Animal Welfare and Ethical Review Body (AWERB)

20/01 A meeting of the Animal Welfare and Ethical Review Body (AWERB) was held in Committee Room 2, Whiteknights House on Thursday 6 February 2020 at 10.00 am.

Present: [Redacted. Sec.40]
[Redacted. Sec.40]
[Redacted. Sec.40]
[Redacted. Sec.40]
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[Redacted. Sec.40]

[Redacted. Sec.40],

Apologies: [Redacted. Sec.40]
[Redacted. Sec.40]

20/02 Minutes of the last meeting

The minutes of the last meeting held on 11 September 2019 were approved as a correct record.

20/03 Matters Arising

19/20 Severity Data

AWERB noted that the data was now available on the website.

19/20 Workshop on the 3Rs

[Redacted. Sec.40] reported that the workshop had taken place.

19/22 Update on aseptic training

It was reported that the aseptic training had taken place

19/22 Communications

It was reported that discussion in regard to the unknown infection had gone quiet. One colleague had contacted the [Redacted. Sec.40] to state that they had evidence of an infection on some histology slides. The [Redacted. Sec.40] had asked for sight of these slides but they had not been provided.

19/23 ASPel System

[Redacted. Sec.40] reported that key colleagues had been provided with the link. Several members of AWERB stated that they had found problems with completing the system, particularly for new applicants.

20/04 Mid and End Term Reviews

The Board received presentations from [Redacted. Sec.40] and [Redacted. Sec.40] in respect of their current Project Licences.

[Redacted. Sec.40]*:*

1) *The regulation of platelet function as a central mechanism for the control of cardiovascular function and development*
   - Mice were used to study the regulation of the function of platelets, to establish the importance of the mechanisms identified in human platelets for blooding clotting and thrombosis. The goal was to develop new strategies to prevent thrombosis, which causes heart attacks and strokes. The use of animals was unavoidable because platelets performed their functions in flowing blood in the presence of many other cells and biochemical factors, and particularly under flowing conditions. A great deal of work was done *in vitro* using human platelets and the groups strived to find new approaches to minimise the use of animals. A core element to this work in the last 3 years had been the further development of mathematical and computational approaches to model the complex processes of platelet regulation. All of this work had focussed on the use of human blood, avoiding the need for mouse experiments.
   - It was noted that strategies to ensure reduction in animal usage were used, such as: efficient statistical design to increase precision, NC3R tool for experimental design, efficient breeding protocols, use of cryo-preservation, efficient laboratory techniques.
   - It was noted that [Redacted. Sec.40] had responded to reviewers that requested that animal experiments be repeated using a different experimental models that this was not ethically defensible.

- It was noted that animal usage was likely to be lower than predicted in the licence application. The numbers quoted in the licence were higher due to an overestimation on the numbers required for the move to the new unit
- There was a possibility that numbers would further reduce as fish work increased
- There was little difference between the transgenic mice and the wild type; the transgenic mice looked completely normal and healthy
- Work to generate platelets from stem cells was progressing and, in the future, would become an important tool in reducing animal use
- [Redacted. Sec.40] agreed that there was a need to share good practice on reducing animal use with researchers. The School ran a PhD Summer School which was an opportunity to introduce good practice. The NC3R workshop on experimental design and planning was also helpful.

AWERB noted that [Redacted. Sec.40] was also holding a second licence. No work was being undertaken at present on this project.

[Redacted. Sec.40]*:*

1) *Novel therapies for disorders of the immune system*
2) *Novel therapeutics for pain*

- It was noted that there had been no opportunity as part of the project to replace animals with non-animal methods. The in vivo models described in the licence application were employed to generate information about how the whole body responded once it had been given a compound. It was neither possible, nor ethical, to use human volunteers in early drug discovery. In the process of new drug discovery, it was therefore necessary to use other whole-body systems, animals, to find out how a living organism responds.

- The number of animals required per group and the experimental design had been determined on the basis of power analysis, advice from statisticians, published data and previous results.
- In regard to opportunities to refine techniques and procedures to reduce the pain, suffering and distress caused to animals:
    - Cupping had been adopted as the technique of choice to pick up mice in longer term studies
    - Following discussion with the [Redacted. Sec.40] post-operative analgesia had been introduced into the rate neuropathic pain model (Medetomidine was now use routinely for post-operative analgesia in the rat model of neuropathic pain)
- AWERB queried whether each compound should be considered by a sub-group of the AWERB before testing. [Redacted. Sec.40] stated that the ethical justification was pre-set, the company concerned would agree the model appropriate for the study and that by having the licence approve in the first place the benefits would be appreciated.
- It was noted that different methodologies were considered but that within the [Redacted. Sec.40] field it was generally expected that a ‘gold’ standard would be used to provide confidence. This had led to inertia in developing other methodologies.

