8607

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: North Carolina State University College of Veterinary Medicine
Address: Clinical Pathology Lab, Room C-269
1052 William Moore Drive
Raleigh, NC 27607
Email:_____
Tel: 919 513-6550 Fax: 919 513-6556

Billing Contact:_____ TAX ID:_____
Email:_____ Tel:_____

Patient Name: B6
Species: K9
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

04/26/2018 2:06PM (GMT-04:00)

HOLTER REPORT

Patient: B6 ID: B6
Address: Telephone:
Doberman

Sex: MC Age: 4y Ht: Wt: Pacer:

Medications:

Symptoms:

ICD-10-CM: Hookup By:

Ref. Physician: B6 ID:
Address: Telephone:

Scanned By:

Conclusions: B6

Reviewed By: Dr. Darcy Adin Date: 5/16/2018

Settings:				
	Tachycardia Rate:	> 180 BPM	Sensitivity:	High
	Bradycardia Rate:	< 40 BPM	Irreg. Sensitivity:	100 percent
	Minimum Pause Interval:	> 3.0 seconds	Algorithm:	Standard
	SVE Percent:	> 40 percent		
	SVT Percent:	> 50 percent		
	ST Level:	> 1.5 mm		

Recorder Serial Number: 03018
Trillium 5000

Software Version: 02.12/04.39

IDEXX VetConnect 1-888-433-9987

Client: B6
Patient:
Species: CANINE
Breed: DOBERMAN_PINSCH
Gender: MALE NEUTERED
Age: 4Y

Date: 05/24/2018
Requisition #: 111508549
Accession #: 4501646140
Ordered by: B6
B6

B6

Account B6

HEALTHCHEK PLUS : CHEM 25 w/ SDMA

Test	Result	Reference Range	Low	Normal	High
ALP	B6	5 - 160 U/L			HIGH
ALT		18 - 121 U/L			
AST		16 - 55 U/L			
CREATINE KINASE		10 - 200 U/L			
GGT		0 - 13 U/L			
ALBUMIN		2.7 - 3.9 g/dL			
TOTAL PROTEIN		5.5 - 7.5 g/dL			
GLOBULIN		2.4 - 4.0 g/dL			
TOTAL BILIRUBIN		0.0 - 0.3 mg/dL			
BILIRUBIN CONJUGATED		0.0 - 0.1 mg/dL			
BUN		9 - 31 mg/dL			
CREATININE		0.5 - 1.5 mg/dL			
CHOLESTEROL		131 - 345 mg/dL			
GLUCOSE		63 - 114 mg/dL			
CALCIUM		8.4 - 11.8 mg/dL			
PHOSPHORUS		2.5 - 6.1 mg/dL			
TCO2 (BICARBONATE)		13 - 27 mmol/L			
CHLORIDE		108 - 119 mmol/L	LOW		
POTASSIUM		4.0 - 5.4 mmol/L			
SODIUM		142 - 152 mmol/L			
ALB/GLOB RATIO		0.7 - 1.5			
BUN/CREATININE RATIO					
BILIRUBIN UNCONJUGATED		0.0 - 0.2 mg/dL			
NA/K RATIO		28 - 37			
HEMOLYSIS INDEX					
LIPEMIA INDEX					
ANION GAP		11 - 26 mmol/L			
SDMA		0 - 14 ug/dL			

B6

Comments:

1. Index of N, 1+, 2+ exhibits no significant effect on chemistry values.
2. Index of N, 1+, 2+ exhibits no significant effect on chemistry values.
3. BOTH SDMA AND CREATININE ARE WITHIN THE REFERENCE INTERVAL which indicates kidney function is likely good. Evaluate a complete urinalysis and confirm there is no other evidence of kidney disease.

HEALTHCHEK PLUS : T4

Test	Result	Reference Range	Low	Normal	High
T4	B6	1.0 - 4.0 ug/dL	LOW	B6	

Comments:

1. Interpretive ranges:
   <1.0 Low
   1.0-4.0 Normal
   >4.0 High
   2.1-5.4 Therapeutic

   Dogs with no clinical signs of hypothyroidism and results within the normal reference range are likely euthyroid. Dogs with low T4 concentrations may be hypothyroid or "euthyroid sick". Occasionally, hypothyroid dogs can have T4 concentrations that are low normal. Dogs with clinical signs of hypothyroidism and low or low normal T4 concentrations may be evaluated further by submission of free T4 and canine TSH. A high T4 concentration in a clinically normal dog is likely variation of normal; however elevations may occur secondary to thyroid autoantibodies or rarely thyroid neoplasia. For dogs on thyroid supplement, acceptable 4-6 hour post pill total T4 concentrations generally fall within the higher end or slightly above the reference range.

HEALTHCHEK PLUS : CBC STANDARD

Test	Result	Reference Range	Low	Normal	High
WBC	B6	4.9 - 17.6 K/uL		B6	
RBC		5.39 - 8.70 M/uL			
HGB		13.4 - 20.7 g/dL			
HCT		38.3 - 56.5 %			
MCV		59 - 76 fL			
MCH		21.9 - 26.1 pg			
MCHC		32.6 - 39.2 g/dL			
% RETICULOCYTE		%			
RETICULOCYTE		10 - 110 K/uL			
% NEUTROPHIL		%			
% LYMPHOCYTE		%			
% MONOCYTE		%			
% EOSINOPHIL		%			
% BASOPHIL		%			
PLATELET		143 - 448 K/uL			
NEUTROPHIL		2940 - 12670 /uL			
LYMPHOCYTE		1060 - 4950 /uL			
MONOCYTE		130 - 1150 /uL			
EOSINOPHIL		70 - 1490 /uL			

BASOPHIL	B6	0 - 100 /uL	B6

Comments:

1. AUTOMATED CBC

Patient History Report

Client: B6
Phone:
Address:

Patient: B6
Species: Canine
Age: B6
Color: BLACK/BROWN
Breed: Pinscher, Doberman
Sex: Neutered Male

Date	Type	Staff	History
5/10/2018	C	B6	Medical Note Report from NCSU CVM cardiology .
5/3/2018	C		Medical Note B6
5/2/2018	L		Chemistry results from IDEXX Reference Laboratory Requisition ID: 110976938 Posted Final

Test	Result	Reference Range
ALB	B6	2.7 - 3.9
ALKP		5 - 160
ALT		18 - 121
ANION GAP		11 - 26
AST		16 - 55
BICARB		13 - 27
BUN/UREA		9 - 31
Ca		8.4 - 11.8
Chloride		108 - 119
CHOL		131 - 345
CREA		0.5 - 1.5
DBIL		0.0 - 0.1
GGT		0 - 13
GLU		63 - 114
IBIL		0.0 - 0.2
PHOS		2.5 - 6.1
Potassium		4.0 - 5.4
TBIL		0.0 - 0.3
TP		5.5 - 7.5
Sodium		142 - 152
A/G Ratio		0.7 - 1.5
B/C Ratio		
Na/K Ratio		28 - 37
GLOB		2.4 - 4.0
CK		10 - 200
SDMA		0 - 14

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 medl note, V:Vital signs

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Phone:
Address:

Patient: B6
Species: Canine
Age: B6
Color: BLACK/BROWN

Breed: Pinscher, Doberman
Sex: Neutered Male

Date	Type	Staff	History

LYMPHS	
MCH	21.9 - 26.1
MCHC	32.6 - 39.2
MCV	59 - 76
MONOS	
NEUT SEG	
PLATELETS	143 - 448
RBC	5.39 - 8.70
RETIC CNT	
WBC	4.9 - 17.6
ABS BASO	0 - 100
ABS EOS	70 - 1490
ABS LYMPHS	1060 - 4950
ABS MONOS	130 - 1150
ABS NEUTS	2940 - 12670
ABS RET	10 - 110

B6

Ascn: B6

AUTOMATED CBC

B6

5/2/2018 C — Medical Note
B6

4/20/2018 C — Medical Note
B6

4/20/2018 P — 42.00 tablet o B6 MG (1662)
B6

4/20/2018 C — Medical Note
Report from NCSU CVM cardiology

4/11/2018 C — Medical Note
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

From:	Peloquin, Sarah </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8607f880df2b494aa639e6d9a3874132-Sarah.Peloq>
To:	'lisa.freeman@tufts.edu'
Sent:	9/14/2018 1:36:02 PM
Subject:	800.267 FDA Case Investigation for B6
Attachments:	02-Vet-LIRN-NetworkProceduresVets-12.22.2015.pdf; 03-Vet-LIRN-Network ProceduresOwners-12.22.2015.pdf

Good morning Dr. Freeman,

Thank you for submitting a few more consumer complaints to FDA!

As part of our investigation, we'd like to request:

- **Full Medical Records**
  - Please email (preferred) or fax (301-210-4685) copies of B6 and B6 **entire** medical history (not just this event), including any referral diagnostics/records.
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Thank you kindly,

Dr. Peloquin

Sarah K. Peloquin, DVM
Veterinary Medical Officer

U.S. Food & Drug Administration
Center for Veterinary Medicine
Veterinary Laboratory Investigation and Response Network
tel: 240-402-1218
fax: 301-210-4685
e-mail: sarah.peloquin@fda.hhs.gov

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Peloquin, Sarah
Sent: 9/14/2018 1:44:20 PM
Subject: RE: 800.267 FDA Case Investigation for B6 (EON-364568) and B6 (EON-365002)
Attachments: RDVM records1.pdf; RDVM records2.pdf; RDVM records3.pdf

Hi Sarah
I sent additional records on B6 directly to Dr. Jones since there were too many to upload individually. I think that should have everything you need on him but if not, please let me know
The owner is happy to talk to you.

Attached are RDVM records on B6 I also have a food sample for her. I'll need to confirm it's ok to contact
Thanks
Lisa

Lisa M. Freeman, DVM, PhD, DACVN
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Friedman School of Nutrition Science and Policy
Tufts Clinical and Translational Science Institute
Tufts University
www.petfoodology.org

From: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Sent: Friday, September 14, 2018 9:36 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>
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From: Peloquin, Sarah </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8607f880df2b494aa639e6d9a3874132-Sarah.Peloq>
To: 'Freeman, Lisa'
CC: Jones, Jennifer L
Sent: 9/14/2018 1:51:03 PM
Subject: RE: 800.267 FDA Case Investigation for B6 (EON-364568) and B6 (EON-365002)

Hi Lisa, thanks so much for passing those along. Sorry for the multiple emails—it looks like we've received everything we need for these two.

Please let me know when you confirm permission to contact B6 owner.

Thanks!
Sarah

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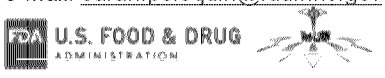

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Peloquin, Sarah
CC: Jones, Jennifer L
Sent: 9/15/2018 2:26:49 PM
Subject: RE: 800.267 FDA Case Investigation for B6

Hi Sarah

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Sent: Friday, September 14, 2018 9:51 AM
To: Freeman, Lisa <lisa.freeman@tufts.edu>
Cc: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
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To: Peloquin, Sarah
Sent: 9/15/2018 2:27:37 PM
Subject: RE: 800.267 FDA Case Investigation for B6 (EON-364568) and B6 (EON-365002)

Hi Sarah,
B6 mom is fine with you contacting her. Email is best for initial contact
B6
Please let me know if you need more info on this case
Thanks
Lisa

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From:	Peloquin, Sarah </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8607f880df2b494aa639e6d9a3874132-Sarah.Peloq>
To:	Rotstein, David; Carey, Lauren; Palmer, Lee Anne; Queen, Jackie L
CC:	Jones, Jennifer L; Reimschuessel, Renate; Ceric, Olgica
Sent:	9/21/2018 6:09:51 PM
Subject:	800.267 EON-364568 B6 Rachael Ray
Attachments:	Mrx.zip

Interview and food pending
Will request previous rdvm records from O

B6 – 6 yr FS FS Aussie mix
Prior Mhx: B6 1/2018, no murmur then *(limited rdvm mrx)*, eats RR Nutrish

8/6/18: rdvm exam for gagging, panting more (other dog fine); 2/6 murmur, pulses weak, HR 90, RR 30, panting w/ min exertion; rads à cardiomegaly, pulmonary edema; brief u/s concern for pericard effusion; B6 ec immediate referral to Tufts
8/6/18: cardio eval; 3-4/6 murmur, fair arterial pulses, premature beats, gallop rhythm, eupneic w/ normal BV sounds; echo à thin LV walls w/ decr contract, LV cavity marked enlarg, FS 16.47%, thick MV/TV, no valve prolapse, RH subject mild enlarg, no pleural/pericard effusion,; EKG à sinus rhythm w/ signs consistent with LA/LV enlarg, freq multifocal VPCs; tau B6 WB B6 plasma; Na 152, AGAP 22, A/G ratio 1.8; dx DCM and ventric arrhythmia; B6
8/23/18: rdvm recheck, doing well at home, switched to RC boxer diet as rec per cardio; 2/6 murmur, clear lung sounds, B6

From: Rotstein, David
Sent: Friday, September 7, 2018 4:35 PM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Glover, Mark <Mark.Glover@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: Tufts DCM case-FW: Rachel Ray Nutrish real beef and brown rice (barcode 7119000095): Lisa Freeman - EON-364568

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From: PFR Event <pfreventcreation@fda.hhs.gov>
Sent: Friday, September 07, 2018 4:32 PM
To: Cleary, Michael * <Michael.Cleary@fda.hhs.gov>; HQ Pet Food Report Notification <HQPetFoodReportNotification@fda.hhs.gov>; B6
Subject: Rachel Ray Nutrish real beef and brown rice (barcode 7119000095): Lisa Freeman - EON-364568

A PFR Report has been received and PFR Event [EON-364568] has been created in the EON System.

A "PDF" report by name "2054744-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 "2054744-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-364568
ICSR #: 2054744
EON Title: PFR Event created for Rachel Ray Nutrish real beef and brown rice (barcode 7119000095); 2054744

AE Date	08/06/2018	**Number Fed/Exposed**	
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Stable
Breed	Mixed (Dog)		
Age	6 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2054744
Product Group: Pet Food
Product Name: Rachel Ray Nutrish real beef and brown rice (barcode 7119000095)
Description: Diagnosed with DCM and CHF
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 Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Rachel Ray Nutrish real beef and brown rice (barcode 7119000095)		

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:
https://eon.fda.gov/eon//browse/EON-364568

To view the PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction!viewReport.jspa?decorator=none&e=0&issueType=12&issueId=381302

==========

From: B6
Sent: Friday, February 2, 2018 10:41 AM
To: Jones, Jennifer L
Cc: B6
Subject: Re: Vet-LIRN request for Metals Testing (800.218)

Follow Up Flag: Follow up
Flag Status: Flagged

Jennifer

WADDL can accept the samples.

All, these would be billed to the VetLIRN infrastructure account.

B6

On Feb 2, 2018, at 4:10 AM, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov> wrote:

Good morning B6,
We have 5 commercial dog food samples we'd like to test for:

- Selenium, Cobalt, Calcium, Phosphorous, Magnesium, Copper, Iron, and Zinc

We received reports of dogs developing dilated cardiomyopathy after consuming these foods-often a grainfree diet with a chicken/kangaroo and/or lentil based diet.
Please let me know if you accept, and I'll send the samples Monday. Please plan to bill the infrastructure grant.
Please also report the results on a dry matter basis.
Thank you kindly and have a nice weekend,
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: B6
To: B6 Jones, Jennifer L
CC: B6
Sent: 2/16/2018 11:58:11 PM
Subject: RE: Vet-LIRN request for Metals Testing (800.218)

This case was logged yesterday as WADDL 2018-2078. Samples had been shipped directly to ASL.

B6

From: B6
Sent: Friday, February 02, 2018 7:41 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Cc: B6
B6
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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

Client: B6 Patient: B6 B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

*Documents are available as separate attachments or files.

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

Non-visit note

Client: B6 Patient: B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

B6

*Documents are available as separate attachments or files.

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 25-May-2012 to 08-Feb-2019

B6

B6 B6

MEDICAL HISTORY

24-Mar-2019 to 19-May-2019

Client

B6

Patient

B6

Canine Tri

Hound Mix Male / Neutered - 102 lb (19-May-2019)

Most recent visit date: 19-May-2019

Microchip No.: B6

Rabies tag ID / date : B6 / 03-Jun-2018

Patient Alerts: B6

Current medical overview: as of 21-May-2019

B6

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 24-Mar-2019 to 19-May-2019

Medications (since 19-May-2018)	Amount	Disp. Date
B6		

Client: B6 Patient: B6

MEDICAL HISTORY: 24-Mar-2019 to 19-May-2019

B6

Outpatient visit (24-Mar-2019 to 24-Mar-2019)

B6

*Documents are available as separate attachments or files.

B6

B6

Client B6 Patient B6

B6

MEDICAL HISTORY: 24-Mar-2019 to 19-May-2019

B6

Client B6 Patient: B6

B6

MEDICAL HISTORY: 24-Mar-2019 to 19-May-2019

B6

B6

Client: B6 Patient: B6

B6

MEDICAL HISTORY: 24-Mar-2019 to 19-May-2019

B6

Documents*

19-May-2019 B6

*Documents are available as separate attachments or files.

B6

Phone: B6
Email:
Date of Report:

Sun May 19 6:00 AM - 5:00 PM EDT
Mon May 20 6:00 AM - 5:00 PM EDT
Tue May 21 6:00 AM - 5:00 PM EDT

Powered by B6 Medical Ventures

Client: B6
Patient:

CBC/chem 5/21/2019

Tufts Cummings School Of Veterinary Medicine

200 Westboro Road
North Grafton, MA 01536

DUPLICATE

Name/DOB: B6)
Patient ID:
Phone number:
Collection Date: B6 7:56 AM
Approval date: 10:34 AM

Sex: CM
Age: 11
Species: Canine
Breed: Treeing Walker Coonhound

Provider: B6
Order Location: Foster Hospital for Small Animals
Sample ID: 1905210012

CBC, Comprehensive, Sm Animal

		Ref. Range/Males
TFRANK		
WBC (ADVIA)		4.40-15.10 K/uL
RBC (Advia)		5.80-8.50 M/uL
Hemoglobin (ADVIA)		13.3-20.5 g/dL
Hematocrit (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
CHCM		
RDW (ADVIA)		11.9-15.2
Platelet Count (Advia) 05/21/19 10:29 AM	B6	173-486 K/uL
Mean Platelet Volume (Advia) B6 8:13 AM		8.29-13.20 fl
Platelet Crit B6 8:13 AM		0.129-0.403 %
PDW		
Reticulocyte Count (Advi		0.20-1.60 %
Absolute Reticulocyte Count (Advia)		14.7-113.7 K/uL
CHr		
MCVr		
Comments (Hematology)		

Microscopic Exam of Blood Smear (Advia)

		Ref. Range/Males
TFRANK		
Seg Neuts (%)		43-86 %
Lymphocytes (%)		7-47 %
Monocytes (%)		1-15 %
Eosinophils (%)		0-16 %
Nucleated RBC B6 9 8:13 AM		0-1 /100 WBC
Seg Neutrophils (Abs) Advia	B6	2.800-11.500 K/ul
Lymphs (Abs) Advia		1.00-4.80 K/uL

Sample ID: 1905210012/1
This report continues... (Final)

Reviewed by: _____

Client: B6
Patient:

CBC/chem 5/21/2019

Tufts Cummings School Of Veterinary Medicine

200 Westboro Road
North Grafton, MA 01536

DUPLICATE

Name/DOB: B6
Patient ID:
Phone number:
Collection Date: B6 7:56 AM
Approval date: 10:34 AM

Sex: CM
Age: 11
Species: Canine
Breed: Treeing Walker Coonhound

Provider: B6
Order Location: Foster Hospital for Small Animals
Sample ID: 1905210012

Microscopic Exam of Blood Smear (Advia) (cont'd)

		Ref. Range/Males
TFRANK	B6	
Mono (Abs) Advia		0.10-1.50 K/uL
Eosinophils (Abs) Advia		0.00-1.40 K/uL
WBC Morphology		
RBC Morphology		
B6 10:33 AM		
Polychromasia		

Chemistry Profile - Small Animal (Package) (Cobas)

		Ref. Range/Males
EUNDERWOOD	B6	
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+		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		106-116 mEq/L
Potassium		3.7-5.4 mEq/L
tCO2(Bicarb)		14-28 mEq/L
AGAP		8.0-19.0
NA/K		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		82-355 mg/dL
Triglycerides		30-338 mg/dl
Amylase		409-1250 U/L
Osmolality (calculated)		291-315 mmol/L
Comments (Chemistry)		

Sample ID: 19052100122
REPRINT: Orig. printing on 5/21/2019 (Final)

Reviewed by: _____
Page 2

Client: B6
Patient:

B6 NT-proBNP 5/21/2019

B6

B6

PET OWNER: B6
SPECIES: Canine
BREED: Coonhound, Other
GENDER: Male
AGE: 11 Years
PATIENT ID:

Tufts University Attn: Lisa Freeman
200 Westboro Rd.
North Grafton, MA 01536
508-839-5395
ACCOUNT #: 88933
ATTENDING VET: FREEMAN

LAB ID: 2301481001
ORDER ID: 309861
COLLECTION DATE: 5/20/19
DATE OF RECEIPT: 5/21/19
DATE OF RESULT: 5/22/19

B6 ervices: Cardiopet® proBNP-Canine*

Chemistry

5/21/19 (Order Received)
5/22/19 11:40 AM (Last Updated)

TEST		RESULT	REFERENCE VALUE	
Cardiopet proBNP (Canine)	a	B6	0 - 900 pmol/L	B6

a Cardiopet proBNP >1800pmol/L

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.

Result is greater than 10000 pmol/L

Client: B6
Patient:

Diet Hx 5/22/2019

B6

CARDIOLOGY DIET HISTORY FORM

Please answer the follo[illegible]out your pet

Pet's name: B6 Owner's name : B6 Today's date: 5/22/19

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
   ascites

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*
From an Grainbird grain free	DRY	2 cups	2/day	N/A 3+years
Baked treats us made	DRY	3	3x Day	N/A

**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*
Chondroitin			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): From m/ treats

Client: B6
Patient:

Vitals Results

B6	10:46:34 AM	Quantify IV fluids (mls)	B6
	11:46:39 AM	Temperature (F)	
	12:03:47 PM	Quantify IV fluids (mls)	
	12:04:12 PM	Quantify IV Fluids (CRI) in mls	
	1:11:05 PM	Respiratory Rate	
	1:11:47 PM	Heart Rate (/min)	
	1:12:54 PM	Heart Rate (/min)	
	1:15:32 PM	Temperature (F)	
	1:19:04 PM	Urine Output (mls)	
	1:41:45 PM	Respiratory Rate	
	1:42:10 PM	Heart Rate (/min)	
	2:05:20 PM	Temperature (F)	
	2:40:35 PM	Nursing note	
	3:02:30 PM	Turn patient (note side down)	
	3:03:09 PM	Heart Rate (/min)	
	3:03:39 PM	Quantify IV Fluids (CRI) in mls	
	3:04:06 PM	Quantify IV fluids (mls)	
	3:04:29 PM	Quantify IV fluids (mls)	
	3:04:50 PM	Respiratory Rate	
	3:05:37 PM	Temperature (F)	
	3:05:53 PM	Weight (kg)	
	3:06:31 PM	Nursing note	
	3:42:39 PM	Eliminations	
	3:46:56 PM	Nursing note	
	3:54:58 PM	Heart Rate (/min)	
	3:56:37 PM	Quantify IV fluids (mls)	
	4:02:03 PM	Urine Output (mls)	
	4:50:45 PM	Nursing note	
	5:05:58 PM	Nursing note	
	5:27:13 PM	Temperature (F)	
	5:29:02 PM	Heart Rate (/min)	
	5:30:38 PM	Turn patient (note side down)	
	6:44:31 PM	Respiratory Rate	
	6:44:49 PM	Heart Rate (/min)	
	7:13:16 PM	Heart Rate (/min)	
	7:24:49 PM	Quantify IV fluids (mls)	

Client: B6
Patient:

Vitals Results

B6	7:25:20 PM	Quantify IV Fluids (CRI) in mls	B6
	7:25:50 PM	Temperature (F)	
	7:27:02 PM	Quantify IV fluids (mls)	
	7:27:23 PM	Quantify IV fluids (mls)	
	7:31:16 PM	Urine Output (mls)	
	7:31:38 PM	Heart Rate (/min)	
	7:32:42 PM	Respiratory Rate	
	9:28:37 PM	Temperature (F)	
	9:29:19 PM	Heart Rate (/min)	
	9:47:49 PM	Heart Rate (/min)	
	10:06:26 PM	Turn patient (note side down)	
	10:06:43 PM	Respiratory Rate	
	10:07:33 PM	Nursing note	
	10:08:53 PM	Nursing note	
	11:10:23 PM	Heart Rate (/min)	
	11:13:38 PM	Temperature (F)	
	11:14:49 PM	Quantify IV fluids (mls)	
	11:15:05 PM	Quantify IV fluids (mls)	
	11:15:17 PM	Quantify IV fluids (mls)	
	11:15:36 PM	Quantify IV Fluids (CRI) in mls	
	11:17:10 PM	Urine Output (mls)	
	11:18:17 PM	Respiratory Rate	
	11:33:28 PM	Heart Rate (/min)	
	1:10:14 AM	Heart Rate (/min)	
	1:11:07 AM	Temperature (F)	
	1:11:20 AM	Turn patient (note side down)	
	1:11:38 AM	Respiratory Rate	
	1:31:01 AM	Heart Rate (/min)	
	3:36:24 AM	Quantify IV fluids (mls)	
	3:36:32 AM	Quantify IV Fluids (CRI) in mls	
	3:36:41 AM	Quantify IV fluids (mls)	
	3:36:52 AM	Quantify IV fluids (mls)	
	3:37:02 AM	Heart Rate (/min)	
	3:37:26 AM	Temperature (F)	
	3:37:39 AM	Respiratory Rate	
	3:38:12 AM	Urine Output (mls)	
	3:50:03 AM	Heart Rate (/min)	
	4:39:44 AM	Heart Rate (/min)	
	5:05:07 AM	Turn patient (note side down)	
	5:18:44 AM	Temperature (F)	
	5:18:52 AM	Respiratory Rate	

Client: B6
Patient:

Vitals Results

B6	5:19:05 AM	Heart Rate (/min)	B6
	7:59:02 AM	Urine Output (mls)	
	8:00:35 AM	Heart Rate (/min)	
	8:00:57 AM	Respiratory Rate	
	8:08:32 AM	Quantify IV fluids (mls)	
	8:09:00 AM	Quantify IV fluids (mls)	
	8:09:35 AM	Quantify IV fluids (mls)	
	8:10:03 AM	Quantify IV Fluids (CRI) in mls	
	10:15:29 AM	Nursing note	
	10:25:33 AM	Urine Output (mls)	
	11:56:46 AM	Quantify IV fluids (mls)	
	11:57:01 AM	Quantify IV fluids (mls)	
	11:57:17 AM	Temperature (F)	
	11:57:28 AM	Quantify IV fluids (mls)	
	11:57:41 AM	Heart Rate (/min)	
	11:57:55 AM	Heart Rate (/min)	
	1:22:33 PM	Quantify IV fluids (mls)	
	1:23:09 PM	Quantify IV fluids (mls)	
	1:23:59 PM	Quantify IV fluids (mls)	
	1:31:00 PM	Quantify IV fluids (mls)	
	1:32:47 PM	Heart Rate (/min)	
	2:11:23 PM	Heart Rate (/min)	
	2:15:37 PM	Urine Output (mls)	
	2:15:51 PM	Respiratory Rate	
	2:27:12 PM	Eliminations	
	3:57:35 PM	Heart Rate (/min)	
	3:57:52 PM	Eliminations	
	4:08:56 PM	Temperature (F)	
	4:09:11 PM	Respiratory Rate	
	4:09:28 PM	Heart Rate (/min)	
	5:24:11 PM	Heart Rate (/min)	
	5:48:56 PM	Quantify IV fluids (mls)	
	5:53:29 PM	Quantify IV fluids (mls)	
	5:53:51 PM	Quantify IV fluids (mls)	
	5:54:23 PM	Heart Rate (/min)	
	5:54:41 PM	Quantify IV fluids (mls)	
	5:55:03 PM	Respiratory Rate	
	5:58:31 PM	Urine Output (mls)	
	7:23:34 PM	Heart Rate (/min)	
	7:42:21 PM	Respiratory Rate	
	7:42:37 PM	Heart Rate (/min)	

Client: B6
Patient:

Vitals Results

B6	7:43:05 PM	Eliminations	B6
	7:52:11 PM	Nursing note	
	8:54:18 PM	Heart Rate (/min)	
	9:08:52 PM	Respiratory Rate	
	9:12:09 PM	Quantify IV fluids (mls)	
	9:12:25 PM	Quantify IV fluids (mls)	
	9:12:45 PM	Quantify IV fluids (mls)	
	9:13:09 PM	Temperature (F)	
	9:21:03 PM	Heart Rate (/min)	
	11:30:59 PM	Heart Rate (/min)	
	11:33:23 PM	Respiratory Rate	
	12:20:36 AM	Heart Rate (/min)	
	12:57:32 AM	Heart Rate (/min)	
	1:36:15 AM	Eliminations	
	1:37:30 AM	Quantify IV fluids (mls)	
	1:37:48 AM	Quantify IV fluids (mls)	
	1:38:03 AM	Quantify IV fluids (mls)	
	1:38:15 AM	Quantify IV fluids (mls)	
	1:38:29 AM	Heart Rate (/min)	
	1:38:39 AM	Respiratory Rate	
	2:35:17 AM	Heart Rate (/min)	
	3:14:14 AM	Heart Rate (/min)	
	3:14:28 AM	Respiratory Rate	
	3:48:19 AM	Eliminations	
	5:22:04 AM	Heart Rate (/min)	
	5:30:15 AM	Quantify IV fluids (mls)	
	5:31:00 AM	Quantify IV fluids (mls)	
	5:31:19 AM	Respiratory Rate	
	5:31:31 AM	Quantify IV fluids (mls)	
	5:45:21 AM	Temperature (F)	
	7:52:47 AM	Heart Rate (/min)	
	7:53:37 AM	Respiratory Rate	
	7:53:53 AM	Heart Rate (/min)	
	8:52:47 AM	Eliminations	
	10:10:04 AM	Quantify IV fluids (mls)	
	10:13:09 AM	Temperature (F)	
	10:13:24 AM	Heart Rate (/min)	
	10:13:33 AM	Respiratory Rate	
	11:08:22 AM	Eliminations	
	11:37:31 AM	Respiratory Rate	
	1:24:29 PM	Heart Rate (/min)	

Client: B6
Patient:

Vitals Results

B6

1:24:41 PM	Respiratory Rate	
1:24:52 PM	Nursing note	
1:26:21 PM	Quantify IV fluids (mls)	
2:57:44 PM	Respiratory Rate	
3:53:35 PM	Eliminations	
5:33:58 PM	Respiratory Rate	
5:39:42 PM	Quantify IV fluids (mls)	
5:40:45 PM	Temperature (F)	
5:40:57 PM	Heart Rate (/min)	
5:52:49 PM	Eliminations	
7:05:11 PM	Respiratory Rate	
9:29:59 PM	Respiratory Rate	
9:30:22 PM	Heart Rate (/min)	
9:32:03 PM	Quantify IV fluids (mls)	
9:45:31 PM	Eliminations	
11:31:33 PM	Respiratory Rate	
11:32:24 PM	Eliminations	
1:01:16 AM	Quantify IV fluids (mls)	
1:03:33 AM	Temperature (F)	
1:03:42 AM	Heart Rate (/min)	
1:03:55 AM	Eliminations	
1:04:14 AM	Respiratory Rate	
3:04:27 AM	Eliminations	
3:04:54 AM	Respiratory Rate	
4:36:43 AM	Quantify IV fluids (mls)	
4:36:56 AM	Heart Rate (/min)	
4:37:08 AM	Respiratory Rate	
7:35:35 AM	Eliminations	
7:35:54 AM	Weight (kg)	
7:54:13 AM	Nursing note	
7:54:20 AM	Nursing note	
7:56:09 AM	Respiratory Rate	
9:13:17 AM	Weight (kg)	
9:18:57 AM	Amount eaten	
9:19:23 AM	Quantify IV fluids (mls)	
9:29:30 AM	Heart Rate (/min)	
9:29:31 AM	Respiratory Rate	
9:42:37 AM	Temperature (F)	
10:30:21 AM	Amount eaten	

B6

Client: B6
Patient:

Vitals Results

B6	11:10:41 AM	Eliminations
	1:11:13 PM	Heart Rate (/min)
	1:11:14 PM	Respiratory Rate
	1:11:22 PM	Quantify IV fluids (mls)
	1:15:44 PM	Amount eaten
	3:09:54 PM	Amount eaten
	3:40:16 PM	Eliminations
	5:11:13 PM	Quantify IV fluids (mls)
	5:22:40 PM	Amount eaten
	5:23:20 PM	Heart Rate (/min)
	5:23:21 PM	Respiratory Rate
	5:26:19 PM	Temperature (F)
	7:45:29 PM	Eliminations
	9:14:13 PM	Quantify IV fluids (mls)
	9:14:23 PM	Amount eaten
	9:14:51 PM	Heart Rate (/min)
	9:14:52 PM	Respiratory Rate
	11:26:22 PM	Eliminations
	11:31:57 PM	Weight (kg)
	1:14:41 AM	Heart Rate (/min)
	1:14:42 AM	Respiratory Rate
	1:18:57 AM	Quantify IV fluids (mls)
	1:19:14 AM	Amount eaten
	1:21:07 AM	Temperature (F)
	3:04:40 AM	Eliminations
	5:17:18 AM	Quantify IV fluids (mls)
	5:23:47 AM	Amount eaten
	5:39:33 AM	Heart Rate (/min)
	5:39:34 AM	Respiratory Rate
	7:15:52 AM	Eliminations
	9:09:08 AM	Weight (kg)
	9:09:24 AM	Eliminations
	10:18:24 AM	Quantify IV fluids (mls)
	10:26:26 AM	Heart Rate (/min)
	10:26:27 AM	Respiratory Rate
	10:49:13 AM	Temperature (F)
	10:49:36 AM	Amount eaten

