CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

BIOMEDICAL ETHICAL REVIEW SUB-COMMITTEE (BERSC)

17th April 2014

MINUTES

14/04-01 Apologies

14/04-02 Minutes

The minutes of the meeting held on 13th March 2014 were considered by the Committee and were approved subject to minor amendments.

14/04-03 Matters Arising

No matters arising were discussed.

14/04-04 Chairperson's Items

No Chairperson's items were reported.

14/04-05 Verbal Report from the Director of BMSU

Home Office roadshow on retrospective severity

A Home Office roadshow on retrospective severity and the conditions of licences will take place at Birmingham University on Monday 28th April 2014. All interested parties are encouraged to attend, including BERSC members. Attendance will count towards CPD for licence holders.

Recent visit from the Animal Science Committee (ASC)

It was reported that the recent visit from the ASC went well, and the work of BERSC was explained to the members of the ASC. A letter has been received from the ASC thanking the University for hosting the visit.

Need for a person external to the University on BERSC

The Home Office Inspector has recently noted the need for a person external to the University to sit as a member of each AWERB. As a result of this, a member of the NC3Rs will be invited to join the Committee.

New electronic licencing system

It was reported that almost all licence holders have now been transferred onto the new electronic licencing system. New applications are being turned around in 1-2 days, and the University has received a complementary letter from the Home Office about the quality of its licencing paperwork.

Request for animals for dissection practical

A request has been received from a member of staff in Biosciences to buy in 50 rats for the purposes of a dissection practical for students. Members of BERSC agreed that it would not be appropriate to buy in animals to kill for this purpose if an alternative can be found. It was agreed that an appropriate number of frozen cadavers can be provided from existing studies going on within BMSU, rather than purchasing additional animals.

14/04-06 Report from the Fast Track Procedure

A report from the fast track procedure was tabled.

14/04-07 Project Licence Proposals

14/04-07-1 Application Ref TBA – In vivo testing of novel targeted treatments in leukaemias and lymphomas with DNA Damage Response defect

It was explained that this licence application is still in the early stages of preparation, and further work is likely to be required on the sections detailing possible adverse effects.

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

In the non-technical summary, under the heading 'reduction' it is stated that the researchers, '…will also maximise the results that we can obtain from each animal'. The Committee requested further information, and the PI explained that this referred to the intention to maximise the amount of data to be gathered from each mouse once it has been killed. It was noted that the use of in vivo imaging should help to reduce the impact upon the animal, as it should be possible to

track progression of a tumour and end an experiment before the tumour causes any suffering.

One of the PI's slides indicated that the mice will be killed at a fixed time point, and it was clarified that this would be defined by the progression of the tumour, balanced against the need to minimise any suffering for the animal. The actual time involved may differ between individual animals.

In the presentation, the PI mentioned work with human cells. From a lay perspective, the Committee queried why animal work is still required if work is being done with humans. The PI explained that this relates to work with immortalised human cell lines, and that while these are used as a surrogate to indicate what may happen in vivo, cell lines cease to be fully representative over time, as they undergo genomic changes in the laboratory environment. There are currently no culture systems for primary tumour cells, and primary human tumour cells cannot usually be kept for longer than a couple of weeks – it is therefore necessary to use animal models in addition to work with cell lines. It was also noted that the regulatory framework requires work to have been carried out with animal models before progressing to human subjects in trials.

The Committee requested further information about how the requirement to consider 'replacement' in the 3Rs will be met. It was explained that animal work will only be undertaken after extensive preparatory work, and only those agents already tested in immortalised cell lines will be used in animals. The wording on this in the application will be clarified.

It was queried why, in protocol 2, it is stated that either intra-femoral or intra-splenic injections may be used. The PI explained that this is dependent upon the type of tumour, and can't always be predicted in advance. The most refined method possible will always be used.

It was noted that the use of real-time imaging should be added to the 'refinements' section of the application. It was also explained that the proposed models are familiar to BMSU staff, and have already undergone considerable refinements. Blood sampling will be used to give very accurate feedback on the health of each animal.

Cut and paste errors (including those on pages 13 and 14 of the licence application) will be corrected.

In the section about the expertise of the proposed researchers, it should be stated that they have expertise in intra-femoral and intra-splenic injections.

It was explained that the previous licence, with a duration of 5 years, has now come to an end – this should be explained in the new licence application.

The Committee queried why protocols 2 and 3 are currently separate, and it was explained that this relates to the need to calculate retrospective severity. The only difference is that some of the animals will experience therapy, which is likely to make the work of a higher severity (before treatment) than for those animals who do not experience therapy.

It was suggested that the overall severity of the cumulative experience of the animals is unclear within the licence application. It was noted that some of the animals are likely to experience only a mild cumulative severity.

Noting the proposed size of the groups of animals to be used, the Committee queried whether the PI has received appropriate advice on experimental design and statistics. It was confirmed that appropriate support in this area has been obtained, and this will be mentioned in the application.

The severity limit of protocol 1 will be corrected to 'moderate', as the currently stated 'mild' is an error.

It was queried how easily dosages for the in vivo work can be calculated from the effects in vitro. The PI explained that from experience, preliminary toxicology gives a good indication of the relevant bioavailability, and experiments will start with pilot work in a very low number of animals.

The adverse effects of the cancer model should be stated in the non-technical summary.

It was suggested that the reference in the licence application to 't-tests' should be replaced with 'appropriate tests', to avoid limiting the possible methods that can be used. It was also suggested that preliminary work should be mentioned in justification of the sample sizes to be used.

The Committee discussed the application further after the applicant left the meeting, raising the following points:

(i) It was explained that one of the two presenters is not named in the licence, as she has no Personal licence. She will be providing the clinical samples to the named researchers and works closely with the Proposed Licence Holder.

(ii) It was felt that the focus of the section on 'refinements' should shift from technical refinements of the experiments to refinements in relation to animal welfare.

Resolved that:

Once comments on the application have been received from the Home Office Inspector, the revised version will be circulated for consideration by the Committee. Once agreed via Chair's action, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

More general concern re.'replacement' element of the 3Rs

Prompted by discussion of the application above, the Committee went on to consider the more general issue of how applicants should approach the 'replacement' section of the licence application form. It was noted that the majority of applicants' responses to this question are very similar. It was noted that the Committee should be aware of the possibility of 'partial replacement', i.e. using less animals than would otherwise have been necessary because of the use of certain experimental techniques (and the likely overlap between reduction, refinement and replacement).

14/04-08 Any Other Business

No items were reported

14/04-09 Date of Next Meeting

The date of the next meeting is 5th June 2014.

GLOSSARY

3Rs	Reduction, Refinement and Replacement
ASC	Animal Science Committee
AWERB	Animal Welfare and Ethical Review Board
BERSC	Biomedical Ethical Review Sub-Committee
BMSU	Biomedical Services Unit
CPD	Continuing Professional Development
DNA	Deoxyribonucleic acid
NC3Rs	National Centre for the Replacement, Refinement, & Reduction of Animals in Research
PI	Principal Investigator
PPL	Project Licence
TBA	To Be Announced