

UNIVERSITY OF BRISTOL
ETHICAL REVIEW GROUP

Notes on the meeting held on Tuesday 20th January 2009, in XX, at 2.00pm

Present: XX

1. Attendance

1.1 XX welcomed the members to the meeting, giving special mention to XX who is replacing XX he has now left the university. He also welcomed the two Home Office Inspectors, XX and XX.

1.2 Not invited to attend

None

1.3 Apologies

Apologies were received from XX

2. Notes and comments of the meeting of 18/11/08 (as circulated)

These were accepted as a true and accurate record of the meeting.

3. Matters arising from the notes of the previous meeting

3.1 Item 5.1.1 (p4): XX assured the ERG that he had liaised with XX and that the revised Project Licence application was now at the Home Office.

3.2 Item 5.1.1 (p4): XX confirmed that he had received full applications as requested.

3.3 Item 5.1.1 (p4): XX informed the group that he had written a letter to XX and that he has responded to say that he understands the concerns of the ERG. A copy of the letter is on file in the ASU office.

3.4 Item 5.1.2 (p5): XX confirmed that he had assisted XX with the wording on his licence. They had also made the abstract more suitable for lay readers.

3.4 Item 5.2.1 (pp5&6): XX had investigated whether XX could do her work *in vitro* instead of using immunocompromised mice. He reported that her Project Licence states that the *in vitro* method does not reflect disease progress accurately, therefore she needs to cultivate compounds in the murine model.

4. Chairman's Report

4.1 XX will be retiring at the end of this academic session. XX suggested that perhaps the ERG should think about recruiting a new lay member. Ideally there would be some cross over before XX leaves.

ACTION: ERG to give ideas for possible replacements at next meeting.

4.2 XX (*this section relates to a University administrative matter and not information relating to experimentation on or other work involving live animals*)

5. Project Licences – New Applications

5.1 Normal Track for ERG Review

5.1.1 1 – XX – “*Bacteriophage-based vaccine-delivery system*”

2 - XX – “*Phage therapy for the treatment and prevention of bacterial diseases*”

- XX left the room while XX and XX addressed the ERG. XX said that this was a slightly unusual situation regarding reviewing a project proposal from an ERG colleague. He also asked that both projects be reviewed at the same time.
- XX declared an interest in the proposal as he has been involved in discussions with XX about this project.

- He then explained the background to the research, in which the potential use of phages in vaccination would be investigated. He made reference to Jenner who, nearly 200 years ago, was lucky enough to have a live disease to work with. XX intends to investigate two diseases that are, currently, very important to man.
- With reference to the first application, XX said that it seemed like a straightforward project but he would like to know:
 - 1 - some of the properties of the phage work,
 - 2 – what evidence there is that the phage will exist in the intestine?
 - 3 – why XX is not intending to test tolerance?
 - 4 – whether the harmful effects are minor, as they appear from the proposal?
- With reference to the second application, XX explained that XX intends to introduce *Clostridium difficile* into hamsters and mice. He would like to know:
 - 1 - how XX will assess side effects
 - 2 – whether there will be major effects in mice, although the protocol is described as moderate.
- XX then had some questions of a more general nature:
 - 1 – Animal numbers clarification – The proposal states 2 groups per study, repeated three times. XX confirmed that the entire study would be replicated three times.
 - 2 – Poultry project – how do the results of the poultry project (referred to as background information in the application) influence XX proposed work.
 - 3 – What is the relevance of work in the Eastern Bloc?
 - 4 – Regarding severity limits in mice and hamsters, is 8 hours sufficient between observations if the animals have a severe infection?
- XX then invited questions from the rest of the group. XX said that he thought that the two projects could possibly be incorporated into one project licence application with several protocols. He also noted that hamsters have been used in the past and given a ‘substantial’ severity limit.
- XX asked what the symptoms of *C. difficile* are. XX explained that acute diarrhoea and dehydration would be observed.

XX joined the meeting. XX briefly explained the process of the meeting and the Ethical Review Process and asked XX to consider the two proposals together.