B6

Client: B6
Patient:

Vitals Results

B6	10:50:00 AM	Nursing note
	11:12:56 AM	Eliminations
	1:36:36 PM	Eliminations
	1:50:34 PM	Amount eaten
	2:31:32 PM	Heart Rate (/min)
	2:31:33 PM	Respiratory Rate
	10:12:13 AM	Weight (kg)
	6:09:50 PM	Weight (kg)
	8:20:54 AM	Heart Rate (/min)
	8:20:55 AM	Respiratory Rate
	8:20:56 AM	Temperature (F)
	8:20:57 AM	Weight (kg)
	9:02:46 AM	Respiratory Rate
	9:23:57 AM	Respiratory Rate
	9:24:06 AM	Eliminations
	9:27:44 AM	Cardiac rhythm
	9:27:45 AM	Heart Rate (/min)
	9:29:04 AM	Lasix/Furosemide treatment note
	10:06:20 AM	Eliminations
	11:03:26 AM	Cardiac rhythm
	11:03:27 AM	Heart Rate (/min)
	11:03:41 AM	Respiratory Rate
	11:44:39 AM	Cardiac rhythm
	11:44:40 AM	Heart Rate (/min)
	11:44:56 AM	Respiratory Rate
	12:48:42 PM	Cardiac rhythm
	12:48:43 PM	Heart Rate (/min)
	1:05:03 PM	Respiratory Rate
	2:00:03 PM	Respiratory Rate
	2:00:11 PM	Cardiac rhythm
	2:00:12 PM	Heart Rate (/min)
	4:08:46 PM	Nursing note
	4:16:09 PM	Weight (kg)
	4:16:47 PM	Cardiac rhythm
	4:16:48 PM	Heart Rate (/min)
	4:16:56 PM	Eliminations
	4:29:28 PM	Nursing note
	4:41:09 PM	Respiratory Rate
	4:48:13 PM	Cardiac rhythm

B6

Client: B6
Patient:

Vitals Results

B6

4:48:14 PM	Heart Rate (/min)	
4:55:11 PM	Respiratory Rate	
5:29:36 PM	Amount eaten	
5:33:38 PM	Catheter Assessment	
5:33:46 PM	Lasix/Furosemide treatment note	
5:38:36 PM	Respiratory Rate	
5:55:06 PM	Cardiac rhythm	
5:55:07 PM	Heart Rate (/min)	
7:04:18 PM	Cardiac rhythm	
7:04:19 PM	Heart Rate (/min)	
7:04:29 PM	Respiratory Rate	
7:05:16 PM	Eliminations	
7:08:00 PM	Nursing note	
7:20:35 PM	Eliminations	
7:22:05 PM	Weight (kg)	
7:42:00 PM	Cardiac rhythm	
7:42:01 PM	Heart Rate (/min)	
7:43:54 PM	Respiratory Rate	
8:58:38 PM	Cardiac rhythm	
8:58:39 PM	Heart Rate (/min)	
8:58:57 PM	Respiratory Rate	
9:01:09 PM	Catheter Assessment	
10:03:32 PM	Cardiac rhythm	
10:03:33 PM	Heart Rate (/min)	
10:04:22 PM	Respiratory Rate	
11:03:50 PM	Cardiac rhythm	
11:03:51 PM	Heart Rate (/min)	
11:04:06 PM	Respiratory Rate	
12:28:30 AM	Cardiac rhythm	
12:28:31 AM	Heart Rate (/min)	
12:28:42 AM	Respiratory Rate	
1:05:20 AM	Cardiac rhythm	
1:05:21 AM	Heart Rate (/min)	
1:05:55 AM	Catheter Assessment	
1:06:03 AM	Lasix/Furosemide treatment note	
1:06:19 AM	Respiratory Rate	
1:26:26 AM	Eliminations	
2:15:43 AM	Cardiac rhythm	
2:15:44 AM	Heart Rate (/min)	
2:15:54 AM	Respiratory Rate	

B6

Client: B6
Patient:

Vitals Results

B6

3:13:36 AM	Cardiac rhythm	
3:13:37 AM	Heart Rate (/min)	
3:13:49 AM	Respiratory Rate	
4:06:17 AM	Cardiac rhythm	
4:06:18 AM	Heart Rate (/min)	
4:06:35 AM	Respiratory Rate	
4:47:11 AM	Cardiac rhythm	
4:47:12 AM	Heart Rate (/min)	
5:10:21 AM	Catheter Assessment	
5:23:15 AM	Weight (kg)	
5:23:46 AM	Respiratory Rate	
5:24:00 AM	Amount eaten	
5:59:00 AM	Cardiac rhythm	
5:59:01 AM	Heart Rate (/min)	
5:59:13 AM	Respiratory Rate	
7:24:43 AM	Cardiac rhythm	
7:24:44 AM	Heart Rate (/min)	
7:32:58 AM	Respiratory Rate	
7:54:01 AM	Cardiac rhythm	
7:54:02 AM	Heart Rate (/min)	
7:54:49 AM	Eliminations	
7:59:10 AM	Respiratory Rate	
8:41:21 AM	Cardiac rhythm	
8:41:22 AM	Heart Rate (/min)	
8:44:28 AM	Respiratory Rate	
9:00:17 AM	Respiratory Rate	
9:45:33 AM	Cardiac rhythm	
9:45:34 AM	Heart Rate (/min)	
10:09:01 AM	Catheter Assessment	
10:09:20 AM	Amount eaten	
10:09:38 AM	Eliminations	
10:09:49 AM	Respiratory Rate	
10:48:53 AM	Cardiac rhythm	
10:48:54 AM	Heart Rate (/min)	
10:49:44 AM	Respiratory Rate	
11:48:48 AM	Cardiac rhythm	
11:48:49 AM	Heart Rate (/min)	
12:12:10 PM	Respiratory Rate	
12:39:51 PM	Catheter Assessment	

B6

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
To: Jones, Jennifer L
Sent: 10/15/2018 12:20:38 AM
Subject: FW: Safety Report ID 244723 Submission Confirmation (additional info)
Attachments: B6 echo 1 30 18.pdf; B6 echo DCM Oct 11 2018.pdf; B6 cardio report 1-30-18.pdf

Hi Jen
I'm attaching the original echo report from B6 (Jan, 2018) and B6 most recent one (Oct, 2018).
Also, Dr. B6 reported her whole blood taurine level in Jan was B6
Unclear how much of improvement in size was improved heart rate control and medications. We'll see if her contractility improves and size gets better after the recent diet change.
Thanks
Lisa

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

-----Original Message-----
From: noreply.safetyreporting@hhs.gov <noreply.safetyreporting@hhs.gov>
Sent: Monday, October 08, 2018 2:18 PM
To: Freeman, Lisa <lisa.freeman@tufts.edu>
Subject: Safety Report ID 244723 Submission Confirmation

Your initial Pet Food Safety Report , Submitted by: Lisa Freeman, ID 244723, was successfully submitted on 10/8/2018 2:14:30 PM EST to the FDA, and it was issued an Individual Case Safety Report Number (ICSR) of 2055791.

Thank you for using the Safety Reporting Portal.

Please do not reply to this message. Replies to this message are routed to an unmonitored mailbox. If you have questions please refer to the Portal's Contact Us page for further instructions.

B6

B6

Echocardiography Examination Report

Patient ID: B6	Exam Date: **10/11/2018**
Client Name B6	
Pet name	Cardiologist B6, **DVM, DACVIM / DECVIM (Cardiology)**
Age: **2**	
Breed **Bloodhound Mix**	
Weight: **35.1 kg**	
Sex: **Female**	

CARDIAC DIAGNOSES AND ASSESSMENT:

DCM- Evidence of reverse remodelling vs 9 months ago when first echod (especially, reduction of LAE), but LV still severely dilated and very poor systolic function; mild AS
Clinically stable

RECOMMENDATIONS:

Remains at risk for CHF, SD
Revist in the event of exercize intolerance, syncope, tachypnea, anorexia
Reecho 6 mo.

MEDICAL HISTORY

9 months ago detected DCM. Taste of the Wild Diet, grain free
Stoppe this diet 1 wk ago
Pet doing clinically ok

STUDY INDICATION:

follow up

CARDIOVASCULAR EXAMINATION:

B6

ECHOCARDIOGRAPHIC FINDINGS:

B6

RADIOGRAPHY AND OTHER IMAGE FINDINGS

NA

MEASUREMENTS

2D		M-Mode		DOPPLER	
IVSd Ao Diam LA Diam LA/Ao	B6	IVSd LVIDd LVPWd IVSs LVIDs LVPWs EDV(Teich) ESV(Teich) EF(Teich) %FS SV(Teich)	B6	MV E Vel MV A Vel Lat E' E/Lat E' A' MV E/A Ratio AV Vmax AV maxPG RVOT Vmax RVOT maxPG TR Vmax TR maxPG	B6

IMAGES: IMAGES:

B6

Sonographer B6, DVM
(Cardiology Resident)

Reviewed by:
B6, DVM, DACVIM / DECVIM
(Cardiology)

B6

Cardiology Examination

Date: 1/30/2018

Client: B6 Patient: B6 Sex: Spayed Female

Patient ID#: DOB: Species: Canine

Phone: B6 Age: B6 Breed: Bloodhound Mix

rDVM: B6

rDVM contact info: B6

Vital Signs:

Medical History:
Progressive exercize intolerance, then incr. respiratory rate and cough past 10 days or so
Echo suggested DCM; chest radiograph indicated CHF (PE)
Rx and pet improved, but clinical sign of incr RR persist

appetite ok- commercial food bison protein source

	Comments
Other	

Reason For Visit:

cardiac consultation

Current Medications:

None
Aminophylline
Amlodipine (Norvasc)
Aspirin
Atenolol
Benazepril
Clopidogrel (Plavix)
Digoxin (digitalis)
Diltiazem HCl
Dilacor
Enalapril
Hycodan (Tussigon)
Lasix (Furosemide)
Methimazole (Tapazole)
Mexiletine
Pimobendan (Vetmedin)
Sildenafil (Viagra)
Sotolol
Spironolactone
Theophylline XR
Other

B6

Referral Diagnostics:

- ☐ Echocardiogram
- ☐ Blood Tests

☐ ECG
☑ Radiographs cardiomegally; pulmonary edema (last week)
☐ Other

Heart Sounds:

☐ Gallop ☐ S_4 ☑ S_3 ☐ Summated ☐ Cannot Distinguish ☐ Systolic click ☐ Split S_2

Heart Rate/Rhythm:

Heart Rate BPM: 180
☑ Sinus tachycardia
☐ Other Arrhythmia

Heart Murmur:

☐ No murmur
☐ Systolic:

Mitral Valve	☐ 1/6	☑ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Tricuspid Valve	☐ 1/6	☑ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Aortic Valve	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Pulmonic Valve	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Left Parasternal	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Right Parasternal	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6

Murmur Quality_____
☐ Continuous
☐ Diastolic

Diet:

Previous CHF: ☑ Yes ☐ No

Dates: approximately one week ago

Comments:

Physical Exam:

Normal		Comments
☑	Mucous Membrane / Capillary Refill Time	
☑	Ears	
☑	Eyes	
☑	Oral Cavity - Dental Disease	
☑	Nose/Throat	
☑	Peripheral Lymph Noces	
☑	Skin	
☑	Abdomen	
☑	Musculoskeletal	mild loss muscle mass noted
☑	CNS	
☑	Urogenital	

Body Condition Score

☐ 1 ☐ 2 ☐ 3 ☑ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9

Respiratory:

☐ Eupenic Respiratory Rate (Breaths per minute) 55 ☑ Tachypneic ☐ Dyspneic ☐ Orthopneic

Auscultation Lungs:

				Location
☐	Clear			
☐	Wheezes	insp ☐	expir ☐	
☐	Crackles	insp ☐	expir ☐	
☐	Muffled	☐ R. Chest	☐ L. Chest	
☑	Harsh			bilaterally

Jugular venous distention or pulsations:

☐ Jugular venous distention or Pulsations none

Femoral arterial pulse pressure
- ☐ Normal
- ☐ Hyperkinetic
- ☑ Hypokinetic

Diagnostics:

☑	Examination	
☑	Echo	
☐	Radiographs	
☐	Blood Tests	
☐	Blood Pressure	_ _mm Hg. _ _Cuff _ _Site
☑	Other	**whole blood taurine**

Assessment:
DCM with severe B6
B6

Prognosis:
guarded

Plan:
follow up with B6 enal panel and eval. in 5-7 d; monthly exams there to assure HR/rhythm and overall reponse to Rx

Therapy:

B6

Monitoring: all vitals, esp RR/RE

Client Communication:
As above- poor prognosis in most affected dogs. short term goal is to reestablished normal breathing rate and effort. need to check blood panel in a week to assure renal function not affected
Then recheck monthly to assess HR/rhythm, and overall status a B6

expect wt loss

taurnine assay submitted

B6

Cardiology Examination

Date: 1/30/2018

Client:	B6	Patient:	B6	Sex:	Spayed Female
Patient ID#:	B6	DOB:	B6	Species:	Canine
Phone:	B6	Age:	B6	Breed:	Bloodhound Mix
rDVM:	B6				
rDVM contact info:	B6				

Vital Signs:

Medical History:
Progressive exercize intolerance, then incr. respiratory rate and cough past 10 days or so
Echo suggested DCM; chest radiograph indicated CHF (PE)
Rx and pet improved, but clinical sign of incr RR persist

appetite ok- commercial food bison protein source

	Comments
Other	

Reason For Visit:

cardiac consultation

Current Medications:

None	B6	
Aminophylline		
Amlodipine (Norvasc)		
Aspirin		
Atenolol		
Benazepril		
Clopidogrel (Plavix)		
Digoxin (digitalis)		
Diltiazem HCl		
Dilacor		
Enalapril		
Hycodan (Tussigon)		
Lasix (Furosemide)		
Methimazole (Tapazole)		
Mexiletine		
Pimobendan (Vetmedin)		
Sildenafil (Viagra)		
Sotolol		
Spironolactone		
Theophylline XR		
Other		

Referral Diagnostics:

- ☐ Echocardiogram
- ☐ Blood Tests

☐ ECG
☑ Radiographs cardiomegally; pulmonary edema (last week)
☐ Other

Heart Sounds:

☐ Gallop ☐ S_4 ☑ S_3 ☐ Summated ☐ Cannot Distinguish ☐ Systolic click ☐ Split S_2

Heart Rate/Rhythm:

Heart Rate BPM:_____180_____
☑ Sinus tachycardia
☐ Other Arrhythmia

Heart Murmur:

☐ No murmur
☐ Systolic:

Mitral Valve	☐ 1/6	☑ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Tricuspid Valve	☐ 1/6	☑ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Aortic Valve	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Pulmonic Valve	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Left Parasternal	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6
Right Parasternal	☐ 1/6	☐ 2/6	☐ 3/6	☐ 4/6	☐ 5/6	☐ 6/6

Murmur Quality_____
☐ Continuous
☐ Diastolic

Diet:

Previous CHF: ☑ Yes ☐ No

Dates: approximately one week ago

Comments:

Physical Exam:

Normal		Comments
☑	Mucous Membrane / Capillary Refill Time	
☑	Ears	
☑	Eyes	
☑	Oral Cavity - Dental Disease	
☑	Nose/Throat	
☑	Peripheral Lymph Nodes	
☑	Skin	
☑	Abdomen	
☑	Musculoskeletal	mild loss muscle mass noted
☑	CNS	
☑	Urogenital	

Body Condition Score
☐ 1 ☐ 2 ☐ 3 ☑ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9

Respiratory:

☐ Eupenic Respiratory Rate (Breaths per minute) 55 ☑ Tachypneic ☐ Dyspneic ☐ Orthopneic

Auscultation Lungs:

				Location
☐	Clear			
☐	Wheezes	insp ☐	expir ☐	
☐	Crackles	insp ☐	expir ☐	
☐	Muffled	☐ R. Chest	☐ L. Chest	
☑	Harsh			bilaterally

Jugular venous distention or pulsations:

☐ Jugular venous distention or Pulsations none

Femoral arterial pulse pressure
- ☐ Normal
- ☐ Hyperkinetic
- ☑ Hypokinetic

Diagnostics:

☑	Examination	
☑	Echo	
☐	Radiographs	
☐	Blood Tests	
☐	Blood Pressure	_ _mm Hg. _ _Cuff _ _Site
☑	Other	**whole blood B6**

Assessment:
DCM with severe, global myocardial failure
sinus tachycardia, pulmonary edema

Prognosis:
guarded

Plan:
follow up with B6 renal panel and eval. in 5-7 d; monthly exams there to assure HR/rhythm and overall reponse to Rx

Therapy:

B6

Monitoring: all vitals, esp RR/RE

Client Communication:
As above- poor prognosis in most affected dogs. short term goal is to reestablished normal breathing rate and effort. need to check blood panel in a week to assure renal function not affected
Then recheck monthly to assess HR/rhythm, and overall status at B6

expect wt loss

B6 assay submitted

From:	Lockeed, Matthew </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A2FE9A22E8F940FA8761FAD18EF37DD0-MATTHEW.LOC>
To:	Earley, Rosemary; Norris, Anne
CC:	Edwards, David; DeLancey, Siobhan; Jones, Jennifer L; Peloquin, Sarah; Reimschuessel, Renate; Palmer, Lee Anne; Carey, Lauren; Rotstein, David; Burkholder, William; Conway, Charlotte; Dewitt, Susan J; Goddard, Kristina; Benton, Denise; Rebello, Heidi; Haake, Lindsay; Peddicord, Sarah; Heard, Alexandra; Colonius, Tristan; Thompson, Alison; Glasner, Aliza; Hattis, Daniel; Emmitt, Keenan; AskOSC; Stamper, Carmela; Thorpe, Valarie; Kimberly, Brad; Cepeda, Sandra; Beckerman, Peter
Sent:	6/27/2019 3:48:40 PM
Subject:	RE: DCM Announcement - 11:00 AM Today (final comms attached)

OL outreach is complete. The call with Rep. Comer's office was friendly and they appreciated the heads-up. I will keep folks posted on any additional communication with Comer's office. Thanks for the quick turnaround on helpful RQAs.

Matt

From: Earley, Rosemary
Sent: Thursday, June 27, 2019 11:22 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

OCA outreach is completed.
Thank you,
Rosie

FDA
Rosemary Earley, DVM| *Congressional Affairs Specialist*
Office of Congressional Appropriations
Office: (301) 796-6186
Cell: B6
rosemary.earley@fda.hhs.gov

From: Hattis, Daniel
Sent: Thursday, June 27, 2019 11:19 AM
To: Earley, Rosemary <Rosemary.Earley@fda.hhs.gov>
Subject: FW: DCM Announcement - 11:00 AM Today (final comms attached)

From: Norris, Anne
Sent: Thursday, June 27, 2019 11:10 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

We are now live! CVM links are below and OMA will reply all to this thread with the press release link shortly. Huge thanks to everyone involved in this ongoing saga!

CVM Update

Web Update – DCM Investigation

Web QA (Updated)

Vet-LIRN Update

DCM Complaint Spreadsheet – 1/1/14 - 4/30/19

Best,
Anne

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:15 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan

<Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

Thanks, Ashley.

All, we're going to stick with the adjusted 11:00 start time. We appreciate your flexibility!

From: Zborowsky, Ashley
Sent: Thursday, June 27, 2019 10:07 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

Thanks Anne – I actually just got off the phone with Pete and we don't have any concerns, so this is good to go. I appreciate your patience! Apologies for the false alarm.

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:02 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra

<Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>; Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

In response to a request from OCC, we are holding on this until approximately 11:00 am ET. The timeline is updated below.

From: Norris, Anne
Sent: Thursday, June 27, 2019 9:41 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jeanette Murphy (Jenny.Murphy@fda.hhs.gov) <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; Siobhan DeLancey - FDA (Siobhan.Delancey@fda.hhs.gov) <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J (Susan.Dewitt@fda.hhs.gov) <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Daniel Hattis (Daniel.Hattis@fda.hhs.gov) <Daniel.Hattis@fda.hhs.gov>; Keenan Emmitt (Keenan.Emmitt@fda.hhs.gov) <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>
Subject: DCM Announcement - 10:30 AM Today (final comms attached)

Good morning,

At 10:30, we'll be sending our DCM investigative update live, including a CVM Update, Web Update, Vet-LIRN Update, Updated Web QA, and a spreadsheet of complaints submitted to the agency through 4/30/19. OMA is issuing a press release. When the pages are live I will circulate links for outreach. Attached are the final comms documents and the comms plan tick-tock is pasted below. Please reach out with any questions or concerns.

Thursday, June 27 - *Date of Announcement*

11:00 am EST
- Publish CVM Update, Web Update, Web QAs, Vet-LIRN Update, Redacted Complaint File (Denise Benton)
- Publish Press Release (OEA/OMA Web)

11:15 am EST: Immediately following email with live comms links (Anne Norris)
All outreach taking place simultaneously:
- CVM Stakeholder Outreach (Martine Hartogensis, Jenny Murphy, Dave Edwards, Jennifer Jones)
- OL Outreach (Tristan Colonius/Matt Lockeed)
- OCA Outreach (Dan Hattis/Keenan Emmitt)
- Mainstream Media Outreach (Lindsay Haake)
- Trade Media Outreach (Anne Norris)

11:45 am EST (upon completion of outreach)
- Email CVM Update to subscriber list (Denise Benton)
- Email Press Release to subscriber list (OEA/OMA Web)
- Publish tweets/Facebook post (Kristina Goddard, Valarie Thorpe)

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

From: Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: B6 @covance.com; msn.nutritional@covance.com
CC: Ceric, Olgica
Sent: 8/3/2017 3:41:03 PM
Subject: head's up: FDA samples shipping today: taurine, carnitine
Attachments: 800.218-Covance-Sub Form-8.2.2017.xls.html

Hi B6
We're shipping a dog food sample for testing. It should arrive tomorrow morning.
Tracking: 1ZA4420T1392373895
Thank you,
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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	B6 @covance.com; msn.nutritional@covance.com
CC:	Ceric, Olgica; Kaurup, Sean
Sent:	7/21/2017 1:14:30 PM
Subject:	head's up: FDA samples shipping today: Thiamine, Taurine, Protein, Fat, Moisture
Attachments:	800.216-Covance-Sub Form-7.19.2017.xls.html

Hi B6

This is a heads up that we are sending 2 samples today. The tracking is: 1ZA4420T0192171465

Please charge to a task order 2.

We are requesting testing for thiamine, taurine, protein, fat, and moisture.

Thanks and have a nice weekend,
Jennifer

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
U.S. Food & Drug Administration
Center for Veterinary Medicine
Office of Research
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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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
CC:	Ceric, Olgica; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'
Sent:	7/11/2017 3:38:21 PM
Subject:	Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Vet will submit PFR online à
2 dogs-unrelated miniature schnauzers

Dog 1: 2 yr à presented 2/2017 with fulminant CHF à severe DCM on echo, taurine/carnitine normal, infectious disease testing negative, died on the ventilator, necropsy done-myocardial changes were subtle but could be similar to moldy corn toxicity in pigs à plasma, urine, serum, and myocardial tissue available

Dog 2: 7 yr, had a syncopal episode ~2/2017 but presented to vet for progressive frequency of syncopal episodes à 6/2017 for CHF, diagnosed with DCM similar to housemate, nearly same image on Echo, taurine/carnitine normal, infectious disease testing negative, they have changed the diet (Hill's) and dog is responding to treatment; plasma, urine, and serum available

Dogs were eating California Naturals (different bag than from 2/2017) and treats (Milo's Kitchen); Vet has samples of food and treats

Jennifer L. A. Jones, DVM
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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>
Sent:	4/16/2018 12:21:39 PM
To:	Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; 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>
Subject:	hold-call with Dr. Adin re: DCM cases
Location:	WebEx Virtual Meeting
Start:	4/20/2018 3:00:00 PM
End:	4/20/2018 4:00:00 PM
Recurrence:	(none)
Meeting Status:	Meeting organized
Required Attendees:	Jones, Jennifer L; Rotstein, David; Norris, Anne; DeLancey, Siobhan; Darcy Adin

-- Do not delete or change any of the following text. --

Join WebEx meeting

Meeting number (access code): B6

Meeting password: B6

Join by phone

+1-210-795-0506 US Toll

+1-877-465-7975 US Toll Free

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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.

From:	Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'
CC:	Ceric, Olgica
Sent:	7/19/2017 11:07:02 AM
Subject:	Info on Vet-LIRN requests to DAF-2016 & 2017
Attachments:	2016-2017-Vet-LIRN-DAF Case Requests.xls.html

Of the 40 cases started in 2016, Vet-LIRN submitted 1 request to DAF. CERT submitted another to evaluate regulatory taurine levels.
Of the 10 complete cases started in 2017, Vet-LIRN submitted 3 requests to DAF. CERT/CIN-DO submitted another 3 for evaluation.

F:\4-ADMIN-OR reporting\04-updates for mangmt\2017-Vet-LIRN-DAF requests

Jennifer L. A. Jones, DVM
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fax: 301-210-4685
e-mail: *jennifer.jones@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Ceric, Olgica </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=OLGICA.CERIC>
To: Nemser, Sarah
CC: Jones, Jennifer L
Sent: 12/12/2014 2:19:00 PM
Subject: Invoice for PO 25
Attachments: 25-Invoice-B6pdf.html

25	***invoice submitted 12/12/2014***	*OC*	**B6**		*800.95-EON-186243-necropsy*	B6

Please pay B6 remaining charges are previous balance.

Olgica Ceric, DVM, PhD
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tel: 301-210-4262
fax: 301-210-4685
e-mail: ***olgica.ceric@fda.hhs.gov***
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Ceric, Olgica
Sent: Friday, December 12, 2014 9:10 AM
To: 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'
Cc: Jones, Jennifer L; Nemser, Sarah; Rotstein, David
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Necropsy report from veterinarian attached-page 3.

More as an FYI that we received it-very few details.

Olgica Ceric, DVM, PhD
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fax: 301-210-4685
e-mail: ***olgica.ceric@fda.hhs.gov***
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Tuesday, December 09, 2014 8:05 AM
To: Reimschuessel, Renate; Ceric, Olgica; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Yep!!

Worth the effort!

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Reimschuessel, Renate
Sent: Tuesday, December 09, 2014 8:02 AM
To: Ceric, Olgica; Rotstein, David; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Good we had them take the B6

Renate Reimschuessel V.M.D. Ph.D. Vet-LIRN
Phone/Fax(301)210-4024
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Ceric, Olgica
Sent: Tuesday, December 09, 2014 7:49 AM
To: Rotstein, David; Reimschuessel, Renate; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Update: Preliminary report from B6 attached. Possible viral etiology.

Olgica Ceric, DVM, PhD
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e-mail: *olgica.ceric@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Ceric, Olgica
Sent: Thursday, November 13, 2014 7:26 PM
To: Rotstein, David; Reimschuessel, Renate; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Medical records from primary veterinarian for your review. I also received radiographs from them, but can't open the file since it's .dcm file for which I don't have the program. I put in request for installation.

Olgica Ceric, DVM, PhD
Veterinary Medical Officer
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fax: 301-210-4685
e-mail: *olgica.ceric@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Thursday, November 13, 2014 3:48 PM
To: Reimschuessel, Renate; Ceric, Olgica; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Agreed!!!

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Reimschuessel, Renate
Sent: Thursday, November 13, 2014 3:45 PM
To: Rotstein, David; Ceric, Olgica; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

If the vet has trouble getting out the spinal cord– she could remove the top 1/3 of the vertebral column and then we ship that – much smaller box than the 85 pound body.

Renate Reimschuessel
Phone and fax- 301-210-4024
Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Reimschuessel, Renate
Sent: Thursday, November 13, 2014 3:38 PM
To: Rotstein, David; Ceric, Olgica; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Excellent!

Renate Reimschuessel
Phone and fax- 301-210-4024

Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Thursday, November 13, 2014 3:28 PM
To: Ceric, Olgica; Reimschuessel, Renate; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 **B6** Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Just spoke with the vet.

She will be coming in to do the necropsy tomorrow and that's it. She has removed spinal cords before and will attempt; if feels can't do it, she'll let us know. She will be removing the brain.

Thanks!
dave

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Ceric, Olgica
Sent: Thursday, November 13, 2014 3:20 PM
To: Reimschuessel, Renate; Rotstein, David; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 **B6** Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Additional records-bloodwork.

Olgica Ceric, DVM, PhD
Veterinary Medical Officer
U.S. Food & Drug Administration
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Office of Research
Veterinary Laboratory Investigation and Response Network (Vet-LIRN)
8401 Muirkirk Road, G704
Laurel, Maryland 20708
tel: 301-210-4262
fax: 301-210-4685
e-mail: *olgica.ceric@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Ceric, Olgica
Sent: Thursday, November 13, 2014 2:46 PM
To: Reimschuessel, Renate; Rotstein, David; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 **B6** Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

2 hours drive.

Olgica Ceric, DVM, PhD

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fax: 301-210-4685
e-mail: ***olgica.ceric@fda.hhs.gov***
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Ceric, Olgica
Sent: Thursday, November 13, 2014 2:46 PM
To: Reimschuessel, Renate; Rotstein, David; Carey, Lauren; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Dog has 85 pounds. We are lchecking how close vet is t B6

Olgica Ceric, DVM, PhD
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fax: 301-210-4685
e-mail: ***olgica.ceric@fda.hhs.gov***
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Reimschuessel, Renate
Sent: Thursday, November 13, 2014 2:44 PM
To: Rotstein, David; Carey, Lauren; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Ok – duh – we have a diagnostic lab in state – we could ask vet to send carcass there for the neuro or the full necropsy.

Renate Reimschuessel
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Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Rotstein, David
Sent: Thursday, November 13, 2014 2:33 PM
To: Reimschuessel, Renate; Carey, Lauren; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

B6

David Rotstein, DVM, MPVM, Dipl. ACVP

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7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Reimschuessel, Renate
Sent: Thursday, November 13, 2014 2:28 PM
To: Rotstein, David; Carey, Lauren; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619- B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Where is the animal?

Renate Reimschuessel
Phone and fax- 301-210-4024
Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Thursday, November 13, 2014 2:08 PM
To: Carey, Lauren; Reimschuessel, Renate; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619- B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

J bonesaw I can handle, it's the bandsaw that still freaks me out!!!

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Carey, Lauren
Sent: Thursday, November 13, 2014 2:05 PM
To: Rotstein, David; Reimschuessel, Renate; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619- B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Ah! I see. Just thinking to my days in the back room with just a blade and some formalin jars + 1 tech staring on. No bone saw for me!

From: Rotstein, David
Sent: Thursday, November 13, 2014 2:03 PM
To: Carey, Lauren; Reimschuessel, Renate; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619- B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Lauren,

Yes-it would be the whole CNS. I figured that the brain would be sampled (and could be figuring wrong!!! L) but that most people don't sample the spinal cord.

There maybe a few things going on here and it may be better if we could get the head and spinal cord to a Vet-LIRN lab…or to any interested pathologists .."hint" J

d.

David Rotstein, DVM, MPVM, Dipl. ACVP
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7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Carey, Lauren
Sent: Thursday, November 13, 2014 2:00 PM
To: Reimschuessel, Renate; Rotstein, David; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Sorry, just finally read the MRx. B6 If we are submitting for the spinal cord, would a full CNS exam, including the brain be possible?

From: Reimschuessel, Renate
Sent: Thursday, November 13, 2014 5:42 AM
To: Rotstein, David; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Olga – either you or Dave should discuss with vet the need and potential options.

I'm at White Oak today – in meetings – you guys work out between yourselves who should call.

Renate Reimschuessel
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Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Rotstein, David
Sent: Wednesday, November 12, 2014 10:51 PM
To: Reimschuessel, Renate; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

B5

B5

d.

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Reimschuessel, Renate
Sent: Wednesday, November 12, 2014 9:44 PM
To: Rotstein, David; Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Local vet – probably unlikely—
Olga – if they can't do the neuro stuff, consider shipping dog carcass to a vet-LIRN path lab after the local vet does the organ harvesting if Dave thinks it is worth the effort/cost.

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Alternate FAX 301-210-4685
renate.reimschuessel@fda.hhs.gov
Vet-LIRN
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Wednesday, November 12, 2014 9:42 PM
To: Ceric, Olgica; Reimschuessel, Renate; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: Re: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Hope they can get spinal cord or portion of spine with cord
Sent from BlackBerry

From: Ceric, Olgica
Sent: Wednesday, November 12, 2014 07:30 PM Eastern Standard Time
To: Reimschuessel, Renate; Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Attached are the medical records from B6 They will be performing necropsy.

Dog was a new patient-two pages only. Veterinarian suspected B6

B6

I will contact primary veterinarian tomorrow, they have additional medical records.

B6 will also send bloodwork and x-rays (done at primary vet, sending by fax tomorrow).

