Assessment and recommendations:

Normal cardiac structure, although the contractile function is mildly decreased. This may be indicative of early cardiomyopathy. Taurine levels were submitted for analysis, and the patient will be switched off of the grain-free diet. If contractile function is not improved at the 4 month rechecked despite change in diet, then we should submit a NT-proBNP to help us diagnose if the changes is indicated of primary DCM and not diet related.

Final Diagnosis:

Mild MMVD
R/O diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:

ISACHC Classification:

☑ Ia
☐ IIIa

☐ Ib
☐ II
☐ IIIb

ACVIM Classification:

☐ A
☑ B1
☐ B2
☐ C
☐ D

M-Mode

IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
%FS		%
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm

M-Mode Normalized

IVSdN	B6	(0.29 - 0.52)
LVIDdN		(1.35 - 1.73)
LVPWdN		(0.33 - 0.53)
IVSsN		(0.43 - 0.71) !
LVIDsN		(0.79 - 1.14) !
LVPWsN		(0.53 - 0.78) !
Ao Diam N		(0.68 - 0.89)
LA Diam N		(0.64 - 0.90)

2D

SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
LVId A4C		cm
LVEDV MOD A4C		ml
LVIs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV A Vel		m/s
MV E/A Ratio		
E'		m/s

A'		m/s
E/E'		
PV Vmax	B6	m/s
PV maxPG		mmHg
AV Vmax		m/s
AV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

Patient
Name: B6
Species: Canine
Black/Tan Female (Spayed) Doberman
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

Admit Date B6 3 PM
Discharge D

Diagnoses:
Mild decreased contractile function

Clinical Findings:
Thank you for bringing B6 **to Tufts for her recheck echocardiogram (ultrasound of the heart).**

On physical examination today B6 **vital parameters (heart rate, respiratory rate, and temperature) were within normal limits. We performed an echocardiogram (ultrasound of the heart) in order to reassess her mild decreased contractile function. As we discussed, just by looking at the pictures everything appeared stable. However, when we got the official measurements, the chambers of her heart measured slightly bigger than previously and her contractile function measures slightly lower as well.**

As we discussed it is possible that those changes are just a variation of normal for B6 **. However, we cannot rule out that this is the early sign of dilated cardiomyopathy. In order to get more information on her cardiac status, we submitted a blood test called NT-proBNP. We will have the results by tomorrow and will call you in order to discuss the next step for** B6 **.**

Monitoring at home:
B6

B6

Diet Recommendations:
Please continue feeding B6 **her Purina Pro Plan Weight Management dry food and Hill's Science Diet adult beef and barley entree. These foods are low in sodium and do not have low calories despite the name.**

Exercise Recommendations:
B6 **does not need any exercise restriction at this time.**

Recommended Medications:
B6 **does not need any cardiac medications at this time.**

Recheck Visits:
A recheck appointment March 6th 11 am with B6 **At this time we will recheck an echocardiogram.**

Thank you for entrusting us with B6 **care. Please contact our Cardiology liaison at (508)-887-4696 or email us at cardiovet@tufts.edu for scheduling and non-emergent questions or concerns.**

Sincerely,
B6

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

Patient ID: B6
B6 Canine
rs Old Female (Spayed) Doberman
Black/Tan

Cardiology Appointment Report

Date: 12/12/2018

Attending Cardiologist:
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

Presenting Complaint:
Mild MMVD
Mild decreased contractile function R/O diet-related vs. primary DCM related mild decrease in contractile function vs normal variation
DCM Study

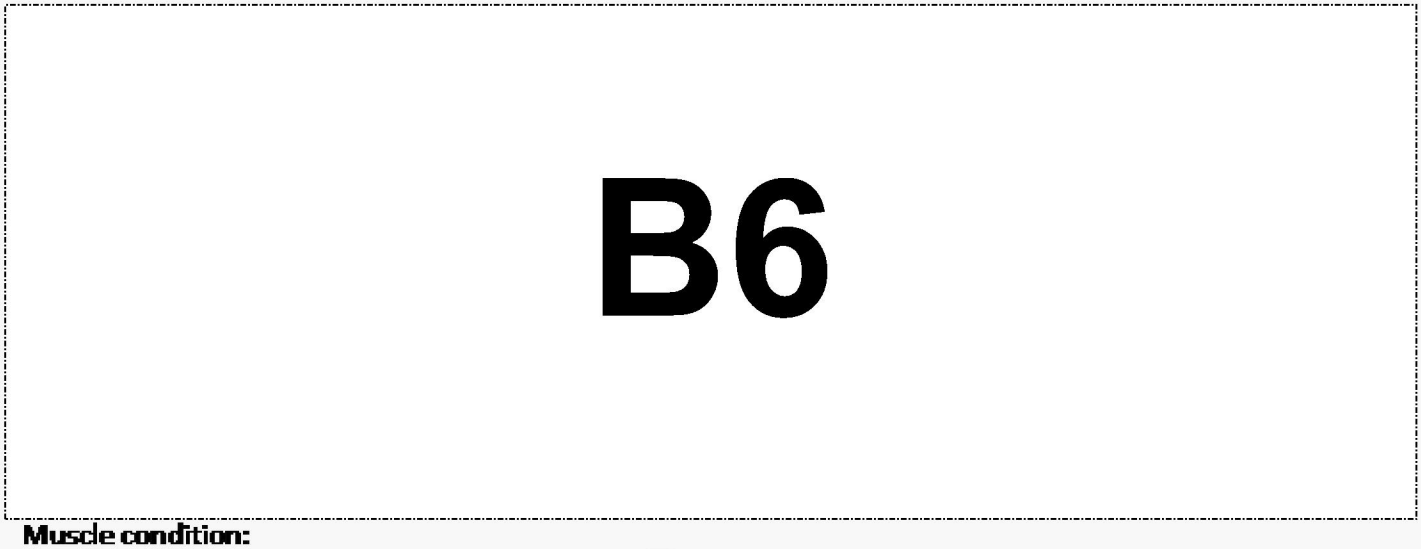
B6

General Medical History:
Normal behavior, eating and drinking well, no v/d/s, occasional coughing, no more than normal
No more voiding uncontrollably in sleep, some leaking, but O feels urinary incontienence has greatly improved with diet

Diet and Supplements:
Purina Pro Plan (Weight Management) 1.5c AM w/ Hill's Sci Diet canned (1/4 can) AM and PM, 1 cup afternoon
Has stopped Fish Oil - has questions about causing bloat

Cardiovascular History:

Prior CHF diagnosis? N
Prior heart murmur? N
Prior ATE? N
Prior arrhythmia? Sinus arrhythmia
Monitoring respiratory rate and effort at home? Not as much, frequent panting
Cough? Occasional, no change from prior
Shortness of breath or difficulty breathing? N
Syncope or collapse? N
Sudden onset lameness? N
Exercise intolerance? N - will occasionally wheeze with cold



Muscle condition:

- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:

Murmur Grade:

- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:

- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:

- [ ] Weak
- [ ] Fair
- [ ] Good
- [x] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:

- [ ] None
- [x] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:

- [ ] Yes
- [ ] Pronounced

- [x] No
- [ ] Intermittent
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
Mild MMVD
Mildly decreased contractile function r/o diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Diagnostic plan:
- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:
General/2-D findings:
Normal LV wall thickness with fair contractile function that is slightly decreased compared to previously. The LV cavity is slightly bigger than previously although not when compared with SMOD. The LA is normal in size. The MV is mildly thickened with no prolapse or ruptured chordae. The PA is smaller than the aorta. The RH is subjectively within normal limits. No pleural or pericardial effusion. No B-lines.

Doppler findings:
No MR
No TR
Normal aortic velocity
Normal pulmonic velocity

Mitral inflow:
- [ ] Summated
- [ ] Normal
- [x] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:
Sinus rhythm during the echocardiogram.

Assessment and recommendations:
Subjectively today's echo appeared very similar than previously but when comparing the numbers it appears that the contractile function is slightly decreased. Depending on which measurement is assess, the LV cavity appears stable to slightly bigger. It is unclear if the changes visualized today are just a variant of normal for this patient versus true progression of a heart disease. The patient was switched

diet since the last appointment and Taurine level were also normal. Since the significance of today's findings is unclear, an NT-proBNP was submitted today. If the level is higher than normal for a Doberman (i.e. >550) then we would most likely recommend starting pimobendan BID. A recheck echocardiogram is recommended in 3 months or sooner if the patient develops clinical signs consistent with worsening heart disease such as increased RR/RE, cough, exercise intolerance, or syncope.

Final Diagnosis:
- Very early DMVD
- Mild decreased contractile function r/o diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Heart Failure Classification Score:
ISACHC Classification:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

M-Mode		
IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
Max LA		cm

2D		
SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm

LVPWs	B6	cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LVId A4C		cm
LVEDV MOD A4C		ml
LVIs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

Patient
Name: B6
Species: Canine
Black/Tan Female (Spayed) Doberman
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: B6

Attending Cardiologist:
B6

Cardiology Resident:
B6

B6

Cardiology Technician:
B6

Student: B6

Admit Date: 3/6/2019 10:59:12 AM
Discharge Date: 3/6/2019

Diagnoses:
Mild decreased contractile function that is improved compared to previously.

Case summary:
Thank you for bringing B6 to Tufts cardiology service for her recheck echocardiogram.

Today we performed a recheck echocardiogram (ultrasound of the heart) which revealed that B6 heart is slightly smaller than before and her contractile function appears better than before although still not completelyet normal. This is excellent news! At this time it is unclear if the changes visualized are secondary to the recent addition of pimobendan versus the recent change in diet.

As discussed, B6 has occasional isolated premature beats on electrocardiogram (ECG, which measures the electrical rhythms of the heart), meaning that her heart occasionally beats sooner than it should. Today we discussed possible diagnostics – such as a Holter monitor, which records an ECG over 24 hours – and possible treatment options. At this time you elect to use the Holter monitor prior to starting any treatment. We will send B6 home wearing the monitor and a journal to record her activities. We will see B6 again tomorrow to remove the monitor. It will take 1-2 weeks to get the ECH recording analysis finalized and we will contact you in order to decide if we need to start new cardiac medications or not.

Monitoring at home:
B6

B6

Recommended Medications:

B6

Diet suggestions:
Please continue feeding B6 **her Purina Pro Plan Weight Management dry food and Hill's Science Diet adult beef and barley entree. These foods are low in sodium but contain appropriate calories.**

Exercise Recommendations:
B6 **does not need any exercise restriction at this time.**

Recheck Visits:
Please bring B6 **in tomorrow to have her Holter monitor removed.**

We would like B6 **to have a recheck echocardiogram in 3 months as part of the DCM study, as long as she continues to do well at home. She has an appointment schedule with** B6 **June 11th at 11am.**

Thank you for entrusting us with B6 **care. Please contact our Cardiology liaison at (508)-887-4696 or email us at cardiovet@tufts.edu for scheduling and non-emergent questions or concerns.**

Sincerely,
B6

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

Patient ID: B6
B6 Canine
ears Old Female (Spayed) Doberman
Black/Tan

Cardiology Appointment Report
ENROLLED IN DCM DIET STUDY

Date: 3/6/2019

Attending Cardiologist:

B6

Cardiology Resident:

B6

(primary)

Cardiology Technician:

B6

Studen B6

Presenting Complaint:
Mild MMVD
Mild decreased contractile function R/O diet-related vs. primary DCM related mild decrease in contractile function vs normal variation
DCM Study

B6

General Medical History:
Doing well at home, owner has no concerns. Asymptomatic.

Diet and Supplements:
Purina Pro Plan (Weight Management) 1.5c AM w/ Hill's Sci Diet canned (1/4 can) AM and PM, 1 cup afternoon

Cardiovascular History:
Prior CHF diagnosis? N

Prior heart murmur? N
Prior ATE? N
Prior arrhythmia? Sinus arrhythmia
Monitoring respiratory rate and effort at home? Not as much, frequent panting
Cough? Occasional, no change from prior
Shortness of breath or difficulty breathing? N
Syncope or collapse? N
Sudden onset lameness? N
Exercise intolerance? N

Current Medications Pertinent to CV System:
Medication: Thyro-Tabs 0.8 mg tablets
Formulation/Tab Size: 1 tab PO BID
Administration Frequency: q 12 hrs
Need refills? No

Medication: Pimobendan
Formulation/Tab Size: 10mg tiny tab
Administration Frequency: 1 tab PO BID
Need refills? Just got refilled, via Wedgewood

Cardiac Physical Examination:
General PE:
MM Color and CRT: pink, moist, crt <2s
BCS (1-9): 4
BW (kg): 35.8 kg

Heart rate: 144
Respiratory rate: panting
Temp (if possible):

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [x] Good
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [ ] None
- [x] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:

- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:

- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [x] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:

- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:

Mild MMVD

Mildly decreased contractile function r/o diet-related vs. primary DCM related mild decrease in contractile function vs normal variation

Elevated proBNP

Diagnostic plan:

- [x] Echocardiogram
- [ ] Chemistry profile
- [x] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:

General/2-D findings:

Normal LV wall thickness with fair contractile function that is slightly improved compared to previously. The LV cavity is smaller today compared to the previous examination on all the measurements. The LA is normal in size. The MV is mildly thickened with no prolapse or ruptured chordae. The PA is smaller than the aorta. The RH is subjectively within normal limits. No pleural or pericardial effusion. No B-lines.

Doppler findings:

No MR

No Tr

Normal aortic velocity

Normal pulmonic velocity

Mitral inflow:

- [ ] Summated
- [ ] Normal
- [x] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:

Heart rate: 160

P wave height: 0.2 mV (<0.4 mV)

P wave duration: 0.04s (<0.04s)

PR interval: 0.08s (0.06-0.13s)
R wave height: 1.5 mV (< 3.0 mv)
QRS duration: 0.08s (<0.06s) QRs morphology
RR interval: 0.4s
QT interval: 0.20s (0.15-0.25s)
MEA: +30
Interpretation: Sinus tachycardia with frequent APCs and left-sided, isolated, VPCs

Assessment and recommendations:
Echocardiogram reveals improvement of the cardiac dimensions and contractile function. All of the measurements obtained today were improved compared to the previous examination. It is unclear if the changes visualized are secondary to the start of pimobendan vs. being on a new diet for a longer period of time. B6 did had relatively frequent VPCs today which were all isolated. However, due to her breed and predisposition for arrhythmia, there is some concern that she has more malignant arrhythmia. A Holter was placed today in order to assess the amount and severity of arrhythmia and decide if we want to start a beta-blocker vs. sotalol vs. amiodarone. No blood was pulled today. A recheck echocardiogram and ECG are recommended in 3 months or sooner if the patient develops clinical signs consistent with worsening heart disease.

Final Diagnosis:
- Very early DMVD
- Mild decreased contractile function that is improved compared to last examination.

Heart Failure Classification Score:
ISACHC Classification:

- ☐ Ia
- ☑ Ib
- ☐ II
- ☐ IIIa
- ☐ IIIb

ACVIM Classification:

- ☐ A
- ☐ B1
- ☑ B2
- ☐ C
- ☐ D

M-Mode	B6	
IVSd		cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
TAPSE		cm

EPSS	B6	cm
M-Mode Normalized		
IVSdN	B6	(0.290 - 0.520)
LVIDdN		(1.350 - 1.730)
LVPWdN		(0.330 - 0.530)
IVSsN		(0.430 - 0.710)
LVIDsN		(0.790 - 1.140)
LVPWsN		(0.530 - 0.780)
Ao Diam N		(0.680 - 0.890)
LA Diam N		(0.640 - 0.900) !
2D		
SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LV Major		cm
LV Minor		cm
Sphericity Index		
LVLd A4C		cm
LVEDV MOD A4C		ml
LVLs A4C		cm
LVESV MOD A4C		ml
LVEF MOD A4C		%
SV MOD A4C		ml
Doppler		
MV E Vel	B6	m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
S'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s

PV maxPG

B6

mmHg

Product Name	Lot Number or ID	Best By Date
Freshpet select roasted meals chicken flavor		

Sender information

B6

USA

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-383014

ICSR:	2064400
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-21 20:24:19 EDT
Reporter is the Animal Owner:	Yes

Reported Problem:

Problem Description:	My dog was diagnosed with congestive heart failure and cardiomyopathy. He eats freshpet dog food. I don't know if that's why he got it but I've read some dog foods can cause this, especially grain free. This has oats so I don't know if that's considered grain free or not but in case it is helpful I am sharing.
Date Problem Started:	01/03/2016
Concurrent Medical Problem:	Yes
Outcome to Date:	Worse/Declining/Deteriorating

Product Information:

Product Name:	Freshpet select roasted meals chicken flavor
Product Type:	Pet Food
Lot Number:	
Package Type:	BAG
Package Size:	5.5 Pound
Possess Unopened Product:	Yes
Storage Conditions:	I buy a new bag of freshpet every week and a half
Product Use Information:	

Description:	He has been on the same type of food for probably four or five years. I don't know if this food contribute to him developing dilated cardiomyopathy and congestive heart failure or not. He also has a heart murmur. But then I heard that that grain-free dog food can be related to congestive heart failure. Also I heard it's not that common in a shitzu he is a shitzu bichon dog. I just want to report it in case there may be some sort of connection.
Product Use Stopped After the Onset of the Adverse Event:	No
Perceived Relatedness to Adverse Event:	Possibly related

Manufacturer /Distributor Information:	
Purchase Location Information:	

Animal Information:

Name:	B6
Type Of Species:	Dog
Type Of Breed:	Shih Tzu
Gender:	Male
Reproductive Status:	Neutered
Weight:	20 Pound
Age:	10 Years
Assessment of Prior Health:	Good
Number of Animals Given the Product:	1

	Number of Animals Reacted:	1	
	Owner Information:		
	Healthcare Professional Information:	Practice Name:	B6
		Contact: Name:	B6
		Phone:	
		Type of Veterinarian:	Primary/regular veterinarian
Sender Information:	Name:		
	Address:	B6	
		United States	
	Contact:	Phone:	B6
		Email:	
	Reporter Wants to Remain Anonymous:	No	
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
	Reported to Other Parties:	None	
Additional Documents:			

B5

Document properties

Author: B6
Company
Template: Normal.dotm
Page count: 1
Paragraph count: 48
Line count: 63
Word count: 395
Character count (spaces excluded): 3536
Character count (spaces included): 4090

From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>

To: Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Peloquin, Sarah; Queen, Jackie L; Rotstein, David

Sent: 3/21/2019 4:17:43 PM

Subject: DCM cases 3/21/2019 1200

Attachments: 2064344-report.pdf; Acana Lamb and Apple singles: Lisa Freeman - EON-372606; Acana Lamb and Apple singles: Lisa Freeman - EON-382951; Acana Puppy and Junior: B6 EON-382870; American Journey Grain-free Salmon & Sweet Potato Recipe: B6 EON-382903; American Journey-Salmon and Sweet Potato: B6 EON-382867; American Journey-Salmon and Sweet Potato: B6 EON-382867; CANIDAE- ALL LIFE STAGES-CHICKEN MEAL & RICE FORMULA--DRY DOG FOOD: Lisa Freeman - EON-381040; CANIDAE- ALL LIFE STAGES-CHICKEN MEAL & RICE FORMULA--DRY DOG FOOD: Lisa Freeman - EON-382878; CANIDAE- ALL LIFE STAGES-CHICKEN MEAL & RICE FORMULA--DRY DOG FOOD: Lisa Freeman - EON-382884; FROMM Salmon Tunalini: B6 B6 EON-382921; Homecooked diet - see diet history in medical record: Lisa Freeman - EON-374789; Homecooked diet - see diet history in medical record: Lisa Freeman - EON-382947; Horizons pulsar grain free diet: B6 EON-382952; Kirkland Signature Nature's Domain Cat Food: B6 EON-382911; Nutrisource Large breed puppy Grain free: S B6 - EON-382807; Nutrisource Large breed puppy Grain free: B6 - EON-382807; Nutro MAX Adult Recipe With Farm Raised Chicken Mini Chunk Dry Dog Food: B6 EON-382838; Taste of the Wild Grain Free: B6 B6 EON-382849

Please note:

American Journey (382867)- histopath findings included. B5

B5

B5

B5

FDA-CVM-FOIA-2019-1704-002555

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 12/3/2018 2:36:39 PM

Subject: Acana Lamb and Apple singles: Lisa Freeman - EON-372606

Attachments: 2059540-report.pdf; 2059540-attachments.zip

A PFR Report has been received and PFR Event [EON-372606] has been created in the EON System.

A "PDF" report by name "2059540-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2059540-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-372606
ICSR #: 2059540
EON Title: PFR Event created for Acana Lamb and Apple singles; 2059540

AE Date	11/08/2018	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Irish Wolfhound		
Age	3 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2059540
Product Group: Pet Food
Product Name: Acana Lamb and Apple singles
Description: Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable

Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Acana Lamb and Apple singles		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information

B6

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-372606

ICSR:	2059540		
Type Of Submission:	Initial		
Report Version:	FPSR.FDA.PETF.V.V1		
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)		
Reporting Type:	Voluntary		
Report Submission Date:	2018-12-03 09:27:13 EST		
Reported Problem:	**Problem Description:**	Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months	
	Date Problem Started:	11/08/2018	
	Concurrent Medical Problem:	Yes	
	Pre Existing Conditions:	Chronic diarrhea Hx of anaplasmosis	
	Outcome to Date:	Stable	
Product Information:	**Product Name:**	Acana Lamb and Apple singles	
	Product Type:	Pet Food	
	Lot Number:		
	Package Type:	BAG	
	Product Use Information:	**Description:**	Fed since 2016
	Manufacturer /Distributor Information:		
	Purchase Location Information:		
Animal Information:	**Name:**	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Irish Wolfhound	
	Gender:	Male	
	Reproductive Status:	Intact	
	Weight:	82.7 Kilogram	
	Age:	3 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:	**Owner Information provided:**	Yes
		Contact:	**Name:** B6 **Phone:** **Email:**
		Address:	B6 United States
	Healthcare Professional Information:	**Practice Name:**	Tufts Cummings School of Veterinary Medicine
		Contact:	**Name:** Lisa Freeman **Phone:** (508) 887-4523

		Email:	lisa.freeman@tufts.edu
		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States

Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	

Additional Documents:		
	Attachment:	**B6** compiled records.pdf
	Description:	Medical records
	Type:	Medical Records

B6

All Medical Records

Client:
Address: B6

Patient: B6
Breed: Irish Wolfhound
DOB: B6

Species: Canine
Sex: Male

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Emergency

SOAP Text Mar 28 2016 10:34PM - B6

B6

Exam:

Client: B6
Patient:

B6

Referral Diagnostics:

Diagnostics Completed:

Diagnostics Pending:

Treatments Completed:
0.2mg/kg butorphanol SQ as an antitussive

Assessment (A)
A1: Infectious tracheobronchitis - recent exposure to other dogs, young dog

Plan (P)
TGH
600 doxycycline PO BID
10mg hycodan PO BID PRN for coughing

Communication Summary: Owner was concerned for pneumonia - discussed with owner that all of B6 signs were upper respiratory and that while infectious tracheobronchitis can progress to pneumonia, B6 s does not show any signs of that at this time. He seems very stable and I recommended treating with oral antibiotics and and antitussive to keep him from coughing so much. Owner ok with this plan, discussed reasons he would need to be rechecked or signs that B6 us was getting worse.

Additional requests submitted:

Estimate given: $ Deposit collected: $

Initial Complaint:
Emergency

SOAP Text Jun 7 2017 10:44PM - B6

6/8/2017 5:57:00 AM EXAM, GENERAL

Ingestion of wooden skewer this evening

Subjective (S)

Client: B6
Patient:

B6

Objective (O)

B6

Assessment (A)
A1: Skewer Ingestion

Plan (P)

B6

SOAP completed by B6 DVM

6/7/2017 10:45:00 PM

B6

Initial Complaint:
wooden skewer ingestion

SOAP Text Jun 8 2017 12:55PM - B6

6/8/2017 12:57:58 PM NEW VISIT (ER)

Doctor: B6
Student: ---
Presenting complaint: Ate wooden skewer ~12 inches, with beef teriyaki, doesn't think he chewed it ~12-18 hours ago
Referral visit? seen by ER last night
Diagnostics completed prior to visit -

Client: B6
Patient:

HISTORY:
B6 2yo IM Wolfhound presenting for ingestion of ~12" wooden skewer 12-18 hours ago. Seen by ER last night right after, attempted to induce emesis with apomorphine - no emesis. Discussed with them imaging vs. endoscopy vs. surgery - at the time owner didn't have money for a deposit and sent home with high fiber diet and instructions to monitor. Since discharge B6 vomited small amount last night, had decreased appetite this morning. Owner got together money for a deposit today is is interested in addressing the issue now.

EXAM:

B6

Assessment (A)
A1: Skewer Ingestion

PLAN:

B6

SOAP approved (DVM to sign): B6 DVM MS

Initial Complaint:
New - echo, low taurine

SOAP Text Nov 8 2018 12:33PM - B6

Client:
Patient: B6

Disposition/Recommendations

B6

Client:	B6
Veterinarian:	
Patient ID:	337144
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Irish Wolfhound
Sex:	Male
Age:	B6 Years Old

Lab Results Report

Nova Full Panel-ICU **6/8/2017 1:13:25 PM** **Accession ID:** B6

Test	Results	Reference Range	Units
SO2%	B6	94 - 100	%
HCT (POC)		38 - 48	%
HB (POC)		12.6 - 16	g/dL
NA (POC)		140 - 154	mmol/L
K (POC)		3.6 - 4.8	mmol/L
CL(POC)		109 - 120	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
MG (POC)		0.1 - 0.4	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
CREAT (POC)		0.2 - 2.1	mg/dL
TCO2 (POC)		0 - 0	mmol/L
nCA		0 - 0	mmol/L
nMG		0 - 0	mmol/L
GAP		0 - 0	mmol/L
CA/MG		0 - 0	mol/mol
BEecf		0 - 0	mmol/L
BEb		0 - 0	mmol/L
A		0 - 0	mmHg
NOVA SAMPLE		0 - 0	

Client:
Patient: B6

FiO2		0 - 0	%
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

B6

Nova Full Panel-ICU **11/8/2018 3:31:21 PM** **Accession ID:** B6 **9454**

Test	Results	Reference Range	Units
Troponin I Research - FHSA	B6	0 - 0.08	mg/dl

B6

stringsoft

Printed Monday, December 03, 2018

Client: B6
Patient:

Administrative Adjustment Form

B6

FOSTER HOSPITAL FOR SMALL ANIMALS
REQUEST FOR DISCOUNT

Date: 04-04-16 Patient ID No: 337144

Requested by: B6 Client Name: B6

TYPE OF DISCOUNT: Animal Name:

☐ Courtesy Allowance (26) ☐ Travis (5)

☐ Professional Discount (28) ☐ Travis Intern Account (5A)

☒ Administrative Adjustment (27)

Clinician to be assigned the deduction: _____
(Must be filled in by Hospital Administration)

☐ Zeus Varia Fund (8):

_____ Dr. Lisa Barber / Dr. Kristine Burgess _____ Date

B6

Justification:

Client unhappy with diagnosis + dog went to another hospital did have pneumonia. We were extremely busy here when dog presented, would have started sedation for chest rads, + not a definite indication at that time.

Reason for Adjustment (Code 1, 2, 3, 4, 5 as noted below): 1, 3

Owner Contacted: Yes (✓) By Whom: B6

Hospital Administrator: _____ Richard Harding _____ Date

Medical Director: _____ Dr. Marston Stanton _____ Date

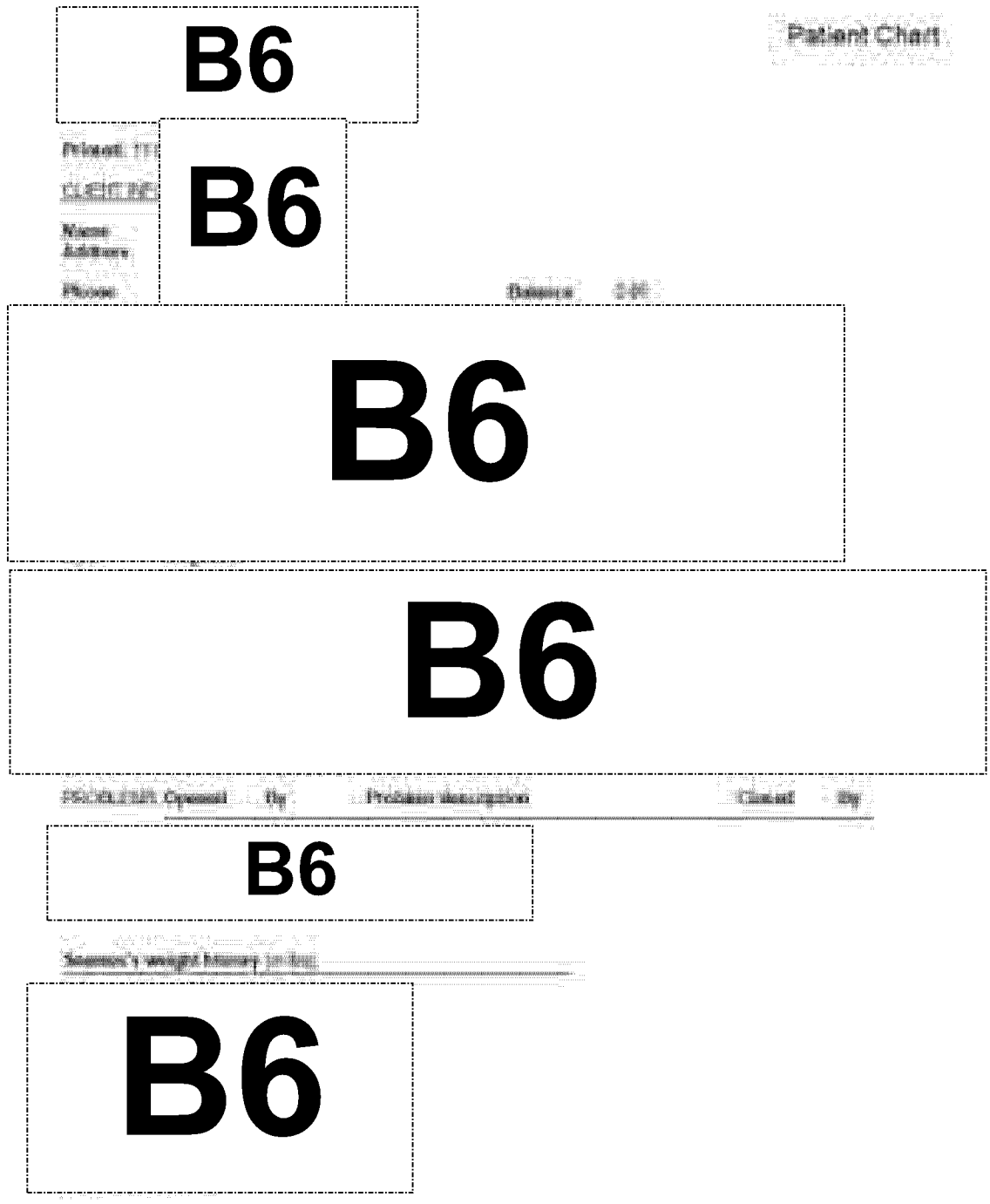
Assoc. Medical Directors: B6 _____ 04-04-16 Date

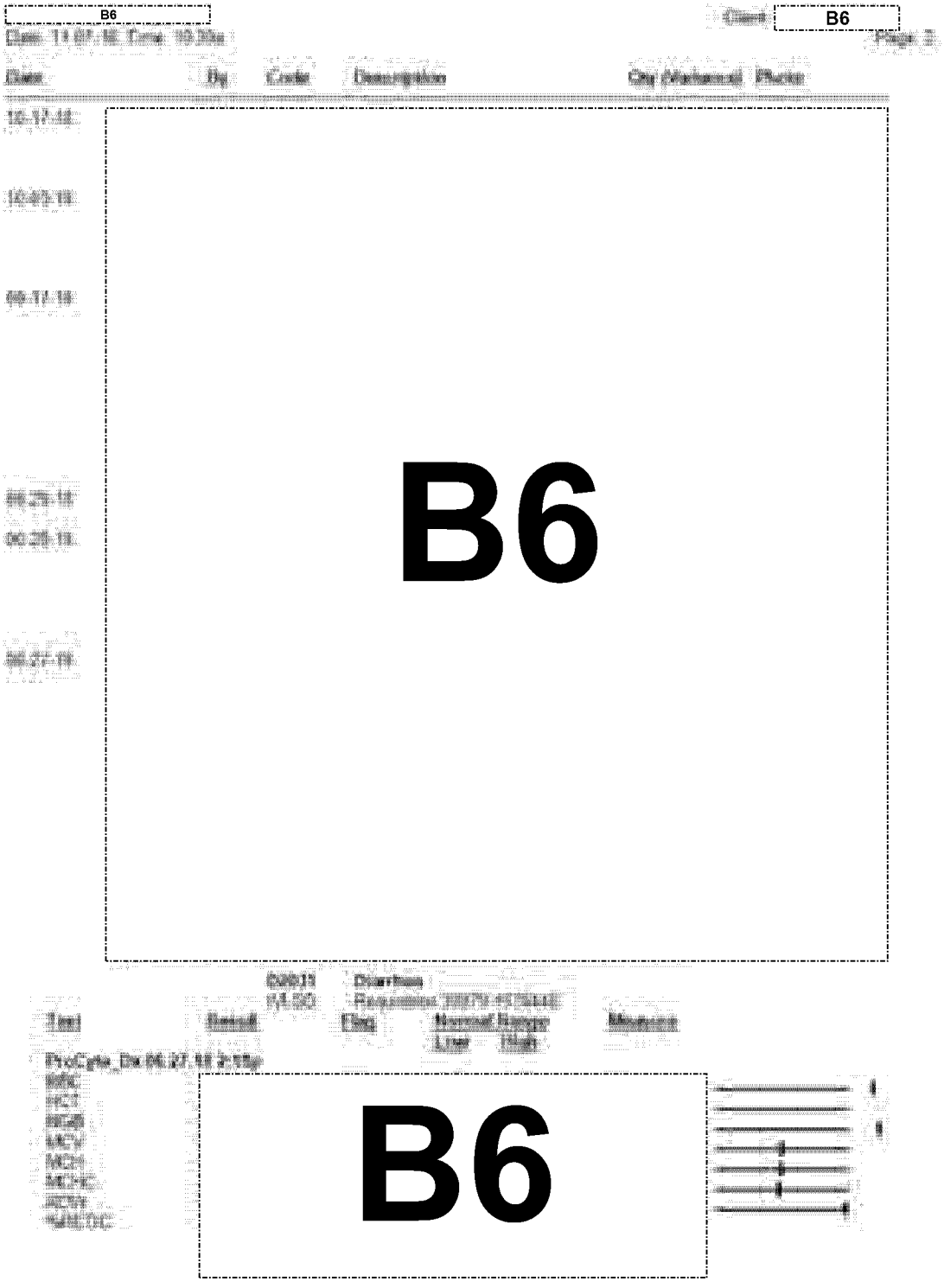
Accounting Manager: _____ Dorothy Dawson _____ Date

Billing Coordinator II: _____ Nancy Cronin _____ Date

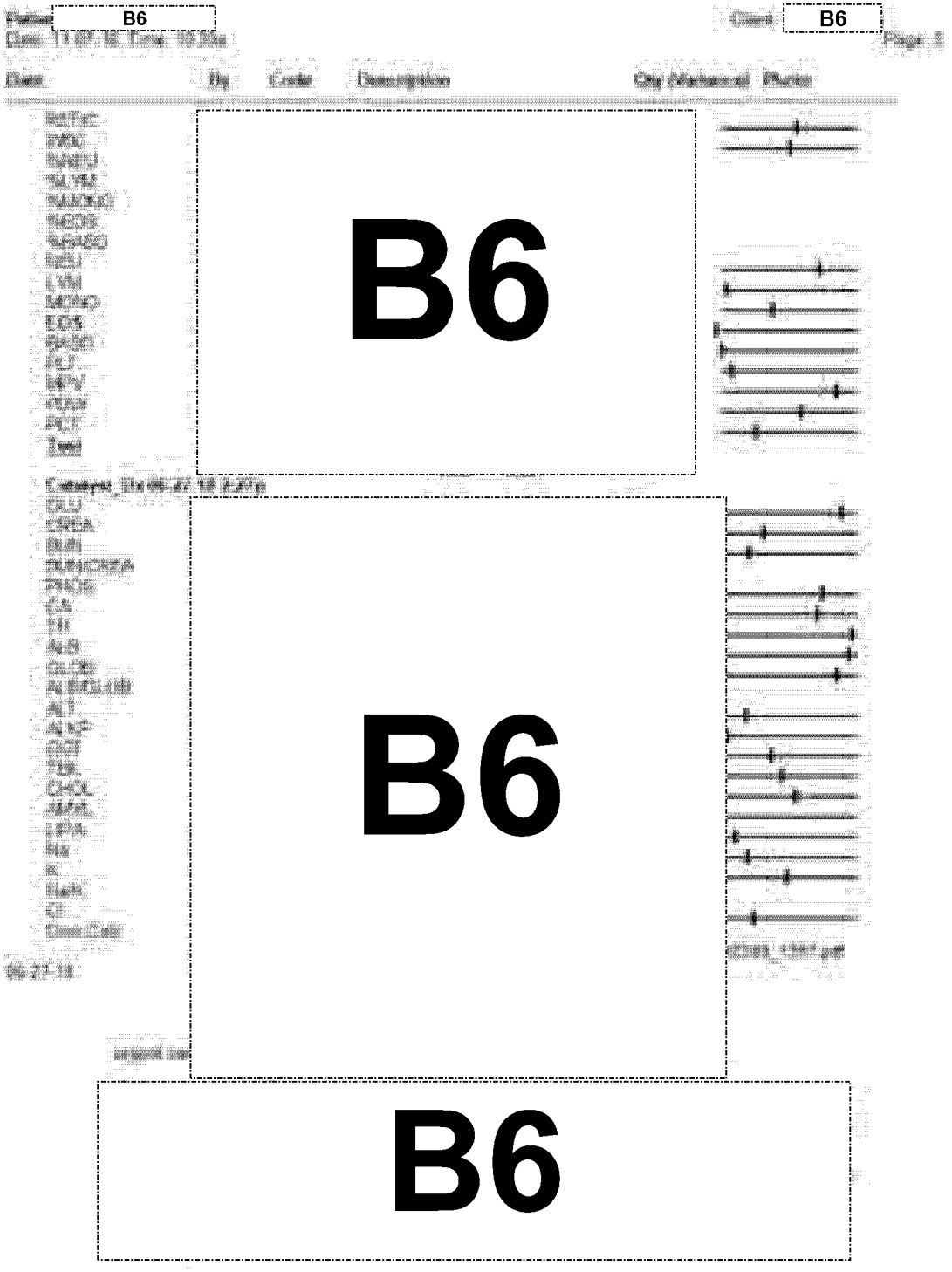
Accounting Asst Supv: (Less than $100) _____ Date

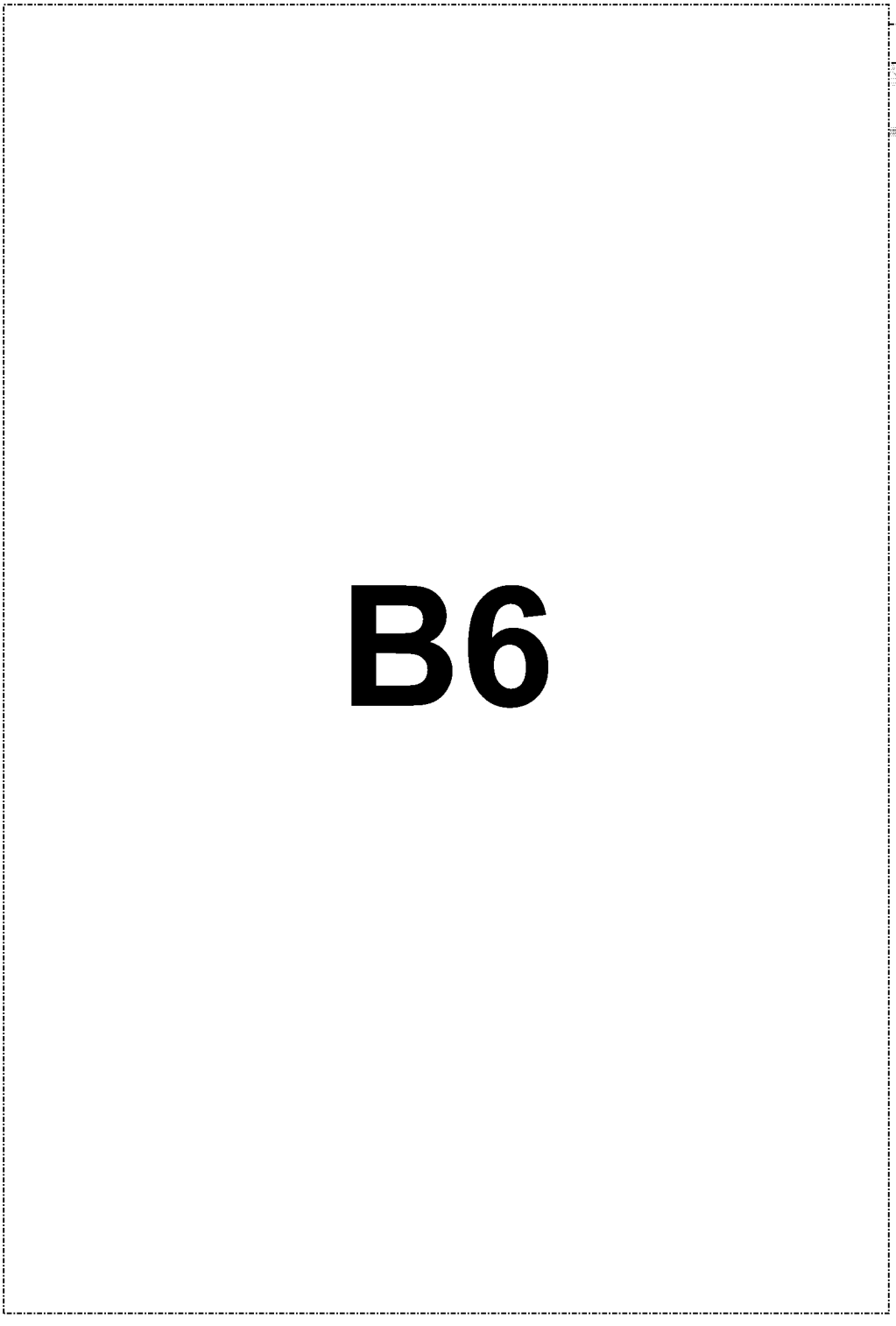
Codes:
1) Communication
2) Misc. Errors / Issues
3) Medical Treatment
4) Financial Asst. Only
5) Unfounded / Goodwill Only





