



# Vet-LIRN Update on Investigation into Dilated Cardiomyopathy

February 2019

This update describes FDA and Vet-LIRN's investigative efforts through November 2018 at a level of technical detail geared toward veterinarians. For more general information, please visit FDA Investigation into Potential Link between Certain Diets and Canine Dilated Cardiomyopathy (</animal-veterinary/news-events/fda-investigation-potential-link-between-certain-diets-and-canine-dilated-cardiomyopathy>).

In July 2018, the FDA alerted (</animal-veterinary/cvm-updates/fda-investigating-potential-connection-between-diet-and-cases-canine-heart-disease>) the public about an investigation into reports of canine dilated cardiomyopathy (DCM) in dogs eating certain pet food. DCM itself is not considered rare in dogs, but these reports are unusual because many of the reported cases occurred in breeds of dogs not typically genetically predisposed to the disease and were reported to have been fed diets containing legumes like peas or lentils, other legume ingredients (pulses) or potatoes as main ingredients. Many of these products are labeled as “grain-free” or “zero-grain.”

Since then, the FDA's Center for Veterinary Medicine (CVM) has taken a multi-pronged approach to the investigation. CVM veterinarians, nutritionists, pathologists and epidemiologists are collaborating with several sectors of the animal health world to collect and evaluate information about the DCM cases and the diets pets ate prior to becoming ill. A key partner in the investigation is the Veterinary

Laboratory Investigation and Response Network (Vet-LIRN), a collaboration of government and veterinary diagnostic laboratories.

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## Food Testing

### Minerals and Elements

Prior to FDA's July 2018 notice about the investigation, Vet-LIRN collected and tested case-related food samples and purchased store-bought products labelled "grain free" for:

- Calcium
- Phosphorous
- Magnesium
- Cobalt
- Copper
- Zinc
- Selenium
- Iodine

The products tested within normal nutrient concentrations recommended in the Association of American Feed Control Officials (AAFCO) Dog and Cat Food Nutrient Profiles published in the AAFCO Official Publication (OP).

## Nutritional Screening and Amino Acid Content

Because some products labelled “grain free” and containing legumes and/or potato products were potentially associated with DCM, Vet-LIRN collected case-related food samples and purchased store-bought products labelled “grain free”. These products were tested, as well as grain-containing products not associated with development of DCM, to investigate any nutritional differences that could explain the development of DCM. As of November 30, 2018, Vet-LIRN has tested grain-free products and grain-containing products for the following:

- protein, fat, moisture
- crude fiber, total dietary fiber, soluble fiber, insoluble fiber
- total starch, resistant starch
- cystine, methionine, and taurine

The average percent protein, fat, total taurine, total cystine, total methionine, total methionine-cystine, and resistant starch content on a dry matter basis were similar for both grain-free and grain-containing products (Table 1).

**Table 1. Average values for grain-free and grain-containing products shown on a dry matter basis**

Measurement	Average Grain-Containing	Average Grain-Free

Protein	28.8 %	29.6 %
Fat	15.2 %	16.6 %
Total Taurine	0.13 %	0.14 %
Total Cystine	0.3 %	0.29 %
Total Methionine	0.59 %	0.55 %
Total Methionine-Cystine	0.89 %	0.84 %
Total Dietary Fiber	8.6 %	12.1 %
Crude Fiber	2.5 %	4.6 %
Insoluble Fiber	7.2 %	11.7 %
Soluble Fiber	1.46	<1.41
Starch	37.4 %	26 %
Resistant Starch	<2.15 %	<2.15 %
Choline Chloride	3289 ppm	2731 ppm
Choline	2453 ppm	1979 ppm

All but one of the grain-free products had methionine-cystine values above the minimum nutrient concentration recommended in the AAFCO OP of 0.65% for adult maintenance foods for dogs. The grain-free foods had greater total dietary fiber, crude fiber, and insoluble fiber, and less starch and choline on average than the grain-containing products. One grain-free product contained choline levels below the minimum concentration recommended for adult maintenance food for dogs, as published in the AAFCO OP.

The FDA is still trying to better understand if (and how) taurine, cystine, and methionine metabolism (both absorption and excretion) may have a role in DCM in the

context of the foods being fed.

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## Case Information

Between January 1, 2014 and November 30, 2018, the FDA received reports of 325 dogs and 10 cats diagnosed with DCM. The FDA additionally received many reports of non-DCM cardiac disease in dogs and cats during this timeframe. In an effort to better understand the reported cardiac diseases, FDA investigated many of the DCM cases, as well as some of these non-DCM cardiac cases by reviewing medical records and performing dietary and environmental exposure interviews. Additionally, FDA is working to determine whether there is a disease continuum that includes cardiac changes that could indicate developing DCM or if there are other cardiac changes of importance.

