



---

University Court  
Minutes of Welfare and Ethical Use of Animals Committee

---

A meeting of the Committee was held on 25th April 2024.

Present: The Convener, the Director of Biological Services (DBS), the University Veterinary Surgeon (UVS, online), two Named Animal Care and Welfare Officers (NACWOs), the training coordinator, the Named Information Officer (NIO), one Personal Licence (PIL) holder, four Project Licence (PPL) holders, one independent and two lay members.

Apologies: Three members had sent apologies.

1 **MINUTES OF LAST MEETING**

The last meeting was held on 25<sup>th</sup> January 2024 and were approved.

2 **MATTERS ARISING**

- a. **Replacements meeting report.** The Convenor, a PIL from the committee and two other PILs attended a 3Rs Replacement meeting in Edinburgh in April. A paper was shared detailing current developments and advances. The conclusions were that there are no suitable alternatives applicable to animal use for the current research in Dundee, but advances are encouraging.
- b. **Antibody generation in sheep.** Following a Home Office change in Policy, projects which raise antibodies in animals must now discuss each antibody generation study with the AWERB. Previously, Dundee had instigated a similar process to maintain local oversight for an antibody raising project licence held by a Dundee researcher, but where the work was authorised elsewhere, as a matter of good practice. Since the Regulator now requires the other establishment's AWERB to undertake such a review the WEC agreed that local review in addition was an unnecessary administrative burden without additional benefit. It has been agreed with the other establishment that their AWERB will complete the reviews and will share the annual report with Dundee for the one researcher this is relevant to.
- c. **Culture of Care for facility staff.** The DBS conducted a survey of all facility staff covering 4 themes, Communication, Feeling Valued, Management Support and Animal Welfare. The outcomes were positive (83%) with actions having been taken with the aim to further improve this percentage. The outcomes relating to animal welfare were exceptionally positive: 90% of facility staff felt able to challenge managers on animal welfare, 79% of staff felt able to challenge researchers, and those unable to directly challenge a researcher instead approached a colleague to discuss. It was felt this demonstrated that an excellent system was in place in Dundee.
- d. **Guidance on writing a retrospective review.** The Convenor, DBS and NVS shared a paper providing guidance for project licence holders on how to complete their Retrospective Reviews. We will trial this document and update as required.

### 3 AMENDMENTS TO THE POLICY AND WEC TERMS AND REMIT DOCUMENTS

The Committee approved the minor changes to the updated documents prior to the meeting. The DBS has submitted to RGPSC for filing and upload to the University website and shared with the research community.

### 4 REPORTS FROM THE NVS AND NACWO ON ANIMAL WELFARE

[Standing agenda item]

The UVS reported as follows:

**Issue with a GA line from a commercial supplier:** Ongoing issues with a GA mouse line with animals being ill on or within a few days of arrival, with the severity of the clinical signs meaning that the animals had to be humanely killed. There have also been some animals that have shown similar clinical signs (requiring cull on studies), and this can mean it is difficult to interpret whether the illness is due to drug effects of the phenotype seen. Approximately 10% of animals overall are affected, with almost all culls being on the day of, or day after arrival.

A report that was sent to the PPL holder by the NVS has been circulated to committee. There have been additional issues with batch of animal imported since the report (8 out of 67 affected). Three mice were cold, unresponsive, slow, and hunched on arrival and were immediately culled. Another four mice developed clinical signs shortly after and had to be culled. A SC18 report has been submitted to the Home Office with a request for regulatory advice. The supplying company is in discussion with the PPL holder and NVS around whether any more animals can be shipped until the problem has been resolved.

Suggestions have been relayed to the supplier to investigate bile acids based on the liver pathology observed in affected animals. A potential study plan has been drawn up, costed, and passed on to the company. The stress-induced issues caused by transport cannot be resolved by breeding in-house as the original colony was shut down, there is no frozen germplasm to resuscitate the line, and the breeding rights now belong to the supplier.

*Post meeting addendum.* A meeting was held between the supplier, the PPL holder the senior PIL holder at Dundee and NVS for each establishment on 3<sup>rd</sup> May 2024. The actions from the meeting were for the supplier to reduce the transit time from source to destination (16-20 hours to approximately 11 hours). In addition, a blood sample will be taken from all animals around 10 days prior to transport, and again upon receipt in Dundee should there continue to be issues that can be investigated through further clinical analysis. There is a commitment to improve communication between all involved in this issue.