Olgica Ceric, DVM, PhD
Veterinary Medical Officer
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Office of Research
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fax: 301-210-4685
e-mail: *olgica.ceric@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Ceric, Olgica
Sent: Tuesday, November 11, 2014 12:18 PM
To: Reimschuessel, Renate; Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: Re: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

One more save at the last moment :)
Olgica Ceric

From: Reimschuessel, Renate
Sent: Tuesday, November 11, 2014 12:10 PM
To: Ceric, Olgica; Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: Re: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Excellent ! Thanks
RR----------
Sent using BlackBerry

From: Ceric, Olgica
Sent: Tuesday, November 11, 2014 11:18 AM Eastern Standard Time
To: Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Update: I arranged necropsy.

Body was sent to crematorium but clinic contacted them and put the hold on cremation. Crematorium is returning the body to clinic (body is frozen) on Thursday.

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Veterinary Medical Officer
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tel: 301-210-4262

fax: 301-210-4685
e-mail: ***olgica.ceric@fda.hhs.gov***
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Rotstein, David
Sent: Tuesday, November 11, 2014 10:29 AM
To: Ceric, Olgica; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Thanks Olga!!

David Rotstein, DVM, MPVM, Dipl. ACVP
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7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: Ceric, Olgica
Sent: Tuesday, November 11, 2014 10:14 AM
To: Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: RE: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

Vet-LIRN Case Summary Document

Vet-LIRN Case Number:	
EON/CC #:	EON-186243
Vet-LIRN Initiation Date:	11.11.2014
MedRec: Requested:	yes
MedRec: Received:	
MedRec: Significant finding:	
Vet-LIRN Tests (planned):	MRx, necropsy
Vet-LIRN Test Results:	
Result Interpretation:	
IF NFA, justification:	

11.11.2014

Dog: 21 months, Akita,male, neutered

Received new bag of dog food (same variety/flavor as always) 10/27/14. Fed normal feeding that evening. Next couple days dog did not show interest in eating, then finally a small amount mid week, then nothing for few more days. Noticed lethargic behavior. Some drooling. Reported concerns to the distributer B6 who assured me it would be reported to manufacturer immediately. Provided all information from bag. Purchased B6 a new bag, different flavor and from a different supplier as well as some wet food of the same. At time of purchase, a representative of manufacturer was in the store and also took a report who

assured me I would be contacted. This did not happen. Dog ate wet food well. Little of the new dry. But continued to be lethargic and increasingly ill. Visit to veterinarian, including a sample of food for testing on B6 Dog showing signs of paralysis. Again to different veterinarian for further treatment B6 Passed away on B6

Plan: necropsy if possible, MRx

Follow up: OC-called the owner and discussed the case with her. Dog passed away B6 morning and was taken to veterinarian on B6 Owner will call veterinarian and find out if they still have the body or if it was cremated already. If body is available she will ask them to hold it.

Additional information from owner: no vomiting or diarrhea noted. Dog was urinating normally (kept in the kennel during the day while family is at work). Dog was taken to regular veterinarian and new veterinarian (owner will provide email and contact information for other veterinarian). Blood work was done. Owner still has the food with original package, no other pets. No raisins, grapes, chocolate. No vitamins and supplements. Dog was previously healthy. No table scraps. Dog was given one treat each day (Doggy Delirious Peanut butter):

http://www.amazon.com/Doggy-Delirious-Peanut-Butter-1-Pound/dp/B006SU4RMI

Olgica Ceric, DVM, PhD
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U.S. Food & Drug Administration
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Office of Research
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fax: 301-210-4685
e-mail: *olgica.ceric@fda.hhs.gov*
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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From: Ceric, Olgica
Sent: Monday, November 10, 2014 10:09 PM
To: Rotstein, David; CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: Re: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

I will contact owner and vet B6 and see about necropsy, will request med.records.
Olgica Ceric

From: Rotstein, David
Sent: Monday, November 10, 2014 10:01 PM
To: CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Subject: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:

21 MO MN Akita

DOD – B6

Recc: necropsy if possible, med records, talk to vet about what testing was done.

Signs are a bit vague—lethargy to paralysis—differential list is wide unless there is bloodwork. Can't think that the neurologic form of Listeria would be that fast & in a monogastric. But would have to be on the list.

Raw diet--http://www.naturesvariety.com/Instinct/dog/kibble/rawboost/all

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7519 Standish Place, RM 120
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240-506-6763 (BB)

From: PFR Event [mailto:pfreventcreation@fda.hhs.gov]
Sent: Monday, November 10, 2014 9:52 PM
To: B6
Subject: Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition: B6

A PFR Report has been received and PFR Event [EON-186243] has been created in the EON System

A "PDF" report by name "1036619-report.pdf" is attached to this email notification for your reference.

Below is the summary of the report

EON Key: EON-186243
EON Title: PFR Event created for Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition; 1036619

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

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

Product information
Individual Case Safety Report Number: 1036619
Product Group: Pet Food
Product Name: Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition
Description: Received new bag of dog food (same variety/flavor as always) 10/27/14. Fed normal feeding that evening. Next couple days dog did not show interest in eating, then finally a small amount mid week, then nothing for few more days. Noticed lethargic behavior. Some drooling. Reported concerns to the distributer B6 who assured me it would be reported to manufacturer immediately. Provided all information from bag. Purchased B6 a new bag, different flavor and from a different supplier as well as some wet food of the same. At time of purchase, a representative of manufacturer was in the store and also took a report who assured me I would be contacted. This did not happen. Dog ate wet food well. Little of the new dry. But continued to be lethargic and increasingly ill. Visit to veterinarian, including a sample of food for testing on B6 Dog showing signs of paralysis. Again to different veterinarian for further treatment B6 Passed away on B6.
Submission Type: Initial
Report Type: Both
Outcome of reaction/event at the time of last observation: Died Euthanized
Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Sender information

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.

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From: Peloquin, Sarah </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8607f880df2b494aa639e6d9a3874132-Sarah.Peloq>
To: Jones, Jennifer L
Sent: 1/30/2019 2:15:41 PM
Subject: B6

Jen, thank you so much for following up with Dr. Freeman!! I just realized I got her voicemail too.

Sarah Peloquin, DVM
Veterinary Medical Officer
tel: 240-402-1218

From: Jones, Jennifer L
Sent: B6
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Cc: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: B6

Hi Lisa,
Thank you for the head's up. If the owner can bring the body to Tufts for the necropsy, we can authorize and pay for it. I attached the most recent version of the necropsy protocol. Your lab can perform the gross necropsy and histopathology of the non-heart tissues. We'll need a set of slide recuts sent to us for review. We'll need to collect the intact formalin-fixed heart, fresh frozen tissues, and slide recuts. When the time comes, I can send you a box for this with a prepaid shipping label.

If you're willing to do this, please send me an estimate for the necropsy and histopathology with recuts. I'll make the purchase request B6
Thank you for bringing this to our attention,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: B6
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: B6
Importance: High

Hi Jen
I left a message on your machine but in case you're checking email, one of the cases I submitted B6 died B6 The owner has given permission for a necropsy or getting heart samples so I am hoping to get in touch with you asap to see if we can work it out (I'm assuming you're back at work since I got this email from you)

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 <Jennifer.Jones@fda.hhs.gov>
Sent: B6
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Subject: B6

Thank you for the update, Lisa. I'm sorry to hear that he passed away. Can you please forward the records for his case?

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: B6
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: B6

Hi Jen
Wanted to let you know that B6 died unexpectedly due to choking B6 while eating. Owner said he had been doing well and we were going to do a recheck in Feb.
So sad ☹
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: Peloquin, Sarah
Sent: 1/30/2019 2:26:45 PM
Subject: B6

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Peloquin, Sarah
Sent: B6 9:16 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: B6

Jen, thank you so much for following up with Dr. Freeman!! I just realized I got her voicemail too.

Sarah Peloquin, DVM
Veterinary Medical Officer
tel: 240-402-1218

From: Jones, Jennifer L
Sent: B6 7:58 AM
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Cc: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Subject: B6

Hi Lisa,
Thank you for the head's up. If the owner can bring the body to Tufts for the necropsy, we can authorize and pay for it. I attached the most recent version of the necropsy protocol. Your lab can perform the gross necropsy and histopathology of the non-heart tissues. We'll need a set of slide recuts sent to us for review. We'll need to collect the intact formalin-fixed heart, fresh frozen tissues, and slide recuts. When the time comes, I can send you a box for this with a prepaid shipping label.

If you're willing to do this, please send me an estimate for the necropsy and histopathology with recuts. I'll make the purchase reques B6
Thank you for bringing this to our attention,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: B6 4:19 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: B6
Importance: High

Hi Jen
I left a message on your machine but in case you're checking email, one of the cases I submitted B6 died B6 The owner has given permission for a necropsy or getting heart samples so I am hoping to get in touch with you asap to see if we can work it out (I'm assuming you're back at work since I got this email from you)

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 <Jennifer.Jones@fda.hhs.gov>
Sent: B6 10:02 AM
To: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Subject: B6

Thank you for the update, Lisa. I'm sorry to hear that he passed away. Can you please forward the records for his case?

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: B6
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: B6

Hi Jen
Wanted to let you know that B6 died unexpectedly due to choking B6 while eating. Owner said he had been doing well and we were going to do a recheck in Feb.
So sad ☹
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:	Peloquin, Sarah </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8607F880DF2B494AA639E6D9A3874132-SARAH.PELOQ>
To:	Rotstein, David; Carey, Lauren; Ceric, Olgica; Glover, Mark; Jones, Jennifer L; Nemser, Sarah; Palmer, Lee Anne; Queen, Jackie L
Sent:	4/25/2019 5:43:10 PM
Subject:	RE: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

FYI, no necropsy was performed on this one per Dr. Freeman.

Sarah Peloquin, DVM
Veterinary Medical Officer
tel: 240-402-1218

From: Rotstein, David
Sent: Monday, April 22, 2019 11:12 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Glover, Mark <Mark.Glover@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: FW: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

Forwarding this on because the dog died on B6 and unsure of necropsy status

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From: Related PFR Event <pfrsignificantactivitycreation@fda.hhs.gov>
Sent: Monday, April 22, 2019 11:09 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Cleary, Michael * <Michael.Cleary@fda.hhs.gov>; HQ Pet Food Report Notification <HQPetFoodReportNotification@fda.hhs.gov>; B6
Subject: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

A PFR Report has been received and Related PFR Event [EON-385681] has been created in the EON System.

A "PDF" report by name "2066093-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 "2066093-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-385681
ICSR #: 2066093
EON Title: Related PFR Event created for Wellness Complete Health Fish and Sweet Potato dry; 2066093

AE Date	02/22/2019	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Other
Breed	Boxer (German Boxer)		
Age	10.5 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2066093
Product Group: Pet Food
Product Name: Wellness Complete Health Fish and Sweet Potato dry
Description: Arrhythmia dx at RDVM July 2018 (had been "wheezing") Started wheezing again 1 week before admission. Diagnosed with DCM, CHF, and ventricular tachycardia 2/22/19 Was fed Wellness diet until 6/2018 then changed to Royal Canin Boxer (current diet). Taurine and troponin pending. Owner has another Boxer eating same diets - has not been screened Enrolled in DCM study. Changing to different diet (although Boxer diet is probably fine) and will recheck in 7 days and 3 months. Patient passed away at home B6
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: Died Other
Number of Animals Treated With Product: 2
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Wellness Complete Health Fish and Sweet Potato dry		

This report is linked to:
Initial EON Event Key: EON-380848
Initial ICSR: 2063189

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:
https://eon.fda.gov/eon//browse/EON-385681

To view the Related PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction!viewReport.jspa?decorator=none&e=0&issueType=10100&issueId=402809&parentIssueTypeId=12

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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.

From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: Peloquin, Sarah
Sent: 4/30/2019 11:36:11 AM
Subject: RE: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

Thank you, Sarah! :) Will you please update the metrics document under the DCM tab?

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Thursday, April 25, 2019 1:59 PM
To: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Glover, Mark <Mark.Glover@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Subject: RE: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

Thanks

From: Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>
Date: April 25, 2019 at 1:43:11 PM EDT
To: Rotstein, David <David.Rotstein@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>, Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>, Glover, Mark <Mark.Glover@fda.hhs.gov>, Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>, Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>
Subject: RE: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

FYI, no necropsy was performed on this one per Dr. Freeman.

Sarah Peloquin, DVM
Veterinary Medical Officer
tel: 240-402-1218

From: Rotstein, David
Sent: Monday, April 22, 2019 11:12 AM
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Glover, Mark <Mark.Glover@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: FW: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

Forwarding this on because the dog died on B6 and unsure of necropsy status

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

240-506-6763 (BB)

U.S. FOOD & DRUG ADMINISTRATION

From: Related PFR Event <pfrsignificantactivitycreation@fda.hhs.gov>
Sent: Monday, April 22, 2019 11:09 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Cleary, Michael * <Michael.Cleary@fda.hhs.gov>; HQ Pet Food Report Notification <HQPetFoodReportNotification@fda.hhs.gov> B6
Subject: Wellness Complete Health Fish and Sweet Potato dry: Lisa Freeman - EON-385681

A PFR Report has been received and Related PFR Event [EON-385681] has been created in the EON System.

A "PDF" report by name "2066093-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 "2066093-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-385681
ICSR #: 2066093
EON Title: Related PFR Event created for Wellness Complete Health Fish and Sweet Potato dry; 2066093

AE Date	02/22/2019	**Number Fed/Exposed**	2
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Died Other
Breed	Boxer (German Boxer)		
Age	10.5 Years		
District Involved	PFR-New England DO		

Product information
Individual Case Safety Report Number: 2066093
Product Group: Pet Food
Product Name: Wellness Complete Health Fish and Sweet Potato dry
Description: Arrhythmia dx at RDVM July 2018 (had been "wheezing") Started wheezing again 1 week before admission. Diagnosed with DCM, CHF, and ventricular tachycardia 2/22/19 Was fed Wellness diet until 6/2018 then changed to Royal Canin Boxer (current diet). Taurine and troponin pending. Owner has another Boxer eating same diets - has not been screened Enrolled in DCM study. Changing to different diet (although Boxer diet is probably fine) and will recheck in 7 days and 3 months. Patient passed away at home B6

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: Died Other
Number of Animals Treated With Product: 2
Number of Animals Reacted With Product: 1

Product Name	Lot Number or ID	Best By Date
Wellness Complete Health Fish and Sweet Potato dry		

This report is linked to:
Initial EON Event Key: EON-380848
Initial ICSR: 2063189

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:
https://eon.fda.gov/eon//browse/EON-385681

To view the Related PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction!viewReport.jspa?decorator=none&e=0&issueType=10100&issueId=402809&parentIssueTypeId=12

==========

From: Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: Ceric, Olgica
Sent: 8/25/2016 11:48:07 AM
Subject: last one, thank you!!
Attachments: 958500-Taurine.pdf.html; 958501-Taurine.pdf.html; 958504-Taurine.pdf.html

05-800.180-EON-multipl B6 Results: District testing results
F:\6-CASES\1-Working on report\800.180-EON-266814 B6 Merrick-taurine

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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: 'Guag, Jake * (Jake.Guag@fda.hhs.gov)'
Sent: 1/10/2018 1:02:19 PM
Subject: Pet Food collection kit for 800.218

Hi Jake,
Can you please send a box when you have time this week? B6

B6

The box will ship to:

Dr. Darcy Adin
North Carolina State University
NC State Veterinary Hospital
1060 William Moore Drive
Raleigh, NC 27607
919-513-6032

We are collecting dog food-weight 0.36 kg. In a plastic tupperware container-~5" x 5" x 2"
No hazardous materials.
Room temperature.

Thank you, J

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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAVID.ROTSTEIN>
To: CVM Vet-LRN-OR; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Sent: B6 3:01:22 AM
Subject: Possible Necropsy? EON-186243-ICSR-1036619 B6 Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition:
Attachments: 1036619-report.pdf.html

21 MO MN Akita

DOD – B6

Recc: necropsy if possible, med records, talk to vet about what testing was done.

Signs are a bit vague—lethargy to paralysis—differential list is wide unless there is bloodwork. Can't think that the neurologic form of Listeria would be that fast & in a monogastric. But would have to be on the list.

Raw diet--http://www.naturesvariety.com/Instinct/dog/kibble/rawboost/all

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM OSC/DC/ICERT
7519 Standish Place, RM 120
240-276-9213 (Office and Fax)
240-506-6763 (BB)

From: PFR Event [mailto:pfreventcreation@fda.hhs.gov]
Sent: B6 9:52 PM
To: B6; HQ Pet Food Report Notification; B6
Subject: Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition B6

A PFR Report has been received and PFR Event [EON-186243] has been created in the EON System

A "PDF" report by name "1036619-report.pdf" is attached to this email notification for your reference.

Below is the summary of the report

EON Key: EON-186243
EON Title: PFR Event created for Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition; 1036619

To view this PFR Event, please click the link below:
https://eon.fda.gov/eon//browse/EON-186243

To view the PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction.jspa?decorator=none&e=0&issueType=12&issueId=198525

Product information
Individual Case Safety Report Number: 1036619

Product Group: Pet Food
Product Name: Nature's Variety Instinct Raw boost; Duck meal & Turkey meal formula. Grain free edition
Description: Received new bag of dog food (same variety/flavor as always) 10/27/14. Fed normal feeding that evening. Next couple days dog did not show interest in eating, then finally a small amount mid week, then nothing for few more days. Noticed lethargic behavior. Some drooling. Reported concerns to the distributer 11/1/14 who assured me it would be reported to manufacturer immediately. Provided all information from bag. Purchased 11/2/14 a new bag, different flavor and from a different supplier as well as some wet food of the same. At time of purchase, a representative of manufacturer was in the store and also took a report who assured me I would be contacted. This did not happen. Dog ate wet food well. Little of the new dry. But continued to be lethargic and increasingly ill. Visit to veterinarian, including a sample of food for testing o B6 Dog showing signs of paralysis. Again to different veterinarian for further treatment B6 Passed away on B6.
Submission Type: Initial
Report Type: Both
Outcome of reaction/event at the time of last observation: Died Euthanized
Number of Animals Treated With Product: 1
Number of Animals Reacted With Product: 1

Sender information

B6

USA

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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.

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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.

From:	Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
CC:	Ceric, Olgica; Nemser, Sarah; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)'
Sent:	10/31/2016 3:27:14 PM
Subject:	potential report to keep an eye out for-DCM-3 dogs-vegan diet

Per Lisa Freeman at Tufts-"I'm going to have another one for you. 3 unrelated dogs in a family who've developed dilated cardiomyopathy. Supposedly on a commercial vegan diet and then small company;s dog food. Once I get more details, I'll submit that one"

I asked her for the ICSR number-will let you know

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: 'Guag, Jake * (Jake.Guag@fda.hhs.gov)'; 'Andrea Fascetti'; B6
Sent: 10/1/2018 2:54:56 PM
Subject: Questions about Control Urine Samples
Attachments: Normal_dog_ND 79-99.xls; Normal_dog_ND1-22.xls

Hi B6
I hope you're doing well. I imagine things are busy right now ☺ I am preparing the reference ranges for our AAVLD presentation, and I had a few questions about the data you sent.

B5

Thank you again. I'll be forwarding a copy of the powerpoint presentation for your feedback later this week.
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: Reimschuessel, Renate </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS/CN=RREIMSCH>
To: Jones, Jennifer L
Sent: 10/25/2017 5:33:00 PM
Subject: RE: 800.218-Final report for review
Attachments: 800.218-FinalReport B6 raft-10.16.2017.doc

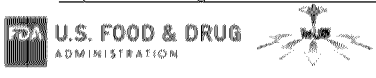
One minor edit

Renate Reimschuessel V.M.D. Ph.D. Vet-LIRN
Phone 1- 240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Jones, Jennifer L
Sent: Monday, October 16, 2017 12:55 PM
To: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: 800.218-Final report for review

F:\6-CASES\1-Working on report\sent to rr for review\800.218-EON-323515-19- B6 -CA Naturals-DCM\6-REPORT

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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
CC:	Ceric, Olgica
Sent:	8/7/2017 11:02:02 AM
Subject:	RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519
Attachments:	800.218-TAMU-[B5] neg.pdf.html; EON-323515-19-[B6]-case summary-8.7.2017.doc.html

FYI-Taurine/carnitine still pending, bu[B5]negative.

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION Vet-LIRN

From: Jones, Jennifer L
Sent: Thursday, July 27, 2017 7:25 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

We received the food and plan to test for[B5]The vet also mentioned two items of interest:

1. She's treated 2 other dogs in last 2 weeks with DCM/CHF and being fed California Natural food. That brings us to 4 DCM dogs recently eating this food.
    a. We can consider taurine and other types of testing?
2. She forwarded me an article abou[B5]
    a. I don't believe our labs or Covance can test for this. Eurofins can test for this.

Thoughts from the group?

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION Vet-LIRN

From: Jones, Jennifer L
Sent: Tuesday, July 18, 2017 8:18 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Ok, thanks, Dave. I'll check[B5]

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION Vet-LIRN

From: Rotstein, David
Sent: Thursday, July 13, 2017 2:54 PM
To: Jones, Jennifer L; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

I think testing is worth pursuing. Oddball question: B5

B5

This would highly unlikely, but wanted to put it out there.

David Rotstein, DVM, MPVM, Dipl.ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Date: July 13, 2017 at 2:44:24 PM EDT
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

B5

Medical Record Review:

B6

Presenting complaint B6: dyspnea, cough of 3 week duration-wheezing type more frequent at nightà rDVM, treated w/ prednisone and doxycycline for kennel coughà B6 inappetance, vomiting à B6 dyspneic and recheck, hospitalized and treated for pneumonia, regurgitatedà B6 treated as outpatient B6 as syring feeding, dog regurgitated and had marked dyspneaà ER à refer to NCSU à B6 put on mechanical ventilator B6 euthanized

B6

B6

B6

tFAST B6 severe cardiomegaly with ventricular hypocontractility

Echo dcm vs. myocarditis vs pacing induce vs. other (severely dilated & hypocontractile left & right ventricles, severely dilated left and right atria)

Necropsy: Lung-severe diffuse alveolar injury with marked fibrin deposition (hyaline) and marked alveolar histiocytosis and multifocal type II pneumocyte hyperplasia; mod to marked diffuse pulmonary edema; mild cardiomegaly with mild mitral valve endocardiosis and mild left ventricular hypertrophy and left atrial dilation; thorax with mild pleural effusion; Suspect primary non-cardiogenic etiology but if clinical cardiac dysfunction then functional cardiac abnormalities cannot be ruled out

Prior MHx: coffee brown urine including clumping after strenuous activity when it is hot outside and resolves with 24-36 hours; also Crystalluria

B6

Presented B6 episodes of collapse, first occurred mid February, fall 6 seconds without losing consciousnessà immediately return to normal à2 weeks later again collapse, then on à 6/3 post 2 hour hike collapsed again; panting more than usual; good appetite for treats but reluctant to eat food since February;à recheck 7/10, doing better, no collapsing episodes except a stumbling moment when excited, respiratory rate normal, diet changed to Hill's

B6

B6

B6

Rads: left sided congestive heart failure

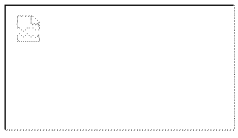
-7/10: moderate left sided cardiomegaly without heart failure, moderate hepatomegaly

Echo: mitral valve endocardiosis with left atrial enlargement and heart failure, decreased left ventricular systolic function, suspected DCM

Thoughts: B5

B5

Jennifer Jones, DVM
Veterinary Medical Officer



From: Rotstein, David
Sent: Tuesday, July 11, 2017 12:44 PM
To: Jones, Jennifer L; Reimschuessel, Renate; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

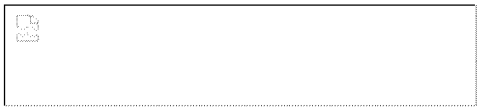
Jen,

B5 so I don't think that could be ruled out.

I do like the exploration of other causes.

d.

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place, RM 120
240-402-5613 (Office) (NEW NUMBER)
240-506-6763 (BB)



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Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Yes, and also, vet talked t B4 who said there was B5 in this food…but that doesn't rule out treats.

B5

Jennifer Jones. DVM
Veterinary Medical Officer

From: Reimschuessel, Renate
Sent: Tuesday, July 11, 2017 11:51 AM
To: Jones, Jennifer L; Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Davis may be able to screen fo B5

Renate Reimschuessel V.M.D. Ph.D. Vet-LIRN
Phone 1-240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

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Cc: Ceric, Olgica; Reimschuessel, Renate
Subject: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Vet will submit PFR online à
2 dogs-unrelated miniature schnauzers

Dog 1: 2 yr à presented 2/2017 with fulminant CHFà severe DCM on echo, taurine/carnitine normal, infectious disease testing negative, died on the ventilator, necropsy done-myocardial changes were subtle but could be similar to moldy corn toxicity in pigsà plasma, urine, serum, and myocardial tissue available

Dog 2: 7 yr, had a syncopal episode ~2/2017 but presented to vet for progressive frequency of syncopal episodesà 6/2017 for CHF, diagnosed with DCM similar to housemate, nearly same image on Echo, taurine/carnitine normal, infectious disease testing negative, they have changed the diet (Hill's) and dog is responding to treatment; plasma, urine, and serum available

Dogs were eating California Naturals (different bag than from 2/2017) and treats (Milo's Kitchen); Vet has samples of food and treats

Jennifer L. A. Jones, DVM
Veterinary Medical Officer
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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=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To: Rotstein, David
Sent: 1/11/2018 3:53:42 PM
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Thank you!

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Thursday, January 11, 2018 10:05 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Here you go!

I couldn't get the original article:

J Am Vet Med Assoc. 1985 Dec 1;187(11):1137-40.

Cardiomyopathy in stranded pygmy and dwarf sperm whales.

Bossart GD, Odell DK, Altman NH.

Abstract

Necropsy and histologic examinations were performed in 23 pygmy sperm whales (Kogia breviceps) and 6 dwarf sperm whales (Kogia simus) that had been stranded singly or in cow-calf pairs along the southeastern coastline of the United States. At necropsy, the gross findings in the adult whales included pale, flabby right ventricles. Microscopically, lesions in the hearts of the whales were characterized by moderate to extensive myocellular degeneration, atrophy, and fibrosis. Similar changes were not seen in 5 of 6 sexually immature whales or in the whale calves. Hepatic changes were consistent with heart failure. The cause of the myocardial lesions was not determined. The systemic effects of failing myocardium probably were a major reason for the stranding of the adult whales.

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

U.S. FOOD & DRUG ADMINISTRATION

to persons not authorized to receive such information. If you are not the intended recipient, any dissemination, distribution, or copying is strictly prohibited. If you think you received this e-mail message in error, please e-mail the sender immediately at david.rotstein@fda.hhs.gov.

From: Jones, Jennifer L
Sent: Thursday, January 11, 2018 9:51 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Thanks, Dave. If you have info readily available that's great. If no, I can look/prompt NCSU to look too.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

From: Rotstein, David
Sent: Thursday, January 11, 2018 9:46 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Thanks Jen.

B5

I didn't get the articles for you, but there is an issue in Kogia (pygmy sperm whales) involving a cardiomyopathy of unknown etiology. There was some work up done on some muscle markers. Not sure if NCSU would be interested in that info or not.

d.

David Rotstein, DVM, MPVM, Dipl. ACVP
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CVM OSC/DC/CERT
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From: Jones, Jennifer L
Sent: Thursday, January 11, 2018 9:36 AM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

FYI-

JJ-Vet emailed-" As additional information, one of our cardiologist colleagues in **B6** posted a question about this association today on our list serve. She has seen 4 cases of DCM in dogs eating kangaroo and lentil (I assume CN but not sure) in the last year - 2 were housemates but related."

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Wednesday, January 03, 2018 2:32 PM
To: Rotstein, David <David.Rotstein@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Tuesday, August 22, 2017 8:39 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Agreed. Thanks Jen

David Rotstein, DVM, MPVM, Dipl. ACVP
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7519 Standish Place
240-506-6763 (BB)

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Tuesday, August 22, 2017 8:37 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

BLUF: **Final Conclusion:** The cause of the two dogs' DCM is unclear. The bloodwork for these dogs showed normal taurine and carnitine levels. Based on the dogs' blood taurine/carnitine levels and the dry dog food test results, it is unlikely that B5 taurine, or carnitine caused the dogs' illness.

Final Conclusion: The cause of the two dogs' DCM is unclear. The bloodwork for these dogs showed normal taurine and carnitine levels. Based on the dogs' blood taurine/carnitine levels and the dry dog food test results, it is unlikely that B5 taurine, or carnitine caused the dogs' illness.

Jennifer Jones, DVM
Veterinary Medical Officer

From: Jones, Jennifer L
Sent: Monday, August 07, 2017 7:02 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

FYI-Taurine/carnitine still pending, but B5 negative.

Jennifer Jones, DVM
Veterinary Medical Officer

From: Jones, Jennifer L
Sent: Thursday, July 27, 2017 7:25 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

We received the food and plan to test for B5 The vet also mentioned two items of interest:

1. She's treated 2 other dogs in last 2 weeks with DCM/CHF and being fed California Natural food. That brings us to 4 DCM dogs recently eating this food.
    a. We can consider taurine and other types of testing?
2. She forwarded me an article abou B5
    a. I don't believe our labs or Covance can test for this. Eurofins can test for this.

Thoughts from the group?

Jennifer Jones, DVM
Veterinary Medical Officer

From: Jones, Jennifer L
Sent: Tuesday, July 18, 2017 8:18 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Ok, thanks, Dave. I'll check B5

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Thursday, July 13, 2017 2:54 PM
To: Jones, Jennifer L; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

I think testing is worth pursuing. Oddball question B5

B5

This would highly unlikely, but wanted to put it out there.

David Rotstein, DVM, MPVM, Dipl.ACVP
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CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Date: July 13, 2017 at 2:44:24 PM EDT
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
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Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

B5

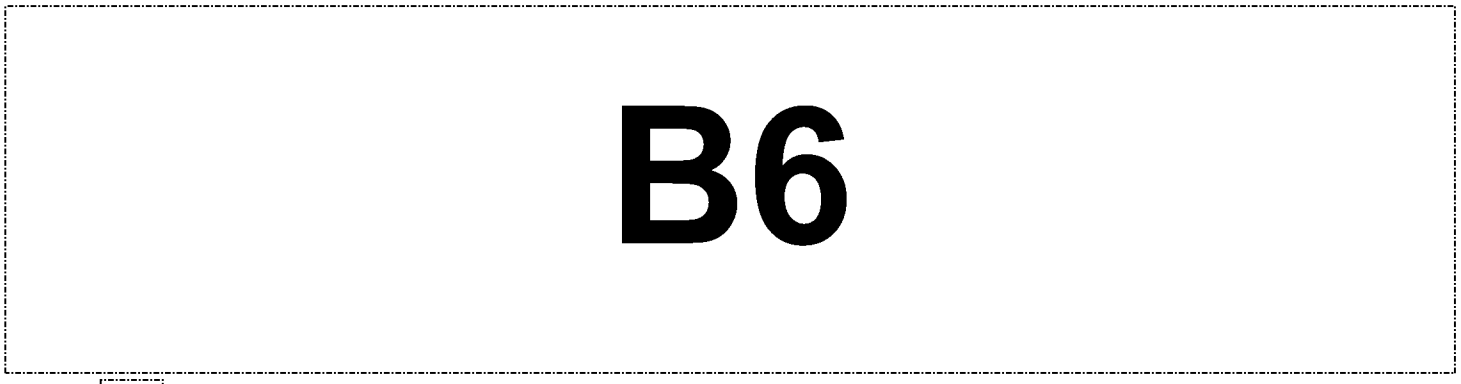
Medical Record Review:

B6

Presenting complaint B6 dyspnea, cough of 3 week duration-wheezing type more frequent at nightà rDVM, treated w/ prednisone and doxycycline for kennel coughà B6 inappetance, vomiting à

B6 dyspneic and recheck, hospitalized and treated for pneumonia, regurgitatedà B6 treated as outpatient B6 as syring feeding, dog regurgitated and had marked dyspneaà ER à refer to NCSU à B6 put on mechanical ventilatorà B6 euthanized

B6



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Echo B6 dcm vs. myocarditis vs pacing induce vs. other (severely dilated & hypocontractile left & right ventricles, severely dilated left and right atria)

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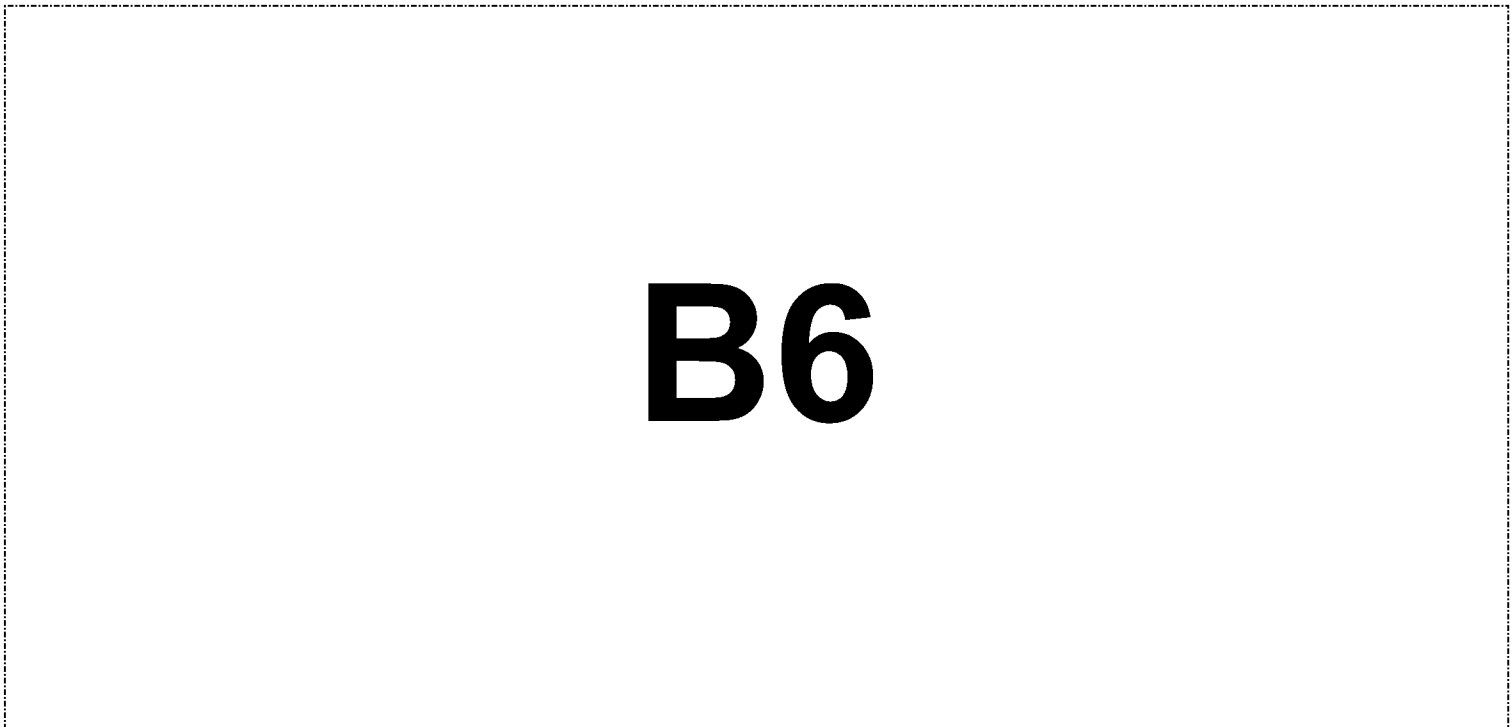

B6

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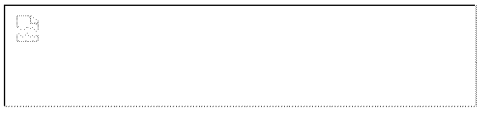
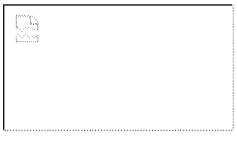
Veterinary Medical Officer





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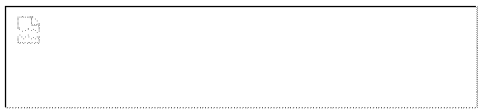

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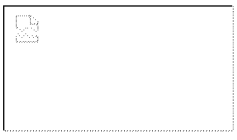

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Davis may be able to screen fo B5

Renate Reimschuessel V.M.D. Ph.D. Vet-LIRN
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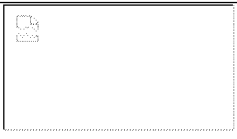
Web: http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm



From:	Jones, Jennifer L </O=FDA/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=JENNIFER.JONESAA8>
To:	Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
CC:	Ceric, Olgica
Sent:	8/22/2017 12:36:53 PM
Subject:	RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

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Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Monday, August 07, 2017 7:02 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: 800.218-Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

FYI-Taurine/carnitine still pending, bu B5 negative.