B6 AH records





B6

B6

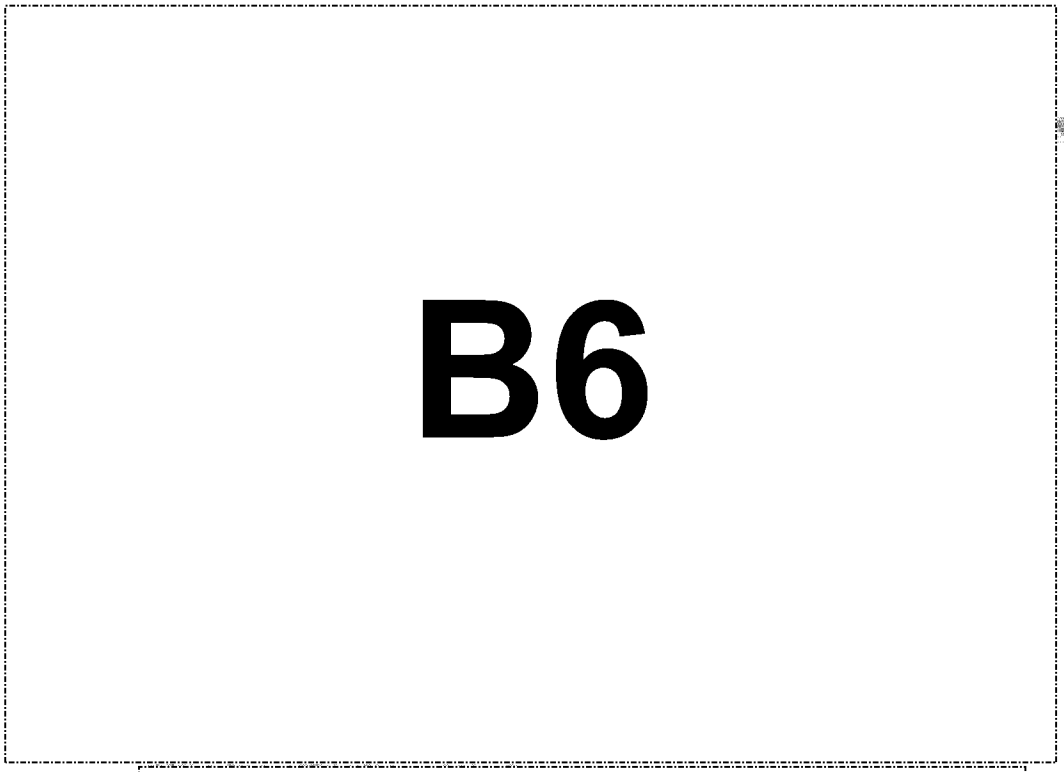
B6

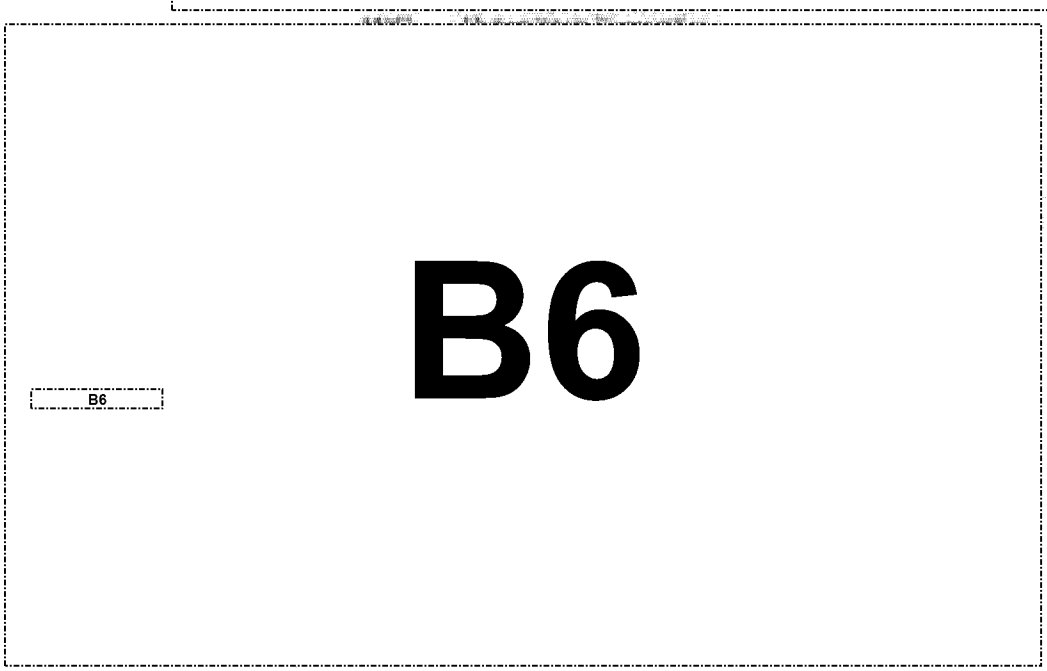
B6

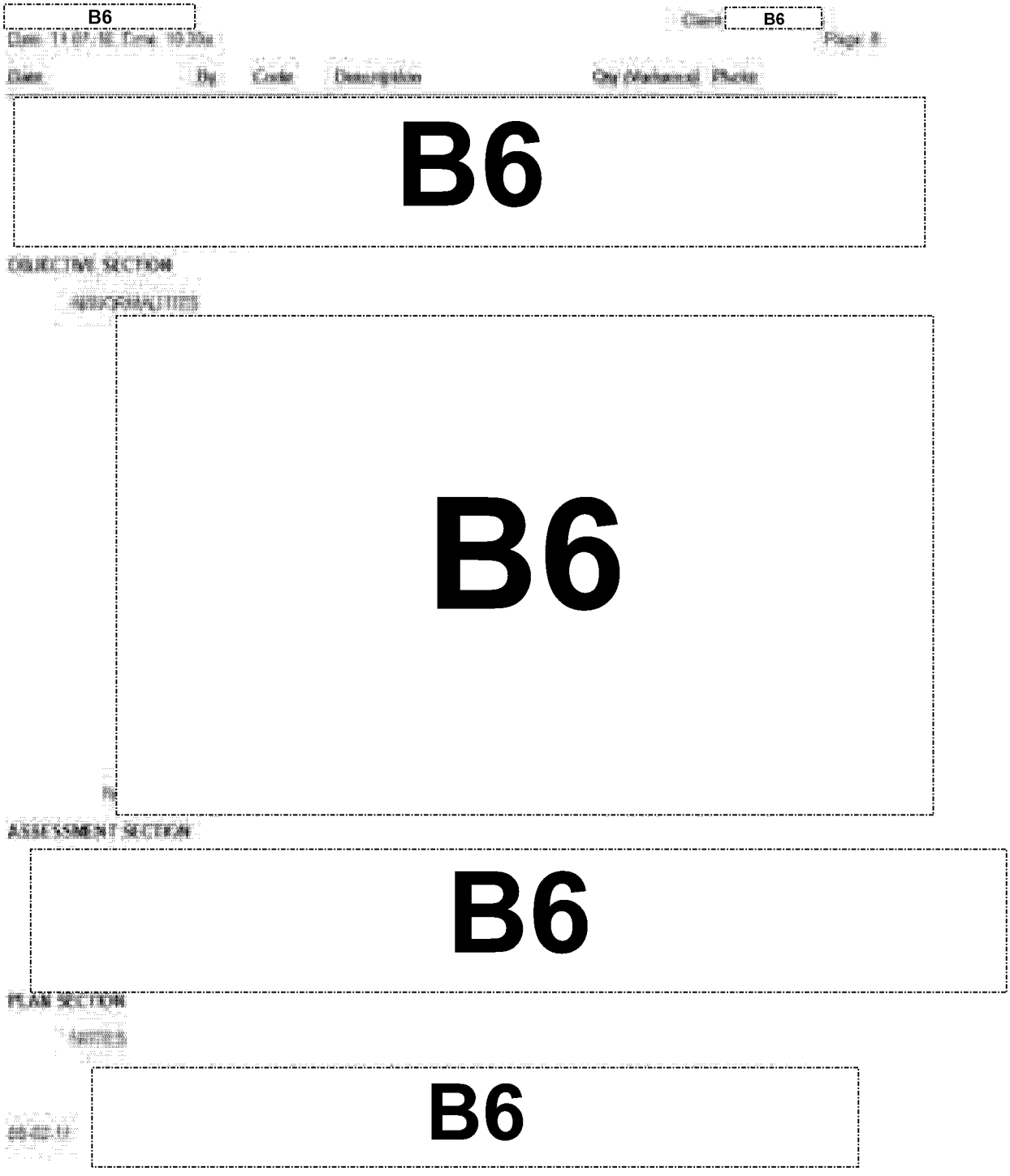
B6

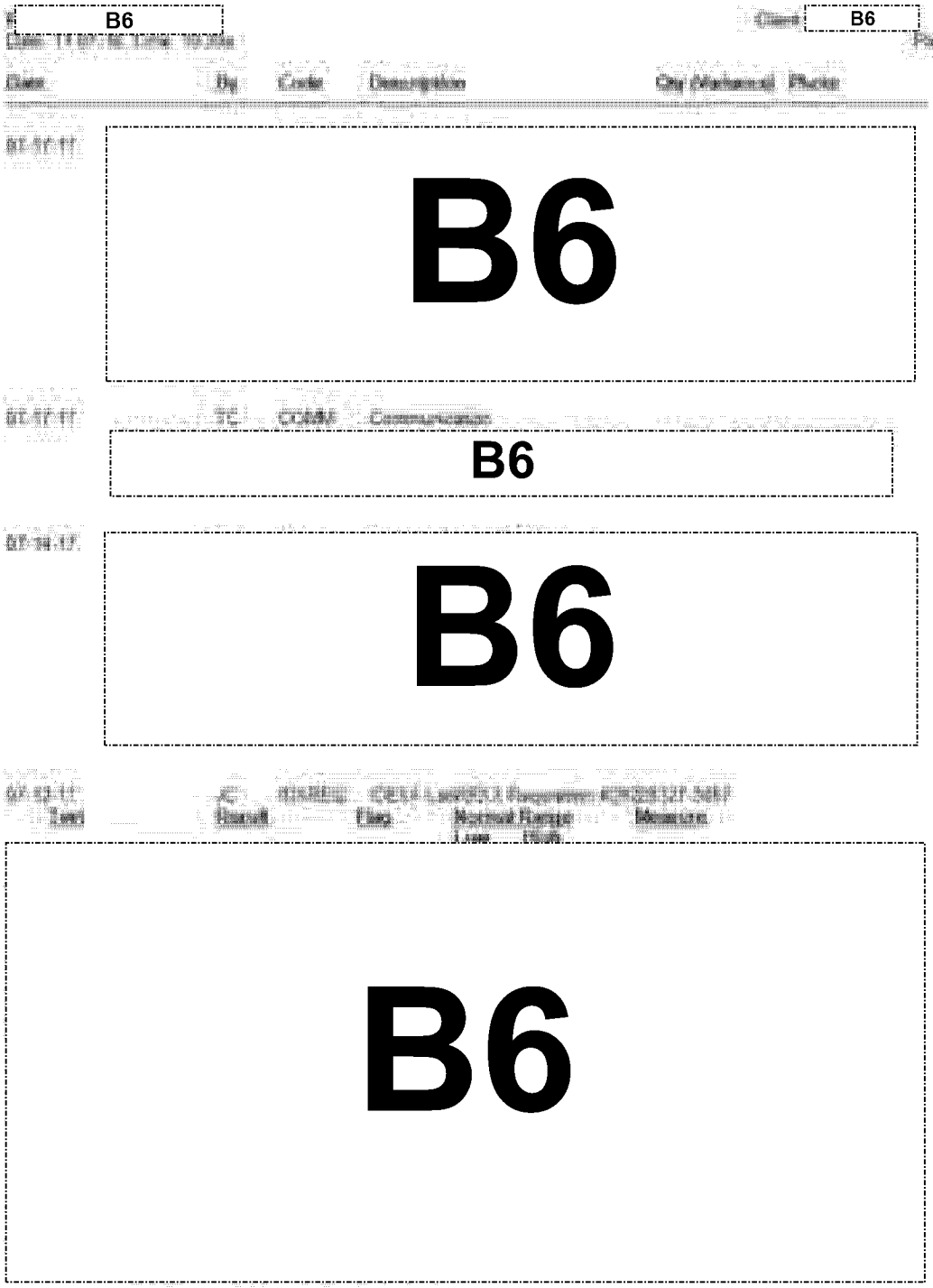
B6

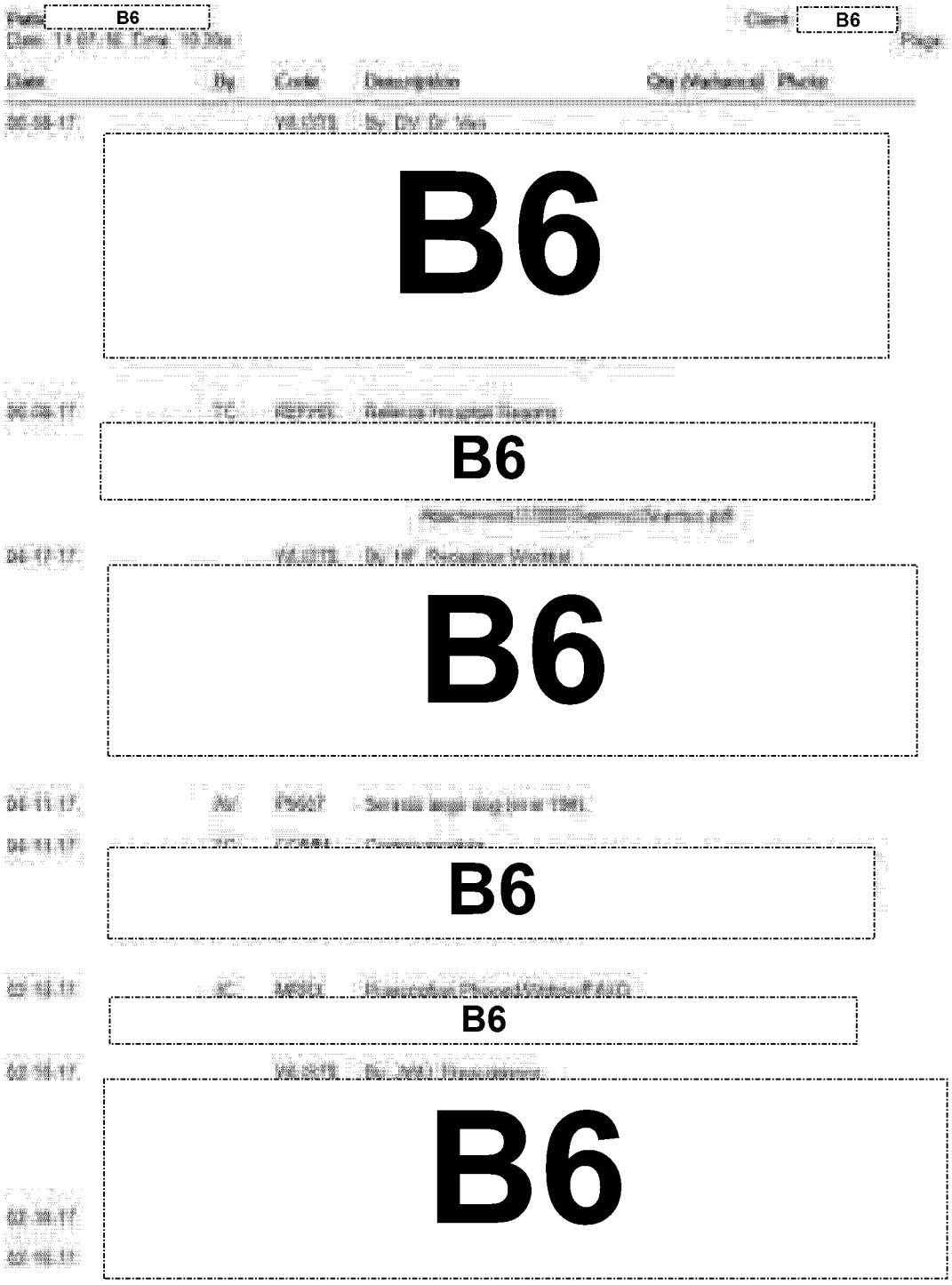
B6 AH records

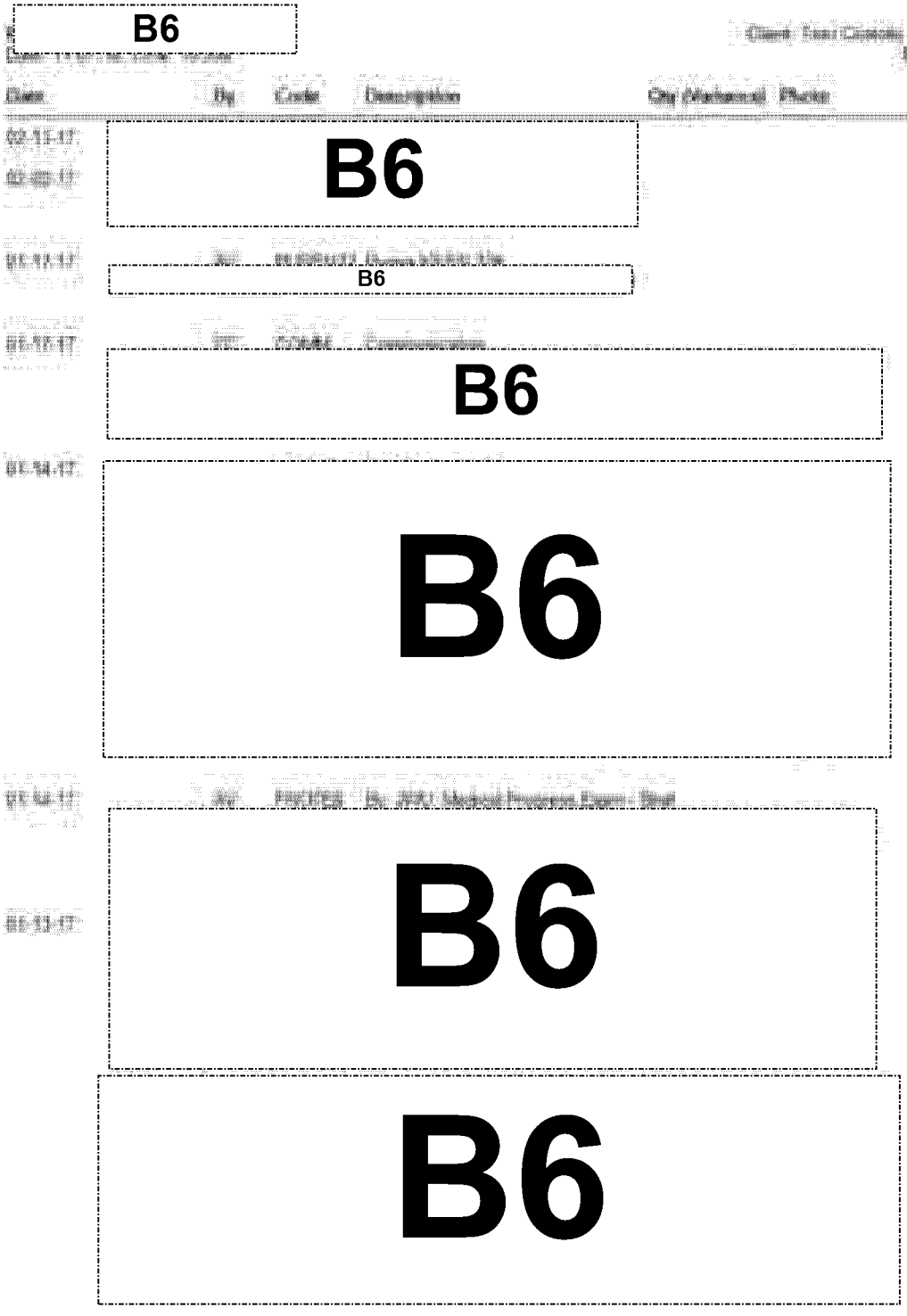












B6

Client B6

Page 11

Date By Code Description Qty Mechanical Photo

Age 20y Weight 12.43 Temp 101.02 Pulse 84.0
CRT: 1 secs

SUBJECTIVE SECTION

B6

OBJECTIVE SECTION

B6

ABNORMALITIES
Mouth

B6

B6

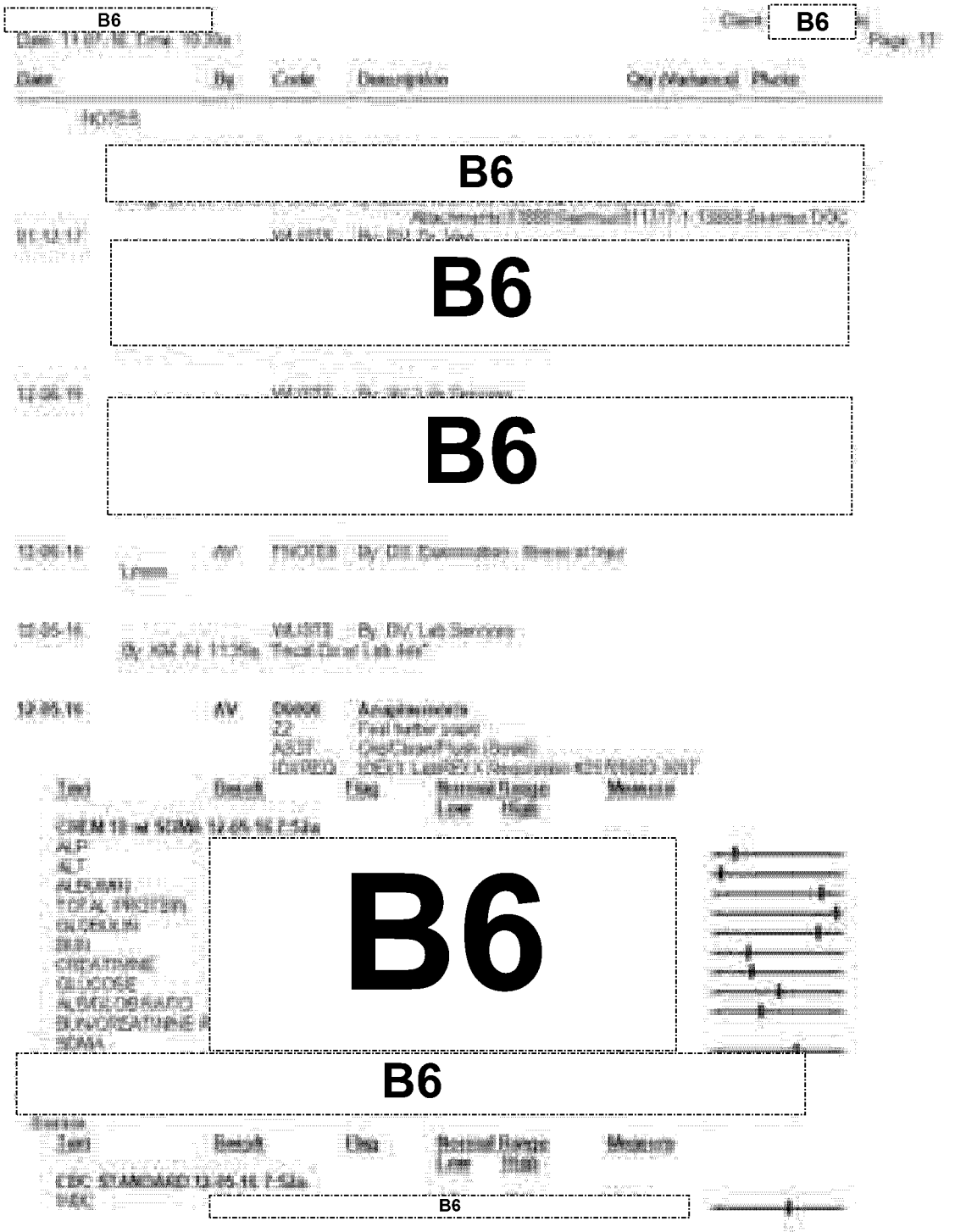
ASSESSMENT SECTION

NOTES

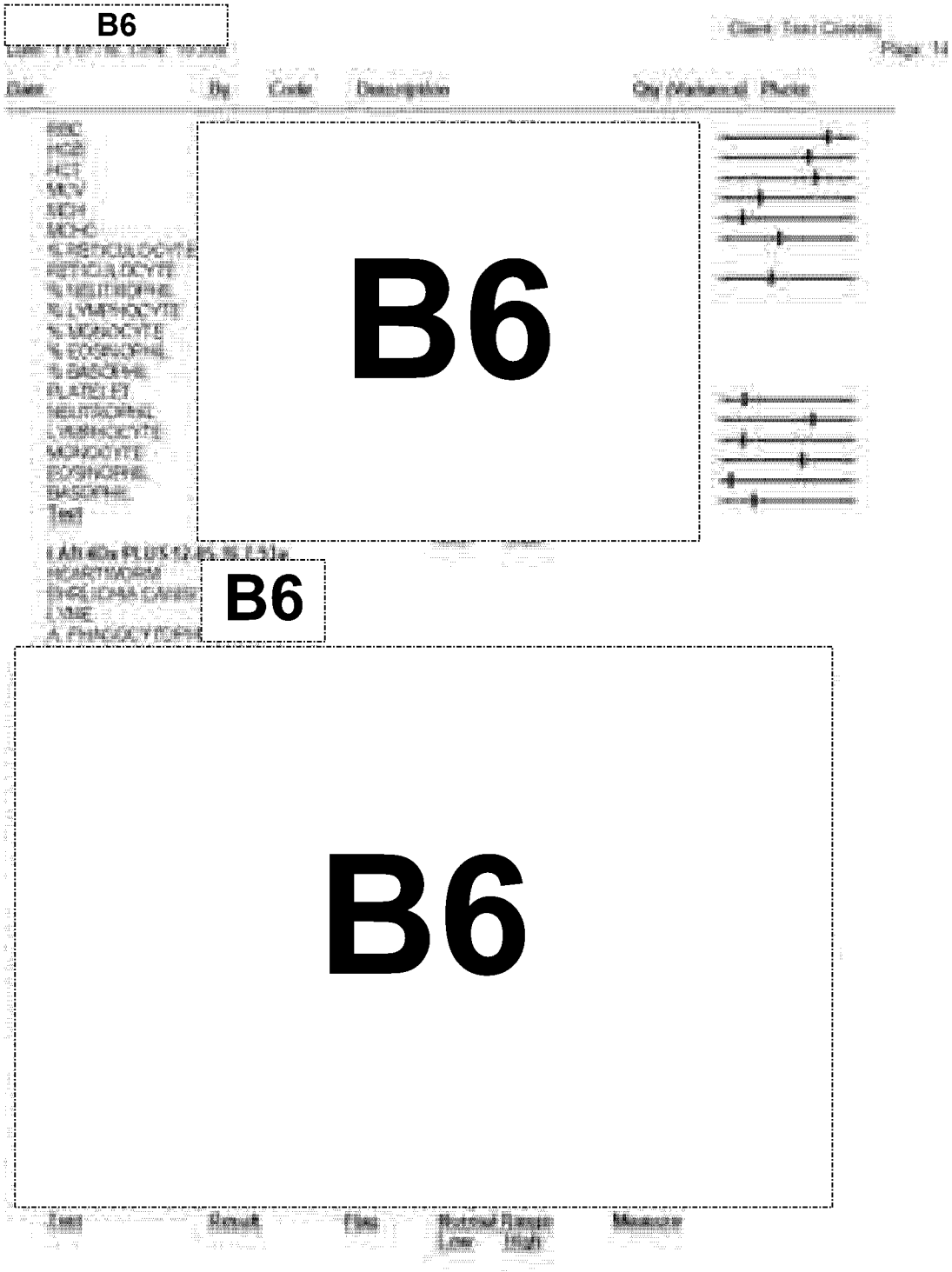
B6

DIAGNOSES
Dentition

PLAN SECTION



B6 **AH records**



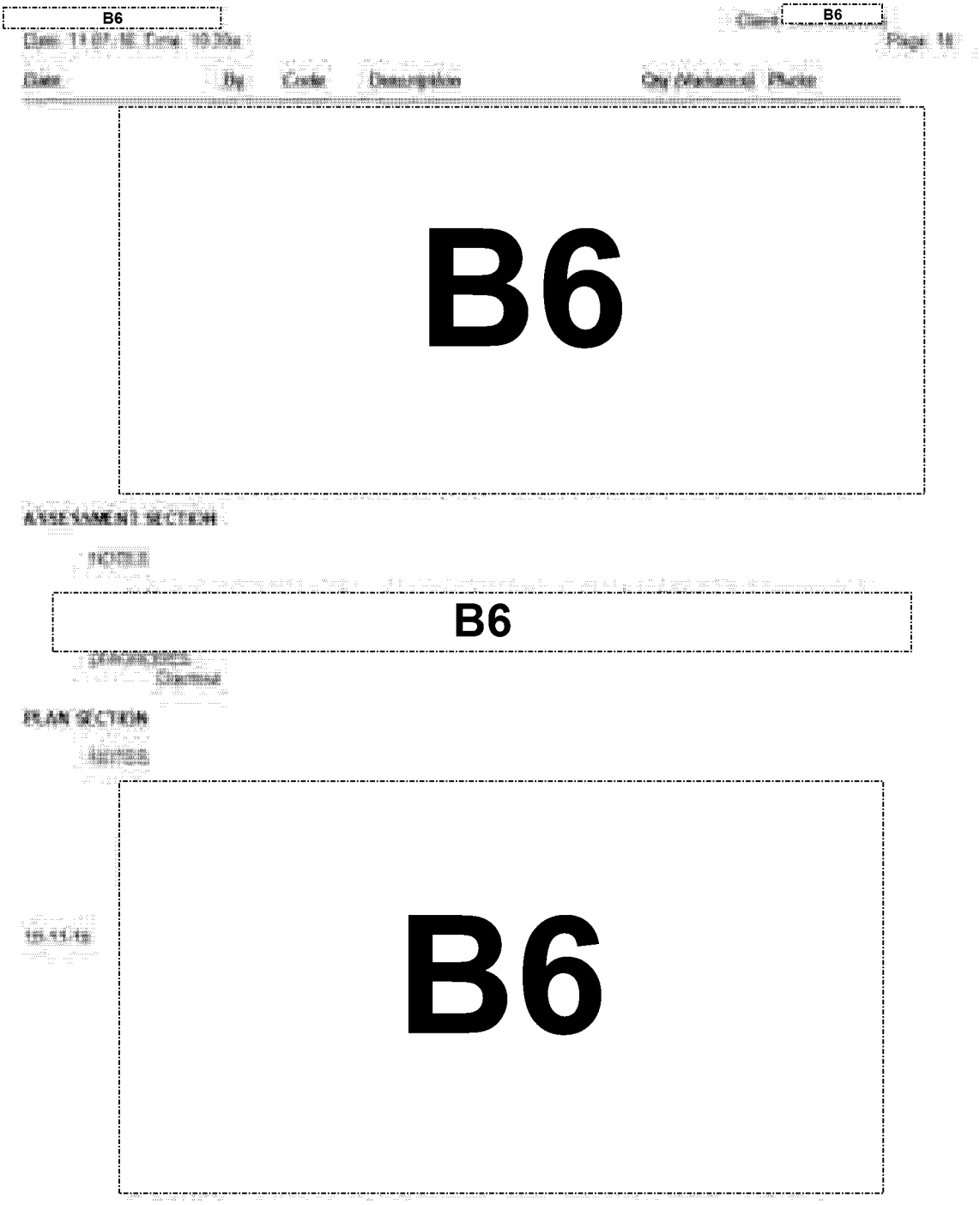
B6

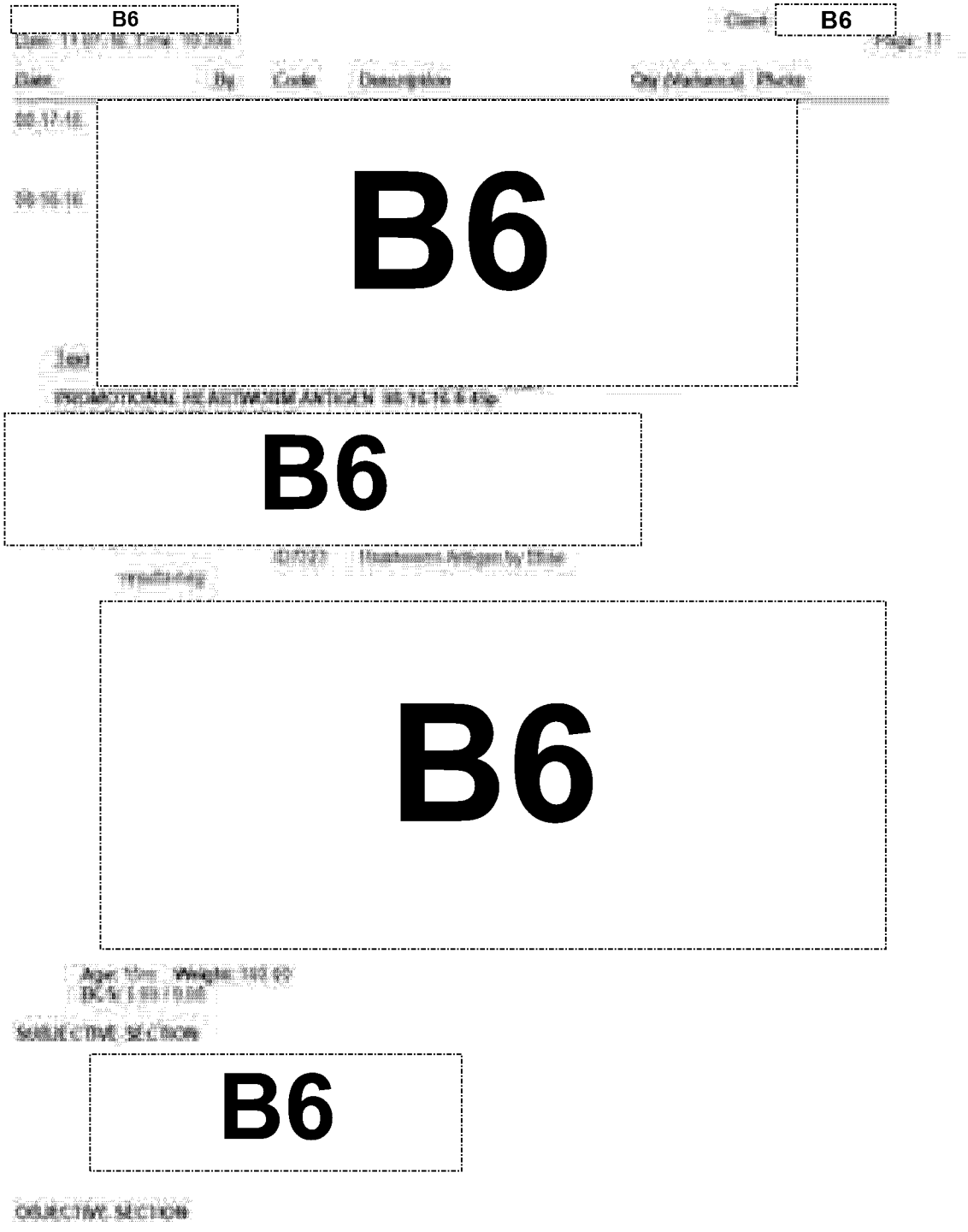
B6

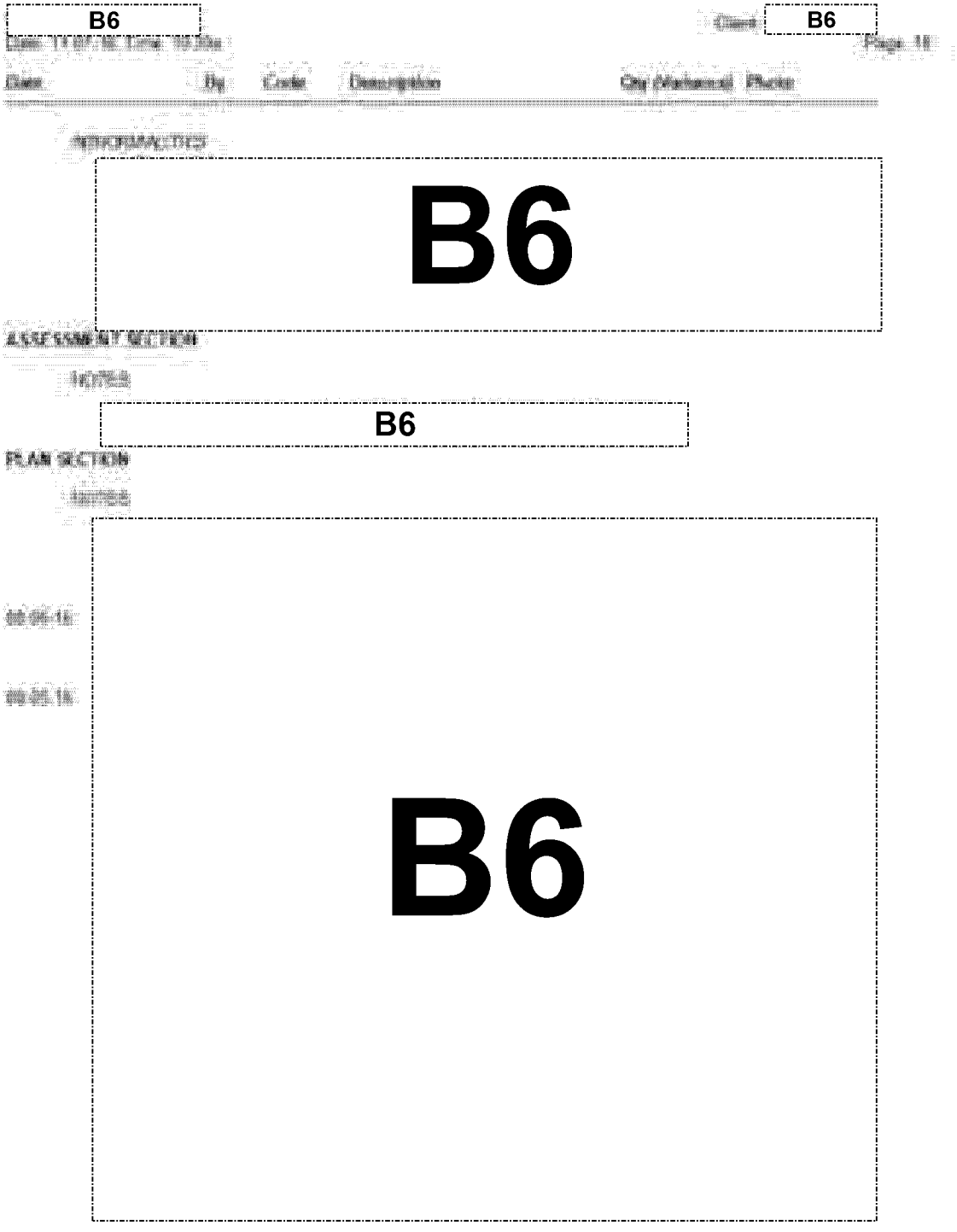
B6

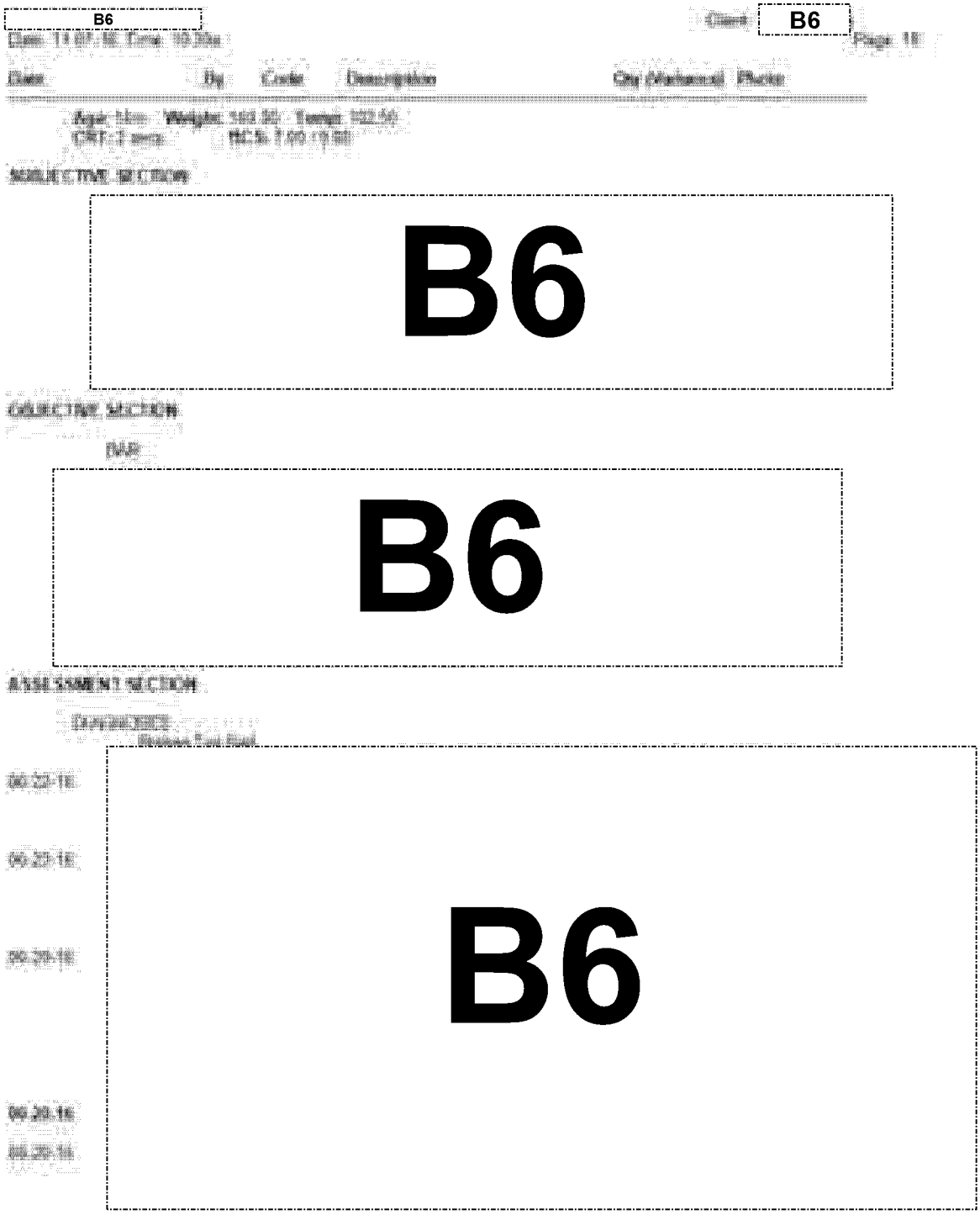
B6

B6







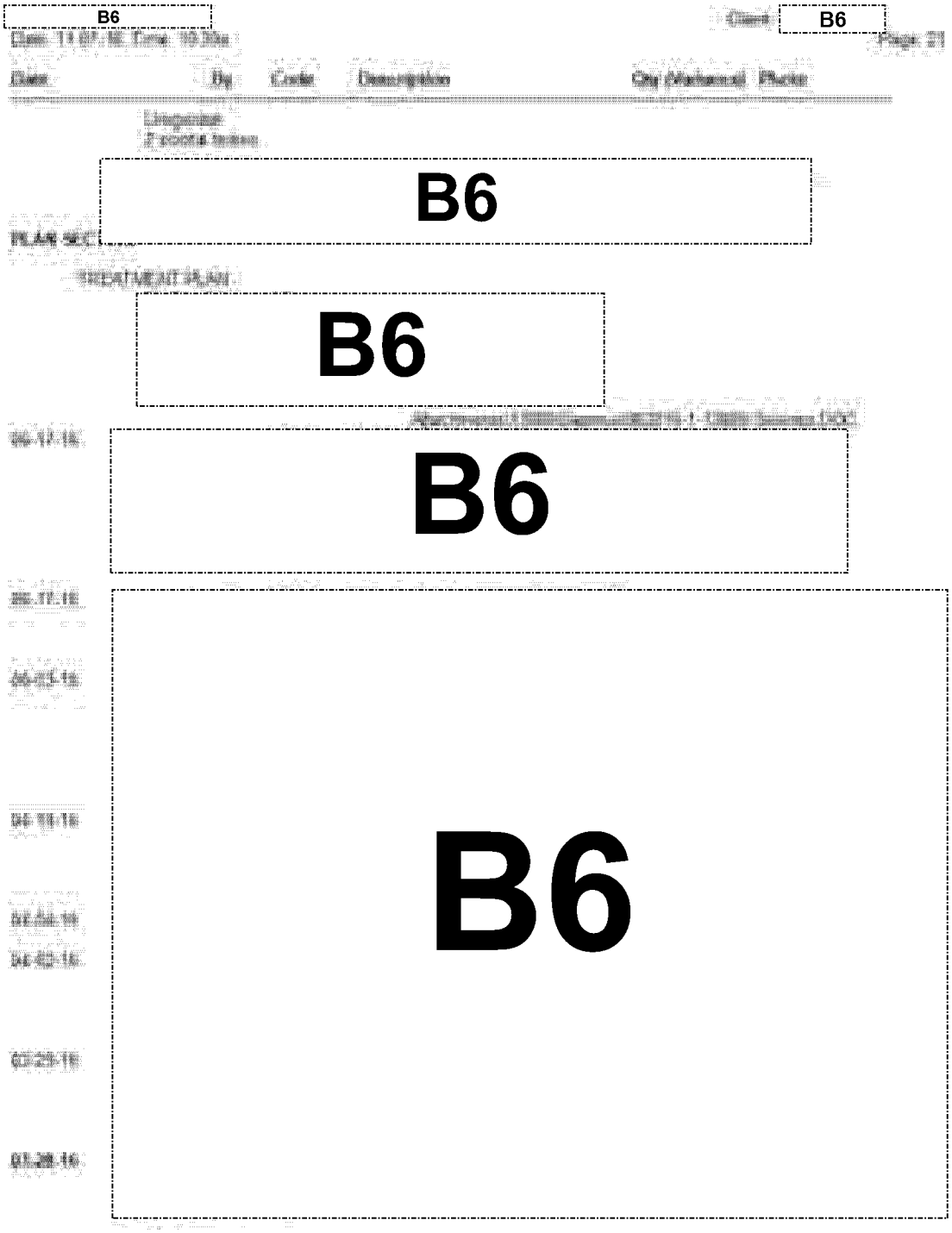


B6

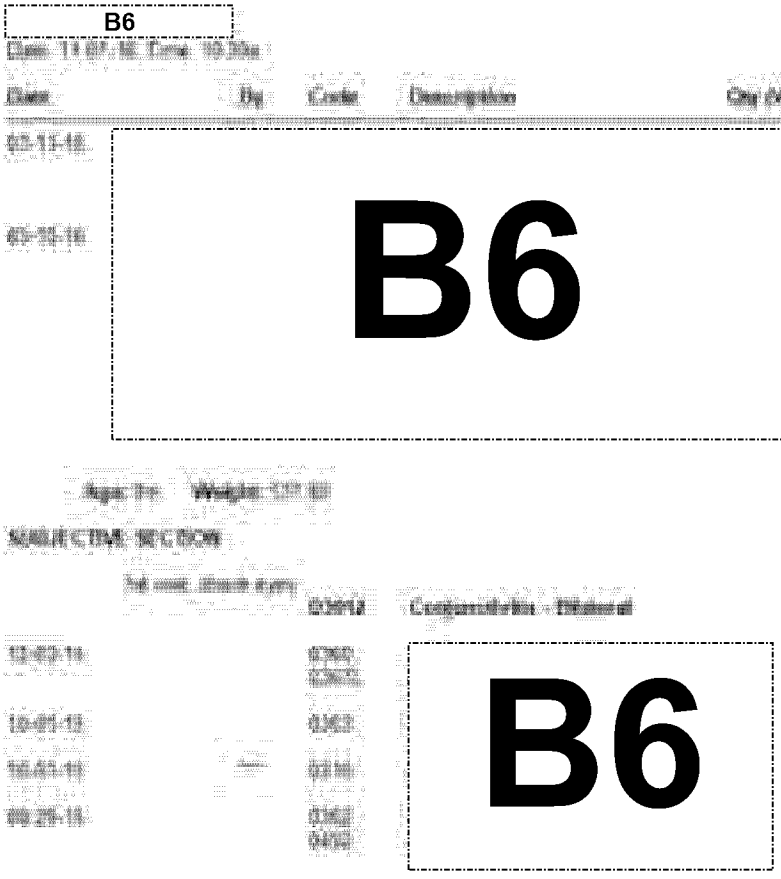
B6

B6

B6

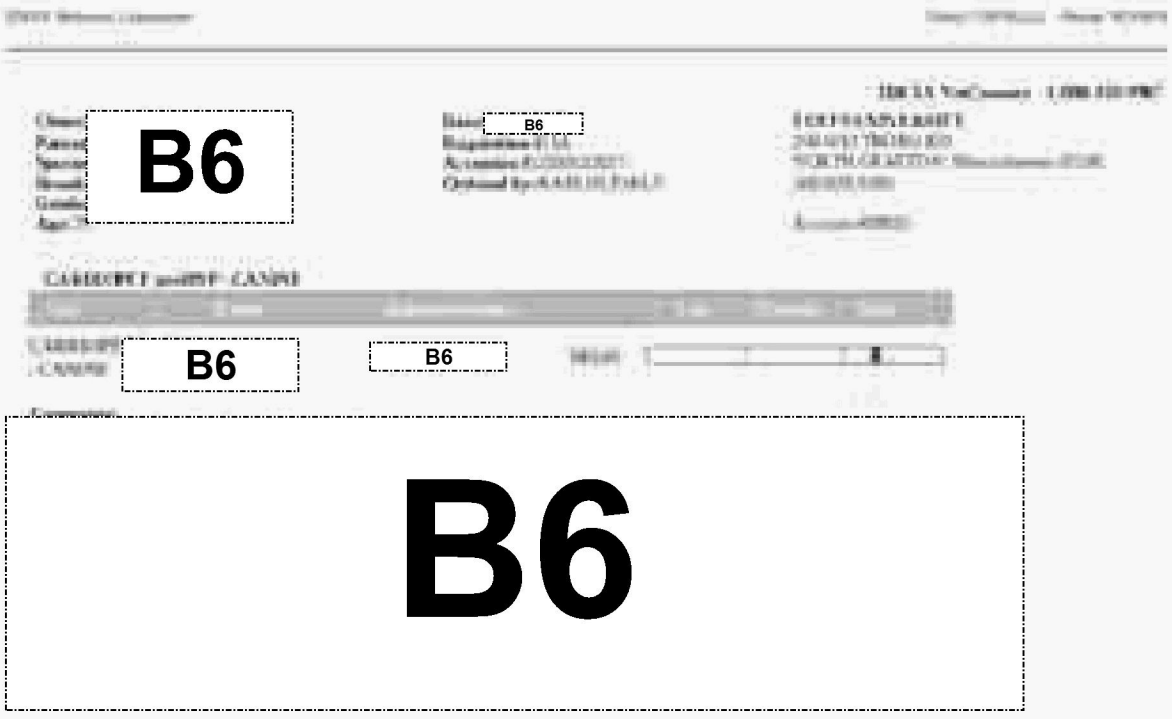


B6 AH records



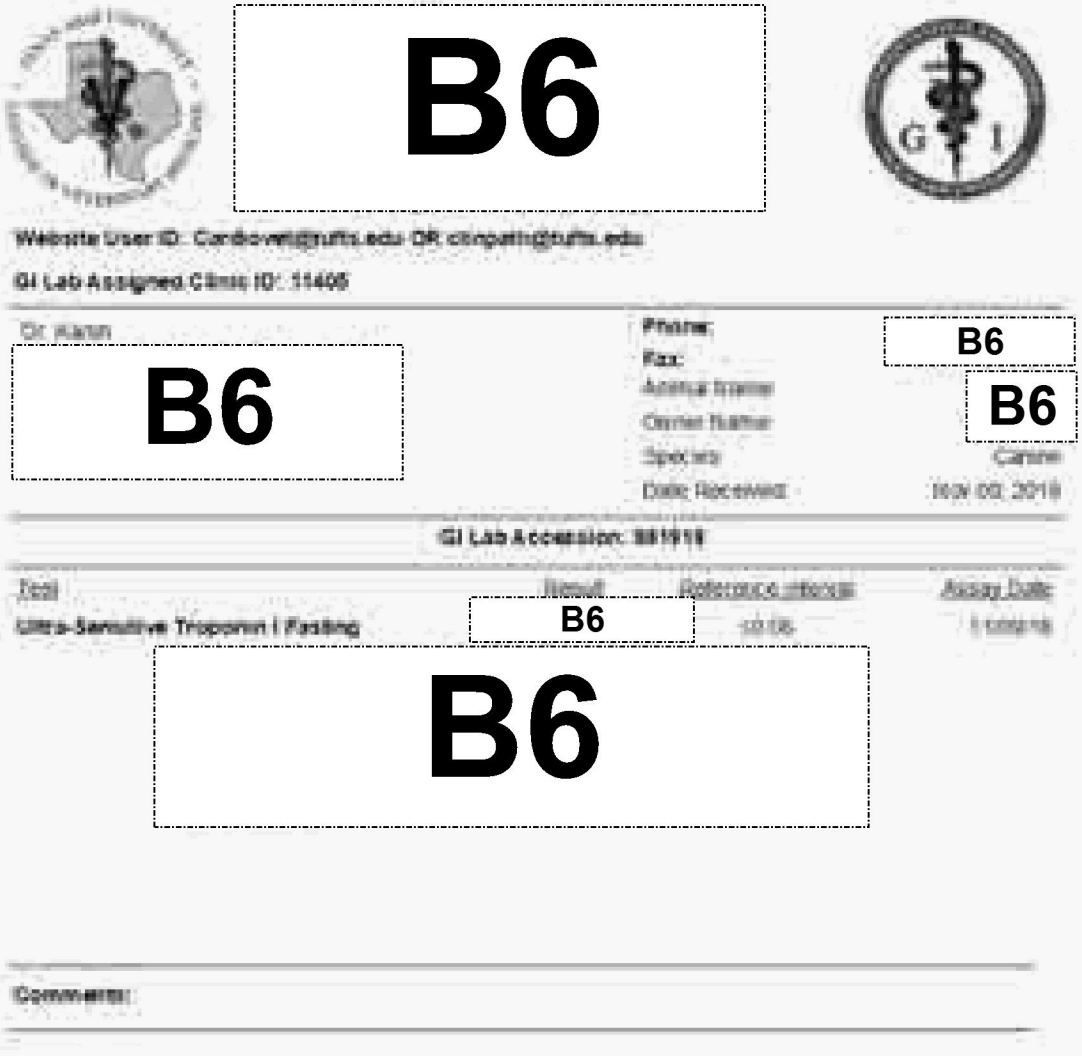
Client: B6
Patient:

Taurine results from UC Davis



Client: B6
Patient: B6

B6 **Troponin**



B6

B6 **Troponin**

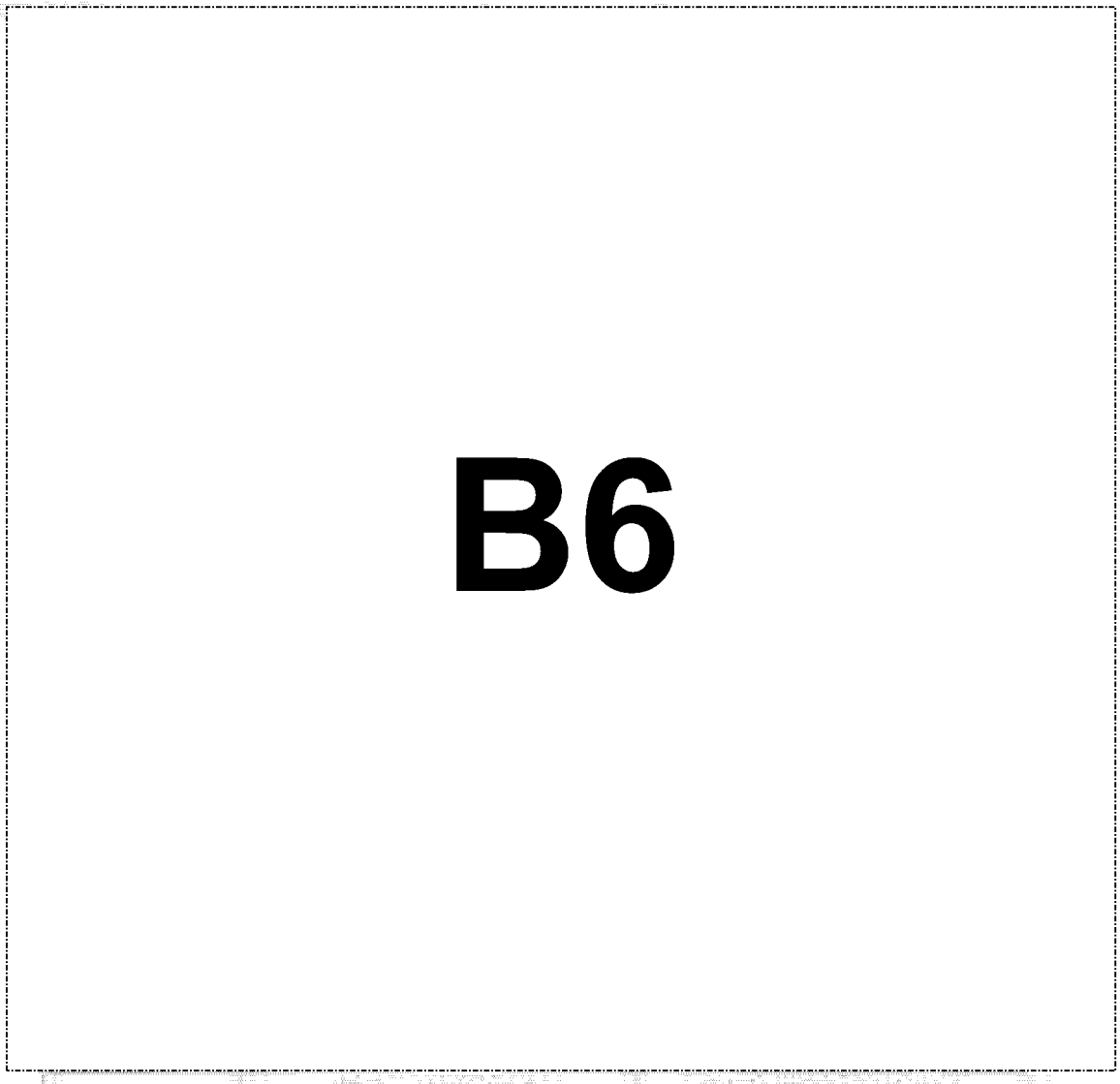
B6

B6

Client: B6
Patient:

UCDavis Taurine Level

[redacted]



	Plasma (nMol/ml)		Whole Blood nMol/ml)	
	Normal Range	No known risk for deficiency	Normal Range	No known risk for deficiency
Cat	80-120	>40	300-600	>300
Dog	60-120	>40	300-350	>150

* Please note with the recent increase in the number of dogs screened for taurine deficiency, we are seeing dogs with values within the reference ranges or above the "no known risk for deficiency range" yet are still exhibiting signs of cardiac disease. Veterinarians are welcome to consult our laboratory for assistance in evaluating your patient's results.

Client: B6
Patient:

Gastrointestinal Lab B6 **11/08/18**

B6

B6

B6

Important Notice: Internal Medicine Conference

Join us for a unique continuing education event in Pattaya, Thailand Oct 29 through Nov 2, 2018. For details see http://internalmedicineconference.tamu.edu

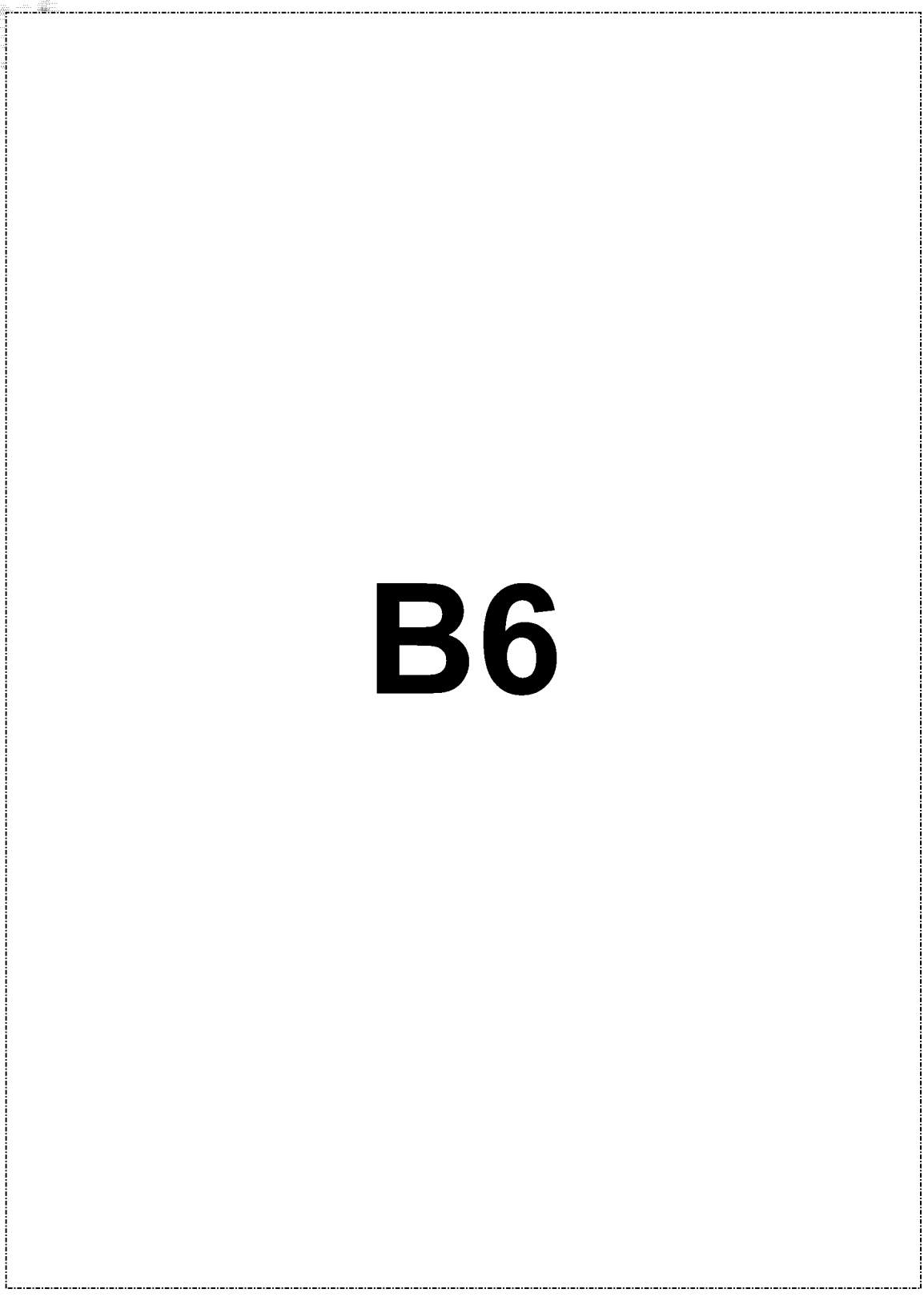
B6

GI Lab Contact Information

Phone: B6
Fax: B6

Email: B6

Lab Results Amino Acid Lab 11/08/18



Lab Results Amino Acid Lab 11/08/18

UNIVERSITY OF CALIFORNIA, DAVIS

B6

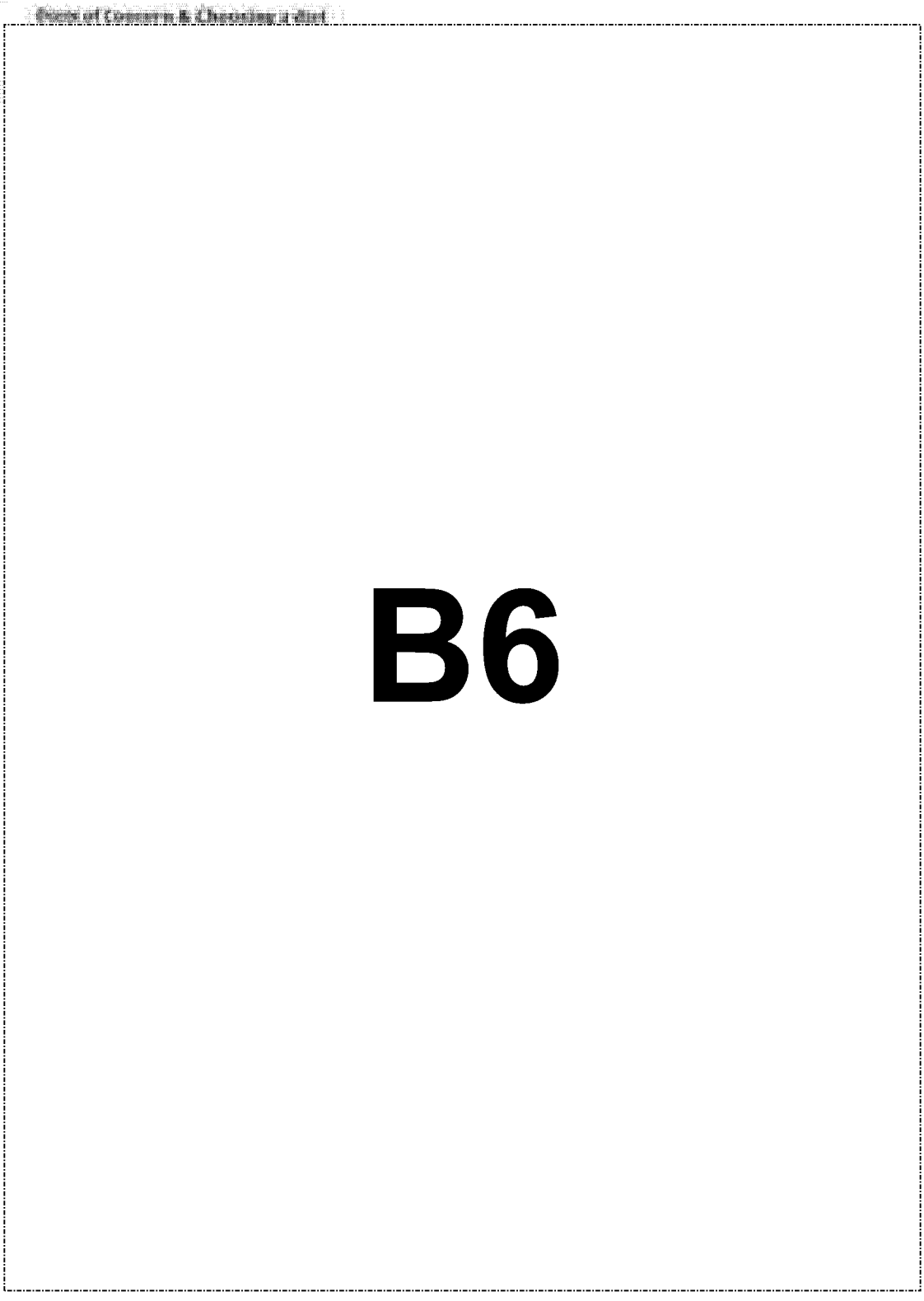
FREQUENTLY REQUESTED INFORMATION REGARDING TAURINE & DILATED CARDIOMYOPATHY IN GOLDEN RETRIEVERS

B6

Lab Results Amino Acid Lab 11/08/18

Clinical Recommendations for Golden Retrievers based on reactor levels

Lab Results Amino Acid Lab 11/08/18



Lab Results Amino Acid Lab 11/08/18

UCDAVIS VETERINARY MEDICINE

CARDIOLOGY SERVICE UPDATES: DOG FOOD & DILATED CARDIOMYOPATHY

B6

Client:
Patient: B6

Diet history 11/8/18

33.3144

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: [illegible]

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
Example: Poor______________|______Excellent

Poor_____________________|Excellent

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
☒ Eats about the same amount as usual ☐ Eats less than usual ☐ Eats more than usual
☐ Seems to prefer different foods than usual ☐ Other_______________

3. Over the last few weeks, has your pet (check one):
☒ Lost weight ☐ Gained weight ☐ Stayed about the same weight ☐ Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

Food (include specific product and flavor) Form Amount How often? Fed since
Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	dry	1.5 cup	2x/day	Jan 2018
85% lean hamburger	microwaved	3 oz	1x/week	Jan 2015
Pupperoni original beef flavor	treat	2	1x/day	Aug 2018
Rawhide	treat	6 inch twist	1x/week	Dec 2018
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

*Any additional diet information can be listed on the back of this sheet

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐ Yes ☒ No If yes, please list which ones and give brands and amounts

		Brand/Concentration	Amount per day
Taurine	☐ Yes ☐ No		
Carnitine	☐ Yes ☐ No		
Antioxidants	☐ Yes ☐ No		
Multivitamin	☐ Yes ☐ No		
Fish oil	☐ Yes ☐ No		
Coenzyme Q10	☐ Yes ☐ No		
Other (please list):			
Example: Vitamin C		Nature's Bounty	500 mg tablets – 1 per day

6. How do you administer pills to your pet?
☐ I do not give any medications
☐ I put them directly in my pet's mouth without food
☒ I put them in my pet's dog/cat food
☐ I put them in a Pill Pocket or similar product
☐ I put them in foods (list foods):_______________

Client: B6
Patient

Vitals Results

B6	7:44 PM	Nursing note
	1:36 PM	Heart Rate (/min)
	1:37 PM	Respiratory Rate
	1:38 PM	Temperature (F)
	0:04:53 AM	Weight (kg)

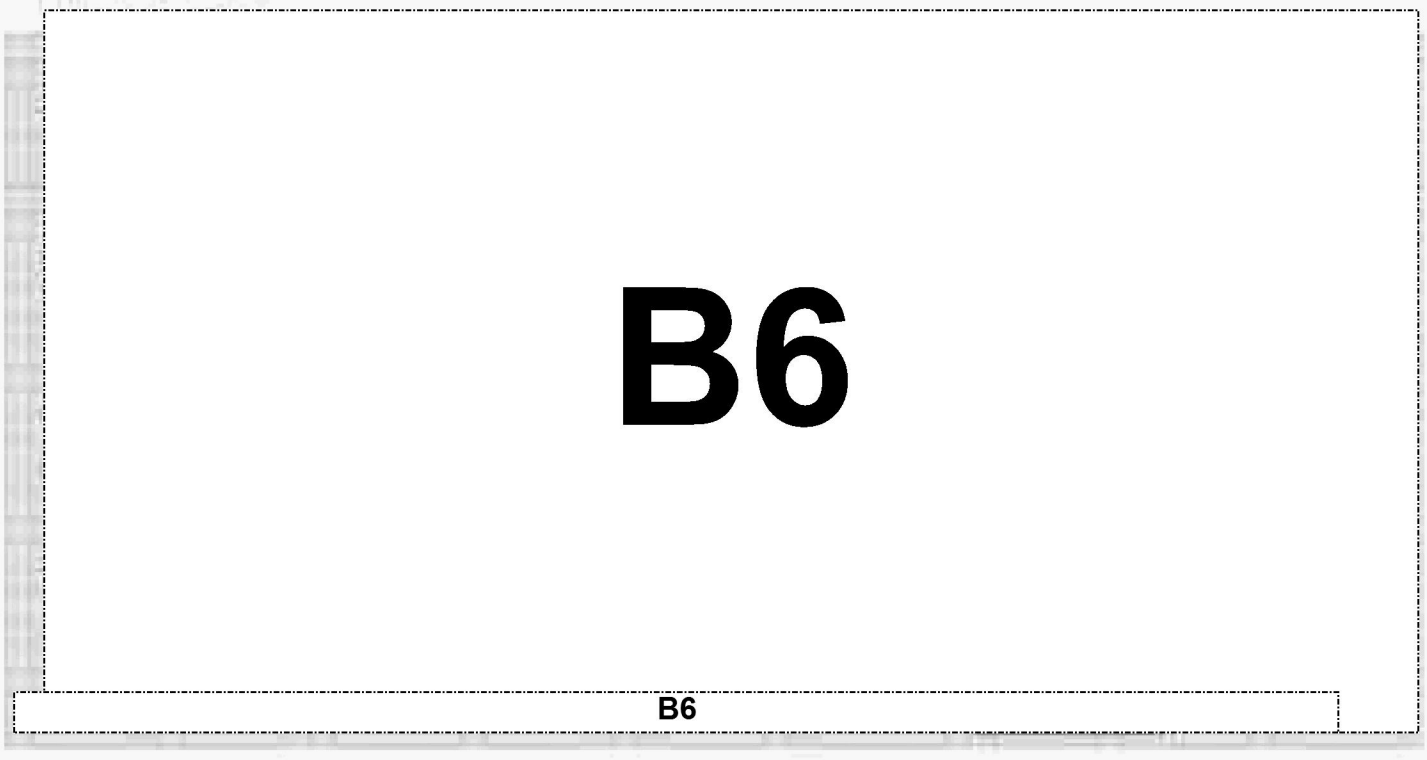
B6

Client: B6
Patient:

ECG from Cardio

B6

B6



Client: B6
Patient:

ECG from Cardio

B6

B6

B6

Client: B6
Patient:

ECG from Cardio

B6

Client: B6
Patient:

Patient History

B6

8:35 PM	UserForm
8:36 PM	Purchase
0:53 PM	Treatment
0:55 PM	Prescription
1:03 PM	UserForm
1:04 PM	Purchase
0:45 PM	Prescription
0:48 PM	Purchase
0:48 PM	Purchase
6:01 AM	UserForm
6:01 AM	Email
1:12 PM	Purchase
2:15 PM	UserForm
3:18 PM	Purchase
3:18 PM	Treatment
3:30 PM	UserForm
3:45 PM	Treatment
3:45 PM	Deleted Reason
3:47 PM	Treatment
3:47 PM	Vitals
4:41 PM	Vitals
4:41 PM	Vitals
4:41 PM	Vitals
2:38 AM	UserForm
2:38 AM	Email
0:40 AM	Appointment
0:04 AM	UserForm
0:04 AM	Vitals
1:07 AM	Treatment
1:14 AM	UserForm
1:30 AM	Purchase
3:31 PM	Labwork
3:34 PM	Purchase
3:34 PM	Purchase
3:34 PM	Purchase

B6

Best Available Copy

Tufts University | Cummings School of Veterinary Medicine

Healing Animals. Helping Humans. Transforming Global Health.

