

Unexpected Outcomes
1/1/2015 – 12/03/2015

Unanticipated p/d reported on annuals (2639; 3443; 2614)** (RIO)

- Mice were reported to be experiencing discomfort during and after IP injections. The protocol was modified to allow ear application, however the project has been halted pending the resolution of solution and delivery issues.
- A pig was reported to have been distressed during administration of anesthesia. A mouth injury required treatment. The methodology for the induction of anesthesia has been changed and has worked better. The research group will also incorporate the use of a sling.
- Death of 3 rats during surgery. These were isolated incidents occurring on a study which conducted many successful surgeries. It was noted that the current protocol form doesn't call out appropriate questions to determine health monitoring during anesthesia or procedures. The difficulties may have been linked to the strain being used.

Mice with enterotoxemia - Some mouse necropsies have shown evidence of enterotoxemia. It was noted that ingestion of regular high carbohydrate diets during post-parturition colostrum production can lead to hemorrhagic digestive tracts. The veterinarian has recommended increased cage monitoring and the administration of a high fat diet. One of the IACUC members suggested that a change in diet could impact the genetic status of the pups, so that should also be monitored.

Adverse event report regarding IS 1640:

- An adverse event was reported in the third year renewal for a two-step tumor project.
- Topical acetone has been causing redness and irritation for some animals. The research team immediately stopped the administration and waited for the skin to heal before any further work was done with the affected animals. The investigator reported that there had been no repeat of the problems with other animals and they suspect that the strain they were working with was particularly sensitive. The issue was considered resolved.

Unanticipated distress in mice - IS04020, 3 year renewal

- During the course of an annual update, an investigator reported the loss of some pups. It was noted that the specific strain produced pups that were small and had trouble eating. The research group changed the protocol to provide high caloric soft food to the pups and there have been no repeated issues.
- No Action required – FYI

Another problem that was noted involved the suture technique in closing abdominal cavities that was corrected by training from the veterinary staff.

A very few number of animals (9 total) have been lost on protocol. Specifically, we have had two transgenic lines where unexpected deaths occurred. We lost 5 out of 50 weanlings in the OT-11/GFP line due to small pup size. We have found that extending soft food at weaning from 4 to 7 days avoids pup death in this strain and we now routinely follow this feeding schedule for this strain. We have also lost 2 adult mice out of ~50 in the same strain due to age related morbidity. We received these mice at older ages, which compounded the problem. We have now replaced older breeders with young mice to avoid this problem in the future.

Finally, we had two adult mice from the MAFIA line die due to age related morbidity. Again, these mice were transferred from the UC Denver facility as older mice, and we have corrected this problem moving forward. .

We do follow protocols in order to ensure that this loss is kept as low as possible-such as regular health checks of our animals and clear communication with vet tech staff when health issues arise. We diligently work to mitigate this source of mortality to the best of our ability.

si RNA-related mortality in mice (Vet. Resident)

- A researcher called in to report a higher than normal mortality rate in a group of animals.
- The problem has been found related to two specific genotypes which are immunocompromised.
- The investigators have continued their study using a lower dose of nanoparticulates and have found no new problems.

Adverse event during swine procedure** (RIO, AV)

- During a transfusion, the researchers noted air in the IV line. DCM was contacted, but the animal became increasingly unstable and was euthanized.
- DCM and the research group figured out that air got into the IV line because the tray that held the plasma was tilted in a manner that allowed air to enter the valve connecting to the IV tubing. Measures have been taken to assure this doesn't happen again including visual monitoring of the IV line prior to starting transfusion.

Unexpected outcome following rabbit orthopedic surgery (Vet Resident)

- Following implant surgery, when the staple sutures were removed, it was noted that some of the skin did not properly adhere. The animal was put on antibiotics for treatment.
- The knot tying procedure was reviewed with the researchers. The veterinarian has recommended using an interrupted suturing pattern with braided material rather than single filament absorbable. Additionally they are recommending a two layer closure with staples.
- The vet will monitor the next procedure.

Mice with lesions: use of corn oil, propylene glycol

- Following the discovery of several mice with ulcerated tumors, there was discussion with the lab regarding procedures that may have been the cause. It was noted that all animals had been given a test agent with a corn oil vehicle and it is suspected that since the corn oil was over a year old that it may have gone bad. A new vehicle has been recommended for use with the remaining mice on the study.
- The animals with tumors have been treated and are being maintained until the next imaging so they can complete the study. Tissues will be collected to determine the exact cause.

- Hind limb paralysis in mice (ISO3764; Clinical Vet)
 - The protocol provides justification and has been approved for withholding post-operative analgesia. A very thorough monitoring process is in place. The paralysis was an unexpected event and the animals were euthanized. The group will continue to monitor their animals for further complications.
 - It was noted that unexpected outcomes should be reported on the Annual Update when it is filed. The Committee was reminded of the system managing the reporting of unexpected complications.

- Sheep death during recovery (ISO3418; Veterinary Residents)
 - Following a routine surgery a ewe died during recovery. It was noted that the ewe was particularly lean, woke up more quickly than expected from anesthesia and started feeding immediately. All sheep are fasted 24 hours pre-operatively to avoid aspiration of stomach contents during surgery.
 - The residents performed a necropsy and found food particles in the trachea. The cause of death appeared to be asphyxiation.
 - It was noted that the research group has over 30 years of experience in this type of surgery and this is the first time in at least 10 years that such an event has occurred. It was noted that there is no appropriate change that could be made to prevent this unique event. The research group will go on a case-by-case basis monitoring particularly lean animals.

One animal died during recovery from sedation. Based on the sudden deterioration of her condition, pulmonary thromboembolism is a possibility. The DCM staff feel that the circumstances of death were atypical, idiosyncratic and do not warrant a reevaluation of DCM anesthesia or emergency resuscitation protocols.