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THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

8th March 2018

MINUTES

Present:

18/03-01 Apologies and introductions

The Home Office Inspector joined the meeting to observe and was introduced to the members present.

18/03-02 Minutes

The minutes of the meeting held on 25th January 2018 were considered by the Committee and were approved subject to minor amendments.

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18/03-03 Matters Arising

In relation to minute 18/01-07-1, it was reported that the NC3Rs Midlands Programme Manager has provided comments to the PI.

In relation to minute 18/01-04, slides from the recent RSPCA Lay Members Forum have been posted on AWERB's shared online site for the Committee's reference.

18/03-04 Chairperson's Items

There were no Chairperson's items to report.

18/03-05 Verbal Reports from the Director of BMSU and Named Persons

Report from the Director of BMSU:

- All annual returns have been received on time and have now been submitted to the Home Office.
- The Director of BMSU attended a recent meeting of AWERB Hub Chairs on behalf of the Chair. From this meeting, it is understood that some hubs are working very well but others less so. Going forward, an ASC member has been assigned to work with each hub in an advisory capacity. Some of the issues discussed at the meeting included the writing of good non-technical summaries and 3Rs sections and these may form the basis of a discussion day within BMSU. There is likely to be some restructuring of the West Midlands Hub to give a better balance of institutions.
- The boilers have now been removed from the BMSU car park and the worst of the anticipated noise and vibration should now be over. It is expected that the disruption will have had some effect on breeding rates, but this was unavoidable.

Report from the Named Veterinary Surgeon:

- The NVS reiterated that the disruption due to building work within BMSU may have affected breeding rates.
- It was reported that BMSU has been working to join up the oversight, maintenance and servicing of all anaesthesia machinery across the University.

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Report from the Named Animal Care and Welfare Officers:

- Given the recruitment of a number of new members of staff within BMSU, refresher training has been provided. The new team is working together well – two members of staff have been upgraded and one has retired, but continues to work two days a week to help train new staff.

- The final microscope will be installed in the intravital suite within the next month and the suite will then be fully equipped. Internal communications and promotional activities are planned to ensure staff are aware of the suite and its capabilities. Training and support will be available for new users at any stage from project planning onwards. The College of Medical and Dental Sciences has very helpfully provided some additional funding for equipment within the suite. Currently, at least one if not both of the two rooms within the suite are being used daily for research.

- Representatives from BMSU will be presenting at the forthcoming Institute of Animal Technology Congress.

- Representatives from BMSU and the NC3Rs Midlands Programme Manager will be giving a presentation at another UK University on the 3Rs in relation to research with fish.

18/03-06 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.

18/03-07-1 Application Ref TBA – The autonomic nervous system and sudden cardiac death

The overall aims of this project are to investigate how the nervous system acts to promote cardiac arrhythmia, by what mechanism(s) these effects occur and what can be done to prevent it.

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

It was explained that the majority of the work in the licence application has received peer review and that the choice of proposed species has already been discussed with reviewers.

The PI is experienced in the majority of the techniques to be used in the licence, apart from the implantation of mini-pumps and appropriate

training will be undertaken for this. All methods have already been used successfully elsewhere.

It was suggested that the number of animals stated on the licence application may be too low. The PI explained that the stated number is reasonable as there is currently only one researcher working on the project and also because one animal can often be used for both the intervention and control work, reducing the number of animals needed.

Whilst protocol two is technically difficult, the PI confirmed that it has been successfully used in previous studies.

It was queried whether the spontaneously hypertensive rat model could be used to avoid the implementation of mini-pumps. The PI will consider this, but it is unlikely to be possible given the need for a control animal and this will be explained in the application.

It was clarified that sudden cardiac death is likely to represent a relatively large proportion of overall cardiac death rates, as it is often difficult to identify once the heart has stopped. This will be explained further in the application.

The PI explained that the angiotensin model is unlikely to give rise to significant side effects over the time period involved.

No more than one mini-pump will be implanted per animal. When correctly used the mini-pumps are generally reliable and produce reproducible effects.