B6

Canine Wolfhound
Patient ID: 337144

STANDARD CONSENT FORM

B6

B6

Owner's name: B6

Owner's address:

Owner's Name: Signature: Date:

If the individual admitting the animal is someone other than the legal owner, please complete the portion below:

The owner of the animal, Teri Costello, has granted me authority to obtain medical treatment and to bind the owner to pay the veterinary medical services provided at Cummings School pursuant to the terms and conditions

B6

B6

Owner's signature:

5/25/16

Date:

B6

Tufts University | Cummings School of Veterinary Medicine

Healing Animals. Helping Humans. Transforming Global Health.

Emergency & Critical Care Liaison: (508) 887-4745

Foster Hospital for Small Animals
56 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-8739
http://vetmed.tufts.edu/

Patient
Name: B6
Species: Canine
Male
Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144

Contact Clinician: B6
Alternate Clinician:
Student:

Discharge Instructions

Admit Date: 3/28/2016 8:36:02 PM
Discharge Date: 3/28/2016

Diagnosis: 1. Productive cough and sneezing with nasal discharge

Procedures: 1. Exam

Medications:
Dispensed: B6

CASE SUMMARY

B6

Patient care instructions:

B6

B6

B6

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
[redacted]
Telephone: (508) 839-5395
Fax: (508) 839-8739
http://vetmed.tufts.edu/

Emergency & Critical Care Line: (508) 887-4745

Patient
Name:
Signalement: B6 [redacted] Wolfhound

Owner
Name:
Address: B6

Patient ID: 337344

Emergency Clinician: B6
Consulting Clinician:

B6

Discharge Instructions

Admit Date: 6/7/2017 8:46:06 PM
Check Out Date: 6/8/2017

Case Summary
Diagnosis:
1. Ingestion of wooden skewer

General Summary:

B6

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:

B6

B6

B6

B6

Ultrasound Request & Report

Patient
Name: B6
Species: Canine
Brindle Male Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144
Date of request: 6/8/2017

Attending Clinician: Mimi Gallo DVM (Small Animal Rotating Intern) Student:

Date of exam: 6/8/17

Patient Location: Ward/Cage: or Weight (kg)

- ☐ Inpatient
- ☐ Outpatient Time:
- ☑ Emergency

Scheduling and Patient Notes: (e.g., waiting for chemo, procedure, need cysto, etc.)

Examination Desired
- ☑ Abdomen
- ☐ Thorax
- ☐ Other:
- ☐ Biopsy or FNA
  Indicate organ(s):
- ☐ Cystocentesis

Permission for sedation
- ☐ Yes
- ☐ No (study may be delayed)

Permission for tissue sampling (if indicated)
- ☐ Yes
- ☐ No

Sedation protocol
- ☐ BA
- ☐ OBA
- ☐ 1/2 dose OBA
- ☐ Dexdomitor/Butorphanol
- ☐ Anesthesia to sedate/anesthetize
- ☐ Clinician to provide

B6

Radiologists
Primary: B6, DVM

Dates
Reported: 6.8.2017

B6

B6

Emergency & Critical Care B6

Patient
Name:
Signalement:

B6

Owner
Name:
Address:

B6

Patient ID: 33744

Emergency Clinician: B6

B6

Discharge Instructions

Admit Date: 6/5/2017 12:10:40 PM
Check Out Date: 6/5/2017

Case Summary
Diagnosis:
1. Wooden skewer ingestion

General Summary:

B6

Patient Care Instructions:

B6

Sincerely,

B6 DVM MS

B6

B6

B6

Radiology Request & Report

Patient
Name: B6
Species: Canine
Brindle Male Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144
Date of request: 6/5/2017

Attending Clinician: B6

Student:

Date of exam: 6/8/17

Patient Location: Ward/Cage:

Weight (kg): 0.00

- ☐ Inpatient
- ☐ Outpatient Time:
- ☐ Waiting
- ☑ Emergency

Sedation
- ☐ IMG
- ☐ OIMG
- ☐ 1/2 dose OIMG
- ☐ DexDomitor/Butorphanol
- ☐ Anesthesia to sedate/anesthetize

Examination Desired: lateral abdomen

Presenting Complaint and Clinical Questions you wish to answer:
Emergency

Pertinent History:

Findings:
ABDOMEN, LATERAL: There is a small amount of gas within the stomach. The small intestines, colon, liver, spleen, kidneys, and bladder are normal. The included thorax and musculoskeletal structures are normal.

Conclusions:
Normal limited abdomen. No evidence of ingested teriyaki stick.

Radiologists
Primary: B6 DVM
Reviewing: B6 DVM, DMCVR

Dates
Reported: 6.8.2017
Finalized: 6.12.2017

B6

Discharge Instructions

Patient
Name: B6
Species: Canine
Breed: Male Irish Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144

Attending Clinician:
B6

Consultation Veterinarian:
B6

B6

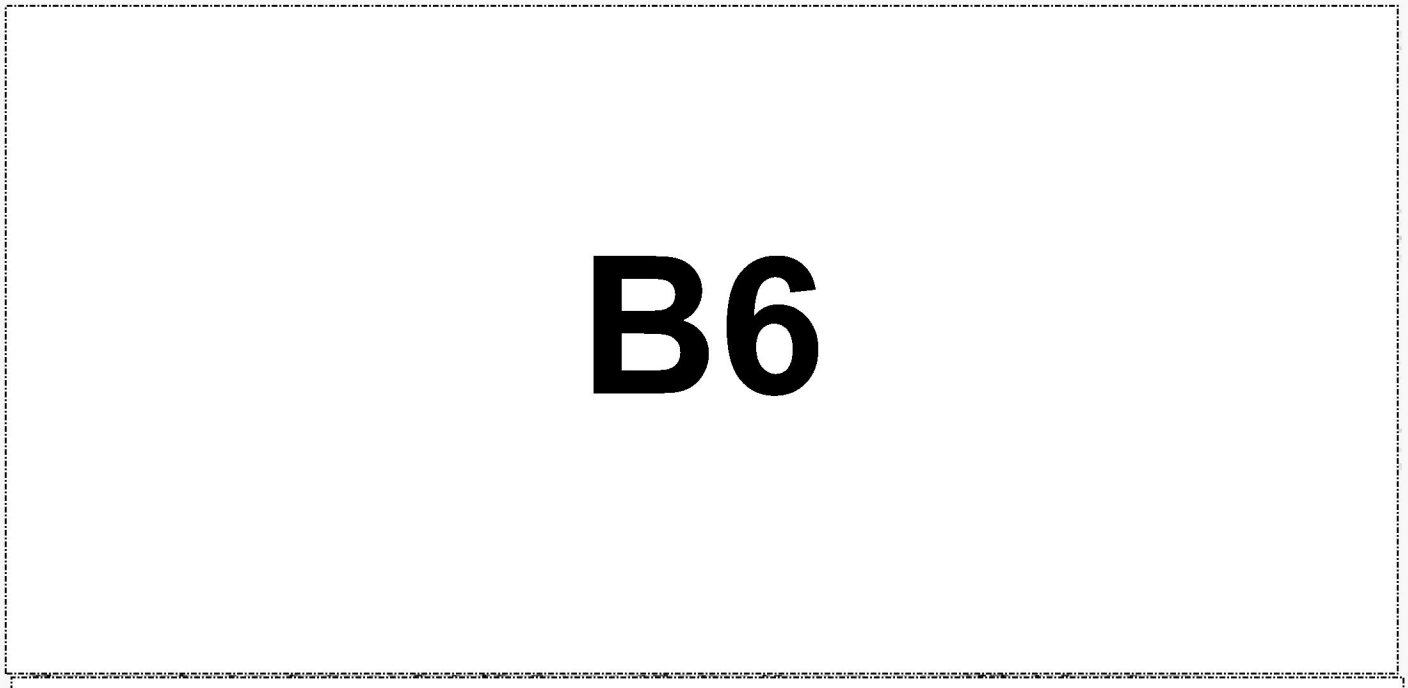
Student: B6

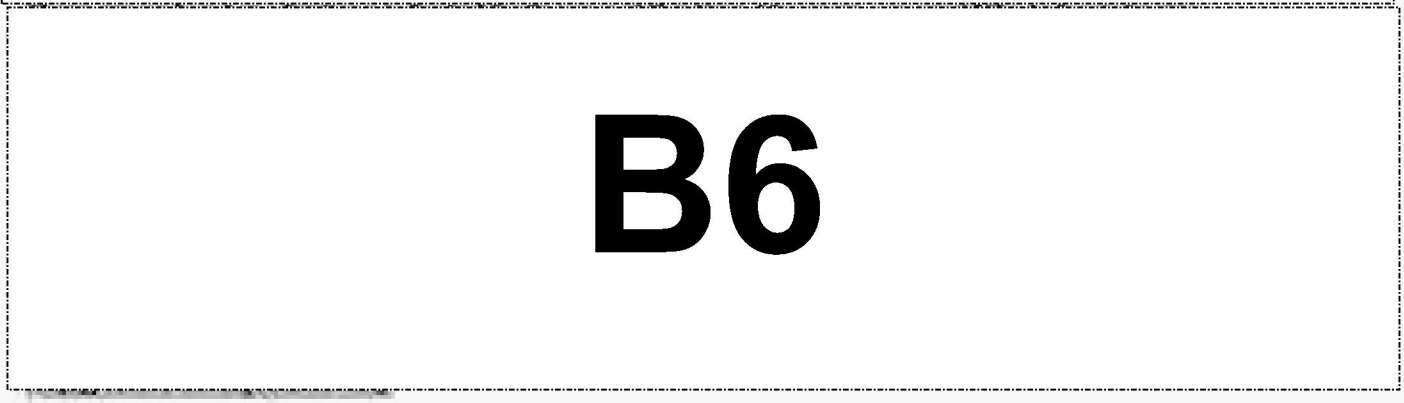
Discharge Date: 11/8/2018

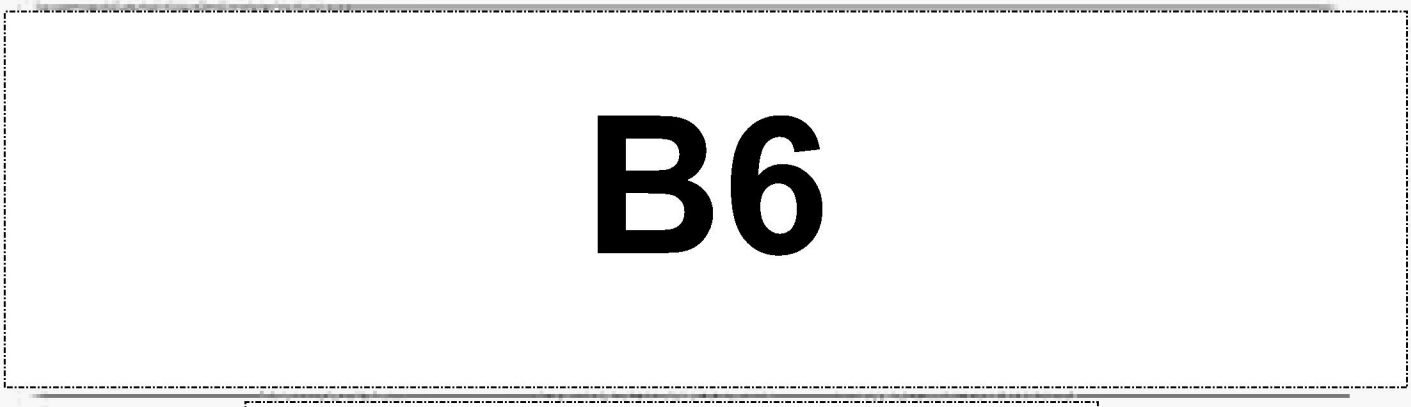
Diagnoses: Mildly low taurine

Clinical Findings:

B6







B6

B6

Cardiology Appointment Report

Date: 11/8/2018

Attending Cardiologist:

B6

Cardiology Resident:

B6

Cardiology Technician:

B6

Student: B6

B6

Presenting Complaint: Screen for DCM

Concurrent Diseases:
Hx of Anaplasmosis Dec. 2016, Dec. 2017
Hx of chronic diarrhea - stable

General Medical History:
B6 has history of chronic diarrhea since puppyhood - owner suspects it's when she changed from puppy food to adult food. Owner acquired B6 as a puppy. Owner reports that B6 pants a lot, but owner feels it is increased. Owner sent sputum to a diagnostic lab to find out allergens and sensitivities. Eating and drinking normally. No c/s/v/PUPD, diarrhea currently resolved with metronidazole. B6 littermate was recently diagnosed with DCM about 6 months ago and was also on a grain free diet. Owner requested taurine levels by rDVM - owner sent blood sample (plasma) to B6 for taurine levels, plasma level was 42. Currently being treated for diarrhea, lost weight during bout of diarrhea and diet change, but has gained weight back.

Diet and Supplements:

B6

Heartgard and Seresto collar

Cardiovascular History:
Prior CHF diagnosis? No
Prior heart murmur? No
Prior ATE? No
Prior arrhythmia? No
Monitoring respiratory rate and effort at home? Normal effort, pants all the time except when sleeping
Cough? No
Shortness of breath or difficulty breathing? No
Syncope or collapse? No
Sudden onset lameness? No
Exercise intolerance? No

Current Medications Pertinent to CV System:
None

Cardiac Physical Examination:

B6

Muscle condition:
- ☑ Normal
- ☐ Mild muscle loss
- ☐ Moderate cachexia
- ☐ Marked cachexia

Cardiovascular Physical Exam:

Murmur Grade:
- ☑ None
- ☐ I/VI
- ☐ II/VI
- ☐ III/VI
- ☐ IV/VI
- ☐ V/VI
- ☐ VI/VI

Jugular vein:
- ☑ Bottom 1/3 of the neck
- ☐ Middle 1/3 of the neck
- ☐ 1/2 way up the neck
- ☐ Top 2/3 of the neck

Arterial pulses:
- ☐ Weak
- ☐ Fair
- ☑ Good
- ☐ Strong
- ☐ Bounding
- ☐ Pulse deficits
- ☐ Pulsus paradoxus
- ☐ Other:

Arrhythmias:
- ☑ None
- ☐ Sinus arrhythmia
- ☐ Premature beats
- ☐ Bradycardia
- ☐ Tachycardia

Gallop:
- ☐ Yes
- ☐ Pronounced

- [x] No
- [ ] Intermittent
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [x] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
Low plasma taurine (42, ref range 60-120)

Differential Diagnoses:
R/o dietary induced taurine deficiency -> DCM

Diagnostic plan:
- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:
General/2-D findings:
Echo performed standing; reduced quality due to panting.
LV walls are normal in thickness with adequate contractile function. LV cavity is normal in size. LA is normal to mildly dilated. RH is dilated. PA appears normal. No masses or dirofilaria visible. No pleural or pericardial effusion. No ascites.

Doppler findings:
AV Vmax 2 m/s

Mitral inflow:
- [ ] Summated
- [x] Normal
- [ ] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:
NSR, HR 80 bpm

Assessment and recommendations:
Echocardiogram reveals relatively normal cardiac structure and function. The LV contractile function is low normal, so early DCM cannot be definitively ruled out. Patient was enrolled in the DCM study, and whole blood and plasma taurine were submitted; recommend supplementing taurine 1000mg PO BID until these results are back. Recheck per study protocol in 3 and 6 months.

Final Diagnosis:

Low plasma taurine
No clear evidence of DCM

Heart Failure Classification Score:
ACVIM Classification:

- [x] A
- [ ] B1
- [ ] B2
- [ ] C
- [ ] D

M-Mode

IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
%FS		%

M-Mode Normalized

IVSdN	B6	
LVIDdN		
LVPWdN		
IVSsN		
LVIDsN		
LVPWsN		

2D

SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LVId A2C		cm
LVEDV MOD A2C		ml
LVIs A2C		cm
LVESV MOD A2C		ml
LVEF MOD A2C		%
SV MOD A2C		ml
LVId LAX		cm
LVAd LAX		cm

LVEDV A-L LAX	B6	ml
LVEDV MOD LAX		ml
LVLs LAX		cm
LVAs LAX		cm
LVESV A-L LAX		ml
LVESV MOD LAX		ml
HR		BPM
EF A-L LAX		%
LVEF MOD LAX		%
SV A-L LAX		ml
SV MOD LAX		ml
CO A-L LAX		l/min
CO MOD LAX		l/min

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
A'		m/s
E/E'		
AV Vmax		m/s
AV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

B6 Male
Affected breed:
337/149

6/8/2017

Dear Dr. B6

B6

If you have any questions, or concerns, please contact us at B6

Thank you,

B6 ergency & Critical Care)

B6

B6

B6

B6 Male
Canine Wolfhound brindle
33/149

6/9/2017

Dear Dr. B6

Thank you for referring B6 with their pet B6 Please see attached discharge for B6

If you have any questions, or concerns, please contact us at B6.

Thank you,

B6

B6

B6

B6 Male
Canine Irish Wolfhound Brindle
33/149

11/13/2018

Dear Dr. B6

Thank you for referring B6 with their pet B6

If you have any questions, or concerns, please contact us at B6

Thank you,

B6 (Cardiology)

From: Related PFR Event <pfrsignificantactivitycreation@fda.hhs.gov>

To: B6 ; Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 3/21/2019 4:00:51 PM

Subject: Acana Lamb and Apple singles: Lisa Freeman - EON-382951

Attachments: 2064360-report.pdf; 2064360-attachments.zip

A PFR Report has been received and Related PFR Event [EON-382951] has been created in the EON System.

A "PDF" report by name "2064360-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2064360-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-382951
ICSR #: 2064360
EON Title: Related PFR Event created for Acana Lamb and Apple singles; 2064360

AE Date	11/08/2018	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Irish Wolfhound		
Age	3 Years		
District Involved	PFR B6 DO		

Product information
Individual Case Safety Report Number: 2064360
Product Group: Pet Food
Product Name: Acana Lamb and Apple singles
Description: Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months Follow-up - NT-proBNP, troponin, echo and ECG
Submission Type: Followup

Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Acana Lamb and Apple singles		

This report is linked to:
Initial EON Event Key: EON-372606
Initial ICSR: 2059540

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information

B6

To view this Related PFR Event, please click the link below:

B6

To view the Related PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

{

Report Details - EON-382951

ICSR:	2064360
Type Of Submission:	Followup
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-21 11:55:12 EDT
Initial Report Date:	12/03/2018
Parent ICSR:	2059540
Follow-up Report to FDA Request:	Yes

Reported Problem:

Problem Description:	Littermate diagnosed with DCM. Initial taurine level (plasma only) was 42. WB taurine submitted = 304 Eats BEG diet Mildly reduced contractile function on echo NT-proBNP = 2766, troponin mildly elevated at 0.1 (istat) and 0.096 at Texas A&M Will recheck in 3-4 months Follow-up - NT-proBNP, troponin, echo and ECG
Date Problem Started:	11/08/2018
Concurrent Medical Problem:	Yes
Pre Existing Conditions:	Chronic diarrhea Hx of anaplasmosis
Outcome to Date:	Stable

Product Information:

Product Name:	Acana Lamb and Apple singles
Product Type:	Pet Food
Lot Number:	
Package Type:	BAG
Product Use Information:	**Description:** Fed since 2016
Manufacturer /Distributor Information:	
Purchase Location Information:	

Animal Information:

Name:	B6
Type Of Species:	Dog
Type Of Breed:	Irish Wolfhound
Gender:	Male
Reproductive Status:	Intact
Weight:	82.7 Kilogram
Age:	3 Years
Assessment of Prior Health:	Good
Number of Animals Given the Product:	1
Number of Animals Reacted:	1

Owner Information:

Owner Information provided:	Yes
Contact:	**Name:** B6
	Phone
	Email
Address:	B6

B6

			United States
	Healthcare Professional Information:	Practice Name:	Tufts Cummings School of Veterinary Medicine
		Contact:	Name: Lisa Freeman
			Phone: (508) 887-4523
			Email: lisa.freeman@tufts.edu
		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States
Sender Information:	Name:		Lisa Freeman
	Address:		200 Westboro Rd North Grafton Massachusetts 01536 United States
	Contact:	Phone:	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:		Yes
	Preferred Method Of Contact:		Email
Additional Documents:			
	Attachment:		Medical Record 2.pdf
	Description:		Follow-up medical records
	Type:		Medical Records
	Attachment:		Medical Record 1.pdf
	Description:		Follow-up medical records
	Type:		Medical Records

Client: B6
Patient:

IDEXX BNP - 3/5/2019

B4 eference Laboratories

Client: B6 Patient: B6

B6

Client: B6
Patient:
Species: CANINE
Breed:
Gender: MALE
Age: 3Y

Date: 03/05/2019
Requisition #: 337144
Accession # B6
Ordered by: FREEMAN

TUFTS UNIVERSITY
200 WESTBORO RD
NORTH GRAFTON, Massachusetts 01536
508-839-5395

Account #88933

CARDIOPET proBNP - CANINE

Test	Result	Reference Range	Low	Normal	High
CARDIOPET proBNP - CANINE	B6	0 - 900 pmol/L	HIGH		

B6

Please note: Complete interpretive comments for all concentrations of Cardiopet proBNP are available in the online directory of services. Serum specimens received at room temperature may have decreased NT-proBNP concentrations.

Page 1 of 1

Client: B6
Patient:

Texas A and M Troponin

B6

B6

B6

Comments:

B6

Client: B6
Patient:

Diet Hx 3/5/19

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name : B6 Today's date: 3/5/19

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)
   Example: ***Poor*** _____|_____ ***Excellent***

   Poor _____|_____ **Excellent**

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
   ☒Eats about the same amount as usual ☐Eats less than usual ☐Eats more than usual
   ☐Seems to prefer different foods than usual ☐Other_____

3. Over the last few weeks, has your pet (check one)
   ☐Lost weight ☐Gained weight ☒Stayed about the same weight ☐Don't know

1. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats and that you have fed in the last 2 years.

   Please provide enough detail that we could go to the store and buy the exact same food - examples are shown in the table

Food (include specific product and flavor)	Form	Amount	How often?	Dates fed
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2016-present*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*June -Aug 2016*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Sept 2016-present*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2018-present*
Hills Prescription Diet i/d digestive Care chicken & vegetable Stew Canned		½ can	2X day	Since 11/18
Hills Presc. diet i/d Chicken flavor dry dog food		3 cups	2X day	Since 11/18
2 months prior to above I was trying him on several types of food due to diarrhea (raw diet Chicken or beef) but continued with diarrhea so went to Hills				

**Any additional diet information can be listed on the back of this sheet*

2. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐Yes ☒No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☒Yes ☐No	Stopped 2 months ago	1000 2X daily x 4 months
Carnitine	☐Yes ☐No		
Antioxidants	☐Yes ☐No		
Multivitamin	☐Yes ☐No		
Fish oil	☐Yes ☐No		
Coenzyme Q10	☐Yes ☐No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

3. How do you administer pills to your pet?
   ☐ I do not give any medications
   ☐ I put them directly in my pet's mouth without food
   ☒ I put them in my pet's dog/cat food when needed
   ☐ I put them in a Pill Pocket or similar product
   ☐ I put them in foods (list foods):_____

Client:
Patient: B6

Vitals Results

B6	7:44 PM	Nursing note	B6
	1:36 PM	Heart Rate (/min)	
	1:37 PM	Respiratory Rate	
	1:38 PM	Temperature (F)	
	0:04:53 AM	Weight (kg)	
	04:41 AM	Weight (kg)	

Client: B6
Patient:

ECG from Cardio

B6

11/8/2018 12:00:47 PM

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

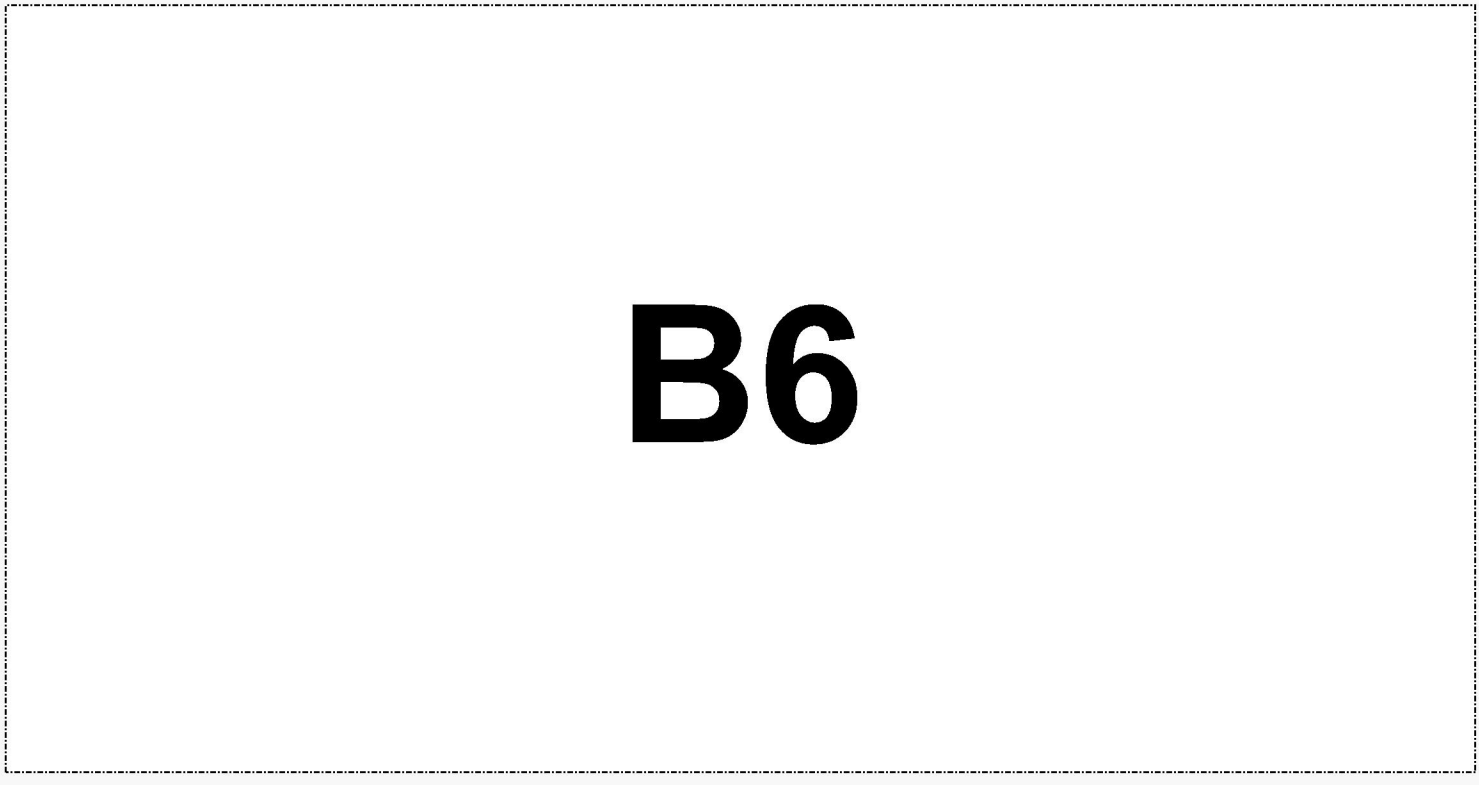
Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient

ECG from Cardio

B6

11/8/2018 12:00:59 PM
Tufts University
Tufts Cummings School of Vet Med
Cardiology



Client: B6
Patient:

Patient History

B6

	08:35 PM	UserForm
	08:36 PM	Purchase
	10:53 PM	Treatment
	10:55 PM	Prescription
	11:03 PM	UserForm
	11:04 PM	Purchase
	10:45 PM	Prescription
	10:48 PM	Purchase
	10:48 PM	Purchase
	06:01 AM	UserForm
	06:01 AM	Email
	01:12 PM	Purchase
	02:15 PM	UserForm
	03:18 PM	Purchase
	03:18 PM	Treatment
	03:30 PM	UserForm
	03:45 PM	Treatment
	03:45 PM	Deleted Reason
	03:47 PM	Treatment
	03:47 PM	Vitals
	04:41 PM	Vitals
	04:41 PM	Vitals
	04:41 PM	Vitals
	02:38 AM	UserForm
	02:38 AM	Email
	10:40 AM	Appointment
	10:04 AM	UserForm
	10:04 AM	Vitals
	11:07 AM	Treatment
	11:14 AM	UserForm
	11:30 AM	Purchase
	03:31 PM	Labwork
	03:34 PM	Purchase
	03:34 PM	Purchase
	03:34 PM	Purchase
	01:04 PM	Appointment
02/19/2019	06:07 PM	Appointment

B6

Client: B6
Patient:

Patient History

B6

09:51 AM	Purchase
09:55 AM	UserForm
09:59 AM	Treatment
10:04 AM	Vitals
10:28 AM	UserForm
11:12 AM	Appointment
11:12 AM	Email
03:03 PM	Purchase

B6

Patient Account History	Description	Qty	price	Extended	Disc	Pmt

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

Patient
Name: B6
Species: B6
Brindle Male Irish Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144

Attending Cardiologist:
B6

Cardiology Resident:
B6

Cardiology Technician:
B6

Student: B6

Discharge Date: 11/8/2018

Diagnoses: Mildly low taurine

Clinical Findings:
Thank you for bringing B6 to Tufts Cardiology Service for screening for dilated cardiomyopathy (DCM).

On physical exam, B6 was bright, alert, and responsive and his vital parameters (heart rate and respiratory rate) were within normal limits. We did not hear any obvious heart murmurs or arrhythmias.

We performed an echocardiogram (ultrasound of the heart) today, which revealed that B6' heart did not show any obvious signs of DCM. However, in early stages of the disease, the ventricles (lower chambers of the heart) are not dilated. Similarly, the atria (upper chambers of the heart) are not obviously dilated. B6 heart had very mildly reduced contractility, which could be normal for him or could possible be an early indication of DCM. Additionally, the speed of blood flow through the aorta, the main artery of the heart that supplies the blood to the rest of the body, is mildly increased, but this is not a concerning finding.

Overall, B6 looks good and he does not appear to have significant heart disease. Given his low taurine levels, we would like to begin taurine supplementation as instructed below.

Our Cardiology and Nutrition team here at Tufts are conducting a study on DCM and its correlation with diet. Although Seamus does not have DCM, the study includes normal cardiac dogs that have a history of a grain-free diet. You have elected to enroll B6 in the study so we pulled some blood for that today.

Diet Suggestions:
B6

B6

- The FDA is currently investigating an apparent association between diet and a type of heart disease called dilated cardiomyopathy. The exact cause is still unclear, but it appears to be associated with boutique diets and those containing exotic ingredient or are grain-free. Therefore, we are currently recommending that dogs do not eat these types of diets.
- We recommend switching B6 to commercial diet made by a well-established company that is not grain-free and does not contain any exotic ingredients, such as kangaroo, duck, lamb, venison, lentils, peas, beans, buffalo, tapioca, barley, and chickpeas.
-
- The FDA issued a statement regarding this issue (https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm613305.htm) and a recent article published by Dr. Lisa Freeman on the Cummings School's Petfoodology blog can further explain these findings (http://vetnutrition.tufts.edu/2018/06/a-broken-heart-risk-of-heart-disease-in-boutique-or-grain-free-diets-and-exotic-ingredients/).

Exercise Recommendations:

B6 may be allowed to dictate his own activity level.

Recommended Medications:

B6

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:
Please check with your primary veterinarian to purchase the recommended diet(s). If you wish to purchase your food from us, please call 7-10 days in advance (508-887-4629) to ensure the food is in stock. Alternatively, veterinary diets can be ordered from online retailers with a prescription/veterinary approval.

Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

---

Case: B6 Owner: B6 Discharge Instructions

B6

B6

Patient ID: 337144
B6 Canine
B6 Years Old Male Irish Wolfhound
Brindle

Cardiology Appointment Report
ENROLLED IN DCM DIET STUDY

Date: 11/8/2018

Attending Cardiologist:

- ☐
- ☐
- ☐
- ☑ B6

Cardiology Resident:

- ☐ B6
- ☑ B6 DVM, MSc

Cardiology Technician:

- ☐
- ☑ B6 CVT, VTS (Cardiology)

Student: B6

Presenting Complaint: Screen for DCM

Concurrent Diseases:
Hx of Anaplasmosis Dec. 2016, Dec. 2017
Hx of chronic diarrhea - stable

General Medical History:
B6 has history of chronic diarrhea since puppyhood - owner suspects it's when she changed from puppy food to adult food. Owner acquired B6 as a puppy. Owner reports that B6 pants a lot, but owner feels it is increased. Owner sent sputum to a diagnostic lab to find out allergens and sensitivities. Eating and drinking normally. No c/s/v/PUPD, diarrhea currently resolved with metronidazole. B6 littermate was recently diagnosed with DCM about 6 months ago and was also on a grain free diet. Owner requested taurine levels by rDVM - owner sent blood sample (plasma) to UC Davis for taurine levels, plasma level was 42. Currently being treated for diarrhea, lost weight during bout of diarrhea and diet change, but has gained weight back.

Diet and Supplements:
Previously fed Taste of the Wild (grain-free)
Acana in 2016
Hill's I/D kibble and canned - for 4 weeks
Fortiflora SID
Metronidazole 750mg PO BID

B12 injections 1x/week
Heartgard and Seresto collar

Cardiovascular History:
Prior CHF diagnosis? No
Prior heart murmur? No
Prior ATE? No
Prior arrhythmia? No
Monitoring respiratory rate and effort at home? Normal effort, pants all the time except when sleeping
Cough? No
Shortness of breath or difficulty breathing? No
Syncope or collapse? No
Sudden onset lameness? No
Exercise intolerance? No

Current Medications Pertinent to CV System:
None

B6

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [x] Good
- [ ] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [x] None
- [ ] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:

- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [x] Normal BV sounds
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

Abdominal exam:
- [x] Normal
- [ ] Hepatomegaly
- [ ] Abdominal distension
- [ ] Mild ascites
- [ ] Marked ascites

Problems:
Low plasma taurine (42, ref range 60-120)

Differential Diagnoses:
R/o dietary induced taurine deficiency –> DCM

Diagnostic plan:
- [x] Echocardiogram
- [ ] Chemistry profile
- [ ] ECG
- [ ] Renal profile
- [ ] Blood pressure
- [ ] Dialysis profile
- [ ] Thoracic radiographs
- [ ] NT-proBNP
- [ ] Troponin I
- [ ] Other tests:

Echocardiogram Findings:

B6

Doppler findings:
AV Vmax 2 m/s

Mitral inflow:
- [ ] Summated
- [x] Normal
- [ ] Delayed relaxation
- [ ] Pseudonormal
- [ ] Restrictive

ECG findings:
NSR, HR 80 bpm

Assessment and recommendations:
Echocardiogram reveals relatively normal cardiac structure and function. The LV contractile function is low normal, so early DCM cannot be definitively ruled out. Patient was enrolled in the DCM study, and whole blood and plasma taurine were submitted; recommend supplementing taurine 1000mg PO BID until those results are back. Recheck per study protocol in 3 and 6 months.

Final Diagnosis:
Low plasma taurine
No clear evidence of DCM

Heart Failure Classification Score:
ACVIM Classification:

- [x] A
- [ ] B1
- [ ] B2
- [ ] C
- [ ] D

M-Mode

IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
%FS		%

M-Mode Normalized

IVSdN	B6	(0.29 - 0.52)
LVIDdN		(1.35 - 1.73)
LVPWdN		(0.33 - 0.53)
IVSsN		(0.43 - 0.71)
LVIDsN		(0.79 - 1.14)
LVPWsN		(0.53 - 0.78)

2D

SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LVLd A2C		cm
LVEDV MOD A2C		ml
LVLs A2C		cm
LVESV MOD A2C		ml
LVEF MOD A2C		%
SV MOD A2C		ml
LVLd LAX		cm

LVAd LAX	B6	cm
LVEDV A-L LAX		ml
LVEDV MOD LAX		ml
LVLs LAX		cm
LVAs LAX		cm
LVESV A-L LAX		ml
LVESV MOD LAX		ml
HR		BPM
EF A-L LAX		%
LVEF MOD LAX		%
SV A-L LAX		ml
SV MOD LAX		ml
CO A-L LAX		l/min
CO MOD LAX		l/min

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
A'		m/s
E/E'		
AV Vmax		m/s
AV maxPG		mmHg

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Discharge Instructions

Patient
Name: B6
Species: Canine
Brindle Male Irish Wolfhound
Birthdate: B6

Owner
Name: B6
Address: B6

Patient ID: 337144

Attending Cardiologist:
- ☐
- ☐
- ☐
- ☑ B6

Cardiology Resident:
- ☐ B6

Cardiology Technician:
- ☐
- ☑ B6 , VTS (Cardiology)
- ☐ CVT

Student: B6

Appointment Date: 3/5/2019

Diagnosis: Stable to slightly improved healthy heart

Clinical Findings:
Thank you for bringing B6 to Tufts Cardiology Service for recheck examination as part of the dilated cardiomyopathy (DCM) study. On physical exam, Seamus was bright, alert, and responsive and his vital parameters (heart rate and respiratory rate) were within normal limits. We did not hear any obvious heart murmurs or arrhythmias.

We performed an echocardiogram (ultrasound of the heart) today, which revealed that Seamus' heart was stable since his last visit and did not show any obvious signs of DCM. He may even have somewhat improved contractile function. Overall, B6 looks good and he does not appear to have significant heart disease. We also took blood samples today to check for biomarkers of heart disease which had been slightly elevated at this last visit. We will call you with the results of these tests.

Diet Suggestions:
It is great that Seamus is doing well on the Hills I/D diet! He has gained over 13 pounds since his last visit so we recommend cutting back just a little bit on how much he is eating. You can start with feeding a total of 5 cups of dry food and 1/2 can of wet food per day. If he is getting treats at home, it is also important to cut back on his regular diet to account for those extra calories.

Exercise Recommendations:
B6 may be allowed to dictate his own activity level.

Recommended Medications:
B6

B6

Please visit our HeartSmart website for more information
http://vet.tufts.edu/heartsmart/

Prescription Refill Disclaimer:
For the safety and well-being of our patients, your pet must have had an examination by one of our veterinarians within the past year in order to obtain prescription medications.

Ordering Food:
Please check with your primary veterinarian to purchase the recommended diet(s). If you wish to purchase your food from us, please call 7-10 days in advance (508-887-4629) to ensure the food is in stock. Alternatively, veterinary diets can be ordered from online retailers with a prescription/veterinary approval.

Clinical Trials:
Clinical trials are studies in which our veterinary doctors work with you and your pet to investigate a specific disease process or a promising new test or treatment. Please see our website: vet.tufts.edu/cvmc/clinical-studies

---

Case: B6 **Owner:** B6 **Discharge Instructions**

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY
Cardiology Liaison: 508-887-4696

B6

Patient ID: 337144
B6 Canine
B6 ears Old Male Irish Wolfhound
Brindle

Cardiology Appointment Report
DCM STUDY

Date: 3/5/2019

Attending Cardiologist:

- [ ]
- [ ]
- [ ]
- [x] B6

Cardiology Resident:

- [ ] B6

Cardiology Technician:

- [ ]
- [x] B6
- [ ]

Student: B6

Presenting Complaint: Recheck DCM study

Concurrent Diseases: Sensitive GI tract -well-controlled with Hills I/D food

General Medical History:
Last seen in November for a DCM screen when a littermate had been diagnosed with DCM on a grain-free diet. B6 had been on a grain free diet and rDVM had previously dx with low taurine. We measured taurine in November which was normal (304 reference range 200-350). B6 has been doing well at home. Since changing diet to Hill I/D has not had any diarrhea and has gained back the weight he had lost. 4 months ago treated for Anaplasmosis with an antibiotic and has not had any lameness issues. Good appetite and energy levels at home. Owner says is doing great with no issues (no c/s/v/d).

Diet and Supplements:
Hills I/D 6 cups dry per day, 1 can split BID; no people food
Taurine supplementation stopped after 2 months (had been doing 1,000 mg BID started November at last appointment)
Vitamin B injections for 3-4 months started for GI issues; stopped 4 months ago

Cardiovascular History:
Prior CHF diagnosis? No
Prior heart murmur? No
Prior ATE? No

Prior arrhythmia? No
Monitoring respiratory rate and effort at home? No, he generaly pants a lot at home
Cough? No
Shortness of breath or difficulty breathing? No
Syncope or collapse? No
Sudden onset lameness? No
Exercise intolerance? None

Current Medications Pertinent to CV System:
No current medications
Heartworm preventative (stops during winter months)

B6

Muscle condition:
- [x] Normal
- [ ] Mild muscle loss
- [ ] Moderate cachexia
- [ ] Marked cachexia

Cardiovascular Physical Exam:
Murmur Grade:
- [x] None
- [ ] I/VI
- [ ] II/VI
- [ ] III/VI
- [ ] IV/VI
- [ ] V/VI
- [ ] VI/VI

Jugular vein:
- [x] Bottom 1/3 of the neck
- [ ] Middle 1/3 of the neck
- [ ] 1/2 way up the neck
- [ ] Top 2/3 of the neck

Arterial pulses:
- [ ] Weak
- [ ] Fair
- [ ] Good
- [x] Strong
- [ ] Bounding
- [ ] Pulse deficits
- [ ] Pulsus paradoxus
- [ ] Other:

Arrhythmia:
- [x] None
- [ ] Sinus arrhythmia
- [ ] Premature beats
- [ ] Bradycardia
- [ ] Tachycardia

Gallop:
- [ ] Yes
- [x] No
- [ ] Intermittent
- [ ] Pronounced
- [ ] Other:

Pulmonary assessments:
- [x] Eupneic
- [ ] Mild dyspnea
- [ ] Marked dyspnea
- [ ] Pulmonary crackles
- [ ] Wheezes
- [ ] Upper airway stridor

☑ Normal BV sounds

Abdominal exam:

☑ Normal
☐ Hepatomegaly
☐ Abdominal distension
☐ Mild ascites
☐ Marked ascites

Problems:

History of low plasma taurine
Normal LV chamber size in November but reduced contractile function so could not rule out early DCM

Differential Diagnoses:

Dietary induced low taurine/DCM vs. congenital

Diagnostic plan:

☑ Echocardiogram
☐ Chemistry profile
☑ ECG
☐ Renal profile
☐ Blood pressure
☐ Dialysis profile
☐ Thoracic radiographs
☐ NT-proBNP
☐ Troponin I
☐ Other tests: taurine level

Echocardiogram Findings:

General/2-D findings:

Echo performed standing; reduced quality due to panting.
LV walls are normal in thickness with adequate contractile function. LV cavity is normal in size. LA is normal to mildly dilated. RH is dilated. PA appears normal. No masses or dirofilaria visible. No pleural or pericardial effusion. No ascites.

Doppler findings:

AV Vmax 1.8 m/s

Mitral inflow:

☐ Summated
☑ Normal
☐ Delayed relaxation
☐ Pseudonormal
☐ Restrictive

ECG findings:

NSR, HR 120 bpm

Assessment and recommendations:

Echocardiogram reveals relatively normal cardiac structure and function. The LV contractile function is slightly higher on all measurements, but this could also be daily variation. Blood work submitted via DCM study. Recheck per study protocol in 3 months.

Heart Failure Classification Score:

ACVIM Classification:

☑ A
☐ B1
☐ B2
☐ C
☐ D

M-Mode

IVSd	B6	cm
LVIDd		cm
LVPWd		cm
IVSs		cm
LVIDs		cm
LVPWs		cm
EDV(Teich)		ml
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
Ao Diam		cm
LA Diam		cm
LA/Ao		
TAPSE		cm

M-Mode Normalized

IVSdN	B6	(0.290 - 0.520)
LVIDdN		(1.350 - 1.730)
LVPWdN		(0.330 - 0.530)
IVSsN		(0.430 - 0.710)
LVIDsN		(0.790 - 1.140)
LVPWsN		(0.530 - 0.780)
Ao Diam N		(0.680 - 0.890) !
LA Diam N		(0.640 - 0.900) !

2D

SA LA	B6	cm
Ao Diam		cm
SA LA / Ao Diam		
IVSd		cm
LVIDd		cm
LVPWd		cm
EDV(Teich)		ml
IVSs		cm
LVIDs		cm
LVPWs		cm
ESV(Teich)		ml
EF(Teich)		%
%FS		%
SV(Teich)		ml
LV Major		cm
LV Minor		cm
Sphericity Index		
LVLd LAX		cm
LVAd LAX		cm

LVEDV A-L IAX	B6	ml
LVEDV MOD IAX		ml
LVLs IAX		cm
LVAs IAX		cm
LVESV A-L IAX		ml
LVESV MOD IAX		ml
HR		BPM
EF A-L IAX		%
LVEF MOD IAX		%
SV A-L IAX		ml
SV MOD IAX		ml
CO A-L IAX		l/min
CO MOD IAX		l/min

Doppler

MV E Vel	B6	m/s
MV DecT		ms
MV Dec Slope		m/s
MV A Vel		m/s
MV E/A Ratio		
E'		m/s
E/E'		
A'		m/s
S'		m/s
AV Vmax		m/s
AV maxPG		mmHg
PV Vmax		m/s
PV maxPG		mmHg

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 3/20/2019 8:28:29 PM

Subject: Acana Puppy and Junior: B6 EON-382870

Attachments: 2064331-report.pdf

A PFR Report has been received and PFR Event [EON-382870] has been created in the EON System.

A "PDF" report by name "2064331-report.pdf" is attached to this email notification for your reference.

Below is the summary of the report:

EON Key: EON-382870
ICSR #: 2064331
EON Title: PFR Event created for Acana Puppy and Junior, Horizon Pulsar Pulses & Chicken formula Grain free, Fromm Adult Gold; 2064331

AE Date	03/11/2019	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Shepherd Dog - Belgian Tervueren		
Age	46 Months		
District Involved	PFR-Foreign Firms DO		

Product information
Individual Case Safety Report Number: 2064331
Product Group: Pet Food
Product Name: Acana Puppy and Junior, Horizon Pulsar Pulses & Chicken formula, Grain free, Fromm Adult Gold
Description: Have fed Acana puppy for a few weeks, Horizon Pulsar, a grain free diet, for 3.5 years, Fromm adult gold for 3 months. Veterinarian detected a heart murmur, we elected to have dog under go an echocardiogram. Cardiologist diagnosed "Given her dietary history, it's certainly possible that B6 suffers from a diet-associated dilated cardiomyopathy". She is now on 3 medications, a new grain based diet and restricted activity for 6-12 months. Hopefully this will correct the problem.
Submission Type: Initial

Report Type: Both
Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 2
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Acana Puppy and Junior		
Horizon Pulsar Pulses & Chicken formula, Grain free		
Fromm Adult Gold		

Sender information

B6

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think

you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-382870			
ICSR:	2064331		
Type Of Submission:	Initial		
Report Version:	FPSR.FDA.PETF.V.V1		
Type Of Report:	Both		
Reporting Type:	Voluntary		
Report Submission Date:	2019-03-20 16:23:03 EDT		
Reporter is the Animal Owner:	Yes		
Reported Problem:	**Problem Description:**	Have fed Acana puppy for a few weeks, Horizon Pulsar, a grain free diet, for 3.5 years, Fromm adult gold for 3 months. Veterinarian detected a heart murmur, we elected to have dog under go an echocardiogram. Cardiologist diagnosed "Given her dietary history, it's certainly possible that B6 suffers from a diet-associated dilated cardiomyopathy". She is now on 3 medications, a new grain based diet and restricted activity for 6-12 months. Hopefully this will correct the problem.	
	Date Problem Started:	03/11/2019	
	Concurrent Medical Problem:	No	
	Outcome to Date:	Stable	
Product Information:	**Product Name:**	Fromm Adult Gold	
	Product Type:	Pet Food	
	Lot Number:		
	UPC:	072705115204	
	Package Type:	BAG	
	Package Size:	15 kilogram	
	Number Purchased:	1	
	Possess Unopened Product:	No	
	Possess Opened Product:	No	
	Storage Conditions:	In a bag in a plastic lidded container in the kitchen pantry.	
	Product Use Information:	**Description:**	1 cup in the morning, 1 cup in the evening
		First Exposure Date:	11/15/2018
		Last Exposure Date:	03/01/2019
		Time Interval between Product Use and Adverse Event:	1 Weeks
		Product Use Stopped After the Onset of the Adverse Event:	Yes
		Adverse Event Abate After Product Stop:	No
		Product Use Started Again:	No
		Perceived Relatedness to Adverse Event:	Possibly related
		Other Foods or Products Given to the Animal	No

	During This Time Period:	
Manufacturer /Distributor Information:		
Purchase Location Information:	Name:	B6
	Address:	B6
Product Name:	Horizon Pulsar Pulses & Chicken formula, Grain free	
Product Type:	Pet Food	
Lot Number:		
UPC:	851094001646	
Package Type:	BAG	
Package Size:	11.4 kilogram	
Number Purchased:	1	
Possess Unopened Product:	No	
Possess Opened Product:	No	
Storage Conditions:	In a bag in a plastic lidded container in the kitchen pantry.	
Product Use Information:	Description:	Approx. 1 cup morning and 1 cup evening
	First Exposure Date:	07/21/2015
	Last Exposure Date:	11/14/2018
	Time Interval between Product Use and Adverse Event:	3 Months
	Product Use Stopped After the Onset of the Adverse Event:	Yes
	Adverse Event Abate After Product Stop:	No
	Product Use Started Again:	No
	Perceived Relatedness to Adverse Event:	Probably related
	Other Foods or Products Given to the Animal During This Time Period:	No
Manufacturer /Distributor Information:		
Purchase Location Information:	Name:	B6
	Address:	B6

	Product Name:	Acana Puppy and Junior
	Product Type:	Pet Food
	Lot Number:	
	UPC:	064992500603
	Package Type:	BAG
	Package Size:	6 kilogram
	Purchase Date:	07/20/2015
	Number Purchased:	1
	Possess Unopened Product:	No
	Possess Opened Product:	No
	Storage Conditions:	In a bag in a plastic lidded container in the kitchen pantry.
	Product Use Information:	**Description:** Approx. 1/3 cup 3 times daily for only a few weeks.
		First Exposure Date: 07/21/2015
		Last Exposure Date: 08/07/2015
		Time Interval between Product Use and Adverse Event: 43 Months
		Product Use Stopped After the Onset of the Adverse Event: Yes
		Adverse Event Abate After Product Stop: No
		Product Use Started Again: No
		Perceived Relatedness to Adverse Event: Possibly related
		Other Foods or Products Given to the Animal During This Time Period: No
	Manufacturer /Distributor Information:	
	Purchase Location Information:	**Name:** B6
		Address: B6
Animal Information:	**Name:**	B6
	Type Of Species:	Dog
	Type Of Breed:	Shepherd Dog - Belgian Tervueren
	Gender:	Female
	Reproductive Status:	Intact
	Pregnancy Status:	Not Pregnant
	Lactation Status:	Not Applicable
	Weight:	47.2 Pound

	Age:	46 Months
	Assessment of Prior Health:	Excellent
	Number of Animals Given the Product:	2
	Number of Animals Reacted:	1
	Owner Information:	
	Healthcare Professional Information:	
Sender Information:	**Name:**	B6
	Address:	B6
	Contact:	**Phone:** B6 **Other Phone:** **Email:**
	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
	Reported to Other Parties:	Store/Place of Purchase Manufacturer Distributor
Additional Documents:		

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 3/21/2019 12:52:52 AM

Subject: American Journey Grain-free Salmon & Sweet Potato Recipe: B6 EON-382903

Attachments: 2064342-report.pdf; 2064342-attachments.zip

A PFR Report has been received and PFR Event [EON-382903] has been created in the EON System.

A "PDF" report by name "2064342-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2064342-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-382903
ICSR #: 2064342
EON Title: PFR Event created for American Journey Grain-free Salmon & Sweet Potato Recipe; 2064342

AE Date	03/10/2019	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Great Dane		
Age	17 Months		
District Involved	PFR- B6 DO		

Product information
Individual Case Safety Report Number: 2064342
Product Group: Pet Food
Product Name: American Journey Grain-free Salmon & Sweet Potato Recipe
Description: Labored breathing, coughing, lack of appetite.
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)
Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 1

Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
American Journey Grain-free Salmon & Sweet Potato Recipe	07 30 20, 19002 7833B 0301, 14:21	

Sender information

B6

USA

To view this PFR Event, nlease click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-382903

ICSR:	2064342
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-20 20:48:01 EDT
Reporter is the Animal Owner:	Yes

Reported Problem:

Problem Description:	Labored breathing, coughing, lack of appetite.
Date Problem Started:	03/10/2019
Date of Recovery:	03/19/2019
Concurrent Medical Problem:	No
Outcome to Date:	Stable

Product Information:

Product Name:	American Journey Grain-free Salmon & Sweet Potato Recipe
Product Type:	Pet Food
Lot Number:	**Lot Number:** 07 30 20, 19002 7833B 0301, 14:21
UPC:	9226812430
Package Type:	BAG
Package Size:	24 Pound
Purchase Date:	03/01/2019
Number Purchased:	2
Possess Unopened Product:	Yes
Possess Opened Product:	Yes
Storage Conditions:	Product was stored unopened till used then sores in a dog food sealed container

Product Use Information:

Description:	Feed **B6** American Journey from when we got him in July, 8 cups a day, puppy food from July and August (3 bags 24 lbs each) August to current (16 bags- 24 lbs each).
First Exposure Date:	03/02/2019
Last Exposure Date:	03/20/2019
Time Interval between Product Use and Adverse Event:	9 Months
Product Use Stopped After the Onset of the Adverse Event:	No
Perceived Relatedness to Adverse Event:	Probably related
Other Foods or Products Given to the Animal During This Time Period:	No

Manufacturer /Distributor Information:

Purchase Location Information:

Name:	Chewy.com

		Address:	B6 United States
Animal Information:	Name:	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Great Dane	
	Gender:	Male	
	Reproductive Status:	Neutered	
	Weight:	117 Pound	
	Age:	17 Months	
	Assessment of Prior Health:	Excellent	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:		
	Healthcare Professional Information:	Practice Name:	B6
		Contact:	Name: Phone: Email: B6
		Address:	B6 United States
		Type of Veterinarian:	Primary/regular veterinarian
		Date First Seen:	03/11/2019
		Permission to Release Records to FDA:	Yes
		Practice Name:	B6
		Contact:	Name: Phone: Email: B6
		Type of Veterinarian:	Referred veterinarian
		Date First Seen:	03/18/2019
		Permission to Release Records to FDA:	Yes
Sender Information:	Name:		
	Address:	B6 United States	
	Contact:	Phone: Email:	B6
	Permission To Contact Sender:	Yes	

	Preferred Method Of Contact:	Email
	Reported to Other Parties:	None
Additional Documents:		

Attachment:	1253[B6]doc
Description:	Ultrasound report done by Dr[B6]
Type:	Analysis

B6

B6

Date of Exam: 3/18/19
Invoice: 12530
Doctor:
Hospital: B6
Phone #:

Patient's Name: B6
Breed: Great Dane
Sex: Male neutered
DOB/Age: 13 months
Weight: 117 lbs.

HISTORY: B6 presented last week with increased respiratory rate, an inconsistent appetite, tachycardia, and ventricular tachycardia. Radiographically he had pulmonary infiltrates with cardiomegaly and an in-house echocardiogram was suggestive of dilated cardiomyopathy, but the owners declined an official echocardiogram at the time. The dog was sent home on Lasix, Benazepril, and Pimobendan as well as Amiodarone for the ventricular tachycardia. A plasma taurine level was run and was 81 (normal is 60-120). The owners consulted another local veterinarian who did not concur and discontinued all the cardiac medications. The dog presented today for an echocardiogram to assess for underlying disease.

EXAM: B6 was appreciably, extremely dyspneic with pale, muddy mucous membranes during the exam. The left atrium was markedly enlarged and there was no evidence of any thrombi or smoke within the atrium. The left ventricle was enlarged in diastole and systole. The myocardium was homogenous with no focal masses or infarcts. The mitral valve was normal thickness and demonstrated normal motion. The EPSS was markedly increased at 2.48 cm indicating annular dilation. The right atrium and right ventricle were enlarged. Contractility was markedly reduced both in real time as well as by measurement of fractional shortening at 15%. The left ventricular outflow tract velocities were reduced, and the right ventricular outflow tract velocities were normal. The tricuspid valve, aortic valve and pulmonic valve were smooth and normal thickness. There was mild focal mitral regurgitation and mild tricuspid regurgitation. There was no evidence of pleural or pericardial effusion nor any masses. Infinity B waves were noted in all lung fields consistent with fulminant pulmonary edema. The EKG demonstrated a normal sinus rhythm and ventricular arrythmias were not noted during the exam.

B6

B6

B6

Canine Echocardiographic Parameters

HR	B6	bpm	LVOT	B6	m/s	E wave	m/s
FS		%	RVOT		m/s	A wave	m/s
IVSd		cm	MR		m/s	E:A ratio	(1-1.9)
Lvd		cm	TR		m/s	IVRT	m/s
LVPWd		cm	AI		m/s	E:IVRT	m/s
LVIds		cm	PI		m/s	AT	m/s
LVIdN 1.27 – 1.85		cm	TR grad		mmHg	ET	m/s
LA/AO		Short axis	VHS			AT:ET	
LA			LVIddN			LVIdsN	B6

DIAGNOSIS: 1. Dilated cardiomyopathy with left atrial enlargement and evidence of congestive heart failure. This dog has been on a grain-free diet and this can be a grain-free diet associated cardiomyopathy; although, this breed of dog is also predisposed to the development of cardiomyopathy and a genetic component is also likely. The normal taurine level does not rule out a diet associated cardiomyopathy as approximately 50% of dogs with this disease have normal taurine levels.

