



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, Maryland 20892-6910
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 480-3387

June 7, 2021

Re: Animal Welfare Assurance
#A4518-01 (OLAW Case F)

Ms. Rana Smith
President and Chief Executive Officer
Chimp Haven, Inc.
13600 Chimpanzee Place
Keithville, LA 71047

Dear Ms. Smith,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 2, 2021 letter reporting an adverse event involving a chimpanzee at Chimp Haven, Inc., following up on an initial telephone report on May 5, 2021. According to the information provided, OLAW understands that a 30 year old female chimpanzee had been introduced to a group of chimpanzees with the intent of forming a new social group. She sustained a leg injury, was given analgesics, anti-inflammatory, and other medications, and was closely monitored by staff. Fighting subsequently occurred among the chimpanzees and the female sustained additional injuries which prevented her from walking. Additional diagnostics and treatments were performed and the animal was separated with a companion. Extensive therapy, treatment, and diagnostics continued with a presumptive diagnosis of spinal disc compression and systemic infection. Despite ongoing treatment and palliative care, the animal's health declined and ultimately the established endpoint criteria had been met.

In conjunction with the Institutional Animal Care and Use Committee, the oversight committee, and a veterinary neurosurgeon the decision was made to euthanize the chimpanzee. A necropsy was conducted which found numerous co-morbid pathologies but the primary one was related to trauma. The other findings probably predisposed her to injury from the conspecifics. The standard operating procedure for separation of groups will be updated based on the information obtained in this case.

Based on the information provided, including the supporting necropsy documents, OLAW is satisfied with the actions taken by the veterinary team, husbandry staff, and others involved in addressing this situation. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

Cc: IACUC Chair
Robert Gibbens, D.V.M., USDA-APHIS-AC



June 2, 2021

Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare, National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982
Phone: 301-594-2061
FAX: 301-402-2803
E-mail: olawdco@mail.nih.gov

RE: Reporting of Adverse Event at Chimp Haven, Assurance A4518-01

Dear Dr.'s Morse, Brown and Wolff:

Chimp Haven is writing to report an adverse event, the euthanasia death of a chimpanzee, within two months of a social introduction. Cleopatra, a hepatitis C positive 30- year old female chimpanzee that arrived to Chimp Haven in 2016 was introduced with her group of seven to another group of six chimpanzees over a total of three days on March 4th, 8th, and 9th, 2021. Cleopatra herself was one of the last chimpanzee's to be introduced on March 9th. The introduction was initially successful and staff were hopeful that the newly formed social group would bond.

On April 6th, Cleopatra was noted to be favoring her left hind limb. She held her stifle at a 70-80 degree angle with no movement from the joint when ambulating. No external wounds were visible. She would pick up her left leg/foot with her hands in order to move. Based on gait characteristics she was suspected to have a primary left stifle injury, possibly an ACL injury. She was started on ibuprofen and famotidine. Due to social dynamics playing a role in Cleopatra's medication acceptance, a co-medicating plan which utilized multiple animal care staff to ensure she was receiving her medications was instituted at this time.

Animal care managers made the decision to continue to give this group additional space due to group volatility and wounding of group members as well as Cleopatra's ongoing mobility issues. Over the following week, Cleopatra's mobility did not improve. She was started on carprofen, famotidine, Cosamin, and tramadol and was taking medications intermittently. Based upon social dynamics and the difficulties with a possible reintroduction, the animal care team felt it was best for her to remain with her group while healing.

On Thursday, April 15th, at a regular weekly meeting, the animal care team discussed concerns about increased volatility within this group and noted that a potential separation may be needed in the future. Additional data collection was to begin the following day by way of a mobility log, cooperative feeding and cooperative medicating logs as well as looking more closely at accumulated data on social dynamics, wounding, and shifting

The morning of Friday, April 16th, the chimpanzees in Cleopatra's group got into a fight in the rain when their indoor bedroom space was reduced for cleaning. Multiple members of the group focused their aggression on Cleopatra, jumped on top of her, and she was unable to flee. Following the fight, the group disbursed and Cleopatra was able to come inside on her own and accept a banana along with her groupmates. The two groups were separated into their original two groups later the same day. After the fight, Cleopatra's tramadol was increased to twice a day.

On Sunday, April 18th, Cleopatra's clinical status declined and she was no longer using either leg to support herself and she was exclusively using her arms to ambulate. Cleopatra was removed from her group with a groupmate to allow for a more focused approach to her treatment including a positive reinforcement based physical therapy plan and extra enrichment.

On Monday, April 19th, Cleopatra was still not using her legs but had some movement in her left toes. She was somewhat stronger in getting around but still tired easily. Handles were placed at each shift door to help her pull herself through.