Only male animals will be used, so there will be no issues relating to female hormones.

The Committee queried whether the mechanism of action of the angiotensin model was relevant, or whether the main interest is in the model's effects. It was acknowledged that there will be some changes to the autonomic nervous system inherent in the model, but this mimics what happens in the equivalent human pathology. The PI will need to consider how best to interpret the results in light of the effects on the autonomic nervous system.

It was explained that guinea pigs will be kept for the minimum time period possible and will be housed in pairs in the largest rat cages available as BMSU does not have dedicated guinea pig housing. They will be small guinea pigs of equivalent size to adult rats.

It was suggested that the wording in the licence application should be revised to make it clear that of the smaller species, mice are the most appropriate for the work to be undertaken.

The PI was commended on a very good NTS, with the only suggestion being that 'long QT syndrome' should be explained (e.g. as an atypical cardiac condition).

The PI was asked whether the use of computer, rather than live animal models had been considered. It was explained that whilst computer models are developing rapidly they are still not at a point where they would be useful for the proposed experiments. The PI has used computer models in other projects, and it is hoped that the data arising from this licence application can be used to inform future development of such models.

The application should be amended to explain why tissue will be taken under terminal anaesthesia rather than after killing by a schedule one method.

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

The NVS felt that the humane endpoints require further work. For example, it would be preferable to allow two separate attempts to measure an animal's blood pressure before requiring the animal to be humanely killed.

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.

18/03-07-2 Application Ref TBA – How does protective immunity develop, function and persist to bacterial pathogens and vaccines?

The overall aim of this project is to address gaps in knowledge that will help us to understand how to better resist infectious diseases and their consequences.

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

It was felt that the reasons for the use of salmonella were not clear in the NTS. The PI explained that there are two forms of salmonella, typhoidal and non-typhoidal, both of which cause many deaths and considerable economic cost each year. Whilst there are three vaccines available against the typhoidal strain there are none which work against the non-typhoidal strain. The reasons for the use of salmonella should be explained more clearly in the application.

Given the stated group size of 4-6 animals, the Committee queried how the PI had calculated the total number of animals to be used. It was explained that the number of researchers within the group will shortly increase and the total number of animals stated represent an upper limit over the five years of the licence, taking into account the number of researchers involved.

The PI confirmed that Freund's adjuvant will not be used in this licence. It was also explained that the adjuvant BCG has been used intraperitoneally in previous studies and has not resulted in any clinical symptoms in the animals. In the planned experiments, it is likely to be used subcutaneously (which will involve looking at localised rather than systemic effects) with a lower starting dose than in previous studies. This represents a refinement.

From previous experience within BMSU, the use of tamoxifen can result in problems such as loss of body weight so a recovery period will be allowed after its administration. Tamoxifen will only be used in a small minority of experiments and this will be clarified in the licence application.

It was felt that as currently described, the adverse effects may be difficult for BMSU staff to interpret and the adverse effects and humane endpoints should be revisited and tightened up in the licence application, in discussion with the NVS.

Given the large size of the spleens in the experimental animals, it was suggested that body weight may not be the most helpful basis for defining humane endpoints. Other indicators such as body condition, coat etc. will therefore also be used and appropriate score sheets are already in use within BMSU. This will be clarified in the application. It was requested that examples of the score sheets be circulated to the Committee for information.

Also regarding the loss of body weight as a humane endpoint, it was noted that different experiments have different stated maximum losses in body weight. The PI explained that this was an effort to make the endpoints more meaningful and tailored to the different types of experiment and this will be stated in the application.

The Committee queried why it is necessary to use virulent salmonella in susceptible mice. The PI explained that this is the gold standard within the literature and is necessary if the research is to be published. It will only represent a minority of the experiments, and will always take place over the shortest possible time span. It is hoped that during the study it will be possible to critique the flaws in this 'gold standard' and to evolve and refine the model.

The PI confirmed that he has consulted the EDA webpages. It was recommended that the EDA app should also be used and the output of this included with the licence application.