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Thursday, July 27, 2017 7:25 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

We received the food and plan to test for B5 The vet also mentioned two items of interest:

1. She's treated 2 other dogs in last 2 weeks with DCM/CHF and being fed California Natural food. That brings us to 4 DCM dogs recently eating this food.
    a. We can consider taurine and other types of testing?
2. She forwarded me an article about B5
    a. I don't believe our labs or Covance can test for this. Eurofins can test for this.

Thoughts from the group?

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION

From: Jones, Jennifer L
Sent: Tuesday, July 18, 2017 8:18 AM
To: Rotstein, David; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

Ok, thanks, Dave. I'll check B5

Jennifer Jones, DVM
Veterinary Medical Officer

U.S. FOOD & DRUG ADMINISTRATION

From: Rotstein, David
Sent: Thursday, July 13, 2017 2:54 PM
To: Jones, Jennifer L; Palmer, Lee Anne; Reimschuessel, Renate; Queen, Jackie L; Carey, Lauren
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

I think testing is worth pursuing. Oddball questior B5

B5

This would highly unlikely, but wanted to put it out there.

David Rotstein, DVM, MPVM, Dipl.ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Date: July 13, 2017 at 2:44:24 PM EDT
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>, Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Queen, Jackie L <Jackie.Queen@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>
Cc: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers-EON-323515-323519

B5

Medical Record Review:

B6

Presenting complaint B6 dyspnea, cough of 3 week duration-wheezing type more frequent at nightà rDVM, treated w/ prednisone and doxycycline for kennel coughà B6 inappetance, vomiting à B6 dyspneic and recheck, hospitalized and treated for pneumonia, regurgitatedà B6 treated as outpatient B6 as syring feeding, dog regurgitated and had marked dyspneaà ER à refer to NCSU à B6 put on mechanical ventilatorà B6 euthanized

B6

B6

B6

tFAST B6 severe cardiomegaly with ventricular hypocontractility

Echo B6**:** dcm vs. myocarditis vs pacing induce vs. other (severely dilated & hypocontractile left & right ventricles, severely dilated left and right atria)

Necropsy: Lung-severe diffuse alveolar injury with marked fibrin deposition (hyaline) and marked alveolar histiocytosis and multifocal type II pneumocyte hyperplasia; mod to marked diffuse pulmonary edema; mild cardiomegaly with mild mitral valve endocardiosis and mild left ventricular hypertrophy and left atrial dilation; thorax with mild pleural effusion; Suspect primary non-cardiogenic etiology but if clinical cardiac dysfunction then functional cardiac abnormalities cannot be ruled out

Prior MHx: coffee brown urine including clumping after strenuous activity when it is hot outside and resolves with 24-36 hours; also Crystalluria

B6

Presented B6 episodes of collapse, first occurred mid February, fall 6 seconds without losing consciousnessà immediately return to normal à2 weeks later again collapse, then on à 6/3 post 2 hour hike collapsed again; panting more than usual; good appetite for treats but reluctant to eat food since February;à recheck 7/10, doing better, no collapsing episodes except a stumbling moment when excited, respiratory rate normal, diet changed to Hill's

B6

B6

B6

Rads: left sided congestive heart failure

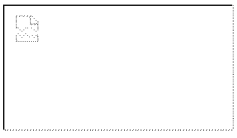
-7/10: moderate left sided cardiomegaly without heart failure, moderate hepatomegaly

Echo: mitral valve endocardiosis with left atrial enlargement and heart failure, decreased left ventricular systolic function, suspected DCM

Thoughts: B5

B5

Jennifer Jones, DVM
Veterinary Medical Officer



From: Rotstein, David
Sent: Tuesday, July 11, 2017 12:44 PM
To: Jones, Jennifer L; Reimschuessel, Renate; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Jen,

B5

d.

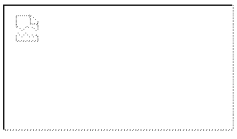
David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place, RM 120
240-402-5613 (Office) (NEW NUMBER)
240-506-6763 (BB)

From: Jones, Jennifer L
Sent: Tuesday, July 11, 2017 12:41 PM
To: Reimschuessel, Renate; Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Yes, and also, vet talked to B4 who said there was B5 in this food…but that doesn't rule out treats.

B5

Jennifer Jones, DVM
Veterinary Medical Officer



From: Reimschuessel, Renate
Sent: Tuesday, July 11, 2017 11:51 AM
To: Jones, Jennifer L; Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica
Subject: RE: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

Davis may be able to screen for B5

Renate Reimschuessel V.M.D. Ph.D. Vet-LIRN
Phone 1- 240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

---

From: Jones, Jennifer L
Sent: Tuesday, July 11, 2017 11:38 AM
To: Rotstein, David; Palmer, Lee Anne; Carey, Lauren; Queen, Jackie L
Cc: Ceric, Olgica; Reimschuessel, Renate
Subject: Head's up-potential DCM case-Dr. Adin-NCSU-2 Schnauzers

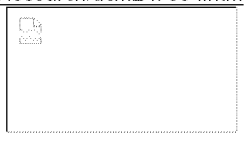
Vet will submit PFR online à
2 dogs-unrelated miniature schnauzers

Dog 1: 2 yr à presented 2/2017 with fulminant CHFà severe DCM on echo, taurine/carnitine normal, infectious disease testing negative, died on the ventilator, necropsy done-myocardial changes were subtle but could be similar to moldy corn toxicity in pigsà plasma, urine, serum, and myocardial tissue available

Dog 2: 7 yr, had a syncopal episode ~2/2017 but presented to vet for progressive frequency of syncopal episodesà 6/2017 for CHF, diagnosed with DCM similar to housemate, nearly same image on Echo, taurine/carnitine normal, infectious disease testing negative, they have changed the diet (Hill's) and dog is responding to treatment; plasma, urine, and serum available

Dogs were eating California Naturals (different bag than from 2/2017) and treats (Milo's Kitchen); Vet has samples of food and treats

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



B6

Patient Information

Patient: B6

Patient Number: B6

Breed: Cocker Spaniel

Exam Date: 09/05/2017 08:21

Age: 4 years

Weight:(kg) 14.80

Sex:

BSA: 0.61

Referring Veterinarian: B6

Cardiologist: B6 DVM, DACVIM (Cardiology)

Client Number: 144203

History: B6 was presented to B6 for evaluation of an enlarged heart and congestive heart failure diagnosed on radiographs on 8/22/17. B6 has no history of a heart murmur. B6 was taken to his regualr vet on B6 for evaluation of a week long progressive cough. The clients report that B6 was coughing about two times per day and the cough became more severe over the course of the week. B6 RDVM ran blood work and took thoracic radiographs at that time. The clients report that initially his RDVM was concerned with pneumonia and prescribed antibiotics, but once the radiographs were reviewed heart failure was diagnosed and B6 were recommended. The clients report that they had not started the antibiotics prior to starting the B6 and B6. The cough went away after starting the B6 but B6 regular vet wanted B6 on the antibiotics as well. The cough is greatly improved, however B6 does still cough every now and then. B6 is currently receiving B6 once daily, B6 mgs in the morning and 2.5 mgs in the evenings, B6 twice daily and B6 mgs twice daily.

Physical Examination: B6 Quiet/distant heart sounds with gallop, no audible murmur on left, grade I/6 systolic murmur left. Regular rhythm. Fine crackles bilaterally. Normal abdominal palpation. Femoral pulses difficult to assess due to shivering, suspect decreased. Palpable jugular pulsation. Good hydration, normal refill, pink mm. Suspect epulis on gingiva associated with left upper canine. Fundic exam WNL.

Diagnostic Tests:

B6

Echo: See Below. ECG during echo showed a sinus tachycardia, heart rate averaging about 200bpm.

Echocardiographic Report

2D ECHO
LA Systolic Diameter LX

DOPPLER
AV Peak Velocity
AV Peak Gradient
Mitral E Point Velocity
MR Peak Velocity

M-MODE
LV Diastolic Diameter MM
LV Systolic Diameter MM
LV Fractional Shortening MM
LV Diastolic Volume Cube
LV Systolic Volume Cube
LV Ejection Fraction Cube
IVS Diastolic Thickness MM
IVS Systolic Thickness MM
IVS Percent Thickening MM

B6

Aortic Root Diameter

PV Peak Velocity
PV Peak Gradient
TR Peak Velocity
TR Peak Gradient

LVPW Diastolic Thickness MM
LVPW Systolic Thickness MM
LVPW Percent Thickening MM
IVS to PW Ratio MM
LV Mass MM
LV Mass Normalized MM
LA Systolic Diameter MM
Aortic Root Diameter MM
MV E Point Septal Separation

B6

Left Ventricle: Moderate dilation with increased sphericity and severe global decrease in contractility.

Left Atrium: Moderate dilation.

Right Ventricle: Mild dilation with decreased contractility.

Right Atrium: Mild dilation with decreased contractility.

Mitral Valve: 3+ central regurgitation, fused inflow.

Aortic Valve: Normal.

Tricuspid Valve: Multiple 2-3+ jets of regurgitation. TR velocity is increased consistent with moderate pulmonary hypertension.

Pulmonic Valve: Normal.

Aorta: Normal.

Pericardium: Normal. No free fluid in the abdomen, distended hepatic vessels.

Diagnosis

Dilated cardiomyopathy - This is a disease characterized by weakening of the heart muscle and dilation of the heart chambers. As the disease progresses, it can lead to congestive heart failure (fluid in the lungs causing shortness of breath and cough). Abnormal heart rhythms are common and can result in sudden death. Most commonly this is an inherited disease, though it can occur secondary to a deficiency in an amino acid called taurine.

Congestive heart failure - We did not repeat radiographs today, but based on the finding of crackles on physical exam, I suspect that there is still some mild fluid in B6 lungs today.

Mild decrease in blood albumin (protein) - This value is increased from the initial bloodwork, though still just mildly low today. We will keep an eye on this, and if it is persistent or progressive we can evaluate further. It is possible that this could be due to heart failure if there had previously been free fluid in B6 abdomen as well as in his lungs.

Recommendations

Please INCREASE:

B6

One thing that can be very helpful for home monitoring is checking sleeping or resting respiratory rates. A recent study showed that even pets with severe heart disease rarely have resting respiratory rates greater than 30 breaths per minute unless they are starting to decompensate for that disease. Elevated respiratory rates at home may be even more sensitive than chest radiographs at picking up early decompensation. Count your pet's respiratory rate when he/she is at rest or sleeping (not within 20 minutes of being active). If his/her respiratory rate is greater than 30 breaths per minute, recheck again in a couple of hours. If persistently elevated above this level, call.

I also recommend considering a new diet with a different protein source. While I do not know of any documented amino acid deficiencies associated with a kangaroo diet, I also have two littermates that I diagnosed with severe dilated cardiomyopathy that were both fed a kangaroo diet for a long time. In that case, an inherited form of disease is possible, and in B6 either an inherited or taurine-associated form of disease is possible, but the connection does bother me. With advanced heart disease, our biggest dietary concerns are adequate calorie content and low sodium content. We aim for less than 80mg sodium per 100 kilocalories (kcal) in patients that have developed congestive heart failure. We do not advise protein restriction unless there is concurrent kidney disease (i.e. kidney diets are not advised unless there is concurrent kidney disease). Please refer to our diet handouts with a list of currently adequate diets and treats, though this list is not exclusive. If you wish to feed a diet that is not on these lists, you will need to call the manufacturer of the diet to obtain a sodium content.

Exercise is also a concern in advanced heart disease. While cage rest is ideal with active heart failure, some exercise is permissible in asymptomatic disease. However, vigorous or extended exercise should be avoided.

I would like to recheck B6 again in another 7-10 days for chest radiographs, kidney panel, and bloodwork on the new medications. Please call if you have any questions or concerns in the meantime. We will call when we receive taurine level results (this can take a couple of weeks sometimes).

B6 DVM, DACVIM (Cardiology)

(Electronically Signed)

Final Date: 05 September 2017 12:17

Amended: 05 September 2017 12:28

Like us on Facebook!

www.facebook.com/ B6

Notes to our clients

-Please bring all medications to your pet's scheduled appointments.

-We require a 48 hour notice for all refills. When you call to request a refill, please leave the pharmacy phone number or clearly indicate if you plan on picking up the medication at our facility. PRESCRIPTION REFILLS ARE NOT AVAILABLE AFTER B6 CARDIOLOGY'S REGULAR BUSINESS HOURS (Evenings, Fridays, holidays and weekends).

-Check out B6 and enter your local zip code to search for the best prices on your medications at your local pharmacies.

-If an emergency arises with your pet B6 Hospital is a 24 hour facility.

B6

Client ID:
Client Name:
Spouse/Other:
Address:

Telephone:

B6

Patient ID:
Name: B6
Breed: Spaniel, Cocker
Sex: Neutered Male
Color: Black/ White/ Brown
Age: B6
DOB: B6

Referring Veterinarian:
Practice:
Phone:
FAX:

B6

Cardiology Reevaluation

Reevaluation of:
Congestive heart failure, left sided, Dilated cardiomyopathy, B6

B6 continues to do well at home, without any weakness or collapse. The owners report that B6 has great energy levels and loves to play. The owners have reported resting respiratory rates at 14-16 bpm, without any coughing. B6 has a normal appetite with normal eliminations, though did vomit clear liquid once 1.5 weeks ago. The owner reports that the mass on B6 gums does not seem to affect his chewing anymore.

Physical Exam:

B6 B6 B6

Vital Sign	
Weight	B6
Attitude	
Temp	
HR	
RR	
RQ	
Muc	
Memb	
CRT	
BP	

Quiet heart sounds. Gallop present. Fair femoral pulses. Regular rhythm. Normal lung sounds. Normal jugular veins. Palpable hepatomegaly. Epidermal collarettes with exudative crusting on ventral abdomen. PLNs WNL. Unchanged appearance to growth on gingiva. MM pink/moist. CRT < 2 sec.

Diagnostics:
Thoracic radiographs: Decrease in heart size as compared to previous films. No evidence of cardiac decompensation.
Renal panel: BUN 32 mg/dL, otherwise unremarkable.
Taurine level: pending, with call with results

Diagnosis:
Congestive heart failure, left sided
Dilated cardiomyopathy
B6

B6

Recommendations:
Please give the following medications as directed:

ITEM DESCRIPTION	DIRECTIONS
B6	Give 1 tablet by mouth in the mornings and 1/2 tablet by mouth in the evenings.
	Give 1 tablet by mouth every 12 hours.
	Give 1 tablet by mouth every 8 hours.
	Give 1 tablet by mouth once every 24 hours.
	Give 1 and 1/2 tablets by mouth every 12 hours.
	Give 1 tablet by mouth every 12 hours.

ADD:
B6 - Give 1 tablet by mouth once every 24 hours for 10 days.
B6 has some lesions on his abdomen that are characteristic of a superficial skin infection. B6 is a good antibiotic for uncomplicated skin infections. B6 should be re-evaluated by your primary veterinarian or a veterinary dermatologist if he does not improve.

We will call you with B6 bloodwork results when they are available.

Please continue to monitor B6 for cough, lethargy and/or changes in respiratory rate/effort.

*** As long as B6 continues to do well at home we would like to re-evaluate him in 3-4 months. At this time we will recheck his kidney values/electrolytes, repeat chest x-rays and repeat an echocardiogram.

Like us on Facebook!!
www.facebook.com B6

Notes to our clients
-Please bring all medications to your pet's scheduled appointments.
-We require a 48 hour notice for all refills. When you call to request a refill, please leave the pharmacy phone number or clearly indicate if you plan on picking up the medication at our facility. PRESCRIPTION REFILLS OUTSIDE OF B6 B6 CARDIOLOGY'S REGULAR BUSINESS HOURS (Evenings, Fridays, holidays, and weekends) MAY BE ASSOCIATED WITH AN AFTER HOURS FILLING FEE.
-Check out B6 and enter your local zip code to search for the best prices on your medications at your local pharmacies.
-If an emergency arises with your pet, B6 is only a phone call away. B6 Hospital is a 24 hour facility and the emergency veterinarians can always reach the cardiologist on-call.
-Please schedule your recommended recheck as soon as possible. Our schedule tends to book up quite quickly and we want to make sure that we see your pet in a timely manner.

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: Account # B6 / Contact: B6 **Date:** 9-5-17
Company Name: B6
Address: B6
B6
Email: B6
Tel: B6 **Fax:** B6

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

Patient Name: B6
Species: K9
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

DOCUMENT PRODUCED IN NATIVE

From:	DeLancey, Siobhan </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A414BA562DCD4C8284B1120074969B9A-SDELANCE>
To:	Jones, Jennifer L; Ask CVM; Norris, Anne
Sent:	3/26/2019 5:45:29 PM
Subject:	RE: Cobalt

This seems reasonable to me, and I don't have concerns about you responding to her directly.

From: Jones, Jennifer L
Sent: Tuesday, March 26, 2019 1:34 PM
To: Ask CVM <AskCVM@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Cobalt

My thought for response was:

We based this on the 25 mg/kg diet for chicks, rats, and sheep per Mineral Tolerances of Animals 2nd Ed, 2005 (NRC). The cobalt in the products we tested was below 1 ppm.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Ask CVM
Sent: Monday, March 25, 2019 5:14 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Cobalt

Adding; Siobhan and Anne.

From: Jones, Jennifer L
Sent: Monday, March 25, 2019 12:31 PM
To: Ask CVM <AskCVM@fda.hhs.gov>
Subject: FW: Cobalt

Hi communications team,
I received this inquiry from a collaborator but need guidance about how to respond. I can provide background about her question, but it's easier to explain the results by phone.
Thanks,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: Saturday, March 23, 2019 11:43 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>

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. Since Co is not an essential nutrient listed in the AAFCO profiles, are you using the max of 10 ppm that is for all species from AAFCO (ie, the level that "will not impair animal performance and should not produce unsafe residues in human food derived from that animal"?

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: Ask CVM </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=614B2D6BBFD341B28EDF346CCFDC9893-ASKCVM>
To: Jones, Jennifer L; DeLancey, Siobhan; Norris, Anne
Sent: 3/25/2019 9:14:04 PM
Subject: RE: Cobalt

Adding; Siobhan and Anne.

From: Jones, Jennifer L
Sent: Monday, March 25, 2019 12:31 PM
To: Ask CVM <AskCVM@fda.hhs.gov>
Subject: FW: Cobalt

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Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: Saturday, March 23, 2019 11:43 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Subject: Cobalt

Hi Jen,
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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: 'Freeman, Lisa'
Sent: 3/26/2019 5:50:16 PM
Subject: RE: Cobalt

Hi Lisa,
We based this on the 25 mg/kg diet for chicks, rats, and sheep per Mineral Tolerances of Animals 2nd Ed, 2005 (NRC). The cobalt in the products we tested was below 1 ppm.
Hope you're well,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION Vet-LIRN

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: Saturday, March 23, 2019 11:43 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
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. Since Co is not an essential nutrient listed in the AAFCO profiles, are you using the max of 10 ppm that is for all species from AAFCO (ie, the level that "will not impair animal performance and should not produce unsafe residues in human food derived from that animal"?

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: Ask CVM; DeLancey, Siobhan; Norris, Anne
Sent: 3/26/2019 5:34:21 PM
Subject: RE: Cobalt

My thought for response was:

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Ask CVM
Sent: Monday, March 25, 2019 5:14 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Subject: RE: Cobalt

Adding; Siobhan and Anne.

From: Jones, Jennifer L
Sent: Monday, March 25, 2019 12:31 PM
To: Ask CVM <AskCVM@fda.hhs.gov>
Subject: FW: Cobalt

Hi communications team,
I received this inquiry from a collaborator but need guidance about how to respond. I can provide background about her question, but it's easier to explain the results by phone.
Thanks,
Jen

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Freeman, Lisa <Lisa.Freeman@tufts.edu>
Sent: Saturday, March 23, 2019 11:43 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
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. Since Co is not an essential nutrient listed in the AAFCO profiles, are you using the max of 10 ppm that is for all species from AAFCO (ie, the level that "will not impair animal performance and should not produce unsafe residues in human food derived from that animal"?

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:	Haake, Lindsay </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=1915C4E4D49F4540A506D48BFABCB046-LINDSAY.HAA>
To:	Lockeed, Matthew; Earley, Rosemary; Norris, Anne
CC:	Edwards, David; DeLancey, Siobhan; Jones, Jennifer L; Peloquin, Sarah; Reimschuessel, Renate; Palmer, Lee Anne; Carey, Lauren; Rotstein, David; Burkholder, William; Conway, Charlotte; Dewitt, Susan J; Goddard, Kristina; Benton, Denise; Rebello, Heidi; Peddicord, Sarah; Heard, Alexandra; Colonius, Tristan; Thompson, Alison; Glasner, Aliza; Hattis, Daniel; Emmitt, Keenan; AskOSC; Stamper, Carmela; Thorpe, Valarie; Kimberly, Brad; Cepeda, Sandra; Beckerman, Peter
Sent:	6/27/2019 3:58:51 PM
Subject:	RE: DCM Announcement - 11:00 AM Today (final comms attached)

Press release is live!

https://www.fda.gov/news-events/press-announcements/fda-issues-third-status-report-investigation-potential-connection-between-certain-diets-and-cases

From: Lockeed, Matthew
Sent: Thursday, June 27, 2019 11:49 AM
To: Earley, Rosemary <Rosemary.Earley@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

OL outreach is complete. The call with Rep. Comer's office was friendly and they appreciated the heads-up. I will keep folks posted on any additional communication with Comer's office. Thanks for the quick turnaround on helpful RQAs.

Matt

From: Earley, Rosemary
Sent: Thursday, June 27, 2019 11:22 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah

<Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

OCA outreach is completed.
Thank you,
Rosie

Rosemary Earley, DVM| *Congressional Affairs Specialist*
Office of Congressional Appropriations
Office: (301) 796-6186
Cell: B6
rosemary.earley@fda.hhs.gov

From: Hattis, Daniel
Sent: Thursday, June 27, 2019 11:19 AM
To: Earley, Rosemary <Rosemary.Earley@fda.hhs.gov>
Subject: FW: DCM Announcement - 11:00 AM Today (final comms attached)

From: Norris, Anne
Sent: Thursday, June 27, 2019 11:10 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

We are now live! CVM links are below and OMA will reply all to this thread with the press release link shortly. Huge thanks to everyone involved in this ongoing saga!

CVM Update

Web Update – DCM Investigation

Web QA (Updated)

Vet-LIRN Update

DCM Complaint Spreadsheet – 1/1/14 - 4/30/19

Best,
Anne

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:15 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

Thanks, Ashley.

All, we're going to stick with the adjusted 11:00 start time. We appreciate your flexibility!

From: Zborowsky, Ashley
Sent: Thursday, June 27, 2019 10:07 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter

<Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

Thanks Anne – I actually just got off the phone with Pete and we don't have any concerns, so this is good to go. I appreciate your patience! Apologies for the false alarm.

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:02 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>; Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

In response to a request from OCC, we are holding on this until approximately 11:00 am ET. The timeline is updated below.

From: Norris, Anne
Sent: Thursday, June 27, 2019 9:41 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jeanette Murphy (Jenny.Murphy@fda.hhs.gov) <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; Siobhan DeLancey - FDA (Siobhan.Delancey@fda.hhs.gov) <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J (Susan.Dewitt@fda.hhs.gov) <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Daniel Hattis (Daniel.Hattis@fda.hhs.gov) <Daniel.Hattis@fda.hhs.gov>; Keenan Emmitt (Keenan.Emmitt@fda.hhs.gov) <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>
Subject: DCM Announcement - 10:30 AM Today (final comms attached)

Good morning,

At 10:30, we'll be sending our DCM investigative update live, including a CVM Update, Web Update, Vet-LIRN

Update, Updated Web QA, and a spreadsheet of complaints submitted to the agency through 4/30/19. OMA is issuing a press release. When the pages are live I will circulate links for outreach. Attached are the final comms documents and the comms plan tick-tock is pasted below. Please reach out with any questions or concerns.

Thursday, June 27 - *Date of Announcement*

11:00 am EST
- Publish CVM Update, Web Update, Web QAs, Vet-LIRN Update, Redacted Complaint File (Denise Benton)
- Publish Press Release (OEA/OMA Web)

11:15 am EST: Immediately following email with live comms links (Anne Norris)
All outreach taking place simultaneously:
- CVM Stakeholder Outreach (Martine Hartogensis, Jenny Murphy, Dave Edwards, Jennifer Jones)
- OL Outreach (Tristan Colonius/Matt Lockeed)
- OCA Outreach (Dan Hattis/Keenan Emmitt)
- Mainstream Media Outreach (Lindsay Haake)
- Trade Media Outreach (Anne Norris)

11:45 am EST (upon completion of outreach)
- Email CVM Update to subscriber list (Denise Benton)
- Email Press Release to subscriber list (OEA/OMA Web)
- Publish tweets/Facebook post (Kristina Goddard, Valarie Thorpe)

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

From:	Earley, Rosemary </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=05737F759EB54E9188CB16CBBE467D12-ROSEMARY.EA>
To:	Norris, Anne
CC:	Edwards, David; DeLancey, Siobhan; Jones, Jennifer L; Peloquin, Sarah; Reimschuessel, Renate; Palmer, Lee Anne; Carey, Lauren; Rotstein, David; Burkholder, William; Conway, Charlotte; Dewitt, Susan J; Goddard, Kristina; Benton, Denise; Rebello, Heidi; Haake, Lindsay; Peddicord, Sarah; Heard, Alexandra; Colonius, Tristan; Lockeed, Matthew; Thompson, Alison; Glasner, Aliza; Hattis, Daniel; Emmitt, Keenan; AskOSC; Stamper, Carmela; Thorpe, Valarie; Kimberly, Brad; Cepeda, Sandra; Beckerman, Peter
Sent:	6/27/2019 3:22:20 PM
Subject:	RE: DCM Announcement - 11:00 AM Today (final comms attached)

OCA outreach is completed.
Thank you,
Rosie

Rosemary Earley, DVM| *Congressional Affairs Specialist*
Office of Congressional Appropriations
Office: (301) 796-6186
Cell B6
rosemary.earley@fda.hhs.gov

From: Hattis, Daniel
Sent: Thursday, June 27, 2019 11:19 AM
To: Earley, Rosemary <Rosemary.Earley@fda.hhs.gov>
Subject: FW: DCM Announcement - 11:00 AM Today (final comms attached)

From: Norris, Anne
Sent: Thursday, June 27, 2019 11:10 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

We are now live! CVM links are below and OMA will reply all to this thread with the press release link shortly.

Huge thanks to everyone involved in this ongoing saga!

CVM Update

Web Update – DCM Investigation

Web QA (Updated)

Vet-LIRN Update

DCM Complaint Spreadsheet – 1/1/14 - 4/30/19

Best,
Anne

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:15 AM
To: Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 11:00 AM Today (final comms attached)

Thanks, Ashley.

All, we're going to stick with the adjusted 11:00 start time. We appreciate your flexibility!

From: Zborowsky, Ashley
Sent: Thursday, June 27, 2019 10:07 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra

<Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

Thanks Anne – I actually just got off the phone with Pete and we don't have any concerns, so this is good to go. I appreciate your patience! Apologies for the false alarm.

From: Norris, Anne
Sent: Thursday, June 27, 2019 10:02 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Murphy, Jeanette <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Benton, Denise <Denise.Benton@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Hattis, Daniel <Daniel.Hattis@fda.hhs.gov>; Emmitt, Keenan <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>; Beckerman, Peter <Peter.Beckerman@fda.hhs.gov>; Zborowsky, Ashley <Ashley.Zborowsky@fda.hhs.gov>
Subject: RE: DCM Announcement - 10:30 AM Today (final comms attached)

In response to a request from OCC, we are holding on this until approximately 11:00 am ET. The timeline is updated below.

From: Norris, Anne
Sent: Thursday, June 27, 2019 9:41 AM
To: Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Moxley, Shera <Shera.Moxley@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>; Schell, Timothy <Timothy.Schell@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jeanette Murphy (Jenny.Murphy@fda.hhs.gov) <Jenny.Murphy@fda.hhs.gov>; Edwards, David <David.Edwards@fda.hhs.gov>; Siobhan DeLancey - FDA (Siobhan.Delancey@fda.hhs.gov) <Siobhan.Delancey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Peloquin, Sarah <Sarah.Peloquin@fda.hhs.gov>; 'Reimschuessel, Renate (Renate.Reimschuessel@fda.hhs.gov)' <Renate.Reimschuessel@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>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Conway, Charlotte <Charlotte.Conway@fda.hhs.gov>; Dewitt, Susan J (Susan.Dewitt@fda.hhs.gov) <Susan.Dewitt@fda.hhs.gov>; Goddard, Kristina <Kristina.Goddard@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Haake, Lindsay <Lindsay.Haake@fda.hhs.gov>; Peddicord, Sarah <Sarah.Peddicord@fda.hhs.gov>; Heard, Alexandra <Alexandra.Heard@fda.hhs.gov>; Colonius, Tristan <Tristan.Colonius@fda.hhs.gov>; Lockeed, Matthew <Matthew.Lockeed@fda.hhs.gov>; Thompson, Alison <Alison.Thompson@fda.hhs.gov>; Glasner, Aliza <Aliza.Glasner@fda.hhs.gov>; Daniel Hattis (Daniel.Hattis@fda.hhs.gov) <Daniel.Hattis@fda.hhs.gov>; Keenan Emmitt (Keenan.Emmitt@fda.hhs.gov) <Keenan.Emmitt@fda.hhs.gov>; AskOSC <AskOSC@fda.hhs.gov>; Stamper, Carmela <Carmela.Stamper@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Kimberly,

Brad <Brad.Kimberly@fda.hhs.gov>; Cepeda, Sandra <Sandra.Cepeda@fda.hhs.gov>
Subject: DCM Announcement - 10:30 AM Today (final comms attached)

Good morning,

At 10:30, we'll be sending our DCM investigative update live, including a CVM Update, Web Update, Vet-LIRN Update, Updated Web QA, and a spreadsheet of complaints submitted to the agency through 4/30/19. OMA is issuing a press release. When the pages are live I will circulate links for outreach. Attached are the final comms documents and the comms plan tick-tock is pasted below. Please reach out with any questions or concerns.

