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THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

19th April 2018

MINUTES

Present:

18/04-01 Apologies and introductions

18/04-02 Minutes

The minutes of the meeting held on 8th March 2018 were considered by the Committee and were approved.

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18/04-03

Matters Arising

In relation to minute 18/03-07-1, it was reported that the application was approved in good time following the last meeting.

In relation to minute 18/03-07-2, the application is almost ready to be approved with a few last minor changes.

18/04-04

Chairperson's Items

- The Chair has circulated information about the forthcoming NC3Rs workshop entitled, 'Improving peer review of in vivo research proposals'. A member of AWERB will be attending on behalf of the University and will feed back to the Committee.
- Following her attendance at the last meeting of AWERB, the Home Office Inspector has reiterated that she is happy with the operation of the Committee and has no concerns.

18/04-05

Verbal Reports from the Director of BMSU and Named Persons

Report from the Director of BMSU:

- Charles River will be holding a seminar at the University on 24/05/18. Attendance is free and members of AWERB and researchers are encouraged to attend.
- An FOI request has recently been received for information on any usage within the University of puppies for the purpose of stress relief of students and staff during exam periods. There is currently no such activity to report.
- The Universities of Aston and Birmingham will jointly host the next meeting of the AWERB hub at Birmingham on 22/05/18. It is hoped that this will include a speaker from the North West hub and also a presentation on what makes a good NTS. This meeting will be open to all members of the relevant AWERBs and a JISCMail list will be set up to help with hub communications.
- Information from the ARMIS system was circulated which showed the problems which can arise when inbreeding with C57 as a background rather than buying in wild-type mice. The buying in of wild type mice is strongly encouraged and animals

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showing any signs of hydrocephalus or overgrown teeth should not be used for breeding.

- It was reported that the building work in BMSU has now almost finished and there should be little further disruption.
- The Home Office Inspector is now looking at new applications very quickly. The Home Office team which is working on the development of the new Project Licence application form will be shadowing the Inspector next week.
- Following its recent move to Croydon, the Home Office is currently short of staff to deal with licensing issues and has a considerable backlog.
- Discussions are underway about an existing surgical model which may be considered unacceptable as it involves a longer than necessary spinal incision. AWERB expressed concerns about this and the researcher will be advised that a more refined approach should be used instead.

Report from the Named Veterinary Surgeon:

- A slight rise in intestinal protozoa has been picked up during routine health screening. It is possible that this is related to the stress caused by recent building work. There are no implications for animal welfare or for ongoing research projects, but it will be looked into and monitored.

Report from the Named Animal Care and Welfare Officers:

- No issues to report.

18/04-06

Report from the Fast Track Procedure

The fast track procedure is up-to-date and a record of matters discussed is stored on the Committee's Collaborate pages.

18/04-07-1

Application Ref TBA – The microenvironment in organ homeostasis and disease

The overall aims of this project are to find out i). how liver disease occurs, ii). how the liver repairs itself following injury and iii). what happens when regeneration goes wrong and whether this leads to liver cancer formation.

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The PI gave a presentation explaining the application to the Committee.

It was stated in the presentation that diphtheria toxin-mediated deletion will be used at the same time as the dietary models of liver disease. It was highlighted that this combination is likely to take the licence into the 'severe' classification and further advice about this will be sought from the Home Office Inspector. It was noted that the likely effects of the models will be minimised in several ways: the particular strain of mouse chosen, the use of half the usual dosage of toxin, the administration of just one injection per day and the use of a 3 rather than 10 week dietary model. It was explained that weight loss problems are very much strain-dependent, and there is some evidence that the strain to be used is not susceptible to these. This will be referenced in the application and the strain to be used will be specified.

All researchers working with the diphtheria toxin model will have to be appropriately vaccinated.

It was noted that the last step in each of the protocols is unclear and it was queried whether any of the studies will be carried out under terminal anaesthesia. The PI will revise the wording to make this clearer.

The NTS should be amended to state that 10,000 rather than 5,000 animals will be used, to allow for the 5,000 used for breeding purposes. Overall, it was suggested that the stated numbers should be revisited as they were considered to be an over-estimation, particularly given that this is the PI's first Project Licence and there will be no other researchers involved.

In the NTS, the Committee asked for further information about the anticipated condition of the mice and it was suggested that the wording should be tightened up to more accurately reflect the anticipated adverse effects (e.g. 'lethargy' rather than 'lack of mobility').

The reference in the application to 'animal surgery' was queried and the PI explained that this refers to the possibility of carrying out laparotomies. This will be clarified in the application.

The NTS should be revised where necessary to ensure that it is written in language understandable to a lay person.

The references to humane endpoints and monitoring should be reworded to clarify that monitoring will take place throughout, not just when the humane endpoints are reached.

The potential adverse effects of tamoxifen should be explained in the application. It should be explained that tamoxifen will be given via

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food or gavage, rather than in drinking water.

It was noted that as jaundice is related to the experimental goal, it should not be stated as a humane endpoint; instead, endpoints such as those relating to weight loss will be used.

After the PI left the meeting, the Committee continued its discussions.

The Committee agreed that this application involves some potentially difficult models and that pilot studies will be important at the beginning of the work. The pilot studies to establish the diphtheria toxin deletion should be included in the programme of work.

The Committee noted that the worst likely experience for animals involved in the study will be some weight loss, but their condition otherwise will usually be fine.