FDA's review of medical records for reports is ongoing and the following data is a summary for only a subset of collected medical records for both DCM and non-DCM cardiac cases. Of 168 dogs and 6 cats whose medical records were reviewed, 104 dogs and 2 cats were DCM cases with heart changes characteristic of DCM on cardiac ultrasound – including decreased ventricular systolic function and dilation. Approximately 67% of dogs (n=71) of those with confirmed DCM had progressed to congestive heart failure. Of the pets with confirmed DCM, approximately 18% (n=19) also had evidence of degenerative valvular disease and 11% (n=12) had atrial fibrillation. Approximately 42% (n=45) of dogs with DCM had a history of allergies or sensitivities to an environmental allergen and/or food that was manifested as dermatitis, otitis, or gastrointestinal disease. Approximately 9% (n=9) and 8% (n=8) of dogs with DCM had a history of hypothyroidism and one or more tick-borne diseases (e.g. Lyme, Anaplasmosis), respectively.

According to the medical records reviewed for the non-DCM cardiac disease cases, other cardiac changes were present on echocardiogram, including degenerative valvular disease, tricuspid and mitral valve regurgitation, and borderline to decreased left ventricular systolic function. For animals without DCM, there may be a spectrum of cardiac changes visualized on echocardiogram (e.g. borderline decreased left systolic function in the absence of left ventricular dilation) if the animal is progressing toward or recovering from DCM. While not DCM, these cases are important to report to FDA, so we may better understand if they could be related to development of DCM or associated with certain diets.

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## **Taurine Levels and Cardiac Disease Status**

Eighty-three dogs and 2 cats (including both DCM and non-DCM cases) had both a taurine measurement and an echocardiogram (Table 2). A full summary of the taurine status and echocardiogram findings for the pets with a taurine measurement and echocardiogram is included in Table 2. Approximately 64% of dogs with DCM had a taurine measurement. Of the pets diagnosed with DCM, approximately 38% had at least one low blood taurine value (Table 4). Golden Retrievers represented approximately one third of all dogs with low taurine and DCM and approximately half of all dogs with low blood taurine regardless of type of cardiac findings. Table 3 shows the reported breed frequency for each category by breed of dog. Table 4 shows the taurine results for all dogs and cats with DCM.

**Table 2. Number of pets with various taurine levels (either whole blood and/or plasma) and echocardiogram changes based on medical record review for dogs with a taurine test.**

Status	Count
Low taurine with DCM	39 (37 dogs, 2 cats)
Normal taurine with DCM*	18 dogs
High taurine with DCM	11 dogs
Low taurine with non-DCM heart changes	10 dogs
Low taurine with normal heart	6 dogs
Normal taurine with non-DCM heart changes	1 dog
Normal taurine and normal heart	2 dogs

\*One dog with DCM had a low plasma taurine and normal whole blood. This dog was considered Normal Taurine with DCM.

**Table 3. Pet breeds grouped by taurine (Tau) status and echocardiogram changes for dogs with a Tau test.**

Breed	Low Tau DCM	Normal Tau DCM	High Tau DCM	Low Tau non-DCM	Normal Tau non-DCM	Low Tau Normal heart	Normal Tau Normal heart
Boxer Mix	1		1				
Doberman Pinscher		3					
German Shepherd		1	1				

Goldendoodle	1	1		1			
Golden Retriever	14	1	1	8	1	6	2
Great Dane	1	2	2				
Labrador Retriever	3	2	1				
Miniature Schnauzer		1	1				
Bluetick Coonhound	2						
Cat	2						
Cocker Spaniel	2						
Blueheeler Mix	1						
Doberman Mix	1						
French Bulldog	1						
Golden Retriever Mix	1						
Maltese	1						
Pitbull	1						
Pitbull Mix	1						
Samoyed	1						
Sheepadoodle	1						
Standard Poodle	1						
Viszla Mix	1						



White Shepherd	1						
Australian Shepherd Mix		1					
Boston Terrier		1					
Labrador Retriever Mix		1					
Shetland Sheepdog		1					
Shih Tzu		1					
Wheaten Terrier		1					
American Staffordshire Terrier			1				
Catahoula Leopard Dog			1				
Pug			1				
Yorkshire Terrier			1				
Flat Coated Retriever				1			
<b>Sum</b>	38	17	11	10	1	6	2

**Table 4. Taurine results for dogs and cats with confirmed DCM.**

<b>Taurine Status* and Sample Type</b>	<b>Count</b>
Low Taurine, Whole blood only	21 dogs
Low Taurine, Plasma only	10 dogs, 2 cats

Low Taurine, Whole blood and Plasma	5 dogs
Low Taurine, Plasma with Normal Whole blood	1 dog
Low Taurine, unknown sample type	1 dog
Normal, Whole blood only	12 dogs
Normal, Plasma only	2 dogs
Normal, Whole blood and Plasma	2 dogs
Normal, unknown sample type	1 dog
High Taurine, Whole blood only	8 dogs
High Taurine, Plasma only	1 dog
High Taurine, Whole blood and Plasma	1 dog
High Taurine, Whole blood with Normal Plasma	1 dog

\*The taurine status is based on reference ranges used by the laboratory that performed the test.

