



Department of Veterans Affairs Medical Center
John D. Dingell Medical Center
4646 John R
Detroit, MI 48201-1932

March 27, 2020

FOIA Request No.: 20-03120--F

Mr. Russ Kick
New England Anti-Vivisection Society
333 Washington Street, Suite 850
Boston, MA 02108

Dear Mr. Russ Kick:

This letter is the initial agency decision to your December 23, 2019, request under the Freedom of Information Act (FOIA), 5 U.S.C. § 552, submitted to the John D. Dingell VAMC for a copy of the following that concerns the "Institutional Animal Care and Use Committee (IACUC) at the John D. Dingell VA Medical Center."

- 1a) According to *The Guide for the Care and Use of Laboratory Animals (The Guide)*, 8th edition, all entities must have a system in place for anyone (insiders or members of the public) to report concerns regarding animal welfare at a facility. These reports are either made directly to the IACUC Chair or a designated representative, or they eventually are routed to the IACUC Chair/representative. *We request all such reported concerns received by the Chair since January 1, 2019.*
- 1b) *Further, for all such reported concerns deemed supported, you are requesting the notification sent to the Institutional Official.* The time frame is January 1, 2019, to present.
- 2a) Per *The Guide*, all entities must have a system in place for investigators to notify the IACUC and/or attending veterinarian of adverse events, unexpected or unanticipated outcomes, violations of protocols, and other incidents involving animal welfare that occur during their studies/experiments. *You request all such notifications received by the IACUC or AV since January 1, 2019.*
- 2b) *Further, you are requesting all notifications sent to the Institutional Official regarding these reported incidents.* The time frame is January 1, 2019, to present.

This would encompass all appendices, annexes, attachments, and accompanying documents, including photos and videos in their original formats and resolution.

As an affiliate with Wayne State University, the Assistant General Counsel, conducted a search for documents responsive to your request. The John D. Dingell VA Medical Center does not have its own "Institutional Animal Care and Use Committee" (IACUC). The search was conducted by using Emails. The conclusion of the search



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revealed, 3 (three) documents, totaling 40 (forty) pages, were determined to be responsive to your request.

My review of the documents revealed that they contained information that falls within the disclosure protections of FOIA Exemption 6, 5 U.S.C. § 552(b)(6). FOIA Exemption 6 permits VA to withhold a document or information contained within a document if disclosure of the information would constitute a clearly unwarranted invasion of a living individual's personal privacy. Stated another way, VA may withhold information under FOIA Exemption 6 where disclosure of the information, either by itself or in conjunction with other information available to either the public or the FOIA requester, would result in an unwarranted invasion of an individual's personal privacy without contributing significantly to the public's understanding of the activities of the federal government.

Specifically, the information I am withholding, as indicated on the enclosed documents, under FOIA Exemption 6 consists of names and email addresses, phone numbers of other individuals included in the records as the individuals associated with this information have a personal privacy interest in it.

The coverage of FOIA Exemption 6 is absolute unless the FOIA requester can demonstrate a countervailing public interest in the requested information by demonstrating that the individual is in a position to provide the requested information to members of the general public and that the information requested contributes significantly to the public's understanding of the activities of the Federal government. Additionally, the requester must demonstrate how the public's need to understand the information significantly outweighs the privacy interest of the person to whom the information pertains. Upon consideration of the materials provided, I have not been able to identify a countervailing public interest of sufficient magnitude to outweigh the privacy interest in this case. The individuals associated with this information have a personal privacy interest in information that outweighs any public interest served by disclosure of their identities under FOIA. Consequently, I am denying your request for this information under FOIA Exemption 6, 5 U.S.C. § 552 (b)(6).

If you disagree with my determination to withhold the information under FOIA Exemption 6, please be advised you may appeal to:

Office of the General Counsel (024)
Department of Veterans Affairs
810 Vermont Avenue, N.W.
Washington, D.C. 20420
Email: ogcfoiaappeals@va.gov



Department of Veterans Affairs Medical Center
John D. Dingell Medical Center
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If you should choose to file an appeal, your appeal must be postmarked or electronically transmitted no later than ninety (90) calendar days from the date of this letter. Please include a copy of this letter with your written appeal and clearly state why you disagree with the determinations set forth in this response.

You may also seek assistance and/or dispute resolution services for any other aspect of your FOIA request, excluding the release determination, from VHA's FOIA Public Liaison and or Office of Government Information Services (OGIS) as provided below:

VHA FOIA Public Liaison:

Email Address: vhafioa2@va.gov

Phone Number: (877) 461-5038

Office of Government Information Services (OGIS)

Email: ogis@nara.gov

Fax: (202) 741-5769

Mailing address: Office of Government Information Services


National Archives and Records Administration

8601 Adelphi Road

College Park, MD 20740-6001

Thank you for your interest in VA. If you have any further questions, please feel free to contact me at (313) 576-1464.

Sincerely,


Toysan Jennings
FOIA Officer

(b) (6) 022719 (16-02-042)

02/27/19 An AE involving administration of MnCL for imaging was reported during the meeting. It was also reported that Dr. (b) (6) had advised Dr. (b) (6) to provide supportive care to her rats prior to administration of MnCL, and that this did not occur in the rats that experienced AE's. The IACUC asked me to follow up and report as potential non-compliance at a future meeting.

From AE Report

3 rats (711, 701, 718) presented with adverse outcomes post-MnCl injection.

711- found dead, injected on 11/8/18, 701- euthanized, injected on 10/25/18, 718- euthanized due to resp. distress, injected on 1/17/19

Veterinary instructions from 11/6/18 was to meet and discuss supportive care options prior to proceeding. At that time the laboratory indicated that this was not going to be done again in the near future. There have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting.

02/27/19 Dr. (b) (6) forwarded (b) (6) the following email strings –

EMAIL STRING ONE -

From: (b) (6)

Sent: Wednesday, February 27, 2019 1:45 PM

To: (b) (6)

Subject: Fw: Supportive care for MnCl injections

From: (b) (6)

Sent: Tuesday, November 6, 2018 1:56 PM

To: (b) (6)

Cc: (b) (6) Gerry Hish; (b) (6)

Subject: Re: Supportive care for MnCl injections

Ok, thanks for letting me know. I look forward to hearing from you soon.

From: (b) (6)

Sent: Tuesday, November 6, 2018 1:42:37 PM

To: (b) (6)

Cc: (b) (6) Gerry Hish; (b) (6)

Subject: Re: Supportive care for MnCl injections

Hello,

I am out of town until Friday, but I am in discussion with the lab to identify possible causes.