Thursday, June 27 - *Date of Announcement*

11:00 am EST
- Publish CVM Update, Web Update, Web QAs, Vet-LIRN Update, Redacted Complaint File (Denise Benton)
- Publish Press Release (OEA/OMA Web)

11:15 am EST: Immediately following email with live comms links (Anne Norris)
All outreach taking place simultaneously:
- CVM Stakeholder Outreach (Martine Hartogensis, Jenny Murphy, Dave Edwards, Jennifer Jones)
- OL Outreach (Tristan Colonius/Matt Lockeed)
- OCA Outreach (Dan Hattis/Keenan Emmitt)
- Mainstream Media Outreach (Lindsay Haake)
- Trade Media Outreach (Anne Norris)

11:45 am EST (upon completion of outreach)
- Email CVM Update to subscriber list (Denise Benton)
- Email Press Release to subscriber list (OEA/OMA Web)
- Publish tweets/Facebook post (Kristina Goddard, Valarie Thorpe)

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

From:	Hartogensis, Martine </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02DF91D554D34B948FC58433D0E42073-MHARTOGE>
To:	Norris, Anne; Jones, Jennifer L; Burkholder, William; Palmer, Lee Anne; Reimschuessel, Renate; Carey, Lauren; Rotstein, David
CC:	DeLancey, Siobhan
Sent:	8/16/2018 11:28:07 PM
Subject:	RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

Hi Anne,

B5

Thank you Anne for the reminder!

Martine

From: Norris, Anne <Anne.Norris@fda.hhs.gov>
Date: August 16, 2018 at 5:12:13 PM EDT
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>, Burkholder, William <William.Burkholder@fda.hhs.gov>, Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>, Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>, Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>, Carey, Lauren <Lauren.Carey@fda.hhs.gov>, Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

Circling back on this. The editor just emailed to confirm that instead of Andrea Fascetti, it'll be Lisa Freeman.

B6

Thanks,
Anne

From: Norris, Anne
Sent: Tuesday, August 14, 2018 12:51 PM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

Thanks for flagging that, Jen.

Apparently Dr. Aldrich's articles are kept in a premium subscriber space on the website that's subject to a separate fee. The editor provided a code for free access to his articles below. And attached is his article, one

page per document to get rid of the ads.

B5

The code is B6 (It's good for 12 months after you first use it.)

From: Jones, Jennifer L
Sent: Tuesday, August 14, 2018 11:56 AM
To: Burkholder, William <William.Burkholder@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

For your situational awareness-VetLIRN does have a contract with Dr. Fascetti at UC Davis dealing with urine amino acid quantification.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Burkholder, William
Sent: Tuesday, August 14, 2018 11:32 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

Bill

From: Norris, Anne
Sent: Tuesday, August 14, 2018 11:26 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

I reached out to gather additional information. Greg Aldrich was the author of this pesky article that we weren't able to read in full. Maybe I can ask the editor to do me a solid and share. Any concerns with him being on the panel? Otherwise, it seems like it could be a good fit for FDA.

B5

B5

From: Palmer, Lee Anne
Sent: Monday, August 13, 2018 11:23 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

B5

From: Norris, Anne
Sent: Monday, August 13, 2018 11:09 AM
To: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

I completely agree with that. B5

B5

Thanks,
Anne

From: Reimschuessel, Renate
Sent: Monday, August 13, 2018 11:06 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

Renate Reimschuessel V.M.D. Ph.D. Director Vet-LIRN
Phone 1- 240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Norris, Anne
Sent: Monday, August 13, 2018 10:58 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: FW: Invitation to participate in webinar on legume seeds and cardiomyopathy

Hi all,

B5

Thanks,
Anne

From: Tim Wall [mailto:TWall@wattglobal.com]
Sent: Monday, August 13, 2018 9:42 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: Debbie Phillips <B6>
Subject: Invitation to participate in webinar on legume seeds and cardiomyopathy

Hi Anne,
My colleagues would like to conduct a webinar on the correlation between dilated canine cardiomyopathy and certain pet food ingredients. Petfood Industry's editor-in-chief, Debbie Phillips-Donaldson, would like to include a representative from the FDA. Please let me know if someone may be available or if you have any questions about participation. We don't have a date or time yet.

Here's my editor's description of the webinar:
"This would be a webinar for pet food professionals who are curious and concerned about the investigation; we are hoping to also include a veterinary expert with a background in nutrition and a nutritionist/formulator. Each person would have about 15 minutes to present, then we'd have a Q&A period of about 15 minutes.

So it would mean a commitment of about 90 minutes the morning of the webinar, plus a brief coordination call (20-30 minutes) about a week before. It would be up to the person whether he or she would present slides, though having at least a few would be helpful considering webinars are somewhat visual."

Thanks for your help.
Best Regards,

TIM WALL | Staff Reporter - Petfood Industry | WATT Global Media
Mobile: +B6 | Office: +1.815.966.5432
Skype: timwall.watt | twall@wattglobal.com

From:	Norris, Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=891982B43D804C9396555BAF36C73DE1-ANNE.NORRIS>
To:	Jones, Jennifer L; Burkholder, William; Palmer, Lee Anne; Reimschuessel, Renate; Hartogensis, Martine; Carey, Lauren; Rotstein, David
CC:	DeLancey, Siobhan
Sent:	8/14/2018 4:50:40 PM
Subject:	RE: Invitation to participate in webinar on legume seeds and cardiomyopathy
Attachments:	1807PETpg_040.pdf; 1807PETpg_041.pdf; 1807PETpg_043.pdf

Thanks for flagging that, Jen.

Apparently Dr. Aldrich's articles are kept in a premium subscriber space on the website that's subject to a separate fee. The editor provided a code for free access to his articles below. And attached is his article, one page per document to get rid of the ads.

B5

The code is **B6** (It's good for 12 months after you first use it.)

From: Jones, Jennifer L
Sent: Tuesday, August 14, 2018 11:56 AM
To: Burkholder, William <William.Burkholder@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

For your situational awareness-VetLIRN does have a contract with Dr. Fascetti at UC Davis dealing with urine amino acid quantification.

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Burkholder, William
Sent: Tuesday, August 14, 2018 11:32 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

Bill

From: Norris, Anne
Sent: Tuesday, August 14, 2018 11:26 AM
To: Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

I reached out to gather additional information. Greg Aldrich was the author of this pesky article that we weren't able to read in full. Maybe I can ask the editor to do me a solid and share. Any concerns with him being on the panel? Otherwise, it seems like it could be a good fit for FDA.

B5

From: Palmer, Lee Anne
Sent: Monday, August 13, 2018 11:23 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

From: Norris, Anne
Sent: Monday, August 13, 2018 11:09 AM
To: Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

Thanks,
Anne

From: Reimschuessel, Renate
Sent: Monday, August 13, 2018 11:06 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: RE: Invitation to participate in webinar on legume seeds and cardiomyopathy

B5

Renate Reimschuessel V.M.D. Ph.D. Director Vet-LIRN
Phone 1- 240-402-5404
Fax 301-210-4685
http://www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm

From: Norris, Anne
Sent: Monday, August 13, 2018 10:58 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@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>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>
Subject: FW: Invitation to participate in webinar on legume seeds and cardiomyopathy

Hi all,

B5

Thanks,
Anne

From: Tim Wall [mailto:TWall@wattglobal.com]
Sent: Monday, August 13, 2018 9:42 AM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: Debbie Phillips <DPhillips@wattglobal.com>
Subject: Invitation to participate in webinar on legume seeds and cardiomyopathy

Hi Anne,
My colleagues would like to conduct a webinar on the correlation between dilated canine cardiomyopathy and certain pet food ingredients. Petfood Industry's editor-in-chief, Debbie Phillips-Donaldson, would like to include a representative from the FDA. Please let me know if someone may be available or if you have any questions about participation. We don't have a date or time yet.

Here's my editor's description of the webinar:
"This would be a webinar for pet food professionals who are curious and concerned about the investigation; we

are hoping to also include a veterinary expert with a background in nutrition and a nutritionist/formulator. Each person would have about 15 minutes to present, then we'd have a Q&A period of about 15 minutes.

So it would mean a commitment of about 90 minutes the morning of the webinar, plus a brief coordination call (20-30 minutes) about a week before. It would be up to the person whether he or she would present slides, though having at least a few would be helpful considering webinars are somewhat visual."

Thanks for your help.
Best Regards,

TIM WALL | Staff Reporter - Petfood Industry | WATT Global Media
Mobile: + B6 | Office: +1.815.966.5432
Skype: timwall.watt | twall@wattglobal.com

B4

B4

From:	Hartogensis, Martine </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02DF91D554D34B948FC58433D0E42073-MHARTOGE>
To:	Putnam, Juli; Carey, Lauren; Jones, Jennifer L; Norris, Anne
CC:	DeLancey, Siobhan; Forfa, Tracey; Rotstein, David; Eisenman, Theresa; Nemser, Sarah; Reimschuessel, Renate
Sent:	7/20/2018 3:14:27 PM
Subject:	RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Ok, thanks Juli! I am looping in Sarah Nemser and Renate in case they know, but no worries if not.

Thanks again!

Martine

From: Putnam, Juli
Sent: Friday, July 20, 2018 11:02 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>; Eisenman, Theresa <Theresa.Eisenman@fda.hhs.gov>
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

B5

Thanks, and hope everyone has a good weekend!

Best,
Juli

From: Hartogensis, Martine
Sent: Friday, July 20, 2018 10:21 AM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Hi Juli,

B5

Martine

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From: Carey, Lauren
Sent: Friday, July 20, 2018 9:50 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
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Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

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Sent: Friday, July 20, 2018 8:02 AM
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Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Thanks Jen.

B5

Martine

From: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>
Date: July 20, 2018 at 6:47:01 AM EDT
To: Carey, Lauren <Lauren.Carey@fda.hhs.gov>, Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>, Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>, Norris, Anne <Anne.Norris@fda.hhs.gov>
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Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

U.S. FOOD & DRUG ADMINISTRATION

From: Carey, Lauren
Sent: Thursday, July 19, 2018 4:12 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
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Jen should have an answer for you on that.

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Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Hi Juli,

Just looping in the dream team again. **B5**

TIA!

Martine

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Sent: Thursday, July 19, 2018 3:58 PM
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Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

B5

From: Hartogensis, Martine
Sent: Thursday, July 19, 2018 3:43 PM
To: Norris, Anne <Anne.Norris@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Great points, thank you Anne!

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Sent: Thursday, July 19, 2018 3:42 PM
To: Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
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B5

Thanks,
Anne

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Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>
Subject: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Hi Martine,
Are you willing to do another interview on DCM tomorrow morning? Washington Post is now writing too.
Please advise.
Thanks!
Juli

Reporter: Kate Furby
Outlet: Washington Post
Deadline: 7/20
Background: Kate would like to write a story on FDA's alert regarding DCM and its potential link to dog food. This would be for the Health, Environment, Science section of the Post. She is contacting a few vets at universities now as well.
Questions:
She said her questions would just be standard ones about the FDA alert on dog food and canine heart health.

- Questions about DCM – what is it, what are symptoms, how is it detected, how common is it, etc.
- Questions about legumes and potatoes in dog diets.

Juli Putnam
Press Officer

Office of Media Affairs
Office of External Affairs
U.S. Food and Drug Administration
Tel: 240-402-0537 / Cell: B6
Juli.Putnam@fda.hhs.gov

From: Putnam, Juli </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=45A45E85E6E94413A4BD2C9FDBB3DE1B-JULIANN.PUT>
To: Hartogensis, Martine; Carey, Lauren; Jones, Jennifer L; Norris, Anne
CC: DeLancey, Siobhan; Forfa, Tracey; Rotstein, David; Eisenman, Theresa
Sent: 7/20/2018 3:02:29 PM
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

B5

Thanks, and hope everyone has a good weekend!

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Thanks Jen.

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Press Officer

Office of Media Affairs
Office of External Affairs
U.S. Food and Drug Administration
Tel: 240-402-0537 / B6
Juli.Putnam@fda.hhs.gov

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To: Putnam, Juli; Carey, Lauren; Jones, Jennifer L; Norris, Anne
CC: DeLancey, Siobhan; Forfa, Tracey; Rotstein, David
Sent: 7/20/2018 2:20:50 PM
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

Hi Juli,

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B5

Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421
U.S. FOOD & DRUG ADMINISTRATION

From: Carey, Lauren
Sent: Thursday, July 19, 2018 4:12 PM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
Cc: DeLancey, Siobhan <Siobhan.Delancey@fda.hhs.gov>; Forfa, Tracey <Tracey.Forfa@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
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Hi Juli,

Just looping in the dream team again. **B5**

TIA!

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Juli Putnam
Press Officer

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Tel: 240-402-0537 / Cell: B6
Juli.Putnam@fda.hhs.gov

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To:	Jones, Jennifer L; Carey, Lauren; Putnam, Juli; Norris, Anne
CC:	DeLancey, Siobhan; Forfa, Tracey; Rotstein, David
Sent:	7/20/2018 2:08:16 PM
Subject:	RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

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Sent: Friday, July 20, 2018 8:07 AM
To: Hartogensis, Martine <Martine.Hartogensis@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
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U.S. FOOD & DRUG ADMINISTRATION

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To: Hartogensis, Martine; Jones, Jennifer L; Putnam, Juli; Norris, Anne
CC: DeLancey, Siobhan; Forfa, Tracey; Rotstein, David
Sent: 7/20/2018 1:49:51 PM
Subject: RE: Media inquiry request - Washington Post - DCM - Deadline: 7/20

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From: Hartogensis, Martine
Sent: Friday, July 20, 2018 8:02 AM
To: Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Carey, Lauren <Lauren.Carey@fda.hhs.gov>; Putnam, Juli <JuliAnn.Putnam@fda.hhs.gov>; Norris, Anne <Anne.Norris@fda.hhs.gov>
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To: Jones, Jennifer L; Carey, Lauren; Putnam, Juli; Norris, Anne
CC: DeLancey, Siobhan; Forfa, Tracey; Rotstein, David
Sent: 7/20/2018 12:01:35 PM
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U.S. FOOD & DRUG ADMINISTRATION

Withheld in Full as B5

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From: Jones, Jennifer L </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0F6CA12EAA9348959A4CBB1E829AF244-JENNIFER.JO>
To: Carey, Lauren; Ceric, Olgica; Glover, Mark; Nemser, Sarah; Palmer, Lee Anne; Queen, Jackie L; Reimschuessel, Renate; Rotstein, David
Sent: 3/20/2018 12:59:57 PM
Subject: RE: Acana Lamb & Apple Singles Formula Dog Food: B6 - EON-349594
Attachments: Listserve on kangaroo and lentil diets.pdf

B5

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Jennifer Jones, DVM
Veterinary Medical Officer
Tel: 240-402-5421

FDA U.S. FOOD & DRUG ADMINISTRATION

From: Carey, Lauren
Sent: Friday, March 16, 2018 1:42 PM
To: Ceric, Olgica <Olgica.Ceric@fda.hhs.gov>; Jones, Jennifer L <Jennifer.Jones@fda.hhs.gov>; Glover, Mark <Mark.Glover@fda.hhs.gov>; Nemser, Sarah <Sarah.Nemser@fda.hhs.gov>; Palmer, Lee Anne <LeeAnne.Palmer@fda.hhs.gov>; Queen, Jackie L <Jackie.Queen@fda.hhs.gov>; Reimschuessel, Renate <Renate.Reimschuessel@fda.hhs.gov>; Rotstein, David <David.Rotstein@fda.hhs.gov>
Subject: FW: Acana Lamb & Apple Singles Formula Dog Food: B6 - EON-349594

I don't think I saw this one sent out. Unknown if there's any product left over or any lot #. The cardiologist made the report.

10yo, 65lb, MN Golden Retriever – dxed DCM, CHF, low blood taurine. Stopped food, supplemented taurine. Dog's values markedly improved and dog is being taken off medications.

From: PFR Event [mailto:pfreventcreation@fda.hhs.gov]
Sent: Friday, March 16, 2018 8:28 AM
To: Cleary, Michael * <Michael.Cleary@fda.hhs.gov>; HQ Pet Food Report Notification

<HQPetFoodReportNotification@fda.hhs.gov> B6
Subject: Acana Lamb & Apple Singles Formula Dog Food: B6 - EON-349594

A PFR Report has been received and PFR Event [EON-349594] has been created in the EON System.

A "PDF" report by name "2043914-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 "2043914-attachments.zip" and is attached to this email notification.

Below is the summary of the report:

EON Key: EON-349594
ICSR #: 2043914
EON Title: PFR Event created for Acana Lamb & Apple Singles Formula Dog Food; 2043914

AE Date	10/25/2017	**Number Fed/Exposed**	1
Best By Date		**Number Reacted**	1
Animal Species	Dog	**Outcome to Date**	Better/Improved/Recovering
Breed	Retriever - Golden		
Age	10 Years		
District Involved	PFR B6		

Product information
Individual Case Safety Report Number: 2043914
Product Group: Pet Food
Product Name: Acana Lamb & Apple Singles Formula Dog Food
Description: Suspected that Acana Lamb and Apple Singles Formula diet provides insufficient levels of taurine, contributing to development of B6 dilated cardiomyopathy. B6 presented to his primary care veterinarian October 21, 2017 for progressive panting at night over the past 3-4 months. Chest radiographs revealed cardiomegaly and congestive heart failure (CHF). We examined B6 on 10/25/17 and was diagnosed with dilated cardiomyopathy (DCM) and CHF. A whole blood taurine level was tested on 10/25/17 and the result was low B6 reference range 200-350 nmol/ml). This is suspected to be due to dietary deficiency. B6 has been on Acana's limited-ingredient Lamb and Apple grain-free diet for the entirety of his life for the management of B6. After diagnosis of DCM and CHF, treatment included: B6 and supplementation with taurine and l-carnitine. His diet was also switched from Acana Lamb and Apple diet to a commercial veterinary prescription diet (Hill's i/d). Since starting medications and supplementation with taurine/l-carnitine and changing the diet, he has had remarkable improvement in his cardiac size and function. He is no longer at risk for CHF and is being tapered off the B6. His systolic function is near normal. We do not see these improvements with medical therapy alone - only with taurine deficiency. - Normal left atrial size - previously severe - Moderate left ventricular enlargement - mildly improved - Mild to moderate right atrial and right ventricular dilation - improved - Low normal, improved decrease in systolic function - previously severe decrease

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: Better/Improved/Recovering
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 & Apple Singles Formula Dog Food		

Sender information

B6

USA

Owner information

B6 USA

To view this PFR Event, please click the link below:
https://eon.fda.gov/eon//browse/EON-349594

To view the PFR Event Report, please click the link below:
https://eon.fda.gov/eon//EventCustomDetailsAction!viewReport.jspa?decorator=none&e=0&issueType=12&issueId=365923

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From:	Palmer, Lee Anne </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CF7C8BD53B6C45A39318A596ACEA7C53-LPALMER>
To:	Hart, Ellen
Sent:	2/20/2019 4:47:52 PM
Subject:	Adin 2019
Attachments:	Adin 2019.pdf

Here ya go! Happy reading.

Lee Anne M. Palmer, VMD, MPH
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Journal of Veterinary Cardiology (2019) 21, 1–9

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Echocardiographic phenotype of canine dilated cardiomyopathy differs based on diet type

Darcy Adin, DVM*, Teresa C. DeFrancesco, DVM , Bruce Keene, DVM , Sandra Tou, DVM , Kathryn Meurs, DVM, PhD , Clarke Atkins, DVM , Brent Aona, DVM , Kari Kurtz, DVM , Lara Barron, DVM , Korinn Saker, DVM, PhD

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Received 30 May 2018; received in revised form 24 October 2018; accepted 6 November 2018

KEYWORDS
Nutritional;
Heart failure;
Dog;
Taurine

Abstract *Introduction:* Canine dilated cardiomyopathy (DCM) can result from numerous etiologies including genetic mutations, infections, toxins, and nutritional imbalances. This study sought to characterize differences in echocardiographic findings between dogs with DCM fed grain-free (GF) diets and grain-based (GB) diets.
Animals: Forty-eight dogs with DCM and known diet history.
Methods: This was a retrospective analysis of dogs with DCM from January 1, 2015 to May 1, 2018 with a known diet history. Dogs were grouped by diet (GF and GB), and the GF group was further divided into dogs eating the most common grain-free diet (GF-1) and other grain-free diets (GF-o). Demographics, diet history, echocardiographic parameters, taurine concentrations, and vertebral heart scale were compared between GB, all GF, GF-1, and GF-o groups at diagnosis and recheck.
Results: Dogs eating GF-1 weighed less than GB and GF-o dogs, but age and sex were not different between groups. Left ventricular size in diastole and systole was greater, and sphericity index was less for GF-1 compared with GB dogs. Diastolic left ventricular size was greater for all GF compared with that of GB dogs. Fractional shortening, left atrial size, and vertebral heart scale were not different between groups. Taurine deficiency was not identified in GF dogs, and presence of congestive heart failure was not different between groups. Seven dogs that were

Presented in abstract form at the American College of Veterinary Internal Medicine Forum, Seattle, WA, June 2018.

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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:	2/25/2019 2:19:28 PM
Subject:	DCM - More from L Freeman 2/25/2019 0915
Attachments:	Acana lamb and apple dry: Lisa Freeman - EON-380747; Wellness Core grain-free ocean fish dry-Wellness core grain free turkey: Lisa Freeman - EON-380742; Wellness CORE Grain-Free Ocean Whitefish dry-Wellness Core grain free turkey: Lisa Freeman - EON-380743

Note: 380742 & 380743 are from the same household. Other dogs in household – 2 not tested yet & 1 normal BNP

David Rotstein, DVM, MPVM, Dipl. ACVP
CVM Vet-LIRN Liaison
CVM OSC/DC/CERT
7519 Standish Place
240-506-6763 (BB)

From:	Palmer, Lee Anne </o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cf7c8bd53b6c45a39318a596acea7c53-LPALMER>
To:	Peterson, Glenn A
Sent:	2/27/2019 4:40:54 PM
Subject:	DCM papers
Attachments:	Adin 2019.pdf; Freeman 2018 javma.253.11.1390.pdf; Freeman_Nutrition and CM 2007 10.1007_s11897-007-0005-6.pdf; Mansilla 2019 J Anim Sci.pdf

Hi – here you go…

Thanks, Lee Anne

Lee Anne M. Palmer, VMD, MPH
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From: U.S. Food and Drug Administration <fda@info.fda.gov>
To: Palmer, Lee Anne
Sent: 2/19/2019 4:01:15 PM
Subject: FDA Provides Update on Investigation into Potential Connection Between Certain Diets and Cases of Canine Heart Disease

If your email program has trouble displaying this email, view it as a web page.

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA Provides Update on Investigation into Potential Connection Between Certain Diets and Cases of Canine Heart Disease

The U.S. Food and Drug Administration today is providing an update on its investigation into reports of dilated cardiomyopathy (DCM) in dogs eating certain pet foods. The update covers reports of DCM received by FDA through November 30, 2018.

This update does not include reports received in December and January due to the lapse in appropriations from December 22, 2018, to January 25, 2019. Because the Anti-Deficiency Act does not except activities that are solely related to protecting "animal health," FDA was not able to continue its investigation during that time.

The FDA first alerted the public about this investigation in July 2018. Since then, the FDA's Center for Veterinary Medicine (CVM) has taken a multi-pronged approach to the investigation, collaborating with a variety of components of the animal health sector to collect and evaluate information about the DCM cases and the diets pets ate prior to becoming ill.

Based on the information gathered as part of our investigation to date, our advice to pet owners remains consistent. The agency has not identified specific recommendations about diet changes for dogs who are not displaying DCM symptoms, but encourages pet owners to consult directly with their veterinarians for their animal's dietary advice.

Continue reading.

You are subscribed to updates from FDA's Center for Veterinary Medicine.

U.S. Food and Drug Administration
10903 New Hampshire Avenue, Silver Spring, MD 20993
1-888-INFO-FDA (1-888-463-6332)

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Plasma and whole blood taurine in normal dogs of varying size fed commercially prepared food

By S. J. Delaney[1], P. H. Kass[2], Q. R. Rogers[3] and A. J. Fascetti[3]

Summary

The objective of the present study was to examine the effect of signalment, body size and diet on plasma taurine and whole blood taurine concentrations. A total of 131 normal dogs consuming commercially prepared dog food had blood drawn 3–5 h post-prandially to be analysed for plasma amino acids and whole blood taurine. Body weight and morphometric measurements of each dog were taken. Plasma and whole blood taurine concentrations were 77 ± 2.1 nmol/ml (mean ± SEM) and 266 ± 5.1 nmol/ml (mean ± SEM), respectively. No effect of age, sex, body weight, body size, or diet was seen on plasma and whole blood taurine concentrations. Mean whole blood taurine concentrations were lower in dogs fed diets containing whole grain rice, rice bran or barley. The lowest whole blood concentrations were seen in dogs fed lamb or lamb meal and rice diets. Plasma methionine and cysteine concentrations were lower in dogs fed diets with animal meals or turkey, and whole grain rice, rice bran or barley. Fifteen of 131 dogs had plasma taurine concentrations lower than, or equal, to the previously reported lowest mean food-deprived plasma taurine concentration in normal dogs of 49 ± 5 nmol/ml (mean ± SEM) (Elliott et al., 2000). These findings support the theory that taurine deficiency in dogs may be related to the consumption of certain dietary ingredients. Scientific and clinical evidence supports the hypothesis that dilated cardiomyopathy is associated with low blood taurine concentration in dogs; therefore, further work is indicated to determine the mechanism by which diet can affect taurine status in dogs.

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DR. JUSTIN SHMALBERG

Dilated Cardiomyopathy and Grain-Free Diets: Thoughts on the FDA Update

July 03, 2019

Fatal heart disease from pet foods? This is the alarming suggestion circling the internet again following the release of more information from the FDA. It's important to view such information in a rational context and to use the opportunity to think about your pet's nutrition broadly.

What do we know?

Veterinary cardiologists suggested that a heart condition known as Dilated Cardiomyopathy (DCM) was occurring more commonly in Golden Retrievers and other breeds not commonly thought to be genetically predisposed (breeds in that latter category include Dobermans, Boxers, Great Danes). DCM has of course been reported in other breeds in smaller numbers, generally other medium- to large-breeds, but there was a concern that the overall number of atypical cases was higher than previously recognized. Some cardiologists suggested that many atypical dogs were fed grain-free diets. This led to interest from veterinarians, breed groups (specifically Golden Retriever owners), the public, and the FDA. The FDA has been accumulating data for months at the present time, and in the last week provided some more details than previously available.

What is DCM?

DCM is broadly a condition characterized by poor contraction of the heart muscle, which can lead to heart failure, a potentially fatal condition. Dogs may have no signs at all, nonspecific signs (poor appetite or energy level), or in advanced stages coughing due to fluid in the lungs or enlargement of the heart, fluid in the belly, severe weakness, collapse, or even death.

Is DCM always a nutritional problem?

Not usually, as the genetic predisposition is thought to be the cause in most cases. However, deficiency of taurine is known to cause a potentially reversible form of DCM (non-nutritional DCM is managed but not reversed). So what is taurine? Taurine is an amino acid made by dogs (but not cats) from other precursor amino acids, specifically methionine (an essential amino acid) which is then converted to another amino acid, cysteine. We can group these together and call them sulfur-containing amino acids (SCAA) since they, you guessed it, contain sulfur. If you give a cat a diet with little or no taurine, DCM is a real possibility. If you give a dog a diet without taurine that is low in SCAA or has SCAA that are not available (not well digested), DCM is also possible. This is what happened nearly 2 decades ago when low-protein diets without adequate or digestible SCAAs (lamb is naturally low) were fed to dogs. It occurred in cats fed diets low in natural taurine without supplementation. Now, most pet foods contain supplemental taurine for cats, and either supplemental taurine or SCAA for dogs (unless they are very high protein diets with naturally occurring amounts). It's important to note

that measuring amino acids or nutrients in general isn't the whole story because it only tells you what theoretically can be digested, not what is actually unlocked from the food and absorbed. Basically, a number can look good but not produce real-world effects.

What is the scope of atypical DCM?

Unfortunately, this is not known. The FDA has reviewed information from 560 dogs and 14 cats between January 1, 2014 and April 30, 2019, with 119 and 5 deaths in those pets, respectively. My cardiologist colleagues tell me that some owners are not reporting their animals, especially now since the problem is more widely publicized - many probably feel it's not worth the effort or won't help to unlock what is happening. There is no streamlined or central reporting system for veterinary cardiologists to input their suspected cases and so the FDA is likely a lower estimate. Some of the dogs reported were in breeds with predispositions (25 Great Danes, 15 Dobermans, 11 Boxers). Unfortunately detailed information is not always available for each dog, and so if a dog was of a predisposed breed and showed signs of reversal, we would think it more likely to not be genetic DCM which isn't known to dramatically improve.

Not all of the cases above have been confirmed to have DCM - the FDA reported that 202 dogs (35% of total reports) and 6 cats (42.8%) had both medical records reviewed and met the DCM definition. Of those reviewed, 59.4% had findings consistent with DCM while others were classified as non-DCM (which included those with decreased left ventricular function (which might be pre-DCM) or other heart changes which may not be related to DCM). Based on a comment below, this paragraph was edited, and I also would emphasize here as I did elsewhere that there certainly are some number of pet parents who did not report cases similar to what the FDA has collected.

It's important to remember that the total number of atypical DCM cases in previous years also isn't known so we have no baseline to which we can compare the current numbers. It's still safe to say that DCM is very uncommon in dogs fed any specific pet food.

What about breed?

Golden retrievers were the most common breed identified (95 cases). This could be because they are truly over-represented or just because their owners were very active in mobilizing as a group and reporting cases. If Goldens are truly more frequently affected, then it's possible that they have a unique genetic predisposition in some families - previous reports have found this for taurine deficiency in Goldens. There could be previously identified genetic predispositions in the other breeds on the list (like Labradors and other retrievers). Or perhaps, it's a combination between genes, diet, the microbiome and a host of unknown factors, especially in those Goldens with normal taurine levels.

It's important to note that almost all of the breeds reported are medium to large (as has been seen in atypical cases before). The only small breeds were Shih Tzus (5 cases) and potentially 'unknown' (13 cases) or maybe some mixed breed dogs (62 cases). We have no frame of reference to compare to previous years in atypical

DCM breed distribution. This would only be identified through a consortium of cardiologists working to identify all previous cases - something that is very challenging to do.

Is taurine to blame for the current cases?

Taurine levels were only available for 64% of dogs with confirmed DCM, and less than half of those had low taurine (42%). Generally speaking, it would be safe to say that low taurine was less common than a normal or high taurine across the dogs reported.

For Golden Retrievers, it's a bit different. The FDA lists taurine results for confirmed Golden DCM cases (24 total). 79.2% had a low taurine, 16.7% normal taurine, and 4.2% high levels. In normal Golden Retrievers, 7 dogs had low taurine and 4 normal. In Goldens with other heart changes (non DCM), 13/17 had low values and 4/17 had normal values. Across the board, with or without DCM, the reported Goldens seem more likely to have low taurine. It is previously known that Goldens can have issues with taurine causing DCM on a familial basis.

The type of sample submitted can influence results. It is known that taurine will yield potentially different results if run on whole blood (the blood that comes straight from the vein) or on the fluid portion of the blood (plasma) and there were differences in what type of samples submitted that could be significant. Some cardiologists are now also suggesting a new taurine reference interval just for Golden retrievers.

In cats, there's really not enough information to make any conclusions.

Taurine was a part of treatment in many dogs that improved (in addition to diet change, medications, and other supplements like fish oil). Taurine is known to help encourage normal contraction of the heart (which is why DCM is caused with true taurine deficiency - remember that DCM is characterized by the heart not contracting well). Taurine may help even genetic DCM to some degree - this has never been really studied to my knowledge. As so many treatments were initiated at the same time, it's nearly impossible to tell if taurine alone was helpful. Certainly taurine is not harmful but the evidence is presently inconclusive that taurine is to blame in many cases. Additional work is needed in Golden retrievers to determine relationships between DCM and taurine.

Is diet to blame at all?

There is no proven association between any dietary strategy or specific diet and DCM. The FDA is testing reported foods but has released limited information. They have stated that the macronutrients, SCAAs, and taurine are similar between tested grain-free and grain-containing foods.

There are a number of guesses, which are just that - guesses, about what could be going on IF a dietary link to these cases were proven. These include:

- Poor availability of SCAAs and taurine in the diet, meaning they are there but not well absorbed

- Legumes or legume proteins at high amounts providing less digestible amino acids, antinutritional factors, and soluble fiber that interacts with digestion and the bacterial flora in the gut (microbiome)
- Poorly digestible ingredients especially those providing protein (meat meals with high bone content (ash), vegetable sources of protein). Remember that poor quality, high ash meals are less expensive than others and that for some meats that may be all that's commonly available.
- Processing changes to SCAAs, especially during extrusion (kibble formation)
- Lack of testing for taurine and SCAAs (although the FDA is saying levels are similar in their testing)
- High fiber amounts that impact the recycling of taurine in the gut (taurine is a part of bile salts found in the bile that get resorbed at different levels depending on the diet)
- Genetic predispositions to differences in handling nutrients or in production of taurine from SCAA, such as previously identified in Golden retrievers

Unfortunately, the information about brand does nothing for nutritionists to be able to look into these potential factors. A detailed list of complaints, some of which contain specific products within brands, is found here. It will take some time to aggregate the information by specific food, and it's not clear that will be done by the FDA.