**Issue with an in-house GA line:** Staff have identified a tremor in mice from another GA line (moderate breeding protocol) and have commented on their docility, so we suspect that, in addition to the changed head shape and potentially related middle ear disease previously reported, these animals have a neurological phenotype. We have also had two (relatively unrelated) animals, with hydronephrosis - one found dead, and one detected at the time of ear notching due to abdominal distention – this latter was affected bilaterally and was wild type for the gene. At this time, although this condition has been seen in humans with genetic deletion, it looks like these are unrelated to genotype and so are background C57B6J issues. We hope that these are just two coincidental instances but, because of initial brother x sister matings (PPL holder did not take the advice to backcross the line when initially rederived) the

incidence may be higher than expected. The colony is now on backcross and all weaned animals are on weekly weighing and increased monitoring until we are confident that these are one offs.

The NACWO reported as follows:

**Wheat grain enrichment:** New option for foraging enrichment, wheat grains successfully trialled – mice love them. They form a constituent of normal diet and so are an option for foraging where no sunflower seeds can be used on dietary studies. Currently considering best approach for stock animals between combining sunflower seeds and wheat grains together, alternating them or sometimes doing one and sometimes the other. The facility manager is currently seeing how long the bag lasts so we can look at relative costs.

**3Rs champion group:** The group has recently formed and is comprised of technicians from both facilities and chaired by the facility manager and NIO. This group will provide support for the adoption of 3Rs approaches on the ground at a local level considering the research priorities, species used and the culture of the institution. Outputs will be shared with/ discussed with DBS and UVS and will have input as appropriate. All information will be shared as they are trialled and developed.

*[Action: NIO/DBS to generate a terms and remit for this group]*

**Steam incident:** There was an out of hours emergency with a damaged steam pipe in the Containment Level 3 area of the facility (22.00 on a Sunday night). The facility manager was called out and found the rooms like a sauna, filled with steam and the temperature at >40 degrees Celsius. The NVS was called for advice and the decision was taken to move the animals (which had already started on study in that they had been infected and were in the chronic stage of infection) to the Containment Level 2 suite adjoining the CL3 area (which has similar levels of biocontainment). Normally animals do not leave CL3 area, other than after euthanasia via the autoclave for decontamination, however, culling them in the room would have been just about impossible and would have put the facility manager at serious risk of being bitten (which is a possible transmission route for the pathogens). The facility manager assessed that the animal's welfare was fine other than some being wet from steam condensing in the cages (those cages were changed immediately). The NVS felt that, since after they have been injected, the animals pose a risk only via biting/ blood to blood contact (e.g. contact with tissues postmortem), once moved, they posed no immediate health and safety risk. As no adverse effects were seen in relation to the animals' experience, and type of study meant that they might still be useful scientifically, it was decided to keep the animals alive until it could be discussed with the researchers whether the animals could still complete the study. The DBS was also phoned, the PIL and PPL emailed, and information relayed on decisions made. Unfortunately, a vital piece of imaging equipment needed for the study was damaged by the steam and the researchers are waiting to see whether it can be replaced or fixed in time to complete the study. Unfortunately, if this can't be done in the next week or so, the animals will be too old to use for the duration of the study without the risk of their age causing welfare issues during the study and will need to be culled.

A report has been generated by the facility as well as by the estates team to identify the root cause and to reflect on action taken.

**Water alarm:** The core breeding facility has an automatic watering system where an alarm should go off if the water gets stuck on and the cage is at risk of flooding (can be caused by bedding getting stuck in nozzle or the mouse pushing their house against the nozzle). The alarm is malfunctioning. The facility manager is in discussion with the supplier and digital services to resolve.

## 5 REPORT FROM THE UVS ON COMPLIANCE

[Standing agenda item]

The UVS reported as follows:

**SC18 reports:** Since the previous meeting there have been three SC18 reports submitted to the Home Office (yellow highlighting). Responses have been received back from ASRU for these three reports, plus a further four submitted last year.

### **Submitted 16/03/23, returned 19/02/24:**

- Animal found dead on infection study, with treatment with recombinant proteins (1 of group of 5, 25 animals on study) at day 12 post infection (pi).
- One animal in the same cage had required cull (day 9 pi) due reaching its humane endpoint (subdued and piloerection, although weight loss <10%)
- A post-mortem dissection was carried out on both animals. For the animal that was culled the stomach contained food, intestines contained parasites (as expected), the levels of which were considered within the normal parasite load. However, the intestines were inflated with fluid and appeared very red. The NVS reviewed photos taken at the postmortem examination of both the animals that was culled, and the animal found dead. NVS considers that the level of gut distension in the culled animal was abnormal and could related to gut motility problems. In addition, there were some signs of possible mucositis. The spleen was considered large, but there was no evidence of septicaemia. There was no clear cause of death for the found dead animal and autolysis mean that it was difficult to interpret the state of the GIT.
- On NVS advice, study continued and completed.
- Incident closed with request to inform of any similar incidents (none since).