Thank you,

~~~~~

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)  
[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]

On Nov 6, 2018, at 7:28 AM, (b) (6) wrote:

In talking with (b) (6) it sounds like multiple MnCl injections are no longer administered, as is stated in the protocol, but please respond with your thoughts regarding recommendations to improve outcomes following MnCl injections. If you don't foresee moving forward with this procedure for awhile, we can discuss another time, but before proceeding. Let me know if it would be easier to set up a meeting to discuss further.

Thanks!

P.S. The incision repair is looking great!

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**From:** (b) (6)  
**Sent:** Friday, November 2, 2018 12:32:10 PM  
**To:** (b) (6)  
**Cc:** Gerry Hish; (b) (6)  
**Subject:** Re: Supportive care for MnCl injections

Thanks for the additional information! In the protocol, it appeared that animals could receive several MnCl injections over the course of the study. Is that not the case?

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**From:** (b) (6)  
**Sent:** Friday, November 2, 2018 12:09:28 PM  
**To:** (b) (6)  
**Cc:** Gerry Hish; (b) (6)  
**Subject:** Re: Supportive care for MnCl injections

Hello Dr. (b) (6)  
All our animals are receiving only one MnCl injection.  
These two animals from this morning (the one that was found dead and the one we are going to euthanize after imaging) received MnCl injection yesterday.  
Thank you,

(b) (6)  
[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]

(b) (6)

**From:** (b) (6)  
**Sent:** Friday, November 2, 2018 11:38 AM  
**To:** (b) (6)  
**Cc:** Gerry Hish; (b) (6)  
**Subject:** Supportive care for MnCl injections

Hi all,

I am providing a summary of my verbal recommendation earlier today that was given in light of recent (3 of 3 animals affected July 2018) and today's adverse outcomes with MnCl injection. Also, can you please let me know how many MnCl injections did these two rats receive in the past, as well as the doses for each injection?

In your protocol, it is noted that some animals can develop illness after MnCl administration, and that supportive care will be given if needed AND more than 36 hours will elapse prior to euthanasia. Based on the potential severity of toxicity/outcome (death) and inability to pre-determine which animals will be negatively affected following MnCl injection, I strongly recommend that all animals receiving MnCl injection also get SQ fluids and an analgesic (carprofen) at the same time as MnCl injection and on the following day, and then as needed thereafter. Some researchers on campus use lower MnCl doses and achieve good contrast for imaging procedures, so we could also consider lowering the dose, but also with this in mind, I am not overly concerned about concurrent fluid administration affecting MnCl elimination to the degree that contrast would be ineffective at the time of imaging.

I would like to have this resolved ASAP (i.e. before proceeding with additional MnCl injections), and so that animals currently injected can receive supportive care ASAP.

Thanks for your time and attention to this matter,

(b) (6)

(b) (6)

**EMAIL STRING TWO -**

**From:** (b) (6)  
**Sent:** Wednesday, February 27, 2019 2:05 PM  
**To:** (b) (6)  
**Subject:** Fw: (b) (6) rats

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**From:** (b) (6)  
**Sent:** Thursday, January 24, 2019 7:21 AM  
**To:** (b) (6)  
**Subject:** Re: Holt rats

737 - inj 1/15/19 no issues  
738 - inj 1/15/19 no issues  
739 - inj 1/17/19 no issues  
717 - inj 1/19/19 - scratching at cap no other issues

715- inj 11/16/19. 1/18/19 hunched, tucked abdomen, vocal when touched. ulcerative dermatitis on rump/tail. (sorry this was my 5th one that i thought was injected after the first of the year but the cge card holder was hiding the other 1 for 11.)

It seems that we are seeing issues popping up about 2 months after injection.

let em know if you need anything else.

(b) (6)



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**From:** (b) (6)  
**Sent:** Thursday, January 24, 2019 7:10 AM  
**To:** (b) (6)  
**Cc:** (b) (6) Gerry Hish  
**Subject:** Re: (b) (6) rats

Hi (b) (6)  
I am going to follow up with the lab. However, can you give me the animal number for the 5 you mentioned and describe any clinical issues we have observed.

Thank you,

(b) (6)

(b) (6)  
[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]

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**From:** (b) (6)  
**Sent:** Thursday, January 24, 2019 6:43 AM  
**To:** (b) (6)  
**Subject:** Re: (b) (6) rats

ok so I currently have 5 rats that were injected since the first of the year. please see email below as well.

(b) (6)  
[Redacted]  
[Redacted]

---

**From:** (b) (6)  
**Sent:** Thursday, January 24, 2019 5:59 AM  
**To:** (b) (6)  
**Subject:** Re: (b) (6) rats

Good morning Dr. (b) (6) sorry I didnt get to this yesterday afternoon things were a bit crazy over here. The dates I sent you yesterday came straight from (b) (6)  
The cages cards have Mn2+ (66mg/kg IP) on them, I am assuming this is the same thing as MnCl... if not I have something else I need to look into today.

Thanks,  
(b) (6)  
[Redacted]  
[Redacted]

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**From:** (b) (6)  
**Sent:** Wednesday, January 23, 2019 12:51 PM



To: (b) (6)  
Subject: Re: (b) (6) rats

Hi (b) (6),  
What is the abbreviation listed on the cagecard? Who did you speak with from the lab regarding the injection date?

Thanks  
(b) (6)

On Jan 23, 2019, at 12:23 PM, (b) (6) wrote:

Rat that was found dead (711) was injected with Mn on 11.8.18.  
Rat that was euthanized on Friday (701) was injected with Mn on 10.25.18.  
Rat that was euthanized yesterday (718) was injected on 1.17.19.

I believe that i have 3 other cages that have been injected as well in the last month. they seem to be using a different abbreviation of the drug so I am not totally sure.

Thanks,

(b) (6)

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From: (b) (6)  
Sent: Wednesday, January 23, 2019 6:16 AM  
To: (b) (6)  
Subject: Re: (b) (6) rats

So number 715 was injected one 11/16 I will contact (b) (6) for the info on the euthanized and found dead rats.

(b) (6)

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From: (b) (6)  
Sent: Tuesday, January 22, 2019 12:53 PM

To: (b) (6)  
Subject: (b) (6) rats

Hi (b) (6)

Could you give me the injection dates of MnCl for the Holt rats which he observed health concerns with. The animal you found dead last week when did it receive MnCl?

Thanks,

(b) (6)

02/28/19 (b) (6) found two active protocols in eProtocol; 16-02-042 and 17-06-284. Protocol 16-02-042 included Manganese enhanced imaging. 17-06-284 did not.

(b) (6) phoned Lande and spoke with (b) (6). She is the new leader as (b) (6) has retired. (b) (6) was not able to provide the protocol number for the AE's, and (b) (6) was working at Applebaum.

(b) (6) phoned Applebaum – and went to (b) (6) voice mail.

02/28/18 (b) (6) sent the following email –

From: (b) (6)

Sent: Thursday, February 28, 2019 9:28 AM

To: (b) (6)

Cc: (b) (6)

(b) (6)

Subject: RE: (b) (6) rats

Hi Dr. (b) (6)

Can you provide the protocol number for the AE's described below?

Thanks,

(b) (6)

02/28/19 Dr. Baker Replied –

From: (b) (6)

Sent: Thursday, February 28, 2019 10:02 AM

To: (b) (6)

Cc: (b) (6)

Subject: Re: (b) (6) rats

The protocol number is 16-02-042.

Thanks!

02/28/19 (b) (6) drafted the following email to Dr. (b) (6) and sent it to Dr. Hish and Dr. Malek for review (as previously instructed by Dr. Cunningham)

Hi Dr. (b) (6)

I am contacting you to inquire about a potential compliance issue that occurred with rats on your approved IACUC protocol 16-02-042. An event was reported during a convened IACUC meeting on 02/27/19 involving rats that presented with adverse outcomes post-MnCl injection. It was also reported that you received veterinary instructions on 11/6/18 to meet and discuss supportive care options prior to proceeding with future MnCl injections. At that time your laboratory had indicated that this was not going to be done again in the near future.

Since there have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting; the IACUC asked me to follow-up on this as a potential non-compliance and report back to them at a future meeting.

Per the IACUC policy "Investigation and Remediation of Non-Compliance and Animal Welfare", within 24 – 48 hours please respond to the accuracy of this report, and if accurate please include a plan to resolve this issue.

Again, the potential issue of concern is not following veterinary recommendation to provide analgesics and SQ fluids to rats before injections of MnCl, or to meet with the vets to discuss supportive care before injecting MnCl.

Thank you,

(b) (6)  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

02/28/19 (b) (6) sent the following email to Dr. Malek and Dr. Hish for review.

**From:** (b) (6)

**Sent:** Thursday, February 28, 2019 10:26 AM

**To:** Moh Malek (b) (6) Gerald Hish (b) (6) (b) (6)

**Cc:** Philip Cunningham (b) (6)

**Subject:** Draft (b) (6) Letter

Hi Dr. Malek and Dr. Hish,

Please review the draft letter below involving the potential issue that the IACUC asked me to look into during yesterday's meeting.

Thanks,

(b) (6)

+++++

Hi Dr. (b) (6)

I am contacting you to inquire about a potential compliance issue that occurred with rats on your approved IACUC protocol 16-02-042. An event was reported during a convened IACUC meeting on 02/27/19 involving rats that presented with adverse outcomes post-MnCl injection. It was also reported that you received veterinary instructions on 11/6/18 to meet and discuss supportive care options prior

to proceeding with future MnCl injections. At that time your laboratory had indicated that this was not going to be done again in the near future.

Since there have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting; the IACUC asked me to follow-up on this as a potential non-compliance and report back to them at a future meeting.

Per the IACUC policy "Investigation and Remediation of Non-Compliance and Animal Welfare", within 24 – 48 hours please respond to the accuracy of this report, and if accurate please include a plan to resolve this issue.

Again, the potential issue of concern is not following veterinary recommendation to provide analgesics and SQ fluids to rats before injections of MnCl, or to meet with the vets to discuss supportive care before injecting MnCl.

Thank you,

(b) (6)  
(b) (6)  
(b) (6)  
(b) (6)  
(b) (6)

03/02/19 (Saturday) Dr. (b) (6)

From: (b) (6)

Sent: Saturday, March 2, 2019 7:51 PM

To: (b) (6) Gerry Hish (b) (6)

Cc: Philip Cunningham (b) (6)

Subject: RE: Draft (b) (6) Letter

Hi (b) (6)

Here is my iterations/question (see red font).