Is there a type of food more commonly reported?

Kibble is the most common food type reported (452 reports) as compared to those feeding multiple types (24), unknown (26), and raw (9). One instance each of home-cooked, refrigerated, semi-moist, and tubbed are reported. We do know that kibble is by far the most commonly fed type of pet diet, so the data may just reflect that. However, it's interesting that canned and fresh diets are not generally reported here (especially canned which would be second most commonly fed). This may be because there is no true association between diet or if there is, that it is not as likely to cause issues because of different ingredients or because of different cooking/processing.

The brand list - should they always be avoided?

Every brand produces a number of foods and this is where the incidence of specific diets would be helpful. In looking through the reports of DCM, many lack complete information about the specific product being fed. Many owners were feeding multiple diets together or rotating (even between brands) which complicates the picture. Examining those brands with 50 or more reports, which are Acana, Zignature, and Taste of the Wild, I searched the reports for specific products. Remember that the data is not easy to search or manipulate in the form provided by the FDA so please interpret these findings with caution and apologies in advance for inaccuracies identified. This said, for Zignature, the kangaroo product appeared 43 times (when reported as the only diet fed), trout 6 times, and turkey 4. Other products were below that. For Acana, lamb appeared 19 times, followed by pork 5, duck 5, and a combination of only duck and pork flavors 5 times. For Taste of the Wild, Pacific Stream appeared by itself 8 times (fish), High Prairie (poultry) 8 times, and Pine Forest (venison) 6 times, followed by other products. This was a very cursory glance, but you can appreciate the diversity of products and the distribution. This data also would be best compared to the sales of the particular brands and individual diets. If a

company is more popular, it might appear more frequently in any list and the same would be true for a particular food.

The absence of generally less expensive kibble diets (by this I mean the cheapest diets you can find on grocery store shelves) may be a bias because of the fact that pet parents feeding those diets may be less likely to see a veterinary cardiologist for screening of heart disease.

So should you avoid particular brands? Likely not, based on the information so far. If there is an association, it will likely be related to food type (processing) and ingredients more than a particular brand. Also remember the vast majority of dogs on all these foods don't have any issue. Most companies are working with nutritionists to continuously evaluate their products especially in light of the present concerns. As nutritionists, we have very limited information to tell them except for those related to ingredients as described below.

Are foods which have been evaluated through feeding trials the answer or foods meet meeting 'WSAVA standards'?

This was added based on a comment you can read below (as well as my reply which contains more detailed information), but I do not believe there is evidence that feeding trials would be preventative for designing a food which avoids this issue if and when causation is determined. Feeding trials conforming to only AAFCO standards are a very low bar to clear, and foods that meet feeding trials can actually have nutrient values outside AAFCO standards. You can read more in the comments below about my take on feeding trials at this stage. WSAVA guidelines for selecting a pet food are helpful, and the majority of listed foods likely meet WSAVA recommendations. Remember the WSAVA provides very few actual recommendations except for ensuring that a food is formulated to meet AAFCO standards OR has been tested with feeding trials for the appropriate life stage of your pet. There is a list of questions to ask, without any opinion given by WSAVA as to what the answer should be. It is my opinion as a nutritionist that foods should, feeding trial or not, have been testing for a nutrient profile after they are formulated and then produced. Remember that there is no evidence that listed foods have a nutrient deficiency, which is consistent with FDA's reported testing.

What about ingredients - any learnings from the FDA data?

The FDA approach to ingredients has not done any favors for the analysis. They include main ingredients as those before vitamins and minerals - as a result, these ingredients could be present in 1% to say 80% of the diet. A big difference nutritionally. It of course is very difficult to determine the concentration of any ingredient based on the ingredient list. They are listed in descending order as-fed (which means with water). A fresh meat will contribute fewer calories than a meal when first on an ingredient list - this is an example of how complicated this becomes. The FDA does say 90 percent were labeled grain-free and 93 percent had legumes (peas, lentils, chickpeas). Potatoes and sweet potatoes in a lesser number - 42%. But unfortunately we don't learn anything from the recent FDA filing on the actual percentage of calories provided by these ingredients - something admittedly difficult to get from manufacturers.

We also need to keep in mind that grain-free diets are extremely popular in the pet-owning population, especially I suspect in those that have regular veterinary care. So we should expect in any list to see a high background of grain-free diets. Certainly if an association exists, the high prevalence of legumes may be important. But the inclusion rate is even more important - there's a big difference between 3% peas and 50% peas or pea derivatives (pea protein, pea starch). Low amounts of legumes have been fed to pets for a long time without any observed issues, and modest amounts of potatoes have also been included in diets, including kibble, for some time.

The animal proteins in the diets appear to be distributed across a range (chicken most common, followed closely by lamb, then salmon, whitefish, kangaroo, turkey, beef, pork, venison, etc.). Of course, for kangaroo, this is mostly reflective of a couple of specific diets as compared to chicken which is a wider range (but of course not many companies make a kangaroo diet nor is kangaroo sold as commonly as chicken).

Take-home messages: if you're avoiding foods based on the list, the ingredients appearing most frequently are legumes. Here again, the amount of legumes isn't addressed which is a big deficiency in our current knowledge of these diets when it comes to ingredients. It would be difficult to believe that 5% or less would be a problem, but in a larger amount, that's a relatively recent phenomenon in pet food production driven by the push for grain-free diets.

What about detailed nutritional information?

Detailed information about the nutritional profiles of the diets has not yet been released from FDA testing. The guaranteed analyses are available for many of the diets, but keep in mind some have changed in the past few years. It's also worth considering that the guaranteed analysis is not a good way to compare pet foods, a subject I and other nutritionists have talked about extensively.

At the present time, we'll have to wait on this data. Of course, if there ends up not being an association between diet and DCM, it may not be particularly relevant anyway.

Why are some dogs improving with diet change?

Individual reports within the FDA data as well as reports from veterinary cardiologists suggest that pets improved following a diet change. This is a bit of an over-simplification because of the fact that many dogs were also given supplemental taurine at very high doses (higher than in pet foods), carnitine (a nutritional supplement which may have benefits in DCM), fish oil, and in severe cases, drugs. Even if a new diet helped, did it help because a particular dog or breed has a higher requirement for a nutrient than an 'average' dog? This would not be the manufacturer's fault per se since they used the best available scientific information to formulate. The effect of diet alone is very difficult to isolate. In addition, the diets to which dogs were changed are often unknown and not compared to the previous diet.

This is a very complicated scientific problem with the need for careful analysis, and we don't yet have the level of analysis required to draw any conclusions or even to compare dogs with and without DCM, of similar breed and age, fed the same foods. It's also important to compare how often DCM occurs on a particular diet within the entire population fed that food as compared to the background incidence (how often DCM occurs in all dogs (or by breed)). For example, if 1 out of 10,000 dogs get DCM when fed any diet, and 1 out of 1,000 develop DCM on diet X, then diet X is certainly worth investigating. The total number of cases reported needs to be compared by the FDA to the number of total dogs exposed. If diet X is 10 times more commonly fed than diet Y, the total number of DCM cases would be expected to be 10 times higher for diet X than Y (even if diet X did not contribute to DCM - more dogs are exposed in the general population). In veterinary studies, we also talk of confounding variables, which basically means other factors that could complicate the ability to establish cause and effect, and this data that the FDA has obtained is complicated by confounding variables like drugs, supplements, breed, age, duration of feeding, calorie intake, microbiome differences, genetic mutations, etc. (which is not entirely their fault since the quality of data from these reports can be difficult to standardize and the amount of data needed is enormous). This is one of the most complex questions to answer that I've seen be asked in pet nutrition.

BEG (Boutique, Exotic, and Grain-free) - is this an appropriate guide?

This is a term being used by some veterinarians to describe the diets in question. I think any attempt at simplification at this point is misplaced. We just don't have enough information. There are brands on the list that I wouldn't consider to be boutique - and this really has no meaning anyway. Brands are often owned by a large pet food company, or their foods manufactured by a larger company, which is the case in the foods reported (including some of the biggest names in pet nutrition). Nevertheless, because a brand is smaller or sold in independent retailers or direct to consumer, are they inherently less reputable or capable? I think not, and some positive innovation in pet food is driven by smaller companies (some of which the large companies purchase or invest in when they recognize this). In full disclosure, I've consulted with companies of all sizes as a nutritionist.

What about exotic - the ingredients aren't particularly exotic looking at the list of proteins and the individual diets being fed - certainly kangaroo diets may appear more frequently than we might expect since they are not as commonly sold as others but this needs to be examined with real data (rather than my impression). Is kangaroo itself likely to be a cause if there was an association between DCM and food? Doubtful if used appropriately and analyzed for nutritional content; if instead high ash meats (or any animal) were being used, it's possible the protein and amino acids were not as digestible as they seem on paper. Remember that many meats and meals used in many pet foods contain cuts or trimmings of meat as well as bone after processing and can vary significantly from supplier to supplier and even from batch to batch. It's also possible kangaroo being expensive was mixed with more legumes - again, we don't have the data. In any respect, I encourage clients to reserve exotic proteins for food trials (testing for food allergies when necessary). But looking at the data, there are certainly a number of poultry, lamb, and fish diets - far more than exotic proteins - so it doesn't seem if there was a definite link that it would be related specifically to the protein source (unless that protein source were not balanced with other proteins or that supplemental amino acids were not added to account for deficiencies in a

final formula). Remember, however, that the FDA has said so far the testing of SCAAs and taurine appears similar in the diets tested.

Grain-free diets have been around for some time, long before it was a frequent appearance on the label. Remember the duck and potato diets for allergy testing - these have been fed for decades. There have been significant changes in how grain-free diets are formulated including the use of legumes and legume protein in higher amounts than done historically. This could be another area where the values look good in testing, but where there isn't optimal absorption of nutrients (or possible interactions between nutrients which were unpredictable). Admittedly, there is no evidence that grain-free foods are superior to grain-containing foods when nutritional composition is similar, but we don't yet have enough information to say all grain-free diets are harmful (and I'm absolutely positive this won't be the case).

Nutrition isn't simple, and the best diet for any pet is usually one that is individualized. Applying any cute label to a complicated and unproven problem does a disservice to the attempt to characterize the problem fully and give pet parents facts, not slogans.

How am I advising pet parents?

The first is to approach the situation as calmly as possible. The vast majority of pets are fed many of these diets without any reported DCM (whether DCM is related to food or not in the end) - it's heartbreaking when any pet is sick and certainly every precaution should be taken as information becomes available. It's understandable that trust in pet food has been eroded because of contamination, recalls, and controversies. Talking to your veterinarian about your pet, which is not the same as any other pet, is helpful as again, the best diet is individualized. I underscore that we haven't yet proven a link between diet and certainly not what part of the diet or diet-pet interaction is to blame. These tips may prove helpful, however:

1. Consider feeding a higher protein diet. Dogs have requirements for essential amino acids (protein) and fatty acids (fat) but not for carbohydrates (although carb-containing ingredients, including peas and potatoes, provide energy along with a host of phytonutrients and other benefits in moderation). A diet with more than 75 grams of protein per 1000 calories is a good place to start, especially if your pet is overweight, doesn't eat a lot of food, has a known heart condition, or is active to give pertinent examples. This is determined by calling the company or estimating from a guaranteed analysis. Feeding more protein generally provides more SCAAs, those taurine precursors I mentioned earlier.
2. Consider a diet with additive taurine. We again don't yet know that taurine is a preventative or treatment factor in atypical DCM cases, but it has a high margin of safety. Diets with supplemental methionine can also be helpful and represent an alternate option (since that's a taurine precursor in dogs). You can always ask a company how they determined if additional taurine or methionine was or wasn't required - but you may not get an answer to such a technical question.
3. Avoid diets at the current time which appear to rely heavily on legumes to meet the protein content of the diet. This is difficult to evaluate on the label. If a fresh meat is first on the ingredient list, followed by a legume or legume protein, it's likely the *legume* that provides more contribution to the diet since it's dry

whereas the meat is mostly water. Similarly, if there's a number of legumes listed and only one meat, that could also be a sign. Or if a legume is the first or second ingredient. Legumes can afford some nutritional benefits, but their history as a significant protein source is less well known. It may end up being perfectly safe, but the reason for higher inclusions (vs. meat) is generally for sustainability, processing, or cost. There's no reason to avoid legumes or potatoes entirely, and I've formulated diets of all types with both ingredients but at low inclusion rates, in the interest of full disclosure.

4. Consider varying the diet. I'm not a proponent of feeding the same diet for the life of any dog or cat. Nutritional variety helps to overcome any particular issues with a certain formulation. Also consider different types of diets - if you're feeding kibble, other options can be explored in addition or alone (canned foods, pasteurized foods, fresh foods, balanced home-prepared diets, etc.).
5. Talk to pet food companies about their testing and formulation process. Do they work with nutritionists to formulate? Do they test the final product to ensure it meets the requirements? Both are preferable.
6. If you have a Golden Retriever on any diet, screening is an option both in terms of an echocardiogram and taurine level until we know more. There certainly are some Golden retrievers that may have DCM from taurine deficiency, and this may be due to genes and not diet alone.
7. Remember that vets and other industry experts (including those at companies) aren't trying to be evasive when not giving answers about the potential DCM association to diet. Simply put, no one has conclusive answers and there are a number of people working to sort this out but it will unfortunately take time.

Comments on this blog below:

I'm an admittedly reluctant blogger, but felt it important to express my thinking on this issue for my clients. I will try to respond to comments as I'm able, and remember that the information above is my opinion and my opinion only based on the published data accessible to everyone (I know there is an unknown amount of unpublished data circulated in parts throughout the internet). I hope, like all pet parents, that definitive answers are coming. I believe the tips above are sound advice generally, and I admit that I do not have the answers (but also think no one yet has those). If you draw any conclusion, it's that we need to be talking about diets, not brands, nutrients not impressions, and specifics rather than generalizations. It's always easier to make a sweeping generalization, but in nutrition, that's when we're often wrong.

Justin Shmalberg 13 Comments 25 Likes Share

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Colton Stricklin 5 hours ago · 0 Likes

Dr. Shmallberg, I want to thank you for your objective, fact-based commentary on this topic. As a scientist myself in another field of study, you are correct in your take of this issue, i.e., there is just not enough information available to be drawing questionable conclusions and simplifying this subject by painting all-dog food manufacturers other than the Big 5-named brands (Purina, Hill's Royal Canin, Iams & Eukanuba) as "boutique" companies who are only interested in profits and continue to sell "dangerous" products. You'll get an eyeful if you take a good look at the Facebook page Dr. Skibbe boasts of "administering" entitled, "Taurine Deficient (Nutritional) Dilated Cardiomyopathy. This site claims that it is strictly "science-based" but tolerates no questions or challenges that they view as "rocking the boat". If someone dares to ask a question or make a statement that is viewed as "controversial", these shills will first point you to their "educational units" (presumably because you haven't educated yourself to their point of view) and if you persist, they will delete and silence you in a manner that will make any third-world despot proud! Here are some examples of the double-talk they employ to keep the lemmings fooled:

.....They have consistently told site members that all foods containing legumes, peas, etc should be avoided at all costs but when some astute members asked why, if these ingredients were so harmful, were the Big 5 companies including them in their formulas, the answer was that the Big 5 have the "expertise" and "science" behind them to know how to properly handle and process these ingredients! Its surprising they didn't go a step further and claim that the Big 5 have a "specials strain" of peas and legumes that only they, have access to and that are totally safe in their exclusive formulas!

.....They continuously point out that one of the criteria for selecting a dog food brand is that it has followed WSAVA recommendations that feeding trials have been conducted, (which the Big 5 companies supposedly do). What Dr. Skibbe and friends leave out is that WSAVA itself, states that feeding trials are not always reliable and in many cases, mean nothing.

.....The Taurine Deficient (Nutritional) Dilated Cardiomyopathy Facebook Page doesn't ever disclose that WSAVA is funded by the Big 5 brands as is shown on WSAVA's website nor is it ever disclosed that the "Veterinary Nutritionists" who are promoting the WSAVA "Standards" are all receiving funding from some or all of the Big 5 Brands.

Slight conflict of interest? Shocking!
.....The Taurine Deficient (Nutritional) Dilated Cardiomyopathy Facebook Page has hundreds of "armchair quarterbacks" who think they are subject-matter experts on this topic, have no veterinary and/or nutritional certifications or credentials, and yet are being allowed to give out veterinary and nutritional advise on an hourly basis.

Again, thank you for your refreshing, objective commentary and hope that continued research on this topic will begin to separate fact from fiction and speculation.

Joshua Stern 19 hours ago · 0 Likes

I'm pleased to see more and more specialists are now paying attention to this issue! There are a couple points here that need clarification and may represent the importance of seeing these cases in the clinic in order to fully appreciate the issue.

Dogs ARE getting better with diet change. In some cases with diet change alone and in some with diet change and supplements. Many of these dogs who get better are then transitioned off of all heart medication and supplements - leaving them without evidence of disease and on the new diet for many months. Many companies have hidden behind this to say that it can't be diet alone, and in some cases this is likely because they know that changing only diet would be unethical in advanced DCM (thus being able to continue their anti-science propaganda). I'm sure this blog only means to stress that this is a complex issue that requires continued study. However, to state that this isn't a diet problem is in my opinion reckless at this point.

This problem is relatively new and the case reports to the FDA demonstrate this well. There has been a recurring suggestion that this problem is generated by a subset of dogs with special needs. That assumption is incorrect . Many diets have been apparently meeting these "special needs" without issue. If this blog is implying that breeds like the Golden Retriever have differing taurine requirements for example, this may be true. However, they didn't wake up that way all of a sudden in 2017; their genetics didn't change abruptly. Are we really OK with companies saying that one of the most popular dog breeds in the world has special needs that can't be met with a diet marketed for dogs?

The suggestion to rotate diets to avoid this issue seems out of place. If you read the FDA update it becomes apparent that owners could rotate many brands, yet still end up with a feeding regime completely comprised of diets associated with DCM. I don't mind the idea of rotating diets, so long as owners rotate formulas that avoid suspect ingredients and are produced by companies that meet WSAVA guidelines. Of course, feeding a single diet with these characteristics appears to be just as good for avoiding NM-DCM.

Finally, it is poor form to suggest that the type of food a person feeds is directly tied to the veterinary care they seek for their pet. There is no research to support such a claim. This is an issue that causes heart failure and sudden death. Both of these outcomes are pretty easily noticed. At one of the busiest academic cardiology centers in the world we see a great number of dogs on diets that meet WSAVA guidelines and many that eat grocery store brands. Many people that care about their dogs and seek advanced treatment do still shop at Target for their pet food. A few years ago I had a client sell her car to pay for a pacemaker in her dog. My own chihuahua eats Beneful because he is 15.5yrs old and he likes it. In short, this statement was inappropriate and feeds into the marketing that got us into this problem to begin with. How do we change the narrative so that pet owners believe that loving and protecting their dog starts by feeding a well-researched dog food?

Dr Schmalberg- you have an excellent opportunity to join forces with a top researcher in the clinical entity that is Nutritionally-mediated DCM at U of F! Please please work with Dr Adin there and help move this research forward for the sake of dogs and the pet food industry!

Joshua A. Stern, DVM, PhD, DACVIM

https://ccah.vetmed.ucdavis.edu/areas-study/genetics/nutritionally-mediated-dcm

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Justin Shmalberg 5 hours ago · 0 Likes

Hi Dr. Stern,

Thanks for taking the time to post and to share your expertise.

I would start by saying I do, in comments and in the above, carefully mention that my thoughts are based on the universally available knowledge about cases, which is to my knowledge only found in the FDA release and a few journal articles or abstracts. I absolutely appreciate that clinical impression is important, and I definitely acknowledge that as information is aggregated and made available scientifically, we may well have different scientific conclusions (some of which may match current clinical impression). In the overview publication of which you are an author in JAVMA, the following is quoted directly: "Regardless, the apparent link between BEG diets and DCM may be due to the grain-free nature of these diets (ie, use of ingredients such as lentils, chickpeas, or potatoes to replace grains), other common ingredients in BEG diets (eg, exotic meats, flaxseed, fruits, or probiotics), possible nutritional imbalances, or inadvertent inclusion of toxic dietary components. Or, the apparent association may be spurious." It sounds like your recent research has revealed that this is a definite association and not spurious. As a follow-up then, can you tell the readers how specifically that conclusion has been reached? Is it

unpublished clinical data and if so can you tell me how many additional dogs this involves at the current time?

It is extremely discouraging to be told a post which fundamentally relates that causation has not yet been *scientifically* established is "reckless". I most certainly did not say it wasn't an issue, only that if it is an issue, the FDA data and other published data hasn't uncovered the reason nor has it suggested definitively what to avoid. Moreover, I absolutely agree that there are some diets that can produce taurine deficiency - but this was previously known and corrected relatively easily by reformulation with taurine in the past (which seems to not be the case here). In the previously-mentioned article you co-authored, the following was said about non-taurine cases: "Notably, however, some dogs improved after a diet change from one grain-free diet to another, and this finding, along with the differences identified between dogs fed various BEG diets, suggested that DCM was not necessarily tied to the grain-free status of the diet. Taurine supplementation was prescribed for many of these dogs despite the lack of apparent deficiency, and it is unclear what role taurine may have played in their recovery." Are there enough cases now to suggest that in some diet alone is definitely sufficient and in others diet and taurine (are numbers available)? Were new diets different in taurine or just different in some other capacity? One frustration I have as a nutritionist is that no one is detailing which diets have been fed after diagnosis, and in many cases, nutritionists are then asked to make a recommendation in the absence of any information to suggest what the dietary link is or what specific diets may be used in treatment successfully.

I would take issue with a narrative that companies are hiding behind statements or uncertainty in the data. Every company I've heard discuss this issue is desperate for causation to be proven and identified so that corrective action can be taken. When you can't tell companies what specifically they've done wrong, it certainly is difficult to induce positive change. I also am not sure there is rampant anti-science propaganda - I think to the contrary owners are concerned when sweeping generalizations are made. I hope you are not left with the impression I'm trying to foster an anti-science narrative - to the contrary, I'm trying to give folks a window into how complicated causation is to prove scientifically with so many confounding variables (not to mention scattered sources of case reporting).

In terms of diet and genetics, my hope would be that reformulation could prevent any diet-related cases regardless of breed (but we of course won't prevent DCM entirely with diet, depending on the actual genes involved much like no one is suggesting DCM in Dobermans can be prevented by diet). But here again, we would have to know specifically what change would need to be made to know how to prevent or the feasibility. Your team related that many of the Goldens were eating less than expected, and I've always encouraged companies to formulate for a very low calorie intake assumption. Is it just adding supplemental taurine, is it therapeutic taurine (maybe 10-20x what's in foods commonly), is it taurine only when legumes are present (at a certain inclusion level)? Or is it some other factor of prevention? I don't know what happened to the numbers of Goldens with DCM before and after 2017 because the incidence has not to my knowledge been

quantified for different periods - do you have this data? If these companies asked you today how to fix the problem for Golden Retrievers (or any breed), what would you say?

In terms of rotation, you're confident that WSAVA guidelines (which are met by many companies on the list, unless again we are changing those standards) and avoiding suspect ingredients is the solution to the problem and that there are data to support this at present? Is the recommendation provided in the JAVMA article still sufficient in your mind: we should recommend the owner change the diet to one made by a "well-established manufacturer that contains standard ingredients (eg, chicken, beef, rice, corn, and wheat)"? And by well-established, I assume this means they have existed for some indeterminate period of time? If the issue were to end up being related only to legumes at a certain amount, as a hypothetical, would the current recommendation not be an over-simplification of an admittedly complex issue?

With respect to diets and veterinary care, I suggested only that I did not know the answer to the question (as with all questions I have posed). Is there a difference in diet being fed between dogs seeing a cardiologist and the general public? I honestly don't know. Do we have data? I understand you have a clinical impression. I think it's important to know what the background of diets being fed by owners who have a dog that sees a cardiologist is so we can compare it to dogs with DCM and to the general population. Would that not be helpful? Certainly not all cases of DCM see a cardiologist (although they may not be diagnosed with DCM without an echo). Is it "poor form" to ask questions to which we don't know the answer? If you believe I was insinuating that people that feed food X don't see a cardiologist because they don't care about their pet, that seems like an oversimplification of the data analysis I was proposing and definitely not accurate to my intention.

Finally, I do think we need to address the following comment: "loving and protecting their dog starts by feeding a well-researched dog food". Can you tell me specifically what research would have definitively prevented the current situation? This is my point - when we say feed brands X,Y,Z because they do research or otherwise give a vague statement, without knowing what specifically brands did to avoid an issue (if anything), it only makes pet parents feel divided in the sense they're being told all 'BEG diets' are bad or the manufacturers on the FDA list are careless. Remember, the most well-researched companies in the world have had their own issues of even greater scope which I raise in the comments below (eg melamine). Many veterinarians and veterinary academic clinicians took issue in the mid-2000s when the reactionary recommendation to melamine was not to ever again feed any of the foods from the largest pet food companies because melamine was thought by many to represent a failure of ingredient sourcing and adulteration prevention. It's not marketing entirely to blame for current divisions in pet food and for different feeding strategies, it's an erosion of trust by pet parents based on a number of factors. I personally believe part of that is oversimplification of nutritional advice.

My overall point here is how do we provide concrete, evidence-based recommendations to clients that aren't sweeping generalizations that further divide and fracture pet parents, the veterinary community, and pet food manufacturers? My questions are designed about the current *available to everyone* data, and I look forward to the continued dissemination of more information from yourself and other leading researchers. At UF, my understanding is that we have not seen the numbers of cases being reported elsewhere, but I do look forward to any involvement or contribution I can make. I also appreciate your leadership in advancing the science here.

Thanks so much for the comments.

Link for article referenced above: https://avmajournals.avma.org/doi/full/10.2460/javma.253.11.1390

Darleen Newlin 19 hours ago · 0 Likes

I thank you for your comments. May I ask you about nomnomnow? Would rotating between protein sources be a sufficient rotation or should another food be considered entirely. I do believe fresh sounds better and I know you formulate nomnom but what about quality control and other scientists being involved. Thank you I am very interested in nomnom for both my cats and dogs.

Justin Shmalberg 5 hours ago · 0 Likes

Thanks for your comment Darleen. I'd prefer to avoid a discussion of specific brands on this blog, whether I formulate them or not. I'm sure the company would be happy to provide information on testing and formulation directly. Many foods are quite different within brands and if this is the case, I will commonly recommend that rotation. In other cases where a brand's diets are all similar nutritionally, I may encourage brand rotation for healthy pets. In clinical nutrition practice, I consider a host of factors about each dog and cat to try to customize specific recommendations (which is where veterinary nutritionists can be helpful generally). As I always say, the best diet is individualized to the needs of any specific pet. Thanks again!

Chris Griffin 3 days ago · 0 Likes

In terms of supplementation, would giving freeze-dried meats help increase levels of taurine? The dogs love it. We use Taste of the Wild since its closest to the brand our breeder feeds (the brand they use is not available in town). We tend to switch between different tastes because I figure it can't hurt.

Thank you for writing this up! I am a biochemist and physiologist by trade and I appreciate the rigor in your post.

Justin Shmalberg 3 days ago · 0 Likes

Thanks for your thoughts Chris. It would likely take a fair amount of additive meat to a kibble to push the concentration of taurine up significantly from what's in the kibble. I would say that many companies, on the list or not, are increasing the amount of taurine in commercial pet food since this happened (often by supplementation with purified taurine) - again whether or not taurine plays a role. I'm a strong advocate for dietary rotation which you mention - it's never made any sense to me that any specific diet would be the best diet for all pets (and if such diets did exist, we certainly wouldn't need veterinary nutritionists!). Rotating foods introduces nutrient and ingredient variability which is likely positive for ensuring individualized nutrient needs are met. Best wishes to you and your dogs!

Kim Skibbe 3 days ago · 0 Likes

Thanks for the reply and for editing on the "cost" issue. I'll make just a quick clarification of my view on "companies" where indeed I probably should have just said brands. It varies by company whether the same team is formulating all of their brands or if they have different divisions. I will however stick with the idea that "formulation, research, and experience matters more than ingredients". Royal Canin has a hydrolyzed soy diet for dogs with allergies; no evidence of DCM or other problems there. Kangaroo is another example: the Kangaroo diet developed by the Iams company and then transferred to Royal Canin in the acquisition has existed since the 1990s with no evidence of DCM problems. But I am told by nutritionists it is a difficult protein to work with, and it appears that perhaps Pets Global {Zignature) might have lacked either the expertise or research to formulate with it.

WSAVA guidelines can obviously be interpreted differently by different people, but in short what we are seeing (in a group where we have collected 500 DCM case reports ourselves) is that the companies that have research centers and a full team of experts aren't having this problem, in spite of ingredients. One example here is Fromm, who had a grain-inclusive diet DCM case mentioned in Dr Stern's study. Read Fromm's own "company timeline" and it shows they abandoned research about 1990 and turned to ingredient-based marketing.

Another one of the brands reported in the FDA graph was, to my understanding, formulated by a veterinary nutritionist. But he did not have the benefit of a full team of nutritionists, toxicologist, food scientist and a research center.

I wouldn't buy a family vehicle because it had the right kind of metal or brake fluid, if they didn't use a full team of engineers and safety testing.

We indeed may find an anti-nutrient or some other causative effect of legumes, but it's clear from other cases (lamb/rice diet lesson of the 1980s, homemade diets that periodically cause DCM, ultra low protein or high fiber) that there are a multitude of ways to get poor nutrition and possible DCM with it.

Again, thanks for your comments. It takes a multitude of inputs to sort out a problem like this and I hope spreading the message helps save dog's lives and prevents more family heartache.

Justin Shmalberg 3 days ago · 0 Likes

Thanks again for your comments and for taking the time to work on this important issue. I did want to offer a few other thoughts:

You won't find any objections to the point that more research and testing on any product is better. However, I worry that readers might infer that the current issue could have been prevented by research and testing - we just don't have data to support that at this time. We've seen issues in the past from companies that had teams and experience. Lamb-based diets which caused DCM due to taurine deficiency were released because the association was not yet recognized. It was only after they were on the market that the issue was identified by academic institutions. Similarly, the melamine recalls were not prevented by large teams because no one thought it would be an intentional contaminant by Chinese suppliers of ingredients. Melamine disproportionately affected some of the companies with the most experience in pet food. More recently, vitamin D excesses were not prevented either by a robust team, research, and experience. I'm absolutely a proponent for as much safety and formulation science as possible, but that doesn't prevent issues when the cause of an issue is unknown and it doesn't mean that every diet produced by company X has that level of diligence. I'm sure if anyone knew of a cause for DCM based on the formulations reported, they would suggest it now regardless of the company they worked for. It's just not yet clear that any testing or scientists could have prevented any relationship between DCM and food based on current scientific knowledge (or to use your specific example that Fromm's level of research effort could have prevented a case). If and when an issue is known, no doubt there will be testing and procedures put in place to prevent it from happening. Then, we will also be able to evaluate whether it could have been prevented. In the end we may find something very specific, say for example, that certain dogs, dog breeds, or lines (families) of dogs are predisposed to DCM that improves (or is prevented) by a certain nutritional profile that isn't optimal or needed for the rest of the dog population. Diet or supplements might even play more of a role in the treatment of DCM from any cause than we previously realized (since it wasn't studied previously).

For potential adverse events from pet food with a low incidence, it would take tens of thousands of dogs to be fed for it to manifest. Regardless of the findings of this investigation, we know the situation will fall into this category. If it's your dog that's affected and it was related to food, this would undoubtedly not provide any solace. And I truly do feel for any pet parent that has a dog with DCM of any cause. I only say this to illustrate that even feeding trials which contained echocardiograms would not likely detect the issue at hand - and echos during feeding trials aren't commonplace in any company to my knowledge. There certainly are other ways we know foods can cause DCM which you mention, but these all seem more classically related to taurine, unlike many of the current reported cases.

My fear with the current DCM conversation is that professionals and pet parents will use it to polarize around previously-held beliefs and assumptions. At present, one could simply look at the list and say this seems to be a kibble problem, so perhaps no one should ever feed kibble. Is that more or less justified at present than saying no one should ever feed grain-free diets? I hope we all, myself included, can see through any biases in the search of the truth.

Emily 2 days ago · 0 Likes

Hi Justin - thanks so much for taking the time write all of this and to respond to comments.

I am a veterinarian that has taken a special interest in nutrition. My interest and studies have been a result of the grain free movement. I felt like that movement spread a lot of misinformation about byproducts, grains, protein meal and most upsetting veterinarians. I would go on various food websites to defend the truth and find ways to effectively talk to people online so I had the knowledge and the confidence to do it in the exam room.

That being said, as someone who absolutely hates grain free for the political issues, I agree this is not just a grain free problem. I would say the majority of us veterinarians trying to educate and increase awareness about this terrible issue, will tell people that this is occurring in both grain free and grain inclusive diets.

I personally feel this isn't a grain free issue but rather a lack of research issue. I respect that you think that research most likely wouldn't have prevented this. I disagree with that thought mainly because there hasn't been ANY correlation with NM-DCM and diets that have extensive research and feeding trials. We both know formulating a diet on paper doesn't mean the diet is the same once manufactured and produced. Isn't that where research and feeding trials come into place ?