COMMENTS: B6

B6

B6

B6

B6

B6

B6

B6

Document properties

Title: UNPROOFED REPORT (MAY CONTAIN ERRORS)
Author: B4, B6
Company:
Template: Building Blocks.dotx
Page count: 2
Paragraph count: 86
Line count: 186
Word count: 986
Character count (spaces excluded): 5038
Character count (spaces included): 6024

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 3/20/2019 8:12:46 PM

Subject: American Journey-Salmon and Sweet Potato; B6 EON-382867

Attachments: 2064327-report.pdf

A PFR Report has been received and PFR Event [EON-382867] has been created in the EON System.

A "PDF" report by name "2064327-report.pdf" is attached to this email notification for your reference.

Below is the summary of the report:

EON Key: EON-382867
ICSR #: 2064327
EON Title: PFR Event created for American Journey Salmon and Sweet Potato; 2064327

AE Date	B6	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Naturally
Breed	Bulldog		
Age	B6 Years		
District Involved	PFR- B6 DO		

Product information
Individual Case Safety Report Number: 2064327
Product Group: Pet Food
Product Name: American Journey Salmon and Sweet Potato
Description: She presented for lethargy, presumed by the owner to be due a recent lameness onset. During her exam, we noted that her heart rate was over 200 but her pulses were weak and occurred at 100 per minute. An immediate ECG was ordered but she collapsed before we could get her to the treatment area. We initiated CPR but she had no cardiac electrical activity on our monitor. We continued CPR for 20 minutes but she did not respond. We sent myocardium to B6 and received the following report: Description Three sections of myocardium are examined. In these sections of myocardium, there are thin strands of fibrous connective tissue interspersed between myocardial fibers. Also interspersed between myocardial fibers are abundant accumulations of adipose tissue. Some of the entrapped myocardial fibers are

atrophic while other myocardial fibers are hypertrophic. Histopathologic Diagnosis Myocardium (three specimens): Multifocal myocardial fibrosis and steatosis with multifocal fiber atrophy Comments The histologic lesions observed in the examined sections of myocardium are compatible with underlying cardiomyopathy. Presumably, arrhythmias associated with cardiomyopathy were the primary underlying cause of the clinical syndrome and death. Authorized by: B6 DVM, PhD, DACVP Histopathology Section Head & Veterinary Pathologist

Submission Type: Initial

Report Type: Adverse Event (a symptom, reaction or disease associated with the product)

Outcome of reaction/event at the time of last observation: Died Naturally

Number of Animals Treated With Product: 1

Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
American Journey Salmon and Sweet Potato		

Sender information

B6

USA

Owner information

B6 USA

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade

secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-382867

ICSR:	2064327
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-20 16:08:48 EDT

Reported Problem:

Problem Description:	She presented for lethargy, presumed by the owner to be due a recent lameness onset. During her exam, we noted that her heart rate was over 200 but her pulses were weak and occurred at 100 per minute. An immediate ECG was ordered but she collapsed before we could get her to the treatment area. We initiated CPR but she had no cardiac electrical activity on our monitor. We continued CPR for 20 minutes but she did not respond. We sent myocardium to B6 B6 and received the following report: Description Three sections of myocardium are examined. In these sections of myocardium, there are thin strands of fibrous connective tissue interspersed between myocardial fibers. Also interspersed between myocardial fibers are abundant accumulations of adipose tissue. Some of the entrapped myocardial fibers are atrophic while other myocardial fibers are hypertrophic. Histopathologic Diagnosis Myocardium (three specimens): Multifocal myocardial fibrosis and steatosis with multifocal fiber atrophy Comments The histologic lesions observed in the examined sections of myocardium are compatible with underlying cardiomyopathy. Presumably, arrhythmias associated with cardiomyopathy were the primary underlying cause of the clinical syndrome and death. Authorized by: B6 , DVM, PhD, DACVP Histopathology Section Head & Veterinary Pathologist
Date Problem Started:	B6
Concurrent Medical Problem:	Yes
Pre Existing Conditions:	She had been on Oclacitinib in 2017 for allergy
Outcome to Date:	Died Naturally
Date of Death:	B6

Product Information:

Product Name:	American Journey Salmon and Sweet Potato
Product Type:	Pet Food
Lot Number:	
UPC:	unknown, ask owne
Package Type:	BAG
Package Size:	24 Pound
Purchase Date:	03/01/2019
Number Purchased:	1
Possess Unopened Product:	No
Possess Opened Product:	Yes
Storage Conditions:	unknown

Product Use Information:

Description:	Fed twice daily
First Exposure Date:	03/01/2019
Last Exposure Date:	B6
Time Interval between Product Use and Adverse Event:	4 Years
Product Use Stopped After the Onset of the	Yes

		Adverse Event:	
		Adverse Event Abate After Product Stop:	Not Applicable
		Product Use Started Again:	No
		Perceived Relatedness to Adverse Event:	Possibly related
		Other Foods or Products Given to the Animal During This Time Period:	Unknown
	Manufacturer /Distributor Information:		
	Purchase Location Information:	Name:	chewy.com
		Address:	United States
Animal Information:	Name:	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Bulldog	
	Gender:	Female	
	Reproductive Status:	Neutered	
	Weight:	57 Pound	
	Age:	4.5 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:	Owner Information provided:	Yes
		Contact: Name:	B6
		Phone:	
		Address:	B6 United States
	Healthcare Professional Information:	Practice Name:	B6
		Contact: Name:	B6
		Phone:	
		Email:	
		Address:	B6 United States
Sender Information:	Name:		
	Address:	B6	

		B6 United States
	Contact:	Phone: Email: B6
	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
	Reported to Other Parties:	None
Additional Documents:		

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification; B6

Sent: 3/20/2019 8:12:46 PM

Subject: American Journey-Salmon and Sweet Potato B6 - EON-382867

Attachments: 2064327-report.pdf

A PFR Report has been received and PFR Event [EON-382867] has been created in the EON System.

A "PDF" report by name "2064327-report.pdf" is attached to this email notification for your reference.

Below is the summary of the report:

EON Key: EON-382867
ICSR #: 2064327
EON Title: PFR Event created for American Journey Salmon and Sweet Potato; 2064327

AE Date	B6	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Naturally
Breed	Bulldog		
Age	4.5 Years		
District Involved	PFR- B6 DO		

Product information
Individual Case Safety Report Number: 2064327
Product Group: Pet Food
Product Name: American Journey Salmon and Sweet Potato
Description: She presented for lethargy, presumed by the owner to be due a recent lameness onset. During her exam, we noted that her heart rate was over 200 but her pulses were weak and occurred at 100 per minute. An immediate ECG was ordered but she collapsed before we could get her to the treatment area. We initiated CPR but she had no cardiac electrical activity on our monitor. We continued CPR for 20 minutes but she did not respond. We sent myocardium to B6 and received the following report: Description Three sections of myocardium are examined. In these sections of myocardium, there are thin strands of fibrous connective tissue interspersed between myocardial fibers. Also interspersed between myocardial fibers are abundant accumulations of adipose tissue. Some of the entrapped myocardial fibers are

atrophic while other myocardial fibers are hypertrophic. Histopathologic Diagnosis Myocardium (three specimens): Multifocal myocardial fibrosis and steatosis with multifocal fiber atrophy Comments The histologic lesions observed in the examined sections of myocardium are compatible with underlying cardiomyopathy. Presumably, arrhythmias associated with cardiomyopathy were the primary underlying cause of the clinical syndrome and death. Authorized by B6 DVM, PhD, DACVP Histopathology Section Head & Veterinary Pathologist

Submission Type: Initial

Report Type: Adverse Event (a symptom, reaction or disease associated with the product)

Outcome of reaction/event at the time of last observation: Died Naturally

Number of Animals Treated With Product: 1

Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
American Journey Salmon and Sweet Potato		

Sender information

B6

USA

Owner information

B6 USA

To view this PFR Event, please click the link below:

B6

To view the PFR Event Report, please click the link below:

B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade

secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-382867

ICSR:	2064327
Type Of Submission:	Initial
Report Version:	FPSR.FDA.PETF.V.V1
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)
Reporting Type:	Voluntary
Report Submission Date:	2019-03-20 16:08:48 EDT

Reported Problem:

Problem Description:	She presented for lethargy, presumed by the owner to be due a recent lameness onset. During her exam, we noted that her heart rate was over 200 but her pulses were weak and occurred at 100 per minute. An immediate ECG was ordered but she collapsed before we could get her to the treatment area. We initiated CPR but she had no cardiac electrical activity on our monitor. We continued CPR for 20 minutes but she did not respond. We sent myocardium to B6 B6 and received the following report: Description Three sections of myocardium are examined. In these sections of myocardium, there are thin strands of fibrous connective tissue interspersed between myocardial fibers. Also interspersed between myocardial fibers are abundant accumulations of adipose tissue. Some of the entrapped myocardial fibers are atrophic while other myocardial fibers are hypertrophic. Histopathologic Diagnosis Myocardium (three specimens): Multifocal myocardial fibrosis and steatosis with multifocal fiber atrophy Comments The histologic lesions observed in the examined sections of myocardium are compatible with underlying cardiomyopathy. Presumably, arrhythmias associated with cardiomyopathy were the primary underlying cause of the clinical syndrome and death. Authorized by: B6 DVM, PhD, DACVP Histopathology Section Head & Veterinary Pathologist
Date Problem Started:	B6
Concurrent Medical Problem:	Yes
Pre Existing Conditions:	She had been on Oclacitinib in 2017 for allergy
Outcome to Date:	Died Naturally
Date of Death:	B6

Product Information:

Product Name:	American Journey Salmon and Sweet Potato
Product Type:	Pet Food
Lot Number:	
UPC:	unknown, ask owne
Package Type:	BAG
Package Size:	24 Pound
Purchase Date:	03/01/2019
Number Purchased:	1
Possess Unopened Product:	No
Possess Opened Product:	Yes
Storage Conditions:	unknown

Product Use Information:

Description:	Fed twice daily
First Exposure Date:	03/01/2019
Last Exposure Date:	B6
Time Interval between Product Use and Adverse Event:	4 Years
Product Use Stopped After the Onset of the	Yes

		Adverse Event:	
		Adverse Event Abate After Product Stop:	Not Applicable
		Product Use Started Again:	No
		Perceived Relatedness to Adverse Event:	Possibly related
		Other Foods or Products Given to the Animal During This Time Period:	Unknown
	Manufacturer /Distributor Information:		
	Purchase Location Information:	Name:	chewy.com
		Address:	United States
Animal Information:	Name:	B6	
	Type Of Species:	Dog	
	Type Of Breed:	Bulldog	
	Gender:	Female	
	Reproductive Status:	Neutered	
	Weight:	57 Pound	
	Age:	4.5 Years	
	Assessment of Prior Health:	Good	
	Number of Animals Given the Product:	1	
	Number of Animals Reacted:	1	
	Owner Information:	Owner Information provided:	Yes
		Contact:	Name: B6
			Phone:
		Address:	B6
			United States
	Healthcare Professional Information:	Practice Name:	B6
		Contact:	Name:
			Phone: B6
			Email:
		Address:	B6
			United States
Sender Information:	Name:		
	Address:	B6	

		B6 United States
	Contact:	Phone: Email: B6
	Permission To Contact Sender:	Yes
	Preferred Method Of Contact:	Email
	Reported to Other Parties:	None
Additional Documents:		

From: PFR Event <pfreventcreation@fda.hhs.gov>

To: Cleary, Michael *; HQ Pet Food Report Notification B6

Sent: 2/27/2019 7:00:50 PM

Subject: CANIDAE- ALL LIFE STAGES-CHICKEN MEAL & RICE FORMULA--DRY DOG FOOD: Lisa Freeman - EON-381040

Attachments: 2063286-report.pdf; 2063286-attachments.zip

A PFR Report has been received and PFR Event [EON-381040] has been created in the EON System.

A "PDF" report by name "2063286-report.pdf" is attached to this email notification for your reference. Please note that all documents received in the report are compressed into a zip file by name "2063286-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-381040
ICSR #: 2063286
EON Title: PFR Event created for CANIDAE® ALL LIFE STAGES CHICKEN MEAL & RICE FORMULA DRY DOG FOOD; 2063286

AE Date	02/25/2019	**Number Fed/Exposed**	3
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Doberman Pinscher		
Age	B6 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2063286
Product Group: Pet Food
Product Name: CANIDAE® ALL LIFE STAGES CHICKEN MEAL & RICE FORMULA DRY DOG FOOD
Description: DCM and CHF diagnosed 2/25/19. Eating BEG diet. 2 other dogs in household will be screened. Will change diet on B6 and reassess in 3 months. Just being discharged today. Taurine and troponin pending
Submission Type: Initial
Report Type: Adverse Event (a symptom, reaction or disease associated with the product)

Outcome of reaction/event at the time of last observation: Stable
Number of Animals Treated With Product: 3
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
CANIDAE® ALL LIFE STAGES CHICKEN MEAL & RICE FORMULA DRY DOG FOOD		

Sender information
Lisa Freeman
200 Westboro Rd
North Grafton, MA 01536
USA

Owner information
B6 USA

To view this PFR Event, please click the link below:
B6

To view the PFR Event Report, please click the link below:
B6

==========

This email and attached document are being provided to you in your capacity as a Commissioned Official with the U.S. Department of Health and Human Services as authorized by law. You are being provided with this information pursuant to your signed Acceptance of Commission.

This email message is intended for the exclusive use of the recipient(s) named above. It may contain information that is protected, privileged, or confidential. Any dissemination, distribution, or copying is strictly prohibited.

The information is provided as part of the Federal-State Integration initiative. As a Commissioned Official and state government official, you are reminded of your obligation to protect non-public information, including trade secret and confidential commercial information that you receive from the U.S. Food and Drug Administration from further disclosure. The information in the report is intended for situational awareness and should not be shared or acted upon independently. Any and all actions regarding this information should be coordinated through your local district FDA office.

Failure to adhere to the above provisions could result in removal from the approved distribution list. If you think

you received this email in error, please send an email to FDAReportableFoods@fda.hhs.gov immediately.

Report Details - EON-381040

ICSR:	2063286			
Type Of Submission:	Initial			
Report Version:	FPSR.FDA.PETF.V.V1			
Type Of Report:	Adverse Event (a symptom, reaction or disease associated with the product)			
Reporting Type:	Voluntary			
Report Submission Date:	2019-02-27 13:49:14 EST			
Reported Problem:	**Problem Description:**	DCM and CHF diagnosed 2/25/19. Eating BEG diet. 2 other dogs in household will be screened. Will change diet on B6 and reassess in 3 months. Just being discharged today. Taurine and troponin pending		
	Date Problem Started:	02/25/2019		
	Concurrent Medical Problem:	Yes		
	Pre Existing Conditions:	Lick granulomas		
	Outcome to Date:	Stable		
Product Information:	**Product Name:**	CANIDAE® ALL LIFE STAGES CHICKEN MEAL & RICE FORMULA DRY DOG FOOD		
	Product Type:	Pet Food		
	Lot Number:			
	Product Use Information:	**Description:**	Fed this diet most of his life	
	Manufacturer /Distributor Information:			
	Purchase Location Information:			
Animal Information:	**Name:**	B6		
	Type Of Species:	Dog		
	Type Of Breed:	Doberman Pinscher		
	Gender:	Male		
	Reproductive Status:	Intact		
	Weight:	60 Kilogram		
	Age:	B6 Years		
	Assessment of Prior Health:	Excellent		
	Number of Animals Given the Product:	3		
	Number of Animals Reacted:	1		
	Owner Information:	**Owner Information provided:**	Yes	
		Contact:	**Name:** B6	
			Phone:	
			Email:	
		Address:	B6	
			United States	
	Healthcare Professional Information:	**Practice Name:**	Tufts Cummings School of Veterinary Medicine	
		Contact:	**Name:**	Lisa Freeman
			Phone:	(508) 887-4523
			Email:	lisa.freeman@tufts.edu

		Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States
Sender Information:	**Name:**	Lisa Freeman	
	Address:	200 Westboro Rd North Grafton Massachusetts 01536 United States	
	Contact:	**Phone:**	5088874523
		Email:	lisa.freeman@tufts.edu
	Permission To Contact Sender:	Yes	
	Preferred Method Of Contact:	Email	
Additional Documents:			
	Attachment:	rpt_medical_record_preview.pdf	
	Description:	Medical records	
	Type:	Medical Records	

Cummings Veterinary Medical Center AT TUFTS UNIVERSITY

B6

All Medical Records

Client: B6
Address:

Patient: B6
Breed: Doberman Pinscher
DOB: B6

Species: Canine
Sex: Male

Home Phone:
Work Phone:
Cell Phone: B6

Referring Information

B6

Client:
Patient: B6

Initial Complaint:
Emergency

SOAP Text B6 9:28PM - B6

Subjective
NEW VISIT (ER)

Doctor: B6
Presenting complaint: Left hind leg discomfort

HISTORY:
-Left hind lameness today - no trauma noted
-Uncomfortable and unable to sleep or get up on bed or couch. Struggling to get up and down
Prior medical history: History of acral lick granulomas - have been there a while. Use e-collar to control. Have been doing a lot for them with their rDVM. No other medical history

B6

EXAM:

B6

Client: B6
Patient:

B6

ASSESSMENT:
A1: Fever: r/o inflammatory (impa vs ticke borne) vs infectious vs neoplasia vs stress vs other
A2: Left hind limb lameness: R/o orthopedic vs soft tissue vs IMPA vs tick borne

PLAN:

B6

Client communication: B6

B6

SOAP approved (DVM to sign): B6 DVM

Initial Complaint:
Emergency

SOAP Text Feb 25 2019 4:46PM - B6

Subjective
NEW VISIT (ER)

Doctor: B6
Student:

Client: B6
Patient:

Presenting complaint: Suspect CHF
Referral visit? Yes
Diagnostics completed prior to visit: 3 view CXR (in e-mail)

HISTORY:

Signalment: 3yo MI Doberman Pinscher
Current history: Presenting today for suspect CHF after visiting rDVM earlier today - according to O, 3 view CXR's showed evidence of pleural effusion. They were referred to Tufts at this time. O reports that B6 began coughing last Thursday (2/21). The owners contacted their rDVM, who was supicious of URI and prescribed antibiotics (O was unsure of name/dose of abx). The last dose of antibiotics was given yesterday, 2/24. This morning B6 was having increased respiratory effort as well as difficulty getting comfortable while laying down.
Prior medical history: Suspect acral lick dermatitis/granulomas on distal limbs
Current medications: N/A
Diet: Canidae All Life Stages dry food (grain free) - has been eating this for 1.5 - 2 years.
Vaccination status/flea & tick preventative use: UTD (O brought records), HWP monthly, F/T seasonally
Travel history: N/A

EXAM:

B6

B6

ASSESSMENT:
A1: Increased respiratory rate and effort r/o: congestive heart failure (DCM vs other) vs pneumonia
A2: Tachycardic r/o: CHF vs stress
A3: Suspect acral lick dermatitis/granulomas on distal limbs

PLAN:

B6

Client: B6
Patient:

B6

B6

Diagnostics completed:

B6

Diagnostics pending:

B6

SOAP approved (DVM to sign): B6 dvm

Addendum:
Starting at 2:32am, P started having atrial fibrillation >200bpm on telemetry, consistent with auscultation and pulse deficits on physical examination. P clinically well despite cardiac rhythm. rate slowed down for a period of time until re-starting >200bpm at 3:17am where it was sustained. At 4am started 45mg regular (not ER) diltiazem PO q8. Converted to NSR at 6:30 am and discontinued further dilt tx pending cardiology assessment.
SCudney

SOAP Text Feb 26 2019 7:18AM - B6

History:

4 y/o IM Doberman Pinscher presented yesterday to the Tufts ER for suspect CHF after visiting rDVM-3 view CXR's showed evidence of pulmonary edema/pleural effusion. O reports that B6 began coughing last Thursday (2/21). The owners contacted their rDVM, who was supicious of URI and prescribed antibiotics (O was unsure of name/dose of abx). The last dose of antibiotics was given 2/24. B6 was having increased respiratory effort as well as difficulty getting comfortable while laying down.

Overnight: P given 100mg Furosemide IV at ~4:30PM and 150mg Furosemide IV at ~5:30PM. Starting at 2:32am, P started having atrial fibrillation >200bpm on telemetry, consistent with auscultation and pulse deficits on physical examination. P clinically well despite cardiac rhythm. Rate slowed down for a period of time until re-starting >200bpm at 3:17am where it was sustained. At 4am started 45mg regular (not ER) diltiazem PO q8. Converted to NSR at 6:30 am and discontinued further dilt tx pending cardiology assessment.

Subjective:

B6

B6

B6

Overall impression since arrival or since last exam: Stable to improve since presentation. The RR and RE improved overnight and B6 appears more comfortable this morning. He had new onset atrial fibrillation and converted back to sinus rhythm which is quite unusual but is still in sinus rhythm this morning.
Appetite: No interest in food since arrival
Diet History: Canidae All Life Stages dry food (grain free) - has been eating this for 1.5 - 2 years.

Objective:

B6

Diagnostics:

B6

Assessments

B6

Plan

Client: B6
Patient:

B6

SOAP completed by B6 V19
SOAP reviewed by:

B6

SOAP Text Feb 27 2019 7:48AM - B6

History:

4 y/o IM Doberman Pinscher presented yesterday to the Tufts ER for suspect CHF after visiting rDVM-3 view CXR's showed evidence of pulmonary edema/pleural effusion. O reports that B6 began coughing last Thursday (2/21). The owners contacted their rDVM, who was supicious of URI and prescribed antibiotics (O was unsure of name/dose of abx). The last dose of antibiotics was given 2/24. B6 was having increased respiratory effort as well as difficulty getting comfortable while laying down.

-2/25/19 (overnight) P given 100mg Furosemide IV at ~4:30PM and 150mg Furosemide IV at ~5:30PM. Starting at 2:32am, P started having atrial fibrillation >200bpm on telemetry, consistent with auscultation and pulse deficits on physical examination. P clinically well despite cardiac rhythm. Rate slowed down for a period of time until re-starting >200bpm at 3:17am where it was sustained. At 4am started 45mg regular (not ER) diltiazem PO q8. Converted to NSR at 6:30 am and discontinued further dilt tx pending cardiology assessment.

-2/26/19 (overnight): P remained stable overnight, converted to sinus rhythm ~11PM. No interest in food overnight, eager to drink water when bowl placed in front of him.

Subjective:

B6

Overall impression since arrival or since last exam: Stable to improved since presentation. The RR and RE have remained stable since removed from oxygen. No atrial fibrillation since 11PM and normal sinus rhythm this morning.
Appetite: No interest in food since arrival
Diet History: Canidae All Life Stages dry food (grain free) - has been eating this for 1.5 - 2 years.

Objective:

B6

Client: B6
Patient:

B6

Diagnostics:

B6

Assessments

B6

Plan

B6

SOAP completed by B6
SOAP reviewed by:

Disposition/Recommendations

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Client:	B6
Veterinarian:	
Patient ID:	438113
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Doberman Pinscher
Sex:	Male
Age:	B6 Years Old

Lab Results Report

None **1/28/2019 12:19:34 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
Anaplasma (4dx)	B6	0 - 0	
Ehrlichia (4dx)		0 - 0	
Heartworm (4DX) - FHSA		0 - 0	
Lyme (4dx)*		0 - 0	

None **2/25/2019 4:52:25 PM** **Accession ID:** B6

Test	Results	Reference Range	Units
SO2%	B6	94 - 100	%
HCT (POC)		38 - 48	%
HB (POC)		12.6 - 16	g/dL
NA (POC)		140 - 154	mmol/L
K (POC)		3.6 - 4.8	mmol/L
CL(POC)		109 - 120	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
MG (POC)		0.1 - 0.4	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
CREAT (POC)		0.2 - 2.1	mg/dL
TCO2 (POC)		0 - 0	mmol/L
nCA		0 - 0	mmol/L
nMG		0 - 0	mmol/L

GAP	B6	0 - 0	mmol/L
CA/MG		0 - 0	mol/mol
BEecf		0 - 0	mmol/L
BEb		0 - 0	mmol/L
A		0 - 0	mmHg
NOVA SAMPLE		0 - 0	
FiO2		0 - 0	%
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

None **2/25/2019 4:59:11 PM** **Accession ID:** B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

None **2/26/2019 9:37:18 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
T. PROTEIN		5.5 - 7.8	g/dL
ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
POTASSIUM		3.7 - 5.4	mEq/L
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
ALK PHOS		12 - 127	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CHOLESTEROL		82 - 355	mg/dL
OSMOLALITY (CALCULATED)		291 - 315	mmol/L

None **2/26/2019 10:10:37 AM** **Accession ID:** B6

Client:
Patient: B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

None **2/27/2019 10:46:18 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
T. PROTEIN		5.5 - 7.8	g/dL
ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
86 Result(s) verified			
POTASSIUM		3.7 - 5.4	mEq/L
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
ALK PHOS		12 - 127	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CHOLESTEROL		82 - 355	mg/dL
OSMOLALITY (CALCULATED)		291 - 315	mmol/L

None **2/27/2019 10:46:09 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

None **2/27/2019 11:17:25 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
MAGNESIUM 2+		1.8 - 3	mEq/L
T. PROTEIN		5.5 - 7.8	g/dL

Client:
Patient: B6

ALBUMIN		2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
87 Result(s) verified			
POTASSIUM		3.7 - 5.4	mEq/L
tCO2 (BICARB)		14 - 28	mEq/L
AGAP		8 - 19	
NA/K	B6	29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
ALK PHOS		12 - 127	U/L
GGT		0 - 10	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CK		22 - 422	U/L
CHOLESTEROL		82 - 355	mg/dL
TRIGLYCERIDES		30 - 338	mg/dl
AMYLASE		409 - 1250	U/L
OSMOLALITY (CALCULATED)		291 - 315	mmol/L

B6

stringsoft

Printed Wednesday, February 27, 2019

Client:
Patient: B6

CBC/Chem - 2/25/2019

Tufts Cummings School Of Veterinary Medicine

200 Westboro Road
North Grafton, MA 01536

DUPLICATE

Name/DOB: B6
Patient ID: 458113
Phone number:
Collection Date: 2/25/2019 6:09 PM
Approval date: 2/25/2019 7:13 PM

Sex: M
Age: 3
Species: Canine
Breed: Doberman Pinscher

Provider: B6
Order Location: V320559: Investigation into
Sample ID: 1902250140

CBC, Comprehensive, Sm Animal (Research)

			Ref. Range/Males
SMACHUNSKI			
WBC (ADVIA)			4.40-15.10 K/uL
RBC (Advia)	L		5.80-8.50 M/uL
Hemoglobin (ADVIA)	L		13.3-20.5 g/dL
Hematocrit (Advia)	L		39-55 %
MCV (ADVIA)			64.5-77.5 fL
MCH (ADVIA)			21.3-25.9 pg
CHCM			
MCHC (ADVIA)			31.9-34.3 g/dL
RDW (ADVIA)			11.9-15.2
Platelet Count (Advia) 02/25/19 6:51 PM			173-486 K/uL
Mean Platelet Volume (Advia) 02/25/19 6:28 PM			8.29-13.20 fl
Platelet Crit 02/25/19 6:28 PM	H		0.129-0.403 %
PDW			
Reticulocyte Count (Advia)	H		0.20-1.60 %
Absolute Reticulocyte Count (Advia)	H		14.7-113.7 K/uL
CHr			
MCVr			

B6

Microscopic Exam of Blood Smear (Advia)

			Ref. Range/Males
SMACHUNSKI			
Seg Neuts (%)			43-86 %
Lymphocytes (%)	L		7-47 %
Monocytes (%)			1-15 %
Nucleated RBC 02/25/19 6:28 PM	H		0-1 /100 WBC
Seg Neutrophils (Abs) Advia	H		2.800-11.500 K/ul
Lymphs (Abs) Advia	L		1.00-4.80 K/uL
Mono (Abs) Advia			0.10-1.50 K/uL
WBC Morphology			
Polychromasia			

B6

Research Chemistry Profile - Small Animal (B6)

Sample ID: 1902250140/1
This report continues... (Final)

Reviewed by: _____

Tufts Cummings School Of Veterinary Medicine
200 Westboro Road
North Grafton, MA 01536

DUPLICATE

Name/DOB: B6 (5/15/2015)
Patient ID: 438113
Phone number:
Collection Date: 2/25/2019 6:09 PM
Approval date: 2/25/2019 7:13 PM

Sex: M
Age: 3
Species: Canine
Breed: Doberman Pinscher

Provider: B6
Order Location: V3203539: Investigation into
Sample ID: 1902250140

Research Chemistry Profile - Small Animal (B6) (cont'd)

SMACHUNSKI		B6	Ref. Range/Males
Glucose			67-135 mg/dL
Urea			8-30 mg/dL
Creatinine			0.6-2.0 mg/dL
Phosphorus			2.6-7.2 mg/dL
Calcium 2			9.4-11.3 mg/dL
Magnesium 2+	L		1.8-3.0 mEq/L
Total Protein			5.5-7.8 g/dL
Albumin			2.8-4.0 g/dL
Globulins			2.3-4.2 g/dL
A/G Ratio			0.7-1.6
Sodium			140-150 mEq/L
Chloride	L		106-116 mEq/L
Potassium			3.7-5.4 mEq/L
tCO2(Bicarb)			14-28 mEq/L
AGAP			8.0-19.0
NA/K	L		29-40
Total Bilirubin			0.10-0.30 mg/dL
Alkaline Phosphatase			12-127 U/L
GGT			0-10 U/L
ALT			14-86 U/L
AST			9-54 U/L
Creatine Kinase			22-422 U/L
Cholesterol	H		82-355 mg/dL
Triglycerides			30-338 mg/dl
Amylase			409-1250 U/L
Osmolality (calculated)	L		291-315 mmol/L

Client: B6
Patient:

IDEXX BNP - 2/25/2019

B4 eference Laboratories

Client: B6

B6

Client: B6
Patient:
Species: CANINE
Breed: DOBERMAN_PINSCH
Gender: MALE
Age: 3Y

Date: 02/25/2019
Requisition #: JA
Accession #: B6
Ordered by: B6

TUFTS UNIVERSITY
200 WESTBORO RD
NORTH GRAFTON, Massachusetts 01536
508-839-5395

Account #88933

CARDIOPET proBNP - CANINE

Test	Result	Reference Range	Low	Normal	High
CARDIOPET proBNP - CANINE	B6	0 - 900 pmol/L	HIGH		

B6

Please note: Complete interpretive comments for all concentrations of Cardiopet proBNP are available in the online directory of services. Serum specimens received at room temperature may have decreased NT-proBNP concentrations.

Page 1 of 1

Client:
Patient: B6

Vitals Results

B6

10:00:27 PM	Heart Rate (/min)
10:00:29 PM	Temperature (F)
10:00:30 PM	Weight (kg)
4:46:45 PM	Heart Rate (/min)
4:46:46 PM	Temperature (F)
4:46:47 PM	Respiratory Rate
4:58:34 PM	Lasix treatment note
5:23:00 PM	Lasix treatment note
6:19:31 PM	FiO2 (%)
6:19:38 PM	Respiratory Rate
7:34:46 PM	Amount eaten
8:11:13 PM	FiO2 (%)
8:11:35 PM	Cardiac rhythm
8:11:36 PM	Heart Rate (/min)
8:11:47 PM	Respiratory Rate
8:36:39 PM	FiO2 (%)
8:36:47 PM	Respiratory Rate
9:31:47 PM	FiO2 (%)
9:32:00 PM	Eliminations
9:32:13 PM	Cardiac rhythm
9:32:14 PM	Heart Rate (/min)
9:32:36 PM	Respiratory Rate
9:40:39 PM	Lasix treatment note
9:40:47 PM	Catheter Assessment
10:49:51 PM	Cardiac rhythm
10:49:52 PM	Heart Rate (/min)
10:50:28 PM	Respiratory Rate
10:50:37 PM	FiO2 (%)
10:50:47 PM	Eliminations
11:37:53 PM	Cardiac rhythm
11:37:54 PM	Heart Rate (/min)
11:38:31 PM	FiO2 (%)
11:38:38 PM	Respiratory Rate
12:48:55 AM	FiO2 (%)
12:49:03 AM	Respiratory Rate
12:49:20 AM	Cardiac rhythm
12:49:21 AM	Heart Rate (/min)
1:04:45 AM	Lasix treatment note
1:04:55 AM	Catheter Assessment

B6

Client:
Patient: B6

Vitals Results

B6

1:21:13 AM	Eliminations
1:21:57 AM	Eliminations
1:22:08 AM	Cardiac rhythm
1:22:09 AM	Heart Rate (/min)
1:23:39 AM	FiO2 (%)
1:23:48 AM	Respiratory Rate
2:19:46 AM	Cardiac rhythm
2:19:47 AM	Heart Rate (/min)
2:21:02 AM	FiO2 (%)
2:21:09 AM	Respiratory Rate
3:27:16 AM	Respiratory Rate
3:27:34 AM	Cardiac rhythm
3:27:35 AM	Heart Rate (/min)
3:27:56 AM	FiO2 (%)
3:52:05 AM	Eliminations
4:34:17 AM	FiO2 (%)
4:34:34 AM	Cardiac rhythm
4:34:35 AM	Heart Rate (/min)
4:34:54 AM	Respiratory Rate
5:23:41 AM	Lasix treatment note
5:25:58 AM	Amount eaten
5:26:39 AM	FiO2 (%)
5:26:47 AM	Catheter Assessment
5:27:00 AM	Eliminations
5:27:30 AM	Respiratory Rate
5:28:36 AM	Cardiac rhythm
5:28:37 AM	Heart Rate (/min)
6:33:22 AM	FiO2 (%)
6:33:31 AM	Cardiac rhythm
6:33:32 AM	Heart Rate (/min)
6:33:44 AM	Respiratory Rate
6:58:26 AM	FiO2 (%)
6:58:41 AM	Respiratory Rate
7:05:37 AM	Heart Rate (/min)
7:06:38 AM	Cardiac rhythm
7:06:39 AM	Heart Rate (/min)
7:10:40 AM	Temperature (F)
9:07:00 AM	Cardiac rhythm
9:07:01 AM	Heart Rate (/min)
9:07:59 AM	Respiratory Rate
9:08:42 AM	FiO2 (%)

B6

Client: B6
Patient:

Vitals Results

B6

9:35:51 AM	Lasix treatment note
9:36:07 AM	Catheter Assessment
9:36:23 AM	Respiratory Rate
9:36:40 AM	FiO2 (%)
10:08:22 AM	Cardiac rhythm
10:08:23 AM	Heart Rate (/min)
10:36:31 AM	Cardiac rhythm
10:36:58 AM	Heart Rate (/min)
11:09:05 AM	Cardiac rhythm
11:09:06 AM	Heart Rate (/min)
11:09:54 AM	FiO2 (%)
11:10:13 AM	FiO2 (%)
12:19:00 PM	Cardiac rhythm
12:19:01 PM	Heart Rate (/min)
12:19:17 PM	FiO2 (%)
1:05:19 PM	Cardiac rhythm
1:05:20 PM	Heart Rate (/min)
1:05:29 PM	FiO2 (%)
1:15:27 PM	Respiratory Rate
1:41:39 PM	FiO2 (%)
1:41:52 PM	Catheter Assessment
1:42:48 PM	Respiratory Rate
1:56:11 PM	Cardiac rhythm
1:56:12 PM	Heart Rate (/min)
1:56:29 PM	Eliminations
2:47:23 PM	FiO2 (%)
2:47:35 PM	Cardiac rhythm
2:47:36 PM	Heart Rate (/min)
2:47:58 PM	Respiratory Rate
3:38:55 PM	FiO2 (%)
3:39:03 PM	Cardiac rhythm
3:39:04 PM	Heart Rate (/min)
3:40:32 PM	Respiratory Rate
4:08:34 PM	Lasix treatment note
4:56:17 PM	Cardiac rhythm
4:56:18 PM	Heart Rate (/min)
4:56:29 PM	Respiratory Rate
5:07:18 PM	Catheter Assessment

B6

Client: B6
Patient:

Vitals Results

5:28:28 PM	Cardiac rhythm
5:28:29 PM	Heart Rate (/min)
5:28:53 PM	Amount eaten
5:29:10 PM	Respiratory Rate
5:36:02 PM	Eliminations
7:03:18 PM	Cardiac rhythm
7:03:19 PM	Heart Rate (/min)
7:03:59 PM	Respiratory Rate
7:28:32 PM	Cardiac rhythm
7:28:33 PM	Heart Rate (/min)
7:28:47 PM	Respiratory Rate
8:40:39 PM	Cardiac rhythm
8:40:40 PM	Heart Rate (/min)
8:41:22 PM	Respiratory Rate
9:25:13 PM	Cardiac rhythm
9:25:14 PM	Heart Rate (/min)
9:25:24 PM	Catheter Assessment
9:25:35 PM	Respiratory Rate
10:54:11 PM	Cardiac rhythm
10:54:12 PM	Heart Rate (/min)
10:55:00 PM	Respiratory Rate
11:37:22 PM	Cardiac rhythm
11:37:23 PM	Heart Rate (/min)
11:37:58 PM	Respiratory Rate
11:52:29 PM	Lasix treatment note
12:36:51 AM	Cardiac rhythm
12:36:52 AM	Heart Rate (/min)
12:37:38 AM	Respiratory Rate
1:11:31 AM	Catheter Assessment
1:16:20 AM	Eliminations
1:16:29 AM	Respiratory Rate
1:35:41 AM	Cardiac rhythm
1:35:42 AM	Heart Rate (/min)
2:57:22 AM	Respiratory Rate
2:58:12 AM	Cardiac rhythm
2:58:13 AM	Heart Rate (/min)
3:52:42 AM	Cardiac rhythm
3:52:43 AM	Heart Rate (/min)
3:52:55 AM	Respiratory Rate
4:50:20 AM	Cardiac rhythm

B6

B6

Client: B6
Patient:

Vitals Results

B6

	4:50:21 AM	Heart Rate (/min)
	4:50:35 AM	Respiratory Rate
	5:48:38 AM	Catheter Assessment
	5:48:57 AM	Amount eaten
	5:49:04 AM	Eliminations
	5:49:11 AM	Cardiac rhythm
	5:49:12 AM	Heart Rate (/min)
	5:49:50 AM	Respiratory Rate
	6:32:36 AM	Cardiac rhythm
	6:32:37 AM	Heart Rate (/min)
	6:32:47 AM	Respiratory Rate
	6:33:46 AM	Eliminations
	7:17:14 AM	Cardiac rhythm
	7:17:15 AM	Heart Rate (/min)
	7:18:38 AM	Respiratory Rate
	7:40:44 AM	Lasix treatment note
	9:08:24 AM	Cardiac rhythm
	9:08:25 AM	Heart Rate (/min)
	9:08:38 AM	Eliminations
	9:09:00 AM	Catheter Assessment
	9:19:53 AM	Respiratory Rate
	10:15:37 AM	Cardiac rhythm
	10:15:38 AM	Heart Rate (/min)
	10:16:40 AM	Respiratory Rate
	11:06:38 AM	Cardiac rhythm
	11:06:39 AM	Heart Rate (/min)
	11:24:58 AM	Respiratory Rate
	11:51:00 AM	Cardiac rhythm
	11:51:01 AM	Heart Rate (/min)
	11:51:54 AM	Respiratory Rate
	12:30:30 PM	Eliminations
	1:18:22 PM	Cardiac rhythm
	1:18:23 PM	Heart Rate (/min)
	1:18:32 PM	Respiratory Rate
	1:22:54 PM	Eliminations
	1:23:50 PM	Catheter Assessment

B6

Telemetry ECG

B6

Telemetry ECG

B6

Telemetry ECG

B6

Telemetry ECG

B6

Client: B6
Patient:

ECG from Cardio

B6

2/26/2019 10:22:22 AM Page 1 of 2
Tufts University
Tufts Cummings School of Vet Med
Cardiology

B6

Client: B6
Patient:

ECG from Cardio

Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6

2/26/2019 10:25:49 AM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient:

ECG from Cardio

B6

2/26/2019 10:26:06 AM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

B6

rDVM CXR - 2/25/2019

rDVM CXR - 2/25/2019

B6

Patient History

	09:01 PM	UserForm
	10:00 PM	Vitals
	10:00 PM	Vitals
	10:00 PM	Vitals
	10:35 PM	UserForm
	10:44 PM	Treatment
	11:39 PM	Purchase
	11:59 PM	Treatment
	12:04 AM	Treatment
	12:41 AM	Prescription
	12:41 AM	Prescription
	12:53 AM	Purchase
	01:00 AM	Treatment
	06:06 AM	UserForm
	06:15 AM	Email
	11:30 AM	Deleted Reason
	01:39 PM	Appointment
	07:47 AM	Appointment
B6	04:46 PM	Vitals
	04:46 PM	Vitals
	04:46 PM	Vitals
	04:46 PM	Vitals
	04:49 PM	UserForm
	04:51 PM	Purchase
	04:56 PM	Purchase
	04:56 PM	Purchase
	04:56 PM	Purchase
	04:58 PM	Vitals
	04:58 PM	Purchase
	04:59 PM	Labwork
	05:11 PM	Treatment
	05:19 PM	Vitals
	05:19 PM	Vitals
	05:23 PM	Vitals
	05:23 PM	Vitals
	05:23 PM	Purchase
	05:47 PM	UserForm
	06:01 PM	Treatment
	06:13 PM	Prescription

B6

Client: B6
Patient:

Patient History

06:19 PM	Purchase
06:19 PM	Purchase
06:19 PM	Treatment
06:19 PM	Vitals
06:19 PM	Treatment
06:19 PM	Vitals
06:33 PM	Purchase
06:33 PM	Purchase
07:34 PM	Treatment
07:34 PM	Vitals
07:34 PM	Vitals
07:35 PM	Treatment
08:11 PM	Treatment
08:11 PM	Vitals
08:11 PM	Treatment
08:11 PM	Vitals
08:11 PM	Vitals
08:11 PM	Treatment
08:11 PM	Vitals
08:36 PM	Treatment
08:36 PM	Vitals
08:36 PM	Treatment
08:36 PM	Vitals
09:31 PM	Treatment
09:31 PM	Vitals
09:32 PM	Treatment
09:32 PM	Vitals
09:32 PM	Treatment
09:32 PM	Vitals
09:32 PM	Vitals
09:32 PM	Treatment
09:32 PM	Vitals
09:33 PM	Treatment
09:40 PM	Treatment
09:40 PM	Vitals
09:40 PM	Treatment
09:40 PM	Vitals
10:49 PM	Treatment
10:49 PM	Vitals
10:49 PM	Vitals

B6

B6

Patient History

B6

10:50 PM	Treatment
10:50 PM	Vitals
10:50 PM	Treatment
10:50 PM	Vitals
10:50 PM	Vitals
11:37 PM	Treatment
11:37 PM	Vitals
11:37 PM	Vitals
11:38 PM	Treatment
11:38 PM	Vitals
11:38 PM	Treatment
11:38 PM	Vitals
12:48 AM	Treatment
12:48 AM	Vitals
12:49 AM	Treatment
12:49 AM	Vitals
12:49 AM	Treatment
12:49 AM	Vitals
12:49 AM	Vitals
01:00 AM	Treatment
01:04 AM	Treatment
01:04 AM	Treatment
01:04 AM	Vitals
01:04 AM	Treatment
01:04 AM	Vitals
01:21 AM	Vitals
01:21 AM	Treatment
01:21 AM	Vitals
01:22 AM	Treatment
01:22 AM	Vitals
01:22 AM	Vitals
01:23 AM	Treatment
01:23 AM	Vitals
01:23 AM	Treatment
01:23 AM	Vitals
02:19 AM	Treatment
02:19 AM	Vitals
02:19 AM	Vitals
02:21 AM	Treatment
02:21 AM	Vitals

B6

Client: B6
Patient:

Patient History

B6	02:21 AM	Treatment
	02:21 AM	Vitals
	03:27 AM	Treatment
	03:27 AM	Vitals
	03:27 AM	Treatment
	03:27 AM	Vitals
	03:27 AM	Vitals
	03:27 AM	Treatment
	03:27 AM	Vitals
	03:52 AM	Vitals
	03:58 AM	Prescription
	04:04 AM	Treatment
	04:34 AM	Treatment
	04:34 AM	Vitals
	04:34 AM	Treatment
	04:34 AM	Vitals
	04:34 AM	Vitals
	04:34 AM	Treatment
	04:34 AM	Vitals
	05:18 AM	Treatment
	05:23 AM	Treatment
	05:23 AM	Vitals
	05:25 AM	Treatment
	05:25 AM	Vitals
	05:26 AM	Treatment
	05:26 AM	Vitals
	05:26 AM	Treatment
	05:26 AM	Vitals
	05:27 AM	Treatment
	05:27 AM	Vitals
	05:27 AM	Treatment
	05:27 AM	Vitals
	05:28 AM	Treatment
	05:28 AM	Vitals
	05:28 AM	Vitals
	06:01 AM	Purchase
	06:33 AM	Treatment
	06:33 AM	Vitals
	06:33 AM	Treatment
	06:33 AM	Vitals
	06:33 AM	Vitals

B6

Client: B6
Patient:

Patient History

06:33 AM	Treatment
06:33 AM	Vitals
06:58 AM	Treatment
06:58 AM	Vitals
06:58 AM	Treatment
06:58 AM	Vitals
07:05 AM	Vitals
07:06 AM	Treatment
07:06 AM	Vitals
07:06 AM	Vitals
07:10 AM	Vitals
07:13 AM	Treatment
08:26 AM	UserForm
09:07 AM	Treatment
09:07 AM	Vitals
09:07 AM	Vitals
09:07 AM	Treatment
09:07 AM	Vitals
09:08 AM	Treatment
09:08 AM	Vitals
09:08 AM	Treatment
09:35 AM	Treatment
09:35 AM	Vitals
09:36 AM	Treatment
09:36 AM	Vitals
09:36 AM	Treatment
09:36 AM	Vitals
09:36 AM	Treatment
09:36 AM	Vitals
09:37 AM	Purchase
10:05 AM	Treatment
10:08 AM	Treatment
10:08 AM	Vitals
10:08 AM	Vitals
10:14 AM	Labwork
10:27 AM	Purchase
10:36 AM	Vitals
10:36 AM	Vitals

B6

B6

Client: B6
Patient:

Patient History

B6	11:01 AM	Prescription
	11:09 AM	Treatment
	11:09 AM	Vitals
	11:09 AM	Vitals
	11:09 AM	Treatment
	11:09 AM	Vitals
	11:10 AM	Treatment
	11:10 AM	Vitals
	11:31 AM	Purchase
	11:31 AM	Purchase
	11:35 AM	Treatment
	12:19 PM	Treatment
	12:19 PM	Vitals
	12:19 PM	Vitals
	12:19 PM	Treatment
	12:19 PM	Vitals
	01:05 PM	Treatment
	01:05 PM	Vitals
	01:05 PM	Vitals
	01:05 PM	Treatment
	01:05 PM	Vitals
	01:15 PM	Vitals
	01:41 PM	Treatment
	01:41 PM	Vitals
	01:41 PM	Treatment
	01:41 PM	Treatment
	01:41 PM	Vitals
	01:42 PM	Treatment
	01:42 PM	Vitals
	01:56 PM	Treatment
	01:56 PM	Vitals
	01:56 PM	Vitals
	01:56 PM	Treatment
	01:56 PM	Vitals
	02:47 PM	Treatment
	02:47 PM	Vitals
	02:47 PM	Treatment
	02:47 PM	Vitals
	02:47 PM	Vitals

B6

Client: B6
Patient:

Patient History

	02:47 PM	Treatment
	02:47 PM	Vitals
	03:38 PM	Treatment
	03:38 PM	Vitals
	03:39 PM	Treatment
	03:39 PM	Vitals
	03:39 PM	Vitals
	03:40 PM	Treatment
	03:40 PM	Vitals
	04:08 PM	Treatment
	04:08 PM	Vitals
	04:56 PM	Treatment
	04:56 PM	Vitals
	04:56 PM	Vitals
	04:56 PM	Treatment
	04:56 PM	Vitals
	05:07 PM	Treatment
	05:07 PM	Vitals
	05:07 PM	Treatment
B6	05:28 PM	Treatment
	05:28 PM	Treatment
	05:28 PM	Treatment
	05:28 PM	Vitals
	05:28 PM	Vitals
	05:28 PM	Treatment
	05:28 PM	Vitals
	05:29 PM	Treatment
	05:29 PM	Vitals
	05:36 PM	Treatment
	05:36 PM	Vitals
	06:03 PM	Purchase
	06:03 PM	Purchase
	06:39 PM	Prescription
	07:03 PM	Treatment
	07:03 PM	Vitals
	07:03 PM	Vitals
	07:03 PM	Treatment
	07:03 PM	Vitals
	07:28 PM	Treatment

B6

Client: B6
Patient:

Patient History

B6

07:28 PM	Vitals
07:28 PM	Vitals
07:28 PM	Treatment
07:28 PM	Vitals
07:50 PM	Treatment
08:40 PM	Treatment
08:40 PM	Vitals
08:40 PM	Vitals
08:41 PM	Treatment
08:41 PM	Vitals
09:25 PM	Treatment
09:25 PM	Vitals
09:25 PM	Vitals
09:25 PM	Treatment
09:25 PM	Vitals
09:25 PM	Treatment
09:25 PM	Treatment
09:25 PM	Vitals
09:28 PM	Treatment
10:54 PM	Treatment
10:54 PM	Vitals
10:54 PM	Vitals
10:55 PM	Treatment
10:55 PM	Vitals
11:37 PM	Treatment
11:37 PM	Vitals
11:37 PM	Vitals
11:37 PM	Treatment
11:37 PM	Vitals
11:52 PM	Treatment
11:52 PM	Vitals
12:36 AM	Treatment
12:36 AM	Vitals
12:36 AM	Vitals
12:37 AM	Treatment
12:37 AM	Vitals
01:11 AM	Treatment
01:11 AM	Vitals
01:11 AM	Treatment
01:16 AM	Treatment
01:16 AM	Treatment

B6

Client: B6
Patient:

Patient History

	01:16 AM	Vitals
	01:16 AM	Treatment
	01:16 AM	Vitals
	01:35 AM	Treatment
	01:35 AM	Vitals
	01:35 AM	Vitals
	02:57 AM	Treatment
	02:57 AM	Vitals
	02:58 AM	Treatment
	02:58 AM	Vitals
	02:58 AM	Vitals
	03:52 AM	Treatment
	03:52 AM	Vitals
	03:52 AM	Vitals
	03:52 AM	Treatment
	03:52 AM	Vitals
	04:50 AM	Treatment
	04:50 AM	Vitals
	04:50 AM	Vitals
	04:50 AM	Treatment
	04:50 AM	Vitals
	05:48 AM	Treatment
	05:48 AM	Treatment
	05:48 AM	Treatment
	05:48 AM	Vitals
	05:48 AM	Treatment
	05:48 AM	Vitals
	05:49 AM	Treatment
	05:49 AM	Vitals
	05:49 AM	Treatment
	05:49 AM	Vitals
	05:49 AM	Vitals
	05:49 AM	Treatment
	05:49 AM	Vitals
	06:01 AM	Purchase
	06:32 AM	Treatment
	06:32 AM	Vitals
	06:32 AM	Vitals
	06:32 AM	Treatment
	06:32 AM	Vitals
	06:33 AM	Vitals
	07:17 AM	Treatment

B6

B6

Client: B6
Patient:

Patient History

B6

07:17 AM	Vitals
07:17 AM	Vitals
07:18 AM	Treatment
07:18 AM	Vitals
07:40 AM	Treatment
07:40 AM	Treatment
07:40 AM	Vitals
07:41 AM	Treatment
09:08 AM	Treatment
09:08 AM	Vitals
09:08 AM	Vitals
09:08 AM	Treatment
09:08 AM	Vitals
09:09 AM	Treatment
09:09 AM	Vitals
09:19 AM	Treatment
09:19 AM	Vitals
09:49 AM	Purchase
10:12 AM	UserForm
10:15 AM	Treatment
10:15 AM	Vitals
10:15 AM	Vitals
10:16 AM	Treatment
10:16 AM	Vitals
10:26 AM	Purchase
10:26 AM	Treatment
10:46 AM	Purchase
10:46 AM	Labwork
10:51 AM	Treatment
11:06 AM	Treatment
11:06 AM	Vitals
11:06 AM	Vitals
11:17 AM	Purchase
11:17 AM	Treatment
11:24 AM	Treatment
11:24 AM	Vitals
11:51 AM	Treatment
11:51 AM	Vitals
11:51 AM	Vitals
11:51 AM	Treatment

B6

Client: B6
Patient:

Patient History

B6

11:51 AM	Vitals
12:30 PM	Vitals
01:18 PM	Treatment
01:18 PM	Vitals
01:18 PM	Vitals
01:18 PM	Treatment
01:18 PM	Vitals
01:22 PM	Treatment
01:22 PM	Vitals
01:23 PM	Treatment
01:23 PM	Treatment
01:23 PM	Vitals

B6

Appears this way on Original

Appears this way on Original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6

B6

B6 B6 Male
Canine Doberman Pinscher Black
438113

B6

Dear Dr. B6

B6 was seen at Tufts' ER for left hind lameness. Please see attached discharge instructions for more information.

If you have any questions, or concerns, please contact us at 508-887-4988.

Thank you,

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

Notice of Patient Admit

Date: B6 1:21:36 PM **Case No:** 438113
Referring Doctor: B6
Client Name:
Patient Name: B6

Dear Dr. B6

Your patient presented to our Emergency service. Please make note of the following information to facilitate communication with our team.

The attending doctor is: Dr. B6
The reason for admission to the HASA is: DCM, CHF

If you have any questions regarding this particular case, please call 508-887-4988 to reach the Cardiology Service. Information is updated daily, by noon.

Thank you for your referral to our Emergency Service.

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

B6

B6 Male
Canine Doberman Pinscher Black
438113

B6

Daily Update From the Cardiology Service

Today's date: B6
Dear Drs at B6

Thank you for referring patients to the B6
University.

Your patient B6 was admitted and is being cared for by the Cardiology Service.

Today, B6

- [x] is in stable condition
- [x] is still in the oxygen cage
- [ ] is critically ill
- [ ] might be discharged from the hospital today

Today's treatments include:

- [x] bloodwork planned/pending
- [x] echocardiography -
  - DCM with active CHF r/o breed-related vs. diet related.
- [ ] cardiac catheter procedure planned
- [ ] ongoing treatment for CHF
- [ ] ongoing treatment for thrombosis
- [ ] ongoing treatment for arrhythmia

Additional plans:
Please allow 3-5 business days for reports to be finalized upon patient discharge.

Please call (508) 887-4696 before 5pm or email us at cardiovet@tufts.edu if you have any questions.
Thank you!

Attending Clinician: Dr. B6 DVM (Resident, Cardiology)
Faculty Clinician: B6 DVM,DACVIM

Senior student:

Foster Hospital for Small Animals

55 Willard Street
North Grafton, MA 01536
(508) 839-5395

All Medical Records

Client: B6
Address: B6

Patient: B6
Breed: Golden Retriever
DOB: B6

Species: Canine
Sex: Female (Spayed)

Home Phone: B6
Work Phone: ( ) -
Cell Phone: B6

Referring Information

B6

Client: B6
Patient: B6

Initial Complaint:
Emergency

SOAP Text B6 **5:44PM - Clinician, Unassigned** B6

Subjective
NEW VISIT (ER)

Doctor: B6 DVM
Student: B6
Presenting complaint: Referral for suspected pericardial effusion
Referral visit? B6
Diagnostics completed prior to visit: right lateral CXR, CBC/Chemistry

HISTORY:

Current history:
B6 is a 9 yo FS Golden retriever who presented to the Tufts ER as a referral for pericardial effusion. She was seen by her rDVM yesterday to evaluate 6 months of weight loss (62# to 58#). Owner noticed a mild dry cough for the past 2 weeks, no specific time of day, sometimes more with excitement, but usually no eliciting cause. rDVM obtained CXR and were concerned about a globoid heart and pericardial effusion. O report no episodes of exercise intolerance, collapse, or respiratory distress. Owners say that she has a great appetite and now begs for food more, despite losing weight. Owner waited for blood work results before bringing her in today. Eating and drinking normally. No sneezing,

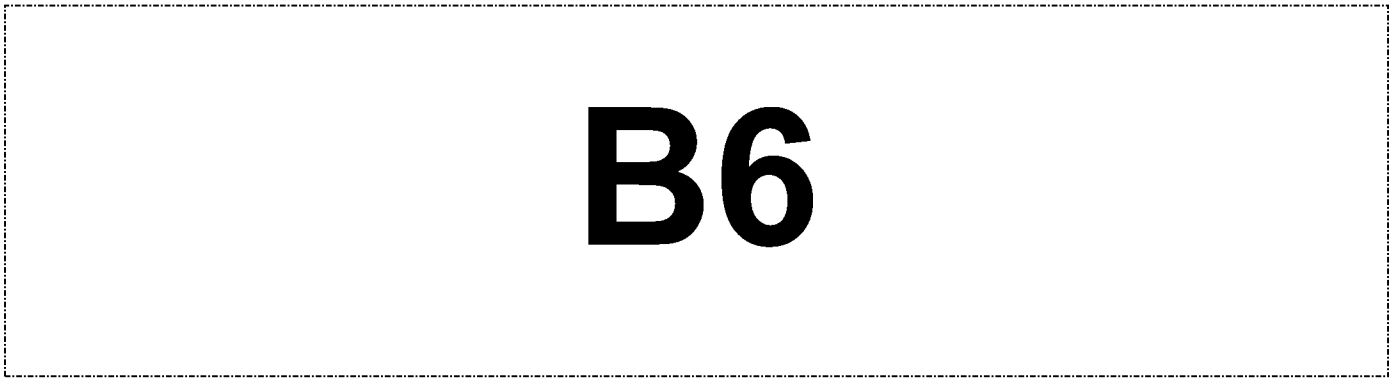
vomiting, or diarrhea. One episode of regurgitation after coughing last week. Not PU/PD at home. She is heart worm tested yearly and receives heart worm prevention every month (Hartguard). She has been on Zigniture Kangaroo Diet for the last 6-8 months. She has no other medical concerns at this time and is not currently receiving medications.