~~~~~

Dear Dr. (b) (6)

I am the Senior Research Compliance Specialist and I'm contacting you to inquire about a potential compliance issue that occurred with rats on your approved IACUC protocol 16-02-042.

An event was reported during a recently convened IACUC meeting on 02/27/19 involving rats that presented with adverse outcomes post-MnCl injection. In addition, it was reported that you received veterinary instructions on 11/6/18 to meet and discuss supportive care options prior to proceeding with future MnCl injections. At that time your laboratory had indicated that the MnCl injections were not going to be performed again in the near future. The potential issue of concern is related to not following veterinary recommendation to provide analgesics and SQ fluids to rats before (b) (6) and Gerry: should this be 'after') injections of MnCl, or to meet with the vets to discuss supportive care before injecting MnCl.

Based on the report, your laboratory injected 5 rats since January 2019, however, there was no communication between your staff and the veterinaries as previously agreed. The IACUC Committee

asked me to follow-up on this potential non-compliance and report back to them at the next meeting (March 27th).

Per the IACUC policy "Investigation and Remediation of Non-Compliance and Animal Welfare," within 24 – 48 hours please respond to the accuracy of this report, and if accurate please include a plan to resolve this issue.

03/04/19 (b) (6) Replied –

From: (b) (6)

Sent: Monday, March 4, 2019 9:10 AM

To: Moh Malek (b) (6) Gerry Hish (b) (6)

Subject: RE: Draft (b) (6) Letter

Hi Moh,

The context was actually intended to read "before continuing injections of MnCl".
If everyone agrees, how about "The potential issue of concern is related to not following veterinary recommendation to provide analgesics and SQ fluids to rats when injecting MnCl, or to meet with the vets to discuss supportive care before injecting MnCl".

Below is the email that was sent by (b) (6)

From: (b) (6)

Sent: Friday, November 2, 2018 11:38 AM

To: (b) (6)

Cc: Gerry Hish; (b) (6)

Subject: Supportive care for MnCl injections

Hi all,

I am providing a summary of my verbal recommendation earlier today that was given in light of recent (3 of 3 animals affected July 2018) and today's adverse outcomes with MnCl injection. Also, can you please let me know how many MnCl injections did these two rats receive in the past, as well as the doses for each injection?

In your protocol, it is noted that some animals can develop illness after MnCl administration, and that supportive care will be given if needed AND more than 36 hours will elapse prior to euthanasia. Based on the potential severity of toxicity/outcome (death) and inability to pre-determine which animals will be negatively affected following MnCl injection, I strongly recommend that all animals receiving MnCl injection also get SQ fluids and an analgesic (carprofen) at the same time as MnCl injection and on the following day, and then as needed thereafter. Some researchers on campus use lower MnCl doses and achieve good contrast for imaging procedures, so we could also consider lowering the dose, but also with this in mind, I am not overly concerned about concurrent fluid administration affecting MnCl elimination to the degree that contrast would be ineffective at the time of imaging.

I would like to have this resolved ASAP (i.e. before proceeding with additional MnCl injections), and so that animals currently injected can receive supportive care ASAP.

Thanks for your time and attention to this matter,

(b) (6)

03/04/19 Dr. Hish Replied –

From: Gerry Hish

Sent: Monday, March 4, 2019 9:47 AM

To: (b) (6) Moh Malek (b) (6)

Subject: Re: Draft (b) (6) Letter

Hi (b) (6)

I have a few suggestions that I will send today.

(b) (6)

SUMMARY for Discussion with Dr. Cunningham on 03/05/19

- An AE in one of Dr. (b) (6) protocols involving administration of MnCL for imaging was reported during the meeting on 02/27/19.
- It was also reported that Dr. (b) (6) had advised Dr. (b) (6) to provide supportive care to her rats prior to administration of MnCL, and that this did not occur in the rats that experienced AE's.
- The IACUC asked me to follow up and report as potential non-compliance at a future meeting.
- Veterinary instructions from 11/6/18 was to meet and discuss supportive care options prior to proceeding.
- There have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting.
- On 02/28/19 Joe drafted a letter to Dr. (b) (6) and sent it to Dr. Hish and Dr. Malek for review.
- On 03/02/19 (Saturday) Dr. Malek replied with one suggestion related to the timing of recommended supportive care.
- On 03/04/19 Dr. Hish said that he had a few suggestions that he would send later that day.
- 03/05/19 I have yet to receive this draft.

03/05/19 The issue was discussed with Dr. Cunningham. He seemed to believe that my wording somehow could be interpreted to mean that I was making the determination of non-compliance. I stated that I use the wording "potential compliance issue", and that the inquiry is meant to be inquisitive and not accusative. I also stated that the title of our SOP is "Investigation and Remediation of Non-Compliance and Animal Welfare".

Dr. Cunningham will look at the letter again and get back to me on any areas where we might want to be more careful. However, we did agree that it might be best to come up with a template to use for these situations.

03/07/19 (b) (6) sent the following reply –

From: (b) (6)
Sent: Thursday, March 7, 2019 1:13 PM
To: Gerry Hish (b) (6) Moh Malek (b) (6)
Subject: RE: Draft (b) (6) Letter

Hi Gerry,

Do you think we will be able to get an inquiry out to Dr. (b) (6) this week?

Thanks,

(b) (6)

03/13/19 (b) (6) met with Dr. Hish and Dr. Malek to discuss the issue. Dr. Hish said it was ok to send out the original draft notification to Dr. (b) (6)

03/13/19 (b) (6) tweaked the original notification slightly, but discussed the changes over the phone with Dr. Malek. He said that it sounded fine, and advised sending it out to Dr. (b) (6) Dr. Malek also asked me to copy Dr. (b) (6) to keep him in the loop.

(b) (6) sent out the following email notification –

From: (b) (6)
Sent: Wednesday, March 13, 2019 2:08 PM
To: (b) (6)
Cc: Moh Malek (b) (6) Gerald Hish (b) (6) (b) (6)
Subject: IACUC Protocol 16-02-042
Importance: High

Dear Dr. (b) (6)

I am contacting you as a Wayne State University Senior Research Compliance Specialist to inquire about a potential compliance issue involving rats on your approved IACUC protocol 16-02-042.

An event was reported during the convened IACUC meeting on 02/27/19 involving rats that presented with adverse outcomes post-MnCl injection. It was also reported that you received veterinary instructions on 11/02/18 strongly recommending "that all animals receiving MnCl injection also get SQ fluids and an analgesic (carprofen) at the same time as MnCl injection and on the following day, and then as needed thereafter". In addition, it was reported that on 11/6/18 you received veterinary instructions to meet and discuss supportive care options prior to proceeding with future MnCl injections. At that time your laboratory had indicated that the MnCl injections were not going to be performed again in the near future.

The potential issue of concern is related to not following veterinary recommendation to provide analgesics and SQ fluids to rats when injecting MnCl, and/or not meeting with the vets to discuss supportive care prior to proceeding with additional MnCl injections.

Based on the report, your laboratory injected 5 rats since January 2019, however, there was no communication between your staff and the veterinarians as previously agreed. The IACUC Committee asked me to follow-up on this potential non-compliance and report back to them at the next meeting (March 27th).

Per the IACUC policy "Investigation and Remediation of Non-Compliance and Animal Welfare," within 24 – 48 hours please respond to the accuracy of this report, and if accurate please include a plan to resolve this issue.

Thank you,

(b) (6)

03/15/19 Dr. (b) (6) sent her reply via email and also phoned me. We discussed the issue, and Dr. (b) (6) explained that (b) (6) thought that the veterinary recommendation was related to multiple injections of MnCL. She thought that since they were only giving single injections that the issue was resolved. She asked about continuing the protocol, and I advised contacting a veterinarian before proceeding with any more injections. They have not injected any more animals since the AE that was reported.