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## Course of Disease

According to recheck echocardiograms in the medical records, some pets with DCM improved after veterinary treatment, diet change, and taurine supplementation, while others improved with appropriate veterinary care and diet change alone. Vet-LIRN has requested 30 additional repeat echocardiograms to better understand DCM heart changes over time. This repeat echocardiogram data is currently being collected and will be compared to the initial echocardiogram parameters to better understand the effects of diet change and/or taurine supplementation on the heart.

One example detailed in Table 4 describes a case in which a dog without taurine deficiency, according to the reference laboratory's reference range, improved with cardiac care and diet change alone. We provide the detailed echocardiogram data to show which parameters changed during recovery and at what rates.

The case involved a 3-year-old male, castrated, Beagle Mix, initially presented with a cough of six weeks duration that was treated with 30 days of doxycycline. The dog had been eating a limited ingredient grain-free diet containing a novel protein source and six legume-based ingredients. The whole blood and plasma taurine levels were above normal reference values. After DCM was diagnosed, the dog was diagnosed with a possible food allergy. This case shows the resolution of DCM at 2 years post presentation after treatment with cardiac prescriptions and diet change only. Taurine was not supplemented. A summary is below (Table 5).

**Table 5. Echocardiogram changes in a 3-year-old Beagle mix over time and with a diet change**

<b>Echocardiogram Parameter</b>	<b>Day 0 Original Diet</b>	<b>1 week Similar to original diet</b>	<b>Approx. 5 months Chicken &amp; Rice</b>	<b>Approx. 1 year Chicken &amp; Rice</b>	<b>Approx. 1.5 years Chicken &amp; Rice</b>	<b>Approx. 2 years Chicken &amp; Rice</b>
LA/Ao	1.28	1.81	1.24	1.31		1.17
IVSd (mm)	9.3	8.6	11.1	7.6	9.2	9.4
LVIDd (mm)	51.4	55.4	51.6	45.8	44.7	45
LVPWd (mm)	8.7	7.9	8.8	9.3	9.5	10.3
IVSs (mm)	10	10.3	14	11.3	12.2	14.6
LVIDs (mm)	41.6	44.6	39.1	33.3	27.9	27.9
LVPWs (mm)	9.3	7.9	11.8	12	11.7	13.8

FS %	18.99	19.4	24.31	27.25	37.48	37.88
EF (Teich) %	41.78	35.78	34.03	33.5	57.13	
Mitral Valve	Mild thickening, Mild mitral regurgitation	Unchanged	Unchanged	Mild thickening, Trace mitral regurgitation	Mild thickening	Normal
Tricuspid Valve	Trace to Mild tricuspid regurgitation	Unchanged	Unchanged	Normal	Normal	Normal
Pulmonary hypertension	Mild	Mild	Mild	Normal	Normal	Normal
Right heart	Enlargement	Unchanged	Unchanged	Unchanged	Unchanged	Normal
AV Vmax (m/s)	1.56	1.49	1.85	1.78	2.14	2.24

MR: mitral regurgitation, TR: tricuspid regurgitation,  
Severity Index: +/- trace, +1 mild, +2 moderate, +3 marked,  
+4 severe

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## Necropsy

As of November 30, 2018, Vet-LIRN has reviewed results of 15 gross necropsies from dogs with suspected heart disease, including 10 necropsies that Vet-LIRN coordinated from cases reported through the FDA Safety Reporting Portal. The dogs either died naturally or were euthanized and did not necessarily have a pre-mortem diagnosis of DCM. Of the 10 necropsies that Vet-LIRN coordinated, there have been 9 canine heart gross examinations, with one heart pending evaluation. During the gross evaluation, we measured dimensions including chamber lumen diameter, chamber wall thickness, and valve circumference. We collected other

tissues for histopathology, including liver, kidney, gastrocnemius muscle, and spleen for 9 of the 10 requested necropsies. The histopathology results and data analysis are pending. The necropsy results will enable Vet-LIRN to evaluate the cases for any common histopathological lesions that could suggest a cause for illness and to confirm the antemortem diagnosis.