Prior medical history: Has had TPLO elsewhere 1 year ago. Hx of UTI, had an AUS of abdomen several years ago. Hx of pruritis, does well with limited ingredient diet. Anaplasma positive since 2011.
Current medications: None
Diet: Zignature kangaroo 1 cup BID dry for the past 6-8 months
Vaccination status/flea & tick preventative use: Seresto, heartgard all year round
Travel history: None

EXAM:

ASSESSMENT:
A1: Cardiomegaly (right >> left ventricular enlargement) - DCM (taurine deficiency vs primary cardiomyopathy) v MVD
A2: Intermittent, non-productive cough - tracheal compression from enlarged heart vs CHF vs primary pulmonary disease (inflammatory v infectious v neoplastic)
A3: Weight loss - suspect cardiac cachexia v other

PLAN:



Diagnostics completed @ rDVM 4/10:
CBC - WNL
Chem - CK 342 (H), otherwise WNL
T4 - 1.5
4DX - anaplasma +, history of + since 2011
Right lateral CXR (in ER email) - enlarged right heart, enlarged left atrium with dorsal tracheal compression

Diagnostics completed @ Tufts:
- Left lateral and VD CXR - generalized cardiomegaly, mild pulmonary vessel enlargement, +/- enlarged caudal vena cava, full report pending
- BP 125 mmHg

Client communication: Discussed exam findings with owner - let O know that she did not have evidence of PCE based on our TFAST, but that her contractile function was slightly diminished and that she had right and left ventricular enlargement (R >> L) B6

B6

Deposit & estimate status B6

Resuscitation code (if admitting to ICU): Yellow

SOAP approved (DVM to sign): B6 DVM (B6 Intern)

SOAP Text B6 **7:21AM - Clinician, Unassigned** B6

Subjective
Exam, cardiology
B6 is a 9yr old FS Golden etriever who presented to the Tufts ER as a referral for pericardial effusion. rDVM obtained CXR and were concerned about a globoid heart and pericardial effusion. She has a 6 mo hx of weight loss, and 2 week hx of dry cough, and hx of UTI. She has been on Zigniture Kangaroo Diet for the last 6-8 months

Diet: Zignature Kangaroo 8/2017-4/2018. Acana duck& pear, Pork & squash 11/2015-7/2017

B6

B6

Assessments
A1: enlarged right heart r/o- DCM, taurine deficiency from diet, DMVD
A2: hx of a cough r/o- CHF, enlarged heart pressing on trachea, primary pulmonary disease (inflammatory vs infectious vs neoplasia)

Plan
P1: Echo
P2: UA (culture)
P3: CBC/CHEM

SOAP completed by: B6
SOAP reviewed by: B6

Initial Complaint:
Recheck: B6

SOAP Text B6 **10:54AM -** B6

Initial Complaint:
Emergency

SOAP Text B6 **3:19AM -** B6

Subjective
NEW VISIT (ER)

Doctor: B6
Student: ---
Presenting complaint: Coughing
Referral visit? No
Diagnostics completed prior to visit

HISTORY:

Signalment: 10 yo SF Golden
Current history:
Owners went to bed and was woken up in middle of night. Sounded like she was trying to vomit and wasn't bringing anything up. Suspect that she was possibly coughing instead. On drive in, no coughing but when she got here she began coughing again. No other concerns at home. Has been doing well at home since last Cardiology visit.

History of eating objects. Owners are concerned she may have eaten an item on Christmas.

Prior medical history: Diagnosed with DCM in April 2018
Current medications: Enalapril, pimobendan, and taurine. Have not needed to give furosemide.
Diet: unknown
Vaccination status/flea & tick preventative use: unknown
Travel history: unknown

EXAM:

ASSESSMENT:
A1: Coughing-- r/o CHF vs bronchial compression vs pneumonia vs bronchitis vs other

PLAN:
Radiographs-- 3 view thorax, 2 view abodmen
Sedation
Butorphanol 1mL IM
TFAST
Furosemide 2mg/kg IM
Discharge

Diagnostics completed:
TFAST-- no PCE, La: Ao 1, LV and RV dilation with R>>>L
Radiographs-- 3 view thorax, 2 view abodmen-- cardiac sillhoutte enlargement, no pulmonary edema, unremarkable

Client: B6
Patient: B6

abdomen

Diagnostics pending:
None

Client communication:

B6

Deposit & estimate status: n/a

Resuscitation code (if admitting to ICU): n/a

SOAP approved (DVM to sign): B6 DVM

Initial Complaint:
Recheck - B6

Disposition/Recommendations

Cummings Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
(508) 839-5395

Client:	B6
Veterinarian:	
Patient ID:	B6
Visit ID:	

Patient:	B6
Species:	Canine
Breed:	Golden Retriever
Sex:	Female (Spayed)
Age:	B6 Years Old

Lab Results Report

Nova Full Panel-ICU **4/10/2018 7:40:25 PM** **Accession ID:** B6

Test	Results	Reference Range	Units
SO2%	B6	94 - 100	%
HCT (POC)		38 - 48	%
HB (POC)		12.6 - 16	g/dL
NA (POC)		140 - 154	mmol/L
K (POC)		3.6 - 4.8	mmol/L
CL(POC)		109 - 120	mmol/L
CA (ionized)		1.17 - 1.38	mmol/L
MG (POC)		0.1 - 0.4	mmol/L
GLUCOSE (POC)		80 - 120	mg/dL
LACTATE		0 - 2	mmol/L
BUN (POC)		12 - 28	mg/dL
CREAT (POC)		0.2 - 2.1	mg/dL
TCO2 (POC)		0 - 0	mmol/L
nCA		0 - 0	mmol/L
nMG		0 - 0	mmol/L
GAP		0 - 0	mmol/L
CA/MG		0 - 0	mol/mol
BEecf		0 - 0	mmol/L
BEb		0 - 0	mmol/L
A		0 - 0	mmHg
NOVA SAMPLE		0 - 0	

FiO2	B6	0 - 0	%
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
PH		7.337 - 7.467	
PCO2		36 - 44	mmHg
PO2		80 - 100	mmHg
HCO3		18 - 24	mmol/L

Nova Full Panel-ICU B6 **8:06:27 PM** **Accession ID:** B6

Test	Results	Reference Range	Units
TS (FHSA)	B6	0 - 0	g/dl
PCV **		0 - 0	%
TS (FHSA)		0 - 0	g/dl

Nova Full Panel-ICU B6 **9:43:01 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
TAURINE P	B6	60 - 120	nmol/mL
TAURINE WB		200 - 350	nmol/mL

Nova Full Panel-ICU B6 **9:44:12 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
WBC (ADVIA)	B6	4.4 - 15.1	K/uL
RBC(ADVIA)		5.8 - 8.5	M/uL
HGB(ADVIA)		13.3 - 20.5	g/dL
HCT(ADVIA)		39 - 55	%
MCV(ADVIA)		64.5 - 77.5	fL
MCH(ADVIA)		21.3 - 25.9	pg
MCHC(ADVIA)		31.9 - 34.3	g/dL
RDW (ADVIA)		11.9 - 15.2	
PLT(ADVIA)		173 - 486	K/uL
MPV (ADVIA)		8.29 - 13.2	fl
PLTCRT		0.129 - 0.403	%
RETIC(ADVIA)		0.2 - 1.6	%
RETICS (ABS) ADVIA		14.7 - 113.7	K/uL

Nova Full Panel-ICU B6 **9:44:27 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
GLUCOSE	B6	67 - 135	mg/dL
UREA		8 - 30	mg/dL
CREATININE		0.6 - 2	mg/dL
PHOSPHORUS		2.6 - 7.2	mg/dL
CALCIUM2		9.4 - 11.3	mg/dL
MAGNESIUM 2+		1.8 - 3	mEq/L
T. PROTEIN		5.5 - 7.8	g/dL

Client: B6
Patient: B6

ALBUMIN	B6	2.8 - 4	g/dL
GLOBULINS		2.3 - 4.2	g/dL
A/G RATIO		0.7 - 1.6	
SODIUM		140 - 150	mEq/L
CHLORIDE		106 - 116	mEq/L
POTASSIUM		3.7 - 5.4	mEq/L
tCO2 (BICARB)		14 - 28	mEq/L
AGAP		8 - 19	
NA/K		29 - 40	
T BILIRUBIN		0.1 - 0.3	mg/dL
D.BILIRUBIN		0 - 0.1	mg/dL
I BILIRUBIN		0 - 0.2	mg/dL
ALK PHOS		12 - 127	U/L
GGT		0 - 10	U/L
ALT		14 - 86	U/L
AST		9 - 54	U/L
CK		22 - 422	U/L
CHOLESTEROL		82 - 355	mg/dL
TRIGLYCERIDES		30 - 338	mg/dl
AMYLASE		409 - 1250	U/L
OSMOLALITY (CALCULATED)		291 - 315	mmol/L

Nova Full Panel-ICU B6 **9:44:10 AM** **Accession ID:** B6

Test	Results	Reference Range	Units
SEGS%	B6	43 - 86	%
LYMPHS%		7 - 47	%
MONOS%		1 - 15	%
EOS%		0 - 16	%
SEGS (AB)ADVIA		2.8 - 11.5	K/ul
LYMPHS (ABS)ADVIA		1 - 4.8	K/uL
MONOS (ABS)ADVIA		0.1 - 1.5	K/uL
EOS (ABS)ADVIA		0 - 1.4	K/uL
WBC MORPHOLOGY	B6	0 - 0	
No Morphologic Abnormalities			
CRENATION		0 - 0	
H-J BODIES		0 - 0	

REFERRAL FORM

TUFTS UNIVERSITY
Cummings School of Veterinary Medicine
Henry and Lois Foster Hospital for Small Animals
Hospital for Large Animals
200 Westboro Road, Route 30
North Grafton, MA 01536
508-839-5395

Service to Which Referred: Cardiology Appointment Date: ______ Time: ______

OWNER INFORMATION:

Name B6 Daytime Phone B6 Evening Phone( ) ______

Address: B6 City: B6 State: B6 Zip Code: B6

PATIENT INFORMATION:

Registered Name/ID: B6

Species: Canine Breed: Golden ret. Sex: FS Age: 9Y

CASE HISTORY

Chief Concern/Provisional Diagnosis: Heart Disease, Pericardial Effusion with cough

Vaccination History: Rabies - 7-7-16 3yr
Dist - 7-7-16 3yr

Other History: ______

Diagnostic Test Results (if possible, please attach results): ______

Are Radiographs enclosed? No - Emailing

Current Therapy & Medication (include dosages): [illegible]
[illegible]

Special Comments/Requests: ______

REFERRING VETERINARIAN INFORMATION

Name: B6 DVM Clinic/Hospital: B6

Phone B6 Fax B6

Address: B6 City: B6 State: B6 Zip Code: ______

If an animal is being referred which has had lab work done at TVDL, please include copies of the lab results or the TVDL accession number. If you are faxing us information about a clinical case which has been referred, please use fax number (508) 839-7951.

Client: B6
Patient: B6

rDVM B6 **Referral and hx 2/23/09-4/10/18**

04-10-2018 7:41 AM B6 → B6 D 1

B4 B4 B4

B6

PET OWNER: B6

SPECIES: CANINE
BREED:
GENDER: FEMALE SPAYED
AGE: B6

B6

ACCOUNT #: B6
ORDERED BY: B6

ACCESSION #: B6
REQUISITION #: B6
DATE OF COLLECTION: 04/10/2018
DATE OF RECEIPT: 04/10/2018
DATE OF REPORT: 04/10/2018

B4 SERVICES: 9999 SAMPLE/TEST INFO NEEDED, 24483999 SENIOR PROF STD FECAL 4DX

HEMATOLOGY

TEST	RESULT	REF. RANGE
RBC [a] *	B6	(5.39 - 8.70) M/uL
Hematocrit		(38.3 - 56.5) %
Hemoglobin		(13.4 - 20.7) g/dL
MCV		(59 - 76) fL
MCH		(21.9 - 26.1) pg
MCHC		(32.8 - 38.2) g/dL
% Reticulocyte		%
Reticulocyte		(10 - 110) K/uL
WBC		(4.8 - 17.6) K/uL
% Neutrophil		%
% Lymphocyte		%
% Monocyte		%
% Eosinophil		%
% Basophil		%
Neutrophil		(2940 - 12670)
Lymphocyte		(1080 - 4850) /uL
Monocyte		(130 - 1150) /uL
Eosinophil		(70 - 1490) /uL
Basophil		(0 - 100) /uL
Platelet		(143 - 448) K/uL

CHEMISTRY

TEST	RESULT	REF. RANGE
Glucose	B6	(83 - 114) mg/dL
IDEXX SDMA [b]		(0 - 14) ug/dL
Creatinine		(0.5 - 1.5) mg/dL
BUN		(8 - 31) mg/dL
BUN:Creatinine Ratio		
Phosphorus		(2.5 - 6.1) mg/dL
Calcium		(8.4 - 11.8) mg/dL
Sodium		(142 - 152)
Potassium		(4.0 - 5.4) mmol/L
Na:K Ratio		(28 - 37)
Chloride		(108 - 119)
TCO2 (Bicarbonate)		(13 - 27) mmol/L
Anion Gap		(11 - 36) mmol/L
Total Protein		(5.5 - 7.5) g/dL
Albumin		(2.7 - 3.9) g/dL
Globulin		(2.4 - 4.0) g/dL
Alb:Glob Ratio		(0.7 - 1.5)
ALT		(18 - 121) U/L
AST		(16 - 55) U/L
ALP		(5 - 160) U/L
GGT		(0 - 13) U/L
Bilirubin - Total		(0.0 - 0.3) mg/dL
Bilirubin - Unconjugated		(0.0 - 0.2) mg/dL
Bilirubin - Conjugated		(0.0 - 0.1) mg/dL
Cholesterol		(131 - 346) mg/dL
Amylase		(337 - 1469) U/L
Lipase		(138 - 755) U/L
H Creatine Kinase		(10 - 200) U/L
Hemolysis Index [c]		
Lipemia Index [d]		

ENDOCRINOLOGY

TEST	RESULT	REF. RANGE
Total T4 *	B6	(1.0 - 4.0) ug/dL

SEROLOGY

TEST	RESULT	REF. RANGE
Heartworm Antigen	B6	
Ehrlichia canis / ewingii		
Lyme (Borrelia burgdorferi)		
Anaplasma phagocytophilum / platys [f]		

Get deeper insights: For complete access to this patient's diagnostic results, including historic values and images, login to: B4

Final report generated April 10, 2018

PAGE 1 of 3

B6 B6 D 2

B4 B4 B4

B6 PET OWNER: B6 DATE OF REPORT: 04/10/2018 ACCESSION #: B6

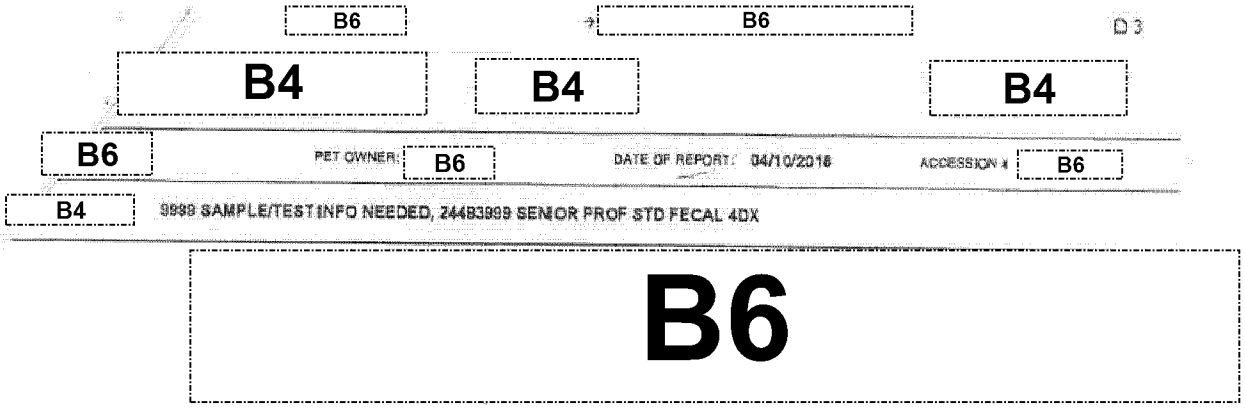
B4 9999 SAMPLE/TEST INFO NEEDED, 24483999 SENIOR PROF STD FECAL 4DX

OTHER

SAMPLE / TEST INFO NEEDED	A fecal specimen was not received. The remainder of requested testing has been performed. Thank you.
	A urine specimen was not received. The remainder of requested testing has been performed. Thank You.

NOTES

B6



Client: B6
Patient: B6

rDVM B6 **Referral and hx 2/23/09-4/10/18**

Owner's Name B6 Animal's Name B6 Page

DATE MO.	DAY	YR.	TREATMENT
4	9	18	B6

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History

4/10/2018 L 1

Hematology results from B4 Reference Laboratory Requisition ID: B6 Posted Final

Test	Result	Reference Range
HCT	B6	38.3 - 56.5
HGB		13.4 - 20.7
MCHC		32.6 - 39.2
WBC		4.9 - 17.6
EOS		
RBC		5.39 - 8.70
MCV		59 - 76
MCH		21.9 - 26.1
LYMPHS		
MONOS		
BASO		
NEUT SEG		
PLATELETS		143 - 448
RETIC CNT		
ABS BASO		0 - 100
ABS EOS		70 - 1490
ABS LYMPHS		1060 - 4950
ABS MONOS		130 - 1150
ABS NEUTS		2940 - 12670
ABS RET		10 - 110

Ascn: B6

AUTOMATED CBC

4/10/2018 L 1

Chemistry results from B4 Reference Laboratory Requisition ID: B6 Posted Final

Test	Result	Reference Range
ALKP	B6	5 - 160
ALT		18 - 121
AST		16 - 55
AMYL		337 - 1469
BUN/UREA		9 - 31
ALB		2.7 - 3.9
Ca		8.4 - 11.8
Chloride		108 - 119
CHOL		131 - 345
CK		10 - 200
CREA		0.5 - 1.5
GGT		0 - 13
GLU		63 - 114
LIPA		138 - 755
PHOS		2.5 - 6.1
Potassium		4.0 - 5.4
Sodium		142 - 152

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History

TBIL	B6	0.0 - 0.3
TP		5.5 - 7.5
GLOB		2.4 - 4.0
DBIL		0.0 - 0.1
SDMA		0 - 14
ANION GAP		11 - 26
BICARB		13 - 27
IBIL		0.0 - 0.2
A/G Ratio		0.7 - 1.5
B/C Ratio		
Na/K Ratio		28 - 37

B6

4/10/2018 L 1

Endocrinology results from B4 Reference
Laboratory Requisition ID: B6 Posted Final

Test	Result	Reference Range
T4	B6	1.0 - 4.0
Ascn:	B6	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medi note, V:Vital signs

Patient History Report

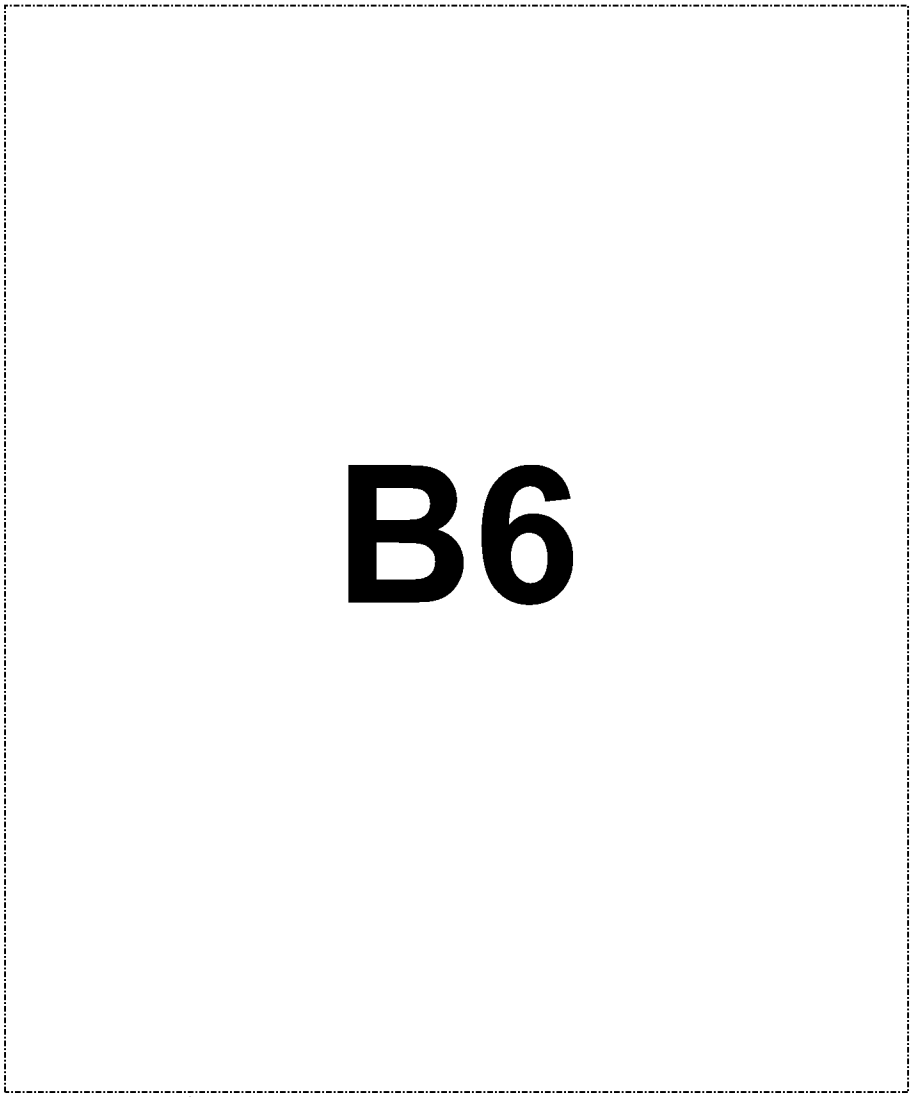
Client: B6
Phone:

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN

Address: B6

Age: 9 Yrs. 8 Mos.
Color: Gold
Sex: Spayed Female

Date	Type	Staff	History
4/10/2018	L	1	



B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN

Address: B6

Age: 9 Yrs. 8 Mos.
Color: Gold
Sex: Spayed Female

Date	Type	Staff	History

B6

4/10/2018 L 1

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Age: 9 Yrs. 8 Mos.
Color: Gold

Breed: RETRIEVER/GOLDEN
Sex: Spayed Female

Date	Type	Staff	History
4/10/2018	PP	1	
4/10/2018	PP	1	
4/9/2018	T	1	
4/9/2018	PP	1	
4/9/2018	B	1	
4/9/2018	B	1	
4/9/2018	B	1	
4/9/2018	B	1	
10/2/2017	L	1	
10/2/2017	CK	1	
10/2/2017	B	1	
10/2/2017	B	1	
10/2/2017	B	1	
10/2/2017	B	1	
10/2/2017	B	1	
10/2/2017	B	1	
10/2/2017	B	1	
6/29/2017	B	B6	
3/31/2017	P	160	
3/31/2017	B	160	
3/23/2017	P	16	
3/23/2017	P	16	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
3/23/2017	V	B6	
3/23/2017	B	16	
3/23/2017	B	16	
3/23/2017	B	16	
3/23/2017	B	16	
2/6/2017	P	11	
2/6/2017	P	11	
2/6/2017	B	11	
2/6/2017	B	11	
2/6/2017	B	11	
1/20/2017	P	1	
1/20/2017	P	1	
1/20/2017	P	1	
1/20/2017	P	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/20/2017	B	1	
1/19/2017	L	15	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing Instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
			ALKP = 23 - 212
			ALT = 10 - 100
			AMYL = 500 - 1500
			BUN/UREA = 7 - 27
			ALB = 2.2 - 3.9
			Ca = 7.9 - 12.0
			CHOL = 110 - 320
			CREA = 0.5 - 1.8
			GLU = 70 - 143
			PHOS = 2.5 - 6.8
			TBIL < 0.0 - 0.9
			TP = 5.2 - 8.2
			GLOB = 2.5 - 4.5
1/19/2017	B	1	
1/9/2017	B	1	
12/7/2016	P	1	
12/7/2016	P	15	
12/7/2016	T	B6	
12/7/2016	T		
12/7/2016	B	15	
12/7/2016	B	15	
12/7/2016	B	15	
12/7/2016	B	15	
11/9/2016	P	11	
11/9/2016	B	11	
7/7/2016	L	1	
7/7/2016	P	1	

B6

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
7/7/2016	P	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
7/7/2016	B	1	
2/29/2016	V	B6	
2/29/2016	B	1	
2/16/2016	P	1	
2/16/2016	P	1	
2/16/2016	B	1	
2/16/2016	B	1	
2/16/2016	B	1	
2/16/2016	B	1	
9/16/2015	P	1	
9/16/2015	P	1	
9/16/2015	T	B6	
9/16/2015	T		
9/16/2015	B	1	
9/16/2015	B	1	
9/16/2015	B	1	
9/16/2015	B	1	
8/20/2015	B	13	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing Instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Age: 9 Yrs. 8 Mos.
Color: Gold

Breed: RETRIEVER/GOLDEN
Sex: Spayed Female

Date	Type	Staff	History
8/3/2015	P	13	
8/3/2015	P	13	
8/3/2015	P	13	
8/3/2015	P	13	
8/3/2015	L	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
8/3/2015	B	13	
9/29/2014	P	11	
9/29/2014	B	11	
8/12/2014	B	B6	
8/12/2014	B		
8/1/2014	B		
7/22/2014	B		

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
7/11/2014	B		
7/11/2014	B		
6/30/2014	B	B6	
6/30/2014	B		
6/30/2014	B		
6/16/2014	P	1	
6/16/2014	P	1	
6/16/2014	V	B6	
6/16/2014	L	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
6/16/2014	B	1	
3/12/2014	P	11	
3/12/2014	B	11	
8/14/2013	P	B6	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
8/14/2013	B	B6	
5/23/2013	B	1	
5/23/2013	B	1	
5/23/2013	B	1	
5/14/2013	P	10	
5/14/2013	B	10	
5/14/2013	B	10	
5/14/2013	B	10	
4/22/2013	P	1	
4/22/2013	P	1	
4/22/2013	V	B6	
4/22/2013	L	11	
4/22/2013	B	1	
4/22/2013	B	1	
4/22/2013	B	1	
4/22/2013	B	1	
4/22/2013	B	1	
4/22/2013	B	1	
4/15/2013	P	1	
4/15/2013	P	1	
4/15/2013	V	B6	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
4/15/2013	B	1	
4/15/2013	B	1	
4/15/2013	B	1	
4/15/2013	B	1	
4/15/2013	B	1	
4/15/2013	B	1	
4/15/2013	B	1	
4/9/2013	B		
1/28/2013	B	B6	
11/27/2012	B		
9/4/2012	P	10	
9/4/2012	B	10	
9/4/2012	B	10	
2/28/2012	L	1	
2/27/2012	P	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B	1	
2/27/2012	B		
8/1/2011	P	B6	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative med note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
8/1/2011	B		
8/1/2011	B	B6	
6/22/2011	B		
4/8/2011	B	10	
4/8/2011	B	10	
4/1/2011	B	B6	
3/4/2011	L	1	
2/24/2011	P	1	
2/24/2011	B	1	
2/24/2011	B	1	
2/24/2011	B	1	
2/24/2011	B	1	
2/24/2011	B	1	
2/24/2011	B	1	
2/24/2011	B	1	
1/3/2011	B		
4/29/2010	B	B6	
4/28/2010	B		
4/20/2010	P		
4/20/2010	B	B6	
4/20/2010	B		
3/10/2010	P	8	
3/10/2010	V		

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative med note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
3/10/2010	B	8	
3/10/2010	B	8	
3/10/2010	B	8	
2/17/2010	L	77	
2/16/2010	V		
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
2/16/2010	B	1	
8/3/2009	P	B6	
8/3/2009	B		
8/3/2009	B	B6	
8/3/2009	B		
7/10/2009	P	8	
7/10/2009	P	1	
7/10/2009	B	1	
7/10/2009	B	8	
7/8/2009	V		

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing Instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN

Address: B6

Age: 9 Yrs. 8 Mos.
Color: Gold
Sex: Spayed Female

Date	Type	Staff	History
7/8/2009	B	1	
6/19/2009	B	B6	
6/17/2009	B	1	
6/17/2009	B	1	
6/9/2009	B	1	
6/8/2009	B	B6	
6/8/2009	B	1	
5/29/2009	P	1	
5/29/2009	L	11	
5/29/2009	B	11	
5/29/2009	B	1	
5/29/2009	B	1	
5/29/2009	B	1	
5/29/2009	B	1	
5/29/2009	B	1	
5/29/2009	B	1	
5/29/2009	B	1	
5/28/2009	B	B6	
5/9/2009	P	1	
5/9/2009	B	1	
4/29/2009	B	B6	
4/27/2009	P	1	
4/27/2009	B	1	
4/27/2009	B	1	
4/23/2009	B	B6	
4/22/2009	P	8	
4/22/2009	B	8	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Address: B6
Age: 9 Yrs. 8 Mos.
Color: Gold
Sex: Spayed Female

Date	Type	Staff	History
4/22/2009	B	8	
4/22/2009	B	8	
4/22/2009	B	8	
4/22/2009	B	8	
4/14/2009	B	B6	
4/14/2009	B		
4/2/2009	P	7	
4/2/2009	B	7	
4/2/2009	B	7	
3/12/2009	B	B6	
3/10/2009	P	1	
3/10/2009	P	1	
3/10/2009	P	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/10/2009	B	1	
3/7/2009	V		
3/7/2009	B	1	
3/7/2009	B	1	
2/24/2009	L	11	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative medl note, V:Vital signs

Patient History Report

Client: B6
Phone:
Address: B6

Patient: B6
Species: CANINE
Breed: RETRIEVER/GOLDEN
Age: 9 Yrs. 8 Mos.
Sex: Spayed Female
Color: Gold

Date	Type	Staff	History
2/24/2009	P	1	
2/24/2009	B	B6	
2/24/2009	B	1	
2/23/2009	V		
2/23/2009	B	1	
2/23/2009	B	1	
2/23/2009	B	1	
2/23/2009	B	1	

B6

B:Billing, C:Med note, CB:Call back, CK:Check-in, CM:Communications, D:Diagnosis, DH:Declined to history, E:Examination, ES:Estimates, I:Departing instr, L:Lab result, M:Image cases, P:Prescription, PA:PVL Accepted, PB:problems, PP:PVL Performed, PR:PVL Recommended, R:Correspondence, T:Images, TC:Tentative med! note, V:Vital signs

Client: B6
Patient: B6

Amino Acid Labs Taurine Panel B6

18509 PL
18510 WB

Sample Submission Form

UC CUSTOMERS ONLY:
Non-federal funds ID/Account Number to bill:_____

Amino Acid Laboratory
University of California, Davis
1020 Vet Med 3B
1089 Veterinary Medicine Drive
Davis, CA 95616
Tel: (530)752-5058, Fax: (530)752-4698

http://www.vetmed.ucdavis.edu/vmb/aal/aal.html

Vet/Tech Contact: B6
Company Name: Tufts Cummings School of Veterinary Medicine
Address: 200 Westboro Road
North Grafton, MA 01536

Email: B6 @tufts.edu
Tel: B6 **Fax:** 508-839-7936

Billing Contact: B6 **TAX ID:**_____
Email: B6 @tufts.edu **Tel:** 508-887-4267

Patient Name: B6
Species: canine
Owner's Name: B6

B6
B6
B6 9:43 AM
TAURINE PANEL
Lithium Heparin

Sample Type: ☒ Plasma ☒ Whole Blood ☐ Urine ☐ Food ☐ Other:_____
Test Items: ☒ Taurine ☐ Complete Amino Acid ☐ Other:_____

Taurine Results (nmol/ml)

Plasma: B6 Whole Blood: B6 Urine:_____ Food:_____

Reference Ranges (nmol/ml)

	Plasma		Whole Blood	
	Normal Range	No Known Risk for Taurine Deficiency	Normal Range	No Known Risk for Taurine Deficiency
Cat	80-120	>40	300-600	>200
Dog	60-120	>40	200-350	>150

B6
B6
B6 9:43 AM Canine
TAURINE PANEL
Lithium Heparin

Client: B6
Patient: B6

Diet history B6

CARDIOLOGY DIET HISTORY FORM

Please answer the following questions about your pet

Pet's name: B6 Owner's name: B6 Today's date: B6

1. How would you assess your pet's appetite? (mark the point on the line below that best represents your pet's appetite)

Example: ***Poor*** _____|_____ ***Excellent***

Poor _____|_____ **Excellent**

2. Have you noticed a change in your pet's appetite over the last 1-2 weeks? (check all that apply)
☒Eats about the same amount as usual ☐Eats less than usual ☐Eats more than usual
☐Seems to prefer different foods than usual ☐Other_____

3. Over the last few weeks, has your pet (check one)
☐Lost weight ☐Gained weight ☒Stayed about the same weight ☐Don't know

4. Please list below ALL pet foods, people food, treats, snack, dental chews, rawhides, and any other food item that your pet currently eats. Please include the brand, specific product, and flavor so we know exactly what you pet is eating.

Examples are shown in the table – please provide enough detail that we could go to the store and buy the exact same food.

Food (include specific product and flavor)	Form	Amount	How often?	Fed since
Nutro Grain Free Chicken, Lentil, & Sweet Potato Adult	*dry*	*1 ½ cup*	*2x/day*	*Jan 2018*
85% lean hamburger	*microwaved*	*3 oz*	*1x/week*	*Jan 2015*
Pupperoni original beef flavor	*treat*	*½*	*1x/day*	*Aug 2015*
Rawhide	*treat*	*6 inch twist*	*1x/week*	*Dec 2015*
Royal Canin Early Cardiac	dry	1½ cup	2x day	April 2018
Bananas		½ banana	2x day	
Greek Yogurt		1 T.	1x day	
Etta-deer Chew STICK,		5" STICK	2x WEEK	April 2017
Veggies - broccoli, zucchini, butternut squash, pumpkin,		½ CUP	3x WK	

**Any additional diet information can be listed on the back of this sheet*

5. Do you give any dietary supplements to your pet (for example: vitamins, glucosamine, fatty acids, or any other supplements)? ☐Yes ☐No If yes, please list which ones and give brands and amounts:

		Brand/Concentration	Amount per day
Taurine	☒Yes ☐No		2,000 mg day
Carnitine	☐Yes ☐No		
Antioxidants	☐Yes ☐No		
Multivitamin	☐Yes ☐No		
Fish oil	☐Yes ☐No		
Coenzyme Q10	☐Yes ☐No		
Other (please list):			
Example: Vitamin C		*Nature's Bounty*	*500 mg tablets – 1 per day*

6. How do you administer pills to your pet?
☐ I do not give any medications
☐ I put them directly in my pet's mouth without food
☐ I put them in my pet's dog/cat food
☐ I put them in a Pill Pocket or similar product
☐ I put them in foods (list foods): Banana

DIETS BEFORE DIAGNOSIS
- ZIGNATURE KANGAROO - 6-8 MONTHS (SEPT 2017 - APRIL 2018)
- ACANA PORK/SQUASH OR DUCK/PEAR BEFORE THAT

Client: B6
Patient: B6

Vitals Results

B6	5:40:32 PM 5:40:33 PM 5:40:34 PM 5:40:35 PM 8:02:29 PM 8:11:31 PM 8:11:45 PM 8:12:00 PM 8:21:56 PM 8:26:30 PM 9:42:33 PM 11:00:07 PM 11:18:07 PM 11:18:35 PM 11:21:05 PM 11:58:41 PM 1:04:34 AM 1:51:32 AM 2:58:23 AM 3:04:17 AM 3:10:25 AM 3:10:31 AM 3:59:04 AM 4:55:24 AM 5:00:41 AM 5:55:00 AM 7:01:46 AM 7:13:45 AM 7:14:23 AM 7:14:51 AM 7:21:17 AM 7:28:11 AM 8:12:43 AM 9:06:14 AM 9:06:22 AM 9:59:21 AM 10:34:11 AM 11:25:53 AM	B6

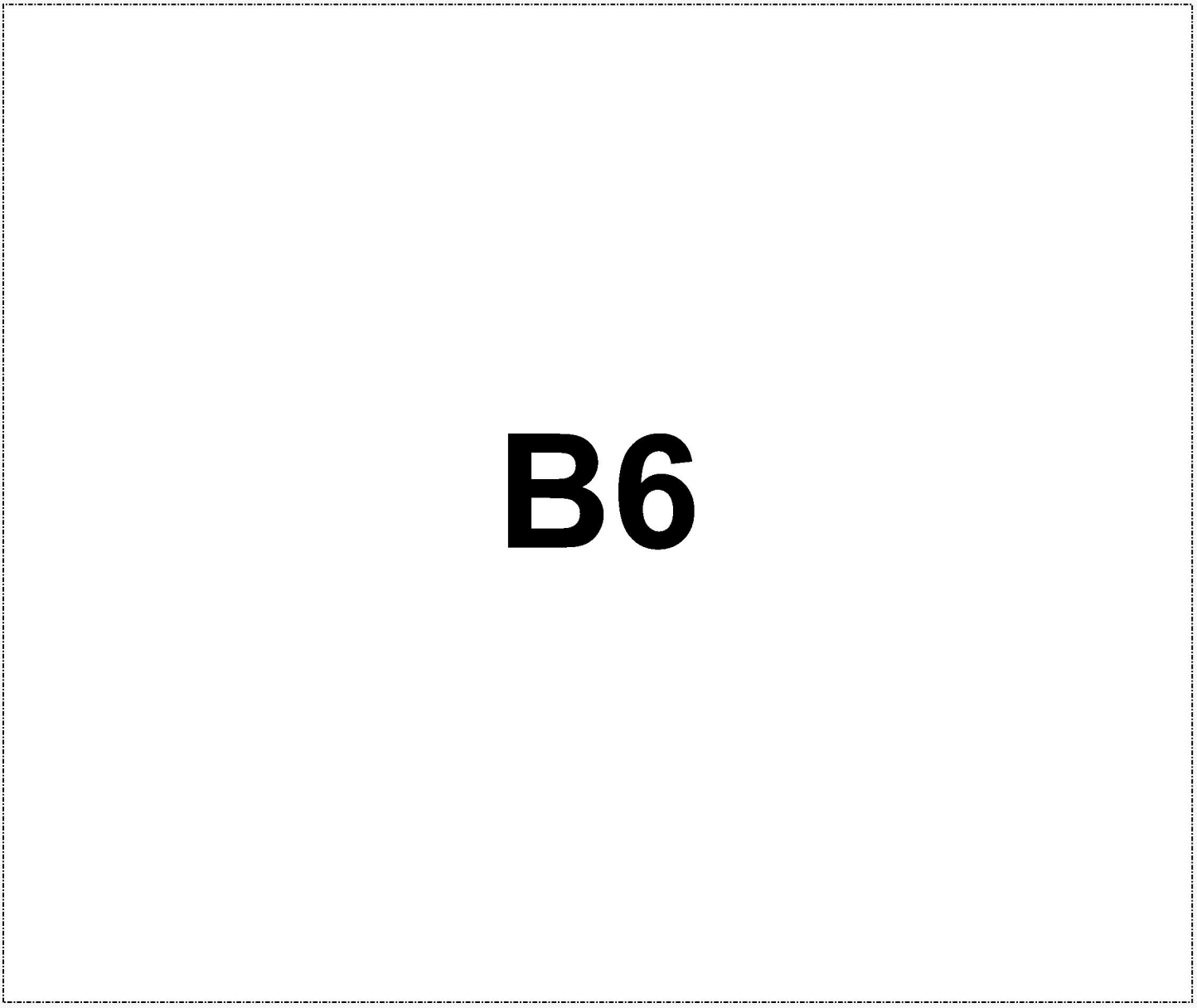
Client: B6
Patient: B6

Vitals Results

B6	11:27:32 AM 11:27:49 AM 11:50:27 AM 1:22:02 PM 1:26:02 PM 1:55:42 PM 3:31:07 PM 3:34:47 PM 3:34:59 PM 3:57:10 PM 1:24:42 AM 2:35:27 AM 2:35:28 AM 2:35:30 AM 5:12:11 AM 15:01 PM	B6

Client: B6
Patient: B6

rDVM B6 **rad** B6 **Thx Right Lat**



Client: B6
Patient: B6

ECG from cardio

B6 B6 10:06:21 AM
Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient: B6

ECG from cardio

B6 B6 10:08:03 AM

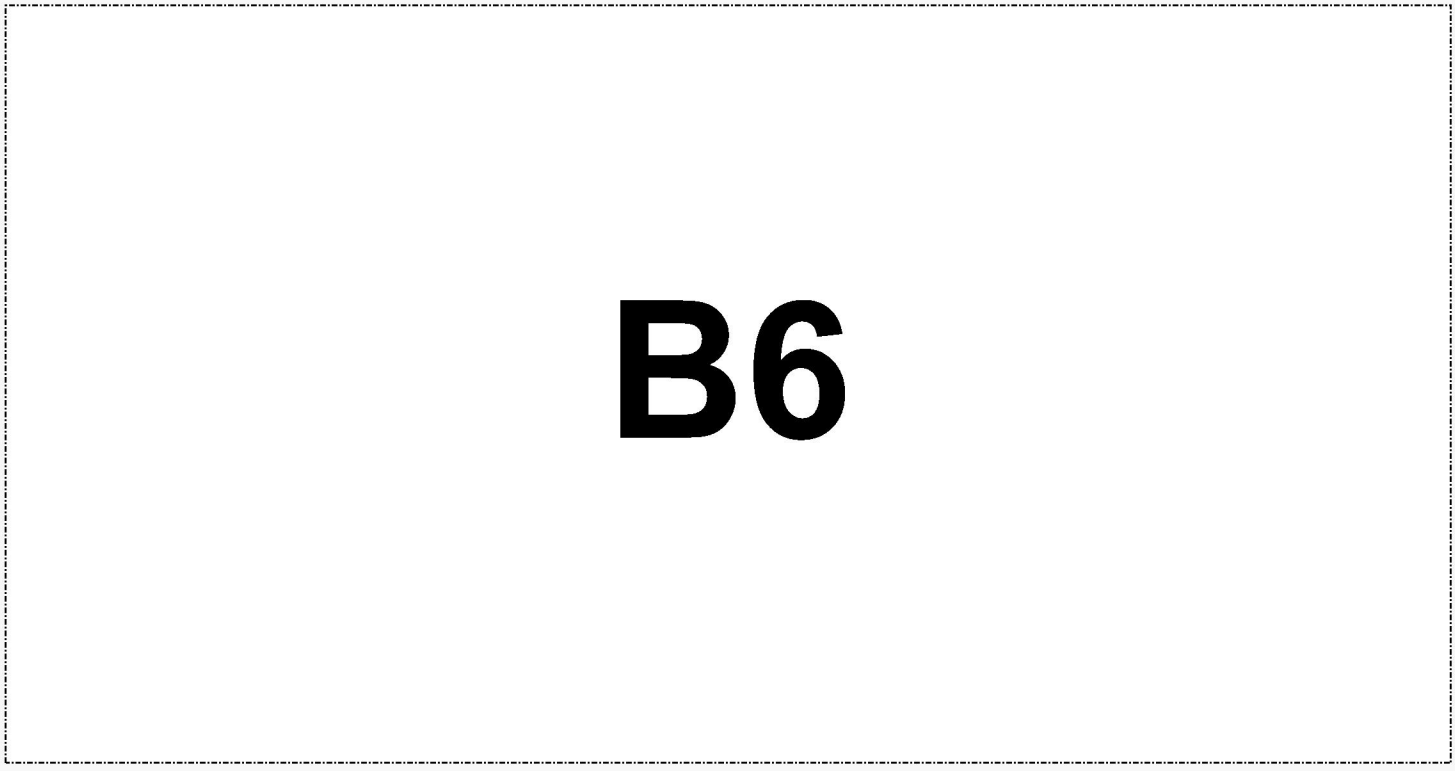
Tufts University
Tufts Cummings School of Vet Med
Cardiology

Client: B6
Patient: B6

ECG from cardio

B6 B6 10:08:03 AM

Tufts University
Tufts Cummings School of Vet Med
Cardiology



Patient History

B6

05:40 PM	Vitals
05:40 PM	Vitals
05:40 PM	Vitals
05:40 PM	Vitals
05:42 PM	UserForm
06:17 PM	UserForm
06:18 PM	UserForm
07:40 PM	Purchase
08:02 PM	Treatment
08:02 PM	Vitals
08:06 PM	Labwork
08:11 PM	Treatment
08:11 PM	Vitals
08:11 PM	Treatment
08:11 PM	Vitals
08:12 PM	Treatment
08:12 PM	Vitals
08:12 PM	Treatment
08:13 PM	Purchase
08:13 PM	Purchase
08:20 PM	Purchase
08:20 PM	Purchase
08:21 PM	Treatment
08:21 PM	Vitals
08:26 PM	Treatment
08:26 PM	Vitals
08:26 PM	Vitals
09:42 PM	Vitals
09:43 PM	Treatment
11:00 PM	Vitals
11:17 PM	Treatment
11:17 PM	Treatment
11:18 PM	Treatment
11:18 PM	Vitals
11:18 PM	Treatment
11:18 PM	Vitals
11:21 PM	Treatment
11:21 PM	Vitals
11:58 PM	Treatment
11:58 PM	Treatment
11:58 PM	Vitals
01:04 AM	Treatment
01:04 AM	Vitals
01:04 AM	Vitals

B6

Client: B6
Patient: B6

Patient History

B6

01:51 AM	Treatment
01:51 AM	Vitals
02:58 AM	Treatment
02:58 AM	Vitals
02:58 AM	Vitals
03:04 AM	Treatment
03:04 AM	Vitals
03:04 AM	Treatment
03:10 AM	Treatment
03:10 AM	Vitals
03:10 AM	Treatment
03:10 AM	Vitals
03:59 AM	Treatment
03:59 AM	Vitals
04:55 AM	Vitals
05:00 AM	Vitals
05:16 AM	Treatment
05:55 AM	Treatment
05:55 AM	Vitals
06:02 AM	Purchase
07:01 AM	Treatment
07:01 AM	Vitals
07:13 AM	Treatment
07:13 AM	Vitals
07:14 AM	Vitals
07:14 AM	Treatment
07:14 AM	Treatment
07:14 AM	Vitals
07:21 AM	Vitals
07:28 AM	Treatment
07:28 AM	Vitals
08:11 AM	Purchase
08:12 AM	Treatment
08:12 AM	Vitals
08:14 AM	Purchase
08:31 AM	UserForm
09:06 AM	Treatment
09:06 AM	Vitals
09:06 AM	Treatment
09:06 AM	Vitals
09:15 AM	UserForm
09:43 AM	Purchase
09:43 AM	Purchase
09:44 AM	Purchase
09:44 AM	Purchase
09:59 AM	Treatment

B6

Client: B6
Patient: B6

Patient History

B6

09:59 AM	Vitals
10:06 AM	Purchase
10:06 AM	Treatment
10:10 AM	Purchase
10:34 AM	Treatment
10:34 AM	Vitals
11:24 AM	Treatment
11:25 AM	Treatment
11:25 AM	Vitals
11:25 AM	Purchase
11:27 AM	Treatment
11:27 AM	Treatment
11:27 AM	Vitals
11:27 AM	Treatment
11:27 AM	Vitals
11:50 AM	Treatment
11:50 AM	Vitals
01:22 PM	Treatment
01:22 PM	Vitals
01:26 PM	Treatment
01:26 PM	Vitals
01:55 PM	Treatment
01:55 PM	Vitals
02:24 PM	Prescription
02:26 PM	Prescription
02:27 PM	Prescription
02:29 PM	Prescription
02:34 PM	Purchase
02:55 PM	Appointment
03:31 PM	Treatment
03:31 PM	Vitals
03:34 PM	Treatment
03:34 PM	Vitals
03:34 PM	Treatment
03:34 PM	Treatment
03:34 PM	Vitals
03:57 PM	Treatment
03:57 PM	Vitals
10:54 AM	UserForm
11:01 AM	Treatment
11:02 AM	Purchase
11:24 AM	Vitals
11:53 AM	Purchase
12:10 PM	UserForm

B6

Client: B6
Patient: B6

Patient History

B6

12:51 PM	Prescription
12:51 PM	Purchase
02:36 PM	Prescription
02:36 PM	Purchase
09:30 AM	Prescription
09:32 AM	Purchase
03:55 PM	Prescription
03:55 PM	Purchase
02:35 AM	Vitals
02:35 AM	Vitals
02:35 AM	Vitals
03:34 AM	UserForm
04:09 AM	Treatment
05:10 AM	Purchase
05:11 AM	Purchase
05:11 AM	Purchase
05:12 AM	Vitals
05:12 AM	Purchase
05:13 AM	Purchase
05:19 AM	Treatment
05:25 AM	UserForm
10:56 AM	Appointment
02:06 PM	UserForm
02:15 PM	Vitals
02:33 PM	Treatment
02:36 PM	Purchase
02:48 PM	UserForm
03:07 PM	Purchase
03:52 PM	Prescription
03:56 PM	Prescription
04:04 PM	Purchase

B6

Appears this way in Original

Appears this way in Original

Appears this way in Original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/
Referring Vet Direct Line 508-887-4988

Notice of Patient Admit

Date: B6 5:41:03 PM **Case No:** B6
Referring Doctor: B6
Client Name: B6
Patient Name: B6

Dear Colleague,

Your patient presented to our Emergency service. Please make note of the following information to facilitate communication with our team.

The attending doctor is: B6
The reason for admission to the FHSA is: Suspect DCM.

If you have any questions regarding this particular case, please call 508-887-4988 to reach the Cardiology Service. Information is updated daily, by noon.

Thank you for your referral to our Emergency Service.

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/Daisy

B6 Female (Spayed)
Canine Golden Retriever Cream
B6

B6

Daily Update From the Cardiology Service

Today's date: 4/11/2018
Dear B6

Thank you for referring patients to the Foster Hospital for Small Animals at the Cummings School of Tufts University.

Your patient B6 was admitted and is being cared for by the Cardiology Service.

Today, B6

- [x] is in stable condition
- [ ] is still in the oxygen cage
- [ ] is critically ill
- [x] might be discharged from the hospital today

Today's treatments include

- [x] bloodwork planned/pending
- [x] echocardiography
- [ ] cardiac catheter procedure planned
- [x] treatment for DCM (primary vs secondary dietary induced)
- [ ] ongoing treatment for thrombosis
- [ ] ongoing treatment for arrhythmia

Additional plans:
Please allow 3-5 business days for reports to be finalized upon patient discharge.

Please call (508) 887-4696 before 5pm or email us at cardiovet@tufts.edu if you have any questions. Thank you!

Attending Clinician: B6
Faculty Clinician: B6 DVM,DACVIM
Senior student:

Appears this way in Original

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6 Female (Spayed)
Canine Golden Retriever Cream
B6

4/24/2018

Dear B6

Thank you for referring B6 with their pet B6

If you have any questions, or concerns, please contact us at 508-887-4988.

Thank you,

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6

Canine Golden Retriever Cream

B6

7/9/2018

Dear B6

Thank you for referring B6 with their pet B6

If you have any questions, or concerns, please contact us at 508-887-4988.

Thank you,

B6

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6 Female (Spayed)
Canine Golden Retriever Cream
B6

B6

Dear B6

Tonight B6 presented to the ER for evaluation of an acutely developed dry non productive cough. She has a history of DCM and is being managed by our Cardiology Service for it. The owners are also concerned that she ingested foreign material on Christmas and her cough may be related to it.

TFAST revealed significant RV enlargement. Thoracic radiographs showed cardiac enlargement without pulmonary edema. Abdominal radiographs (insisted to be performed by owner) were unremarkable.

Hospitalizaiton was recommended so she can be re-evaluated by Cardiology ASAP, but ultimately declined. She was given furosemide 2mg/kg IM and discharged.

If you have any questions, or concerns, please contact us at 508-887-4988.

Thank you,

B6 DVM

Cummings
Veterinary Medical Center
AT TUFTS UNIVERSITY

Foster Hospital for Small Animals
55 Willard Street
North Grafton, MA 01536
Telephone (508) 839-5395
Fax (508) 839-7951
http://vetmed.tufts.edu/

B6

B6 Female (Spayed)
Canine Golden Retriever Cream
B6

1/2/2019

Dear B6

Thank you for referring B6 with their pet B6.

If you have any questions, or concerns, please contact us at 508-887-4988.

Thank you,

B6 (Cardiology)

From:	Norris, Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=891982B43D804C9396555BAF36C73DE1-ANNE.NORRIS>
To:	Solomon, Steven M; Forfa, Tracey; Moxley, Shera; Flynn, William T; Murphy, Jeanette; Hartogensis, Martine; Allen, Mary; Edwards, David; Conway, Charlotte; Jones, Jennifer L; Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Burkholder, William; Benton, Denise; Goddard, Kristina; Dewitt, Susan J; Alvey, Laura - CVM; Stamper, Carmela; Smith-Collier, Chandra E; DeLancey, Siobhan
Sent:	2/15/2019 4:51:30 PM
Subject:	Posting on Tuesday, 2/19: DCM Update
Attachments:	CVMU_DCM_Feb2019.docx; DCM Plan_Feb2019.docx; DCM_Feb2019_Update.docx; DCM_VetLIRN_Feb2019.docx; WebQA_DCM_Feb2019.docx

Good morning,

CVM's public update on the investigation into diet and canine dilated cardiomyopathy is now scheduled for Tuesday (2/19) morning.

The final, fully cleared documents are attached. The CVM Update, web page, Vet-LIRN update, and updated web QA will post at 10:00 am, B5 At 11:00 am, we'll promote the update to email subscribers and through social media.

B5

Please let me know if you have any questions or concerns. When the links are live on Tuesday, we'll be sure to share.

Thanks,
Anne

Anne Norris
Strategic Initiatives

Office of the Director
Center for Veterinary Medicine
U.S. Food & Drug Administration
O: 240-402-0132
M: B6
Anne.Norris@fda.hhs.gov

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: Carey, Lauren; Rotstein, David; Peloquin, Sarah
Sent: 7/12/2019 1:42:25 PM
Subject: RE: Fish & Taurine

Article on Cobia and also other fish.
https://reader.elsevier.com/reader/sd/pii/S0044848607005601?token=F145C6C9CDFD137474AA20B39DA5F05536438CC14F3EE1D768C1E32A09F56

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754659/pdf/srep21231.pdf

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Thursday, July 11, 2019 6:16 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Fish & Taurine

Excellent! Thank you :)

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Carey, Lauren
Sent: Wednesday, July 10, 2019 2:53 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Fish & Taurine

Yup, pretty interesting. It's a Dr. Fascetti article so I think it must have made the rounds, but just in case, especially since we were B5

From: Rotstein, David
Sent: Wednesday, July 10, 2019 2:52 PM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Fish & Taurine

Sarah and Jen may have seen it---very interesting—and states in the very first sentence about the development on DCM on the rice-based diet.

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERRT

7519 Standish Place
B6

From: Carey, Lauren
Sent: Wednesday, July 10, 2019 2:48 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Fish & Taurine

Good thoughts! B5 . Have we seen this one?

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4971673/

From: Rotstein, David
Sent: Wednesday, July 10, 2019 2:44 PM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: RE: Fish & Taurine

B5

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERRT
7519 Standish Place
B6

From: Carey, Lauren
Sent: Wednesday, July 10, 2019 2:42 PM

To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: Fish & Taurine

B5

Thanks,
Lauren

Lauren Carey, DVM
Veterinary Medical Officer / Division of Veterinary Product Safety HFV-242

Center for Veterinary Medicine
Office of Surveillance and Compliance
U.S. Food and Drug Administration
Tel: 240-402-5738
Lauren.Carey@fda.hhs.gov

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Jones, Jennifer L
Sent: 8/8/2018 8:43:16 PM
Subject: as promised
Attachments: Canine DCM protocol external 7-8-18.docx

Hi Jennifer
Below are the WSAVA guidelines and also my blog that expands on the quality control measures.
https://www.wsava.org/WSAVA/media/Arpita-and-Emma-editorial/Selecting-the-Best-Food-for-your-Pet.pdf
http://vetnutrition.tufts.edu/2016/12/questions-you-should-be-asking-about-your-pets-food/

Also, I think I sent the attached to you before but resending in case.
Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Board Certified Veterinary Nutritionist™
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

Vet-LIRN Case Summary Document

Vet-LIRN Case Number:	800.267
EON/CC #:	EON-345858
Owner LAST Name:	
Vet LAST Name:	Multiple
Vet-LIRN Initiation Date:	4/13/2018
MedRec: Requested:	
MedRec: Received:	
MedRec: Significant finding:	
Vet-LIRN Tests (planned):	
Vet-LIRN Test Results:	Covance • Control/non-GF Cys, Met, Tau
Result Interpretation:	
IF NFA, justification:	

COMPLAINT Narrative: Dave and I proactively held a call with communications about the potential for grain free diets to cause DCM. B5

B5

B5

4/20/2018

JJ-We held a call with many cardiologists and nutritionists today. I sent a follow-up to the group with a

B5

B5

Vet-LIRN Plan:

-
-
-

B5

B5

4/24/2018

JJ-I reviewed the list sent by Tufts and compiled it with the PFRs we've received for DCM B5

B4

B5

I looked up the ingredients for each product listed and looked for common product commonalities.

BLUF: The most common ingredients were:

- Flaxseed/Flaxseed oil
- Peas/Pea fiber/Pea flour

On the phone call, one of the cardiologists mentioned B5

B5

Hypotheses if a pet food issue:

B5

B5

4/20/2018

JJ-Lisa Freeman (Tufts) sent a draft dietary history form. I made a few comments and sent back to the group. B5

B5

5/1/2018

JJ-I did some research on B5

B5

B5

B5 *Thoughts?*

Dave previously sent an email about B5

B5

B5

5/4/2018

B5

I prepared the samples (list below), made the lab submission forms, and packed the box. SN will make a shipping label.