Email Reply (with attachment (b) (6) _2019.pdf)

From: (b) (6)

Sent: Friday, March 15, 2019 2:13 PM

To: (b) (6)

Cc: Moh Malek (b) (6); Gerry Hish (b) (6); (b) (6)

Subject: Re: IACUC Protocol 16-02-042

Hello,

I have attached a response to your email below.

I truly believe this was a miscommunication.

Please let me know what the next steps need to be.

Thank you,

(b) (6)

03/15/19 (b) (6) sent the following email (with (b) (6) response attached)–

From: (b) (6)

Sent: Friday, March 15, 2019 3:51 PM

To: Moh Malek (b) (6); Gerald Hish (b) (6); (b) (6)

(b) (6)

Subject: RE: IACUC Protocol 16-02-042

Importance: High

Hi All,

I am attaching Dr. (b) (6) response to the inquiry below. According to our SOP "The IACUC Chair and AV (Attending Veterinarian) (or designated DLAR veterinarian) will have 24 hours to decide on the best course of action based on the information obtained during the inquiry. This may include one or more of the following:

- i. Dismissal of the allegation (unsubstantiated)
- ii. Referral to other appropriate university process
- iii. Immediate corrective action required (implemented by AV and/or IACUC Chair). Immediate action is always taken if there are animal welfare concerns.
- iv. Review at a convened IACUC meeting
- v. Further investigation required by the compliance specialist"

I am assuming "Review at a convened IACUC meeting", but please let me know officially by Monday on how you would like me to proceed.

Thanks,

(b) (6)

03/18/19

03/17/19 Dr. Malek Replied –

From: Moh Malek

Sent: Sunday, March 17, 2019 10:16 PM

To: (b) (6) Gerry Hish (b) (6) (b) (6)

(b) (6)

Subject: RE: IACUC Protocol 16-02-042

Hi (b) (6)

Yes, this will be 'Review at a convened IACUC meeting.'

03/18/19 Dr. Hish Replied –

From: Gerry Hish

Sent: Monday, March 18, 2019 8:15 AM

To: Moh Malek (b) (6) (b) (6) (b) (6)

(b) (6)

Subject: Re: IACUC Protocol 16-02-042

Hi everyone,

I agree. The lab has already reached out to Dr. (b) (6) to discuss supportive measures moving forward but we should review it with the group.

Gerry

Final Report Summary

- An AE involving administration of MnCl for imaging was reported during the convened IACUC meeting on 02/27/19.
- It was also reported that veterinary instructions from 11/6/18 were to meet and discuss supportive care options prior to proceeding with administration of MnCl. At that time the laboratory indicated that this was not going to be done again in the near future.
- There have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting.
- The IACUC asked the Research Compliance Specialist to follow up and report as potential non-compliance at a future meeting.
- The Research Compliance Specialist requested any veterinary correspondence documenting the incident between the vet and the PI.
- **The Compliance Specialist was forwarded the following email notification that was sent to the PI and research staff on November 2, 2018.**
Subject: Supportive care for MnCl injections

Hi all,

I am providing a summary of my verbal recommendation earlier today that was given in light of recent (3 of 3 animals affected July 2018) and today's adverse outcomes with MnCl injection. **Also, can you please let me know how many MnCl injections did these two rats receive in the past, as well as the doses for each injection?**

In your protocol, it is noted that some animals can develop illness after MnCl administration, and that supportive care will be given if needed AND more than 36 hours will elapse prior to euthanasia. **Based on the potential severity of toxicity/outcome (death) and inability to pre-determine which animals will be negatively affected following MnCl injection, I strongly recommend that all animals receiving MnCl injection also get SQ fluids and an analgesic (carprofen) at the same time as MnCl injection and on the following day, and then as needed thereafter.** Some researchers on campus use lower MnCl doses and achieve good contrast for imaging procedures, so we could also consider lowering the dose, but also with this in mind, I am not overly concerned about concurrent fluid administration affecting MnCl elimination to the degree that contrast would be ineffective at the time of imaging.

I would like to have this resolved ASAP (i.e. before proceeding with additional MnCl injections), and so that animals currently injected can receive supportive care ASAP.

Thanks for your time and attention to this matter,

- **The PI's Lab Manager/Research Assistant replied to the above email on November 2, 2018**
Subject: Re: Supportive care for MnCl injections

Hello.....,

All our animals are receiving only one MnCl injection.

These two animals from this morning (the one that was found dead and the one we are going to euthanize after imaging) received MnCl injection yesterday.

Thank you,

- **The WSU Veterinarian sent the following Reply on November 02, 2018**

Subject: Re: Supportive care for MnCl injections

Thanks for the additional information! In the protocol, it appeared that animals could receive several MnCl injections over the course of the study. Is that not the case?

- The WSU Veterinarian sent the following Reply on November 06, 2018
In talking with (*Lab Manager*), it sounds like multiple MnCl injections are no longer administered, as is stated in the protocol, but please respond with your thoughts regarding recommendations to improve outcomes following MnCl injections. If you don't foresee moving forward with this procedure for awhile, we can discuss another time, but before proceeding. Let me know if it would be easier to set up a meeting to discuss further.

Thanks!

P.S. The incision repair is looking great!

- **The PI responded on November 06, 2018**

Subject: Re: Supportive care for MnCl injections

Hello,

I am out of town until Friday, but I am in discussion with the lab to identify possible causes.

Thank you,

- **Veterinary response November 06, 2108**

Subject: Re: Supportive care for MnCl injections

Ok, thanks for letting me know. I look forward to hearing from you soon.

- The Research Compliance Specialist contacted the PI to inquire about the potential compliance issue related to not following veterinary recommendation to provide analgesics and SQ fluids to rats when injecting MnCl, and/or not meeting with the vets to discuss supportive care prior to proceeding with additional MnCl injections.
- The PI's initial response (attached) indicated that she believed there was some confusion in terms of the communication between the lab manager, other lab personnel, and the veterinarian.
- The PI stated, since the animals were only receiving one injection, based on the subsequent email, they thought that the issue with administration of SQ fluids and Carprofen was resolved.

- The PI also indicated that lab personnel did mentioned to the veterinarian that MnCl2+ injections were not going to be performed again in the near future. This was due to the fact that the MRI scanner was slated to be shut down to perform upgrades for at least two months beginning December first.
- The PI was traveling in November at the time of the incident but stated via email that they would discuss the issue with lab. The PI states that they did discuss with the lab how they might improve outcomes after MnCl2+ administration. Since they had several animals receiving MnCl2+ or having surgeries during that time they had a thorough review and discussion of their procedures and outcomes.
- In her initial response the PI also stated that they failed to see the part of the email requiring a meeting with the veterinarian before any new MnCl2+ injections. This was an oversight on their part.
- When they were told that the MRI scanner would continue to be available through January (and now until mid April), they continued with our studies.
- The lab has already reached out to the WSU veterinarian to discuss supportive measures moving forward.
- There have not been any previous non-compliance issues involving this PI.

03/18/19 (b) (6) sent the draft of the final summary, and Dr. (b) (6) reply to Dr. Hish and Malek for review.

From: (b) (6)

Sent: Monday, March 18, 2019 4:00 PM

To: Moh Malek (b) (6) Gerald Hish (b) (6)

Subject: Draft (b) (6) Final

Hi,

I am attaching a draft of the final report of the potential compliance issue involving Dr. (b) (6) protocol. I will redact her initial response (also attached) when sending out to the IACUC.

I included the contents of the email correspondence in the final report because I though it substantiated Dr. (b) (6) assessment that there was some "confusion in terms of the communication between the lab manager, other lab personnel, and the veterinarian".

Please review and let me know if you would like any changes.

Thanks,

(b) (6)

(b) (6)

(b) (6)
(b) (6)
(b) (6)
(b) (6)

03/19/19 Dr. Malek Replied –

From: Moh Malek

Sent: Tuesday, March 19, 2019 7:05 AM

To: (b) (6) Gerry Hish (b) (6)

Subject: RE: Draft (b) (6) Final

Hi (b) (6)

Those look fine to me.

thanks, Moh

03/19/19 (b) (6) sent the following email to Dr. (b) (6) with the final summary and her redacted reply attached.

