MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 10 February 2022

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 16 December 2021 were approved.

Reported: The attendance list on the minutes from the 19 August 2021 meeting were incorrect. An NVS was present however arrived slightly late leading to the error on the minutes. The Secretary will correct the minutes.

2. Applications for New Project Licences

2.1. [redacted], The Impact of Integrin a1b1 Signalling on Polycystic Kidney Disease

Considered: A completed AWERB form and PPL application.

Interviewed: [redacted]

Discussed:

- Sample sizes will be modified once data is collected from the research. The sample sizes used in the application are based on data from the literature.
- The best measure of renal function was discussed. Protein urea will be used instead of the albumen/creatinine ratio mentioned in the draft seen by AWERB members.

Revisions:

- To be harvesting tissue from mice at 4 weeks, presumably the mice will have been genotyped? Please bear in mind the time of tissue sampling and speed of genotyping to ensure mice are identified before more severe disease manifests.
- Page 12 - point 2) should itga1+/+/Pkd1nl/nl be itga1-/- Pkd1nl/nl?
- Page 24 – You discussed in the meeting that you are not going to be using albumen/creatinine ratio but protein urea. The application needs to be updated to reflect this.
- Page 30 – please make it clear in the application which controls you plan on using. During the meeting you explained that you will be looking at animals that have one and two copies of allele and checking to see if there is a difference. This needs to be explained in the licence.
- A number of comments were made regarding your Non-Technical Summary some of which are listed below. Please update your NTS based on the comments and send it to the following lay members for their review [redacted]
    - The non-technical summary should be for a lay audience. The use of scientific and technical language should be avoided and where this is not possible an explanation or definition given the first time it is used.
    - Aims - Please define 'integrin'.
    - Page 3 - Under what will be done to the animals, it might be good to mention blood sampling, mouth swabbing, ear biopsy, and hair sampling.
    - Page 4 - What are the expected impacts and/or adverse effects for the animals during your project? If kidney infection is likely as described on page 27 then consider adding this into the harms section.
    - Page 4 - You say adverse effects are unlikely to occur because the ADPKD mice are killed before symptoms develop though later in the NTS and also in the license you say that approximately 25% of animals are likely to experience moderate levels of severity. It's probably a good idea to make this clearer in the harms section of the NTS and explain what the mice actually experience (when they develop a cyst especially) so we understand why it's a moderate level of suffering
    - Page 5 - In "why were they not suitable?" the terms pkd1 and itga1 appear with no explanation, as does "nanobody". Please given an explanation.
    - Page 5 - Please explain the relevance of the extracellular matrix to cyst formation.
    - Page 6 - Refinement - this contains the simple and direct description of the project that is required somewhere at the beginning of the NTS, but it also uses terms that are not appropriate for the NTS, such as 'Pkd1nl/nl mice'.

- Page 7 - Line 4 A less technical description of 'embryonic lethality and cytogenesis' is needed, e.g cyst formation.

Outcome: The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

2.2. [redacted], Imaging & Radiation Treatment of Cancer

Considered: A completed AWERB form and PPL application.

Interviewed: [redacted]

Discussed:
- [redacted] raised a number of concerns which will be dealt with after the meeting through further contact between the NVS and applicant.

Revisions:
- Please note that the 2010 Workman guidelines are being updated.
- There is a discrepancy in the number of animals you state you will use. Page 6 says 1050, page 17 says 800 and the Cat A form states 800. Please update the licence and Cat A form to be consistent.
- It appears that some copying and pasting has taken place from a previous PPL to this application resulting in steps with multiple unrelated procedures. Please work with the NVS or NACWO to amend this before the licence is submitted to the Home Office.
- The adverse effects and humane endpoints are not tailored to the animal models used and some essential adverse effects are fully omitted (e.g. tumour ulceration) or in contradiction between sections (e.g. maximal size of tumour; sometimes 1.7cm3 and others 1.5cm3). Please contact an NVS to obtain input into this area of the application [redacted]).
- Page 12 - paragraph "regarding identifying patients" needs re-wording.
- Page 14 – "Autoradiography of sections from the xenografts to demonstrate distribution of radioactivity across the tumour. Time 1-2years." Please clarify what the time is related to.
- Page 18 - Protocol 1 Step 1 - animals anaesthetised - needle inserted AA/AB – please check with the BSF staff if AA should be removed if the animal is anaesthetised.
- Page 22 – Step 2. Additional information is required regarding blood samples. What is the sample size and how frequently are the samples to be taken for blood sampling? Where are they taken from? Does the injection of the radioactive compound affect the site of blood sampling?
- A number of comments were made regarding your Non-Technical Summary some of which are listed below. Please update your NTS based on the comments and <u>send it to the following lay members for</u> their review [redacted]
  - The non-technical summary should be for a lay audience. The use of scientific and technical language should be avoided and

where this is not possible an explanation or definition given the first time it is used.

