MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 23 March 2023

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted] (future PPL applicants)

1. **Minutes**

Agreed: That the minutes of the meeting held on 23 February 2023 were approved.

2. **Applications for New Project Licences**

2.1. [redacted]

#1 Biocompatibility & Pharmacology of Novel Nanotechnologies
#2 - Nanotechnologies for Cancer Treatment, Diagnosis & Monitoring
#3 - Nanotechnology & Nanomedicine for Detection & Treatment of Brain Disorders

Considered: A completed AWERB form, PPL applications, and minutes from Local Management Committee Meeting

Interviewed: [redacted]

Panel discussion:
- More clarification is required regarding severity levels.
- The decision to split one licence into three was raised.

- More information from the applicants is requested regarding the live animal imagine.

Discussed with applicant:

- The committee asked the applicant about the cumulative effects on mice and to hear about the justification for why the researchers ensure animals do not exceed the moderate severity limit. The applicants explained how the animals are monitored and that they recover very well in the tumour models.
- The committee explored the hydrodynamic injection with the applicant who explained the procedure in more detail.
- The adverse effects seen with live imaging were explored with the applicant and it was advised to add back in the information that had been removed after the pre-AWERB meeting and include details on how often scans will be and for how long.
- The applicants explained about the hind limb paralysis that they have observed previously and how they minimise this happening.

Revisions: It was explained to the applicant that the committee had provided comments to the Secretariat prior to the meeting and while some would be discussed in the meeting, the list below includes all the comments whether they were raised in the meeting or not.

- There are some minor typographical errors which in the main do not change the meaning of the sentences but which you may wish to correct prior to submission to the Home Office.
- In the sections 'How will experiments and data analysis be randomised and blinded?' you say 'Blinding will be used where possible including in data analysis stages' Please clarify if you really mean that data analysis will be blinded as it is difficult to perform an appropriate analysis if you don't which groups the animals belong to.
- P21/44 (PPL1) and p30/76 (PPL2) – As discussed in the meeting the use of the hydrodynamic (tail vein) injection 100 ml/kg (10% body weight) raised concerns for the wellbeing of the animals if the requested 5 injections in total are given on consecutive days. Please provide information on the frequency of the hydrodynamic tail vein injections given the fact that AWERB would not support consecutive days of this procedure.
- P23/44 (PPL1), P31/76 (PPL2), P27/73 (PPL3) – With regards the statements that <15 % of animals may experience hind limb paralysis after injection of graphene nanomaterial complexes, please include the mitigating actions you described in the meeting where you switch to alternative administration routes if this happens and any other mitigating actions you take to minimise the suffering to animals.
- P23 and 37 (PPL1), p 32/48/65 (PPL2) and 46/65 (PPL3) – As discussed in the meeting, AWERB do not question the need for longitudinal imaging, however details of adverse effects should be included along with details of frequencies and durations. AWERB note that you were advised to remove this previously but AWERB members were in agreement after discussions with you and after you had left that this information should be added.
- Page 25 (PPL1), p35, 51, 68 (PPL2) - It is not clear what "prior to time" means – is this a typographical error?

- Page 23 (PPL1), p29 (PPL2) – is it correct that a body score of 1 or 5 will result in immediate culling?

#1 - Biocompatibility & Pharmacology of Novel Nanotechnologies

- Page 21 - Under "Intracranial administration" there is no indication how many insertions there might be.
- Page 25 - the age at the start needs defining for those animals that will be kept up to 12 months.
- Page 34 - should treatment be a step protocol or is this just antibiotics?
- 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]
    - Please define the terms 'nanomaterials' and 'biocompatibility' (sic) on their first use.
    - Page 3 - minor suggestion - you say under the first question related to benefits the data gathered will also inform health and safety for those exposed to nanomaterial during their "jobs"; I wondered if this knowledge may have wider relevance than that to society more generally - is the public likely to be exposed to nanomaterials? If so this would seem worth flagging as it would imply a higher level of importance to the work proposed; in your answer to the second question the wider societal impact through to home is mentioned.
    - Page 4 - "without an existing phenotype" - could this be expressed in lay language so the lay reader can understand the meaning here? It is somewhat clarified on 7 of 44 ('healthy animals without any disease of clinical phenotype') but it should be explained clearly on the first use for a lay reader in non-technical language.
    - Page 5 - for sake of consistency you might consider "humanely killed" as opposed to culled - throughout all 3 applications because the answer to what happens to the animals is killed.
    - Page 6 - Line 3 Please describe an 'organoid'

#2 - Nanotechnologies for Cancer Treatment, Diagnosis & Monitoring

- Page 29 – is the traffic light system a standard one, for example is it used by CRUK MI and MCRC?
- Page 33, 49 and 66 - Regarding exposure of tumours to TTFs, you say that electrodes may need to be replaced? On how many occasions? Would this require additional anaesthesia?
- Page 34 – please include more details of the 'heat as sham' including how hot the heat will be.
- Page 60 – please include details of where specifically the intracranial injection will go into.
- 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]

- In the non-technical summary the term 'removed' may be better for a lay reader than 'resected'.
- Page 3 - "Cancer remains an unmet clinical need that current technologies and medical approaches have yet been able to overcome." - feels a bit of an overly complicated sentence to express that we need new approaches to cancer therapy so perhaps you can reword this.
- Page 4 – 'imaging modalities', specially the term 'modalities'' may not be easy to understand for lay readers and would benefit from being reworded.