Regardless this is a tragic issue and I personally feel that the only way (beyond research and feeding trials of course!) to move forward and to find an answer is to rebuild the clients trust in their veterinarian. That broken trust is really poisonous in our industry and needs to be fixed. It doesn't matter what cause research uncovers if pet parents are unwilling to trust the research and science since the company they follow and feed to their pets continues to tell them that we are the enemy and can not be trusted !

Justin Shmalberg 4 hours ago · 0 Likes

Hi Emily,

Thanks for your thoughtful post. I agree that misinformation is harmful, but I do welcome a healthy debate with different viewpoints when evaluating diets or dietary strategies. I've been on record before saying that ingredients need to be evaluated independently - what's the source, what's the digestibility, what's the nutritional profile of that ingredient, how do the ingredients interact, what's the potential for contamination, etc.

Regarding research, I don't yet have any data to quantify the amount of research on a particular diet. Most companies don't publish research on individual diets, so do we mean nutritional testing? There are only so many laboratory tests that can be done on pet food and I don't know that the diets on the list had less testing or research than others - is there a source of this information of which I'm unaware? I also don't know that there aren't diets on the list which went through feeding trials - I haven't assessed this information and haven't seen in published. I am highly suspicious that a feeding trial would have identified any issues related to DCM - the number of animals in the trial would likely be too small and the outcome measures not cardiac-specific enough. If some brands had encountered this issue, and not released a food because it caused DCM, I am sure they would release that information to other companies to improve the industry. I'm not anti-research or anti-feeding trial by any means, but someone needs to provide actual information to support this claim. If we don't, it looks to some pet parents like an attempt to bolster some brands over others without evidence (which is what causes polarization in my mind).

I think your point on trust is absolutely critical. I believe that trust is best repaired by being honest, and I honestly can't yet tell owners what caused this nor can I say that research or feeding trials are protective. I believe if we don't know, it's ok to say we don't know. Most pet parents want answers now, which is absolutely

understandable, but I don't think we should reach for a sweeping conclusion before we're ready. Hopefully more information will be available soon!

Justin Shmalberg 3 days ago · 0 Likes

Hi Dr. Skibbe,

Thank you for taking the time to read my comments. I would of course emphasize that these comments are mine and mine alone, and that there is a diversity of opinion. There are also, as you mention, data which are formally available (FDA) and data which are not widely available (pending cases with the FDA or cases unreported by owners, the cases of individual cardiologists or cardiology groups, and information on a variety of public interest websites / social media sites). I also would say I have no relationship with the companies mentioned by the FDA, so I also do not have any internal access to their nutritional profiles or their formulation approaches.

With all unpublished data you reference, my hope is that it is either published or disseminated in a form in which the data are clear. For example, if cardiologists have encountered improvements that now seem to be entirely diet-dependent, it would be helpful to know what diets (not brands) were fed (and for instance, is there a specific diet recommended or did the owner decide based on a provided general criteria (WSAVA), for example?). I receive a number of messages from pet parents who weren't given dietary recommendations and want to know what to do. In my conversations with cardiologist colleagues, there have been a diversity of dietary recommendations made - some specific, some general. My main underlying point in all of this, is that the data are not easy to evaluate based on what the FDA has provided. And data from other sources are also not consolidated or readily accessible to everyone (the hope being that the FDA is able to do this, but it's a massive undertaking).

In terms of 'certain small companies,' I would not consider many of the companies with listed diets small (Champion, Diamond, Mars, Purina). Perhaps you mean brands? Nutro of course being owned by Mars, which owns Royal Canin; Merrick being owned by Purina; Blue being owned by General Mills. Is there something Royal Canin is doing that Nutro is not, Purina branded foods versus Merrick? I'm honestly not sure I have enough internal information to say? In terms of specific brands not listed, this is a fair point but I don't have enough information to say that it's because of the brand. Is it instead because foods in some brands perhaps contain less legumes or contain more taurine or even have lower ash meals? This would be an interesting analysis. We should be talking about individual diets rather than brands at this point, which was a huge part of what I intended to convey. If there ends up being an association, I am almost sure it will be to diets not to brands, which of course makes sense because brands often produce a range of very nutritionally different diets. As veterinarians I think we do ourselves a disservice when talking about brand X versus brand Y, especially before we have conclusive proof and especially without internal knowledge of what companies are actually doing. In the past, I believe we have lost credibility

by advocating brands versus advocating for nutritional strategies. I'm for instance not an advocate for a diet reliant on legumes for substantial amounts of protein, but this would be irrespective of who produced the diet. And my opinion is not yet based on data but rather a shorter period of time in which we've been able to evaluate higher legume diets.

I would caution everyone against being overly confident in feeding trials. In fact the WSAVA guidelines say the same: "While feeding trials help to test for the food's nutritional adequacy, the use of feeding trials does not guarantee that the food provides adequate nutrition under all conditions." Nor does the WSAVA explicitly recommend feeding trials, only that diets should carry an AAFCO statement for the appropriate life stage (either formulated to meet OR have feeding trials). The comment you reference "Change your dog's diet to a dog food brand that meets the World Small Animal Veterinary Association (WSAVA) criteria. These brands have not just been formulated to meet AAFCO nutritional standards, but have actually been tested in feeding trials..." does not seem to be reflective of what the WSAVA has said. In addition, I am not sure that every diet within those brands have been through feedings trials, so this is why talking about the specific diet (rather than brand) is so important.

The emphasis on feeding trials is an interesting one as pet parents might rightly ask; are feeding trials protective for any nutrition-related DCM which may exist? The minimum standard for an AAFCO feeding trial would in my mind never really be able to detect or prevent any diet-related DCM. They are an extremely low standard. If there was an issue with diets without a feeding trial, might it be that some companies "formulating to meet" test their foods after formulation for detailed nutrient profiles versus others who perhaps test for only a limited number of analytes after production? Here again, however, the information we have suggests that diets met current AAFCO standards (which I for one would love to see strengthened but that's a different issue). To my knowledge, nutrient testing and feeding trials on any food have not found DCM or an issue which could contribute to DCM before a food was released to market. I believe the feeding trial association is a weak one until substantiated. This is not to take away from feeding trials, but rather to say we have no evidence feeding trials have or would prevent what's reported and if saying so, it should be qualified to pet parents with actual data not impressions.

I would also add for readers' clarification that to my knowledge many of the listed foods meet WSAVA criteria at least as I read them. I have unfortunately seen some nutritionists and veterinarians say foods don't meet the WSAVA guidelines when in fact that do. Unless, the WSAVA committee is proposing a change to their recommendations of which I'm unaware?

The population from which dogs with DCM are screened is my main emphasis with my examples of brand X versus brand Y, especially after the issue was publicized. It is a fair point that some brands do not appear on the list, but again, I don't have personal knowledge of the background diets being fed to dogs that see cardiologists (and I know many cardiologists who historically did not take a diet history before this happened). In my nutrition practice, the diets on the list were far more commonly encountered than many you mention (but there is likely a bias to nutrition practice that is different from cardiology). Is it also possible that pending cases or unreported cases are of other brands - it's a fair

point about probabilities which you raise of brands that aren't on the list. But I still don't know what company X is doing differently from company Y or what nutrients are different to explain why I am selecting a diet or another. We still don't know what specifically we are avoiding until we have the cause. I agree that there are some trends which appear worth investigation - such as with kangaroo appearing more commonly in cases than I would guess (emphasis on guess) appear in a cardiology practice or in the general population. I believe here again, we will eventually need data like this to sort out what correlations exist. I don't fault my cardiologist colleagues or any other researchers on this topic as this is very difficult data to collect and collate, and as I said, I know everyone is doing their best.

My comment about less expensive brands was actually referring to extremely inexpensive brands found on grocery store shelves, which also do not appear on the list. I would not consider many of the brands you may be advocating to owners (Purina, Royal Canin, etc) to be less expensive and so I appreciate the opportunity to clarify. I will edit the post above to reflect that point.

Thank you for the valid criticism of the way data about non-DCM cases was presented in light of the FDA's progress so far. I have edited the post to reflect the number of non-DCM cases reported out of the total for which records were reviewed. I have no doubt that more reports exist which need to be investigated, and that this investigation strains the resources of the FDA. My hope is that government-research partnerships are able to help over time alleviate this burden to provide more facts. Certainly, there will be some reports which pet parents submit that do not have DCM, have typical DCM, or that have pre-DCM changes of variable magnitude. This will continue to be important to stratify the data and to make sure that the list of foods and other factors is as accurate as possible.

I have no doubt my opinions may be different than colleagues, and that I may not have the personal experience that others have (including my cardiologist colleagues). It remains difficult, however, for the general public and myself to evaluate data which are not available or not specific. I want to emphasize more than anything that the publically-available data does not yet support some of the generalizations being made, and that generalizations are problematic in nutrition. For this reason, my own comments on legumes should be taken as opinion about my approach to pet nutrition generally rather than owing to any clear cause and effect relationship with DCM. It's more challenging to focus on individual diets (rather than companies), nutrients rather than just ingredients, true incidence vs. impressions, but only when we get to that level of analysis do I believe we will find the answers we're looking for. I appreciate your dedication to this issue, and for sharing your information and perspectives.

Kim Skibbe 3 days ago · 1 Like

Dr Schmalberg, Thank you so much for taking the time to write on this concerning issue. Pet owners are worried, and hopefully appreciate a nutritionist's viewpoint on this issue.
As a veterinarian myself and someone who has been following this issue for over a year, I did want to

ask for clarification on a few of your points. I currently administer a facebook page with nearly 90,000 members, and another page with thousands of veterinarians. We are discussing your comments in the veterinary group and wanted to give you the opportunity to reply to our questions before we post your commentary in the larger public group, particularly since one of your comments seems to stand in contrast to the researchers and cardiologists closest to this issue. Because this is such a prominent issue right now, pet owners are taking every quote very seriously.

In regards to your comments on dogs improving with diet change: we are hearing from Dr Stern and other cardiologists that dogs are now coming off of heart medications and supplements. And of course there is the simple fact of the evidence of dietary correlation: one cannot overstate the disproportionate nature of the case reports to certain small companies. As stated in an update from cardiologist Michelle Rose "Change your dog's diet to a dog food brand that meets the World Small Animal Veterinary Association (WSAVA) criteria. These brands have not just been formulated to meet AAFCO nutritional standards, but have actually been tested in feeding trials, and Dr. Robert George and I, AERC's cardiologists, have not seen a single case of nutritional dilated cardiomyopathy from any of these brands. Examples include Hill's Science Diet, Purina Pro Plan, Royal Canin, Iams, and Eukanuba." As a consultant in the pet food industry, I'm sure you are aware that these are the largest companies. While it would therefore not be surprising to see a tiny number of coincidental cases on dogs eating popular brands, there would have to be literally thousands of them to statistically compare to the cases reported on some of these smaller brands.

This is why I particularly question "The absence of generally less expensive kibble diets may be a bias because of the fact that pet parents feeding those diets may be less likely to see a veterinary cardiologist for screening of heart disease." If we are simply stating that the reports are not a perfect representation, then I agree. It's quite possible (for example) that Rachel Ray Nutrish might be causing a higher % of DCM than is indicated by the 10 case reports. But if we are looking at dog food companies overall, the massive size of companies like Purina, Iams, and Royal Canin would make it impossible to overlook nutritional correlations on these foods I practice in a high-income area, I take diet history on all my patients, and had never heard of Zignature or many of these other small brands before I started following the DCM issue. Over 90% of my patients eat a diet that follows WSAVA guidelines. Also, you can look at the OFA website for a partial list of echocardiogram screening clinics that occur in conjunction with dog shows; this is another time where dogs eating popular diets are getting echocardiograms.

Finally, I was surprised to see your sentence "Not all of the cases above have been confirmed to have DCM - the FDA reported that 202 dogs (35% of total reports) and 6 cats (42.8%) had both medical records available and met the DCM definition." I went back to the report to see what I had missed. The FDA phrasing is different by one significant word: they did not say the records were not available on the other dogs but rather that "whose medical records were reviewed with heart changes characteristic of DCM on cardiac ultrasound – including decreased ventricular systolic function and dilation " This would seem at first a meaningless distinction, but it just so happens that we have a support group with

approximately 500 affected owners and most tell me the FDA has not yet interviewed them or requested full records The FDA is clearly unable to deal with all of the case reports on this issue. Adding to the fact that (as you already stated) many have not yet reported to the FDA at all. I fear this is a much larger problem than indicated by the 500 reported cases.

Thank you
Dr Kim Skibbe

Nutrition and Cardiomyopathy: Lessons from Spontaneous Animal Models

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Spontaneously occurring dilated cardiomyopathy in dogs and hypertrophic cardiomyopathy in cats are common diseases and are vastly underutilized as models of human cardiac disease. The goals of nutrition are no longer limited to a low-sodium diet, as research is now showing that nutrients can modulate disease and be an important adjunct to medical therapy. Deficiencies of certain nutrients can contribute to cardiomyopathies, as with taurine, but some nutrients—such as n-3 fatty acids, carnitine, and antioxidants—may have specific pharmacologic benefits. Dogs and cats with spontaneous cardiomyopathies are an exciting and promising model for studying nutritional modulation of cardiac disease.

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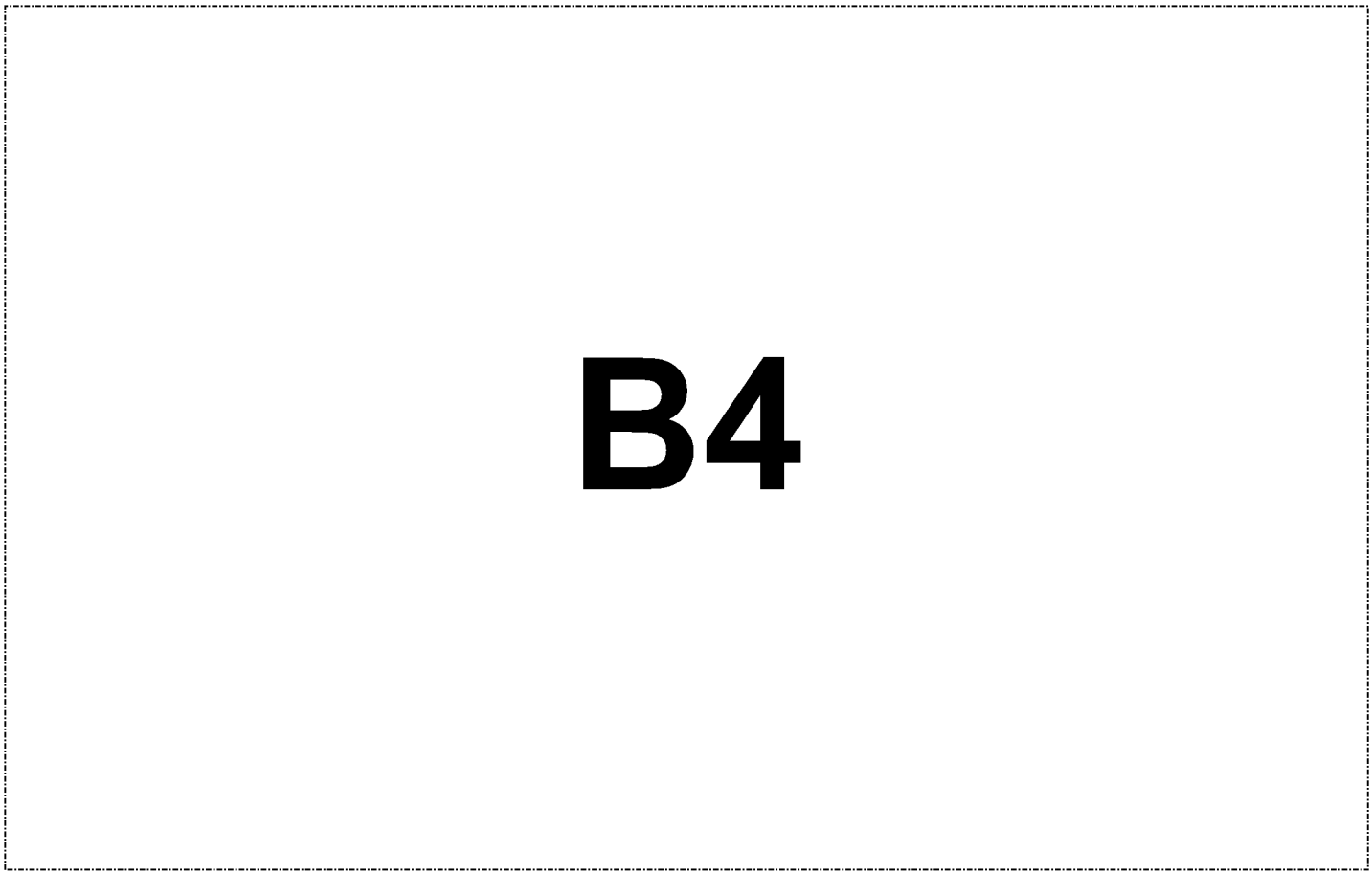

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Review Article

Genetics of Human and Canine Dilated Cardiomyopathy

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Cardiovascular disease is a leading cause of death in both humans and dogs. Dilated cardiomyopathy (DCM) accounts for a large number of these cases, reported to be the third most common form of cardiac disease in humans and the second most common in dogs. In human studies of DCM there are more than 50 genetic loci associated with the disease. Despite canine DCM having similar disease progression to human DCM studies into the genetic basis of canine DCM lag far behind those of human DCM. In this review the aetiology, epidemiology, and clinical characteristics of canine DCM are examined, along with highlighting possible different subtypes of canine DCM and their potential relevance to human DCM. Finally the current position of genetic research into canine and human DCM, including the genetic loci, is identified and the reasons many studies may have failed to find a genetic association with canine DCM are reviewed.

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The Journal of Nutrition
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

Differences in Taurine Synthesis Rate among Dogs Relate to Differences in Their Maintenance Energy Requirement[1–3]

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Abstract

Diet-induced (taurine deficiency) dilated cardiomyopathy is reported more in large than small dogs possibly because taurine biosynthesis rate (TBR) is lower in large than small dogs. The TBR in 6 mongrels (37.9 ± 2.1 kg) and 6 beagles (12.8 ± 0.4 kg) was determined from the fractional dilution rate of urinary [1,2-$^2H_2$]-taurine, (d4-tau). All dogs were given a 15.6% protein, 0.60% sulfur amino acid (SAA) diet in amounts to maintain an ideal body condition score. After 3 mo, 14.6 mg/kg body weight of d4-tau was given orally and TBR determined from d4-tau to taurine ratio in urine collected each d for 6 d. Enrichments of d4-tau were determined by GC-MS. Thereafter, mongrels and beagles were paired by ranking of SAA intake per metabolic body weight per kg$^{0.75}$. Each pair received the same amount of diet/kg$^{0.75}$ for 2 wk, then TBR was again determined. Concentrations of taurine in plasma, blood, and urine and concentrations of plasma thiols were measured during each TBR determination. In Expt. 1, TBR and taurine concentrations in plasma and urine of mongrels were lower ($P < 0.05$) than those of beagles. In Expt. 2, TBR and taurine concentrations in blood and plasma of mongrels were lower ($P < 0.05$) than beagles. Together, the results support the hypothesis that large compared with small dogs have lower TBR when fed diets near-limiting in dietary SAA, but adequate to maintain ideal body condition. J. Nutr. 137: 1171–1175, 2007.

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Plasma Taurine Concentrations in Normal Dogs and in Dogs With Heart Disease

George A. Kramer, Mark D. Kittleson, Philip R. Fox, Julia Lewis, and Paul D. Pion

Plasma taurine concentrations were determined in 76 dogs with dilated cardiomyopathy (DCM), 28 dogs with acquired valvular disease (AVD), and 47 normal (control) dogs. The data were collected at 2 referral centers, The Animal Medical Center, New York, NY (AMC), and the University of California, Davis (UCD), and the studies were conducted independently. Different anticoagulants (sodium citrate at AMC and lithium heparin at UCD) were used to collect the plasma samples. Paired analysis of samples showed a significant difference in plasma taurine concentrations, depending on the anticoagulant used. Consequently, results from each clinic were analyzed separately. Plasma taurine concentrations were significantly higher in dogs with AVD (median, 133 nmol/mL; range, 25 to 229 nmol/mL) than in control dogs (median, 63 nmol/mL; range 44 to 224 nmol/mL) and dogs with DCM (median, 72 nmol/mL; range, 1 to 247 nmol/mL) at AMC ($P < .001$). The number of dogs with AVD at UCD was too small to draw meaningful conclusions. At UCD, the median plasma taurine concentration was 98 nmol/mL (range, 28–169 nmol/mL) in dogs with AVD, 75 nmol/mL (range, 0.1–184 nmol/mL) in dogs with DCM, and 88 nmol/mL (range 52–180 nmol/mL) in control dogs. There were no significant differences in plasma taurine concentrations between dogs with DCM and the control dogs at either hospital. Congestive heart failure and administration of cardiac medication had no significant effect on plasma taurine concentrations. Plasma taurine concentration was low (<25 nmol/mL) in 17% (13/76) of the dogs with DCM. Seven of the 13 dogs with low plasma taurine concentrations were Cocker Spaniels or Golden Retrievers. It was concluded that most dogs with DCM do not have low plasma taurine concentrations. However, certain breeds or individual dogs may have low plasma taurine concentrations in association with DCM. Whether this association is causal or not is unknown. The significance of the high plasma taurine concentrations in dogs with AVD is also unknown.

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Special topic: The association between pulse ingredients and canine dilated cardiomyopathy: addressing the knowledge gaps before establishing causation[1]

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ABSTRACT: In July 2018, the Food and Drug Administration warned about a possible relationship between dilated cardiomyopathy (**DCM**) in dogs and the consumption of dog food formulated with potatoes and pulse ingredients. This issue may impede utilization of pulse ingredients in dog food or consideration of alternative proteins. Pulse ingredients have been used in the pet food industry for over 2 decades and represent a valuable source of protein to compliment animal-based ingredients. Moreover, individual ingredients used in commercial foods do not represent the final nutrient concentration of the complete diet. Thus, nutritionists formulating dog food must balance complementary ingredients to fulfill the animal's nutrient needs in the final diet. There are multiple factors that should be considered, including differences in nutrient digestibility and overall bioavailability, the fermentability and quantity of fiber, and interactions among food constituents that can increase the risk of DCM development. Taurine is a dispensable amino acid that has been linked to DCM in dogs. As such, adequate supply of taurine and/or precursors for taurine synthesis plays an important role in preventing DCM. However, requirements of amino acids in dogs are not well investigated and are presented in total dietary content basis which does not account for bioavailability or digestibility. Similarly, any nutrient (e.g., soluble and fermentable fiber) or physiological condition (e.g., size of the dog, sex, and age) that increases the requirement for taurine will also augment the possibility for DCM development. Dog food formulators should have a deep knowledge of processing methodologies and nutrient interactions beyond meeting the Association of American Feed Control Officials nutrient profiles and should not carelessly follow unsubstantiated market trends. Vegetable ingredients, including pulses, are nutritious and can be used in combination with complementary ingredients to meet the nutritional needs of the dog.

Key words: dilated cardiomyopathy, dogs, feed formulation, grain-free, nutrition, pulse ingredients

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[2]Sprake et al. 2005.

[3]Arslan, 2006.

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PAPER

Canine dilated cardiomyopathy: a retrospective study of signalment, presentation and clinical findings in 369 cases

OBJECTIVE: To review the clinical and diagnostic findings and survival of dilated cardiomyopathy from a large population of dogs in England.

METHODS: A retrospective study of the case records of dogs with dilated cardiomyopathy collected between January 1993 and May 2006.

RESULTS: There were 369 dogs with dilated cardiomyopathy of which all were pure-bred dogs except for four. The most commonly affected breeds were dobermanns and boxers. Over 95 per cent of dogs weighed more than 15 kg and 73 per cent were male. The median duration of signs before referral was three weeks with 65 per cent presenting in stage 3 heart failure. The most common signs were breathlessness (67 per cent) and coughing (64 per cent). The majority of dogs (89 per cent) had an arrhythmia at presentation and 74 per cent of dogs had radiographic signs of pulmonary oedema or pleural effusion. The median survival time was 19 weeks.

CLINICAL SIGNIFICANCE: Dilated cardiomyopathy occurs primarily in medium to large breed pure-bred dogs, and males are more frequently affected than females. The duration of clinical signs before referral is often short and the survival times are poor. Greater awareness of affected breeds, clinical signs and diagnostic findings may help in early recognition of this disease which often has a short clinical phase.

M. W. S. MARTIN, M. J. STAFFORD JOHNSON AND B. CELONA*

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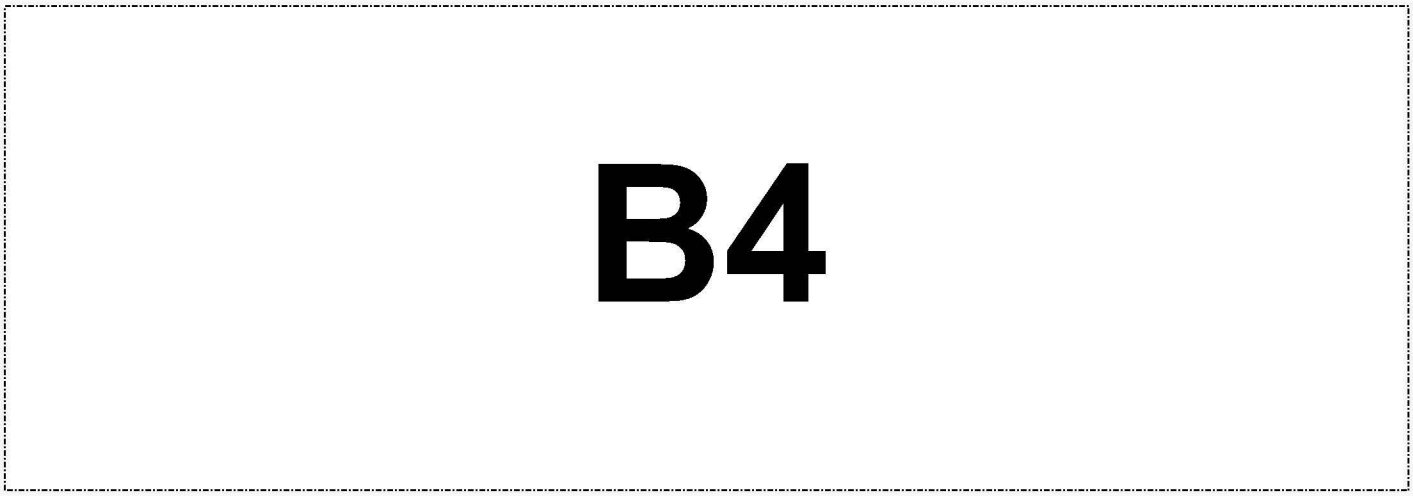

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Iron Overload Cardiomyopathy, Better Understanding of An Increasing Disorder

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Abstract

The prevalence of Iron Overload Cardiomyopathy (IOC) is increasing. The spectrum of symptoms of IOC is varied. Early in the disease process, patients may be asymptomatic while severely overloaded patients can have terminal heart failure complaints that are refractory to treatment. It has been shown that early recognition and intervention may alter outcomes. Biochemical markers and tissue biopsy, that have traditionally been used to diagnose and guide therapy, are not sensitive enough to detect early cardiac iron deposition. Newer diagnostic modalities such as MRI are noninvasive and can assess quantitative cardiac iron load. Phlebotomy and chelating drugs are suboptimal means of treating IOC; hence the roles of gene therapy, hepcidin, and CCBs are being actively investigated. There is a need for the development of clinical guidelines in order to improve the management of this emerging complex disease.

Keywords

Iron overload cardiomyopathy; hemochromatosis; hemosiderosis; T2* MRI; chelation; calcium channel blockers

Introduction

Iron is an essential element that forms an important component of metabolic and biological processes, but when present in excess, it can produce tissue damage due to oxidative stress (1). Excess body iron may accumulate in liver, spleen, heart, bone marrow, pituitary, pancreas and the central nervous system causing damage to these organs. IOC results from the accumulation of iron in the myocardium, and it is the leading cause of death in patients receiving chronic blood transfusion therapy (2). The incidence of IOC is increasing worldwide, and it is usually managed by cardiologists. Noteworthy has been its increase in individuals with hematologic malignancies, especially with the increased use of treatments

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such as bone marrow transplant and stem cell therapy (3). Furthermore, as patients with sickle cell disease and thalassemia live longer, IOC incidence rises. It has been documented that adequate medical therapy can reverse IOC when it is diagnosed before end stage heart failure occurs (4), thus underscoring the importance of early detection of IOC. Thus, it is critical for cardiology care providers to keep updated their knowledge on managing IOC to take advantage of recent progress in this area. In this article, the current status of diagnosis of IOC, particularly using imaging modalities and updated therapeutic approach for IOC, have been reviewed.

Etiology

IOC has been defined as the presence of systolic or diastolic cardiac dysfunction secondary to increased deposition of iron in the heart independent of other concomitant processes (1). Excess iron accumulation in the body usually takes place either by increased gastrointestinal (GI) iron absorption (hemochromatosis) or excess administration of exogenous iron by dietary sources or red blood cell (RBC) transfusions (hemosiderosis). These conditions are described in Table 1.

Increased iron absorption

Hereditary hemochromatosis (HH) is an autosomal disorder in which mutations of specific genes involved in iron metabolism cause iron overload in the body with increased GI absorption (5,6). It has been divided into 4 subtypes as described in Table 1. The association of IOC with HH has been well characterized (7,8). Increased GI absorption with a normal diet is also observed in porphyria cutanea tarda (9), chronic liver disease including nonalcoholic fatty liver disease (10), hepatitis B (11) or C (12), and in ineffective erythropoiesis as seen in sideroblastic anemia (13) and severe thalassemia (14).

Excess administration of exogenous iron

Sub Saharan Africans have a high dietary iron intake as a result of drinking traditional beers fermented in steel drums (African iron overload) (15). This mechanism of iron overload was initially thought to be the etiology of hepatic carcinoma and cardiomyopathy in these patients, but other reports suggest that environmental factors superimposed on genetic predisposition may be a better explanation for the development of these conditions (16,17).

Parenteral iron administration

Chronic blood transfusion is the cornerstone of treatment for hereditary anemias like thalassemia and sickle cell disease. A unit of packed RBC consists of 200 to 250 mg of elemental iron that accumulates in the body as there is no active excretion of iron. Over long periods of repeated transfusions, iron overload occurs with deposition of iron in multiple organs. Earlier detection of these hereditary anemias is associated with a decreased mortality due to improved treatment, but often with persistent chronic transfusion requirements, is one of the reasons for an increasing incidence of iron overload (18-20).

Pathogenesis

Iron kinetics is illustrated in Figure 1. Deposition of iron in the heart is a gradual process and depends on the increasing levels of serum iron. Under normal iron homeostasis, cardiac iron is regulated through transferrin mediated uptake mechanisms. During iron overload, transferrin is saturated, and non transferrin bound iron is released into the circulation and enters cardiac myocytes in the ferrous form through L-type calcium channels(LTCC) as has been described (21). Endosome-mediated uptake might also play a role, but is poorly understood (22). Iron is then bound to ferritin and transported to lysosomes for degradation

and long-term storage in the cardiac myocyte (22). Pathologic iron deposition begins initially within the epicardium and extends to the myocardium and then endocardium, which helps explain the preservation of systolic function until very late in the disease (1). Once the antioxidant capacity of the cell is exceeded, iron is catalyzed by the rapid Fenton reaction producing hydroxyl ions, which is an extremely reactive free radical species that causes lipid peroxidation producing membrane permeability alterations. These modifications create a leak of hydrolytic enzymes which initiate cell damage and subsequent cardiac myocyte death. In cases with concomitant myocardial ischemia, iron overload can accelerate ischemia-induced reperfusion injury, and may lead to an autocatalytic process which results in a cardiomyopathic process (1,23). Initial evidence suggests that deposition of iron in the sarcoplasm of epicardial myocytes in this disease is a problem of storage and is not an infiltrative process. Thus there is the potential for the iron to be removed and for the process to be reversed, which has been the subject of much investigation and influenced the direction therapeutic interventions have followed (24).

Clinical presentation

Because of the wide spectrum of etiologies for IOC, symptoms may be quite varied. Early in the disease process, patients may be totally asymptomatic, while severely overloaded patients can have terminal irreversible heart failure symptoms. Thus, early identification of the disease becomes a very important consideration. Multiple physiologic, biomolecular, and structural factors such as tachycardia, volume overload, eccentric left ventricular hypertrophy, endocrinopathies, genetic predisposition, neurohormonal activation, and proinflamatory cytokines can play a role in affecting cardiac function (4,25,26). Patients' initial presentation is often exertional shortness of breath as a result of left ventricular diastolic dysfunction secondary to a restrictive pathophysiology. This condition may later progress to a dilated cardiomyopathy with left ventricular systolic dysfunction (23,27,28). Iron accumulation occurs in the ventricular myocardium before the atrial myocardium (22). Deposition in the conduction system has also been noted (29) and can lead to nodal disease causing bradyarrythmias and necessitating pacemaker placement. First degree AV blocks and supraventricular arrhythmias correlate with the extent of iron deposition in the atrial myocardium (30). Iron probably is proarrythmic by itself (31), and this fact along with the varied deposition of iron in the tissue leading to nonhomogeneity in conduction velocity or repolarization may explain the increased incidence of atrial and ventricular tachyarrhythmias that have been noted in subjects with iron overload (32). Paroxysmal atrial fibrillation is the most common form of arrhythmia seen in IOC and is invariably associated with myocardial damage (4). Left ventricular dilatation with systolic dysfunction predisposes to more frequent ventricular arrhythmias. Moderate to severe left ventricular dysfunction usually occurs with heavy iron deposition. Right heart failure can also be present early in the course of disease and be independent of, or evolve and progress along with left heart failure. With severe cardiac impairment, average survival is usually less than one year (23,30,33). Iron deposition can also occur in the pericardium and, if extensive enough, result in clinical signs and symptoms.