Samples sent to Covance for Tau/Met/Cys:

Case ID	Product Name	Type	Grains	Clinically	Ingredients in common w/ Top GF ingredients (>14 in our data set)
800.216-sub 2	B4				
800.215-sub 5					
800.210-sub 1					
800.194-sub 1					
800.240-sub 1					
800.240-sub 2					
800.240-sub 3					
800.240-sub 4					
800.250-sub 1					

5/9/2018

JJ-Martine spoke with a B5

B5

5/10/2018
JJ-LAP had some B5

B5

Info from LAP:

If you look at the cases we've received (well – either in the list from Tufts or NC State or reported to CVM not to Tufts/NC) in which the Grain-free status of the primary brand fed (or reported) can be determined, 39 of 41 had exposure to Grain-free foods, including the cats. B5

B5

B5

LAP believes there is a B5

5/17/2018
JJ-We received the results of the Covance control food testing. I updated the xls and made a report for the group.

BLUF-I suspect B5

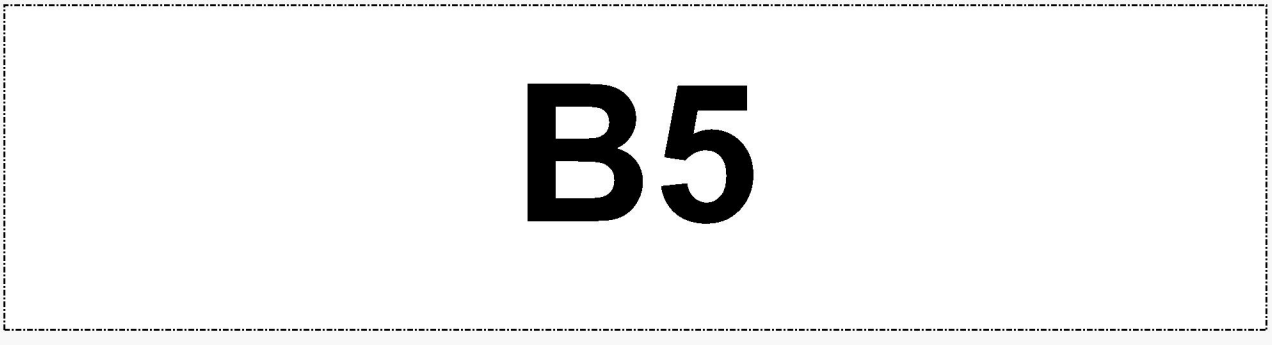
- B5

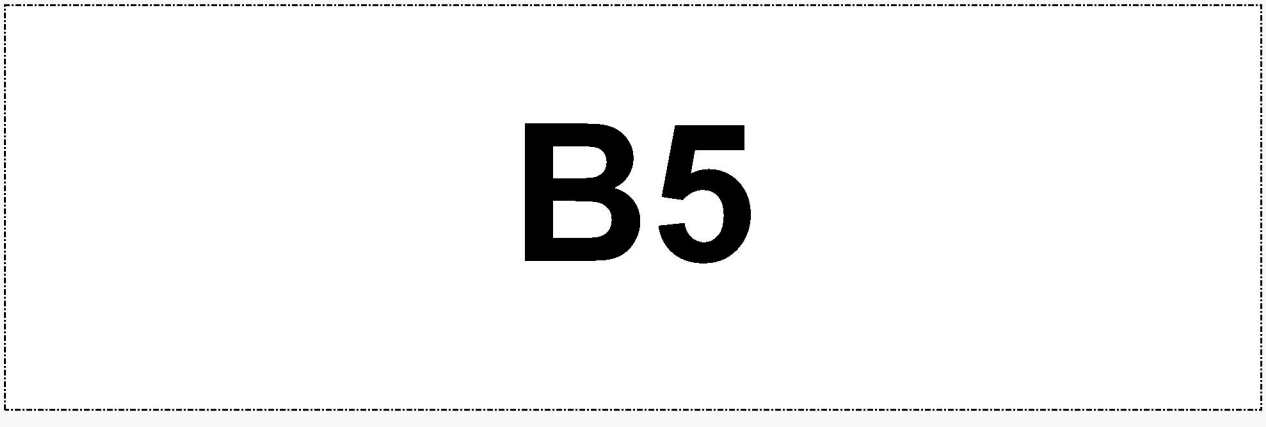
B5

5/18/2018
JJ- LAP filed her initial analysis-

B5


B5


B5


B5

MH mentioned B5

B5

6/13/2018

JJ-OSC plans to B5

B4, B5

We had a call with PFI and discussed the findings from our product testing (without brand names) B5

B5

B5

B5

Source	Case	Typical Breed?	Diagnosis	wb taurine	plasma taurine
Tufts	B6	Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM/CHF	WNL	WNL
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM/CHF, RA mass	/	/
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM/CHF	WNL	WNL
Tufts		Atypical	DCM	WNL	WNL
Tufts		Atypical	DCM/CHF	WNL	WNL
Tufts		Atypical	Murmur but no echo (in for GI issues)	/	/
Tufts		Atypical	DCM/CHF	WNL	WNL
Tufts		Atypical	DCM +/- CHF, V tach	/	/
Tufts		Atypical	DCM	/	/
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM	WNL	WNL
Tufts		Atypical	DCM/CHF	200	40
Tufts		Atypical	DCM/CHF	/	/
Tufts		Atypical	DCM	229	105
NCSU	EON-323515	Atypical	DCM/CHF	adequate-no value(s)	
NCSU	EON-323519	Atypical	DCM/CHF, MV endocardiosis	normal-no value(s)	
B6	EON-345822	Atypical	DCM/CHF, some V-tach	292	/
	EON-345831	Atypical	DCM/CHF, Endocardiosis, A-Fib	236	/
	EON-345833	Atypical	DCM, Endocardiosis	/	/
	EON-345835	Typical	DCM/CHF, low Alb	10	/
	EON-345965	Atypical	DCM, partial retinal detachment	276	/
CVCA	EON-350158	Atypical	DCM/CHF (early CHF)	168	/
CVCA	EON-350263	Typical	DCM/CHF, endocardiosis	/	/
CVCA	EON-350359	Typical	DCM	/	/
B6	EON-351031	Atypical	DCM/CHF	119	/
	EON-351034	Atypical	DCM/CHF	57	/
Tufts	B6	Typical	DCM	39	/
Tufts		Typical	DCM	47	/

supplemented	improved	dob	breed	visit date	sex	age
yes	no		PORTUGUESE WATER DOG		SF	7.2
no			LABRADOR CROSS		CM	11.0
no (died)			SAMOYED		CM	7.2
no			GOLDEN RETRIEVER		CM	10.1
yes	pending		LABRADOR RETRIEVER		CM	8.3
no			GERMAN SHEPHERD		CM	5.0
no			BEAGLE CROSS		CM	3.0
no			GERMAN SHORTHAIR POINTER		M	2.7
no			AUSTRALIAN CATTLE DOG		SF	5.8
no			MIX		CM	5.0
yes	no		LAB		SF	2.5
no			PIT BULL		CM	6.8
no			PHAROAH HOUND		F	0.7
yes	yes		PIT BULL		CM	10.6
no (died)			FRENCH BULLDOG		CM	9.5
no		B6	FRENCH BULLDOG	B6	SF	5.1
yes	no		GOLDEN RETRIEVER		CM	11.0
no			GOLDEN RETRIEVER		SF	11.0
yes	pending		GOLDEN RETRIEVER		SF	9.7
yes	died		Miniature Schnauzer		CM	2.5
no	CHF resolved		Miniature Schnauzer		CM	7
unknown	unknown		LABRADOR RETRIEVER		SF	6
no	stable-slight		LABRADOR RETRIEVER		F	8
no	died		LABRADOR RETRIEVER		SF	5
yes			American Cocker Spaniel		CM	4
yes			Shih Tzu		CM	8
yes	yes		LABRADOR RETRIEVER		SF	13
yes	pending		Bull Terrier		M	8
yes	pending		American Cocker Spaniel		SF	13
yes	pending		GOLDEN RETRIEVER		CM	6
yes	pending		GOLDEN RETRIEVER		SF	11
yes	pending		DOBERMAN PINSCHER		CM	7.3
yes	yes		BOXER		CM	1.7

		800.218-sub 1 Case Sample California Naturals Kangaroo & Lentil	800.218-sub 2 Store-bought California Naturals Kangaroo & Lentil	800.218-sub 6 Case sample California Naturals Kangaroo & Lentil
B4	Ca	1.30%	1%	0.93%
	Mg	0.13%	0.14%	0.15%
	P	0.74%	0.67%	0.68%
	Fe	**30 mg/kg**	**30 mg/kg**	**31 mg/kg**
	Co	0.12 mg/kg	0.14 mg/kg	.14 mg/kg
	Cu	21 mg/kg	19 mg/kg	16 mg/kg
	Zn	240 mg/kg	280 mg/kg	200 mg/kg
	Se	0.7 mg/kg	0.65 mg/kg	.68 mg/kg
	Ca:P	1.76:1	1.49:1	1.37:1
	Cu:Zn	0.09:1	0.07:1	0.08:1
B4	Tau	~0.26%	1.06 mg/g = ~0.11%	1.22 mg/g = ~0.12%
	Cystine	2.32 mg/g = ~0.23%	2.31 mg/g = ~0.23%	2.5 mg/g = ~0.25%
	Met	5.78 mg/g = ~0.58%	5.53 mg/g = ~0.55%	7.78 mg/g = ~0.78%
	Met-Cys	~0.81%	~0.78%	~1.03%
	Cys:Met	0.4 : 1	0.42 : 1	0.29 : 1
	Met: Met+Cys	0.72 : 1	0.71 : 1	0.76 : 1
	Met: Cys	2.52 : 1	2.39 : 1	3.12 : 1
MSU	Iodine	not tested	4.04 ug/g (ppm)	1.87 ug/g (ppm)

800.218-sub 5	800.218-sub 4	800.261	
Case Sample	Case Sample	Store-bought	
California Naturals Chicken Meal	Fromm Heartland Gold Grain Free Large Breed Adult	Zignature Essentials Kangaroo	AAFCO-Adult Maint
1.80%	1.20%		0.5 to 2.5%
0.14%	0.14%		0.06%
1.30%	1%		0.4 to 1.6 %
39 mg/kg	**30 mg/kg**		40 mg/kg
0.14 mg/kg	0.37 mg/kg		25 mg/kg-chicks/rats/sheep max
19 mg/kg	25 mg/kg		7.3 mg/kg
330 mg/kg	170 mg/kg		80 mg/kg
0.66 mg/kg	0.85 mg/kg		0.35 to 2 mg/kg
1.38:1	1.2:1		1:1 to 2:1
0.06:1	0.15:1		0.09:1-not AAFCO
1.08 mg/g = ~0.11%	1.84 mg/g = ~0.18%	pending	0.1% in Cats
3.2 mg/g = ~0.32%	3.15 mg/g = ~0.32%	pending	n/a
6.2 mg/g = ~0.62%	4.75 mg/g = ~0.48%	pending	0.33%
~0.94%	~0.79%	pending	0.65%
0.52 : 1	0.66 : 1	pending	
0.66 : 1	0.61 : 1	pending	
1.94 : 1	1.5 : 1	pending	
3.19 ug/g (ppm)	1.58 ug/g (ppm)	4.2 ug/g (ppm)	1 ppm (min) to 11 ppm (max)

		800.218-sub 1	800.218-sub 2	800.218-sub 6	800.218-sub 5	800.218-sub 4	800.261	800.216-sub 2	800.215-sub 5	800.210-sub 1	800.194-sub 1	800.240-sub 1	800.240-sub 2	800.240-sub 3	800.240-sub 4	800.250-sub 1	
		Case Sample	Store-bought	Case sample	Case Sample	Case Sample	Store-bought	Store-bought	Case	Case		Case	Case	Case	Case	Store-bought	
		California Naturals Kangaroo & Lentil	California Naturals Kangaroo & Lentil	California Naturals Kangaroo & Lentil	California Naturals Chicken Meal	Fromm Heartland Gold Grain Free Large Breed Adult	Zignature Essentials Kangaroo	Wysong Vegan Canine/Feline Formula	Wellness Small Breed Healthy Weight Turkey & Brown Rice-DOG	Rachel Ray Nutrish Chicken & Brown Rice-CAT FOOD	Purina Proplan Focus Indoor Care Cat Food	Iams Proactive Health Mini Chunks Adult 1+	Iams Proactive Health Mini Chunks Adult +1	Iams Proactive Health with Grass Fed Lamb	Iams Proactive Health Small & Toy Breed Adult 1+	Wellness Core Grain Free Original-Dog-No reports****	AAFCO-Adult Maint
B6	Ca	1.30%	1%	0.93%	1.80%	1.20%											0.5 to 2.5%
	Mg	0.13%	0.14%	0.15%	0.14%	0.14%											0.06%
	P	0.74%	0.67%	0.68%	1.30%	1%											0.4 to 1.6 %
	Fe	**30 mg/kg**	**30 mg/kg**	**31 mg/kg**	**39 mg/kg**	**30 mg/kg**											40 mg/kg
	Co	0.12 mg/kg	0.14 mg/kg	.14 mg/kg	0.14 mg/kg	0.37 mg/kg											25 mg/kg-chicks/rats/sheep max
	Cu	21 mg/kg	19 mg/kg	16 mg/kg	19 mg/kg	25 mg/kg											7.3 mg/kg
	Zn	240 mg/kg	280 mg/kg	200 mg/kg	330 mg/kg	170 mg/kg											80 mg/kg
	Se	0.7 mg/kg	0.65 mg/kg	.68 mg/kg	0.66 mg/kg	0.85 mg/kg											0.35 to 2 mg/kg
	Ca:P	1.76:1	1.49:1	1.37:1	1.38:1	1.2:1											1:1 to 2:1
	Cu:Zn	0.09:1	0.07:1	0.08:1	0.06:1	0.15:1											0.09:1-not AAFCO
B6	Tau	MB = **0.26% est DMB**	MB = **0.11% est DMB**	MB = **0.14% est DMB**	DMB = **0.12% est DMB**	MB = **0.2% est DMB**	B = **0.051% est DMB**	B = **~0.19% est DMB**	MB = **0.22% est DMB**	MB = **0.24% est DMB**	MB = **0.24% est DMB**	MB = **0.11% est DMB**	MB = **0.11% est DMB**	MB = **0.11% est DMB**	MB = **0.12% est DMB**	MB = **0.25% est DMB**	0.1% in Cats
	Cystine	MB = **0.26% est DMB**	MB = **0.26% est DMB**	MB = **0.28% est DMB**	DMB = **0.36% est DMB**	MB = **0.34% est DMB**	t DMB = **0.33% DMB**	MB = **0.46% est DMB**	MB = **0.32% est DMB**	MB = **0.42% est DMB**	MB = **0.5% est DMB**	MB = **0.3% est DMB**	MB = **0.3% est DMB**	= **<0.011% est DMB**	= **<0.011% est DMB**	= **<0.011% est DMB**	n/a
	Met	MB = **0.64% est DMB**	MB = **0.61% est DMB**	MB = **0.86% est DMB**	DMB = **0.69% est DMB**	MB = **0.51% est DMB**	MB = **0.4% est DMB**	MB = **0.60% est DMB**	MB = **0.66% est DMB**	MB = **0.78% est DMB**	MB = **0.94% est DMB**	MB = **0.57% est DMB**	MB = **0.6% est DMB**	B = **0.045% est DMB**	B = **0.032% est DMB**	B = **0.032% est DMB**	0.33% dog
	Met-Cys	0.9% est DMB	0.87% est DMB	1.14% est DMB	1.05% est DMB	0.85% est DMB	0.73% est DMB	1.06% est DMB	0.98% est DMB	1.2% est DMB	1.44% est DMB	0.87% est DMB	0.9% est DMB	0.056% est DMB	0.043% est DMB	0.043% est DMB	0.65% dog
	Cys:Met																
	Met: Met+Cys																
	Met: Cys																
MSU	Iodine	not tested	4.04 ug/g (ppm)	1.87 ug/g (ppm)	3.19 ug/g (ppm)	1.58 ug/g (ppm)	4.2 ug/g (ppm)										1 ppm (min) to 11 ppm (max)
		per label moisture max 10%	per label moisture max 10%	per label moisture max 10%	per label moisture max 10%	per label moisture as-is 7.07%	per label moisture max 10%	per label moisture max 10%	per label moisture max 11%	per label moisture max 9%	per label moisture max 12%	per label moisture max 10%	per label moisture max 10%	per label moisture max 10%	per label moisture max 10%	per label moisture max 10%	

Last Name	EON	MRx Req	MRx Rcvd	MRx Summ	Interview Req
B6	EON-359281	x	x	x	x
	EON-359337	x	x	x	x
	EON-359723	x	x	x	x
	EON-359524	x	x	x	x
	EON-361158	x	x	x	x
	EON-361042	x	x	x	NFA
	EON-361105	x	x	x	x
	EON-361132	x2			
	EON-361233	x	x	x	x
	EON-361233	x	x	x	NFA
	EON-359594	x	x	x	x
	EON-359190	x	x	x	x
	EON-359301	x	x	x	x
	EON-359374-359595	x	x	x	x
	EON-361816	x			
	EON-361832	x	x	x	NFA
	EON-361853	x	x	x	x
	EON-361855-57	x	x	x	x
	EON-361866	x	x	x	x
	EON-361903	x	IP		
	EON-362172	x	x	x	x
	EON-361876	x	x	x	x
	EON-362325	x	x	x	x
	EON-362327	x	x	x	x
	EON-362347	x	x	x	x
	EON-362358	x			
	EON-362368	x			
	EON-362411	x	x	x	x
	EON-362570	x	need CC mrx		
	EON-362680	x	x		
	EON-362724	x	x	x	x
	EON-362795	x	IP - x2		
	EON-362796	x			
	EON-358522	x	x	x	x
	EON-360197	x	x	x	NFA
	EON-360030	x	x	JJ	
	EON-364330	x	x	x	x
	EON-361412	x	x	x	x
	EON-361244	x	x	x	x
	EON-361347	x	x	x	x
	EON-361684	x	x	x	x
	EON-363316	x	x	x	x
	EON-363409	x	x		
	EON-363497	x	x	x	x
	EON-363608	x			
	EON-363773	x	x	x	x

B6

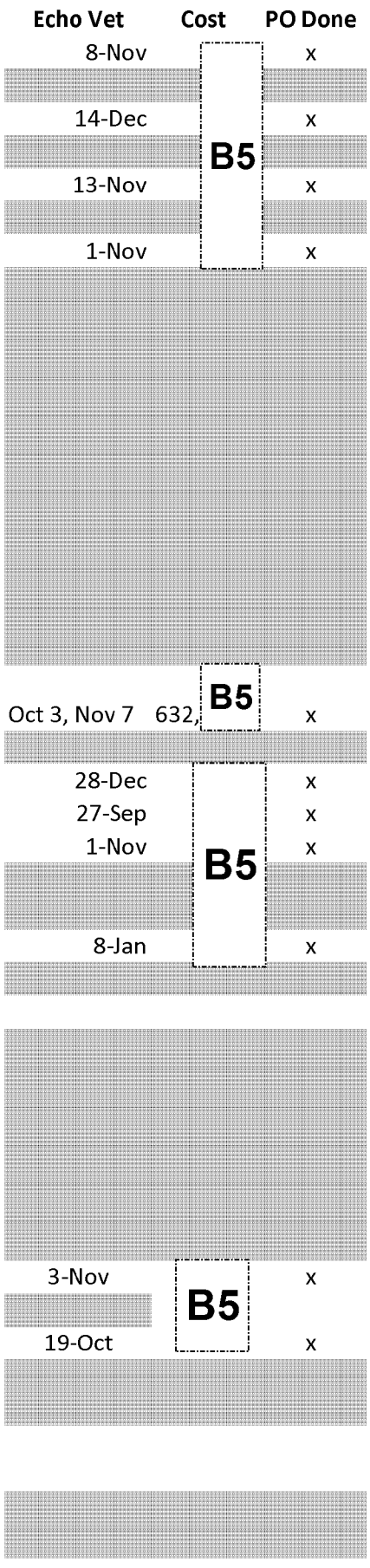
EON-363846	x	x		
EON-363873	x	x	x	x
EON-363894	x2	x	x	x
EON-361320	x	x	x	x
EON-361723	x	x	x	x
EON-363453	necrop?			
EON-363580	x			
EON-364300	echo tau?			
EON-364322	x	NFA	no echo/tau	
EON-364337	x			
EON-364568	x	x	x	x2
EON-365002	x	x	x	x
EON-364590	x	x	x	x
EON-364639	x	x	x	x
EON-364646	x	IP		
EON-364715	x	IP		
EON-364718	x	x	x	x
EON-364891	x	x	x	x
EON-365010	x	x	x	x
EON-365076	x	x	x	x
EON-365839	x	x		yes O perm
EON-366207	x	x		
EON-366509	x	x		
EON-366513	x			
EON-366547	x			
EON-366570	x	x		
EON-366538	x	x	x	NFA
EON-359942	x	x	x	x
EON-368370	x	IP		

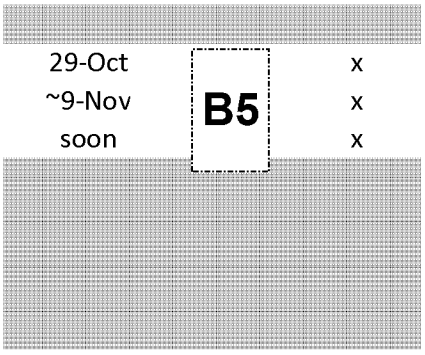
B6

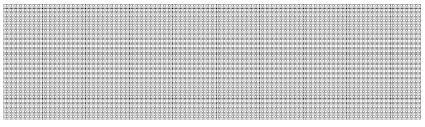
Interview Done	Food Req	Food Avail	Box Sent	Food Rcvd	Necropsy?	Echo O
x	x	No			No	x
x	x	Yes	x	x	No	x2
x	x	Yes	x	x	No	x
x	x	No	NFA		No	
x	x	No			No	x
					No	
x	x	Yes	x	x	No	x
x	x	Yes	x	x	No	
					No	
x	x	No	NFA		No	
x	x	No	NFA		No	
x	x	Yes	x	x	No	
x	NFA				No	
					No	
x	x	Yes	x	x	No	
x	x	No	NFA		No	
x	x	No			No	
x	x	No	NFA		No	x
x	x	No	NFA		No	
x	x	No	NFA		No	x
x	NFA				No	x
x	x	Yes	x	x	No	x
x	x	Yes			No	x
		No			Yes	
x	x	No	NFA		Yes	
					No	
x	x	Yes	x		No	
					No	
x	x	No			Yes	
x	x	No			No	x
x	x	Yes	x	x	No	
x	x	No			No	x
x	x	No			Yes	
					No	
		No				
need tau results						
x	No				No	

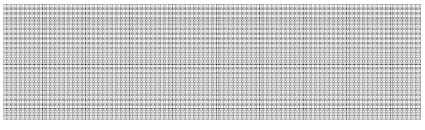
B6

		Yes			No	
x	Yes					
x	Yes	No			No	x
x	No				No	x
x	No				No	x
		Yes LF				
x	Yes	Yes	x			
		Yes				
x	x	Yes vet	JG			
		No				
x	x	Yes	JG			
x	x	No				O asked
x	No					
x	x	Yes	x		No	
No answer					Yes	
		Yes			No	


Echo Vet
Cost
PO Done
8-Nov
x
14-Dec
x
B5
13-Nov
x
1-Nov
x
B5
Oct 3, Nov 7
632,
x
28-Dec
x
27-Sep
x
1-Nov
x
B5
8-Jan
x
3-Nov
x
B5
19-Oct
x


29-Oct
~9-Nov
soon
B5
x
x
x





From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: Rotstein, David; Hartogensis, Martine; Palmer, Lee Anne; Carey, Lauren
Sent: 6/4/2018 5:00:52 PM
Subject: RE: checking in-FW: DRAFT- email to the Divisions about Dilated Cardiomyopathy

I received results from Covance, and I need to update this powerpoint. B5 B5 Please stay tuned.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Monday, June 04, 2018 12:58 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Subject: checking in-FW: DRAFT- email to the Divisions about Dilated Cardiomyopathy

Everyone,

B5

Thanks,
dave

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B5 **(BB)**

U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Thursday, May 24, 2018 10:04 AM
To: Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: DRAFT- email to the Divisions about Dilated Cardiomyopathy

Jackie,

Please take a look when you get a chance:

B5

Thank you,

Dave

Brand	flavor	Firm	Location	FEI	Division

B4, B5

B4, B5

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B4 (BB)

From: Hartogensis, Martine </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02DF91D554D34B948FC58433D0E42073-MHARTOGE>
To: Jones, Jennifer L; Palmer, Lee Anne; Carey, Lauren; Rotstein, David
Sent: 6/13/2018 1:44:20 AM
Subject: RE: Thanks again for the call today re grain-free diets

Oh, interesting. That is hopeful and sounds like early intervention is a very good thing.

Martine

From: Jones, Jennifer L
Sent: Tuesday, June 12, 2018 3:12 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

I reviewed my notes from the call we had with NCSU, Tufts, Davis, etc. The shortest interval the experts saw between consuming the food and developing DCM was ~9 months. One dog had been fed a Kangaroo & Lentil diet for years. B5

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Hartogensis, Martine
Sent: Tuesday, June 12, 2018 12:03 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Ok, thank you Lee Anne!

Martine

From: Palmer, Lee Anne
Sent: Tuesday, June 12, 2018 11:30 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

B5

From: Hartogensis, Martine
Sent: Tuesday, June 12, 2018 10:55 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: FW: Thanks again for the call today re grain-free diets

Good morning.... B5

Martine

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Tuesday, June 12, 2018 10:49 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Great – many thanks, Martine. On a somewhat related note, is FDA monitoring or seeing any similar issue with vegan pet food diets?

Regards,

Peter
O: +1.202.791.9432
M: B6

From: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Sent: Tuesday, June 12, 2018 7:57 AM
To: Tabor, Peter <peter@petfoodinstitute.org>
Subject: RE: Thanks again for the call today re grain-free diets

Thank you and good morning. Here are the slides from Dr. Jones' presentation yesterday. Please let us know if you have any questions.

Martine

Martine Hartogensis, DVM
FDA Center for Veterinary Medicine
Deputy Director, Office of Surveillance & Compliance
(240) 402-7178

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Monday, June 11, 2018 9:27 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: Re: Thanks again for the call today re grain-free diets

Great - many thanks and have a good night, Martine.

Sent using OWA for iPhone

From: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Sent: Monday, June 11, 2018 9:09:16 PM
To: Tabor, Peter
Subject: RE: Thanks again for the call today re grain-free diets

Hi Peter,

Thank you so much for the call today. We really appreciate your willingness to work with us and collaborate on this very interesting issue. I promise to send the slides asap...just need to resolve one minor issue and they are yours!

I apologize for the delay and will get back to you first thing tomorrow.

Thanks again!

Martine

Martine Hartogensis, DVM
FDA Center for Veterinary Medicine
Deputy Director, Office of Surveillance & Compliance
(240) 402-7178

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Monday, June 11, 2018 2:43 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: Thanks again for the call today re grain-free diets

Thanks, Dr Hartogensis, for pulling your colleagues together this morning to share information on FDA and veterinarian findings re grain-free diets and DCM. There was mention, by Jennifer, I think, of slides that could be shared with PFI. We'd like to include those slides in our message to members, if you agree doing so would be appropriate. If so, please send those slides over ASAP. We'd like to include them in our message to members in the next day or so.

Thanks and we'll be in touch.

Regards,

Peter Tabor
Vice President, Regulatory & International Affairs
Pet Food Institute
O: +1.202.791.9432
M: B6
E: peter@petfoodinstitute.org

PFI is an equal opportunity provider and employer. PFI prohibits discrimination and is committed to providing equal access to all programs, activities and materials. For the full text of the PFI nondiscrimination statement, please visit the PFI website (www.petfoodinstitute.org). Persons with disabilities who require special accommodation or alternative means for communication of information (e.g., Braille, large print, sign language translation) or persons who require special dietary accommodations should contact PFI at (202) 791-9440 or info@petfoodinstitute.org.

From: Carey, Lauren </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=F0226BD682844FA2B71EA3750D4FCB82-LAUREN.CARE>
To: Jones, Jennifer L; Hartogensis, Martine; Rotstein, David; Palmer, Lee Anne; Norris, Anne
Sent: 6/13/2018 12:12:00 PM
Subject: RE: Thanks again for the call today re grain-free diets

The pet food section on page 5 is very interesting. I wonde B5

B5

From: Jones, Jennifer L
Sent: Wednesday, June 13, 2018 8:05 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Also, here's a good article on pulses in China from our Canadian colleagues. http://www.agr.gc.ca/resources/prod/Internet-Internet/MISB-DGSIM/ATS-SEA/PDF/6718-eng.pdf

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Hartogensis, Martine
Sent: Wednesday, June 13, 2018 7:54 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Good point. Anne, do you have a contact?

B5

Martine

From: Rotstein, David
Sent: Wednesday, June 13, 2018 7:47 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

I don't. B5

B5

David Rotstein, DVM, MPVM, Dipl. ACVP

CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

From: Hartogensis, Martine
Sent: Wednesday, June 13, 2018 7:40 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Ok, thank you! **B5**

From: Rotstein, David
Sent: Wednesday, June 13, 2018 7:36 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

From: Hartogensis, Martine
Sent: Wednesday, June 13, 2018 7:34 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Hi Dave,

Not a bad idea. B5

B5

Martine

From: Rotstein, David
Sent: Wednesday, June 13, 2018 7:28 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

From: Jones, Jennifer L
Sent: Wednesday, June 13, 2018 6:59 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

From one of our contacts reporting Grain Free DCM cases.

Jennifer Jones, DVM
Veterinary Medical Officer

Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Hartogensis, Martine
Sent: Tuesday, June 12, 2018 9:53 PM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

From: Carey, Lauren
Sent: Tuesday, June 12, 2018 7:32 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

That's an excellent idea. That seems like the sort of thing PFI would track/report on?

From: Jones, Jennifer L
Sent: Tuesday, June 12, 2018 3:12 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Hartogensis, Martine
Sent: Tuesday, June 12, 2018 12:03 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Ok, thank you Lee Anne!

Martine

From: Palmer, Lee Anne

Sent: Tuesday, June 12, 2018 11:30 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

B5

B5

From: Hartogensis, Martine
Sent: Tuesday, June 12, 2018 10:55 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: FW: Thanks again for the call today re grain-free diets

Good morning.. B5

Martine

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Tuesday, June 12, 2018 10:49 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: RE: Thanks again for the call today re grain-free diets

Great – many thanks, Martine. On a somewhat related note, is FDA monitoring or seeing any similar issue with vegan pet food diets?

Regards,

Peter
O: +1.202.791.9432
M: + B6

From: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Sent: Tuesday, June 12, 2018 7:57 AM
To: Tabor, Peter <peter@petfoodinstitute.org>
Subject: RE: Thanks again for the call today re grain-free diets

Thank you and good morning. Here are the slides from Dr. Jones' presentation yesterday. Please let us know if you have any questions.

Martine

Martine Hartogensis, DVM
FDA Center for Veterinary Medicine
Deputy Director, Office of Surveillance & Compliance
(240) 402-7178

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Monday, June 11, 2018 9:27 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: Re: Thanks again for the call today re grain-free diets

Great - many thanks and have a good night, Martine.

Sent using OWA for iPhone

From: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Sent: Monday, June 11, 2018 9:09:16 PM
To: Tabor, Peter
Subject: RE: Thanks again for the call today re grain-free diets

Hi Peter,

Thank you so much for the call today. We really appreciate your willingness to work with us and collaborate on this very interesting issue. I promise to send the slides asap…just need to resolve one minor issue and they are yours!

I apologize for the delay and will get back to you first thing tomorrow.

Thanks again!

Martine

Martine Hartogensis, DVM
FDA Center for Veterinary Medicine
Deputy Director, Office of Surveillance & Compliance
(240) 402-7178

From: Tabor, Peter [mailto:peter@petfoodinstitute.org]
Sent: Monday, June 11, 2018 2:43 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Subject: Thanks again for the call today re grain-free diets

Thanks, Dr Hartogensis, for pulling your colleagues together this morning to share information on FDA and veterinarian findings re grain-free diets and DCM. There was mention, by Jennifer, I think, of slides that could be shared with PFI. We'd like to include those slides in our message to members, if you agree doing so would be appropriate. If so, please send those slides over ASAP. We'd like to include them in our message to members in the next day or so.

Thanks and we'll be in touch.

Regards,

Peter Tabor
Vice President, Regulatory & International Affairs
Pet Food Institute
O: +1.202.791.9432
M: B6
E: peter@petfoodinstitute.org

From: B6
To: Darcy Adin
CC: Lisa Freeman; jstern@ucdavis.edu; rfries@illinois.edu B6 Jones, Jennifer L
Sent: 4/18/2018 9:34:02 PM
Subject: Re: Diet DCM Call

Hi Darcy, I can do 11 on Friday. I made plans at 3, but if others need to do it later, I can change them.

B6 Sent from my iPhone

> On Apr 18, 2018, at 7:09 AM, Darcy Adin <dbadin@ncsu.edu> wrote:
>
> Hi All,
>
> We had originally proposed B4, B5
B4, B5
>
> I'm going to pick 11am EST arbitrarily - please let me know if you can talk then or if a different time is better. I'm available throughout the day.
>
> Thanks Everyone!
> Darcy

From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To: Jones, Jennifer L
Sent: 4/24/2018 4:55:40 PM
Subject: RE: DCM/grain-free - checking in

Jen,

The EON number is 345858

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
B6 (BB)

From: Jones, Jennifer L
Sent: Tuesday, April 24, 2018 12:31 PM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM/grain-free - checking in

B5

B5

B5

B4, B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Norris, Anne
Sent: Friday, April 20, 2018 12:53 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: DCM/grain-free - checking in

Agree wholeheartedly. Thanks for putting that call together, very interesting!

Anne

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 12:42 PM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: DCM/grain-free - checking in

Anne and Siobhan,
Dave and I were talking after the call. B5

B5

What do you think?
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Norris, Anne
Sent: Monday, April 16, 2018 11:07 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: DCM/grain-free - checking in

Following up on our discussion last week, I reached out to B6 She said we no longer have the arrangement with B4 we once did. B5 dead end. Exploring alternatives, will keep you posted.

Thanks,
Anne

From: Jones, Jennifer L
Sent: Friday, April 13, 2018 6:37 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: DCM/grain-free - checking in

Thanks, Anne. I'll be in the office until 9am, B6 B6 .

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG

From: Norris, Anne
Sent: Thursday, April 12, 2018 6:56 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Re: DCM/grain-free - checking in

Wow. What breeds? I'll send a cal invite for tomorrow AM to try to catch you while you're at Vet-LIRN with Jen.

From: Rotstein, David <David.Rotstein@fda.hhs.gov>
Date: April 12, 2018 at 5:59:56 PM EDT
To: Norris, Anne <Anne.Norris@fda.hhs.gov>, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Re: DCM/grain-free - checking in

Anne

I'll be available. I'll be with VetLIRN in the morning.

This sounds great-thanks for moving it forward. We got two new complaints (same submitter) today.

From: Norris, Anne <Anne.Norris@fda.hhs.gov>

Date: April 12, 2018 at 5:36:50 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: DCM/grain-free - checking in

Hi Jen and Dave,

I know it probably looks like nothing has happened [B5] [B5] Most recently, I just talked with Dan McChesney for a while [B5] If you have any availability tomorrow, [B5]

Thanks,
Anne

Anne Norris
Health Communications Specialist

Strategic Communications & Public Engagement Team
Office of Foods and Veterinary Medicine
U.S. Food & Drug Administration
O: 240-402-0132
M: [B6]
Anne.Norris@fda.hhs.gov

From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To: Palmer, Lee Anne; Jones, Jennifer L
Sent: 4/28/2018 1:00:09 AM
Subject: Fwd: DCM cases - proposed diet history
Attachments: diet history form 4-27-18 external.doc

Lee Anne,

Thought you would be interested and could provide any comments/suggestions

---

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu>, B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6

Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and

concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs B6 Freeman B6 Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6

Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting
Meeting number (access code): B6
Meeting password: B6

Join by phone
B6 US Toll
US Toll Free
Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: Rotstein, David; Palmer, Lee Anne
Sent: 4/30/2018 11:23:59 AM
Subject: RE: DCM cases - proposed diet history
Attachments: diet history form 4-27-18 external-jj.doc

I made a few comments and will send back to the group.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Friday, April 27, 2018 9:00 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Fwd: DCM cases - proposed diet history

Lee Anne,

Thought you would be interested and could provide any comments/suggestions

---

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu> B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN

Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; **B6**
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; **B6**
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 Freeman, B6 Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6
Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting

Meeting number (access code): B6
Meeting password: B6

Join by phone

B6 US Toll

US Toll Free

Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--

Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From:	Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To:	'Freeman, Lisa'; Darcy Adin; Joshua A Stern; Fries, Ryan C; B6
CC:	Rotstein, David; Norris, Anne; DeLancey, Siobhan; Ceric, Olgica
Sent:	4/30/2018 11:25:31 AM
Subject:	RE: DCM cases - proposed diet history
Attachments:	diet history form 4-27-18 external-jj.doc

Thank you for sharing, Lisa.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa [mailto:Lisa.Freeman@tufts.edu]
Sent: Friday, April 27, 2018 7:27 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Darcy Adin <dbadin@ncsu.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; **B6**; B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form **B5**

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6

B6

Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6, Freeman, B6, Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med
B6 e
American College of Veterinary Internal Medicine (Cardiology)
Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting

Meeting number (access code): B6
Meeting password: B6

Join by phone

B6 US Toll
US Toll Free

Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From:	Darcy Adin <dbadin@ncsu.edu>
To:	Freeman, Lisa
CC:	Jones, Jennifer L; Joshua A Stern; Fries, Ryan C; B6 David; Norris, Anne; DeLancey, Siobhan; Ceric, Olgica
Sent:	4/30/2018 2:12:38 PM
Subject:	Re: DCM cases - proposed diet history

That is really great Lisa! We have one as well but this is much better / more detailed. Is this OK to share with our group?
Thanks!
Darcy

On Fri, Apr 27, 2018 at 7:26 PM, Freeman, Lisa <Lisa.Freeman@tufts.edu> wrote:

Hi everyone

I'm attaching a proposed diet history form. B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks

Lisa

Lisa M. Freeman, DVM, PhD, DACVN

Professor

Cummings School of Veterinary Medicine

Friedman School of Nutrition Science and Policy

Tufts Clinical and Translational Science Institute

Tufts University

www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM

Veterinary Medical Officer

Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,

Jen

Jennifer Jones, DVM

Veterinary Medical Officer

Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 >; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 Freeman, B6 Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6

Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med

Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,

Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting
Meeting number (access code): B6
Meeting password: B6

Join by phone
B6 US Toll
US Toll Free
Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--

Darcy B. Adin, DVM, DACVIM (Cardiology)

Clinical Assistant Professor of Cardiology

North Carolina State University

NC State Veterinary Hospital

1060 William Moore Drive

Raleigh, NC 27607

919-513-6032

--

Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Darcy Adin
CC: Jones, Jennifer L; Joshua A Stern; Fries, Ryan C; B6 r; Rotstein, David; Norris, Anne; DeLancey, Siobhan; Ceric, Olgica
Sent: 4/30/2018 10:02:18 PM
Subject: RE: DCM cases - proposed diet history

Hi Darcy
You're more than welcome to use it although John has already asked for a few tweaks and I'd love to hear from this group if there are any other edits that you think would be useful so that it could be widely used.
Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Monday, April 30, 2018 10:13 AM
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: Re: DCM cases - proposed diet history

That is really great Lisa! We have one as well but this is much better / more detailed. Is this OK to share with our group?
Thanks!
Darcy

On Fri, Apr 27, 2018 at 7:26 PM, Freeman, Lisa <Lisa.Freeman@tufts.edu> wrote:
Hi everyone
I'm attaching a proposed diet history form B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor

Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 ; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 Freeman B6, Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting

Meeting number (access code): B6
Meeting password: B6

Join by phone

B6 US Toll
US Toll Free

Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Rotstein, David; Jones, Jennifer L
Sent: 5/1/2018 1:40:27 PM
Subject: RE: DCM cases - proposed diet history

Oops – I see the answer to question 1. In that case, my comment about the people/raw food example may be more pertinent. Would love to join you on the discussion calls if it's feasible. Thanks!

I'm attaching a proposed diet history form B5

B5

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:39 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Thanks – this is a great dietary history. My only comments:

B5

Thanks for the opportunity to comment!

Lee Anne

From: Rotstein, David
Sent: Friday, April 27, 2018 9:00 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Fwd: DCM cases - proposed diet history

Lee Anne,

Thought you would be interested and could provide any comments/suggestions

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu>, B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form. B5
sending out to all clients (dog and cat) to have them fill it out ahead of time and bring it with them to the appointment.

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6
B6
>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 ; B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 ; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 , Freeman, B6 , Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting
Meeting number (access code): B6
Meeting password: B6

Join by phone
B6 US Toll
US Toll Free
Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Rotstein, David; Jones, Jennifer L
Sent: 5/1/2018 1:56:59 PM
Subject: RE: DCM cases - proposed diet history

Sorry, stream of thought thing going on.

Perhaps one more idea that I find helpful:

B5

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:40 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Oops – I see the answer to question 1. In that case, my comment about the people/raw food example may be more pertinent. Would love to join you on the discussion calls if it's feasible. Thanks!

I'm attaching a proposed diet history form. B5

B5

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:39 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Thanks – this is a great dietary history. My only comments:

B5

Thanks for the opportunity to comment!

Lee Anne

From: Rotstein, David
Sent: Friday, April 27, 2018 9:00 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Fwd: DCM cases - proposed diet history

Lee Anne,

Thought you would be interested and could provide any comments/suggestions

---

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu>, B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form. B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 n>;
B6
>

Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; B6 ; Lori Hitchcock <acvimcardiosecretary@gmail.com>; B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and

concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6, Freeman, B6, Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6

Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6

Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting

Meeting number (access code): B6
Meeting password: B6

Join by phone

B6 US Toll

US Toll Free

Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--
Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From:	Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To:	Rotstein, David; Jones, Jennifer L
Sent:	5/1/2018 3:08:12 PM
Subject:	Last one, I promise: DCM cases - proposed diet history
Attachments:	diet history form 4-27-18 external.doc

If they can add a question to each food: are you still feeding it? I tried to add edits to the form as well. (I did a rough job, though L).

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:57 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Sorry, stream of thought thing going on.

Perhaps one more idea that I find helpful:

B5

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:40 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Oops – I see the answer to question 1. In that case, my comment about the people/raw food example may be more pertinent. Would love to join you on the discussion calls if it's feasible. Thanks!

I'm attaching a proposed diet history form **B5**

B5

From: Palmer, Lee Anne
Sent: Tuesday, May 1, 2018 9:39 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: DCM cases - proposed diet history

Thanks – this is a great dietary history. My only comments:

B5

B5

Thanks for the opportunity to comment!

Lee Anne

From: Rotstein, David
Sent: Friday, April 27, 2018 9:00 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Fwd: DCM cases - proposed diet history

Lee Anne,

Thought you would be interested and could provide any comments/suggestions

---

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Date: April 27, 2018 at 7:27:27 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>, Joshua A Stern <jstern@ucdavis.edu>, Fries, Ryan C <rfries@illinois.edu>, B6
B6
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>, DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: DCM cases - proposed diet history

Hi everyone
I'm attaching a proposed diet history form B5

B5

Once I get some input from you, I can make into a fillable form so we can send out electronically.

B5

Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
Professor
Cummings School of Veterinary Medicine
Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University

From: Jones, Jennifer L [mailto:Jennifer.Jones@fda.hhs.gov]
Sent: Friday, April 20, 2018 3:50 PM
To: Darcy Adin <dbadin@ncsu.edu>; Freeman, Lisa <Lisa.Freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 >; B6 >
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases
Importance: High

My apologies for the repeat email. After further internal discussion, in lieu of submitting Consumer Complaints, you can just email me a spreadsheet with the data.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Friday, April 20, 2018 1:19 PM
To: 'Darcy Adin' <dbadin@ncsu.edu>; Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C <rfries@illinois.edu>; B6 >; B6 >
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: hold-call with Dr. Adin re: DCM cases

Thank you again for joining us on the call and providing the information about your cases. To help us catalogue and potentially act on these adverse events, please file an official consumer complaint. Instructions on how to report a pet food report can be found at: https://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm182403.htm. The complaint can be submitted through the Safety Reporting Portal: https://www.safetyreporting.hhs.gov. You can attach documents already created that compile your case data. We will review the data and may contact you for possible follow-up.

In the meantime, if you have a dog with DCM on a grain free diet that dies or is euthanized, please do not dispose of the animal's body or any remaining food. Please submit an individual consumer complaint for that dog, and mention that you have been instructed to submit the report by Vet-LIRN. We will review the complaint for potential follow-up and may be able to offer a necropsy. I attached a copy of our Vet-LIRN network procedures that describe how we operate. I also included a version for animal owners.

Please email or call me with any questions. Thank you again for your time and expertise,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Darcy Adin [mailto:dbadin@ncsu.edu]
Sent: Thursday, April 19, 2018 11:00 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>; Joshua A Stern <jstern@ucdavis.edu>; Fries, Ryan C

<rfries@illinois.edu>; B6 ;
Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Rotstein, David <David.Rotstein@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: Fwd: hold-call with Dr. Adin re: DCM cases

Dear Dr. Jones,

We are all able to meet tomorrow, Friday April 20th at 11 am EST to discuss our clinical observations and concerns surrounding a potential relationship between grain-free canine diets and Dilated Cardiomyopathy.

Drs. B6 Freeman, B6 Fries and Stern - the call details are in the forwarded email below.

Just a brief introduction for the FDA group:

B6
Dr. Lisa Freeman is a Professor of Clinical Nutrition at Tufts University, College of Vet Med

B6
Dr. Ryan Fries is a Clinical Assistant Professor of Cardiology at Illinois, College of Vet Med
Dr. Josh Stern is an Associate Professor of Cardiology at UC Davis, College of Vet Med

Thank you everyone for making time in your schedule! I am looking forward to this.

Sincerely,
Darcy Adin

---------- Forwarded message ----------
From: **Jones, Jennifer L** <Jennifer.Jones@fda.hhs.gov>
Date: Thu, Apr 19, 2018 at 7:16 AM
Subject: hold-call with Dr. Adin re: DCM cases
To: "Rotstein, David" <David.Rotstein@fda.hhs.gov>, "Norris, Anne" <Anne.Norris@fda.hhs.gov>, "DeLancey, Siobhan" <Siobhan.Delancey@fda.hhs.gov>, Darcy Adin <dbadin@ncsu.edu>

-- Do not delete or change any of the following text. --

Join WebEx meeting
Meeting number (access code): B6
Meeting password: B6

Join by phone
B6 US Toll
US Toll Free
Global call-in numbers | Toll-free calling restrictions

Can't join the meeting?

If you are a host, go here to view host information.

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.

--

Darcy B. Adin, DVM, DACVIM (Cardiology)
Clinical Assistant Professor of Cardiology
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

From: Carey, Lauren </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=F0226BD682844FA2B71EA3750D4FCB82-LAUREN.CARE>
To: Jones, Jennifer L; Rotstein, David; Palmer, Lee Anne; Queen, Jackie L
CC: Ceric, Olgica; Reimschuessel, Renate; Nemser, Sarah
Sent: 5/3/2018 4:26:27 PM
Subject: RE: 800.267-EON-345858-DCM Cluster

Hi Jen,

I think B5

Thanks,
Lauren

From: Jones, Jennifer L
Sent: Tuesday, May 01, 2018 9:06 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: 800.267-EON-345858-DCM Cluster

B5 I wonder about eithe B5

B5 Thoughts?

Dave previously sent an email about lentils being deficient in Cystine and Methionine. I found the same information about peas (attached). For Growing labrador dogs, if cystine is limited (~ 0.2%), a Cys:Met cutoff may lie somewhere between 0.32 : 1 and 0.38 : 1. **Above that ratio, the dogs in the study here did poorly** B4.

In chickens (Sarwar article), a Cys/Met ratio of 0.2 : 1 in low protein diets causes lower 2 wk weight gain, food intake, BUN, and taurine-conjugated bile acids in weanling rats B5

B5

In pigs, there is absolute methionine and cystine values but also the met : met+cys ratio is important. For pigs the ratio is between 30-70% but the Qiao says 54.15%. I wonder B5

B5

Also-This is an older study in beagles, B5 (https://academic.oup.com/in/article-abstract/111/12/2117/4771254?redirectedFrom=fulltext. B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To: Carey, Lauren; Jones, Jennifer L; Palmer, Lee Anne; Queen, Jackie L
CC: Ceric, Olgica; Reimschuessel, Renate; Nemser, Sarah
Sent: 5/3/2018 4:33:53 PM
Subject: RE: 800.267-EON-345858-DCM Cluster

Agreed!

From: Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Date: May 3, 2018 at 12:26:29 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: 800.267-EON-345858-DCM Cluster

Hi Jen,

I think testing some non-grain free samples would be an interesting comparison.

Thanks,
Lauren

From: Jones, Jennifer L
Sent: Tuesday, May 01, 2018 9:06 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: 800.267-EON-345858-DCM Cluster

B5 I wonder about either B5

B5 Thoughts?

Dave previously sent an email about lentils being deficient in Cystine and Methionine. I found the same information about peas (attached). For Growing labrador dogs, if cystine is limited (~ 0.2%), a Cys:Met cutoff may lie somewhere between 0.32 : 1 and 0.38 : 1. **Above that ratio, the dogs in the study here did poorly** (https://academic.oup.com/jn/article-abstract/112/11/2033/4554028?redirectedFrom=fulltext).

In chickens (Sarwar article), a Cys/Met ratio of 0.2 : 1 in low protein diets causes lower 2 wk weight gain, food intake, BUN, and taurine-conjugated bile acids in weanling rats. B5

B5

In pigs, there is absolute methionine and cystine values but also the met : met+cys ratio is important. For pigs the ratio is between 30-70% but the Qiao says 54.15%. I wonder B5

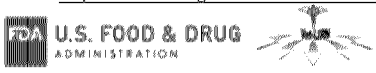
B5

B5

Also-This is an older study in beagles, B5
(https://academic.oup.com/jn/article-abstract/111/12/2117/4771254?redirectedFrom=fulltext. B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm



From: Rotstein, David </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0A3B17EBFCF14A6CB8E94F322906BADD-DROTSTEI>
To: Jones, Jennifer L; Palmer, Lee Anne; Queen, Jackie L; Carey, Lauren
CC: Reimschuessel, Renate; Ceric, Olgica; Nemser, Sarah
Sent: 5/4/2018 4:00:40 PM
Subject: RE: DCM cases-food-Iodine screening results

B5

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Date: May 4, 2018 at 10:03:44 AM EDT
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

There is no minimum for dogs…it is apparently a conditionally essential amino acid because dogs can make it from methione and cystine.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:01 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Interesting…so the AAFCO minimum for cats is 0.1% DMB, **B5**
B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 9:46 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Jones, Jennifer L
Sent: Monday, April 23, 2018 10:32 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: DCM cases-food-Iodine screening results

FYI-Iodine < 10ppm for the foods tested. B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Rotstein, David; Jones, Jennifer L; Queen, Jackie L; Carey, Lauren
CC: Reimschuessel, Renate; Ceric, Olgica; Nemser, Sarah
Sent: 5/4/2018 4:07:01 PM
Subject: RE: DCM cases-food-Iodine screening results

B5 If you look at the cases we've received B5

B5

From: Rotstein, David
Sent: Friday, May 4, 2018 11:59 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Lee Anne

This is excellent. Based on what is found moving forward, B5

B5

From: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>
Date: May 4, 2018 at 11:15:20 AM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:35 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>

Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Yes. B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:21 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

I know dogs can synthesize taurine B5 .. B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:04 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

There is no minimum for dogs…it is apparently a conditionally essential amino acid because dogs can make it from methione and cystine.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:01 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Interesting…so the AAFCO minimum for cats is 0.1% DMB, B5
B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 9:46 AM

To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

One more nutritional deficiency-Taurine low based on AAFCO's Feline Minimum for Extruded foods. The dog consuming the product had a low whole blood Taurine level.

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Jones, Jennifer L
Sent: Monday, April 23, 2018 10:32 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: DCM cases-food-Iodine screening results

FYI-Iodine < 10ppm for the foods tested. B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: Palmer, Lee Anne; Rotstein, David; Queen, Jackie L; Carey, Lauren
CC: Reimschuessel, Renate; Ceric, Olgica; Nemser, Sarah
Sent: 5/4/2018 4:12:45 PM
Subject: RE: DCM cases-food-Iodine screening results

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 12:07 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5 If you look at the cases we've received B5

B5

B5

From: Rotstein, David
Sent: Friday, May 4, 2018 11:59 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Lee Anne

This is excellent. Based on what is found moving forward, B5

B5

From: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>
Date: May 4, 2018 at 11:15:20 AM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>

Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:35 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Yes. I'm going to B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:21 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

I know dogs can synthesize taurine, B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:04 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

There is no minimum for dogs…it is apparently a conditionally essential amino acid because dogs can make it from methione and cystine.

Jennifer Jones, DVM

Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:01 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Interesting...so the AAFCO minimum for cats is 0.1% DMB, B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 9:46 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Monday, April 23, 2018 10:32 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: DCM cases-food-Iodine screening results

FYI-Iodine < 10ppm for the foods tested. B5

B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Jones, Jennifer L; Rotstein, David; Queen, Jackie L; Carey, Lauren
CC: Reimschuessel, Renate; Ceric, Olgica; Nemser, Sarah
Sent: 5/4/2018 4:33:54 PM
Subject: RE: DCM cases-food-Iodine screening results
Attachments: Ingredients DCM reports per Jen's table v.2.docx

Just an initial quickie count of Jen's data in JMP B6

B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 12:13 PM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 12:07 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

From: Rotstein, David
Sent: Friday, May 4, 2018 11:59 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Lee Anne

This is excellent. Based on what is found moving forward, **B5**

B5

From: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>
Date: May 4, 2018 at 11:15:20 AM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:35 AM

To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Yes. B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:21 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

I know dogs can synthesize taurine B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 10:04 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

There is no minimum for dogs…it is apparently a conditionally essential amino acid because dogs can make it from methione and cystine.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Palmer, Lee Anne
Sent: Friday, May 04, 2018 10:01 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

Interesting…so the AAFCO minimum for cats is 0.1% DMB, B5

B5

From: Jones, Jennifer L
Sent: Friday, May 4, 2018 9:46 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: RE: DCM cases-food-Iodine screening results

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG

From: Jones, Jennifer L
Sent: Monday, April 23, 2018 10:32 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>
Subject: DCM cases-food-Iodine screening results

FYI-Iodine < 10ppm for the foods tested B5

B5

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To: Jones, Jennifer L; Rotstein, David; Carey, Lauren; Pohl, Aurelie
Sent: 8/15/2019 4:31:06 PM
Subject: Brief update on cardiomyocyte idea (and metabolomics)
Attachments: Harikrishnan 2019 microbiome and heart failure.pdf; Nsbshomo and tang 2015.pdf; Yoshida et al. 2018 gut flora.pdf

Hi all – just a brief update for you and then more info and meetings ahead where we all can be involved!
Marilyn Martinez from ONADE approached me about 2 weeks ago B5

B5

Interesting things to consider:

B5

B5

Thanks!

Lee Anne
Lee Anne M. Palmer, VMD, MPH
Acting Director, Division of Veterinary Product Safety

Center for Veterinary Medicine
Office of Surveillance and Compliance
U.S. Food and Drug Administration
Tel: 240-402-5767
Leeanne.palmer@fda.hhs.gov

Diet, the Gut Microbiome and Heart Failure

Sivadasanpillai Harikrishnan

Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India

Abstract

The collection of microorganisms that live in coexistence within or on the host body has been referred to as the microbiota. In humans, such cohabitation is mostly seen in the gut, mainly in the colon. The gut microbiome is acquired from the environment and is modified mostly by the diet. There are preliminary data to show that gut microbia can directly influence the pathogenetic disease processes in heart failure (HF). HF leads to bowel wall oedema and regional hypoxia, causing a change in the microbial flora of the gut, which can initiate or perpetuate certain pathogenetic process in HF. The structural component of the microbiota itself, such as lipopolysaccharides or the substances produced by the bacteria, such as trimethylamine N-oxide, is implicated in the pathogenesis of HF. This process is termed as the 'heart–gut axis' in HF. Manipulating the gut microbia or targeting products from the microbia may become treatment options for HF in future.

Keywords

Heart failure, gut microbia, microbiota, trimethylamine N-oxide, lipopolysaccharide.

Disclosure: The author has no conflicts of interest to disclose.
Received: 7 November 2018 **Accepted**: 15 January 2019 **Citation**: *Cardiac Failure Review* 2019;5(2):119–22. **DOI**: https://doi.org/10.15420/cfr.2018.39.2
Correspondence: Sivadasanpillai Harikrishnan, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, 695011, India.
E: drharikrishnan@outlook.com

"All diseases begin in the gut."
– Hippocrates (460–370 BC)

In recent years many researchers have described the relationship between the gut microbiota and many diseases, including heart disease, hypertension, diabetes and obesity.[1,2] Diet is one of the major factors that influence the pattern of the gut microbiota.[3] This article discusses how the gut microbiota affects heart failure.

What is the Human Gut Microbiome?

The collection of micro-organisms that co-exists within or on the host body has been referred to as the microbiota.[1] There are more than 2,000 species of commensal organisms (mostly bacteria) that co-exist with the human body, the vast majority in the gut. A healthy human adult has approximately 100 trillion bacteria in the gut, mostly in the colon.[1,4]

The gut microbiome is acquired from the environment, it is not genetically acquired, and the gut is usually sterile in the womb. For example, the fetus acquires different microbiota during caesarean section and during vaginal delivery.[5] Subsequently, the fetus acquires different types of microbiome depending on diet and the environment to which it is exposed.[6,7]

The human gut microbiome is dominated by five phyla: *Bacteroidetes*, *Firmicutes*, *Actinobacteria*, *Proteobacteria* and *Cerrucomicrobia*.[1,8] Usually the gut microbiota is stable within the individual and family. In the healthy gut, the anaerobic groups *Bacteroidetes* and *Firmicutes* contribute to more than 90% of the total bacterial species.[8]

What Decides the Pattern of an Individual's Gut Microbiome?