- XX stated that these project proposals are a result of two years work. Phages are viruses, which target bacteria without harming the animal. They were used as antibiotics before the advent of antibiotics.
- With reference to the second project, XX explained that it was aimed at using phage to treat *C. difficile*. It is a hospital acquired infection and especially targets those over 65 years old receiving antibiotic treatment, the reason being that antibiotics disrupt the normal balance of micro-organisms in the gut and leave people susceptible to gastrointestinal infections. As *C. difficile* proliferates, the disease becomes more apparent as a result of increasing levels of toxins. Current treatment is further antibiotic treatment, therefore there is not a high success rate due to the gut flora being destabilised. *C. difficile* is present in a large percentage of the population with no ill effects. Disease only sets in when overgrowth occurs. XX explained that it is, therefore, not necessary to eradicate it, just suppress its numbers. Phage success is a 100-10,000 times reduction in *C. difficile* population, allowing commensal gut flora to re-establish. He said that it could be used in advance because it is known who is susceptible and which operations are causal. This should reduce the emergence of the clinical disease.
- With regard to the first project, XX explained that phage is used in a different way. The idea is to introduce a gene into phage to code for an antigen to provide protection to the patient. So, GM phage is introduced to the patient where it builds up in the gut flora, and certain of these organisms, in turn, produce the antigen. Outcome predictions are: the induction of mucosal immunity or, alternatively, the induction of oral tolerance. It may be a way of turning off adverse reactions. XX is unsure what the results will show but, either way, they will be of great interest as vaccines or as immunocompromising agents.
- XX asked about work in the Eastern Bloc. XX said that there is huge evidence of efficacy but nothing has been published on *C. difficile* in English. A lot of work has been done in the Eastern Bloc but, unfortunately, it is not often translated into English so the results have not often been taken seriously. He added that it is, unquestionably, a very effective way of coping with enteric disease. He knows this from his own research on Campylobacter in poultry.
- XX then asked for more details of the poultry work. XX said that it achieved the aims of the study but as the species is very tolerant to high numbers of Campylobacter it would not be useful for further research. He added that it would be difficult to deliver treatment to individual birds within a poultry shed housing 20,000-30,000 birds. He explained that once Campylobacter enters the human population it results in food poisoning.

- XX observed that it is clear that we want the properties of the phages, although they will be used very differently in the two studies. XX said that once a phage goes into the gut, it will reduce the population of *C. difficile* to start with as it is a predator-prey relationship, resulting in an initial plunging drop in numbers. The population then climbs back up to about 10%. Therefore, the *C. difficile* population is always 90-99% suppressed but will still persist. He confirmed that phages are usually extremely specific, to within a single strain of bacteria, although there is one particular phage that will attack *C. difficile* and Salmonella. There are 13 strains of *C. difficile* but 70% of clinical cases are due to just three strains. XX checked that one could be sure of not affecting other populations. XX replied that it would be prudent to use a cocktail to attack all 13 strains because if treatment were started at a species level, effective treatment could be delayed by several days.
- XX asked if there was a reason that XX had not included a protocol on tolerance. XX responded that he intends to add this in as per XX advice. XX does not think that it should change the overall severity banding. XX agreed that all the animals would suffer was oral gavage in the vaccine study. He thinks that the clinical disease study would probably be given a moderate banding.
- In response to XX query about severity limits, XX confirmed that in hamsters, the disease is very acute. Animals will die within 48 hours if not treated, and therefore they will be checked every 8 hours to ensure that suffering is minimised. If an animal shows any signs of diarrhoea it will be culled. He also said that in the initial trial, he would not use a cocktail of phages. He would first trial ones with known results to build up data for MRC in view of funding.
- In response to a query as to whether laboratory hamsters are clean of *C. difficile*, XX replied that he did not know, but he did know that it is a very common occurrence for hamsters to suffer stomach upsets induced by antibiotics.
- XX enquired whether XX considered 8 hours between animal observations was sufficient. He thought that it was. He said that mice could tolerate longer but hamsters needed more frequent checks.
- XX asked if hamsters become pyrexia and then die. XX confirmed this, so XX suggested that XX implant a few animals with thermal probes to monitor their body temperature during the experiment. XX thought that this was a good idea and he would incorporate it into his proposal.
- XX informed the ERG that the hamster model is generally more accepted as it is useful for studying the acute phase of the disease but that the mouse model is more useful for studying the chronic phase.
- XX asked what sex hamsters would be used. XX thought that this was not relevant. XX said that it is relevant because he would need to provide single housing for males as they would fight if kept together. XX commented that females may well fight too, especially in the presence of males. XX suggested that XX may wish to consider this in his application.