The PI was asked to justify the replication experiments, and it was explained that the reproducibility of experiments is important when working with complex systems. The Committee discussed the arguments for carrying out a properly powered study once, versus replicating a lesser powered study. It was also noted that in vaccine studies, replication is useful to account for variation in the quality and preparation of the vaccine. The rationale for replication will be included within the licence application.

It was explained that subcutaneous peri-ankle injections are likely to only moderately affect movement and pain relief will be given. The use of peri-ankle injections is a refinement, as previous versions of the procedure involved injections into the footpad and caused considerable swelling. Further information about this refinement will be included in the licence application.

For some antigens, it will be possible to take lymph nodes from the other side of the animal (i.e. not the side used for the experimental procedure) to use as a control, and this can be seen as a reduction.

It was agreed that the NTS was appropriate, with just a few terms requiring further explanation.

The reference to the use of local anaesthetic gel for intraperitoneal injections will be removed, as it is unnecessary.

The hope that this research may have an impact on the problem of multi-drug resistant bacteria should be emphasised in the licence application.

Where necessary, the application should be corrected to remove references to protocols 13-16 as these will no longer be part of the licence.

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

It was agreed that there is some work to be done on the humane endpoints, the background to the study, the NTS and the 3Rs section of the application.

Feedback on the application has already been provided by the Home Office Inspector and input will be provided on the 3Rs by the NC3Rs Midlands Programme Manager.

A query was raised about the number of mice required for breeding versus the number to be used in experiments. It was explained that almost all of the animals bred will be used in experiments and most are homozygous. Wild type mice will be bought in.

Resolved that:

The amended licence application will be made available to the Committee with a deadline for any further comments. After this, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

18/03-08 Matters relating to the 3Rs

Report from the NC3Rs Midlands Programme Manager

Activities undertaken recently:

- A meeting with post-doctoral researchers to discuss NC3Rs Crack IT opportunities and possible funding.
- A presentation was given at the University's IMI Forum and at an early careers research event.

Upcoming activities will include:

- A workshop on the 3Rs in research using fish, focussing on surface swabbing as an alternative to fin clipping.
- Work with one of the main genotyping service providers on technical issues relating to fish swabbing.
- A 3Rs symposium on 19th September 2018. Work is underway to identify appropriate speakers and poster submissions, suggestions relating to this were welcomed.
- Relating to the recent award of an NC3Rs Training Fellowship and several studentships to members of the University, contact will be made with the Press Office to generate appropriate communications material.
- A paragraph on the use of ARRIVE and the EDA will be included in the BMSU newsletter, as it is felt that whilst researchers do mention these tools in their licence applications, they don't necessarily understand what they are and how to use them. Links to other relevant resources will be included. The Home Office Inspector is encouraging Universities to use the new NC3Rs systematic review tool, and this will also be

publicised in the newsletter.

18/03-09 Any Other Business

- The Committee was reminded that the licence application previously discussed under minute 17/11-07-1 has been recirculated and the deadline for comments is today.

- With the agreement of the Registrar and Secretary, the name of this Committee has been changed from the 'Biomedical Ethical Review Sub-Committee (BERSC)' to the 'Animal Welfare and Ethical Review Body (AWERB)', in line with other institutions and the terminology used in the legislation.

- Animal usage figures for 2017 will be shortly added to the BMSU website.

18/03-11 Date of Next Meeting

The date of the next meeting will be 19th April 2018.

GLOSSARY

3Rs	Replacement, Reduction and Refinement
ARRIVE	Animal Research: Reporting of In Vivo Experiments
AWERB	Animal Welfare and Ethical Review Body
BCG	Bacillus Colmette-Guérin – an adjuvant
BERSC	Biomedical Ethical Review Sub-Committee
BMSU	Biomedical Services Unit
EDA	Experimental Design Assistant
IMI	Institute of Microbiology and Infection
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NTS	Non-Technical Summary
NVS	Named Veterinary Surgeon
PI	Principal Investigator
QT	Measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. Long QT syndrome is an abnormal cardiac condition.
RSPCA	Royal Society for the Prevention of Cruelty to Animals
TBA	To Be Announced
UK	United Kingdom