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THE UNIVERSITY OF BIRMINGHAM
BIOMEDICAL ETHICAL REVIEW SUB-COMMITTEE (BERSC)

21st January 2016

MINUTES

Present:

16/01-01 Apologies

A new lay member was welcomed to the meeting.

16/01-02 Minutes

The minutes of the meeting held on 17th December 2015 were considered by the Committee and were approved subject to amendments.

16/01-03 Matters Arising

An update was requested on the progress of the application discussed in minute 15/12-07-1; it was explained that the application is still being finalised and comments have been received from the Home Office. Also in relation to this application further clarification was requested from the PI on why it would be almost impossible to carry out the work using human cells.

16/01-04 Chairperson's Items

There were no Chairperson's items for discussion.

16/01-05 Verbal Reports from the Director of BMSU and Named Persons

CONFIDENTIAL MATERIAL

Report from the Director of BMSU:

- Work has been progressing on the new quarantine room for initial exploratory experiments on animals from external sources (see minute 15/12-05). It is hoped that this will be ready within the next few months.
- The most recent routine health screening of animals within BMSU showed no problems. A low level of helicobacter was identified, but this has no implications for animal welfare or for the science of the experiments carried out within the Unit.
- The Committee was informed that a forum for AWERB members is being organised by the RSPCA, LASA, LAVA and IAT and it will take place on 12th May 2016 (flyer circulated). BMSU is prepared to fund two members of BERSG to attend.

Report from the Named Veterinary Surgeon:

- The new batch of Xenopus frogs are continuing to thrive and are laying well.
- Considerable work is being undertaken on the development of local regulations and procedures for work involving the exercising of mice.

CONFIDENTIAL MATERIAL

16/01-06

Report from the Fast Track Procedure

The fast track procedure is up-to-date, and there are no outstanding issues.

16/01-07-1

Application Ref TBA – Investigating a novel treatment for heart failure

The objectives of this project are to identify the mechanisms underlying the development of left ventricular hypertrophy and heart failure and to assess if and how perhexiline and novel derivatives delay the progression from left ventricular hypertrophy to heart failure.

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

It was noted that using mice in the weight range of 21-23g significantly reduces variability and improves the outcomes of the work, allowing a reduction in the number of animals required. This reduction should be explained in the 3Rs section of the application.

It was clarified that after three weeks the animals used in these experiments will develop symptoms of heart failure. The symptoms will include peripheral and pulmonary oedema and fatigue. A clear score sheet will be used to rate such symptoms and specific humane endpoints will be identified.

This model will be classified as ‘severe’ by the Home Office because of the potential mortality rate of 25% over the first seven days after surgery, which is inherent in the model. During the initial training period, this mortality rate may be increased. It is the possibility of unexpected deaths which will render this model severe, although the experience of the majority of the animals may actually be moderate when assessed retrospectively. This should be made clear in the application. The application should be amended to clarify that there will be an increased risk of mortality for up to seven days after surgery; the current wording of ‘24 hours or 7 days after surgery’ may cause confusion.

If an animal does die suddenly after surgery, it was queried whether it will have suffered. The PI will clarify this with collaborators carrying out similar work at other institutions. Post-mortems will be carried out on any animals which die suddenly, to learn more about the reason for the death.

Further information was requested about how the animals will be monitored during the seven day period after surgery. The PI explained that the surgeon and BMSU staff will observe the animal constantly on

CONFIDENTIAL MATERIAL

the day of surgery; continuous monitoring will then be carried out over the following days, based on the advice of the NVS.

Echocardiography will be carried out under recovery anaesthesia. It will be used to assess the progression of heart failure and will be used to monitor symptoms to ensure that the relevant humane endpoints are not exceeded. This represents a refinement when compared to a reliance on time-based humane endpoints as some animals' symptoms may progress more quickly than others'. The Committee queried whether there will be any additional risks in anaesthetising animals which are developing heart failure and the PI explained that she will draw on the experience of a collaborating institution in relation to this. It is thought that additional risks are minimal as the anaesthesia will only be very light, much less than that required for surgery.