The specific patterns of gut microbiota are called enterotypes.[9] An unwelcome change in the gut microbiome is called dysbiosis.[10] One of the most important factors that influences the enterotype is the individual's long-term diet. For example, diets high in animal protein and fat will show high levels of *Bacteroides* and low levels of *Prevotella* (also part of the *Bacteroidetes* genus).[11] On the contrary, diets high in carbohydrates and low in animal protein and fat will have low levels of *Bacteroides* and high levels of *Prevotella*. Another example of the diet–gut microbial interaction is found in Japanese people. Their guts contain *Bacteroides plebeius*, which produces an enzyme that aids in seaweed digestion.[12]

Other factors that influence the gut microbial pattern other than the diet are environmental changes, hygiene, antibiotic use and disease states.[1,6]

How the Gut Microbiota Affects the Host

The gut microbiome has many functions.[13] One of its functions is a protective function via pathogen displacement, nutrient and receptor competition and production of antimicrobial factors.[1] The gut microbiota also secretes some vitamins.

One of the most important functions of the gut microbiome is metabolic, as it aids in the digestion of food components. For example, gut bacteria are involved in the breakdown of sugars (e.g. glycans, which are complex sugars that cannot be cleaved by any human

enzymes) by glycoside hydrolase. Gut microbiota participates in the human digestive process through two main catabolic pathways – saccharolytic or proteolytic.[14] Both pathways lead to the production of short-chain fatty acids (SCFAs). The second catabolic pathway also produces toxic molecules such as ammonia, various amines, thiols, phenols and indoles, which are cleared by the kidneys but will accumulate if there is renal dysfunction.[1,14,15]

It is reasonable to view the microbiome as an 'organ' that weighs approximately 1–2 kg, although it is without a distinct structure. The microbiome constantly makes compounds, some of which are absorbed and are biologically active. Thus, it can be considered as an endocrine organ producing biologically active entities that diffuse into the bloodstream and act at distant sites.[1]

The gut microbiota are separated from the lamina propria by a single layer of intestinal epithelium. The intestinal epithelium deploys a variety of mechanisms to restrict commensal bacteria to the intestinal lumen and to prevent egression of these microbiota to the underlying tissue.[16] The gut microbiota in turn have evolved to evade the host's immune system and circumvent the antimicrobial host response.[16]

The intestinal barrier mechanism has a dual role to play – it protects against the invasion of microorganisms and absorption of bacterial toxins, but also enables the absorption of essential products, electrolytes and nutrients.[17]

The gut microbiota produces many substances that are able to enter the bloodstream and subsequently influence pathobiological processes. The permeability of these substances is dependent on the functional and structural integrity of the mucosal barrier. Potential barrier disruptors include hypoperfusion of the gut, infections, toxins, drugs and other lifestyle factors.[17] Sometimes it may be a structural component of the microbiota itself, such as lipopolysaccharides (LPS) or peptidoglycans, that interact with host mucosal surface cells through pattern recognition receptors.[1,18]

In addition, molecules produced by microbial organisms can also gain entry to cause various effects. Some identified pathways include the trimethylamine N-oxide (TMAO) pathway, the SCFA pathway and the bile acid pathway.[1] The precursor of TMAO is l-carnitine or choline, which is present in food substances such as red meat. If a person has a high intake of red meat, TMAO production is increased, which is implicated in the pathogenesis of heart disease.[2]

How Do We Study the Gut Microbiome?

It is not easy to study the gut microbiome because it contains millions of bacteria and thousands of species. There are also fungi and viruses present, which can pose difficulties because their genetic material interferes with the identification of the bacterial genome in question. A further issue with studying the gut microbial genome is that the microbial community is distinct in different regions of the intestine, and also because the genome changes frequently due to horizontal gene transfer.[19]

The traditional method is culture, but it is tedious and time consuming. Bacterial genomic sequencing is the next most suitable method. One popular method is 16S ribosomal RNA (rRNA) gene amplicon analysis. Metagenomic sequencing, another method that is gaining popularity, is usually more expensive but offers increased resolution, enabling a more specific taxonomic and functional classification.[20] Wang et al. explained this as: "16S rDNA sequence attempts to reveal 'who's there?' in a given microbial community, while shotgun metagenomic sequencing can be used to answer the complementary question of 'what can they do?'."[21]

Association of the Gut Microbiota with Heart Disease

There are many recent publications on the association between the gut microbiota and heart disease, especially heart failure.[22–26] Changes in the gut microbiota can lead to the development of risk factors for atherosclerotic vascular disease and directly influence pathogenetic disease processes such as acute coronary syndromes and heart failure.[27]

Obesity is one example. Its pathology is associated with changes in the relative abundance of two dominant bacterial divisions, *Bacteroidetes* and *Firmicutes*.[28] Obese patients have been shown to display high *Firmicutes* counts. It has also been found that the obese microbiome has an increased capacity to harvest energy from the diet, and that the obese "trait" is transmissible: colonisation of germ-free mice with an obese microbiota results in a significantly greater increase in total body fat than colonisation with a lean microbiota, with the same diet.[29]

In addition, hypertension and diabetes have also been found to have associations with specific gut microbial patterns, and researchers have discovered certain links in the pathogenesis of these diseases and bacterial interactions.[22,30,31]

In a study comparing patients who had coronary heart disease (CHD) with those who did not, it was found that in patients who had CHD, the proportion of the phylum *Bacteroidetes* was lower, with a higher proportion of *Firmicutes*.[32] Increased TMAO levels were found to be associated with an increased risk of incident major adverse cardiovascular events (MACEs) in a cohort of 4,007 patients who underwent coronary angiography followed up for 3 years.[33] In another study, a Cleveland clinic cohort of 530 patients presenting to the emergency department with chest pain showed elevated plasma TMAO levels at presentation that were independently associated with risk of MACEs.[34] The *Bacteroidetes:Firmicutes* ratio is known to be altered in all chronic diseases and therefore may not be a reliable identifier of a particular disease.

Raised TMAO levels are implicated in endothelial and smooth muscle cell activation, foam cell formation, and myocardial and renal fibrosis.[2] In a recent systematic review and meta-analysis (16 publications, 19,256 patients), elevated concentrations of TMAO and its precursors were associated with increased risks of MACEs and all-cause mortality, independent of traditional risk factors.[35] Another meta-analysis and systematic review of 26,167 patients also showed a positive dose-dependent association between TMAO plasma levels and increased cardiovascular risk and mortality.[36]

Association of the Microbiota with Heart Failure

The gut microbiota is also implicated in the pathogenesis of heart failure (HF). In HF, due to reduced ejection fraction, there is a reduction in intestinal blood flow and low oxygen delivery. This predisposes the gut to the growth of pathogenic types of anaerobic bacteria.[37]

Patients with chronic HF also develop bowel wall oedema due to venous congestion that impedes the absorptive function of the gut and permits bacterial overgrowth in the mucus layer adjacent to the apical surface of the colonic mucosa.[36] Increased intestinal permeability, assessed by the sugar cellobiose test, has also been reported in patients with HF, and this increased permeability correlates with right atrial pressure and C-reactive protein levels.[38,39]

These bacteria produce many harmful substances including TMAO and endotoxin (LPS), which predisposes or leads to worsening of HF. These discoveries have led to the hypothesis of the heart–gut axis of HF (*Figure 1*).[40,41] Higher LPS concentrations have been found in patients with decompensated HF, which correlates with the increased level of bowel wall oedema, as discussed earlier. LPS decreases after 're-compensation'. According to Sandek et al., this suggests a cause and effect relationship between the oedematous gut wall, epithelial dysfunction and translocating LPS.[42]

High TMAO levels are found in patients with HF, which predict higher long-term mortality, even after adjusting for traditional risk factors and cardiorenal indexes.[41] TMAO has been found to be a prognostic factor in HF patients, and higher levels predict a poor prognosis at 1-year follow-up. A combination of TMAO and the traditional marker N-terminal pro-brain natriuretic peptide are able to provide additional prognostic information.[43]

Why do TMAO levels increase to such an extent in HF? The changes in bacterial composition, as discussed earlier, appear to be the primary driver of TMAO levels.[25] Renal impairment and changing dietary patterns may also contribute.[25] How TMAO affects the pathobiology of HF is not clear. Proposed theories include stimulation of cytokines such as tumour necrosis factor-alpha, which can aggravate myocardial fibrosis, microvascular dysfunction in the heart independent of its proatherosclerotic effects, neurohormonal derangements, and so on, but we do not yet have a clear answer.[25]

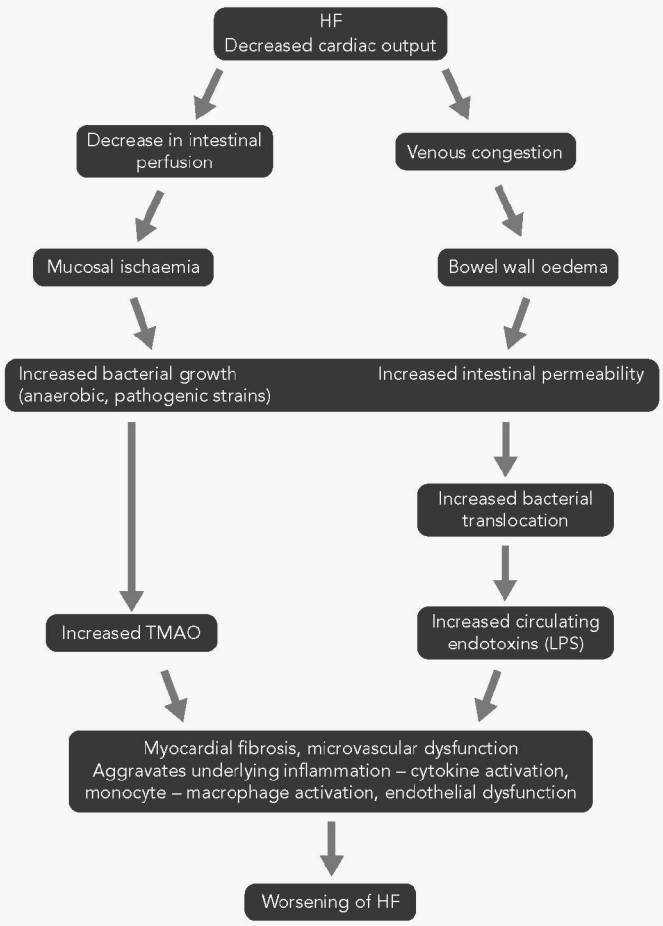
Can We Manipulate the Gut Microbiome to Treat Disease?

There are some studies on manipulation of the gut microbiome that give us hope in treating related diseases. Manipulation can be achieved in many ways. We can alter the diet to change the type of microbiota, we can target the chemicals produced by the gut microbiota, or we can directly alter the microbial flora by the addition of probiotics.

If we reduce red meat in the diet, we reduce the intake of choline and lecithin, and thereby reduce TMAO, which has a positive impact on the risk of heart disease. For example, changing to a Mediterranean diet has been shown to reduce markers of HF. Another method is to administer nonabsorbable antibiotics that kill specific microbiota and thus alter the overall microbial pattern.

Probiotics is another method that can alter the gut's microbial pattern. Probiotics are live beneficial bacteria (*Bifidobacteria*, *Lactobacilli*, *Streptococci* and non-pathogenic strains of *Escherichia coli*) that can be ingested to create an appropriate intestinal microbial balance. There are studies using *Saccharomyces boulardii* in HF that have shown benefit. However, the positive effects of probiotics only apply to a restricted group of microbial species and potential hazards exist, including the possibility of turning these microbiota into opportunistic pathogens in immunocompromised individuals.[44]

Figure 1: Hypothesis of the Heart–Gut Axis in Heart Failure



HF = heart failure; LPS = lipopolysaccharides; TMAO = trimethylamine N-oxide.

The ongoing Gut-Heart trial has randomised 150 patients with stable HF and a left ventricular ejection fraction <40% to receive the antibiotic rifaximin, the probiotic yeast *S boulardii* (ATCC 74012) or no treatment in a 1:1:1 fashion.[45] The primary endpoint is ejection fraction at 3 months. The outcome of the trial will shed some light into the possible therapeutic avenues in the future targeting gut microbiome.

The last – and very interesting – method that is gaining popularity in the treatment of many gastrointestinal diseases is faecal transplantation. Faecal transplantation from lean volunteers was found to show a benefit in weight reduction as well as a reduction in risk factor levels for HF.[46]

We are not yet sure of the best method to alter the gut microbiota; however, the most safe and promising option may be to rely on alteration of the diet.

Conclusion

Millions of years of co-evolution have created diverse ecosystems of gut microbiota that contribute to the maintenance of human metabolic homeostasis. We are slowly discovering the various ways that these co-habitants work in health and disease. We are therefore not alone – we are linked with our gut microbiota, which controls our systems remotely. Understanding and manipulating the microbiota may hold future answers for health and disease. ■

1. Tang WH, Kitai T, Hazen SL. Gut microbiota in cardiovascular health and disease. *Circ Res* 2017;120:1183–96. https://doi.org/10.1161/CIRCRESAHA.117.309715; PMID: 28360349.
2. Brown JM, Hazen SL. Microbial modulation of cardiovascular disease. *Nat Rev Microbiol* 2016;16:171–81. https://doi.org/10.1038/nrmicro.2017.149; PMID: 29307889.
3. Tang WW, Hazen SL. Dietary metabolism, gut microbiota and acute heart failure. *Heart* 2016;102:813–4. https://doi.org/10.1136/heartjnl-2016-309268; PMID: 26980719.
4. Tang WH, Hazen SL. The contributory role of gut microbiota in cardiovascular disease. *J Clin Invest* 2014;124:4204–11. https://doi.org/10.1172/JCI72331; PMID: 25271725.
5. Jakobsson HE, Abrahamsson TR, Jenmalm MC, et al. Decreased gut microbiota diversity, delayed Bacteroidetes colonisation and reduced Th1 responses in infants delivered by Caesarean section. *Gut* 2014;63:559–66. https://doi.org/10.1136/gutjnl-2012-303249; PMID: 23926244.
6. Tamburini S, Shen N, Wu HC, Clemente JC. The microbiome in early life: implications for health outcomes. *Nat Med* 2016;22:713–22. https://doi.org/10.1038/nm.4142; PMID: 27387886.
7. Thursby E, Juge N. Introduction to the human gut microbiota. *Biochem J* 2017;474:1823–36. https://doi.org/10.1042/BCJ20160510; PMID: 28512250.
8. Qin J, Li R, Raes J, et al. A human gut microbial gene catalog established by metagenomic sequencing. *Nature* 2010;464:59–65. https://doi.org/10.1038/nature08821; PMID: 20203603.
9. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome. *Nature* 2011;473:174–80. https://doi.org/10.1038/nature09944; PMID: 21508958.
10. Gorvitovskaia A, Holmes SP, Huse SM. Interpreting Prevotella and Bacteroides as biomarkers of diet and lifestyle. *Microbiome* 2016;4:15. https://doi.org/10.1186/s40168-016-0160-7; PMID: 27068581.
11. Johnson EL, Heaver SL, Walters WA, Ley RE. Microbiome and metabolic disease: revisiting the bacterial phylum Bacteroidetes. *J Mol Med Berl Ger* 2017;95:1–8. https://doi.org/10.1007/s00109-016-1492-2; PMID: 27900395.
12. Hehemann JH, Correc G, Barbeyron T, et al. Transfer of carbohydrate-active enzymes from marine bacteria to Japanese gut microbiota. *Nature* 2010;464:908–12. https://doi.org/10.1038/nature08937; PMID: 20376150.
13. Bäckhed F, Ley RE, Sonnenburg JL, et al. Host–bacterial mutualism in the human intestine. *Science* 2005;307:1915–1920. https://doi.org/10.1126/science.1104816; PMID: 15790844.
14. Sekirov I, Russell SL, Antunes LC, Finlay BB. Gut microbiota in health and disease. *Physiol Rev* 2010;90:859–904. https://doi.org/10.1152/physrev.00045.2009; PMID: 20664075.
15. Nallu A, Sharma S, Ramezani A, Muralidharan J, Raj D. Gut microbiome in chronic kidney disease: challenges and opportunities. *Transl Res J Lab Clin Med* 2017;179:24–37. https://doi.org/10.1016/j.trsl.2016.04.007; PMID: 27187743.
16. Zhang K, Hornef MW, Dupont A. The intestinal epithelium as guardian of gut barrier integrity. *Cell Microbiol* 2015;17:1561–9. https://doi.org/10.1111/cmi.12501; PMID: 26294173.
17. Bischoff SC, Barbara G, Buurman W, et al. Intestinal permeability – a new target for disease prevention and therapy. *BMC Gastroenterol* 2014;14:189. https://doi.org/10.1186/s12876-014-0189-7; PMID: 25407511.
18. Brown JM, Hazen SL. The gut microbial endocrine organ: bacterially derived signals driving cardiometabolic diseases. *Annu Rev Med* 2015;66:343–59. https://doi.org/10.1146/annurev-med-060513-093205; PMID: 25587655.
19. Lerner A, Matthias T, Aminov R. Potential effects of horizontal gene exchange in the human gut. *Front Immunol* 2017;8:1630. https://doi.org/10.3389/fimmu.2017.01630; PMID: 29230215.
20. Jovel J, Patterson J, Wang W, et al. Characterization of the gut microbiome using 16S or shotgun metagenomics. *Front Microbiol* 2016;7:459. https://doi.org/10.3389/fmicb.2016.00459; PMID: 27148170.
21. Wang W-L, Xu SY, Ren ZG, et al. Application of metagenomics in the human gut microbiome. *World J Gastroenterol* 2015;21:803–14. https://doi.org/10.3748/wjg.v21.i3.803; PMID: 25624713.
22. Yang Q, Lin SL, Kwok MK, et al. The roles of 27 Genera of human gut microbiota in ischemic heart disease, type 2 diabetes mellitus, and their risk factors: a mendelian randomization study. *Am J Epidemiol* 2018;187:1916–22. https://doi.org/10.1093/aje/kwy096; PMID: 29800124.
23. Jie Z, Xia H, Zhong SL, et al. The gut microbiome in atherosclerotic cardiovascular disease. *Nat Commun* 2017;8:845. https://doi.org/10.1038/s41467-017-00900-1; PMID: 29018189.
24. Luedde M, Winkler T, Heinsen FA, et al. Heart failure is associated with depletion of core intestinal microbiota. *ESC Heart Fail* 2017;4:282–90. https://doi.org/10.1002/ehf2.12155; PMID: 28772054.
25. Nagatomo Y, Tang WH. Intersections between microbiome and heart failure: revisiting the gut hypothesis. *J Card Fail* 2015;21:973–80. https://doi.org/10.1016/j.cardfail.2015.09.017; PMID: 26435097.
26. Kitai T, Kirsop J, Tang WH. Exploring the microbiome in heart failure. *Curr Heart Fail Rep* 2016;13:103–9. https://doi.org/10.1007/s11897-016-0285-9; PMID: 26886380.
27. Yu D, Shu XO, Rivera ES, et al. Urinary levels of trimethylamine-N-oxide and incident coronary heart disease: a prospective investigation among urban Chinese adults. *J Am Heart Assoc* 2019;8:e010606. https://doi.org/10.1161/JAHA.118.010606; PMID: 30606084.
28. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature* 2006;444:1022–3. https://doi.org/10.1038/4441022a; PMID: 17183309.
29. Turnbaugh PJ, Ley RE, Mahowald MA, et al. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006;444:1027–31. https://doi.org/10.1038/nature05414; PMID: 17183312.
30. Pevsner-Fischer M, Blacher E, Tatirovsky E, et al. The gut microbiome and hypertension. *Curr Opin Nephrol Hypertens* 2017;26:1–8. https://doi.org/10.1097/MNH.0000000000000293; PMID: 27798455.
31. Upadhyaya S, Banerjee G. Type 2 diabetes and gut microbiome: at the intersection of known and unknown. *Gut Microbes* 2015;6:85–92. https://doi.org/10.1080/19490976.2015.1024918; PMID: 25901889.
32. Cui L, Zhao T, Hu H, et al. Association study of gut flora in coronary heart disease through high-throughput sequencing. *BioMed Res Int* 2017;2017:3796359. https://doi.org/10.1155/2017/3796359; PMID: 28497047.
33. Tang WH, Wang Z, Levison BS, et al. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. *N Engl J Med* 2013;368:1575–84. https://doi.org/10.1056/NEJMoa1109400; PMID: 23614584.
34. Li XS, Obeid S, Klingenberg R, et al. Gut microbiota-dependent trimethylamine N-oxide in acute coronary syndromes: a prognostic marker for incident cardiovascular events beyond traditional risk factors. *Eur Heart J* 2017;38:814–24. https://doi.org/10.1093/eurheartj/ehw582; PMID: 28077467.
35. Heianza Y, Ma W, Manson JE, et al. Gut microbiota metabolites and risk of major adverse cardiovascular disease events and death: a systematic review and meta-analysis of prospective studies. *J Am Heart Assoc* 2017;6:pii:e004947. https://doi.org/10.1161/JAHA.116.004947; PMID: 28663251.
36. Schiattarella GG, Sannino A, Toscano E, et al. Gut microbe-generated metabolite trimethylamine-N-oxide as cardiovascular risk biomarker: a systematic review and dose-response meta-analysis. *Eur Heart J* 2017;38:2948–56. https://doi.org/10.1093/eurheartj/ehx342; PMID: 29020409.
37. Sandek A, Swidsinski A, Schroedl W, et al. Intestinal blood flow in patients with chronic heart failure: a link with bacterial growth, gastrointestinal symptoms, and cachexia. *J Am Coll Cardiol* 2014;64:1092–102. https://doi.org/10.1016/j.jacc.2014.06.1179; PMID: 25212642.
38. Sandek A, Bauditz J, Swidsinski A, et al. Altered intestinal function in patients with chronic heart failure. *J Am Coll Cardiol* 2007;50:1561–9. https://doi.org/10.1016/j.jacc.2007.07.016; PMID: 17936155.
39. Pasini E, Aquilani R, Testa C, et al. Pathogenic gut flora in patients with chronic heart failure. *JACC Heart Fail* 2016;4:220–7. https://doi.org/10.1016/j.jchf.2015.10.009; PMID: 26682791.
40. Kamo T, Akazawa H, Suzuki JI, Komuro I. Novel concept of a heart-gut axis in the pathophysiology of heart failure. *Korean Circ J* 2017;47:663–9. https://doi.org/10.4070/kcj.2017.0028; PMID: 28955383.
41. Tang WH, Wang Z, Fan Y, et al. Prognostic value of elevated levels of intestinal microbe-generated metabolite trimethylamine-N-oxide in patients with heart failure: refining the gut hypothesis. *J Am Coll Cardiol* 2014;64:1908–14. https://doi.org/10.1016/j.jacc.2014.02.617; PMID: 25444145.
42. Sandek A, Bjarnason I, Volk HD, et al. Studies on bacterial endotoxin and intestinal absorption function in patients with chronic heart failure. *Int J Cardiol* 2012;157:80–5. https://doi.org/10.1016/j.ijcard.2010.12.016; PMID: 21190739.
43. Suzuki T, Heaney LM, Bhandari SS, et al. Trimethylamine N-oxide and prognosis in acute heart failure. *Heart* 2016;102:841–8. https://doi.org/10.1136/heartjnl-2015-308826; PMID: 26869641.
44. Kothari D, Patel S, Kim SK. Probiotic supplements might not be universally-effective and safe: a review. *Biomed Pharmacother Biomedecine Pharmacother* 2018;111:537–7. https://doi.org/10.1016/j.biopha.2018.12.104; PMID: 30597307.
45. Mayerhofer CCK, Halvorsen S, Seljeflot I, et al. Design of the GutHeart-targeting gut microbiota to treat heart failure-trial: a Phase II, randomized clinical trial. *ESC Heart Fail* 2018;5:977–84. https://doi.org/10.1002/ehf2.12332; PMID: 30088316.
46. Marotz CA, Zarrinpar A. Treating obesity and metabolic syndrome with fecal microbiota transplantation. *Yale J Biol Med* 2016;89(3):383–8. PMID: 27698622.

Review Articles

Intersections Between Microbiome and Heart Failure: Revisiting the Gut Hypothesis

YUJI NAGATOMO, MD, PhD,[1] AND W. H. WILSON TANG, MD[1,2]

Cleveland, Ohio

ABSTRACT

Microbes play an important role in human health and disease. In the setting of heart failure (HF), substantial hemodynamic changes, such as hypoperfusion and congestion in the intestines, can alter gut morphology, permeability, function, and possibly the growth and composition of gut microbiota. These changes can disrupt the barrier function of the intestines and exacerbate systemic inflammation via microbial or endotoxin translocation into systemic circulation. Furthermore, cardiorenal alterations via metabolites derived from gut microbiota can potentially mediate or modulate HF pathophysiology. Recently, trimethylamine *N*-oxide (TMAO) has emerged as a key mediator that provides a mechanistic link between gut microbiota and multiple cardiovascular diseases, including HF. Potential intervention strategies which may target this microbiota-driven pathology include dietary modification, prebiotics/probiotics, and selective binders of microbial enzymes or molecules, but further investigations into their safety and efficacy are warranted. (*J Cardiac Fail 2015;21:973–980*)

Key Words: Microbiome, TMAO, heart failure.

B4

B4

B4

B4

B4

B4

B4

B4

diseases

MDPI

Review

Gut Microbiome and Cardiovascular Diseases

Naofumi Yoshida, Tomoya Yamashita * and Ken-ichi Hirata

Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe 6500017, Japan; kouchiboy@hotmail.com (N.Y.); hiratak@med.kobe-u.ac.jp (K.H.)

* Correspondence: tomoya@med.kobe-u.ac.jp; Tel.: +81-78-382-5111; Fax: +81-78-382-5859

Academic Editor: Luis Vitetta

Received: 8 June 2018; Accepted: 29 June 2018; Published: 29 June 2018

Abstract: Recent evidence has suggested that the gut microbiome is involved in human health and diseases, such as inflammatory bowel disease, liver cirrhosis, rheumatoid arthritis, and type 2 diabetes. Cardiovascular diseases, which are associated with high morbidity and mortality across the world, are no exception. Increasing evidence has suggested a strong relationship between the gut microbiome and the progression of cardiovascular diseases. We first reported such a relationship with coronary artery disease two years ago. Next-generation sequencing techniques, together with bioinformatics technology, constantly and dramatically expand our knowledge of the complex human gut bacterial ecosystem and reveal the exact role of this bacterial ecosystem in cardiovascular diseases via the functional analysis of the gut microbiome. Such knowledge may pave the way for the development of further diagnostics and therapeutics for prevention and management of cardiovascular diseases. The aim of the current review is to highlight the relationship between the gut microbiome and their metabolites, and the development of cardiovascular diseases by fostering an understanding of recent studies.

Keywords: gut microbiome; cardiovascular diseases; *Bacteroides*

1. Introduction

The human gastrointestinal tract harbors several hundred trillion bacteria that are collectively referred to as the gut microbiome, which is called the "forgotten organ" because of its important roles beyond digestion and metabolism [1,2]. Growing evidence suggests that the gut microbiome is associated with the pathogenesis of both intestinal and extra-intestinal disorders, such as obesity and other related metabolic diseases, inflammatory bowel disease, and non-alcoholic steatohepatitis, among others [3–5]. Next-generation sequencing techniques and multi-omics approaches have constantly and dramatically expanded our knowledge of the microbial world. A new era is dawning with the recognition of the gut microbiome as a "multifunctional organ". Unsurprisingly, cardiovascular diseases (CVDs) are no exception to this association [6].

CVDs are the leading causes of mortality and morbidity in many developed and developing countries, despite the widespread use of medical therapy in the last decade [7–9]. CVDs are responsible for 17.7 million deaths every year (31% of all global deaths), including one of every three deaths in the United States and one of every four deaths in Europe and Japan [8]. By 2030, 40.5% of the US population is projected to have some form of CVD. Between 2010 and 2030, the real, total direct medical costs of CVD are predicted to triple from $273 billion to $818 billion, and the real, indirect costs (owing to lost productivity) for all CVDs are estimated to increase by 61% ($172 billion to $276 billion) [10]. These data strongly support the idea that effective and inexpensive prevention and therapeutic strategies are needed for patients with CVDs. The gut microbiome contributes to human metabolism and the immune system, and is being currently investigated as a diagnostic and therapeutic target for CVDs. Thus, the aim of this review is to discuss the evidence for the relationship

between the gut microbiome and CVDs to promote an understanding of the latest perspectives of the role of the gut microbiome in CVDs. Moreover, we have raised several issues that should be considered when interpreting previous evidence.

2. Trimethylamine-*N*-oxide and CVDs

A close relationship between the gut microbe-dependent production of trimethylamine-*N*-oxide (TMAO), derived from specific dietary nutrients such as choline and carnitine, and future cardiovascular events has been widely recognized [10]. Trimethylamine (TMA), which is produced by the gut microbial enzymes TMA lyases, is a precursor of TMAO. TMAO can be measured by liquid chromatography-mass spectrometry. Elevated blood TMAO levels have been directly linked to poor outcomes in patients with CVDs, such as coronary artery disease and acute and chronic heart failure (Table 1) [11–16]. Tang et al., investigated the relationship between the fasting plasma levels of TMAO and the incidence of major adverse cardiovascular events (death, myocardial infarction, or stroke) during three years of follow-up in 4007 patients undergoing elective cardiac catheterization [13]. They found that the patients in the highest quartile for circulating TMAO levels had a 2.5-fold increased risk of major adverse cardiovascular events, compared with the patients with values in the lowest quartile. Of note, even after adjustment for traditional risk factors, an elevated TMAO level could predict an increased risk of major adverse cardiovascular events [13]. Additionally, high TMAO levels were observed in patients with stable heart failure compared to healthy subjects [11]. This result suggests that the gut microbiome may play a role in the development and progression of heart failure. They also showed that elevated TMAO levels were associated with a 2.2-fold increase in the risk of mortality, after an adjustment for traditional risk factors and the brain natriuretic peptide. Moreover, the blood TMAO levels were associated with coronary plaque vulnerability, as assessed by optical coherence tomography, and the long-term risks of cardiovascular events in patients with acute coronary syndrome [14]. The latest metagenome-wide association study demonstrated the microbial characterization of coronary artery disease (CAD) patients and showed that the gut microbial enzymes that produce TMA were enriched in the patients with CAD compared to the healthy controls [17].

As different gut microbial compositions generate different levels of TMAO [18], higher blood TMAO levels and an increased CVD risk can be attributed to a TMA-producing microbiome harboring TMA lyases. These findings support the idea that prevention of CVD is feasible through gut microbial modulation. However, the area under the receiver operating characteristic curve, based on TMA lyases, was not sufficient to predict the incidence of CAD (Area Under the Curve = 0.63). Moreover, a recent clinical trial has shown that fish consumption increases the circulating TMAO levels, highlighting the substantial limitations in our current understanding of the relationship between diet and gut microbial TMAO production [18]. Moreover, all available clinical studies are cross-sectional studies or cohort studies, not interventional studies. Further research is needed to elucidate whether TMAO contributes directly to the progression of CVD or reflects the presence of a deleterious colonic microbial metabolism, dietary habits, or renal tubular dysfunction. In addition, the distribution of TMAO levels in the general population is unknown, and standard reference values are not currently available [19]. A detailed understanding of the biological role of TMAO in CVD patients is crucial for evaluating the feasibility of developing drugs that affect the TMAO levels or the possibility of using TMAO as a marker of CVD.

Table 1. Major clinical reports demonstrating the impact of circulating trimethylamine-*N*-oxide (TMAO) levels on cardiovascular diseases (CVD).

Year	Study Population	Number of Subjects	Main Outcome	Follow-Up Period	Results
2013 *N. Engl. J. Med.*	Patients who were undergoing elective diagnostic cardiac catheterization	4007 in USA	Major cardiovascular events (myocardial infarction, stroke), or death	3 years	Increased TMAO levels were associated with an increased risk of major adverse cardiovascular events or death
2014 *J. Am. Coll. Cardiol.*	Stable heart failure patients underwent elective coronary angiographic evaluation	720 in USA	All-cause mortality (death)	5 years	Elevated TMAO levels portended higher long-term mortality risk
2015 *J. Card Fail*	Chronic systolic heart failure with comprehensive echocardiographic evaluation	112 in USA	Adverse clinical events (death/transplantation)	5 years	Higher TMAO levels were associated with a higher incidence of death/transplantation
2016 *Heart*	Acute heart failure	972 in UK	All-cause mortality (death) and a composite of death or re-hospitalization due to heart failure (death/HF)	1 year	Elevated levels were associated with a higher incidence of death/HF
2016 *Am. J. Cardiol.*	Coronary artery disease	26 in China	Coronary plaque vulnerability assessed by optical coherence tomography	-	Plasma TMAO level was significantly higher in patients with plaque rupture than in those without plaque rupture
2017 *Clin. Chem.*	Acute myocardial infarction	1079 in UK	Composite of all-cause mortality and re-infarction (death/myocardial infarction)	2 years	TMAO levels were associated with death/MI

3. Other Gut Microbial Metabolites and CVD

There are a number of other gut microbial metabolites in addition to TMA. These metabolites have also been reported to have a link to CVDs. Indoxyl sulfate is produced by gut microbial tryptophanases that convert dietary tryptophan into indole, which is then converted to indoxyl and indoxyl sulfate in the liver by the sequential actions of cytochrome P450 enzymes and sulfotransferase 1A1. Indoxyl sulfate has been shown to have pro-inflammatory and pro-oxidant effects in cardiomyocytes and cardiac fibroblasts. Furthermore, recent reports have shown that indole and indoxyl sulfate affect the arterial blood pressure via peripheral and central mechanisms that depend on serotonin signaling in rats [20].

Short chain fatty acids (SCFAs), produced by the colonic bacterial fermentation of dietary fiber, contribute a significant proportion of the daily energy requirement [21]. SCFAs, especially butyrate and propionate, play an important role in regulatory T cell differentiation and intestinal tract immune regulation. The increased production of acetate by the gut microbiota of rodents leads to the activation of the parasympathetic nervous system, which promotes increased glucose-stimulated insulin secretion, hyperphagia, and obesity. However, no reports have described the direct impact of SCFAs on the incidence and progression of cardiovascular diseases [22].

The gut microbiome utilizes sulfur-containing compounds to produce hydrogen sulfide. Hydrogen sulfide is an important biological mediator that is involved in various physiological processes, including the regulation of arterial blood pressure [23]. Moreover, phenylacetylglutamine is a product that is formed by the conjugation of phenylacetate and glutamine. High serum levels of phenylacetylglutamine have been observed in patients with advanced chronic kidney disease, and as a strong and independent risk factor for overall mortality and cardiovascular diseases [24]. P-cresyl sulfate, a secondary metabolism of p-cresol, is also a microbial metabolite. Increased levels of p-cresyl sulfate are associated with worse outcomes in patients with chronic kidney disease [25].

These results suggest that gut microbial metabolites may play an important role in the development of CVD. Further studies are warranted to elucidate the causal relationship between these metabolites and CVD.

4. Alterations of the Gut Microbial Structure Associated with CVD

Several studies have been conducted to elucidate which gut bacterial species are involved in the incidence and progression of CVD (Table 2) [17,26–28]. We were the first to report that the incidence of CAD was linked to an alteration of the gut microbial composition [28,29]. We have reported a lower abundance of the phylum *Bacteroidetes* and a higher abundance of the order *Lactobacillales* in patients with CAD compared to non-CAD patients with coronary risk factors, such as diabetes, hypertension, or dyslipidemia, and healthy volunteers using terminal restriction fragment length polymorphism analysis, which is one of the most well-established and reliable 16S rRNA-based methods. The *Firmicutes/Bacteroidetes* ratio, an indicator of dysbiosis, increased in the CAD patients compared with the non-CAD controls. Interestingly, our data revealed that the CAD patients were significantly more likely to be categorized as enterotype III, which is characterized by low levels of *Bacteroides*, compared with the non-CAD controls. Last year, a metagenome-wide association study of fecal samples from 218 CAD patients and 187 healthy subjects from China was reported [17]. The abundance of *Enterobacteriaceae* was significantly higher in the CAD patients compared to the healthy subjects. The abundance of *Streptococcus* spp. was also significantly higher in the patients with CAD than in the healthy subjects. This may be due to the use of proton pump inhibitors in CAD patients [30]. Consistent with our results, *Bacteroides* spp. were significantly depleted in the CAD patients. Given that *Bacteroides* spp. are known to have an important role in maintaining a healthy gut ecosystem [31], and that the abundance of *Bacteroides* spp. was found to decrease in patients with atherosclerotic ischemic stroke and transient ischemic attack [27], *Bacteroides* spp. may have the potential to regulate atherosclerosis progression. Furthermore, *Faecalibacterium prausnitzii*, which exhibits anti-inflammatory effects [32], was also significantly depleted in the CAD patients. Of note, the co-abundance network structure differed between the two groups. The negative

correlations between *Streptococcus* spp. and *Bacteroides* spp. were observed only in the CAD patients. On the other hand, the positive correlation between *Bacteroides* spp. and *Erysipelotrichaceae* bacterium was seen only in the healthy subjects. These results implied that a peculiar inter-species relationship in the gut microbiome may exist in CAD patients compared to healthy subjects.

Additionally, there are some studies that have demonstrated the relationship between the gut microbiome and heart failure (HF). Kamo et al., first reported the gut microbial difference in Japanese heart failure patients [33]. They performed a 16S rRNA gene sequencing analysis of fecal samples from 12 HF patients and 12 age-matched healthy subjects. They further compared the gut microbiome in HF patients according to age; the gut microbiome in the 12 HF patients younger than 60 years of age were compared with those of the 10 HF patients 60 years of age or older. Although the richness and diversity of the gut microbiota were not significantly different between the HF patients and healthy subjects, *Dorea* and *Clostridium* were less abundant in the HF patients than in the healthy subjects. Moreover, older HF patients had a lower abundance of *Bacteroidetes* and a higher abundance of *Proteobacteria* compared to the younger HF patients. There is also a report from China that shows a metagenomic analysis of fecal samples from patients with chronic HF [34]. They enrolled 53 HF patients and 41 controls with risk factors and compared the compositions of their gut microbiomes. *Ruminococcus*, *Acinetobacter*, and *Veillonella* increased in the HF patients, whereas *Alistipes*, *Faecalibacterium*, and *Oscillibacter* decreased. In line with the previous report, *Faecalibacterium prausnitzii* decreased in the HF patients compared to the controls. The results of these studies suggest that an altered gut microbiome may have an impact on the development and progression of heart failure. This evidence paves the way for further studies investigating the gut microbiome in the prevention and management of CVD.

Table 2. Clinical reports demonstrating the gut microbiome in patients with CVD.

Year	Study Population	Country	Analysis	Results
2012 *Nat. Commun.*	12 patients with symptomatic atherosclerosis (myocardial infarction or cerebrovascular events) and 13 age- and sex-matched healthy individuals.	Sweden	Gut metagenome	*Collinsella* ↑, *Eubacterium* ↓, *Roseburia* ↓ in patients with symptomatic atherosclerosis.
2015 *J. Am. Heart Assoc.*	141 patients with stroke and transient ischemic attack (stroke/TIA patients) and 94 asymptomatic controls.	China	16S rRNA V4 region	*Enterobacteriaceae* ↑, *Proteobacteria* ↑, *Escherichia/Shigella* ↑, *Bacteroidetes* ↓, *Bacteroidales* ↓, *Bacteroidaceae* ↓, *Bacteroides* ↓ in stroke/TIA patients.
2016 *J. Atheroscler. Thromb.*	39 coronary artery disease (CAD) patients, 30 age- and sex-matched no-CAD controls with coronary risk factors, and 50 healthy volunteers without coronary risk factors.	Japan	Terminal restriction fragment length polymorphism	*Firmicutes/Bacteroidetes* ratio ↑, *Lactobacillales* ↑, *Bacteroides* + *Prevotella* ↓ in CAD.
2017 *Nat. Commun.*	218 individuals with atherosclerotic cardiovascular disease (ACVD) and 187 healthy controls.	China	Gut metagenome	*Enterobacteriaceae* (*Escherichia coli, Klebsiella* spp., and *Enterobacter aerogenes*), *Streptococcus* spp., *Lactobacillus salivarius, Solobacterium moorei, Atopobium parvulum, Ruminococcus gnavus, Eggerthella lenta* ↑, *Roseburia intestinalis* ↓, *Faecalibacterium* cf. *prausnitzii* ↓, *Bacteroides* spp. ↓, *Prevotella copri* ↓, *Alistipes shahii* ↓ in ACVD.

5. Alternations in Gut Microbial Function Associated with CVD

In addition to the compositional characteristics, the functional characteristics of the gut microbiome have been investigated in order to delineate the mechanisms related to the development of CVD. Although metagenomic shotgun sequencing analysis is the main method to examine the functional characteristics, methods are being developed to predict functional profiles from taxonomic profiles. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) is a bioinformatics software package designed to predict metagenomic functional content from the 16S rRNA gene [35]. The Kyoto Encyclopedia of Genes and Genomes (KEGG) modules are usually used to construct a functional map of the gut microbiome [36].

The first shotgun sequencing of the gut metagenome in patients with symptomatic atherosclerotic plaques in their carotid arteries was a study with a small number of samples [27]. They showed that genes that encode proteins involved in peptidoglycan synthesis were enriched, and those that encode phytoene dehydrogenases were depleted in the patients compared to these genes in healthy subjects. Considering that gut bacterial function differs even within the same strain, a metagenomic shotgun sequencing study must provide us with further detailed information. Five years later, Jie et al., have reported a metagenomic shotgun sequencing study with 218 CAD patients and 187 healthy subjects [30]. They revealed alterations in gut microbial functional modules in CAD patients, such as the phosphotransferase system, amino acid transporters, vitamin metabolism, lipopolysaccharide biosynthesis, and the activities of SCFAs and TMA lyases.

With regard to HF, Cui et al., have investigated the metabolic patterns of the gut microbiome in patients with chronic HF to provide direct evidence and a comprehensive understanding of gut microbial dysbiosis [34]. Fifty-three chronic HF patients (ischemic cardiomyopathy, n = 29; dilated cardiomyopathy, n = 24) and 41 controls with risk factors were enrolled. They found an elevation in the microbial genes for lipopolysaccharide biosynthesis, tryptophan, and TMAO generation in the chronic HF patients. This result provides a convincing explanation for the increased plasma lipopolysaccharide levels in HF patients [37], because the main source of lipopolysaccharides is the gut/gut microbiome. Moreover, increased expression of the genes for phosphotransferase systems and decreased gene expression for the synthesis and transport of amino acids, nucleotide sugar biosynthesis, and the iron transport system were observed in the HF patients compared with the controls. These disease-dependent unique features in the functional capacity may give us clues for novel therapeutic approaches.

6. Issues to Be Considered When Interpreting the Studies

Most clinical studies compare the gut microbial composition between patients and healthy controls. Administration of medication has a substantial effect on the gut microbiome, and medication-matched controls are required to elucidate the impact of the gut microbiome on disease progression. Moreover, the studies mentioned above have provided useful characterization of the fecal microbial profile in patients with CVD; however, we are still struggling with these descriptive data. A specific gut microbiome-based target to prevent CVD has yet to emerge, which is the greatest challenge that we are currently facing. It may take a little more time to conduct a large cohort study or a translational study to promote a deeper understanding of how the gut microbiome directly contributes to CVD. While we already know that diet, prebiotics, probiotics, a specific IgA antibody, and enzymes can modulate the gut microbiome and its function [38,39], these interventions for patients with CVD are constrained by ethical considerations or funding limitations. In such cases, an in vitro fermentation system simulating the human intestinal tract may help to evaluate the functionality or safety of these interventions under highly reproducible conditions without the ethical issues [40]. Specifically, we can culture feces from patients with prebiotics or probiotics in an in vitro fermentation system and analyze how the gut microbiome, and its metabolites and functions, are changed after the intervention. Of note, we have observed some discrepancies between the findings in humans and mice. These may be due to

the differences in the natural gut microbiome. It is important to pay attention to the complexities of translating the findings from an animal model to humans.

7. Conclusions

In summary, recent evidence on the potential interaction between the gut microbiome and cardiovascular diseases is intriguing. With increasing awareness of the relationship between the gut microbiome and CVD, we have high expectations for the clinical application of gut microbiome modulation. Further studies, focusing on a more specific and mechanistic understanding of the gut microbiome in the pathogenesis of CVD, are necessary to develop novel diagnostic and therapeutic strategies for CVD.

Author Contributions: T.Y. conceived and wrote the manuscript and made critical revisions. N.Y. conceived and wrote the manuscript. K.H. searched the bibliography and made critical revisions.

Funding: This research was funded by JSPS KAKENHI Grant Number 24591114, 16K09516 (T.Y.) and 17K09497 (K.H.), The Japanese Circulation Society Translational Research Foundation (K.H.), Uehara Memorial Foundation (K.H.), Takeda Scientific Foundation (T.Y.), Senshin Medical Research Foundation (T.Y.), Yakult Bioscience Research Foundation (T.Y.), Hyogo Science and Technology Association (T.Y. and K.H.), and Kondou Kinen Medical Foundation (T.Y.). Article Processing Charges was sponsored by MDPI.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Turnbaugh, P.J.; Ley, R.E.; Mahowald, M.A.; Magrini, V.; Mardis, E.R.; Gordon, J.I. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* **2006**, *444*, 1027. [CrossRef] [PubMed]
2. Macpherson, A.J.; Harris, N.L. Interactions between commensal intestinal bacteria and the immune system. *Nat. Rev. Immunol.* **2004**, *4*, 478–485. [CrossRef] [PubMed]
3. Zhao, L. The gut microbiota and obesity: From correlation to causality. *Nat. Rev. Microbiol.* **2013**, *11*, 639–647. [CrossRef] [PubMed]
4. Imajo, K.; Fujita, K.; Yoneda, M.; Nozaki, Y.; Ogawa, Y.; Shinohara, Y.; Kato, S.; Mawatari, H.; Shibata, W.; Kitani, H.; et al. Hyperresponsivity to low-dose endotoxin during progression to nonalcoholic steatohepatitis is regulated by leptin-mediated signaling. *Cell Metab.* **2012**, *16*, 44–54. [CrossRef] [PubMed]
5. Gevers, D.; Kugathasan, S.; Denson, L.A.; Vázquez-Baeza, Y.; Van Treuren, W.; Ren, B.; Schwager, E.; Knights, D.; Song, S.J.; Yassour, M.; et al. The treatment-naïve microbiome in new-onset Crohn's disease. *Cell Host Microbe* **2014**, *15*, 382–392. [CrossRef] [PubMed]
6. Tang, W.H.W.; Kitai, T.; Hazen, S.L. Gut Microbiota in Cardiovascular Health and Disease. *Circ. Res.* **2017**, *120*, 1183–1196. [CrossRef] [PubMed]
7. Ridker, P.M.; Danielson, E.; Fonseca, F.A.H.; Genest, J.; Gotto, A.M.J.; Kastelein, J.J.P.; Koenig, W.; Libby, P.; Lorenzatti, A.J.; MacFadyen, J.G.; et al. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. *N. Engl. J. Med.* **2008**, *359*, 2195–2207. [CrossRef] [PubMed]
8. Benjamin, E.J.; Virani, S.S.; Callaway, C.W.; Chang, A.R.; Cheng, S.; Chiuve, S.E.; Cushman, M.; Delling, F.N.; Deo, R.; de Ferranti, S.D.; et al. Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association. *Circulation* **2018**. [CrossRef] [PubMed]
9. Shimokawa, H.; Miura, M.; Nochioka, K.; Sakata, Y. Heart failure as a general pandemic in Asia. *Eur. J. Heart Fail.* **2015**, *17*, 884–892. [CrossRef] [PubMed]
10. Heidenreich, P.A.; Trogdon, J.G.; Khavjou, O.A.; Butler, J.; Dracup, K.; Ezekowitz, M.D.; Finkelstein, E.A.; Hong, Y.; Johnston, S.C.; Khera, A.; et al. Forecasting the Future of Cardiovascular Disease in the United States: A Policy Statement From the Am. Heart Association. *Circulation* **2011**, *123*, 933–944. [CrossRef] [PubMed]
11. Tang, W.H.; Wang, Z.; Fan, Y.; Levison, B.; Hazen, J.E.; Donahue, L.M.; Wu, Y.; Hazen, S.L. Prognostic value of elevated levels of intestinal microbe-generated metabolite trimethylamine-*N*-oxide in patients with heart failure: Refining the gut hypothesis. *J. Am. Coll. Cardiol.* **2014**, *64*, 1908–1914. [CrossRef] [PubMed]
12. Suzuki, T.; Heaney, L.M.; Bhandari, S.S.; Jones, D.J.L.; Ng, L.L. Trimethylamine *N*-oxide and prognosis in acute heart failure. *Heart* **2016**, *102*, 841–848. [CrossRef] [PubMed]

13. Tang, W.H.; Wang, Z.; Levison, B.S.; Koeth, R.A.; Britt, E.B.; Fu, X.; Wu, Y.; Hazen, S.L. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. *N. Engl. J. Med.* **2013**, *368*, 1575–1584. [CrossRef] [PubMed]
14. Fu, Q.; Zhao, M.; Wang, D.; Hu, H.; Guo, C.; Chen, W.; Li, Q.; Zheng, L.; Chen, B. Coronary Plaque Characterization Assessed by Optical Coherence Tomography and Plasma Trimethylamine-*N*-oxide Levels in Patients With Coronary Artery Disease. *Am. J. Cardiol.* **2016**, *118*, 1311–1315. [CrossRef] [PubMed]
15. Tang, W.H.W.; Wang, Z.; Shrestha, K.; Borowski, A.G.; Wu, Y.; Troughton, R.W.; Klein, A.L.; Hazen, S.L. Intestinal Microbiota-Dependent Phosphatidylcholine Metabolites, Diastolic Dysfunction, and Adverse Clinical Outcomes in Chronic Systolic Heart Failure. *J. Card. Fail.* **2015**, *21*, 91–96. [CrossRef] [PubMed]
16. Suzuki, T.; Heaney, L.M.; Jones, D.J.; Ng, L.L. Trimethylamine *N*-oxide and Risk Stratification after Acute Myocardial Infarction. *Clin. Chem.* **2017**, *63*, 420–428. [CrossRef] [PubMed]
17. Jie, Z.; Xia, H.; Zhong, S.-L.; Feng, Q.; Li, S.; Liang, S.; Zhong, H.; Liu, Z.; Gao, Y.; Zhao, H.; et al. The gut microbiome in atherosclerotic cardiovascular disease. *Nat. Commun.* **2017**, *8*, 845. [CrossRef] [PubMed]
18. Cho, C.E.; Taesuwan, S.; Malysheva, O.V.; Bender, E.; Tulchinsky, N.F.; Yan, J.; Sutter, J.L.; Caudill, M.A. Trimethylamine-*N*-oxide (TMAO) response to animal source foods varies among healthy young men and is influenced by their gut microbiota composition: A randomized controlled trial. *Mol. Nutr. Food Res.* **2017**, *61*. [CrossRef] [PubMed]
19. Schiattarella, G.G.; Sannino, A.; Toscano, E.; Giugliano, G.; Gargiulo, G.; Franzone, A.; Trimarco, B.; Esposito, G.; Perrino, C. Gut microbe-generated metabolite trimethylamine-*N*-oxide as cardiovascular risk biomarker: A systematic review and dose-response meta-analysis. *Eur. Heart J.* **2017**, *38*, 2948–2956. [CrossRef] [PubMed]
20. Huć, T.; Nowinski, A.; Drapala, A.; Konopelski, P.; Ufnal, M. Indole and indoxyl sulfate, gut bacteria metabolites of tryptophan, change arterial blood pressure via peripheral and central mechanisms in rats. *Pharmacol. Res.* **2018**, *130*, 172–179. [CrossRef] [PubMed]
21. Kimura, I.; Inoue, D.; Maeda, T.; Hara, T.; Ichimura, A.; Miyauchi, S.; Kobayashi, M.; Hirasawa, A.; Tsujimoto, G. Short-chain fatty acids and ketones directly regulate sympathetic nervous system via G protein-coupled receptor 41 (GPR41). *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 8030–8035. [CrossRef] [PubMed]
22. Ohira, H.; Tsutsui, W.; Fujioka, Y. Are Short Chain Fatty Acids in Gut Microbiota Defensive Players for Inflammation and Atherosclerosis? *J. Atheroscler. Thromb.* **2017**, *24*, 660–672. [CrossRef] [PubMed]
23. Tomasova, L.; Dobrowolski, L.; Jurkowska, H.; Wróbel, M.; Huc, T.; Ondrias, K.; Ostaszewski, R.; Ufnal, M. Intracolonic hydrogen sulfide lowers blood pressure in rats. *Nitric Oxide* **2016**, *60*, 50–58. [CrossRef] [PubMed]
24. Poesen, R.; Claes, K.; Evenepoel, P.; de Loor, H.; Augustijns, P.; Kuypers, D.; Meijers, B. Microbiota-Derived Phenylacetylglutamine Associates with Overall Mortality and Cardiovascular Disease in Patients with CKD. *J. Am. Soc. Nephrol.: JASN* **2016**, *27*, 3479–3487. [CrossRef] [PubMed]
25. Gryp, T.; Vanholder, R.; Vaneechoutte, M.; Glorieux, G. p-Cresyl Sulfate. *Toxins* **2017**, *9*, 52. [CrossRef] [PubMed]
26. Karlsson, F.H.; Fåk, F.; Nookaew, I.; Tremaroli, V.; Fagerberg, B.; Petranovic, D.; Bäckhed, F.; Nielsen, J. Symptomatic atherosclerosis is associated with an altered gut metagenome. *Nat. Commun.* **2012**, *3*, 1245. [CrossRef] [PubMed]
27. Yin, J.; Liao, S.X.; He, Y.; Wang, S.; Xia, G.H.; Liu, F.T.; Zhu, J.J.; You, C.; Chen, Q.; Zhou, L.; et al. Dysbiosis of Gut Microbiota With Reduced Trimethylamine-*N*-Oxide Level in Patients With Large-Artery Atherosclerotic Stroke or Transient Ischemic Attack. *J. Am. Heart Assoc.* **2015**, *4*, e002699. [CrossRef] [PubMed]
28. Emoto, T.; Yamashita, T.; Sasaki, N.; Hirota, Y.; Hayashi, T.; So, A.; Kasahara, K.; Yodoi, K.; Matsumoto, T.; Mizoguchi, T.; et al. Analysis of Gut Microbiota in Coronary Artery Disease Patients: A Possible Link between Gut Microbiota and Coronary Artery Disease. *J. Atheroscler. Thromb.* **2016**, *23*, 908–921. [CrossRef] [PubMed]
29. Emoto, T.; Yamashita, T.; Kobayashi, T.; Sasaki, N.; Hirota, Y.; Hayashi, T.; So, A.; Kasahara, K.; Yodoi, K.; Matsumoto, T.; et al. Characterization of gut microbiota profiles in coronary artery disease patients using data mining analysis of terminal restriction fragment length polymorphism: Gut microbiota could be a diagnostic marker of coronary artery disease. *Heart Vessels* **2017**, *32*, 39–46. [CrossRef] [PubMed]

30. Jackson, M.A.; Goodrich, J.K.; Maxan, M.-E.; Freedberg, D.E.; Abrams, J.A.; Poole, A.C.; Sutter, J.L.; Welter, D.; Ley, R.E.; Bell, J.T.; et al. Proton pump inhibitors alter the composition of the gut microbiota. *Gut* **2016**, *65*, 749–756. [CrossRef] [PubMed]
31. Wexler, A.G.; Goodman, A.L. An insider's perspective: Bacteroides as a window into the microbiome. *Nat. Microbiol.* **2017**, *2*, 17026. [CrossRef] [PubMed]
32. Sokol, H.; Pigneur, B.; Watterlot, L.; Lakhdari, O.; Bermúdez-Humarán, L.G.; Gratadoux, J.-J.; Blugeon, S.; Bridonneau, C.; Furet, J.-P.; Corthier, G.; et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 16731–16736. [CrossRef] [PubMed]
33. Kamo, T.; Akazawa, H.; Suda, W.; Saga-Kamo, A.; Shimizu, Y.; Yagi, H.; Liu, Q.; Nomura, S.; Naito, A.T.; Takeda, N.; et al. Dysbiosis and compositional alterations with aging in the gut microbiota of patients with heart failure. *PLoS ONE* **2017**, *12*, e0174099. [CrossRef] [PubMed]
34. Cui, X.; Ye, L.; Li, J.; Jin, L.; Wang, W.; Li, S.; Bao, M.; Wu, S.; Li, L.; Geng, B.; et al. Metagenomic and metabolomic analyses unveil dysbiosis of gut microbiota in chronic heart failure patients. *Sci. Rep.* **2018**, *8*, 635. [CrossRef] [PubMed]
35. Langille, M.G.; Zaneveld, J.; Caporaso, J.G.; McDonald, D.; Knights, D.; Reyes, J.A.; Clemente, J.C.; Burkepile, D.E.; Vega Thurber, R.L.; Knight, R.; et al. Predictive functional profiling of microbial communities using 16S rRNA marker gene sequences. *Nat. Biotechnol.* **2013**, *31*, 814–821. [CrossRef] [PubMed]
36. Kanehisa, M.; Furumichi, M.; Tanabe, M.; Sato, Y.; Morishima, K. KEGG: New perspectives on genomes, pathways, diseases and drugs. *Nucleic Acids Res.* **2017**, *45*, D353–D361. [CrossRef] [PubMed]
37. Sharma, R.; Haehling, S.; Rauchhaus, M.; Bolger, A.P.; Genth-Zotz, S.; Doehner, W.; Oliver, B.; Poole-Wilson, P.A.; Hans-Dieter, V.; Coats, A.J.S.; et al. Whole blood endotoxin responsiveness in patients with chronic heart failure: The importance of serum lipoproteins. *Eur. J. Heart Fail.* **2005**, *7*, 479–484. [CrossRef] [PubMed]
38. Okai, S.; Usui, F.; Yokota, S.; Hori, I.Y.; Hasegawa, M.; Nakamura, T.; Kurosawa, M.; Okada, S.; Yamamoto, K.; Nishiyama, E.; et al. High-affinity monoclonal IgA regulates gut microbiota and prevents colitis in mice. *Nat. Microbiol.* **2016**, *1*, 16103. [CrossRef] [PubMed]
39. Mizoguchi, T.; Kasahara, K.; Yamashita, T.; Sasaki, N.; Yodoi, K.; Matsumoto, T.; Emoto, T.; Hayashi, T.; Kitano, N.; Yoshida, N.; et al. Oral administration of the lactic acid bacterium Pediococcus acidilactici attenuates atherosclerosis in mice by inducing tolerogenic dendritic cells. *Heart Vessels* **2017**, *32*, 768–776. [CrossRef] [PubMed]
40. Wilson, B.A.; Takagi, R.; Sasaki, K.; Sasaki, D.; Fukuda, I.; Tanaka, K.; Yoshida, K.-I.; Kondo, A.; Osawa, R. A Single-Batch Fermentation System to Simulate Human Colonic Microbiota for High-Throughput Evaluation of Prebiotics. *PLoS ONE* **2016**, *11*, e0160533.