XX left the meeting.

XX summarised the discussion, saying that XX seemed happy to incorporate the two studies into one project licence application, as per XX suggestion. He also appeared keen to monitor the core body temperature in some animals. XX said that this would back up the 8-hour monitoring that he intends to do. XX noted that it seems to be a useful piece of research.

The ERG approved this application.

5.1.2 XX – “Phage therapy for the treatment and prevention of bacterial diseases”

- See section 5.1.1 above.

As the meeting was running ahead of schedule, it was decided to proceed to item 5.2.

5.2 Fast Track for ERG Ratification

5.2.1 XX – “Studies of the biology of parasitic nematodes”

- XX told the ERG that XX is an immunoparasitologist. The ERG looked at a recent project licence application of his on immunity in wild rodents. He now plans to continue his work with rats, investigating the parasite ‘Strongyloides’.
- In the first protocol, he uses the animals as a host for the production of worms, which he will later harvest and study. He has a developmental engineered model gut to monitor growth and behaviour of the

worms because it is difficult to study these things within the animal. However, it does not maintain the worms so he still requires animals as hosts.

- The second protocol looks at immune responses in rats with immune systems altered with drugs, given larvae systemically or via the skin. XX will take blood samples, give drugs to alter the immune system and treat some rats ready for a second challenge. These are all mild interventions. The aim of XX work is not to stop infestation by the parasites but rather to take a more fundamental interest in the biology of the parasites, especially with reference to their gene profile.
- XX asked what is new about this project compared with his earlier work. XX replied that XX is interested in the nutrients taken by the worms from the animal's gut and the consequent interaction between the two organisms.

The ERG ratified this application.

5.2.1 XX – “*The control of cardio-respiratory activity*”

- XX explained that XX is from the department of XX. His group focuses on the effects of hypertension. He has several models of hypertension including use of mice and rats. He is particularly interested in the role of the autonomic nervous system and brain control. The research group has established several techniques whereby blood pressure control mechanisms can be altered; e.g. by inserting genes into the brain and then implanting a transducer with a probe into the aorta, which gives 24-hour readings of blood pressure. This process of telemetry is very informative as it allows the animal to recover.
- XX is also interested in the role of chronic pain in hypertensive animals, which justifies not using analgesics because they would interfere with the results. This work, therefore, has a ‘Substantial’ severity limit.
- XX will introduce DNA into sperm (rather than the usual method of using ova), which should be a straightforward way of producing genetically altered (GA) animals. Drugs will be delivered to the animals via peripheral blood vessels.
- XX agreed that this group has been extremely successful in their work and it is highly relevant as it is currently unknown why hypertension suddenly develops. It is as if the set point for blood pressure becomes reset by an unknown factor, or set of factors.
- XX said that other researchers had had problems with Wistar Kyoto (WKY) rats. XX said that perhaps he will use more GA mouse strains depending on his results.
- XX enquired how long the animals are kept alive for. XX replied that this was a difficult question because he did not want to set a figure ‘out of the blue’ and then find that he would like to keep the animal alive longer because he was getting interesting results and the animal appeared relatively well. XX suggested that if a low limit was set, it would limit the work being carried out. XX and XX discussed the point further.
- XX said that in Section 19b Page 9 (Induction of neuropathic pain), XX does not say when he would call a halt, i.e. in terms of behaviour. XX stated that self-mutilation would not be expected so if that were to occur, XX would have to cull the animal. XX suggested that other indicators, beyond autotomy, should be considered.
- XX wanted to know how the number of animals was worked out as it was not clear from the abstract. XX and XX assured XX that XX had submitted very detailed workings.
- XX asked how successful people are at predicting total numbers over five years. He thought that it might possibly be more important to predict per experiment. XX commented that it is important to allow enough animals to complete the work. XX noted that a quarter to a third of all project licences have a nil return.

The ERG ratified this application.

