Animals (Scientific Procedures) Act 1986

Non-technical summaries for project licences granted during 2015

Volume 6

Projects with a primary purpose of: Translational and applied research – Human gastrointestinal disorders including liver

Project Titles and keywords

1. **A piglet model for environmental enteric dysfunction (EED) and acute secretory diarrhoea (ASD) in infants in developing countries**
    - Infant, diarrhoea, piglet, malabsorbtion

2. **The development of intervention strategies for foodborne pathogens**
    - Campylobacter, poultry, colonisation, interventions

3. **Function of innate lymphoid cells in the liver and role in liver disease**
    - Immune, liver, obesity, NAFLD, NASH

4. **Mechanistic strategies for tackling liver disease**
    - Liver fibrosis, portal hypertension, treatment

5. **Development of remote controlled capsule endoscopy**
    - Remote cytology, microbiology, tissue, capsule

6. **Dietary regulation of intestinal epithelial cells**
    - Crohn’s, Dietary treatment, Intestinal inflammation

Project 1	**A piglet model for environmental enteric dysfunction (EED) and acute secretory diarrhoea (ASD) in infants in developing countries**	
Key Words (max. 5 words)	Infant, diarrhoea, piglet, malabsorbtion	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
	X	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	Current rodent models do not do predict the likely success of treatments arid diagnostics for EED and ASDD, and our objectives are to develop such a model in piglets, to validate it against existing data from infants, and to use it to identify possible novel diagnostic and therapeutic approaches.	
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	There is a need for an experimental model of ASD and EED, both of which are important diseases of human infants, which reliably predicts whether particular treatments or diagnostic approaches will be successful. The main benefit of the work will be to provide a model of these diseases in which we can test new medicines. Currently, many drugs which have shown promise in tests in mice do not work when applied to human infants, wasting time and resources and delaying the development of other, potentially more promising medicines. By testing new therapies in piglets before they are tried in humans,	

	we can eliminate some of these, identify those most likely to be effective, and speed up the process of finding appropriate treatments.
What species and approximate numbers of animals do you expect to use over what period of time?	Pigs. Approximately 60 animals.
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	We expect the adverse effects to be extremely variable between piglets, as is the case with EED and ASD in human infants. Adverse effects may include diarrhoea and weight loss, and the expected levels in individual pigs may be moderate. All piglets will be killed using an overdose of an anaesthetic agent at the end of the experiment.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The causes of EED and ASD in human infants are complex and incompletely understood. Until they are understood, it will be impossible to develop a reliable non-animal model
2. Reduction Explain how you will assure the use of minimum numbers of animals	Studies have already been published showing how variable are the effects we will measure. This will allow us to calculate the minimum number of animals necessary to see the effects of the procedures we will carry out.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Pigs are increasingly seen as good models for humans because of the similarity of their digestion, metabolism and immune system. This is particularly true of young piglets, where weaning produces a syndrome which looks similar to the early stages of EED. By using weaned piglets, which already have a degree of enteric dysfunction, we have the best opportunity to develop a model of EED/ASD similar to that in humans.

Project 2	**The development of intervention strategies for foodborne pathogens**	
Key Words (max. 5 words)	Campylobacter, poultry, colonisation, interventions	
Expected duration of the project (yrs)		
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
	X	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	The overall aims of the project are to understand why Campylobacter colonises poultry so well, and hopefully to develop measures to control it and other food-borne pathogens.This will be done by: 1. Identifying factors that allow *Campylobacter* spp to colonise chickens and turkeys so readily. 2. Testing potential control measures for their ability to reduce colonisation of chickens and turkeys by *Campylobacter* spp, *Salmonella*, *Enterococcus spp* and *E. coli*.	
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	The social and economic costs of food-borne bacterial diseases are considerable. Broadly speaking, the data generated by this research will enable the development of human and animal health policies and of policies for food production both in the UK and world-wide. Handling/consumption of poultry is a major source of human Campylobacter infections, so a reduction in the extent of poultry	

	infection should result in a drop in the number of human cases. It is likely data will be produced that can be used to provide informed opinion on the feasibility of the intervention strategies aimed at reduction. The results generated from publicly funded work (eg Defra, BBSRC) will be disseminated through peer-reviewed journals and in reports accessible to the public. Data dissemination from commercial work would be according to the relevant companies' policies/wishes. Specifically, in the short term, the work could lead to the identification and understanding of the factors that allow the organism to colonise poultry so well. In the long term, this knowledge may be used in the development of successful intervention strategies, eg vaccines. The work also aims to help in the development of control therapies such as probiotics and antimicrobial therapies, including refinements to antibiotic therapies in order to limit the development of antibiotic resistance. Successful intervention techniques could then be used by the poultry industry to reduce the number of food-borne pathogens in their flocks.
What species and approximate numbers of animals do you expect to use over what period of time?	Chickens and turkeys. Up to 300 of each over 5 years
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	No adverse reactions are expected. Determining the outcomes of these studies involves analysis of clinical samples obtained post mortem, so all animals will be killed by humane methods at the end of each study
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The aim of these studies is to understand how the bacteria colonise birds and to develop and test control measures ultimately intended for use in the poultry industry. This can only be achieved using appropriate animal models.