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: B6
Sent: 9/14/2018 2:16:03 PM
Subject: RE: FDA study
Attachments: 800.267-Sample Testing Procedures-v11.doc

Thank you, B6 This is helpful feedback. I've again, updated the procedures to reflect your comments.

Have you submitted a report to the Safety Reporting portal? If so, please let me know the ICSR # (confirmation number). After we get the report, I'll send the box to collect the samples.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: B6 @cvcavets.com>
Sent: Wednesday, September 12, 2018 4:46 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: FDA study

Hi Jennifer,

I have collected all the samples from the first patient in the study and they are in the freezer. I have attached the submission form for the study. I understand you will now be sending us the container to send you the samples in.

I also wanted to let you know that the directions for the B4, B5

B4, B5

B6

From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: B6
CC: Andrea Fascetti
Sent: 8/20/2019 6:06:11 PM
Subject: RE: Question about results

Great, thank you for the clarification. This helps tremendously.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: B6
Sent: Tuesday, August 20, 2019 1:53 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Andrea Fascetti <ajfascetti@ucdavis.edu>
Subject: Re: Question about results

Good Morning Dr. Jones,

ND and NLD are the same meaning below detection limits (sorry for the inconsistency) . From our B6 results using B5 our BLD results normally fall into a range from B5 B5 Statisticians may be able to give some meaningful suggestions about how to deal with this problem.

Kind regards,
B6

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Sent: Tuesday, August 20, 2019 4:44 AM
To: B6
Cc: Andrea Fascetti <ajfascetti@ucdavis.edu>
Subject: Question about results

Good morning Josh and Andrea,
I had two quick general questions about the B5

B5

Thank you in advance,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685

e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Andrea Fascetti <ajfascetti@ucdavis.edu>
To: Jones, Jennifer L
Sent: 3/25/2019 8:14:08 PM
Subject: Re: reference ranges for plasma amino acids

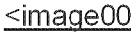
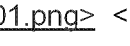
Hi Jen - We use the Delaney reference ranges - especially when looking at a complete AA analysis. Remember cysteine will be low unless samples are treated with SSA at the time of collection.

I hope this works.

Andrea

On Mar 25, 2019, at 2:57 PM, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov> wrote:

Hi Andrea,
Do you have specific reference ranges for canine plasma amino acids in your lab? I looked at the Delaney et al paper but didn't know if there was a set range you used.
Thank you in advance,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm
 

From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: B6
CC: Andrea Fascetti
Sent: 5/29/2019 4:22:06 PM
Subject: RE: Heads up: Vet-LIRN shipped 800.267-CO samples

Great! Thank you.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: B5
Sent: Wednesday, May 29, 2019 12:11 PM
To: Guag, Jake <Jake.Guag@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: Andrea Fascetti <ajfascetti@ucdavis.edu>
Subject: Re: Heads up: Vet-LIRN shipped 800.267-CO samples

Dear Dr. Jones and Jake,

I have added the WB taurine in. Please find the updated results in attachment. The # 10 WB & PL taurine results seem off. We will check them as soon as we can.

Thanks,
B6

From: Guag, Jake <Jake.Guag@fda.hhs.gov>
Sent: Wednesday, May 29, 2019 4:49 AM
To: Jones, Jennifer L; B6
Subject: RE: Heads up: Vet-LIRN shipped 800.267-CO samples

Hi,
I asked B6 and replied with some results. He will add WB results.

Jake

From: Jones, Jennifer L
Sent: Wednesday, May 29, 2019 6:54 AM
To: Guag, Jake <Jake.Guag@fda.hhs.gov>; B6
Subject: RE: Heads up: Vet-LIRN shipped 800.267-CO samples

Good morning B6
I wanted to check-in on the samples and see if you had any results.
Thanks so much and hope you had a nice vacation,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Guag, Jake
Sent: Thursday, May 16, 2019 10:15 AM
To: B6
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: RE: Heads up: Vet-LIRN shipped 800.267-CO samples

Hi B6
Both boxes are arrived in your location yesterday. Could you please check package and sample condition and provide the sample inventory forms?

Thanks
Jake

From: B6
Sent: Tuesday, May 14, 2019 2:38 PM
To: Guag, Jake <Jake.Guag@fda.hhs.gov>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Re: Heads up: Vet-LIRN shipped 800.267-CO samples

Hi Jake,

Thanks for the update. Will let you know when they arrive.

Kind regards,
B6

From: Guag, Jake <Jake.Guag@fda.hhs.gov>
Sent: Tuesday, May 14, 2019 6:57 AM
To: B6
Cc: Jones, Jennifer L
Subject: Heads up: Vet-LIRN shipped 800.267-CO samples

Hi B6
We shipped 800.267-CO samples on dry ice to you this morning. Box #1 has urine samples and Box #2 has whole blood and plasma samples.
Both boxes will be your location tomorrow (May 15, 2019), and their tracking numbers are 1ZA4420T0198935852 (Box#1) and 1ZA4420T0195716460 (Box#2) with UPS.
Inside box, you will find an inventory form. Please check and provide us (Fax or Scan)

Note:
Please charge the urine sample testing under AA contract, and submit invoice for whole bold and plasma sample testing.
For each CO case, we shipped 1 tube blood and plasma tube and 2 tubes for urine samples except CO-08 and CO-10 (only 1 tube available)

Thank you,
Jake

Jake Guag, MPH, CPH
Biologist (FDA/CVM/OR/Vet-LIRN)
8401 Muirkirk Road
Laurel, Maryland 20708

Email: jake.guag@fda.hhs.gov
Tel: 240-402-0917

Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997–2001)

Andrea J. Fascetti, VMD, PhD, DACVN, DACVIM; John R. Reed, DVM, MS, DACVIM;
Quinton R. Rogers, PhD, DACVN; Robert C. Backus, DVM, PhD

Objective—To determine signalment, history, clinical signs, blood and plasma taurine concentrations, electrocardiographic and echocardiographic findings, treatment, and outcome of dogs with low blood or plasma taurine concentrations and dilated cardiomyopathy (DCM).

Design—Retrospective study.

Animals—12 client-owned dogs with low blood or plasma taurine concentrations and DCM.

Procedure—Medical records were reviewed, and clinical data were obtained.

Results—All 12 dogs were being fed a commercial dry diet containing lamb meal, rice, or both as primary ingredients. Cardiac function and plasma taurine concentration improved with treatment and taurine supplementation. Seven of the 12 dogs that were still alive at the time of the study were receiving no cardiac medications except taurine.

Conclusions and Clinical Relevance—Results suggest that consumption of certain commercial diets may be associated with low blood or plasma taurine concentrations and DCM in dogs. Taurine supplementation may result in prolonged survival times in these dogs, which is not typical for dogs with DCM. Samples should be submitted for measurement of blood and plasma taurine concentrations in dogs with DCM, and taurine supplementation is recommended while results of these analyses are pending. (*J Am Vet Med Assoc* 2003;223:1137–1141)

B4

B4

B4

B4

B4

B4

From: Andrea Fascetti <ajfascetti@ucdavis.edu>
To: Jones, Jennifer L
Sent: 7/9/2018 3:42:06 PM
Subject: Paper and link to Pet Food Industry Magazine
Attachments: torres paper.pdf

Hi Jen - Thank you again for taking my call. I have attached the paper by Dr. Torres on cyst(e)ine and its stability (or lack thereof) in plasma.

It also occurred to me that you may be already subscribed to Pet Food Industry Magazine, but if not you may wish to consider. It is free to receive. They do have some good articles by folks such as Dave Dzanis and Greg Aldrich on pet food production. In fact the issue I just got has an article on legumes. I have attached the latest version (which just landed in my in box) below.

Take care - Andrea

Begin forwarded message:

Petfood Industry - July 2018
If you are having trouble viewing this e-mail, open the online version.

PetfoodIndustry.com | Magazines | Newsletters | Webinars | Top Petfood Companies | Videos

Follow Us

In the July issue:

Blue Dog Bakery: mass market premium treat success

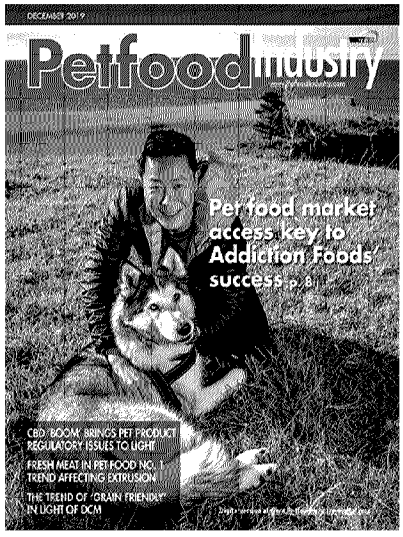
New cat food, treat products reflect pet ownership

The importance of transparency in the pet food industry

Brazil, Mexico lead Latin America in pet food consumption

Experts address Chinese pet food market, new regulations

High-protein pet food: popular ingredient has challenges



Petfood Industry
July 2018

Don't Miss an Issue!
Renew Now ▶

Human vs. pet food labeling: How do they differ?

Legume see oligosaccharides: How much is just right in dog and cat diets?

How shifting pet ownership economics impact pet food

See the full Table of Contents

If you think a colleague might be interested in this publication please feel free to share this e-mail with them.

Sincerely,

Debbie Phillips-Donaldson
Editor-in-chief, Petfood Industry
dphillips@wattglobal.com

From: Jones, Jennifer L </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0f6ca12eaa9348959a4cbb1e829af244-Jennifer.Jo>
To: 'Andrea Fascetti'
Sent: 7/9/2018 3:37:27 PM
Subject: Link to Article I mentioned

Hi Andrea,
Thanks again for the call. Here's a link to the free article I mentioned.
https://academic.oup.com/jn/article/131/2/276/4687012

Take care,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Andrea Fascetti <ajfascetti@ucdavis.edu>
To: Jones, Jennifer L
Sent: 7/9/2018 3:46:48 PM
Subject: Re: Link to Article I mentioned

Thanks! I should have guessed George Fahey was involved. He is a nutrition rock star! He has officially retired but is still active last I heard. He is a great resource and has done a ton of research on fiber/digestibility /bioavailability of feed ingredients in canine and feline diets. B6 who has continued some of his work but seems to have more of an emphasis on the microbiome these days.

Best regards -

Andrea

On Jul 9, 2018, at 8:37 AM, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov> wrote:

Hi Andrea,
Thanks again for the call. Here's a link to the free article I mentioned.
https://academic.oup.com/jn/article/131/2/276/4687012

Take care,
Jen

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
new tel: 240-402-5421
fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm
<image001.png> <image004.png>

Plasma amino acid and whole blood taurine concentrations in cats eating commercially prepared diets

Cailin R. Heinze, VMD; Jennifer A. Larsen, DVM, PhD; Philip H. Kass, DVM, PhD; Andrea J. Fascetti, VMD, PhD

Objective—To establish comprehensive reference ranges for plasma amino acid and whole blood taurine concentrations in healthy adult cats eating commercial diets and to evaluate the relationships of age, sex, body weight, body condition score (BCS), dietary protein concentration, and dietary ingredients with plasma amino acid and whole blood taurine concentrations.

Animals—120 healthy adult cats.

Procedures—Blood samples and a complete health and diet history were obtained for each cat, and reference intervals for plasma amino acid and whole blood taurine concentrations were determined. Results were analyzed for associations of age, breed, sex, body weight, BCS, use of heparin, sample hemolysis and lipemia, dietary protein concentrations, and dietary ingredients with amino acid concentrations.

Results—95% reference intervals were determined for plasma amino acid and whole blood taurine concentrations. A significant difference in amino acid concentrations on the basis of sex was apparent for multiple amino acids. There was no clear relationship between age, BCS, body weight, and dietary protein concentration and amino acid concentrations. Differences in amino acid concentrations were detected for various dietary ingredients, but the relationships were difficult to interpret.

Conclusions and Clinical Relevance—This study provided data on plasma amino acid and whole blood taurine concentrations for a large population of adult cats eating commercial diets. Plasma amino acid and whole blood taurine concentrations were not affected by age, BCS, or body weight but were affected by sex and neuter status. Dietary protein concentration and dietary ingredients were not directly associated with plasma amino acid or whole blood taurine concentrations. (*Am J Vet Res* 2009;70:1374–1382)

The past 4 decades have been a time of dramatic advances in knowledge of feline nutrition, especially the relationships between protein metabolism and numerous disease states. Blood amino acid concentrations have been used for years to aid in the assessment of nutritional and protein status of cats and have a pivotal role in the diagnosis of specific medical conditions. The ability to measure whole blood and plasma taurine concentrations in cats aided in the discovery that taurine deficiency was a major cause of central retinal degeneration[1] and dilated cardiomyopathy[2] in cats. These discoveries have saved many cats from these debilitating and potentially fatal diseases. Without the ability to analyze blood amino acid concentrations, these important connections may never have been made. Amino acid analysis has also been of benefit in investigating many other disease processes, including liver disease,[3] diabetes mellitus,[4,5] heart disease,[6] and even brain injury,[7] in humans and other animals, but comparatively little of this research has focused on cats.

Abbreviations

BCS	Body condition score
NRC	National Research Council
SSA	Sulfosalicylic acid

Blood amino acid concentrations are dynamic and can be reflective of the most recently consumed diet when samples are obtained during the immediate postprandial period.[8,9] Alternatively, they can reflect the mean amino acid concentrations in protein-malnourished animals that eat a constant diet, thus allowing detection of severe and chronic amino acid deficiencies.[10]

Despite a long history of the use of amino acid concentrations for diagnostic and research purposes, there

Received September 12, 2008.
Accepted January 4, 2009.
From the Veterinary Medical Teaching Hospital (Heinze), and the Departments of Molecular Biosciences (Larsen, Fascetti) and Population Health and Reproduction (Kass), School of Veterinary Medicine, University of California-Davis, Davis, CA 95616. Dr. Heinze's present address is Department of Animal Science, College of Agricultural and Environmental Sciences, University of California-Davis, Davis, CA 95616.
Supported by grants from the Center for Companion Animal Health, School of Veterinary Medicine, University of California-Davis, and the Morris Animal Foundation and by the Nestlé Purina PetCare Company. Dr. Heinze was supported by an educational grant from the Nestlé Purina PetCare Company.
The authors thank Dr. Zengshou Yu, Deborah Bee, and Tiffany Chan for technical assistance.
Address correspondence to Dr. Fascetti (ajfascetti@ucdavis.edu).

are few reports of typical amino acid concentrations in plasma and whole blood of adult cats eating commercial diets. Although plasma amino acid concentrations for adult cats eating commercial diets have been published in 2 studies,[6,11] neither of those studies was designed to establish representative reference ranges; therefore, data were reported for only small numbers of healthy cats (29 and 24 cats, respectively) used as control animals in those studies. Additionally, neither study specifically addressed the diets being fed to the cats.

Currently, published reference values for feline amino acid concentrations have come primarily from studies[12–15] in which investigators evaluated amino acid requirements and protein metabolism in growing kittens consuming purified diets. Those diets were formulated with crystalline amino acids or protein concentrates (such as casein and soy protein), and the bioavailability of amino acids in such diets is extremely high.[16,17] In contrast, commercial foods undergo processing that may negatively impact the bioavailability of some amino acids, such as lysine, tryptophan, methionine, and cysteine.[10,18–20] Additionally, those studies[12–15] used only small numbers of growing kittens that were closely related and lacked the genetic diversity inherent in the general feline population. The potential problem with the use of data obtained from genetically similar animals consuming purified diets to develop reference ranges and nutritional recommendations was addressed in 2006 in the recent version of an NRC publication.[10] That publication acknowledged the differences between diet types and provided nutrient requirement recommendations based on the availability of nutrients in ingredients commonly used in foods commercially available for pets.

Our intent in the study reported here was to establish reference ranges for plasma amino acid and whole blood taurine concentrations in cats. We hypothesized that there would be associations between amino acid concentrations and dietary protein concentrations and ingredients. The first objective was to obtain samples from a large number of cats to facilitate the creation of new reference ranges to more accurately reflect the general feline population. A second objective was to analyze the collected data for relationships between plasma amino acid concentrations and signalment, body weight, BCS, dietary protein, and dietary ingredients. Other studies have not adequately addressed how sex, age, body weight, and BCS affect plasma amino acid concentrations, and such information allows for better interpretation of plasma amino acid values in clinically affected animals. In another study[21] conducted by our laboratory group, we detected a relationship between dietary ingredients and plasma amino acid concentrations, particularly taurine, methionine, and cysteine, in dogs. This relationship may also be relevant in cats because there has been a shift toward increasing the use of plant-based protein sources in commercially available pet foods. These ingredients can have lower concentrations of essential amino acids that may also be preferentially impacted by processing, which can result in a decrease in digestibility and bioavailability.[22–25]

Materials and Methods

Animals—Blood samples were obtained from 120 cats consuming commercially prepared feline diets. All cats were free of apparent systemic illness; obesity was not considered grounds for exclusion. The study population consisted of pet cats belonging to students, faculty, and staff of the School of Veterinary Medicine at the University of California-Davis, as well as a lesser number of university-owned cats housed in 2 separate colony facilities. Owners of participating pet cats provided written consent for use of their cats in the study. This study was reviewed and approved by the Institutional Animal Care and Use Committee of the University of California-Davis.

Development of reference intervals—All owners were instructed to feed their cats 3 to 5 hours before blood collection because blood amino acid concentrations are affected by meals and food deprivation.[26] Age, sex, neuter status, breed, body weight, BCS (9-point scale),[27] and current health status (detection of vomiting, diarrhea, sneezing, or coughing or changes in appetite, body weight, urination, or water intake) were recorded at the time of sample collection. One investigator (CRH) assigned a BCS to each privately owned cat and the cats from one of the university facilities. A staff veterinarian assigned the BCS for each cat at the second university facility. Both of these people used the same criteria[27] to assign each BCS and were experienced with the technique. Some university-owned cats were fed ad libitum, and samples were obtained at various intervals after eating (estimated time ranged from the immediate postprandial period up to 5 hours after eating).

Collection of blood samples—A blood sample (1 to 2 mL) was obtained from each cat with a heparinized or unheparinized syringe via jugular or medial saphenous venipuncture. Heparin supplies were unexpectedly interrupted because of a major recall[28] during the sample collection period; thus, heparin was not available for all samples (heparin was available at the beginning and end but not during the middle of the sample collection period). Regardless of whether the syringe was heparinized, all blood samples were immediately transferred to lithium heparin blood tubes; tubes were then gently inverted several times. When ≥ 1.5 mL of blood was collected, 0.5 mL of the sample was placed in a separate tube and frozen at –80°C for determination of whole blood taurine concentration. The remainder of the blood sample was centrifuged within 1 hour after collection. After centrifugation, plasma was immediately harvested and placed in labeled 1.5-mL microcentrifuge tubes. Plasma from most of the pet cats and cats from 1 university colony (n = 94) was subjectively assessed for lipemia and hemolysis by 1 investigator (CRH), who assigned a grade of mild, moderate, or severe. Two hundred microliters of plasma was removed, and an equal volume of 6% SSA (with a norleucine internal standard) was added to precipitate protein in the sample. All samples were maintained at –80°C until analysis. Interval between sample collection and analysis ranged from 1 to 60 days.

Assessment of amino acids—Plasma amino acid and whole blood taurine concentrations were analyzed

as described elsewhere.[29] Briefly, an automated amino acid analyzer[a] was used to perform cation-exchange high-pressure liquid chromatography separation and ninhydrin-reactive colorimetric detection. Complete plasma amino acid analysis (of 24 amino acids) was performed for all pet cats. One of the colony facilities mandated specific husbandry and security protocols that precluded immediate treatment of the samples with SSA; thus, cysteine concentrations could not be determined for all cats.[30] Furthermore, whole blood taurine concentration was only determined in cats when ≥ 1.5 mL of blood was obtained.

Evaluation of the effect of signalment, body weight, BCS, and diet on amino acid concentrations—All owners of pet cats completed a questionnaire on diet history. The questionnaire included information on the diet or diets fed, amount fed per day, number of times fed per day, amount of time fed the current diet or diets, food storage method, treats, treat amounts, treat frequency, supplemental products, amount of supplemental products, frequency of supplemental products, access to other animals' food, any medications, and exercise frequency. Information on diet and health history was obtained from university records for all university-owned cats. Only cats fed a single diet were included in the analysis to determine whether diet affected plasma amino acid concentrations. Dietary protein content (in g/100 kcal) was obtained from the diet manufacturer or calculated from the guaranteed analysis by use of modified Atwater factors.[10]

Statistical analysis—Statistical analysis was performed with computer software programs.[b–d] Results for tests of normality as well as the mean; median; SD; 0, 2.5th, 50th, 97.5th, and 100th percentile values; and 95% reference intervals based on percentiles were determined for each amino acid.

Multiple linear regression was used to assess relationships of age, body weight, and BCS with plasma amino acid concentrations. Population measures and dietary data were described by use of median, mean, and SD when appropriate. Kruskal-Wallis tests were used to evaluate potential relationships between sex-neuter status and plasma amino acid concentrations. Mann-Whitney tests were used to investigate the potential association of heparin use during blood collection with amino acid concentration, and Jonckheere-Terpestra tests were used to assess the association between ordinal categories of lipemia and hemolysis with amino acid concentration. Values of $P \leq 0.05$ were considered significant. Values of $R^2 > 0.5$ were considered indicative of a strong linear correlation.

Relationships between dietary ingredients and plasma amino acid concentrations were investigated by use of Kruskal-Wallis tests followed by pairwise dietary comparisons with results adjusted for multiple comparisons to preserve a nominal type 1 error rate of 5%. Significant pairwise comparisons were reported as $P \leq 0.05$.

Results

The majority (83/120) of cats were pets. The remaining 37 cats were university-owned animals. Age ranged from 8 months to 16 years (median, 3 years; mean ± SD, 4.4 ± 3.13 years). Body weight ranged from 2.55 to 8.7 kg (median, 4.51 kg; mean, 4.76 ± 1.33 kg), and BCS ranged from 2.5 to 8 (median, 5.5; mean, 5.6 ± 1.06). Eighteen (15%) cats were considered obese (BCS ≥ 7). Fifty-six cats were neutered males, 29 were spayed females, 7 were sexually intact males, and 28 were sexually intact females. All of the sexually intact cats were university-owned animals. Breeds represented included domestic shorthair (n = 79), domestic medium-hair (10), mixed-breed cat (12), domestic longhair (7), Persian (7), Bengal (2), Siamese (1), Ragdoll (1), and Manx (1). The Persian and Bengal cats were part of a university colony, whereas the Siamese, Ragdoll, and Manx were pet cats. Domestic shorthair cats were represented in both university and pet cat populations. There was not a sufficient number of breeds represented to enable assessment of the relationship between breed and plasma amino acid concentrations.

University-owned cats were part of 2 separate colony facilities. The 2 facilities had no blood lines in common. At 1 facility (n = 13 cats), there were several sets of siblings and some parent-offspring pairs as well as unrelated cats from which blood samples were collected. At the second facility (n = 24 cats), there were siblings, half-siblings, and 1 parent-offspring pair from which blood samples were collected. There were some sibling groups in the pet cats and probably some parent-offspring pairs as well; however, these relationships were harder to assess because parentage information was not collected for the pet cats.

Insufficient blood samples (< 1.5 mL) were obtained from 31 cats; thus, whole blood taurine concentrations were determined for only 89 cats. Similarly, some samples obtained from university-owned cats were not treated with SSA immediately after collection; therefore, cysteine concentrations were determined for only 96 cats. Samples were collected into both heparinized (n = 54 samples) and unheparinized (66) syringes prior to being placed in lithium heparin tubes. There was a significant (range of P values, < 0.001 to 0.048) difference between heparinized syringe and unheparinized syringe samples for concentrations of the amino acids arginine, citrulline, glutamic acid, glycine, isoleucine, leucine, methionine, ornithine, threonine, tryptophan, and valine. Mean amino acid concentrations typically were lower in heparinized samples, although this was not the case for all amino acids, and not all concentrations differed significantly.

Increases in degree of lipemia had a significant (P = 0.008) positive association with threonine concentrations. Increases in degree of hemolysis had a significant positive association with the concentrations of isoleucine (P = 0.040), tryptophan (P = 0.030), and valine (P = 0.021) and a significant (P = 0.013) negative association with glutamic acid concentrations. The majority (17/25) of the amino acids assayed did not have a normal distribution, so nonparametric methods based on percentiles were used to determine the 95% reference intervals (**Table 1**).

Concentrations of arginine, asparagine, aspartic acid, cysteine, glutamic acid, glycine, hydroxyproline, isoleucine, lysine, ornithine, serine, threonine, trypto-

phan, and valine differed significantly (range of *P* values, < 0.001 to 0.038) among the 4 sex classifications (sexually intact male, castrated male, sexually intact female, and spayed female). Sexually intact females had higher concentrations of arginine, isoleucine, and valine, compared with the 3 other groups (all *P* values < 0.001). There were no significant differences between spayed females and castrated males; however, sexually intact females had significantly higher amino acid concentrations of arginine, isoleucine, tryptophan, and valine (range of *P* values, < 0.001 to 0.038) and significantly lower concentrations of aspartic acid ($P = 0.019$) than sexually intact males. Although there was a significant negative linear relationship between age and amino acid concentration for arginine ($P = 0.019$), glutamic acid ($P = 0.035$), and ornithine ($P = 0.029$), the linear correlation was weak ($R^2 = 0.045$, 0.037, and 0.040, respectively). As body weight increased, there was a significant ($P = 0.032$) positive linear relationship for plasma concentrations of histidine, whereas there was a significant (range of *P* values, < 0.001 to 0.032) negative relationship for concentrations of alanine, arginine, glutamic acid, glycine, hydroxyproline, isoleucine, lysine, ornithine, serine, and valine. Arginine, glutamic acid, glycine, hydroxyproline, isoleucine, lysine, ornithine, serine, and valine concentrations had a significant (range of *P* values, < 0.001 to 0.049) positive linear relationship with increases in BCS, whereas methionine concentrations had a significant ($P = 0.007$) negative relationship. The linear correlation was weak for concentrations of all amino acids for body weight (range of R^2, 0.039 to 0.123) and BCS (range of R^2, 0.033 to 0.139).

Fifty-four (39 dry, 13 canned, and 2 frozen-raw) diets were fed to the cats. Twelve diets were widely available at grocery and discount stores, 12 were veterinary prescription diets, and the other 30 were available from large pet supply chains or specialty stores. The 12 prescription diets included weight management diets (n = 6 diets), dental diets (2), renal diets (2), a urinary diet (1), and a gastrointestinal diet (1). Both renal diets were fed in addition to maintenance diets to healthy cats because other cats in the households had renal disease. The urinary diet was fed to a cat without recent or current clinical signs of urinary tract disease. The gastrointestinal diet had been prescribed to treat a cat with diarrhea 6 years prior to the study, and the owner opted to continue feeding it despite resolution of the problem.

University-owned cats were fed 6 diets; 10 cats were the most that were fed one of these diets. Pet cats were fed 48 diets; 13 cats were the most that were fed one of these diets. All the diets used in this study exceeded the NRC recommended allowance for dietary crude protein concentration for adult feline maintenance (5 g/100 kcal)[10] and had passed feeding trials or were formulated to meet Association of American Feed Control Officials minimum nutrient profiles for adult maintenance. All but 7 cats had been fed the same diet or combination of diets for at least 1 month before the study, with many cats being fed the same diet for 1 year or more prior to the study. All 7 cats with a more recent dietary change obtained most of their daily calories from the same diet for at least 1 week before blood samples were collected.

Twenty-three cats were fed specific amounts at each meal, 58 cats were fed ad libitum, and the remaining 39 cats were fed unknown or varying amounts, often because > 1 cat shared a feed bowl in multiple-cat households. Twenty-six of the 120 cats were fed > 1 diet, and many of the owners did not know the amount of each diet fed and sometimes did not know the diet or diets being fed at the time of sample collection. These 26 cats were excluded from analysis of the effects of diet on plasma amino acid and whole blood taurine concentrations.

None of the cats were fed supplemental products. Twenty-eight (23%) cats were fed treats, either commercial treats created for cats or treats in the form of foods consumed by humans. Of these 28 cats, only 9 were reportedly fed treats daily. The remaining 19 cats received treats from several times a week to once a month or less often. For 7 of the 9 cats that received treats daily, the treats did not provide a substantial (< 10%) portion of daily caloric intake. The other 2 cats that received treats daily obtained approximately 13% of their daily calories from treats. Because of the inconsistency of treat administration and the low percentage of daily calories provided by treats, this information was not included in the analysis to investigate potential associations between dietary protein and ingredients and plasma amino acid and whole blood taurine concentrations.

Data from the 94 cats eating only 1 diet were used to determine the relationship between diet and plasma amino acid concentrations. Of the 30 diets fed to this group of cats, 26 were dry expanded kibble, 2 were frozen-raw, and 2 were canned diets. Seven diets (6 dry and 1 canned) were veterinary prescription diets. Nineteen of the 94 cats received treats, with only 6 of the 19 cats receiving treats daily. Two cats obtained approximately 13% of their daily calories from commercial treats. Twenty-five of the 30 diets were supplemented with taurine, 14 were supplemented with methionine, 9 were supplemented with lysine, and 1 was supplemented with tryptophan.

Because of a lack of specific food intake information, protein intake could not be determined for most of the cats. Therefore, the protein content of the diet on a caloric basis (rather than the actual intake of each cat) was used for analysis. Dietary protein concentration ranged from 7.3 to 23.1 g/100 kcal (median, 9.32 g/kcal; mean ± SEM, 11.31 ± 5.19 g/kcal), with all but 3 diets containing between 7.3 and 12.0 g/100 kcal (the protein concentration for those 3 diets ranged from 18.6 to 23.1 g/100 kcal).

Protein concentration of the diet had a significant (range of *P* values, < 0.001 to 0.030) effect on amino acid concentrations for 15 amino acids. There were positive correlations between dietary protein concentration and plasma concentrations of arginine, glutamic acid, glycine, hydroxyproline, isoleucine, lysine, ornithine, serine, and valine, whereas plasma concentrations of aspartic acid, histidine, methionine, phenylalanine, proline, and taurine were negatively correlated with dietary protein concentration. However, none of these relationships had a strong linear correlation (range of R^2, 0.043 to 0.403). When only diets with ≤ 12 g of protein/100 kcal were examined, there were no significant

Table 1—Plasma amino acid and whole blood taurine concentrations in 120 adult cats eating commercially prepared diets.

Amino acid	95% reference interval (nmol/mL)	Median (nmol/mL)	Mean (nmol/mL)	SD	SEM	*P* value for test of normality
Alanine	270–925	425	462	160	15	< 0.001*
Arginine	46–200	84	95	38	3	< 0.001*
Asparagine	52–143	88	91	25	2	0.099
Aspartic acid	8–67	26	28	12	1	< 0.001*
Citrulline	9–30	17	18	6	1	0.031*
Cysteine†	12–42	24	26	9	1	< 0.001*
Glutamine	430–953	648	664	134	12	0.129
Glutamic acid	25–160	62	73	38	4	< 0.001*
Glycine	217–975	323	398	279	26	< 0.001*
Histidine	68–164	115	116	24	2	0.817
Hydroxyproline	21–145	60	63	31	3	< 0.001*
Isoleucine	30–141	55	63	29	3	< 0.001*
Leucine	78–278	135	146	49	5	< 0.001*
Lysine	44–282	89	108	61	6	< 0.001*
Methionine	20–128	61	64	28	3	0.003*
Ornithine	7–55	17	21	12	1	< 0.001*
Phenylalanine	38–103	71	70	15	1	0.615
Proline	104–423	248	258	76	7	0.572
Serine	92–413	159	179	85	8	< 0.001*
Taurine	37–252	108	118	55	5	< 0.001*
Whole blood taurine‡	275–701	455	457	103	11	0.154
Threonine	77–287	169	173	54	5	0.244
Tryptophan	30–104	57	60	17	2	0.003*
Tyrosine	31–86	56	57	15	1	0.236
Valine	85–302	148	164	62	6	< 0.001*

*Values of $P \leq 0.05$ were not compatible with a normal distribution; nonparametric methods based on percentiles were used to determine all 95% reference intervals. †Represents results for 96 cats. ‡Represents results for 89 cats.

associations between dietary protein concentration and plasma amino acid concentrations.

Supplementation of diets with taurine and methionine was significantly ($P = 0.007$ and $P = 0.015$, respectively) correlated with higher plasma concentrations of these amino acids. However, taurine supplementation was not significantly ($P = 0.360$) correlated with whole blood taurine concentrations, and lysine supplementation was not significantly ($P = 0.440$) correlated with plasma lysine concentrations. An analysis of plasma tryptophan concentrations was not conducted because only 1 diet was supplemented with tryptophan.

Seventy-four cats were fed diets that contained an animal-source product as the first ingredient listed. The remaining 20 cats were fed diets with a plant-source product as the first ingredient listed. The second ingredient listed was of plant origin in diets fed to 57 cats, whereas the second ingredient listed was of animal origin in diets fed to 37 cats. Twenty cats were fed diets that had animal products as the first 2 ingredients listed.

Regardless of the first 4 dietary ingredients listed, there were no significant associations between ingredients and plasma concentrations of aspartic acid, citrulline, cysteine, hydroxyproline, tryptophan, and tyrosine or whole blood concentrations of taurine. There were significant correlations with some amino acid concentrations and dietary ingredients, but they were not consistent throughout the ingredient list. For example, plasma concentrations of arginine, asparagine, glutamine, isoleucine, lysine, ornithine, proline, and valine were significantly (all *P* values, < 0.001) lower when chicken by-product meal was the first ingredient listed than when corn was the first ingredient listed. However, when chicken by-product meal was the second ingredient listed, plasma concentrations of histidine, leucine, lysine, ornithine, and proline were all significantly (all *P* values, < 0.001) higher than when the second ingredient listed was corn.

When the first ingredients listed were divided into plant-source versus animal-source products, there were significant (range of *P* values, < 0.001 to 0.031) differences in plasma concentrations of alanine, asparagine, aspartic acid, glutamine, histidine, leucine, methionine, phenylalanine, proline, taurine, threonine, and tyrosine. All of these amino acid concentrations were higher when the first ingredient listed was a plant-source product than when the first ingredient listed was an animal-source product. When the second ingredient listed was an animal-source product, as opposed to a plant-source product, plasma concentrations of alanine, arginine, glutamine, glutamic acid, glycine, hydroxyproline, isoleucine, leucine, lysine, ornithine, proline, serine, threonine, and valine were significantly (range of *P* values, < 0.001 to 0.023) higher.

Discussion

The objective of the study reported here was to develop reference ranges for plasma concentrations of amino acids and whole blood concentrations of taurine in healthy cats eating commercial diets and to determine the effect of age, sex, body weight, BCS, dietary protein, and dietary ingredients on these findings. A

power calculation determined that 120 animals were required to establish reliable reference intervals.[31] To our knowledge, we compiled data on amino acid concentrations from the largest population of adult cats eating commercial diets that has been reported to date (120 cats for all amino acids, except for whole blood taurine [89 cats] and cysteine [96 cats]).

This study population, although not an exact representation of the general cat population, is likely a close enough representation for these reference ranges to be meaningful. Twelve (10%) cats of the study population were purebred cats, which corresponded to the percentage of purebred cats in the general population in another report.[32] Unfortunately, these 12 cats did not represent a sufficient number of cats to assess differences in amino acid concentrations among breeds. The percentage of overweight and obese cats (BCS ≥ 6) in the study was 41% (49/120), which is higher than the 35% reported for the general cat population in another study.[33] The mean BCS was 5.6 for the cats in this study; only 18 of 120 (15%) cats had a BCS ≥ 7. It is possible that the subjective nature of assigning a BCS influences the proportion of overweight and obese cats reported by different sources.[34] Although some associations between body weight or BCS and plasma amino acid concentrations were significant, linear correlations were weak and no additional relationships could be discerned from the data. This finding was consistent with reported plasma and whole blood taurine concentrations in dogs[21] and plasma amino acid concentrations in adult cats.[11]

Castrated male cats outnumbered spayed female cats in a ratio of almost 2:1 in the study population, despite results of a recent survey[32] in which it was reported that female cats were kept as pets more often than are male cats. Because only pet cats with amiable dispositions were used in our study, it is possible that more female than male cats were adverse to procedures involved with collection of blood samples. Alternatively, this owner population may have specifically sought out male cats over female cats for other reasons. University-owned cats were included in the study population to introduce sexually intact cats into the study population because all the pet cats in the study population were spayed or neutered, whereas 87% of the overall pet cat population are spayed or neutered.[32] With the inclusion of the university-owned cats, 85 of 120 (71%) cats in the study population were spayed or neutered.

Significant differences among the 4 sex classifications were detected for concentrations of multiple amino acids. It was interesting that there were no significant differences between spayed females and neutered males, but there were differences between sexually intact males and females. These results suggest that hormonal differences between the sexes are likely affecting plasma amino acid concentrations. Studies in other species have also revealed an association between sex and plasma or serum amino acid concentrations. A study[35] in humans revealed that women have lower serum concentrations of proline, leucine, isoleucine, and tyrosine, compared with concentrations in men. In another study,[36] it was reported that elderly women have lower serum concentrations of essential amino acids, compared with concentrations in elderly men. A similar sex effect has been found in rats, with female rats having lower plasma concentrations of almost all amino acids than the concentrations in male rats.[37] It is unclear in these studies as to the factors responsible for the sex differences because each study examined a different population and not all populations involved hormonally active individuals. Further assessment of cats in all 4 sex classifications that are eating the same diet would be necessary to further clarify the true effect of sex and neuter status.

Although there was a significant relationship between age and amino acid concentration for several amino acids, the linear correlations were weak. In contrast, investigators in a study[6] of adult cats found an inverse relationship between plasma taurine concentration and age, but they did not examine all of the amino acids or the association with diet. However, that result was detected in a population of cats older than the population of cats in our study (mean ages, 8.3 and 8.9 years vs 4.4 years for the study reported here). Additionally, that study[6] was designed to assess plasma taurine concentrations in cats with heart disease, and it is possible that the correlation with age was more related to underlying disease than to age of the cats.

Only adult cats were used in the aforementioned study[6] and the study reported here. It is likely that actively growing kittens have plasma amino acid profiles that differ substantially from those of adult cats. Data from a study[13] in kittens indicated higher mean plasma concentrations of all amino acids, except citrulline, compared with the plasma concentration in our study population of adult cats. Investigators in another study[38] reported higher mean plasma concentrations for alanine, arginine, asparagine, cysteine, glutamic acid, glycine, histidine, lysine, methionine, ornithine, proline, threonine, and tryptophan, whereas the mean plasma concentrations of glutamine, isoleucine, phenylalanine, and tyrosine were lower, compared with the concentrations determined in our study. Mean concentrations of leucine and valine in that study[38] were similar to those in our study. However, an effect of diet cannot be ruled out because both of those previous studies[13,38] used animals fed purified diets. Because both of those studies used the same analytic methods as the study reported here, it is unlikely that this factor accounts for the differences observed.

Amino acid concentrations typically were lower for most amino acids in samples collected in heparinized syringes, compared with concentrations for samples collected in unheparinized syringes, which suggested that dilution of the samples may have been responsible for the difference. Because variable amounts of blood were collected from the cats, the effect of dilution was not consistent for all samples and could not be quantitatively tested. Although some of these concentration differences were significant, they were of small magnitude and unlikely to have a major clinical impact. It was unlikely to be a population bias contributing to these results because once heparin became unavailable, both cat populations (pet cats and university-owned cats) were affected equally. Amino acid concentrations were assayed in plasma rather than serum; thus, it was important that blood samples did not

clot prior to analysis. Therefore, the authors recommend the use of heparinized syringes to ensure that a plasma sample is obtained.

The effect of sample hemolysis on plasma amino acid concentrations in this study likely reflected the higher concentrations of amino acids in RBCs, compared with concentrations in plasma.[9] It is established that conditions that alter the concentration of cellular components in the blood affect plasma amino acid concentrations.[39] The finding that glutamic acid concentration was negatively correlated with hemolysis was unexpected because glutamic acid concentrations are higher in RBCs than in plasma.[9] It is possible that this result may have been artifactual. Because of the variability in plasma amino acid concentrations and the few moderately (6/94 [6%]) and severely (2/94 [2%]) hemolyzed samples, the effects of this sampling artifact could not be clearly defined. Additionally, the assessment of both hemolysis and lipemia in this study was subjective. Further investigation of the impact of hemolysis and lipemia via objective measurements of these changes (such as absorbance data from spectrophotometry) is needed.

Treats composed a small percentage of the daily caloric intake of the cats; thus, they were not included in the calculations of dietary protein or the ingredient comparisons. Twenty-three percent of the study cats received treats at least monthly. It has been reported[40] that approximately 26% of pet cats receive treats daily and 44% receive treats at least once per week.

It was impossible to calculate protein intake for most of the cats fed ad libitum or fed vague or varying amounts of food. In addition, many cats were fed > 1 diet. For these reasons, dietary protein concentration (rather than actual intake) was assessed, and only cats fed 1 diet were included in the analysis. Although the dietary protein concentration was examined on a caloric basis, it is still possible that cats may have had higher or lower energy requirements than expected and thus were consuming more or less protein than predicted. All of the diets exceeded NRC recommendations for feline maintenance of 5 g/100 kcal of protein, with protein concentrations ranging from 7.3 to 23.1 g/100 kcal. All diets, except for 3, provided protein concentrations of ≤ 12.0 g/100 kcal. Although dietary protein concentration was significantly correlated with plasma amino acid concentrations for 15 amino acids, these were weak linear correlations. When the data for the 3 diets containing the highest concentrations of protein (18.6 to 23.1 g/100 kcal) were excluded, the correlations were no longer significant.

The essential amino acid requirements for cats were originally determined with growth response curves as well as by comparing plasma amino acid concentrations obtained when feeding diets containing varying concentrations of the amino acid of interest.[10] In other species, it has been determined that plasma amino acid concentrations remain low until the requirement is met and then increase markedly.[41] Studies[42,e] have revealed that when lysine is provided in excess of dietary requirements in cats, plasma amino acid concentrations do not reliably predict the relative proportion of the excess. Data from these studies[41,e] and the study reported here suggest that diets providing amino acids and crude protein concentrations in excess of the recommended allowances for adult feline maintenance established by the NRC should not necessarily be expected to cause higher plasma amino acid concentrations than diets providing amino acids and crude protein concentrations closer to the minimal requirements. This effect may be especially relevant in cats consuming commercially available foods, compared with cats consuming purified diets.

The relationships of ingredients to amino acid concentrations were unexpected. In this study, amino acid concentrations, including many essential amino acids, were lower in cats consuming diets that contained animal protein as the first ingredient listed. Although plant proteins are poorer sources of taurine and other sulfur-containing amino acids, compared with many animal proteins, cats consuming diets containing a plant-source ingredient (usually a grain) as the first ingredient listed had higher mean taurine concentrations than cats consuming diets with an animal protein as the first ingredient listed. It is likely that other factors were involved because diets that contained higher proportions of protein from plant sources may be more consistently and aggressively supplemented with taurine. The concentrations of supplemental amino acids are not required to be reported on the label of feline diets, which makes it difficult to compare diets.

Taurine and methionine supplementation of diets was correlated with higher plasma concentrations of these amino acids. However, taurine supplementation was not correlated with whole blood taurine concentrations. This finding is not surprising because plasma taurine concentrations are thought to be more indicative of recent meals than are whole blood taurine concentrations.[26]

Lysine supplementation was not correlated with plasma lysine concentrations. The diets with added lysine may have been sufficiently limiting in this amino acid before supplementation such that additional lysine only brought them up to the concentrations in the unsupplemented diets. The lack of correlation between lysine supplementation and plasma lysine concentrations is likely to be a dietary factor rather than a biological factor unique to the cats eating the supplemented diets.

Whole blood taurine concentration is considered to be a more accurate measure of taurine status than is plasma taurine concentration[9] in cats and reflects skeletal muscle concentrations more accurately than do plasma taurine concentrations.[43] In the study reported here, 3 cats had plasma taurine concentrations that would be considered a risk factor for development of dilated cardiomyopathy (< 40 nmol/mL).[10] However, whole blood taurine concentrations in these cats were considered to be reflective of normal physiologic taurine status (> 200 nmol/mL).[10] It was later determined that 2 of the 3 cats had been placed under substantial caloric restriction (relative to calculated energy needs) by their owner in an attempt to maintain a lean body condition while feeding a diet designed for adult cats with normal energy requirements. Because nutrient requirements are established with the assumption of av-

erage energy needs, animals with lower than expected calorie requirements will consume less total nutrients from a diet designed to support a typical animal. This likely explains the low plasma taurine concentrations determined in these 2 cats. The findings in this study support the contention that whole blood taurine concentrations should always be assessed in addition to plasma taurine concentrations to determine true taurine status.

Alterations in plasma amino acids attributable to differences in dietary ingredients have been reported. Because of the association of dilated cardiomyopathy with taurine deficiency in dogs and cats, most studies have concentrated on this amino acid. The substitution of rice bran[44] and soy protein[29] for corn starch and casein in purified diets, respectively, can decrease plasma taurine concentrations in cats. In another study,[21] diets containing whole grain brown rice as the first plant ingredient listed were associated with lower whole blood taurine concentrations in dogs, compared with results for diets with ground corn as the first plant ingredient listed, whereas diets containing lamb meal and rice were associated with lower mean whole blood taurine concentrations than were diets containing other combinations of animal and plant ingredients. In the study reported here, we found no correlation between any of the first 4 ingredients listed and whole blood taurine or plasma cysteine concentrations.

In our study, we found that feeding taurine-supplemented diets resulted in significantly higher plasma taurine concentrations, independent of other dietary ingredients. However, dietary ingredients still had an impact on plasma taurine concentration. Plasma taurine concentrations were significantly higher when the first ingredient listed was corn instead of beef or chicken; all diets, except for 1, in which corn was the first ingredient listed were supplemented with taurine. However, plasma taurine concentrations were significantly lower when the second ingredient listed was rice or beef liver rather than chicken by-product meal, despite the fact that all of the diets, except for 1, with rice or beef liver as the second ingredient listed were supplemented with taurine. This discrepancy was likely attributable to the contribution of ingredient interactions and, possibly, other confounding factors such as variable amounts of supplemental taurine in the diets or variable caloric intake by the cats consuming them. Differences in associations between ingredients and amino acid concentrations between this study and the data reported for a study[21] in dogs may be attributable to differences in the metabolism of sulfur-containing amino acids in cats, compared with metabolism in dogs, or differences in study design. It is likely that diet and population factors also may explain the differences between the studies in cats that examined rice bran[44] and soy protein[29] and plasma taurine concentrations because those studies were performed under more controlled circumstances and used purified diets.

It is difficult to assess the ingredients in a commercial diet that provide the greatest proportions of nutrients because ingredients are listed by order of weight and can be further subdivided into constituent parts. Because of differences in moisture, a diet that has chicken as the first ingredient listed may provide less chicken protein than a diet that has chicken meal as the first ingredient listed. Similarly, an ingredient such as rice may contribute a substantial proportion of the nutrients to a diet despite being listed later in the ingredient list because this component is low in moisture and could appear as rice, brewer's rice, and rice flour in the same diet. Currently, manufacturers are not required to list the amounts of each ingredient in a diet, and this information is generally considered to be proprietary. In our study, the relationships between plasma amino acid concentrations and diet were difficult to interpret because of the number of diets, ingredients, and amino acids assessed. Many of the relationships were inconsistent with results reported in other studies or expected nutrient amounts of certain ingredients. Moreover, the results became more difficult to interpret as ingredients farther down the list (ingredients 3 through 7) were analyzed. This study illustrated the limitations of assessing the nutritional adequacy of diets by use of criteria such as the ingredient list. It is the authors' experience that diets are often assessed solely on the basis of ingredient lists, disregarding the legal definitions for ingredients as well as how ingredient lists are developed by manufacturers within the current regulatory framework.

The study reported here was the first large study to determine plasma amino acid concentrations in cats eating commercial diets. Despite some limitations, the plasma amino acid and whole blood taurine concentrations reported here are likely representative of the general pet cat population. This information will be of value in clinical assessment of patients and should encourage further research into alterations in amino acid concentrations in many disease processes and conditions in cats.

a. Biochrom 30 amino acid analyzer, Biochrom Ltd, Cambridge, England.
b. MedCalc 10.0.2.0, MedCalc Software bvba, Mariakerke, Belgium.
c. StatXact 8.0, Cytel Software Corp, Cambridge, Mass.
d. BMDP PC90, BMDP Statistical Software Inc, Los Angeles, Calif.
e. Larsen JA, Fascetti AJ, Calvert CC, et al. Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis, Calif: Unpublished data, 2009.

References

1. Hayes KC, Carey RE. Schmidt SY. Retinal degeneration associated with taurine deficiency in the cat. *Science* 1975;188:949–951.
2. Pion PD, Kittleson MD, Rogers QR, et al. Myocardial failure in cats associated with low plasma taurine: a reversible cardiomyopathy. *Science* 1987;237:764–768.
3. Strombeck DR, Rogers Q. Plasma amino acid concentrations in dogs with hepatic disease. *J Am Vet Med Assoc* 1978;173:93–96.
4. Albisser AM, Cheng DC, Yamasaki Y, et al. Changes in blood amino acids account for the insulin and glucagon responses to mixed meals in dogs. *Diabetes Res* 1985;2:49–55.
5. Hansen SH. The role of taurine in diabetes and the development of diabetic complications. *Diabetes Metab Res Rev* 2001;17:330–346.
6. McMichael MA, Freeman LM, Selhub J, et al. Plasma homocysteine, B vitamins, and amino acid concentrations in cats with cardiomyopathy and arterial thromboembolism. *J Vet Intern Med* 2000;14:507–512.
7. Borsheim E, Bui QU, Wolfe RR. Plasma amino acid concentra-

tions during late rehabilitation in patients with traumatic brain injury. *Arch Phys Med Rehabil* 2007;88:234–238.
8. Maggs DJ, Nasisse MP, Kass PH. Efficacy of oral supplementation with L-lysine in cats latently infected with feline herpesvirus. *Am J Vet Res* 2003;64:37–42.
9. Zicker SC, Rogers QR. Use of plasma amino acid concentrations in the diagnosis of nutritional and metabolic diseases in veterinary medicine, in *Proceedings*. IVth Cong Int Soc Anim Clin Biochem 1990;1–16.
10. National Research Council ad hoc Committee on Dog and Cat Nutrition. *Nutrient requirements of dogs and cats*. Washington, DC: National Academies Press, 2006.
11. Goldstein RE, Marks SL, Cowgill LD, et al. Plasma amino acid profiles in cats with naturally acquired chronic renal failure. *Am J Vet Res* 1999;60:109–113.
12. Strieker MJ, Morris JG, Rogers QR. Increasing dietary crude protein does not increase the essential amino acid requirements of kittens. *J Anim Physiol Anim Nutr (Berl)* 2006;90:344–353.
13. Rogers QR, Morris JG. Essentiality of amino acids for the growing kitten. *J Nutr* 1979;109:718–723.
14. Hargrove DM, Rogers QR, Calvert CC, et al. Effects of dietary excesses of the branched-chain amino acids on growth, food intake and plasma amino acid concentrations of kittens. *J Nutr* 1988;118:311–320.
15. Hammer VA, Rogers QR, Morris JG. Dietary crude protein increases slightly the requirement for threonine in kittens. *J Nutr* 1996;126:1496–1504.
16. Lewis AJ, Bayley HS. Amino acid bioavailability. In: Ammerman CB, Baker DH, Lewis AJ, eds. *Bioavailability of nutrients for animals: amino acids, minerals and vitamins*. San Diego: Academic Press Inc, 1995;35–52.
17. Morris JG, Rogers QR, O'Donnell JA. Lysine requirement of kittens given purified diets for maximal growth. *J Anim Physiol Anim Nutr (Berl)* 2004;88:113–116.
18. Rutherfurd SM, Rutherfurd-Markwick KJ, Moughan PJ. Available (ileal digestible reactive) lysine in selected pet foods. *J Agric Food Chem* 2007;55:3517–3522.
19. Rutherfurd SM, Moughan PJ. Determination of sulfur amino acids in foods as related to bioavailability. *J AOAC Int* 2008;91:907–913.
20. Hurrell RF, Finot PA. Food processing and storage as a determinant of protein and amino acid availability. *Experientia Suppl* 1983;44:135–156.
21. Delaney SJ, Kass PH, Rogers QR, et al. Plasma and whole blood taurine in normal dogs of varying size fed commercially prepared food. *J Anim Physiol Anim Nutr (Berl)* 2003;87:236–244.
22. Burns RA, LeFaivre MH, Milner JA. Effects of dietary protein quantity and quality on the growth of dogs and rats. *J Nutr* 1982;112:1843–1853.
23. Major EJ, Batterham ES. Availability of lysine in protein concentrates as determined by the slope-ratio assay with chicks and comparisons with rat, pig and chemical assays. *Br J Nutr* 1981;46:513–519.
24. Williams PA, Hodgkinson SM, Rutherfurd SM, et al. Lysine content in canine diets can be severely heat damaged. *J Nutr* 2006;136:1998S–2000S.
25. Ousterhout LE, Grau CR, Lundholm BD. Biological availability of amino acids in fish meals and other protein sources. *J Nutr* 1959;69:65–73.
26. Pion PD, Lewis J, Greene K, et al. Effect of meal-feeding and food deprivation on plasma and whole blood taurine concentrations in cats. *J Nutr* 1991;121:S177–S178.
27. Laflamme D. Development and validation of a body condition score system for cats: a clinical tool. *Feline Pract* 1997;25(5–6):13–18.
28. FDA Recall Information Web site. Baxter to proceed with recall of remaining heparin sodium vial products. Available at: www.fda.gov/oc/po/firmrecalls/baxter02_08.html. Accessed Aug 13, 2008.
29. Kim SW, Morris JG, Rogers QR. Dietary soybean protein decreases plasma taurine in cats. *J Nutr* 1995;125:2831–2837.
30. Torres CL, Miller JW, Rogers QR. Determination of free and total cyst(e)ine in plasma of dogs and cats. *Vet Clin Pathol* 2004;33:228–233.
31. Jennen-Steinmetz C, Wellek S. A new approach to sample size calculation for reference interval studies. *Stat Med* 2005;24:3199–3212.
32. American Pet Products Manufacturers Association. *2007–2008 APPMA National Pet Owners Survey*. Greenwich, Conn: American Pet Products Manufacturers Association Inc, 2008.
33. Lund EM, Armstrong PJ, Kirk CA, et al. Prevalence and risk factors for obesity in adult cats from private US veterinary practices. *Intl J Appl Res Vet Med* 2005;3:88–96.
34. Burkholder WJ. Use of body condition scores in clinical assessment of the provision of optimal nutrition. *J Am Vet Med Assoc* 2000;217:650–654.
35. Tomiya M, Fukushima T, Watanabe H, et al. Alterations in serum amino acid concentrations in male and female schizophrenic patients. *Clin Chim Acta* 2007;380:186–190.
36. Pitkanen HT, Oja SS, Kemppainen K, et al. Serum amino acid concentrations in aging men and women. *Amino Acids* 2003;24:413–421.
37. Chance WT, Grossman CJ, Newrock R, et al. Effects of electromagnetic fields and gender on neurotransmitters and amino acids in rats. *Physiol Behav* 1995;58:743–748.
38. Taylor TP, Morris JG, Willits NH, et al. Optimizing the pattern of essential amino acids as the sole source of dietary nitrogen supports near-maximal growth in kittens. *J Nutr* 1996;126:2243–2252.
39. Backus RC, Howard KA, Rogers QR, et al. Leukocytosis and thrombocytosis caused by consumption of a low magnesium and high calcium diet elevates whole-blood taurine concentration in cats. *J Nutr* 1998;128:2581S–2583S.
40. Laflamme DP, Abood SK, Fascetti AJ, et al. Pet feeding practices of dog and cat owners in the United States and Australia. *J Am Vet Med Assoc* 2008;232:687–694.
41. Zimmerman RA, Scott HM. Interrelationship of plasma amino acid levels and weight gain in the chick as influenced by suboptimal and superoptimal dietary concentrations of single amino acids. *J Nutr* 1965;87:13–18.
42. Fascetti AJ, Maggs DJ, Kanchuk ML, et al. Excess dietary lysine does not cause lysine-arginine antagonism in adult cats. *J Nutr* 2004;134:2042S–2045S.
43. Pacioretty L, Hickman MA, Morris JG, et al. Kinetics of taurine depletion and repletion in plasma, serum, whole blood and skeletal muscle in cats. *Amino Acids* 2001;21:417–427.
44. Stratton-Phelps M, Backus RC, Rogers QR, et al. Dietary rice bran decreases plasma and whole-blood taurine in cats. *J Nutr* 2002;132:1745S–1747S.