6. Project Licences – Amendments for ERG Ratification

6.1 **30/2353** XX “*An evaluation of strategies to improve convection-enhanced delivery*”

XX reported that XX wants to add stereotaxic injections to the licence. Her work involves delivery of drugs through the blood-brain barrier. If an animal is injected directly into the brain there is the chance of drug tracking back through the wound. This can be toxic if a whole dose is delivered in one go. XX confirmed that XX is endeavouring to refine her technique.

The ERG approved the amendment.

6.2 **30/2270** XX “*Pathophysiology of autoimmune uveitis*”

XX would like to amend his licence to allow him to use viral vectors. XX noted that this would be an opportunity to try something that XX couldn't have anticipated at the time of writing his original project licence application. He thought it could have a promising outcome.

The ERG approved the amendment.

6.3 **30/2255** XX “*Early pathogenesis of prion disease*”

The amendment involves a change of licence holder from XX to XX as XX has now taken up a post in Ireland. XX confirmed, at XX request, that the proposed deputy has been on all the appropriate courses.

The ERG approved the amendment.

6.4 **30/2297** XX “*Cytotoxic T lymphocyte responses to self-antigens: ‘Tolerance versus autoimmunity’*”

XX reported that this amendment concerns the refinement of the adverse effects stated in the licence. An end point on animal weight has been given.

The ERG approved the amendment.

7. Project Licences – Mid Term Reviews

7.1 **XX 30/2302** – “*Molecular and cellular therapy for neurodegeneration*” [Tabled]

XX reported that a number of grant proposals are being considered. He is not aware of any welfare issues in the studies undertaken so far. XX applauded the fact that XX is looking at *in vitro* options before moving into *in vivo* work.

The ERG approved the review as satisfactory.

7.2 **XX 30/2288** – “*Mechanisms underlying opioid tolerance*”

XX reported that this work is linked to human drug abuse, where progressively higher levels of the abused substance are used as the body appears to develop a tolerance. This is probably due to a de-sensitising effect. It has been found that there is a respiratory repressive effect, which is reverted by low levels of alcohol. It was previously thought that morphine abusers who were found dead, had become tolerant and therefore used higher levels finally resulting in respiratory collapse but XX argues not. He made a case for abusers calculating accurately but other factors involved causing death.

XX asked about the interaction between heroin and ketamine. XX replied that this appeared to be a novel observation in laboratory animals, although there is anecdotal information on the interaction in humans. Paramedics are able to instantly identify when a person has taken ketamine due to the involuntary body movements: their first question is apparently to ask what else the patient has been taking because they are aware of the dangers of mixing these two drugs.

XX (HOI) offered to ask other Home Office Inspectors if they are aware of other ongoing work in this field. It may be useful for further research and in the interests of the 3Rs for the research animals involved.

A question was asked whether sudden deaths like these should be reported to the Home Office. XX responded that they should because they are unexpected deaths. It is both a requirement and useful information for them.

The ERG approved the review as satisfactory.

In view of the time, it was decided to return to item 5.1.3.