### **Submitted 05/04/23, returned 02/04/24:**

- Animal found dead on genetically altered gut parasite study.
- Gross postmortem examination found animal to be in good condition. Weight loss since induction of infection at postmortem 7.6% (had been 3.4% on last per mortem weighing).
- Parasite levels at time of death were either not present or very low.
- Food was present along whole alimentary tract, so death considered to have been very rapid, however caecum was enlarged, and blood and diagnosis made of typhlitis.
- Therefore, recorded as moderate severity and reported only due to unexpectedness of death.
- Typhlitis can be seen in immunosuppressed individuals and triggers are not well understood. It is hard to diagnose or treat and usually fatal, even in people with very intensive treatment.
- Incident closed with request to inform of any similar incidents (none since).

### **Submitted 05/05/23, returned 11/04/24:**

- Animal found dead on house dust mite (HDM) induced asthma study.
- Dosing of HDM allergen is intranasally 5 x per week (under brief anaesthesia).
- Found dead at approximately 11.30am. Dosing the previous day had been performed with no issues. Last check had been 5pm.
- No obvious cause of death; all remaining animals appeared fine and were only 2 days from completion, so NVS gave permission for study to continue.
- Incident closed with request to inform of any similar incidents (none since).

**Submitted 23/05/23, returned 24/04/24:**

- Animal on infection study found dead at day 127 post infection.
- No obvious cause. Postmortem exam not possible due to H & S limitations.
- Incident closed with request to inform of any similar incidents (none since).

**Submitted 20/02/24, returned 04/03/24:**

- Animal found dead on drug PKPD study.
- Compound was well characterised and so toxicity would have been very unexpected.
- The group perform dose analysis on all studies and subsequent dose analysis of this study identified that there was a dose preparation error.
- All calculations are checked by a second person and were correct but in this instance, there was a human error in the sample preparation that led to over-dosing on this instance.
- As all doses are analysed, the group is can confirm that this is a one off, extremely rare event, based on the evidence of their analysis.
- Incident closed.

**Submitted 18/03/24, returned 03/04/24:**

- Mouse found dead on intracranial tumour and drug efficacy study.
- No previous symptoms.
- No identifiable cause of death at gross postmortem examination.
- No evidence of stroke on histopathology report.
- Incident closed.

**Submitted 04/04/24, returned 24/04/23:**

- GA line exceeding limits on PPL (Refer to item 4).
- Additional information has been sought and advice that a PPL amendment may be required (We had asked to speak to an inspector for advice on what changes were needed).
- We are seeking regulatory advice on what changes to PPL are needed.
- Any PPL amendment will come to WEC for consideration.

## **6 REPORT FROM THE TRAINING COORDINATOR**

[standing agenda item]

Training is proceeding as normal. Since the last meeting there have been: 45 DOPS assessments, 48 Online Modules, 2 New PIL AB, 2 persons currently on PIL Theory Training, 1 person on PPL training, 1 Staff Member completed Mouse Embryo and Spermatozoa Cryopreservation Course, 20 Staff/Users attended Necropsy Course. All facility staff attended a CPD session in March and dates are schedule for PIL / PPL Holders 2024 Training, Colony Manager Training 2024 TBA and we are investigating NC3Rs Training (survey with researchers on preferences).

In line with current best practice, we have made changes in the use of carbon dioxide as a means of Schedule 1 humane killing. This information has been shared with the scientific community and training provided.

## **7 REPORT FROM THE NIO ON 3Rs**

[standing agenda item]

**National Presence:** Four University of Dundee posters were presented by four members of facility staff at the Institute for Animal Technology (IAT) Congress 2024. The data was generated via collaboration of research staff and facility staff and demonstrates following 3Rs.

#### **Replacement.**

- See Minutes Section 2a.
- PPL refresher training courses for 2024 will include information on literature searches aimed at the replacement of animals by suitable experimental alternatives wherever possible. NIO has recently completed USDA Animal Welfare Information Center's (AWIC) "Meeting the Requirements of the Animal Welfare Act" which provided training on focused literature searches. Following on from PPL refresher training course in 2024, information on efficient literature searching will be shared with the scientific community in Dundee.