On Wednesday, April 21st, Cleopatra was sedated and there was no significant crepitus in any joints and only mild joint effusion in the left knee. She had mild intermittent hypertension, which is historical for her. Cleopatra was starting to form a decubital ulcer on her right hip. She was treated with some IV fluids and bilateral knee injections of a joint supplement. Lumbar, hip, stifle, and ankle radiographs were obtained and she also received laser therapy of both knees. Following Cleopatra's sedation, we received bloodwork and the radiologist's report of her spine and lower extremities with the results listed below:

1. Systemic infection with probable kidney involvement. She was started on a systemic antibiotic to help control infection.
2. Significantly elevated potassium of 8.8. She was started on a short course of a low dose potassium binder in attempts to help slowly bring down her blood potassium.
3. The radiographs did not show any underlying causes for Cleo's paresis, per the radiology report. Radiographs ruled out underlying etiologies such as fractures and dislocations, leaving our primary differential to be a disc compression of the spinal cord. Upon recovery, our clinical veterinarian performed testing for deep pain which was found to be negative on the left and positive on the right. These results were supportive of a spinal or neurological injury.
4. Because of the difficulties with diagnosis, surgery and the recovery process for a spinal injury in a chimpanzee, conservative treatment including strict rest, steroid therapy, and physical therapy was initiated on April 22nd, following Cleopatra's sedation. Other goals of her therapy included laser treatment of the lower spinal column, and the left knee as well as passive range of motion therapy. In addition, modifications were made to her enclosure to include extra handholds, cushions, and lower lixits. Cleopatra was also started on quality of life monitoring at this time. Chimp Haven's IACUC/SCCC was informed regarding Cleopatra's case.

On Monday, April 26th, Cleopatra moved both sets of her toes and ankles. She was variably compliant with medication acceptance and had been unresponsive to further therapy.

On May 3rd, Cleopatra met endpoint criteria. The decision was made to euthanize Cleopatra on May 4th 2021 in consultation with a veterinary neurosurgeon from Baton Rouge based on her grave medical prognosis without surgical intervention. Due to extreme post-operative care requirements, surgery was not a viable option.

A necropsy was performed and the histopathology report is attached. On necropsy, at least one band of each ACL was intact. There was evidence of ante mortem trauma to her left knee. Her ventral lumbar spinal cord was bruised but we were unable to visualize the disc spaces. She had a moderate amount of clear fluid in her abdomen and around her heart. Her liver grew four masses through the diaphragm and into the thoracic cavity, 5cm x 6 cm in size. Her heart muscle was thickened and her left atrioventricular valve had nodular growths. She also had a uterine mass. The main pathology effecting her quality of life was trauma, however she had several co-morbidities that likely predisposed her to injury post introduction.

Chimp Haven collects data in multiple formats after an introduction to gauge how the new groups are doing. Data collection includes proximity, behavior time budgets, and wounding data. We are evaluating our criteria

for separation of groups based on what we have learned from this event and will be modifying and updating our written standard operating procedures as needed.

Dr. Raven Jackson-Jewett notified both our USDA and NIH representatives, Dr. Tomlinson and Sheri Hild respectively, of Cleopatra's euthanasia and the circumstances surrounding it.

Please let me know if you require any further information.

Sincerely,

(b) (6)

Rana Smith
President and CEO, Institutional Official
rsmith@chimphaven.org

CC: Chimp Haven SCCC/IACUC, AAALAC accredit@aaalac.org

13600 Chimpanzee Place Keithville, LA, 71047

(b) (6)

chimphaven.org



(b) (4)

(b) (4)

FINAL

(b) (4)

Patient: Chimp Haven, Cleopatra

Chimp Haven

Accession:

Species: Primate

Hospital #: (b) (4)

Veterinarian: Novak, Lauren

Breed: Not Provided

13600 Chimpanzee Way

Patient MRN:

Age: 30 yrs

Keithville, LA 71047

Received Date: 5/11/2021 6:16 AM EA

Gender: Female Intact

(318)925-9575

Reported Date: 5/19/2021 12:50 PM

Test Requested: Necropsy in a jar

Test Name	Result	Units	Flag	Reference Range/Cutoff
Necropsy in a jar				Run on 5/19/2021 12:46:00 PM

(b) (4)

Reviewed By: _____

Date: _____

Originally Printed On: 5/19/2021 12:50 PM

Printed: 5/19/2021 12:50 PM

Page: 1/1

STAT[S] Corrected [C] Amended [A]

Accession (b) (4) Patient #: 552937

Lab Results for: Chimp Haven, Cleopatra

(b) (4)

(b) (4)

Pathology Accession:

(b) (4)