5.1.3 XX – “Development of novel therapies to treat diseases of the Central Nervous System”

- XX reminded the ERG about this application by XX on behalf of XX in a completely new area of work. XX is a contract research business operating with the University. He said that at the end of the discussion at the September 2008 ERG meeting, the ERG had recommended that it could not approve the application in its current state. He then tabled a letter that he had written to XX with the accompanying relevant section of the minutes. XX informed the group that XX has now resubmitted the application and XX has reviewed it, as he was one of the original reviewers.
- XX said that XX has an impressive track record in drug testing and immunology. He noted that this proposal was a slightly unusual commercial arrangement, in which well-established models of neurological disease would be offered. Most issues raised last time (Sept '08) have been resolved except the following points:
 - 1 – XX needs to be very clear about the numbers of animals to be used, especially for model validation because the models are already established but have not been transferred to the University of Bristol.
 - 2 – The work has been split into two phases, which is a positive step. Phase 1 looking at existing models and Phase 2 testing new drugs on a commercial basis once the models are available here.
 - 3 – XX has a lack of expertise in these models. XX would like to have seen supporting statements. He thought the ERG should apply the same rules as research councils in this area.
 - 4 – At the last meeting it was considered appropriate for XX to appoint a second deputy, considering the wide scope of the proposal but XX could not find a new deputy in the revised licence.
- XX noted that XX had given some revised animal figures, including some genetically altered (GA) mice. XX was reasonably happy with the overlap of the use of rats and mice but if XX wants to use transgenic animals, they would need to repeat in normal mice. He thought this process could be streamlined. He also noted that there were inconsistencies in the animal numbers between the Home Office lay abstract and the project licence application. XX and XX noted that the numbers in the abstract were ‘per year’ and the numbers in the application were ‘over the lifetime of the project’ but this still did not account for the discrepancies.
- XX said that the severity limit had been increased from ‘Moderate’ to ‘Severe’ [Substantial] but that XX had highlighted that an existing project licence using the same model had been given a ‘Moderate’ label.
- Additional experts had been listed and they were all established neuroscientists but there were not a lot of published records for them although plenty of *in vivo* animal experience.
- XX said that he still had concerns about the proposal as he was not convinced that XX had answered the points that the ERG had put to him. There were no supporting references to XX (deputy) experience in many models, in Bristol or elsewhere. Therefore, he read it as starting *de novo*. XX then noted his other comments, as follows:
 - XX claims that bringing the GM mice from XX will be straightforward but there is no evidence of linking with XX to help validate it.
 - References to the work of XX have been included on knee and ankle chronic pain.
 - In Section 18 Objective 3, a section has been inserted on diabetic neuropathy as a model of chronic pain but it has not been mentioned elsewhere.
 - It is not obvious that there is a clear time sequence. For example, will XX validate the work and only then start offering the service OR will they stage it and validate and offer one model at a time?
 - XX expressed concern that lesions of the saphenous and sural nerves have been quoted as established models of chronic pain. This requires qualification as some kinds of nerve injury are symptom-free while others may show evidence of a sensory disturbance.
- XX thought there was no clear answer regarding the assessment of pain responses from certain stimuli, e.g. acetone and heat application. XX wanted to know if these were acceptable methods. XX confirmed that these were established methods.
- XX would like a definition of ‘regular’. She would like to know the actual frequency of observations of the animals following procedures.
- XX reminded the ERG that ‘Substantial’ is the proper label for the upper severity limit, not ‘Severe’ (in connection with XX comment earlier). He also noted that XX and XX have both been fairly recently granted project licences with a ‘Substantial’ banding.
- XX reassured the group that the animals would be seen daily by the ASU staff and that any observations by researchers would be in addition to this.
- XX wanted to know the normal feeding pattern for a mouse and, therefore, what would be the impact of not eating for 22 hours. XX stated that mice have a strong drive to find food and spend most of their waking hours doing so. He confirmed that they might well be becoming hypoglycaemic by this point.

XX and his deputy, XX, joined the meeting. XX reminded them of the process of the meeting and the Ethical Review Process. He asked them to focus on the issues raised last time the proposals had been considered and how they believed they had addressed them in the revised application.

