Inspection Report

OKLAHOMA STATE UNIVERSITY
101 McElroy Hall Annex
STILLWATER, OK 74078

Customer ID: **502460**
Certificate: **73-R-0121**
Site: 001
OKLAHOMA STATE UNIVERSITY

Type: ROUTINE INSPECTION
Date: 29-JUN-2021

2.31(c)(7) Critical

Institutional Animal Care and Use Committee (IACUC).

There are multiple deviations from the procedures described in Protocols 1 and 2.

- On 2 June 2020 the primary investigator for Protocol 1 injected a guinea pig with a solution containing a "Cremophor® EL-based vehicle". The protocol was approved for a solution using a DMSO base. The Primary Investigator chose to use a different base and felt that it would be safe for the animals. The guinea pig subsequently had an allergic response to the injection and died soon after. On 15 June 2020 the IACUC chose to permanently suspend the protocol in question. The suspension was reported to USDA on 17 June 2020.

Protocol 2 describes an experimental design starting with "Objective 1" in Year 1 and progressing to "Objective 2" in year 2 of the study.

- Two dogs, "Richie – ID OOV-9" and "Milo – ID KQB-0" had the chemical procedure performed on 13 March 2020 under Objective 2 procedures. This was three months before the actual Objective 1 dose optimization study was conducted (between 20 May 2020 and 1 June 2020) on a group of 10 dogs. The primary investigator chose to ignore this schedule and initiate the project with a long-term study involving Richie and Milo. This was a significant deviation that impacted these dogs and should have been submitted to the IACUC as a protocol amendment prior to conducting the procedure.
- Ten dogs were utilized under Objective 1 of the protocol between 20 May 2020 and 19 June 2020. According to this

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protocol, the dogs would be surgically castrated 1-3 hours after chemical injection. They would be monitored over the next 24 hours for a variety of pain factors such as panting, vocalization, and antisocial behavior. Pain evaluation would be recorded using a 0-3 scale. The dogs would also be "monitored for the development of fever post CTA". Study records provided did not show any of these monitoring procedures for the ten dogs used in the study.

- Four dogs "Milo – KQB-0", "Richie – OOV-9", "Lyle – LY80" and a dog with ID "HCB-0" were utilized under the Objective 2 section of this protocol. The protocol states dogs in this objective would be evaluated for "stress markers in blood" over a 2-week period post injection. The protocol further states that a CBC and serum testosterone levels would be checked on each dog at "0 min, 30 min, 60 min, 180 mins, 24 h and 72 h and once each month". Study records did not demonstrate that any of this monitoring was conducted on the four dogs.

Animal Care and Use Protocols must be reviewed and approved by the IACUC. Any amendments or significant changes to a protocol must also be approved by the IACUC. Protocols 1 and 2 had significant deviations from the approved procedures that were not presented to the IACUC for review and approval. These deviations had a dramatic impact on the animals, including the death of a guinea pig and a significant health and welfare impact on numerous dogs. The IACUC must approve and monitor all procedures on regulated animals to assure adherence to the allowed procedures. Correct from this point forward

2.31(d)(1)(i) Critical

Institutional Animal Care and Use Committee (IACUC).

- Two dogs, "Milo" and "Richie" were started on the long-term protocol prior to any dose optimization or pain scale testing being conducted. Four days after the injection, "Milo" was surgically castrated due to the formation of scrotal ulceration. "Richie", per facility records, did not appear to have any effect from the injections. He was placed in a foster home for approximately one year, then returned to the study and given a second injection on 25 April 2021. He was then surgically castrated on 28 April 2021 due to ulceration of the scrotum.

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- A dog named "Lyle – ID LY80" was utilized under Protocol 2 and subjected to 4 separate major operative procedures. The AWA definition of a major operative procedure is any surgical intervention that penetrates and exposes a body cavity or any procedure which produces permanent impairment in physical or physiological functions. The procedure of chemical castration is designed to permanently impair the testicular tissue. Study records indicate that Lyle received an injection in the left testicle on 12 June 2020, and in the right testicle on 13 June 2020. Lyle then had surgery on 16 June 2020 to remove the right testicle due to ulceration of the scrotum. The left testicle was removed in a separate procedure on 16 October 2020.

Procedures involving animals will avoid or minimize discomfort, distress, and pain. The Primary Investigator did not complete Objective 1 for Protocol 2 which was designed to "determine the best dose that provides the maximum effectiveness of the CTA method" and to monitor clinical signs that indicate pain and distress. Failing to complete this portion of the protocol resulted in unnecessary discomfort and distress to "Milo", "Richie", and "Lyle". In addition, Lyle was subjected to multiple painful procedures including two separate surgical castrations. Primary investigators must follow IACUC approved protocols to ensure animal pain and distress is minimized.

Correct from this point forward

2.31(e)(3) Critical

Institutional Animal Care and Use Committee (IACUC).

- On Protocol 2, ten dogs were utilized under the "Objective 1" portion of the protocol. The primary investigator failed to fully describe the intended use of the animals. The procedures in this portion of the protocol are frequently vague and unclear. The experiment is intended to test methods of chemical castration in dogs. The protocol describes the injection method and dose determination but does not specify other details of this procedure. Study records indicate that 6 of the 10 dogs had one testicle injected, with the other testicle left as a control. Three of the other 4 dogs received "2X" dose in each testicle. One received "2X" dose in the left, and "1.5X" in the right. The protocol does not make any reference to

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varying the doses in this manner.

- The same section of this protocol continues by stating that “if needed, temperature sensors” will be inserted in the testicles to confirm “core heating”. There is no explanation of this procedure, nor any indication of expected temperature findings or baseline parameters.

Protocols must contain a complete explanation of the intended use of animals. Protocols that are vaguely worded or lacking details do not give a clear, thorough description of the intended experimental procedures. This protocol must be amended to give a complete and accurate description of intended animal use.

Correct from this point forward

This inspection and exit interview were conducted with facility representative.

Additional Inspectors:

DEBBIE CUNNINGHAM, VETERINARY MEDICAL OFFICER

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United States Department of Agriculture
Animal and Plant Health Inspection Service

Customer: 502460
Inspection Date: 29-Jun-2021

Species Inspected

Cust No	Cert No	Site	Site Name	Inspection
502460	73-R-0121	001	OKLAHOMA STATE UNIVERSITY	29-JUN-2021

Count	Scientific Name	Common Name
000007	*Felis silvestris catus*	CAT ADULT
000018	*Canis lupus familiaris*	DOG ADULT
000020	*Equus caballus*	DOMESTIC HORSE
000056	*Bos taurus*	CATTLE / COW / OX / WATUSI
000026	*Oryctolagus cuniculus*	DOMESTIC RABBIT / EUROPEAN RABBIT
000003	*Ovis aries aries*	SHEEP INCLUDING ALL DOMESTIC BREEDS
000010	*Cavia porcellus*	DOMESTIC GUINEA PIG
000035	*Microtus ochrogaster*	PRAIRIE VOLE
000175	**Total**	