From: (b) (6)

Sent: Tuesday, March 19, 2019 9:11 AM

To: (b) (6)

Cc: Moh Malek (b) (6) Gerry Hish (b) (6) (b) (6)

Subject: IACUC Protocol 16-02-042

Importance: High

Dear Dr. (b) (6),

I am contacting you to inform you that the IACUC Chair and Attending Veterinarian have determined that the best course of action involving the potential issue(s) with your protocol is "review at a convened IACUC meeting".

I am attaching the final report summary, and your redacted initial response that will be distributed to the IACUC for review at the convened meeting on 03/27/19.

Per Wayne State University's SOP "Investigation and Remediation of Non-Compliance and Animal Welfare" you have 5 business days to provide a written response to the attached report. You also have the opportunity to attend the IACUC meeting on 03/27/19.

Thank you,

(b) (6)

03/27/19 (b) (6) sent the following email to Dr. (b) (6) with her redacted response and final summary attached.

From: (b) (6)

Sent: Wednesday, March 27, 2019 10:21 AM

To: (b) (6)

Subject: IACUC Protocol

Hi Dr. (b) (6)

Attached is the report and your reply that will be discussed at the IACUC meeting today.
Were you planning to attend?

Thanks,

(b) (6)

(b) (6)

***Attached Document "031919_Final Report Summary"**
Final Report Summary for 03/27/19 IACUC Meeting

- An AE involving administration of MnCl for imaging was reported during the convened IACUC meeting on 02/27/19.
- It was also reported that veterinary instructions from 11/6/18 were to meet and discuss supportive care options prior to proceeding with administration of MnCl. At that time the laboratory indicated that this was not going to be done again in the near future.
- There have been 5 rats injected since the beginning of the year and the lab did not contact the veterinary staff to meet prior to starting.
- The IACUC asked the Research Compliance Specialist to follow up and report as potential non-compliance at a future meeting.
- The Research Compliance Specialist requested any veterinary correspondence documenting the incident between the vet and the PI.
- **The Compliance Specialist was forwarded the following email notification that was sent to the PI and research staff on November 2, 2018.**
Subject: Supportive care for MnCl injections

Hi all,

I am providing a summary of my verbal recommendation earlier today that was given in light of recent (3 of 3 animals affected July 2018) and today's adverse outcomes with MnCl injection. **Also, can you please let me know how many MnCl injections did these two rats receive in the past, as well as the doses for each injection?**

In your protocol, it is noted that some animals can develop illness after MnCl administration, and that supportive care will be given if needed AND more than 36 hours will elapse prior to euthanasia. **Based on the potential severity of toxicity/outcome (death) and inability to pre-determine which animals will be negatively affected following MnCl injection, I strongly recommend that all animals receiving MnCl injection also get SQ fluids and an analgesic (carprofen) at the same**

time as MnCl injection and on the following day, and then as needed thereafter.

Some researchers on campus use lower MnCl doses and achieve good contrast for imaging procedures, so we could also consider lowering the dose, but also with this in mind, I am not overly concerned about concurrent fluid administration affecting MnCl elimination to the degree that contrast would be ineffective at the time of imaging.

I would like to have this resolved ASAP (i.e. before proceeding with additional MnCl injections), and so that animals currently injected can receive supportive care ASAP.

Thanks for your time and attention to this matter,

- **The PI's Lab Manager/Research Assistant replied to the above email on November 2, 2018**

Subject: Re: Supportive care for MnCl injections

Hello.....,

All our animals are receiving only one MnCl injection.

These two animals from this morning (the one that was found dead and the one we are going to euthanize after imaging) received MnCl injection yesterday.

Thank you,

- **The WSU Veterinarian sent the following Reply on November 02, 2018**

Subject: Re: Supportive care for MnCl injections

Thanks for the additional information! In the protocol, it appeared that animals could receive several MnCl injections over the course of the study. Is that not the case?

- The WSU Veterinarian sent the following Reply on November 06, 2018
In talking with (*Lab Manager*), it sounds like multiple MnCl injections are no longer administered, as is stated in the protocol, but please respond with your thoughts regarding recommendations to improve outcomes following MnCl injections. If you don't foresee moving forward with this procedure for awhile, we can discuss another time, but before proceeding. Let me know if it would be easier to set up a meeting to discuss further.

Thanks!

P.S. The incision repair is looking great!

- **The PI responded on November 06, 2018**

Subject: Re: Supportive care for MnCl injections

Hello,

I am out of town until Friday, but I am in discussion with the lab to identify possible causes.

Thank you,

- **Veterinary response November 06, 2108**

Subject: Re: Supportive care for MnCl injections

Ok, thanks for letting me know. I look forward to hearing from you soon.

- The Research Compliance Specialist contacted the PI to inquire about the potential compliance issue related to not following veterinary recommendation to provide analgesics and SQ fluids to rats when injecting MnCl, and/or not meeting with the vets to discuss supportive care prior to proceeding with additional MnCl injections.
- The PI's initial response (attached) indicated that she believed there was some confusion in terms of the communication between the lab manager, other lab personnel, and the veterinarian.
- The PI stated, since the animals were only receiving one injection, based on the subsequent email, they thought that the issue with administration of SQ fluids and Carprofen was resolved.
- The PI also indicated that lab personnel did mention to the veterinarian that MnCl₂+ injections were not going to be performed again in the near future. This was due to the fact that the MRI scanner was slated to be shut down to perform upgrades for at least two months beginning December first.
- The PI was traveling in November at the time of the incident but stated via email that they would discuss the issue with lab. The PI states that they did discuss with the lab how they might improve outcomes after MnCl₂+ administration. Since they had several animals receiving MnCl₂+ or having surgeries during that time they had a thorough review and discussion of their procedures and outcomes.
- In her initial response the PI also stated that they failed to see the part of the email requiring a meeting with the veterinarian before any new MnCl₂+ injections. This was an oversight on their part.
- When they were told that the MRI scanner would continue to be available through January (and now until mid April), they continued with their studies.
- The lab has already reached out to the WSU veterinarian to discuss supportive measures moving forward.
- There have not been any previous non-compliance issues involving this PI.

*Attached Document (b) (6) Response (b) (6) _2019"

March 15, 2019

Dear Mr. (b) (6)

I appreciate the opportunity to provide a response to this issue. I believe there was some confusion in terms of the communication between my lab manager, other lab personnel, and the veterinarian. First, since the animals were only receiving one injection, based on the subsequent email, we thought that the issue with administration of SQ fluids and Carprofen was resolved. Second, my lab personnel mentioned to the veterinarian that MnCl₂+ injections were not going to be performed again in the near future. This was due to the fact that the MRI scanner was slated

to be shut down to perform upgrades for at least two months beginning December first. Since then the date for the MRI upgrades have been delayed on several occasions. I was traveling in November at the time of the incident and stated via email that I would discuss the issue with lab. I did discuss with the lab how we could improve outcomes after MnCl₂+ administration. Since we had several animals receiving MnCl₂+ or having surgeries during that time we had a thorough review and discussion of our procedures and outcomes. We failed to see the part of the email requiring a meeting with the veterinarian before any new MnCl₂+ injections. This was an oversight on our part. When we were told that the MRI scanner would continue to be available through January (and now until mid April), we continued with our studies. We would like to meet with the veterinarian to discuss our MnCl₂+ protocol and what we have learned. Please let us know the best course of action from this point forward. Best regards,

(b) (6)

03/27/10 IACUC Meeting

After considerable discussion the IACUC voted (7-6) that this represents noncompliance. They voted 11 in favor, 2 abstain that this represents minor noncompliance.

03/28/19 (b) (6) sent the following email –

From: (b) (6)

Sent: Thursday, March 28, 2019 9:36 AM

To: (b) (6)

Cc: Moh Malek (b) (6) Gerald Hish (b) (6) (b) (6)

(b) (6)

Subject: IACUC Protocol 16-02-042

Importance: High

Dear Dr (b) (6)

I am writing to inform you that the inquiry report involving potential non-compliance with your protocol 16-02-042 was discussed during the convened IACUC meeting on 03/27/19. The Committee also reviewed your response to the non-compliance inquiry. The incident involved not following veterinary recommendation to provide analgesics and SQ fluids to rats when injecting MnCl, and/or not meeting with the vets to discuss supportive care prior to proceeding with additional MnCl injections.

After careful discussion, the committee members voted that the incident constitutes minor noncompliance and acknowledged that you are currently working with veterinarians to address the issue to prevent further occurrences.