- XX began by stating that the key thing was the models they intended to bring to Bristol from XX University. He admitted that animal numbers needed firming up and that he was not an expert in the area, so, additional expertise would be needed. He said that he had brought a letter from XX to the Animal Services Unit (ASU) saying that she was happy to support him and train his staff in setting up the models and in dealing with any issues that may arise during transfer. He said that XX had experience of validating pain studies with “gold standard” compounds. XX had also delivered a letter to the ASU from XX, where the unique mouse strain is held. He believed that a huge number of animals should not be needed to set up the model.
- XX had also asked XX to help them with setting up models of Alzheimer’s and Parkinson’s disease and subsequently assessing signs of disease. She is currently using some of the methods for clinical assessment that they intend to use e.g. the water maze.
- XX has also agreed to provide support in pharmaceutical models. XX asked for details about her as he had not heard of her. XX stated that she is an independent consultant, based in XX, who has, in the past, worked for XX.
- In each model, XX stated that they would run with a small number of animals for each compound to assess the appropriate dose. They would then validate it against a control group. He said that he thought the ERG was comfortable with the fact that he could not be exact about these figures. XX agreed.
- With regard to pain levels, XX said that they had originally put ‘Moderate’ on the application because they had referred to XX project licence with similar procedures. He has now taken the advice of XX and changed it to ‘Substantial’.
- XX said that he understood there were difficulties in giving exact numbers but that currently there were three different sets of figures. XX confirmed that they should have added up. XX gave an example of 2400 mice in the licence application but 2100 somewhere else. XX said that he would correct it and that he must have made a mistake. XX reiterated that the numbers would need to be checked in every part of the application.
- XX next point concerned the lack of a time sequence for Phases 1 and 2. XX said that he will expand on this. He has limited resources and does not intend to leap into using all the models at the same time. He will probably go with one or two models at a time, initially, scopolamine and the pain models as XX staff are experienced in these areas. They would then prepare for others, e.g. Parkinson’s.
- XX did not have any information regarding the additional expertise (the letters referred to earlier by XX) so XX said he would summarise it for the ERG later as XX had just passed him the details.
- XX asked how regularly animals would be assessed in the section concerning the minimisation of adverse effects. XX responded that the ASU technical staff would carry out daily checks, which should make clear any signs of distress as they would inform the licence holder. XX staff would also check but less often, although, more regularly with acute models.
- XX wanted to know who would be supporting XX with the diabetic neuropathy model. XX replied that it would be a researcher with whom XX had worked before. He is not based at the University of Bristol and she could not remember his name. Nor could XX, so he said that he could provide assurance before they started, if necessary.
- XX then informed XX that lesions of the saphenous and sural cutaneous nerves would not necessarily give a model of chronic pain. This knowledge is based on personal experience of research in the area. XX asked what the ERG would like them to do. XX suggested removing it from the proposal. XX and XX responded that XX had suggested putting it into the application, so they will consult with her. [Note added after the ERG meeting: XX does have experience of a partial nerve injury model of rat saphenous nerve where there is evidence of sensory disturbance (allodynia) but not necessarily neuropathic pain]. He thanked the ERG for their advice. XX commented that it is only a useful procedure if it is relevant to what they will be doing.

XX and XX left the meeting.

- XX confirmed that he did now have letters from the following people:
 - XX of UoB, confirming that she will help XX
 - XX of XX University, who will help assure the Parkinson’s disease and Lewy bodies disease models are valid
 - XX of UoB, stating that she will provide support and advice on Alzheimer’s disease, although she acknowledges that she has not used the exact models that XX intend to use. However, she has used similar ones.

- XX, providing a CV showing that she was publishing original papers up until 2004. XX remarked that it was disappointing that the ERG did not have that information beforehand as it would have made reading the revised application easier.
- XX gave an overview of the discussion.
 - He said that the animal numbers still needed to be corrected but that this should be possible.
 - Clarification of the implementation of Phases 1 and 2 is still needed.
 - The severity limit of 'Substantial' will be used, although XX would prefer to use 'Moderate. XX noted that he does not have an option.
 - Additional expertise has been sought.
 - A section on diabetic neuropathy had been added in. XX said, and XX confirmed, that just inducing diabetes does not automatically cause pain. XX said that it is possible that the mice might be put on insulin. XX would like more information on this.
- XX commented that the whole application seems a rag bag of bits and pieces. XX said that this might be because they want to include lots of pieces of expertise to be commercially attractive.
- XX thought that staging which protocols would be established first was very important because, in theory, they could have a number of protocols established, which, at any point in time, may not actually be needed by anybody.
- XX noted that XX seemed very casual about things, especially with regard to animal numbers. As the ERG had already asked for revision of the numbers she thought it disappointing that there were still inconsistencies. In light of the fact that the work is to be available commercially, and in the public eye, XX thought that XX attitude should be less casual.
- XX commented that XX had not done what the ERG had requested, i.e. staging the work.

XX asked the ERG whether, if everything was in place, i.e. staging, neuropathic pain, animal numbers and so on, they would be happy to recommend it.