- Title - might the title be "Improving imagining and radiation treatment of cancer" as this indicates the aim of the work to the lay reader.
- Page 3 - As a lay reader I found it a little challenging to extract from the 'why is it important' section what the actual areas of improvement were to be; on p.4 there are two outputs (optimization of cancer marker drugs and identifying markers on hypoxic (cells?) to target TR agents. I wondered if these are the two main aims of the project then could the text on p.3 be clarified about these two outputs/objectives?
- Page 5 - it would be helpful if the indicators of the tumour volumes, in terms of cubic centimetres, were accompanied by some examples from everyday life. This would aid the lay reader in being able to visualise just how big tumour actually is.
- Page 6 – please explain that xenograft refers to the implanted cancer.
- Page 6 - Dosimetry should be explained in the NTS
- Page 7 - Typo "in the literature" repeated twice.
- The NTS should include that only one flank will be used.
- The NTS should include details of hyperthermia.
- The NTS could do with a little more on what the animals experience, noting stress that is caused by the various procedures: injection with non-radioactive and radioactive drugs; imaging under anaesthesia; subcutaneous insertion of a microchip. Details of how often these procedures performed should also be included.

Outcome: The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

2.3. [redacted], Understanding Gene Function in Cardiovascular Disease

Considered: A completed AWERB form and PPL application.

Interviewed: [redacted]

Discussed:
- It is a large licence with many protocols.
- The inclusion of a severe protocol required particular consideration by AWERB members.

Revisions:
- For some steps the adverse effects listed are actually mild and transient so these can be removed and sometime the question can be answered “No” (e.g. Cardiac phenotyping). Some adverse effects listed are also more likely related to the competency of the operator and hence should not be listed as adverse effect (e.g. Blood sampling, oral gavage). The occurrence of complication is quite rare but the Home Office Inspector will likely be happy to be kept updated in case such complication occurred. If you have questions about this point please contact the NVS [redacted].

- It would be useful if abbreviations were specified the first time they appear. This occurs at multiple places in the application.
- The body weight at which animals are killed is variously reported as 10% and 15%; sometimes it is not obvious why this is so and sometimes the text is confusing. Please can you clarify is this is correct or if one percentage should be used.
- Page 61 - Does not floor feeding and the provision of chew blocks improve the welfare of older mice and should therefore be considered as a refinement in the NTS? Can the use of Mini-pumps and radio telemetry be considered refinements as well? Please seek advice from the BSF staff and NVS about this.
- Page 67 - Tail blood sampling is said to occur up to 6 times. Please clarify how are these times determined and what is the minimum time between each sample.
- Page 85 – please given the intervals for sample times for unconscious ECG and other none invasive imaging which are said may occur up to 3 times.
- Page 141 – The proportion of animals that will experience this severity is listed as 15%, however on page 142 you talk about 25% of mice dying following ligation of the coronary artery. Please can you check if the proportion should be amended to be 25% instead of 15%.
- A number of comments were made regarding your Non-Technical Summary which are listed below. Please update your NTS based on the comments and send it to the following lay members for their review [redacted]
    - Thank you for the detailed answers to the questions on what will be done to the animals and adverse effects. I suspect these answers can be pared down somewhat substantially, while still leaving the relevant content. Overall, though comprehensive, I found the NTS to be rather long with quite a bit of repetition. Most of the information needed is there, it just needs to be pared down to the minimum I feel, so the document can be read more easily by the non-scientific public. Having said that, it would be helpful to add in the NTS that a proportion of the animals will undergo induction of gene alterations by treatment with tamoxifen and that there are potential impacts such as weight loss associated with this. And also explain they will experience procedures such as oral gavage (I know this is transient, but it's still surely stressful), glucose or insulin tolerance tests which involve 8 hours of fasting.
    - Aims - suggest 'of' is added to Development of Heart Failure.
    - Page 4 - Could possibly remove "including the PMCA, MAPK and Hippo pathways" as a bit technical for the lay reader and the sentence conveys the point in a simple way without the detail.
    - Page 4 - "made visible" - shared? Some of this detail could be placed in ways to maximise outputs section to avoid repetition.

Outcome: The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

3. Retrospective Assessments of Project Licences requiring full committee review

3.1. [redacted], Preclinical evaluation of cancer therapeutics

Considered: Completed questions from the ASPeL system for a Retrospective Assessment.

Interviewed: [redacted]

Discussed:
- The version will need changing to be more lay friendly given that the Retrospective Assessments are publically available documents.
- The version that is submitted to the Home Office needs to be anonymous and have any mention of names researchers and the company removed.
- Sharing of negative results should be discussed with clients and you should urge companies to publish negative results to avoid unnecessary duplication of studies.
- Animals were reported as going into the severe banding on a moderate protocol but not on the severe protocol. It was discussed that the extra monitoring on the severe protocol may have been accountable for this.

Outcome: AWERB endorse submission of this Retrospective Assessment based on the revisions being made.