Result ID: NJ-21-00273

Chimp Haven
13600 Chimpanzee Way
Keithville, LA 71047
(318) 925-9575

Date Received: 05/11/2021
Date Reported: 05/19/2021

Veterinarian: Dr. Lauren Novak

Patient	Species	Breed	Sex	Age	Clinical MRN
Chimp Haven, Cleopatra Non Human Primate		Chimpanzee	F	29	552937

DIAGNOSIS:

DIFFUSE, LYMPHOHISTIOCYTIC PORTAL HEPATITIS WITH FIBROSIS AND BILE DUCT HYPERPLASIA

SEVERE, CHRONIC, VENTRICULAR MYOCARDIAL HYPERTROPHY WITH INTERSTITIAL FIBROSIS, ARTERIOSCLEROSIS, AND MITRAL VALVULAR DEGENERATION (ENDOCARDIOSIS)

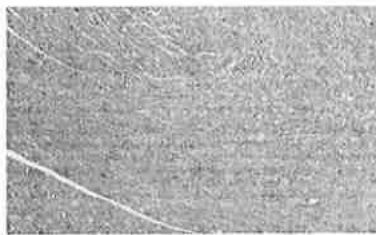
BILATERAL, CHRONIC RENAL DISEASE

CHRONIC, LYMPHOHISTIOCYTIC TO EOSINOPHILIC ENTEROCOLITIS WITH VILLOUS BLUNTING

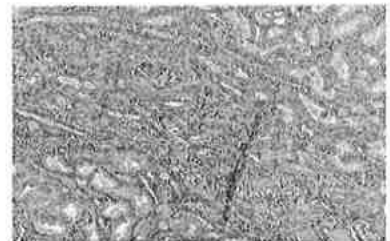
UTERINE LEIOMYOMA



High magnification of the hepatitis



High magnification of the hypertrophic cardiomyopathy



High magnification of the chronic renal disease

(b) (4)

(b) (4)

(b) (4)

Pathology Accession:

(b) (4)

Chimp Haven
13600 Chimpanzee Way
Keithville, LA 71047
(318) 925-9575
Veterinarian: Dr. Lauren Novak

Result ID: NJ-21-00273

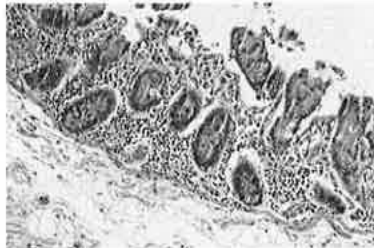
Date Received: 05/11/2021

Date Reported: 05/19/2021

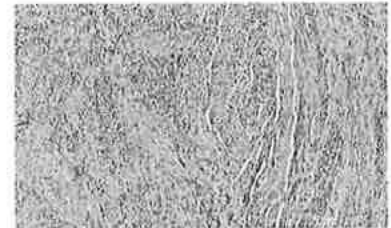
Patient	Species	Breed	Sex	Age	Clinical MRN
Chimp Haven, Cleopatra Non Human Primate		Chimpanzee	F	29	552937



High magnification of the enteritis



High magnification of the colitis



High magnification of the uterine leiomyoma

CASE COMMENT:

The sudden decline in health is attributed to the trauma (likely spinal cord as noted grossly). However, there are many significant comorbidities that could have caused enough morbidity to result in Cleopatra being picked on and not be able to defend herself.

The lesions within the kidneys and heart are severe and considered to be the main causes of this chimpanzee's illness. This is consistent with cardiorenal syndrome. This syndrome is characterized by glomerular sclerosis and tubulointerstitial fibrosis with myocardial fibrosis. The chronic renal disease can compound heart disease due to increased resistance in the renal vascular bed, and conversely heart disease can lead to renal disease through poor perfusion and/or from primary hypertension. I suspect heart failure with chronic hypertension was the initiating lesion.

The hepatitis is consistent with a chronic Hepatitis C infection. I did not find any hepatic neoplasia in these sections, but based on the clinical history provided I suspect there was. There is also a enterocolitis which could be secondary to a bacterial infection or hypersensitivity type reaction (which I suspect in this case). Both likely contributed to the overall morbidity. There is a uterine leiomyoma which is considered to be an incidental finding in this case. Please contact me with any questions about this case.

MICROSCOPIC DESCRIPTION:

Liver: Multifocally, extending from portal areas (which commonly bridge) into sinusoids are mild to moderate areas of fibrosis, bile duct hyperplasia, and increased numbers of lymphocytes, histiocytes, and few neutrophils. The lobular hepatic parenchyma is irregular and occasionally nodular.