- XX still has concerns about how Section 17 is written, especially the part saying that XX is 'an expert in neuropathic pain' as there is no evidence for this.
- XX wondered why, if the saphenous and sural nerve work has been published by people like XX, XX and XX had not picked up on this.
- XX noted that it is such a different type of application for XX and the ERG that it is difficult to deal with. XX agreed and said that the ERG has to take the letters of recommendation at face value. XX said that they had no reason to disbelieve them.
- XX would like further discussion on endpoints. He did not think it is necessary for any animal to end up chewing their digits. He would suggest that if there was any sign of autotomy, the animal should be culled, therefore using similar wording to that of XX recent application with a paper reference provided also XX would very much support XX in this. XX could understand where XX had sourced his figure due to papers published abroad, which used this limit.

XX asked the ERG if they would be happy to leave it with XX and XX to see through. The ERG agreed.

ACTION: XX and XX to give a progress report at the next ERG meeting.

- XX (HOI) wished to make a few comments. He said that sometimes spinout/contract research companies from universities are successful but not all. He suggested that the ERP was not set up to assess this on an ongoing basis and that the ERG might need to revise the procedure. He would want to know more about XX and their referees and supporters. He was concerned that XX had mentioned 'limited resources' as this appeared to be an expensive enterprise. He would also want to know the relevance of diabetic neuropathy. He would also request further information on validation, including endpoints.
- XX noted that XX presentation had sounded more like an application for funding than for a licence. He would need to be convinced that the project is practically possible. The work would also need to be to GLP or equivalent to be useful to industry.
- XX enquired as to the connection with the ASU. Are XX buying their services? XX responded that he is in the process of negotiating this. The ASU does not have the staff cadre at the moment to compete commercially. Although the technicians are good, they have to deal with a much wider range of animals and procedures and are, therefore, not as speedy as employees of a commercial pharmaceutical company.
- XX then asked if XX was offering something unique. XX would also like to know how competitive they would be. XX discussed with some ERG members the details of how spinout companies and universities have interacted in the past and how this information could be applied to the current situation.
- XX said he will take advice on organising a meeting with PVC Research elect, XX and XX, regarding spinout companies of this sort. Alternatively, he might raise the matter as part of the ASU review.

- XX commented that he would not like to put off the university from proceeding; he just wished to note that the University of Bristol has concerns as does the Home Office. He thought that every point made during the meeting was relevant.

8. Final Reviews

8.1 XX 30/2151 – “*Plaque rupture*”

XX remarked that all the final reviews being considered today had a common theme, i.e. a lack of funding that had meant fewer studies, and hence less use of animals, than had been planned originally. However, this project had been an extremely worthwhile piece of work. XX wished to make the point that an amendment had been required during the licence due to skin irritation and self mutilation due to the feeding of a high fat diet. He had therefore been required to implement procedures to keep an eye on the situation, i.e. ASU technicians checked the animals thoroughly each day and this was backed up by researchers checking them three times per week.

The ERG was happy with this review.

8.2 XX 30/2132 – “*Mechanisms of intestinal inflammation*”

It was disappointing that there had been no publications from this work due to a lack of funding. XX wished to note that XX spends only 4/10 of his time in the UK and 6/10 in Sweden.

The ERG was happy with this review.

8.3 XX 30/2293 – “*Antimicrobial resistance associated with livestock production*” [Tabled]

This Final Review has been carried forward from the November 2008 meeting and replaces a Mid Term Review.

XX reported that the technicians had enjoyed working with XX on this project and that it had gone well.

The ERG was happy with this review.

8.4 XX 30/2054 – “*Study of infectious diseases of cats*” [Tabled]

XX commented that very few people work with cats in the current climate. This work used cats for the benefit of cats in the future. There had been some very positive results in one particular section of work.

The ERG was happy with this review.

9. Report on UIN Applications

9.1 Approved

9.1.1 XX UB/08/038 – “*Regulation of neurotransmitter receptors*”

This work will involve Schedule 1 killing and subsequent use of brain tissue.

The ERG ratified this UIN.

9.1.2 XX UB/08/039 – “*Social behaviour in the domestic cat*”

XX reported that this work is purely observational. XX is investigating whether cats prefer social isolation or to live in groups within a household. The intent is to determine whether or not cats living in a communal environment are more stressed than ones who have the house to themselves.

The ERG ratified this UIN.

9.1.3 XX UB/08/040 – “*Responses of domestic dogs to ‘Tellington touch’ therapy*”

XX explained that ‘Tellington touch’ is a massaging technique used to calm dogs and reduce stress. The concern is that it is used inappropriately and instead of better techniques in some situations. XX will use volunteer owners and their dogs, in a purely observational study, to investigate whether the therapy can mask underlying conditions.