Reoccurrence(s) of this issue, or other non-related noncompliance issues, may result in a finding of serious and/or continuing non-compliance by the IACUC which, by federal law, would require reporting to WSU's Institutional Official (IO). The IO would be required to report the incident to The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), the Office of Laboratory Welfare (OLAW) and funding agencies *if PHS or NSF funded*, the Office of Research Oversight *if VA funded*, and/or the Department of Defense *if funded by the DOD*.

Thank you for your prompt response in resolving this matter when it was identified.

You have 5 business days to appeal this decision in writing.

(b) (6) [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

(b) (6)_DLAR_042419 (16-12-179)

04/24/19 Dr. Hish reported the following AE –

"On 4/1/2019 a dead, partially cannibalized female mouse was found in a large, Group II cage at the VA. Five additional female mice were present in the cage and were all found to have mild dehydration and mildly decreased body condition. The cage had food but no water bottle. The laboratory stated that they had not manipulated the cage in the previous week and DLAR staff (3 different technicians) had documented observation of food and water in all cages in the previous week. The cage had last been changed on 3/27/19 according to the room log".

"A water bottle and soft chow was immediately supplied. All animals responded well".

Dr. Hish said it was unlikely that the mice would have been in the condition noted if the water bottle had not been present at the time of the cage change on 03/27/19, and asked me to initiate a non-compliance inquiry with both the PI and DLAR. **However, I will not use the wording "non-compliance" in the inquiry. Rather just state that the "IACUC has asked me to look into a situation involving the water bottle".**

04/24/19 Dr. Hish forwarded (b) (6) the following email string –

From: Gerry Hish

Sent: Wednesday, April 24, 2019 2:46 PM

To: (b) (6)

Subject: Fwd: (b) (6) cage J1933b-2-J1930b, case # 4639 Update

Email regarding cage without bottle.

From: (b) (6)

Sent: Thursday, April 4, 2019 1:09 PM

To: Gerry Hish; (b) (6)

Cc: (b) (6)

Subject: Re: (b) (6) cage J1933b-2-J1930b, case # 4639 Update

All the mice are a/a, BC3 with normal hydration. I have d/c monitoring of this case.

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

From: (b) (6)
Sent: Monday, April 1, 2019 4:35 PM
To: Gerry Hish; (b) (6)
Cc: (b) (6)
Subject: (b) (6) cage J1933b-2-J1930b, case # 4639

On Monday, 4/1/2019 at approximately 2 p.m., while checking room LL349, (b) (6) protocol 16-12-179, I noticed a group 2 mouse poly J1933b-2-J1930b, that contained a deceased mouse (# J2188) which had been cannibalized by its 5 female cage mates. The cage did not have a water bottle. The remaining 5 mice were found to be BC2-3 with mild dehydration. The cage contained scant feces. I promptly gave a water bottle to the cage and soft chow. I reported the incident in person to (b) (6) (b) (6), who maintains the colony and to Dr. (b) (6) by phone. The colony manager had not manipulated the cage the previous week. An illness report was initiated and entered into system late p.m. on 4/1/19 by (b) (6). The body of J2188 was bagged/tagged (marked save) and placed in freezer.

The room had been serviced the previous week as follows:

3/25/19: Room was checked by (b) (6) 7 cages changed as needed, trash removed by (b) (6) (b) (6)

3/26/19: Room was checked by (b) (6) fed an, 3 polys changed as needed, trash removed, 1 shelf unit of filter tops changed, filled food barrel by (b) (6)

3/27/19: Room checked by (b) (6) **Polys and bottles changed**, trash OK, sweep and mopped box checked, air filter box checked, light timer box checked by (b) (6)

3/28/19: Room checked by (b) (6) F/W box checked.

3/29/19: Room checked by (b) (6) F/W box checked, change poly an box checked, trash marked OK, Sweep/Mop marked OK.

3/30/19: Room checked by (b) (6) F/W box marked ok. Poly box marked ok. Comments noted: 2 new litters.

3/31/19: Room checked by (b) (6) F/W box check marked.

Mouse J2188 was born in house on 1/14/19. Weaned 2/4/19. Strain: TGTPH2. Protocol 16-12-179. Room LL349/VA. Pl: (b) (6)

Sincerely,

(b) (6)
(b) (6)
(b) (6)

(b) (6)

04/25/19 (b) (6) sent the following email to Carrie James –

From: (b) (6)

Sent: Thursday, April 25, 2019 11:45 AM

To: (b) (6)

Subject: Kuhn 16-12-179

Hi (b) (6)

Yesterday the IACUC asked me to look into the situation involving the missing water bottle on one of Dr. (b) (6) cages. Dr. Hish has already forwarded me your email report describing the situation and time line.

Can you tell me if there is/was any documentation of lab procedures with this cage between the time of the cage change and the incident discovery?

Also, do you have any idea of how this may have happened?

Thanks,

(b) (6)

(b) (6)

04/25/19 (b) (6) Replied –

From: (b) (6)

Sent: Thursday, April 25, 2019 11:52 AM

To: (b) (6)

Cc: (b) (6)

Subject: Re: Kuhn 16-12-179

I have cc'd (b) (6) the breeder of these mice to provide you with the requested information.

I can not provide any more insight into how this happened, I can only assume that the bottle was not added at time of cage change. The documentation of the room chart is all I have to go by.

If you have additional inquiries, please feel free to call or email me.

(b) (6)

Sincerely,

(b) (6)

04/25/19 (b) (6) replied –
From: (b) (6)
Sent: Thursday, April 25, 2019 12:23 PM
To: (b) (6)
Subject: Re: (b) (6) 16-12-179

Hello,

The cage in question had last been manipulated by me on 2/4/19 - the day of weaning. The cage was placed on the rack at that time. There was no further handling of the mice/cage by me or any of the Kuhn personnel.

Please let me know if there is further information required.

Thanks,

(b) (6)

05/02/19 (b) (6) copied the email strings above and sent the email below to Dr. Hish –
From: (b) (6)
Sent: Thursday, May 2, 2019 9:51 AM
To: Gerald Hish (b) (6)
Subject: (b) (6) Protocol

Hi Gerry,

Can you give me some ideas on how I can help looking into the water bottle situation. I kind of feel like I am at a dead.

Here are the emails that I sent and replied –

Thanks,

(b) (6)

05/22/19 at the convened IACUC meeting the IACUC voted unanimously that the situation was a reportable AE (versus non-compliance), and was to be reported by the IACUC Attending Veterinarian.

05/23/19 (b) (6) sent the following email –

From: (b) (6)
Sent: Thursday, May 23, 2019 8:38 AM
To: Gerald Hish (b) (6)
Cc: Moh Malek (b) (6)
(b) (6)
Subject: Adverse Event 16-12-179

Hi Dr. Hish,

At yesterday's meeting the IACUC voted unanimously that the AE reported at last month's meeting involving the lack of a water bottle on the above protocol to be a "reportable adverse event" (versus non-compliance).

They were made aware that you were going to report the situation to OLAW.

Thank you,

(b) (6)

(b) (6)

(b) (6)



Philip R Cunningham, Ph.D.

(b) (6)

(b) (6)

Animal Welfare Assurance Number: D16-00198

June 3, 2019

Brent C. Morse, DVM, DACLAM, Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892
olawdco@mail.nih.gov

RE: Report of Serious Adverse Event

Dr. Morse:

I am writing to report a serious adverse event that occurred on April 1, 2019.

A dead, partially cannibalized female mouse was found in a large mouse cage with food but no water bottle. Five additional female mice were present in the cage and were all found to have mild dehydration and mildly decreased body condition. A water bottle and soft chow was immediately supplied to the dehydrated mice and all animals responded well.

Upon review of the daily husbandry log for that room and following a discussion with husbandry technicians servicing the room, it was determined that the last recorded handling by husbandry staff had occurred five days prior, on March 27, 2019. Food and water were present in all cages in the room on each day of the previous week according to logbook entries on three separate days by different technicians. The laboratory staff stated that they had not manipulated the cage in the previous week. While it seems unlikely that the remaining five mice could survive for 4-5 days without access to water, no alternative scenario was supported by the available evidence.

The adverse event was reported to the IACUC by the Attending Veterinarian on April 24, 2019 after a preliminary phone consultation with OLAW and the IACUC requested that the Research Compliance Specialist (RCS) investigate the incident. The RCS reported that the investigation yielded no additional information during a convened meeting of the IACUC on May 22, 2019 which determined the event to be a reportable serious adverse event.