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Pathology Accession:

(b) (4)

Chimp Haven
13600 Chimpanzee Way
Keithville, LA 71047
(318) 925-9575
Veterinarian: Dr. Lauren Novak

Result ID: NJ-21-00273

Date Received: 05/11/2021

Date Reported: 05/19/2021

Patient	Species	Breed	Sex	Age	Clinical MRN
Chimp Haven, Cleopatra Non Human Primate		Chimpanzee	F	29	552937

Heart: In all cardiac sections, the myocardium contains numerous patchy areas of dissecting interstitial fibrosis with associated myocyte loss, degeneration, and rare necrosis. The vast majority of myocardial myocytes are hypertrophic with swollen pale cytoplasm and large rectangular to irregular nuclei (karyomegaly). Many coronary arteries are partially occluded by tunica intimal smooth muscle hypertrophy and hyalinization of the entire wall (arteriosclerosis). There is increased interstitial fibrosis surrounding these vessels. The submitted left AV valve is distended by nodular areas of myxomatous extracellular matrix and fibrosis.

Kidneys: Multifocally, the cortex and medullary interstitium contains patchy areas of fibrosis with mild infiltrates of lymphocytes, plasma cells, macrophages, and few neutrophils. There is mild glomerular and tubular loss, with scattered remaining glomeruli being sclerotic or having hyalinized Bowman's capsules. The remaining tubules occasionally have hyalinized basement membranes, and few are mildly ectatic and filled with clear to eosinophilic material.

Small and large intestines: Diffusely, all segments have mildly to moderately increased numerous of lymphocytes, histiocytes, eosinophils, and fewer neutrophils within the lamina propria which occasionally extend into the submucosa. There is blunting of small intestinal villi.

Uterus: A section of uterus wall provided contains irregular smooth muscle bundles (consistent with leiomyoma). No mitotic figures are observed.

No significant histologic abnormalities are observed within the lungs, stomach, pancreas, inguinal and mesenteric lymph nodes, spleen (slightly increase hemosiderosis), adrenal glands, or urinary bladder.

CLINICAL HISTORY & TENTATIVE/WORKING CLINICAL DIAGNOSIS-DIFFERENTIAL DIAGNOSIS:

Clinical history received and the requisition form has been provided to the pathologist, digitized and uploaded to this case. Submitting Clinician Working Clinical Diagnosis or Differential Diagnosis: No preliminary clinical diagnosis or differential diagnosis was provided.

Submitting Veterinarian: Lauren Novak

SPECIMEN(S) GROSS DESCRIPTION:

Necropsy: Jars: 1; Pieces of tissue: M; Tissue Sections: M; Cassettes: 23.

TEST(S) PERFORMED:

NECROPSY IN A JAR

(b) (4)

(b) (4)

(b) (4)

Pathology Accession: (b) (4)

Result ID: NJ-21-00273

Chimp Haven
13600 Chimpanzee Way
Keithville, LA 71047
(318) 925-9575
Veterinarian: Dr. Lauren Novak

Date Received: 05/11/2021

Date Reported: 05/19/2021

Patient	Species	Breed	Sex	Age	Clinical MRN
Chimp Haven, Cleopatra Non Human Primate		Chimpanzee	F	29	552937

(b) (4)

(b) (4)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, June 4, 2021 7:25 AM
To: Rana Smith
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Report of Adverse Event at Chimp Haven, Assurance A4518-01

Thank you for this report, Ms. Smith. We will send a response soon.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Rana Smith <rsmith@chimphaven.org>
Sent: Wednesday, June 2, 2021 6:28 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Amy Fultz <afultz@chimphaven.org>; 'accredit@aaalac.org' <accredit@aaalac.org>
Subject: Report of Adverse Event at Chimp Haven, Assurance A4518-01

Good evening,

Chimp Haven would like to report an adverse event which occurred on Friday, April 16, 2021 resulting in injury/euthanasia for one of our chimpanzees. Please see the attached letter and histopathology report for additional details.

Thank you in advance for your review -- please let me know if you need any additional information.

Cordially,

Rana Smith



Rana Smith | President and Chief Executive Officer
13600 Chimpanzee Place
Keithville, LA 71047
Mobile: (b) (6) | Fax: (b) (6)
chimphaven.org



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Initial Report of Noncompliance

By: (b) (6)

Date: 5/5/21

Time: 12:00

Name of Person reporting: Raven Jackson Bennett

Telephone #: (b) (6)

Fax #:

Email:

Name of Institution: Chimp Haven

Assurance number: A4518

Did incident involve PHS funded activity? _____

Funding component: _____

Was funding component contacted (if necessary): _____

What happened?

Introduction of 30 yr old chimp led to fight +
spinal injury, paralyzed

Species involved: chimpanzee

Personnel involved:

Dates and times:

Animal deaths:

Projected plan and schedule for correction/prevention (if known): _____

Euthanize

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

Case # _____