The ERG ratified this UIN.

9.1.4 XX UB/08/041 – *“The effects of weaning on the feeding behaviour in foals”*

Weaning is a stressful time for any animal but domesticated animals undergo unnatural weaning. They are removed abruptly from the mother and often go straight into isolation. There is evidence in many species that weaning can result in abnormal behaviour patterns. This project looks at whether weaning in horses can lead to stereotypic behaviours later in life, such as crib biting and wind-sucking. It is a purely observational study with volunteer horse owners. XX and XX noted that no animal numbers had been given. XX responded that the numbers used is entirely dependent on XX access to animals.

The ERG ratified this UIN.

9.1.5 XX UB/08/042 – *“Assessment of the incidence of intra-abdominal hypertension in critically ill dogs”*

This work may have consequences for, and compromise, recovery in humans. Hypertension will be monitored through a catheter in the bladder for clinical purposes, not specifically for this study. XX asked whether XX had accounted for the fact that a filled bladder will consequently accommodate extra volume on further filling. He mentioned that this had caused problems with visceral pain research in the past. XX could not answer, so agreed to take the query back to the researcher.

ACTION: XX to contact XX regarding XX query and report back to the ERG at the next meeting.

The ERG ratified this UIN.

9.1.6 XX UB/08/043 – *“Welfare of Pet Guinea Pigs (U-grad project)”*

This work compares group housed and singly housed animals.

Part 1 involves observing the guinea pig when placed onto a lap.

Part 2 involves placing the animal in a novel arena and observing its reaction.

XX hopes to be able to tell whether the animal is stressed in either situation. For example, if it is used to human contact then it may appear stressed when isolated. XX remarked that it seemed a little vague but he could see no suffering so he would not want to stop the work.

The ERG ratified this UIN.

9.1.7 XX UB/08/044 *“Development of novel techniques to assess the cognitive effects of pain in horses”*

Refer to 9.1.11

9.1.8 XX UB/08/045 *“Makgadikgadi zebra migration research project”*

XX reported that an electric fence would be put up in the migration area. The domesticated cattle and donkeys would be fitted with radiocollars to monitor how they share the space with the zebra. The aim is to identify how the different species affect each other’s use of space.

The ERG ratified this UIN.

- 9.1.9 XX UB/08/046 *“A review of the ecological significance of transfrontier parks with specific emphasis on the impact of border security fences on large desert mammal distribution and abundance in the Sonoran Desert of North America”*

XX will be focusing on large animals, above 10kg in weight, and whether they are able to pass through the border security fences. The work is purely observational as he will be using camera evidence.

The ERG ratified this UIN.

- 9.1.10 XX UB/09/001 *“MSc Project: The temporal and spatial association patterns and social structure of Natterer’s bats *Myotis nattereri*, in a box scheme (XX); and the implications for conservation, habitat enhancement, compensation and monitoring schemes”*

The bats will be caught from boxes – already under licence – and fitted with a 0.35g transmitter. This will either fall off or be groomed off in due course. XX is investigating whether bats migrate out of the area.

The ERG ratified this UIN.

- 9.1.11 XX UB/09/002 *“Development of novel techniques to assess the cognitive effects of pain in horses”*

XX confirmed that XX is supervising XX (see 9.1.7) in this project but that they had submitted separate UIN applications.

They will be observing abdominal surgery to identify better ways in which pain can be assessed. They are, therefore, using animals that are already being operated on. The novel technique involves observing the animal’s response to a novel sound or person.

The ultimate aim is to provide advice and guidance on the use of analgesics after surgery.

The ERG ratified this UIN.

10. For Information

- XX mentioned that the January 2009 ASU newsletter is now available on the website.
- XX also wished to note that XX had both recently had their work highlighted on the University of Bristol website. He was pleased that, in both cases, they had mentioned the fact that they had needed to use animals to complete their work successfully.

11. Any Other Business

There was no further business to discuss.

12. Date of the next meeting

The next meeting will be held at 2.00pm on Tuesday 17th March 2009 in Bristol in Room XX.