Other institutions have experienced more difficulties with the diphtheria toxin model than have been seen within BMSU, where the model has been used with minimal difficulties.

It was felt that the parallels with human illness should be emphasised in the NTS.

The excellent flow diagram which was used in the presentation should be included with the application.

Resolved that:

The revisions discussed above will be made and incorporated into the application. Once this has been done, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

18/04-07-2

Application Ref TBA – Identification of pneumococcal genes involved in nasopharyngeal colonisation and disease

The overall aim of this project is to identify bacterial molecules which are important in the ability of streptococci to colonize the respiratory tract and cause pneumonia and use this knowledge to develop new vaccines and treatments.

The PI gave a presentation explaining the application to the Committee.

It was explained that imaging work is not included within this licence as it will not be possible in BMSU given the use of infectious animals and the risk of cross-contamination.

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In relation to a clinical score of 6 on the 'Development of pneumonia and sepsis' scale as a defined end point in protocol 2, it was queried whether it would be possible to humanely kill the animals at an earlier point on the scale as a refinement. The PI will consider this and will look into whether the use of telemetry might be another option. The Committee asked whether animals are likely to improve once they have reached point 6 on the scale and the PI explained that this is possible, depending upon the strain of mouse used and whether a vaccination has been given.

The maximum length of the experiments will be determined by the control group – if a particular strain of mouse reaches a humane endpoint by day 3, the experiments with that strain will last for 3 days.

It was suggested that it might be possible to use subcutaneous injectable microchips to measure temperature, although a study would be needed to test the feasibility of this.

The PI was asked why more of the proposed work couldn't be done using galleria larvae and it was explained that whilst galleria are a good model and it may be possible to establish which genes are important for survival in galleria, it won't be possible to do all of the proposed work with them. The galleria model doesn't mimic respiratory tract infection and any findings from the gut of moth larvae would not be directly comparable.

In relation to the stated aims of the study, the Committee queried where vaccination fits in and how treatment (as mentioned in protocol 2) relates to the aims of the study. As there is no treatment arm of the study, the reference to antibiotics should be removed from the application. An additional aim will be added to reflect the proposed vaccine testing.

500 extra animals should be added to the stated figures for breeding purposes. The proposed figures were considered reasonable for 2 people working on the project over 5 years.

The PI explained that blood sampling will be carried out to monitor levels of bacteraemia, which will usually confirm any symptoms observed. This should be explained in more detail in the application.

As the mouse grimace scale will not be used, reference to it should be removed from the application. Similarly, as local anaesthetic gel will not be used this should be removed from the application.

The NTS should be amended to better explain why the mice used in the colonisation experiments have to be killed at the end of the experiments.

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After the PI left the meeting, the Committee continued its discussions.

It was clarified that the mice will have to be killed before they reach level 6 on the clinical scoring system used (i.e. the point that they become unresponsive to touch), or this will be a severe rather than a moderate application.

The Committee was informed that this work has been ongoing for some years, but new personnel have recently joined the research group. There will need to be appropriate training and management of the new researchers to ensure that the required techniques are correctly carried out and monitored.

It was explained that SyRF is a tool to help with systematic review and meta-analysis and it was agreed that further efforts should be made to raise awareness of it and to explain to researchers what it is for.

The 'Alternative Contact' currently stated in the application will be changed.

Regarding the 3Rs, efforts will be made to encourage the researchers to use telemetry where possible.

Resolved that:

The amended licence application will be made available to the Committee electronically. After this, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

18/04-08

Matters relating to the 3Rs

Report from the NC3Rs representative

Activities undertaken recently:

- The presentation which was recently given at an early careers research event has led to several applications for NC3Rs funding.
- A workshop on the 3Rs in research using fish has taken place and a note of the key points has been circulated.
- Discussions have been ongoing with a researcher who previously used fin clipping, but who will now start to use swabbing instead.

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- BMSU has been working with one of the main genotyping service providers on technical issues relating to fish swabbing. The company has been having some technical difficulties with taking swabs and is now considering the use of a cell scraper to overcome this problem.
- Contact has been made with the University's Press Office to help highlight the 3Rs research programme.

Upcoming activities will include:

- The Midlands 3Rs symposium will be held at Birmingham on 19th September 2018. Work is underway to identify appropriate speakers and poster submissions and the NC3Rs 2017 3Rs prize winner will be the keynote speaker.
- Material will be included in the BMSU newsletter to raise awareness of NC3Rs resources (as noted in minute 18/04-07-2).
- The NC3Rs Midlands Programme Manager has been speaking to a number of research groups about the 3Rs.
- The three institutions which currently fund the NC3Rs Midlands Programme Manager post have reviewed the work carried out to date and are happy to continue to provide funding and to retain the current post holder.

18/03-09

Any Other Business

There were no additional issues to report.

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18/04-11

Date of Next Meeting

The date of the next meeting will be 14th June 2018.

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GLOSSARY

3Rs	Replacement, Reduction and Refinement
ARMIS	Automated biological service unit management system
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
C57	Strain of laboratory mouse
FOI	Freedom of Information
JISCMail	Email discussion lists for the UK Education and Research communities
NACWO	Named Animal Care and Welfare Officer
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NTS	Non-Technical Summary
NVS	Named Veterinary Surgeon
PI	Principal Investigator
SyRF	Systematic Review & Meta-analysis Facility
TBA	To Be Announced