#### **Reduction and Refinement**

**Intravenous (IV) dosing:** IV success rates have greatly improved since team members have been performing schedule 1 culling via IV overdose of anaesthesia on mice ear marked for non-urgent euthanasia. Additional refinements since 2021:

- Improved lighting (Daylight lamp with adjustable brightness).
- Warming apparatus – changed from heat lamps to warming cabinets with a set temperature.
- Changed from insulin syringes (e.g. BD Micro Fine) to hypodermic needles (BD Microlance).
- Rats undergoing administration of substances. Success rates increase from 66% when using needles to 96% when using catheters.
- The primary risks of IV formulations at lower pHs is tachypnoea (rapid breathing, due to a reduction in blood pH ordinarily being interpreted as high CO<sub>2</sub> levels by the body), and inflammation or damage to the tissue surrounding the injection site. These can be mitigated via a slow bolus rate (to prevent rapid changes in blood pH), avoidance of unnecessary damage to surrounding tissue when placing the needle in the vein, and prevention of leakage upon removal of the needle. As such, a slow bolus shall be used, and licensees with high IV success rates shall be selected for dosing these studies. Dose sites shall be monitored for signs of inflammation.

**Review of historical data:** Historical data is being searched for information on an as required basis to look for patterns. The requests for information so far:

- Pup loss. Are there any differences between backcrossing colonies vs non backcrossing colonies? Poster produced and showed pup loss is lower in backcrossed colonies, as well as a lower incidence of illness. This information has been shared nationally in response to queries from other establishments.
- Teeth issues. A rise in C57BL/6j mice reporting teeth issues prompted review. Issue traced back to two batches of mice bought in from a commercial supplier during September 2023.
- Vaginal septum incidence. Incidence increased in 2024 compared to previous years. Transmission may be due to various factors. Commercial supplier will check stock female mice for vaginal septa prior to shipment.
- Do environmental changes e.g. loss of steam and thus changes to humidity affect breeding? No impact found.
- Specific GA strain phenotype queries.

**Refinement database (hints and tips for the research community):** Each study conducted within the facility is captured within a Study Plan. At the end of each study, the research group is required to return a completion report detailing any refinements, advances, or issues. A database is being generated to track all comments on issues encountered during, and refinements applied to completed studies. The aim is to produce an information resource for all users involved in study design and hands on practical work on best practice in methods and case studies evidence. Information collated will be shared with the scientific community.

**Literature searches:** Focused literature searches for 3Rs are now being completed as questions are presented. Queries so far include:

- Voluntary administration of substances
- Colony health and backcrossing
- Sperm storage for archiving.

[Action: NIO to consider a 3Rs' newsletter or a 3Rs' day].

## 8 REPORT FROM THE DBS ON LICENSING MATTERS

[standing agenda item]

A comprehensive review of progress of each application submitted to the committee and to the Home Office since the last meeting was discussed. The turnaround time within the committee is very good. The time taken at the Home Office is on average 40 working days for a new licence application (service level expectation), on most occasions less for minor amendments.

## 9 AOCB

- The Committee welcomed a new lay member.
- The committee were informed that the DBS/UVS and Convenor had reviewed the evidence of committee activities against AWERB expectations and were performing to expected standards. This will become an annual review (and terms and remit will be updated).
- A GA line outsourced for rederivation imported into Dundee could unfortunately not be used due to the expiry of funding following delays to the rederivation process.

## 10 DATE OF NEXT MEETINGS

4<sup>th</sup> July 2024.

31<sup>st</sup> October 2024.

23<sup>rd</sup> January 2025.

24<sup>th</sup> April 2025.

3<sup>rd</sup> July 2025.

2<sup>nd</sup> October 2025.

## 11 ACTION LOG

	<b>Actions</b>	<b>Responsibility</b>	<b>Update</b>
25/04/2024 Item 4	NIO/DBS to generate a terms and remit for the 3Rs Champion group	NIO/DBS	Approved by ELH 29/04/2024
25/04/2024 Item 7	NIO to consider a 3R's newsletter and/or a 3R's day	NIO	Discussion with DBS to materialise
25/01/2024 Item 3	Outstanding Study Plan completion reports from one project licence holder.	PPL holder	27 completion reports were submitted on 23/04/2024