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## **Prospective Diagnostic Sample Testing**

Vet-LIRN has been collaborating with Chesapeake Veterinary Cardiology Associates (CVCA) to collect medical records, an owner interview, and diagnostic samples from pets with DCM diagnosed by a board-certified veterinary cardiologist by echocardiogram. These cases are included in the overall number of DCM cases, but were selected for further study because their ongoing program of care with the practice will be comprehensively documented and provided in full to Vet-LIRN.

Upon confirmation of a DCM diagnosis, CVCA will collect blood (whole blood and plasma), urine, feces, DNA swabs, and food, if the pet is not receiving any supplements (e.g. taurine, cystine, or methionine) and is still eating a diet labeled “grain-free.” Vet-LIRN will test the blood and urine for taurine, cystine, methionine, and other amino acids. Vet-LIRN is archiving feces and DNA from these cases for possible future testing.

CVCA will collect repeat urine, blood, and feces at 1 to 2 months and 6 months after the initial diagnosis and document any treatment or dietary changes, if any, that were recommended by the cardiologist. The repeat urine and blood samples will be tested for amino acid content and the feces archived. At the 6-month recheck, CVCA will also

conduct a repeat echocardiogram to assess any changes to the heart. As of November 11, 2018, CVCA and Vet-LIRN have collected initial samples from 14 dogs. CVCA is currently collecting the 1 to 2-month samples. Two dogs have died and will not complete the sample collection. Vet-LIRN is currently evaluating the heart histopathology from those two dogs.

Vet-LIRN is also collecting food associated with each CVCA case and will test each diet for:

- protein, fat, moisture
- crude fiber, total dietary fiber, soluble fiber, insoluble fiber
- total starch, resistant starch
- free and total cystine, methionine, and taurine

Separate from the ongoing collaboration with CVCA, Vet-LIRN has contracted with a network lab to collect blood (whole blood and plasma), urine, feces, and DNA from healthy dogs without a known breed predisposition to DCM for comparison. The dog must also be consuming a grain-containing primary diet that meets the following criteria:

- not be labelled “grain-free”
- consuming the diet for at least 1 year before the samples are collected
- animal proteins are from either cattle, swine, poultry, and/or fish
- no more than 2 legume, pulse, or potato (including sweet potato) ingredients that must appear after the animal and grain ingredients
- the diet formulation was verified to be nutritionally adequate by animal feeding tests using AAFCO procedures

The blood and urine samples will be tested similarly to those collected in the cases from CVCA collaboration and compared to the values from the dogs diagnosed with DCM.

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## How You Can Help

FDA encourages veterinary professionals to report well-documented cases of DCM in dogs whose illness is suspected of having a link to diet. You can submit information by using the electronic Safety Reporting Portal (<http://www.safetyreporting.hhs.gov/>) or calling your state's FDA Consumer Complaint Coordinators (</safety/report-problem/consumer-complaint-coordinators>). The more information you are able to provide, particularly about feeding history, medical records, and diagnostic testing, the better. Detailed instructions can be found on [How to Report a Pet Food Complaint \(/animal-veterinary/report-problem/how-report-pet-food-complaint\)](/animal-veterinary/report-problem/how-report-pet-food-complaint).

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## Additional Information

- [FDA Investigation into Potential Link between Certain Diets and Canine Dilated Cardiomyopathy \(/animal-veterinary/news-events/fda-investigation-potential-link-between-certain-diets-and-canine-dilated-cardiomyopathy\)](/animal-veterinary/news-events/fda-investigation-potential-link-between-certain-diets-and-canine-dilated-cardiomyopathy)
- [FDA Provides Update on Investigation into Potential Connection Between Diet and Cases of Canine Heart Disease \(/animal-veterinary/cvm-updates/fda-provides-update-investigation-potential-connection-between-certain-diets-and-cases-canine-heart\)](/animal-veterinary/cvm-updates/fda-provides-update-investigation-potential-connection-between-certain-diets-and-cases-canine-heart)  
(February 2019)

- FDA Investigating Potential Connection Between Diet and Cases of Canine Heart Disease (/animal-veterinary/cvm-updates/fda-investigating-potential-connection-between-diet-and-cases-canine-heart-disease) (July 2018)
- Journal of American Veterinary Medical Association - Diet-associated dilated cardiomyopathy in dogs: what do we know?  
(<https://avmajournals.avma.org/doi/full/10.2460/javma.253.11.1390>)  
[↗](http://www.fda.gov/about-fda/website-policies/website-disclaimer) (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>) (December 2018)

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