3.2. [redacted], Development and Optimisation of Infection Models

Considered: Completed questions from the ASPeL system for a Retrospective Assessment.

Discussed:
- This Retrospective Assessment is overdue owing to the licence holder moving to another establishment and resulting administration errors from the Home Office regarding licences held in the researcher's name and two establishments.

Outcome: AWERB endorse submission of this Retrospective Assessment.

4. Report on licences processed from 01/12/2021 to 20/01/2022

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], Understanding The Role of Inflammation in Dementia.
[redacted], Understanding Vision & Developing Therapies for Blindness.
[redacted], Evaluation of Cognitive Function in Animal Models.
[redacted], Treatment & Pathology of Neurological Diseases.

4.2. Amendments to Project Licence [redacted]; Generation, Breeding and Maintenance of Genetically Altered Rodents

[redacted], Generation of Tph2-2A-Flp-V5 Mouse Line Using CRISPR.
[redacted], Generation of CCSP-CreERT2 Mouse Line Using CRISPR.

4.3. Applications for Category C work

[redacted], The Role of Distinct Pools of Synaptic Vesicles in Neurotransmitter Release & The Regulation of Different Modes of Exocytosis.

5. Update on applications outstanding from previous meetings and upcoming Project Licence applications

5.1. The committee were provided with a document showing the status of applications considered previously and those pencilled in for future meetings.

6. NACWO and Directors report

6.1. A document was provided to the committee for this item. No comments or queries were raised.

7. NVS report

7.1. A report was provided to the committee for this item.
7.2. The issue regarding skin constriction in pups was discussed. The NVS had suggested that cream was administered which helped. While not appearing to be in pain and still suckling and gaining weight, the decision was made that some pups should be humanely killed. Using the animals for experiments was not considered suitable.

8. Standard Conditions 18s and non-compliances

8.1. A report was provided to the committee for this item.
8.2. A discussion took place regarding gut torsion. [redacted] explained how this occurs, usually in germ-free mice, and the steps which are being taken to reduce the incidence including enrichment in cages. It was noted that gut torsion is unpredictable and does happen infrequently.

9. 3Rs AWERB subgroup report

9.1. The papers from the 3Rs subgroup meeting on 8 December 2021 were provided to the committee for this item.
9.2. The committee noted the NC3Rs Skills & Knowledge Transfer Award that Dr Hannah Harrison holds. Dr Harrison will be invited to a future AWERB 'away day' to speak on her research and the equipment she is using.

10. NC3Rs Regional Programme Manager update

International 3Rs Prize

1 – The 2021 3Rs prize is now open. The prize is open to researchers across the world who have published an outstanding paper with demonstrable 3Rs impacts in the last three years.

This globally recognised award is sponsored by GSK and consists of a £28k prize grant and a £2k personal award. It is awarded annually to highlight the contributions of individual researchers across the medical, biological and veterinary sciences, and further support the development of their work and career.

If you would like further information please contact [redacted] – deadline for applications is Wednesday 6 April.

Resources

2 – The NC3Rs has updated it's website. We've re-organised some pages, particularly those detailing 3Rs resources, and added more filters to help people find the things they are looking for. If you have any links saved you should be re-directed to the correct page, but if you have any problems please contact Jo Stanley and she can look into this.

3 – The NC3Rs has just published new guidance on rat playpens. The exposure of animals to additional space and enrichment can help them to display natural behaviours that's beneficial to both their physiological and psychological well-being. As well as improving their overall welfare, it can also reduce stress and improve scientific outcomes. The new guidance has details on the various benefits, as well as extensive advice on how to set-up a playpen. You can find the resource here, and can also contact [redacted] if you'd like any advice.

Events

4 – Focus on Fish

This online event, organized by the RSPCA, will be held on Wednesday 23 Feb. It will bring together experts to share cutting-edge knowledge and approaches to refining the use of fish. To find out more or register please visit the following page https://www.nc3rs.org.uk/events/focus-fish-2022.

5 – Just a reminder that we are still running regular live online demonstrations of the EDA tool for anyone interested in getting started, or picking up some tips. Attendance is limited to allow for a detailed Q&A session, particularly for those who have specific questions about the tool. The next demo is on 30 March - for more information or to register please head here https://www.nc3rs.org.uk/events/virtual-demonstration-experimental-design-assistant-0.

11. Any other business

11.1. Draft away day notes from 21 January 2022 for review

The minutes from the away day held on 21 January 2022 were provided to members.

11.2. Documentation provided for Project Licence applications

During the meeting it was noted that the images within Project Licence applications do not appear to be downloading from the ASPeL system correctly. In addition, minutes from pre-AWERB meetings have not been provided for the last couple of meetings.

The next meeting will be on 24 February 2022 at 10am-12.30pm.

Dates of meetings for the 2021/2022 academic year are:

11 November 2021
16 December 2021
10 February 2022
17 March 2022
28 April 2022
9 June 2022
21 July 2022
1 September 2022