20/05 Technical Services Report

The AWERB received the report and in particular noted:

- There had been issues with the heating and air pressure in holding rooms B16 and B17. These rooms were heated by a separate boiler from the rest of the BRU. This boiler was aged and has lost pressure on two occasions and stopped working (causing the room temperatures to drop), Estates were aware of this issue and an action plan had been put in place to prevent heating failures. The fan which served the air handling unit for these rooms switches off ventilation when the outside temperature gets too cold. Estates were over-riding this fan switch off to prevent ventilation being lost to these rooms.
- There had also been issues with the drainage from the unit silting up and blocking, and the temperatures in the controlled temperature room fluctuating. Technical Services were in constant discussion with Estates and there was an understanding of the need to continue to maintain the AMS BRU.
- Groups in the BRU had started to perform surgery according to the new aseptic surgery SOP. Two mandatory training workshops for all users who undertake or intend to undertake surgery had been scheduled, the first was held on 15th January and the second was being held on 12th February, and all groups were engaging in this. BRU staff were also attending these workshops to enable them to be trained as non-sterile surgical assistants.
- Two members of [Redacted. Sec.40] were leaving in February, the interviews for replacements are over the next couple of weeks.
- The new unit was currently scheduled for handover in June 2020. Most of the new equipment was on order and ready for delivery later this year. Users of the BRU were kept up to date with monthly emails of the progress and plans for occupying the building. There was a planned visit from the [Redacted. Sec.40] on the 13th of March. The building would be fairly advanced by then. She would be shown the demonstration room and a number of other areas including the holding rooms and surgery suite.

In regard to temperature issues within the BRU, the AWERB urged colleagues to ensure appropriate mitigation in case of plant failure, for e.g. heaters, extra bedding, fans, as well as a contingency plan for when animals would be moved.

20/06 ASRU communication

The AWERB received and noted the ASRU Operational Newsletter from December
2019.

20/07 Discussion on ethics of service licences

[Redacted. Sec.40] and [Redacted. Sec.40] presented to AWERB on the challenges around services licences.

In particular it was noted that:

- In considering licence applications to AWERB should:
    - Ensure that the application had been prepared to a satisfactory standard
    - Identify ethical and welfare issues and consider a Harm Benefit Analysis
    - Identify any other that might apply to other projects and consider the development of guidance for good practice
    - Propose time-points for mid-term/retrospective review
- Essential questions should include:
    - What was the knowledge gap being addressed
    - What were the clinical/veterinary/agri/conservation benefits?
    - Were all health benefits equally valuable
    - What about using animals to develop cures for life-style related conditions
    - Did an economic benefit justify harm to animals
- The Concordat required signatories to 'provide accurate descriptions of the benefits, harms and limitations of such research and be realistic about the potential outputs of such research'
- Of the total number of procedures carried out on mice and rats in 2018 at the University 6,511 out of 9,395 were undertaken by external clients.
- Other AWERBs had stated that they did not need to know compound name/structures but did need to know: what the therapeutic area was; how far the project was through the drug development pathway; what success would look lie; what would happen next if successful; less diffuse project licences; whether there was an NDA with 3rd party clients; new project licences would require more information.
- Multiple generic projects had their origins in Article 40 of EU Directive 2010/63 and then in ASPA 5(4). There was legal acceptance that these types of projects could be licensed
- The AWERB should explore the possibility of alternatives at the PPL draft stage. Before any animals were sued the PPLh must be able to demonstrate that the use of animal was justified for each individual study, that no alternatives could be used, that the minimum number of animals were used consistent with the scientific objective, each study had been designed to reduce to the minimum any pain, suffering, distress or lasting harm. The PPLh should eb aware of the obligation to implement the 3Rs throughout the project.
- Challenges included: the background cannot be specific since it is not known in advance what might be tested; benefits are also difficult to specify.
- It was important that: there was a robust process in place toc heck that the samples to be tested needed to be tested in the animal model; AWERB should evaluate the processes that the PPLh uses to ensure the requirements are met; AWERB could look at requests prospectively but this could result in time delay.
- Potential issues – the PPLh might have a vested interest in accepting the work, e.g. commercial; what would happen if the AWERB found retrospectively that the work was not justified

Members of AWERB discussed the issues around service licences, and the following comments were made:

- There was support for the formation of a technical sub-committee to consider such applications
- A model was already in place at CEDAR for the Camelids. Meetings were regularly held with the NVS
- There was a need to be blunter with contract research services about AWERBs requirements

AWERB asked that [Redacted. Sec.40], liaise with colleagues at other Universities to ascertain what they do.

Action: [Redacted. Sec.40]

This item would be brought back to the next meeting.

20/08 Any other business

TB on the Farm

It was reported that TB had now spread to the edge of West Berkshire.

During February a reactor had tested positive for the 21A strain and one test was inconclusive. As a result, the herd (1100) was now subject to 60-day test. Only two positive cases had been confirmed to date. It was noted that the two consecutive 60-day tests were required for an all clear.

AWERB were reminded that it was a closed herd. A small loss of animals was unlikely to impact any studies.

Elderly Mice

It was noted that the BRU had instigated a traffic light system for ageing mice

20/09 Dates of meetings in the Session 2019-2020

Thursday 14 May 2020 at 10.00 am