Corrective actions: Signage has been posted throughout all vivaria reminding husbandry and laboratory personnel to check cages for both water and food and the incident has been discussed with husbandry staff as part of focused retraining.

Please contact me if you would like additional information.

Sincerely,

Philip R. Cunningham, Ph.D.
Institutional Official

c.c. Moh Malek, Ph.D., IACUC Chair, (b) (6)
Gary L. Borkowski, D.V.M., M.S., AAALAC International, accredit@aaalac.org

(b) (6) **051417**

05/14/17 (b) (6) received this email from (b) (6)
From: (b) (6)
Sent: Tuesday, May 14, 2019 9:17 AM
To: (b) (6)
Subject: FW: VA Animal Lab Issue

(b) (6) do you have details about this? I don't know anything about it.

Thanks,
(b) (6)

From: (b) (6)
Sent: Tuesday, May 14, 2019 7:57 AM
To: (b) (6)
Subject: VA Animal Lab Issue

Good Morning (b) (6)

I was told that one of Dr. Mateika's animal lab employees made a complaint to IACUC that Dr. Mateika tried to make them do a procedure or procedures that were not approved by IACUC. When they refused, Dr. Mateika pressured them to do the unapproved procedure/s. I wanted to check with you to see if this is correct, and if IACUC will deliberate on this in the next meeting. I appreciate the information!

Thanks,
(b) (6)

(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)

05/14/19 (b) (6) replied -
From: (b) (6)
Sent: Tuesday, May 14, 2019 9:19 AM
To: (b) (6)
Subject: RE: VA Animal Lab Issue

Hi (b) (6)

No one has reported this situation to me.

Thanks,

(b) (6)

05/14/19 (b) (6) was cc'd on the following email –

From: (b) (6)

Sent: Tuesday, May 14, 2019 9:36 AM

To: (b) (6)

Cc: (b) (6)

Subject: RE: VA Animal Lab Issue

(b) (6)

Thanks. I c.c.'d Joe, he will be the person who will look into the allegation.

(b) (6)

From: (b) (6)

Sent: Tuesday, May 14, 2019 9:30 AM

To: (b) (6)

Subject: RE: VA Animal Lab Issue

Not yet, I got this info from the AO of Research (b) (6) I'll look into it further and I'll let you know what I find out. I was also told the employee is planning on leaving the lab because of this incident.

Thanks,

(b) (6)

(b) (6)

(b) (6)

(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)

From: (b) (6)

Sent: Tuesday, May 14, 2019 9:26 AM

To: (b) (6)

Subject: [EXTERNAL] RE: VA Animal Lab Issue

(b) (6)

I checked with (b) (6) Research Compliance Specialist, he hasn't received a complaint from anyone. I haven't either. If anyone in our office spoke with someone she would have referred it to

(b) (6) Have you spoken with the employee to find out who he/she spoke with?

Thanks,

(b) (6)

05/17/19 (b) (6) was copied on the following email –

From: (b) (6)

Sent: Friday, May 17, 2019 10:09 AM

To: (b) (6)

Cc: (b) (6)

Subject: RE: VA Animal Lab Issue

The study staff that are allegedly making the complaint are Janet Wolforth and Mallika Somayajulu. I have not been able to reach them directly yet, but am told they are both looking for new jobs. They could be afraid to make the complaint to Joe, for fear of losing their jobs before they have found another job? I will make every attempt to speak with them.

Thanks,

(b) (6)

(b) (6)
(b) (6)
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05/17/19 (b) (6) sent the following reply with the SOP for reporting animal welfare concerns attached.

From: (b) (6)

Sent: Friday, May 17, 2019 1:23 PM

To: (b) (6)

Subject: RE: VA Animal Lab Issue

Hi (b) (6)

I don't know if it will help, but per the attached SOP they can report anonymously if desired and will be protected from discrimination and reprisal.

Thanks,

(b) (6)

(b) (6) Replied –

From: (b) (6)

Sent: Friday, May 17, 2019 1:56 PM

To: (b) (6)

Subject: RE: VA Animal Lab Issue

Very helpful to know! They are both going to come talk to me on Monday morning, they didn't want to put anything in e-mail. So, I'll let them know about this option. One of them has quit and her last day is early next week. I'll keep you apprised of what happens with our talk on Monday.

Thanks,

(b) (6)

(b) (6) Replied –

From: (b) (6)

Sent: Friday, May 17, 2019 3:55 PM

To: (b) (6)

Subject: RE: VA Animal Lab Issue

(b) (6)

Please let me know if you would like me to be there with you on Monday as well.

Thanks again,

Joe

05/20/19 (b) (6) discussed the potential situation with Dr. Hish, (b) (6) and Dr. Malek at the IACUC agenda meeting this morning, and said that he would forward Amy's report when it was submitted.

05/20/19 (b) (6) received the following email from (b) (6) (with attached Report saved in NC binder)–

From: (b) (6)

Sent: Monday, May 20, 2019 1:06 PM

To: (b) (6)

(b) (6)

(b) (6)

Subject: Report IACUC # 17-01-199

Good Afternoon WSU IACUC Administration,

I have attached a report of problems relayed to me in the following study:

PI: (b) (6)

Title: 5-HT Modulation of Arousal and Chemoreflex Responses in Intact and SCI Mice

17-01-99

Please feel free to reach out to me if you have any questions.

Sincerely,

(b) (6)

(b) (6)

(b) (6)

Attached Report pasted below –
May 20, 2019

WSU IACUC Administration Office
87 East Canfield, Second Floor
Detroit, MI 48201

Dear IACUC Committee:

I am writing to inform you of problems that have come to my attention regarding the following study:

PI: (b) (6)

Study Title: 5HT Modulation of Arousal and Chemoreflex Responses in Intact and SCI Mice
IACUC #: 17-01-199

On 5/20/19 2 employees of Dr. (b) (6) working on the above-named study came to me to discuss some problems that they have encountered involving their work in the lab. Both employee's wish to remain anonymous due to fear of reprisal or intimidation by the PI. The employees relayed that Dr. (b) (6) instructed them to perform a procedure that was not approved by the IACUC and in their estimation, would cause undue suffering to the animal with little chance of scientific gain. The animal in question had already undergone surgical placement of a telemetry unit to monitor activity of the genioglossus muscle and EEG activity (procedures approved by IACUC). The telemetry unit failed, and the PI directed the staff (in an e-mail initially) to perform surgery to remove the failed telemetry until and place a new unit with new leads and sensors. A second surgery for removal and replacement of failed telemetry units is not currently approved in the protocol. During a staff meeting the following working day, the PI again directed them to do the additional surgery. The employee who would be responsible to perform the surgery explained that this additional procedure is not approved by IACUC, and that the animal would not likely survive the second surgery due to the invasiveness of the surgery and the stress on the animal from the first surgery. The employee stated that she would not perform the surgery. The PI was angry, yelled at the staff members and told them to write a protocol modification amendment for the procedure. The surgical staff explained that the IACUC would probably not approve the additional surgery due to the low likelihood of animal survival. The animal was later euthanized. The surgical staff member stated that she had reported and discussed this incident with Dr. (b) (6) (VA Safety Officer) and (b) (6) (VA Administrative Officer for Research).

In addition, both employees relayed that if an animal loses >20% of body weight and has a poor body condition post-operatively, that the animal is to be euthanized per protocol. The PI directs them to inject the animal with subcutaneous fluids before weighing the animals to increase their body weight. The employees communicated that the PI seems to be more concerned about obtaining data than following protocol or the welfare of the animals, in their experience. They also said that the PI "bullies" his employees by yelling at them and questioning their work ethic when they disagree with him or bring up problems with the techniques they are using. They stated that a previous employee of his also made a complaint to the IACUC about him. They expressed feeling intimidated by him.

I provided the employees with a copy of the Wayne State University IACUC SOP titled: Reporting Animal Welfare Concerns, which states that concerned parties may remain anonymous and will be protected from discrimination and reprisal. The SOP also lists the WSU Office of Internal Audit anonymous hotline.

The employees declined to call the hotline, as they felt that reporting to me and the others listed above should be sufficient.

Please feel free to contact me if have any questions.