#3 - Nanotechnology & Nanomedicine for Detection & Treatment of Brain Disorders

- Page 14 – is there a reason why the objective title is in italics?
- Page 23 and page 41 – please can you include information on where in the electrode will be placed in the brain.
- Page 26 and page 44 – please include details on how often intracranial administration will take place – is it just once per animal?
- Page 31 – does PD stand for Parkinson's disease? If so, please can you include this abbreviation the first time you use it.
- Page 56 – please seek advice from the BSF staff on if you need to include details of what types of tumour cells you will be administering.
- 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]
  - The NTS has an excess of technical detail. It would benefit by being succinct and easier to read for the lay reader. In Refinement the first 2 paragraphs could be much abbreviated.
  - Please define the term 'nanomaterials' on its first use.
  - Page 3 – 'drug-refractory' may not be understood by lay reader, therefore could a simpler term be used such as resistant or non-responsive.
  - Page 6 – is there a reason the number of mice are in italics?

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], Repair & Resolution of Cutaneous Wounds & Inflammation.

Considered: A completed AWERB form, PPL application, and minutes from Local Management Committee Meeting

Interviewed: [redacted]

Discussed with applicant:
- The committee explored why zebrafish cannot be used as an alternative model.
- The ovariectomy model was discussed along with the sex of the animals to be used in the research.

Revisions: It was explained to the applicant that the committee had provided comments to the Secretariat prior to the meeting and while some would be discussed in the meeting, the list below includes all the comments whether they were raised in the meeting or not.

- Page 14 - The committee recommend the removal of the information on the rationale for the ovariectomy model as it was not felt the statement added to the application.
- 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]
    - Page 3 - the applicant does not need to evidence their claims in great detail; for instance they may wish to consider the extent to which statements like "in their review of available clinical data, Guest et al. concluded that there had been a 48% increase in wound care costs between 2013 and 2018, with 28% of these wounds being leg ulcers; the average age of a patient requiring wound care was 58" are required; it may be sufficient to simply use the prior sentence.
    - Page 3 – you state "approved by the FDA" - why FDA? is there no UK context? This reference may require explaining as to its meaning (what is the FDA) and why it is important to the project.
    - Page 3 - "Why is it important to undertake this work?" - the second part on psoriasis describes issues but does not quite state clearly what the research project is doing to respond to these challenges. Please include some more detail.
    - Page 5 – will only mice receive pain relief – if yes, why will rats not receive it?
    - Page 5 – 'How will you look to maximise the outputs of this work?'. The bullet points do not address dissemination of the work/knowledge instead it focusses on ensuring quality of data. Please revise.
    - Page 7 – 'Why were they not suitable?' – please define the term 'microbiome'.
    - Page 9 – 'Which animal models and methods will you use during this project?' You state in the last sentence that all mice will be humanely killed; what will happen to the rats?
    - Page 9 - The committee recommend removal of the reference to Zebrafish in the Section 'Why can't you use animals that are less sentient?'

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. Update on refinements for project

3.1. [redacted] - Genes & essential nutrient influences on behaviour.

The researcher gave an update on the new cabinets and the benefit of the cages. Some of the wireless nodes are for the running wheels and some are for passive motion. There are no cables for the animals to chew on which was previously a hazard for them.

4. Report on licences processed from 09/02/2023 to 05/03/2023

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], Understanding & Targeting the Inflammatory Response
[redacted], Central Regulation of Appetite & Body Weight

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

[redacted] Creation of Tg-CopA Mouse Line Using CRISPR

4.3. Applications for Category B work

[redacted], Identifying Astroglial Molecular Contributors to Epileptogenesis

4.4. Applications for Category C work

[redacted], MSci Practical Project: Detection of Immune Cell Populations in Mouse Lymphoid Organs

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. Standard Conditions 18s and non-compliances

6.1. The committee were provided with a table of reports submitted to ASRU along with the reports for each incident.

7. Any other business

7.1. Transnetyx

Transnetyx will be giving a presentation on 18 April 2023 about how biological variability can impact research and discussing the their automated genotyping, genetic monitoring and microbiome analysis services.

The next meeting will be on 27 April 2023 at 10am-12.30pm.

Dates of meetings for the 2022/2023 academic year are:
25 May 2023
22 June 2023
20 July 2023
August break

Dates of meetings for the 2023/2024 academic year are:
21 September 2023
19 October 2023
16 November 2023
14 December 2023
25 January 2024
22 February 2024
21 March 2024
25 April 2024
23 May 2024
20 June 2024
25 July 2024
August break