Diagnosis

A high degree of clinical suspicion is necessary to identify and categorize primary hemochromatosis and secondary iron overload. Diagnosis can be very challenging in the early stages of disease; also an accurate assessment of organ specific iron overload is helpful in planning treatment.

Biochemical markers

To identify patients with iron overload, plasma transferrin saturation of greater than 55% and serum ferritin of greater than 200 ng/ml or 300 ng/ml (for women and men respectively) have been proposed as per the 2005 ACP guidelines (34,35). However, transferrin saturation can miss a substantial population of patients who are homozygous for HFE mutations (36). It can also be elevated along with ferritin levels in Asian and Pacific Islanders without the HFE mutations, and thus have uncertain significance in these populations (37). Ferritin, being an acute phase reactant (38), can be elevated in active inflammatory conditions and also in certain liver diseases (39,40). Serum iron studies are a useful tool in screening patients for total body iron overload, but they are unsatisfactory as a diagnostic tool to detect specific organ overload such as cardiac iron. The level of serum ferritin at which iron deposition is detected in the heart has not been defined. There are reports of heavy cardiac iron deposition despite the presence of low serum ferritin levels (41,42). Serum iron studies give little information on deposition of iron and less on actual tissue location. In addition, serum ferritin levels, in particular, have a wide variability when measured serially, thus making it difficult to use as a marker to determine response to therapeutic interventions.

Tissue biopsy

Tissue biopsy is the traditional gold standard for making the diagnosis of liver iron overload (43), but iron deposition in the heart tends to be patchy (30). Biopsies may thus miss the areas of deposition and provide a false negative result. In myocardial biopsy specimens, the degree and cellular distribution of iron stores known as hemosiderin is best assessed using a Pearls, Prussian stain and a semi-quantitative assessment of iron stores is derived based on the number of myocytes containing stainable iron (24,44) In normal hearts, no stainable iron should be seen and the deposition of iron appears to occur in the sarcoplasm starting in the perinuclear areas and disseminating to the entire sarcoplasm as iron overload progresses (24,30,33,45). The iron concentration can be measured with atomic absorption spectrometry and Olson et al. have reported the average elemental iron in biopsy specimens are 399 μg/g dry weight in normal subjects and 1701 μg/g dry weight in idiopathic hemochromatosis with significant overlap between these two groups (45). A positive result indicates that iron overload is present, but not how extensive the process may be (24,33). Also, biopsy is an invasive procedure and, as a result, is not an ideal tool to screen asymptomatic patients.

Echocardiography

As iron overload proceeds, echocardiography may reveal biventricular dilatation and progressive evidence of a restrictive cardiomyopathy from myocardial damage (46). Echocardiographic evidence of ventricular diastolic dysfunction can be detected early before systolic dysfunction occurs, specifically using tissue Doppler signals (47,48). Lambardo et al. failed to identify diastolic dysfunction using conventional Doppler echocardiographic parameters such as mitral inflow E/A ratio and deceleration time to predict the severity of myocardial iron overload verified by myocardial biopsy in thalassemia patients with preserved left ventricular systolic function (49). Later, however, Vogel et al. reported that a decrease in peak systolic and peak diastolic early filling tissue Doppler wave is frequently seen in the patients with β-thalassemia and cardiac MRI-proven myocardial iron overload (50), and that these declines are more prominent in the left ventricular septum than lateral free wall. Tissue Doppler-derived peak systolic strain has similarly shown to decrease in that population (51). Palka et al. has reported a decrease in peak systolic and diastolic early filling mitral annular tissue velocity as well as prolongation of the duration of atrial reversal wave of pulmonary vein Doppler in HH patients with predominantly normal left ventricular systolic function (47). In our previous investigation in asymptomatic HH subjects, echocardiography has detected enhanced left atrial active contraction even before overt left ventricular diastolic dysfunction appeared, and this may be the earliest detectable

echocardiographic finding of cardiac iron overload in this population (52). Interestingly, diastolic strain rates, measured with color coded tissue Doppler in subjects with iron overload, appears to be related to the level of oxidative stress (53), indicating that these echocardiographic parameters may be a surrogate for iron overload induced oxidative stress (54).

It could be hypothesized that cardiac contractile reserve is impaired in IOC before detectable left ventricular systolic dysfunction occurs at rest, and this abnormality might be detected by stress echocardiography. We have tested this hypothesis in asymptomatic HH subjects, and found that contractile reserve is not decreased in this population as compared with age-gender matched normal volunteers who lacked HH mutations (55). However, unexpectedly, a higher incidence of ischemic stress electrocardiographic responses in HH subjects (33%) compared to normal subjects (10%) was observed. The significance of this finding is unclear, but highlights the necessity of stress echocardiography or other stress imaging when evaluating coronary artery disease in this population (55).

As a result of these considerations, echocardiography has the potential to identify early pathophysiology due to iron overload, although it is not sensitive enough to reveal actual iron deposition in tissues. In addition, echocardiography has been successfully employed to evaluate iron-depleting therapy in idiopathic hemachromatosis as it demonstrated a decrease in the left ventricular mass and wall thickness and these findings correlated with the reversal of myocardial iron infiltration (56).

Computer tomography (CT)

CT scanning can identify high electron density iron in the organs (57,58), but its sensitivity and specificity are poor with high false positive rates associated with fibrosis (59), and it has a low sensitivity for detecting the early stages of iron overload in tissues (60). The clinical usefulness of this diagnostic method for IOC has not been tested.

Magnetic resonance Imaging (MRI)

MRI is the only presently available noninvasive method with the potential to assess quantitatively myocardial iron load. MRI constructs images from transmitted microwave signals induced by exciting protons in the body in a high magnetic field. In non-iron overloaded hearts, these signals are homogenous and relaxation time (time to fade excited signals) lasts for a longer duration (brighter over time). In iron overloaded hearts, however, the iron paramagnetic effect produces changes in MR signal intensity, susceptibility and shortens the relaxation time and darkens the image more quickly (61). MRI scanning can refocus the signals returning from the tissues using a special radiofrequency pulse (spin echo; SE) or by using special small magnet fields called gradients (gradient echo; GE) at specific time intervals (echo time; TE). The time constant of decay for SE induced relaxation time is known as T2 and for GE is T2* and the units are milliseconds (ms). Iron in the tissue shortens the relaxation time (signals fade faster with more iron content), thus, the more the iron content, the shorter are the T2, T2*. Some investigators report rates of signal decay (R2= 1000/ T2 & R2* = 1000/T2*) which are a reciprocal of T2 and T2* and are measured in Hertz or S^{-1}. Earlier studies for quantitative evaluation of the iron content were performed using the SE measurement, and it was noted to have an inverse relation with liver iron concentration (62-64). SE has poor signal to noise ratio at longer echo times, and, with its limited sensitivity, has made the accurate quantification of myocardial iron unsatisfactory (62,63,65,66). On the other hand, GE techniques, which do not have these problems, seem to be more suitable for assessing myocardial iron content. Anderson et al. were the first to use the T2* technique for myocardial iron assessment in subjects with thalassemia major (67). In this study, a single short axis mid ventricular slice was acquired

at nine separate TEs, and each slice was acquired during one breath hold of approximately 20 seconds (Figure 2). It was observed that there was a progressive decline in ejection fraction as the myocardial iron deposition increased, and all patients with ventricular dysfunction had a myocardial T2* of <20 ms (67). The coefficient of variation for inter-study reproducibility of cardiac T2* was 5%. The scanning time of T2* was recently shortened by the use of a multi-GE technique which has the advantage that all slices are acquired in just one breath hold (68). Pepe et al. used a multislice multi-GE T2* technique to achieve segmental analysis of left ventricular myocardial iron content and observed a good correlation between the global T2* (12 segments) and T2* value in the mid ventricular septum (69). They concluded that mid ventricular T2* value was a good marker of entire myocardial iron content. However, they were concerned that mid ventricular T2* would not be sensitive enough to reflect the heterogeneity of composition of myocardial iron overload (cytosolic iron, hemosiderin deposits etc.) (66,70-72) In contrast, the T1-T2 weighted SE method has been proposed as being more sensitive in differentiating cytosolic iron and ferritin (73). Recent optimized breath-hold T2 imaging has shown improved local inter-study reproducibility and inter-site reproducibility with a coefficient of variance of 4.4% and 5.2% respectively as compared with the traditional T2* imaging (74). One potential advantage of newer T2 imaging will be to perform a multisegment analysis to explore regional distribution of myocardial iron. The accuracy of T2* imaging is currently limited to the septum due to susceptibility effect artifacts from anterior and posterior cardiac veins and lungs which contaminate the other left ventricular regional walls. In addition, measuring both T2 and T2* might be beneficial, if different forms of tissue iron might be respectively defined by T2 and T2* measurements (74).

Furthermore, cardiac MRI can provide accurate reproducible measures of left ventricular systolic ejection fraction, volumes, and mass which can be followed over the course of therapy (75). A correlation between the decline in left ventricular ejection fraction and higher myocardial iron content measured with T2* has been noted (76-78). Attempts to assess left ventricular diastolic function in IOC with cardiac MRI using tagging (79) or DENSE sequence (80) is currently under investigation.

In summary, GE T2* technique is still widely used for clinical assessment of entire iron content in IOC; however, the new technical development of cardiac MRI will likely provide methods for more detailed quantification and characterization of deposited iron species in IOC.

Proposed clinical pathway to evaluate for IOC

As a result of our experience with patients with cardiomyopathy, we currently propose the following clinical pathway to evaluate for IOC. This pathway is currently being used by the NIH Clinical Center Cardiology Consult Service (Figure 3).

If the patient is known to be at risk for iron overload due to a previous genetic diagnosis of HH or multiple red blood cell transfusions, transthoracic echocardiography with complete LV diastolic function assessment including tissue velocity measurements of the mitral annulus should be conducted every 1- 2 years. This evaluation should occur regardless of cardiac symptoms or biochemical evidence of iron overload. If either abnormal LV diastolic function and/or decreased peak systolic tissue velocity of mitral annulus are noted, cardiac MRI with T2* assessment following the grading system based on the T2* measurements and listed below should be performed. In cases where idiopathic cardiomyopathy is the primary diagnosis, regardless of iron study results, we recommend cardiac MRI with T2* measurements to rule out IOC since it has been reported to occur with normal iron levels (41,42) and is a treatable condition. Once cardiac T2* is confirmed to be normal (>20 ms), it

is unlikely that IOC will become a cause of idiopathic cardiomyopathy unless the patient is at risk for IOC and develops it in the future.

Conventional therapy

Iron overload is a slow cumulative process; early diagnosis and treatment should be the main goal of therapy to prevent multiorgan failure. Standard treatment currently includes dietary management, phlebotomy, and chelating agents. At present, research using CCBs in IOC, gene therapy to target the genetic mutations in thalassemia and sickle cell disease, and heart transplantation in refractory heart failure are under intense scrutiny.

In order to assist with clinically grading the severity of IOC at this time, people at risk for IOC may be divided into 3 categories based on cardiac T2* values (61).

1) Those with T2* > 20ms (green zone) are at low risk for the imminent development of congestive heart failure.

2) Those with T2* between 10 -20 ms (yellow zone) in whom cardiac deposition has probably occurred, are at intermediate risk of cardiac decompensation.

3) Those with T2* < 10 ms (red zone) are in the high risk category of cardiac decompensation and need immediate review and intensification of chelation therapy.

Although the diagnostic use of cardiac MRI for IOC has been established, the validity of T2* obtained from cardiac MRI as a therapeutic marker is still under investigation. Thus, proper guidelines to follow for evaluating the therapeutic effects of IOC treatment with cardiac MRI measurements still need to be developed.

There is some evidence that with the use of effective chelation therapy, the development of clinically significant cardiac iron overload in patients in the green and yellow zones may be delayed (56,81,82). It is apparent that patients in the red zone with heart failure symptoms need to be treated with aggressive chelation therapy in conjunction with standard heart failure medications including angiotensin converting enzyme inhibitors, diuretics and β-blockers. It remains to be seen whether the addition of chelation therapy will either stop the progression of, or improve LV dysfunction beyond what might be accomplished by aggressive standard heart failure treatment.

Dietary Management

Dietary interventions to minimize or eliminate iron ingestion are not feasible and usually unnecessary as only 0.5 to 1.0 mg of iron is absorbed daily in excess of normal absorption in most persons with hemochromatosis and the total daily absorption is small in comparison with the 200 to 250 mg of iron per unit of blood removed weekly by therapeutic phlebotomy. Diets do not enhance iron excretion, and patients must understand that there is no substitute for iron depletion therapy (83). Patients can eliminate the consumption of iron rich foods such as red meat and still have little effect on total body iron content. Alcohol increases iron absorption and should be minimized (84). Multivitamin tablets containing iron and vitamin C should be avoided (85). Tannates, phytates, oxalates, calcium and phosphates present in food can bind iron and inhibit its absorption, which provides a little benefit (86).

Phlebotomy

Phlebotomy, the gold standard for treating HH, causes iatrogenic anemia by removing 400 – 500 cc of blood (200 to 250 mg of iron) at each session thus mobilizing iron from the organs where it is stored for the production of hemoglobin. Early in the disease, this procedure may be done up to one or two times a week to obtain a target ferritin below 20 ng/ml (87) (88).

Once the therapeutic ferritin level is achieved, the frequency of maintenance phlebotomy is determined with periodical follow up of serum iron and ferritin level with gradual decreasing phlebotomy interval. Generally maintenance phlebotomy requires three to four times phlebotomy a year for men and one to two times for women (89). Routine monitoring of hemoglobin, ferritin, and hematocrit is essential during maintenance phlebotomy (90). Improvements in cardiac function in HH patients with cardiomyopathy and refractory arrhythmias have been noted with aggressive iron removal with phlebotomy, especially when started early in the disease process (91-93).

Chelating Agents

Phlebotomy is not feasible in patients who have significant anemia, malignancy, and some with hemodynamic instability. In such cases, chelation therapy has been effectively used as an alternative. The goal of chelation therapy is to detoxify those organs containing excess iron by binding the iron, removing it, and then excreting the compound in urine and bile. Presently available chelators include deferoxamine, deferasirox and deferiprone.

Deferoxamine is a clinically approved, highly specific hexadentate iron chelating molecule which binds to iron released from the reticuloendothelial system which has scavengered iron after the catabolism of senescent RBC, and excretes it in the urine. It also has a very high affinity to bind with the trivalent ferric ion and is thought to remove cardiac iron by direct interaction with this ion. The benefits of long-term subcutaneous deferoxamine therapy of increasing survival and decreasing cardiac complications in transfusion dependent iron overloaded thalassemia patients is well documented in the medical literature (2,82,94,95). High intravenous doses, instead of traditional subcutaneous infusion, are also used for the rapid removal of cardiac iron from heavily iron loaded patients with cardiac failure (81). Prospective studies confirming the beneficial effect of i.v. deferoxamine in the reduction of myocardial iron content in IOC were reported in patients treated with i.v. deferoxamine for 12 months with MRI derived T2* (96). Reduction in iron levels was associated with an increase in T2* MRI values (5.1 ± 1.9 ms to 8.1 ± 2.8 ms, placebo vs. deferoxamine, $P = 0.003$), significant improvements in left ventricular (LV) ejection fraction (52 ± 7.1% to 63 ± 6.3%, $P = 0.03$), and reductions in LV volume and LV mass index. Unfortunately, deferoxamine has a high maintenance cost, poor oral bioavailability, and the need for frequent administration. These considerations often contribute to poor compliance in patients (97).

Deferiprone is a bidentate chelating agent with good oral bioavailability, rapid absorption from the stomach, and reaches peak levels in 2 hours post administration after being metabolized in the liver. It is being tested on β-thalassemia and sickle cell patients with transfusion iron overload, and its long term efficacy and safety has not been fully established (90). In the USA, it is available only through the FDA treatment use program. Clinical efficacy of deferiprone is less consistent than deferoxamine (98,99). In a randomized double blind placebo controlled trial in 65 patients over 12 months, subcutaneous deferoxamine combined with oral deferiprone therapy reduced myocardial iron and improved the ejection fraction and endothelial function in thalassemia major patients with mild to moderate cardiac iron load when compared to deferoxamine therapy alone (100).

Deferasirox is a tridentate lipophilic oral chelating agent which selectively binds to iron in the ratio of 2:1 and mobilizes iron from stores. The early benefit of using deferasirox has been demonstrated in thalassemia, sickle cell disease, myoproliferative disorders, and Diamond- Blackfan anemia. Results from small-scale randomized phase III trials evaluating the effect on iron overload have been encouraging (101,102). Despite these hopeful results, long-term safety and efficacy beyond 1 year is lacking at this time. Thus, there is insufficient data at present to support the use of deferasirox to treat IOC.

Newer chelating drugs

Deferitrin, desferrithiocin, hydroxybenzylethylenediaminediacetic acid, pyridoxal isonicotinoyl hydrazone, 2-pyridylcarboxaldehyde thiophenecarboxyl hydrazone, and L1NA –II (a deferiprone derivative) are among the newer chelating agents that are under active investigation. A drug with satisfactory oral bioavailability and good long-term efficacy and safety would be extremely useful, and a quest for such an agent is ongoing.

Erythrocytapheresis

Erythrocytapheresis involves an automated exchange of RBCs of patients with hemachromatosis with those of subjects without and thus helps in decreasing the iron overload mainly in the form of hemoglobin (103,104). This procedure is mainly used in treatment and prophylaxis of sickle cell patients by removing the sickle cells and also old RBCs (104). This is a complex and costly procedure with a high risk of infection and further research is needed to prove its efficacy for IOC (105).

Heart Transplant

If a patient has reached stage IV New York Heart Association heart failure symptoms without any improvement in heart failure despite aggressive medical therapy including cardiac resynchronization therapy, heart transplant may be a reasonable option to extend survival and improve quality of life. If heart transplantation becomes a serious consideration, it must be performed in combination with the aggressive application of therapy to reduce iron overload. Recently Caines et al. published a review of 16 IOC end stage heart failure patients who received heart transplantation from 1967 to 2003 with a mean age of 31 years (14-63 years). They had a actuarial 10-year survival rate of 41%, with Kaplan-Meier analysis, with 1, 3 and 5 year survival rates of 81% for all three time intervals (106). Three patients died within one year secondary to infectious complications. Thirty day mortality was 12% (106). When severe IOC and hepatic iron overload co-exist, combined heart-liver transplantation may be considered because transplantation of only a single organ might not improve the outcome (106). There are a limited number of cases available in the literature, and thus more data is needed to validate whether heart transplant actually improves the clinical outcome of patients short and long-term.

Newer mechanistic directed therapeutic options

Role of Calcium channel Blockers

The mechanisms of iron transport into excitable tissues such as cardiac myocytes is under active investigation. Non transferrin bound iron (NTBI) enters the heart in the ferrous form, and the rate of transport increases with augmentation of the iron load (107). Recent evidence has suggested that voltage gated L-type calcium channels (LTCC) may be involved with iron transport into cardiomyocytes. LTCC primarily transport Ca^{+2}, but can also transport other divalent ions such as Fe^{+2}, Zn^{+2} (21,108). The association of LTCC with iron uptake is evident in studies that have shown 1) an increase in iron uptake rates in excitable tissues, i.e. tissues with pacemaker qualities, compared to non excitable tissues as they have more LTCC (107,109), 2) an increased activity of LTCC with increased levels of iron (109-111), and 3) LTCC agonist Bay K 8644 produced a 2.3-fold increase in the nifedipine sensitive Fe^{2+} uptake by the heart by enhancing LTCC activity (21). More definitive evidence of the role of LTCC in iron overload was found when Oudit et al. used therapeutic levels of the LTCC blockers verapamil and amlodipine to treat IOC in mice, and demonstrated that treatment with CCBs inhibited the LTCC current in cardiac myocytes thereby attenuating myocardial iron accumulation and oxidative stress, improved survival, prevented hypotension, and preserved heart structure and function (111). It was also noted that iron-overloaded transgenic mice with cardiac-specific over expression of the LTCC α1-subunit

had twofold higher myocardial iron and oxidative stress levels, as well as greater impairment in cardiac function. LTCC blockade in these mice protected them from iron overload. The above findings indicate the possible preventive and therapeutic role of CCBs in IOC (111). If effective, they may be used in the early stages of IOC, and may also enhance the therapeutic effects of standard chelation therapy. The role of verapamil, but perhaps not the dihydropyridine CCBs, may be limited in the advanced stage of IOC which may be associated with conduction system defects and LV systolic dysfunction, both of which may be exacerbated by verapamil administration. Presently a nonrandomized open label trial sponsored by the National Institute of Diabetes and Kidney Disease is underway to assess the role of nifedipine in iron overload patients.

Hepcidin

The human hepcidin gene HAMP located on chromosome 19 encodes for a precursor protein, 84 amino acid pre-prohepicidin, which is primarily produced in the liver. It undergoes subsequent post translational processing that results in a mature 25 amino acid form, hepcidin, which plays a major role in regulating iron homeostasis in the body. The evidence for this conclusion was observed in hepcidin knockout mice that developed massive iron overload (112) as well as in mice engineered to overproduce hepcidin who developed severe anemia (113). Hepcidin binds to ferroportin resulting in internalization and degradation of ferroportin thereby blocking cellular iron export (114,115). This obstruction results in a decrease in serum iron levels by blocking iron absorption from the intestine, iron recycling from macrophages, and mobilization of stored iron from liver hepatocytes. Hepcidin is thought to be regulated by hemojuvelin, transferrin receptor 2, transferrin, HFE gene, hypoxia, inflammation, and erythroid factors (116). Besides production by the liver, hepcidin is also believed to be produced by macrophages (117), fat cells (118) and the heart (119). Lower levels of hepcidin were observed in studies on HH (120,121) and non-hemachromatosis iron overload diseases (122-124), so hepcidin analysis might provide a role in screening, monitoring, prognosis and therapy of HH. Techniques using mass spectrometry can identify various isoforms of hepcidin in urine and serum (125,126). Augmentation of hepcidin levels by iron reduction, hepcidin inducers, hepcidin supplements and antioxidants may play a role in the future treatment of iron overload conditions. There is still a lot to understand about the full potential of this key regulator of iron homeostasis and additional studies are underway and are needed to determine its role in iron regulation.

Role of gene therapy

Cure of primary genetic diseases like β-thalassemia and sickle cell disease before or after tissues develop iron overload could be an option to prevent IOC. Gene therapy involves correction of the underlying defect by genetically modulating autologous stem cells which are then implanted by a vector into the target cell, thereby facilitating the expression of the desired functional product by the target cells. Lentiviral vectors proved capable of efficiently transmitting complex globin expression cassettes containing transcriptional regulatory sequences from the β-globin locus control region, which are required for high level expression, to treat β-thalassemia (127). Correction of anemia and organ damage in β-thalassemic mouse models has been achieved using both β-globin (128,129) and γ-globin vectors (130,131). Recently Pestina et. al. reported the use of a γ-globin lentiviral vector for hematopoietic stem cell transduction in severe sickle cell disease (127). Similar gene therapy approaches designed to target over expression of hepcidin and inhibition of DMT-1 expression, ferroportin expression, expression of the wild type HFE gene using duodenal stem cells have been postulated to greatly reduce the iron accumulation in HH and are yet to be evaluated in mouse models of HH (132). Though the approach of gene therapy is promising, these techniques have relatively high morbidity and mortality rates and extensive biosafety research is needed to demonstrate that the benefit /safety ratio is acceptable before

it can be accepted as a mainstream medical treatment of IOC. These studies are presently being pursued.

Role of stem cell transplant

It is also hoped that introduction of healthy hematopoietic stem cells in severe congenital anemia lacking appropriate β-hemoglobin production, such as sickle cell disease or β-thalassemia, may reverse the primary pathophysiology in the disease and reduce the need for transfusions. (133). This approach; however, presently is not ready for widespread application because stem cell transplant requires aggressive chemotherapy and radiation unless perfectly matched donor cells are available. Currently, clinical trials are underway to test low-intensity radiation along with immunosuppressant drugs without chemotherapy to accomplish successful stem cell transplantation with a half-matched donor in order to broaden its use.

Conclusions

IOC is a potentially lethal, but treatable disease when diagnosed and treated early in its course. Newer insights into iron homeostasis and the complicated mechanism of iron entry into the heart are now emerging. Improved cardiac imaging techniques are being developed and perfected for the early identification of iron overload and its treatment. New therapeutic options with better chelating agents with increased safety, efficacy, and absorption with therefore better compliance are being evaluated. The role of CCBs, hepcidin, genetic and stem cell therapy are being investigated and may play a role in future disease management. Further studies are needed to define optimal medical care for increasing survival and improving quality of life for these patients. In the interim, it is important to use the techniques presently available for early diagnosis and to utilize the existing therapeutic interventions in a safe manner.

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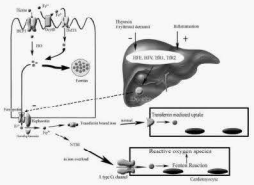

Figure 1. Iron Kinetics. Heme is absorbed by Heme carrier protein-1 (HCP-1) and released from iron by hemoxygenase-1 (HO-1), but heme uptake overall still remains controversial

Non heme iron is reduced by duodenal cytochrome b at the apical membrane of intestinal enterocytes (134), which is taken up by intestinal epithelium by the divalent metal transporter 1 (DMT1) (135,136). Ferrous iron is then transported to the basolateral portion of the cell by iron carriers and later transported into the circulation by the duodenal iron exporter Ferroportin (regulated by hepcidin) when there is a need for iron. Ferrous iron is oxidized by ceruloplasmin in non-intestinal cells and also by a homologue of ceruloplasmin, Hephaestin, in intestinal cells to ferric iron and loaded on to transferrin. With the increase in intracellular concentrations of iron, ferritin synthesis also increases. Once the storage capacity is exceeded, metabolically active iron is released intracellularly in the form of hemosiderin and toxic nontransferrin-bound forms of iron (NTBI).

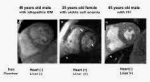

Figure 2. Typical examples of T2* cardiac MRI imaging to assess both myocardial and liver iron overload are shown

T2* images were obtained by using the gradient echo sequence of cardiac MRI employing a 1.5 T scanner as reported by Anderson et al (67). The images captured at TE time of 5 ms are shown. T2* image of 45 year old with idiopathic cardiomyopathy (CM) shows no evidence of iron overload in the liver and heart (panel A; **Heart T2*=39 ms; Liver T2*=27 ms**). T2* image of 35 year old female with sickle cell anemia and a history of multiple transfusions shows iron overload in both the liver (arrowhead) and heart (arrows) (panel B; **Heart T2*=12 ms; Liver T2*<2 ms**). T2* image of a 45 year old male with hereditary hemachromatosis (HH) shows iron overload seen in the liver (arrowhead), but not heart (panel C; **Heart T2*=30 ms; Liver T2*=2 ms**). Please note that iron overloaded tissues appear darker in the images. (The images in this figure were provided by Andrew Arai, M.D., Branch of Cardiac Energetics, National Heart, Lung, and Blood Institute of the National Institutes of Health, Bethesda, MD).

Figure 3. Our proposed clinical pathway to evaluate patients with idiopathic cardiomyopathy or those at risk for iron overload is shown

IOC=iron overload cardiomyopathy, LV=left ventricle.

Table 1

Etiology of Iron overload Disorders

Disease	Mechanism	Molecular correlate	Iron deposition
1. Primary Hereditary Hemochromatosis			
a. Type 1 (HFE related) (AR)	Increased GI absorption with normal diet	*Missense mutation* - C282Y homozygosity - H63D homozygosity - C282Y/H63D heterozygosity - Other mutations of HFE	Liver, heart, endocrine glands
b. Type 2 (Juvenile hemochromatosis) (AR)	Increased GI absorption with normal diet	- Mutation on HJV gene which encodes for hemojuvelin - Rare form where hepcidin is inactivated	Liver, heart, endocrine glands
c. Type 3 (AR)	Increased GI absorption with normal diet	- Mutation of transferring receptor 2	Liver, heart, endocrine glands
d. Type 4 (AD)	Increased GI absorption with normal diet	- Mutation of SLC40A1 which encode for ferroportin	Macrophages, Liver, heart, endocrine glands
2. Secondary			
a. Iron-loading anemias (Transfusion related)			
- Thalassemia	- Transfusion related - In severe thalassemia can have increased GI absorption	Mutation causing defect in synthesis of α- and β-globin chains of hemoglobin	Heart, pancreas, pituitary, Liver
- Sickle cell anemia	- Transfusion related	Substitution of a valine for glutamic acid as the 6th amino acid on the beta globin chain (HbS)	Liver, Heart
- Sideroblastic anemia	- Transfusion related - Increased GI absorption with normal diet	Hereditary or acquired Ineffective erythropoiesis	Neurons, Heart, mitochondria
- Diamond blackfan anemia	- Transfusion related	Congenital hypoplastic anemia with decreased erythroid precursors	Heart, Liver
- Congenital dyserythropoesis anemia	- Transfusion related	Ineffective erythropoiesis	Liver, IIeart, endocrine
- post stem cell transplant patients	- Transfusion related		Liver, Heart
- Chronic kidney disease/ end stage renal failure/ dialysis	- Oral and IV iron supplementation - Transfusion related	- Decreased erythropoietin	Heart, Liver
b. Dietary Overload			
- African Iron overload	- increased dietary intake	- Increased diet with predisposing genetic factors (proposed mechanism)	Heart, Liver, endocrine
c. Miscellaneous			
- Aceruloplasminemia			
- Congenital atransferrinemia			
- Chronic liver diseases			
- Hepatitis C and B			
- Alcohol induced liver disease			
- Porphyria cutanea tarda			
- Fatty liver disease			

Proposed Guidelines for the Diagnosis of Canine Idiopathic Dilated Cardiomyopathy

The ESVC Taskforce for Canine Dilated Cardiomyopathy

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Abstract

Dilated cardiomyopathy (DCM) is a major cause of morbidity and mortality in various dog breeds. The diagnosis of overt DCM is not normally problematic, although the importance of active exclusion of other causes of the dilated, hypokinetic heart is emphasised. Recent interest in human familial DCM has prompted a number of researchers to investigate the genetic basis of canine DCM. Prospective screening of dogs from lines with familial prevalence of DCM may identify dogs with pre-clinical ("occult") DCM. Dogs with other echocardiographic abnormalities or arrhythmias may also be identified. It is clear that dogs, like humans, have a prolonged pre-symptomatic phase of the disease extending over years. The ESVC DCM taskforce was established to provide the veterinary cardiology community with guidelines for the diagnosis of DCM, predominantly based on 2D and M-mode echocardiography. Diagnosis of DCM requires all of the following: (i) Left ventricular dilatation (ii) Reduced systolic function (iii) Increased sphericity of the left ventricle. We propose a scoring system for the identification of dogs in the pre-clinical stages. These include a number of major criteria and minor criteria. Future prospective longitudinal studies are required to test these in different breed populations to assess their predictive power and further refinements may be required. The importance of post mortem confirmation of disease is emphasised, and the two major histopathological features associated with DCM, the attenuated wavy fibre and the fibro-fatty infiltration-degenerative forms, require further investigation to identify the different aetiopathogenetic factors which may be involved.

Key words: Dog, Dilated Cardiomyopathy, Echocardiography, Histopathology, Familial Dilated Cardiomyopathy

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Taurine and Carnitine in Canine Cardiomyopathy

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Dilated cardiomyopathy (DCM) is one of the most common acquired cardiovascular diseases in dogs [1–4]. Although few studies of the prevalence of DCM in the overall population of dogs have been reported, estimates range from 0.5% to 1.1% [5,6]. Only degenerative valvular disease and, in some regions of the world, heartworm infection are more common causes of cardiac morbidity and mortality in dogs. DCM is seen most commonly in large and giant breeds of dogs, although its frequency seems to be increasing in medium-sized breeds, such as the English and American cocker spaniels [4–8]. It has been reported rarely in small and miniature breeds of dogs [9].

DCM is particularly challenging to veterinarians because the cause is often unknown and can vary among dog breeds [10]. Because most cases of DCM in dogs are classified as idiopathic, most therapies can be classified as "Band-Aid therapies" that palliate the effects of this disease for a short duration but do little to address the primary disease process. Therefore, DCM is almost always a progressive disease, and most dogs will eventually succumb to their disease. Survival times in dogs with DCM are variable and can be influenced by several factors, including breed. However, the prognosis for survival of dogs with DCM remains poor, with reported survival rates of 17.5% at 1 year and 7.5% at 2 years [11–13]. Until recently, reported cases of DCM reversal in dogs were very rare.

With advancements in echocardiology, diagnostic capabilities in canine cardiology have improved dramatically over the past 2 decades. Therapeutic advances have made surprisingly little progress. Symptomatic treatment is the standard care and outcome remains poor.

Recently, more promising therapies for dogs with DCM have resulted from a clearer understanding of the importance of biochemistry and nutrition in managing this disease. Nutrition is now widely accepted as an important adjunct to medical therapy in dogs with DCM.

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