Sincerely,

(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(b) (6)

CC: (b) (6) VA Facility Director; (b) (6) Research ACOS; (b) (6) Chair R&D Committee;
(b) (6) WSU Animal Research Compliance

05/20/19 (b) (6) forwarded the above email to Dr. Hish, Malek, and (b) (6)

From: (b) (6)

Sent: Monday, May 20, 2019 1:24 PM

To: Moh Malek (b) (6) Gerald Hish (b) (6) (b) (6) (b) (6)

(b) (6)

Subject: FW: Report IACUC # 17-01-199

Hi,

I just received this report from (b) (6) regarding the incident that we discussed this morning.

Thanks,

05/20/19 (b) (6) discussed with (b) (6) stating his impression that since the lab staff didn't perform the procedures as directed, that (in his opinion) this likely not be considered protocol non-compliance. Non-compliance if any, would likely be related to giving fluids to mask euthanasia criteria. (Not discussed with (b) (6) but a note to self: Still, if fluids are approved to treat dehydration in the protocol, this would be debatable as well.

05/20/19 (b) (6) sent the following reply to Amy -

From: (b) (6)

Sent: Monday, May 20, 2019 1:33 PM

To: (b) (6)

Cc: (b) (6) Gerald Hish (b) (6)

(b) (6); Moh Malek (b) (6)

Subject: RE: Report IACUC # 17-01-199

Hi (b) (6),

Do you know how often (if ever) fluids were given in an effort to mask euthanasia criteria?

Thanks,

(b) (6)

05/20/19 (b) (6) Replied –

From: (b) (6)

Sent: Monday, May 20, 2019 1:48 PM

To: (b) (6)

Cc: Dorinda Monsor (b) (6); Gerry Hish (b) (6); Moh Malek

(b) (6)

Subject: RE: Report IACUC # 17-01-199

No, I'm sorry, they were not that specific as to dates or specific incidents for the fluid injections. I got the impression it was done upon his request, but not how often this occurred.

Thanks,

(b) (6)

05/20/19 Protocol Review – 17-01-199

The protocol approves multiple recovery surgeries in mice for Transducer implantation, hemisection, measurement of upper airway collapsibility, and catheter adjustment. However, the protocol does not approve a second surgery for replacing failed telemetry devices.

Euthanasia –

1. STATE the SPECIFIC CRITERIA for the euthanasia of abnormal or moribund animals (assume someone may have to euthanize animals IN YOUR ABSENCE). Review the Defining Humane Endpoints Guideline.
 - ☐ Not Applicable (e.g. animals are used for tissue harvesting only and will not undergo any procedures prior to death)

Weight loss of 20% or more

Other conditions (examples may include, but are not limited to: a clinical condition that does not respond to treatment, such as an infected surgical site; any condition that a veterinarian deems severe enough to warrant euthanizing the animal). *Please describe below:*

(1) Scratching of incision that cannot be relieved (2) Absence of ambulation 24 hours following surgery. **(3) Severe dehydration which does not improve with oral and SQ fluid therapy** (4) Urinary blockage. **(5) If the mice remain dehydrated resulting in a greater than 20 % reduction in weight, despite oral and SQ re-hydration therapy, and have a body condition of less than 2 out of 5, the animal will be euthanized.**

Summary – Since the lab staff intervened without performing the second surgery for telemetry device replacement, and looking at the fairly specific euthanasia regarding euthanasia criteria and fluid therapy; I think it is very unlikely that the situation reported represents protocol non-compliance.

05/20/19 (b) (6) sent Dr. Cunningham the following email (With (b) (6) report attached)–

From: (b) (6)

Sent: Monday, May 20, 2019 2:42 PM

To: Philip Cunningham (b) (6)

Cc: Moh Malek (b) (6)

Subject: FW: Report IACUC # 17-01-199

Phil,

The IACUC will review this letter from (b) (6) at the meeting this week, but I wanted to make sure you received a copy today.

Thanks,

(b) (6)

05/20/19 (b) (6) sent the following email –

From: (b) (6)

Sent: Monday, May 20, 2019 3:17 PM

To: Moh Malek (b) (6) Gerald Hish (b) (6) (b) (6)

(b) (6)

Cc: Philip Cunningham (b) (6)

Subject: IACUC Protocol 17-01-199

Good afternoon,

I am writing in response to (b) (6) report concerning Dr. (b) (6)

It appears that laboratory staff intervened to prevent a second surgery that if performed, would have been a compliance issue.

Also, I contacted Amy and she was not sure of specific details related to SQ fluids (to circumvent euthanasia) as the letter seemed to imply.

I reviewed the protocol and there is some pretty specific wording related to euthanasia criteria. The protocol reads –

1. STATE the SPECIFIC CRITERIA for the euthanasia of abnormal or moribund animals (assume someone may have to euthanize animals IN YOUR ABSENCE). Review the Defining Humane Endpoints Guideline.

Not Applicable (e.g. animals are used for tissue harvesting only and will not undergo any procedures prior to death)

Weight loss of 20% or more

Other conditions (examples may include, but are not limited to: a clinical condition that does not respond to treatment, such as an infected surgical site; any condition that a veterinarian deems severe enough to warrant euthanizing the animal). *Please describe below:*

- (1) Scratching of incision that cannot be relieved
- (2) Absence of ambulation 24 hours following surgery.
- (3) Severe dehydration which does not improve with oral and

SQ fluid therapy (4) Urinary blockage. (5) If the mice remain dehydrated resulting in a greater than 20 % reduction in weight, despite oral and SQ re-hydration therapy, and have a body condition of less than 2 out of 5, the animal will be euthanized.

Please let me know how you would like me to proceed.

Thank you,

(b) (6)

05/21/19 (b) (6) made the decision that the letter from (b) (6) should not be redacted. I thought that it should have been redacted.

From: (b) (6)

Sent: Tuesday, May 21, 2019 12:00 PM

To: (b) (6)

Gerry Hish (b) (6)

Moh Malek (b) (6)

Cc: Joseph Monsur (b) (6)

Subject: IMPORTANT: Meeting agenda items

Dear all,

We are going to have a very busy meeting tomorrow, primarily because of non-compliance agenda items. I have added an important letter for you to review prior to the meeting from Dr. (b) (6) the VA Research Compliance Office. **She has brought to our attention allegations of potential non-compliance of an investigator at the VA. Because this letter is directly from the VA to the IACUC, it has not been redacted. As you know, we need to keep the utmost confidentiality when it comes to all animal welfare allegations, especially for one as delicate as the one that will be presented tomorrow.**

I encourage **all committee members** to review the letter. It has been posted on Teams under Non-compliance Agenda Items (May 2019 meeting – VAMC letter from Compliance Officer).

If you have questions or are having difficulty accessing Teams, please let me know.

Thanks,

(b) (6)

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(b) (6)

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(b) (6)

05/22/19 The report from (b) (6) was reviewed at the convened IACUC meeting. Dr. (b) (6) asked if there was anything in the protocol describing fluid therapy, and I provided the text in the euthanasia section.

Dr. (b) (6) added that Dr. (b) (6) mice are monitored closely, and that she was the one who recommended the fluid therapy, and wording in the euthanasia section. She said that even with fluid therapy, she could not say that mice were being maintained beyond protocol end points, and not being euthanized appropriately.

The Committee believed that this was a personnel issue, more than a potential non-compliance.

However they were concerned that the situation could worsen when the two individuals leaving the PI's lab are replaced and trained by Dr. (b) (6)

The Committee requested a follow-up PAM once the new individuals are hired.

05/23/19 (b) (6) sent the following email –

From: (b) (6)

Sent: Thursday, May 23, 2019 8:25 AM

To: (b) (6)

Cc: Moh Malek (b) (6)

Subject: IACUC Protocol 17-01-199

Good morning!

Would it be possible for me to be notified when Dr. (b) (6) hires two new people for the above protocol and they receive IACUC approval.

At yesterday's meeting the IACUC requested that I perform post-approval monitoring after the new hires.

Thank you,

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6) Replied –

From: (b) (6)

Sent: Thursday, May 23, 2019 8:47 AM

To: (b) (6)

Cc: Moh Malek (b) (6)

(b) (6)

Subject: RE: IACUC Protocol 17-01-199

Hi (b) (6)

Yes, I will inform you once the amendment to add the new lab personnel is approved.

Thank you,

(b) (6)