The length of time stated in the application for echocardiography is incorrect and should be amended to 5-10 minutes. References to imaging being carried out without anaesthesia should be removed from the application as these have been included in error.

It was explained that the abdominal aortic constriction model is a refinement when compared to the previously used thoracic model. In the thoracic model, the animals are likely to experience more severe heart failure symptoms and the necessary surgery is more difficult and more invasive. The abdominal aortic constriction model involves less suffering, less variability and a slower disease progression. The surgery required for the abdominal aortic constriction model takes a maximum of 30 minutes per animal and the project will benefit from the involvement of a surgeon who is extremely skilled in the required techniques and who will train other members of the research team. It should be possible to carry out between five and ten surgeries per day.

The PI was asked to revisit the lay summary to amend/explain any technical terms and to provide further information about the 3Rs. It was felt that the lay summary should provide a clearer explanation of what will be experienced by the animals and it should be made clear why the model has been classified as severe.

The reference in the application to using animals for another purpose after the experiments relates to dissection and the use of tissues, not the reuse of live animals.

The PI explained that the animals will be pre-treated with the drug before surgery, heart failure will be induced via surgery and then treatment will be given again after three weeks.

It was queried why genetically altered mice will be required and the PI explained that while all initial work will be carried out with wild type mice, relevant genetically altered mice may be used in the later stages of the project if promising metabolic changes are identified.

CONFIDENTIAL MATERIAL

In the application, the PI acknowledges that the estimated number of animals required is generous and that less animals may be required in reality. It was felt that a realistic number of animals should be stated in the application and an amendment should then be submitted if more are required. The numbers of animals stated in various sections of the application should be made consistent.

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

The Committee agreed that the lay summary required significant revisions to ensure that all necessary information is provided (particularly a clear description of what will happen to the animals and discussion of the 3Rs) and that technical terms are avoided or explained.

The researcher was commended on providing an excellent presentation to the Committee.

The Committee considered the ethical implications of receiving funding from pharmaceutical companies. In the case of the project currently being reviewed, the company funding the work is interested in developing its commercial interests and this has been openly explained. It was felt that there may be some risk of such projects not receiving appropriate peer review. It was emphasised that the remit of BERSC is to consider the ethics of the proposed research, rather than the ethics of the wider activities of companies funding research (which are assessed elsewhere within the University).

As a severe licence, this work will have an annual reporting clause and the reports which are sent to the Home Office will be tabled at BERSC for information.

Resolved that:

The revisions discussed above will be made and feedback will be sought from the Home Office Inspector and incorporated into the application. Once the Chair is happy with the changes, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

16/01-08

3Rs meeting with Leicester and Nottingham

Ten places have been allocated for Birmingham delegates at the joint 3Rs meeting to be held at the University of Leicester on 16th March 2016. Project and Personal Licence holders and members of BERSC are invited to express an interest in attending.

CONFIDENTIAL MATERIAL

16/01-09

Any Other Business

The Committee discussed possible ways to improve the quality of the Non-Technical Summaries submitted for review and some form of initial screening by a lay member was suggested. The Director of BMSU will consider this and will report back with options for consideration at the next meeting.

As it is not currently possible to insert page numbers into Project Licence applications on the new electronic system, it was suggested that it would be helpful to manually add page numbers to the versions of the applications circulated to the Committee for review.

16/01-10

Date of Next Meeting

The date of the next meeting is 3rd March 2016.

CONFIDENTIAL MATERIAL

GLOSSARY

3Rs	Reduction, Refinement and Replacement
AWERB	Animal Welfare and Ethical Review Body
BERSC	Biomedical Ethical Review Sub-Committee
BMSU	Biomedical Services Unit
IAT	Institute of Animal Technology
LASA	Laboratory Animal Science Association
LAVA	Laboratory Animals Veterinary Association
NVS	Named Veterinary Surgeon
PI	Principal Investigator
PPL	Project Licence
RSPCA	Royal Society for the Prevention of Cruelty to Animals
TBA	To Be Announced