2. Reduction Explain how you will assure the use of minimum numbers of animals	The advice of one of the establishment's qualified statisticians is sought for each new experimental design to ensure the minimum numbers of birds are used that will provide statistically valid data. Data from previous studies is used to determine the variability in levels of colonisation in control birds. In addition, data from treatment groups from previous studies is provided to the statistician as examples of the kind of data that may be expected in a forthcoming trial. This data is then employed by the statistician in order to determine minimum group sizes that will allow detection of differences between groups. Newly generated data will be fed back to the statistician in order to assess whether the group sizes are still appropriate in subsequent studies.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Chickens and turkeys are an appropriate model for these studies as Campylobacter and the other bacterial species of interest are all naturally found in poultry. Furthermore, the aims of the work are to understand how Campylobacter colonises birds and to develop/test potential therapies/treatments that would be aimed at use by the poultry industry. Animal suffering in the proposed studies will be minimal. Strains and levels of bacteria, and challenge route, will be selected to ensure minimal suffering by the birds.

Project 3	**Function of innate lymphoid cells in the liver and role in liver disease**	
Key Words (max. 5 words)	Immune, liver, obesity, NAFLD, NASH	
Expected duration of the project (yrs)	5	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
		Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
	X	Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	Liver disease is the only cause of death in under-65-year-olds currently increasing in the UK and obesity-related disease is a major contributor to this. It is estimated that 25 – 30% of adults are affected by non-alcoholic fatty liver disease (NAFLD), in which excess fat is stored in the liver, and as many as 5% suffer from the more serious non-alcoholic steatohepatitis (NASH), in which the fatty liver becomes chronically inflamed. 20% of NASH patients go on to develop cirrhosis and liver cancer. The leading risk factor for NASH is obesity and 50% of the UK population is projected to be obese by 2030, so this is a serious and growing public health concern. Furthermore, the fact that NASH has only relatively recently been recognised as a problem means there is an urgent need for more research. A number of new kinds of immune cells (“ILCs”) have recently been discovered, and many of these are found in the liver. What these cells do is not yet known, but there are a number of lines of evidence to suggest that they may be involved in the	

	development of NAFLD and NASH. In this project, we will investigate this by making genetically modified mice which lack certain immune cells of interest but are in every other way normal. We will then establish whether these mice differ from normal mice in their susceptibility to liver disease. This will give us an idea of the importance of these cells for the development of disease.
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	The liver contains large numbers of ILCs, but what these cells do is not known. The major potential for this project to advance science is by addressing this question. There are currently no effective treatments for NAFLD and NASH. Therefore, understanding how ILCs are involved in these diseases could also be clinically important, because it could help in the development of new therapies.
What species and approximate numbers of animals do you expect to use over what period of time?	We will use normal and genetically modified mice. The project will last for 5 years and over this period, we expect to use 1500 mice.
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	The genetically modified mice we propose to use will either be indistinguishable from normal mice or will have defects in their immune systems which mean they are more likely to catch certain diseases. Because we will keep the mice in special cages that keep germs out, all of the mice will still lead normal and healthy lives. Naturally occurring gut bacteria are known to play a role in NAFLD and NASH and the important time at which animals and people are colonised by these bacteria is at and shortly after birth. Therefore we will give some of the pregnant and nursing mice in our breeding protocol antibiotics to prevent this happening. When this has been done in the past, the mice did not suffer any problems from being given antibiotics. The severity of the breeding protocol, together with the administration of antibiotics in some mothers is “mild”. Mice that we have bred in the first part of the project

	will enter the second part, in which we will feed them a “Western-style” diet that is high in fat and sugar. This will cause the mice to become obese and pre-diabetic, and they will also develop a NASH-like disease. Because of this, the mice will not be as healthy as those fed a normal diet, and so the severity is “moderate”. As part of this protocol, the mice will also undergo a few simple procedures. The mice will undergo a “glucose tolerance test” to see if they are becoming pre-diabetic. In this test, the mice eat or drink a dose of sugar and we take multiple small blood samples to see how well their bodies are coping with the sugar. We will take blood samples in order to assess liver injury. Whenever we take blood, we will avoid taking too much by not taking more than 10% of total blood volume on any one occasion, or 15% of blood volume within 28 days. We will also use a local anaesthetic to prevent the mice feeling pain from the needle, where necessary. At the end of the experiment, mice will be killed and their tissues taken for further study.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	In this project, we will use both human clinical samples and mice. Wherever possible, we will work on cells isolated from human tissues and this will reduce the number of mice we have to use. However, access to human tissue is limited and there are also certain kinds of studies that cannot be carried out on humans. Working with mice will allow us to make changes to the animals – such as genetic modification– that would not be ethical or practical in humans. Therefore, using the mice will give us valuable additional information that we could not have collected from our work with human samples alone. We cannot model NAFLD and NASH using cells in a dish because no good way of doing this currently exists.
2. Reduction Explain how you will assure	We will use statistical methods to ensure that we use the minimum number of animals that will give us

the use of minimum numbers of animals	accurate results. In order to get the maximum information from every animal, we will harvest multiple tissues from each animal. We will measure the number and function of their immune cells using “multiparameter” techniques that allow us to ask up to twelve questions of each sample.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	We have chosen to use mice because their physiology and immunology are similar to those of humans, and because a number of genetically modified strains of mouse are already available. The fact that these strains have already been made will mean that we do not have to start from scratch, which would require many more mice. There are a number of ways to give mice a NASH-like disease. We have chosen to do so by feeding them the “Western-style” diet, because this is closest to the situation in humans, both in terms of the diet (high fat and sugar) and the symptoms (obesity, insulin resistance and liver disease).

Project 4	**Mechanistic strategies for tackling liver disease**	
Key Words (max. 5 words)	Liver fibrosis, portal hypertension, treatment	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
	X	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	Liver disease is the largest cause of death in the UK. Liver fibrosis (scarring) is a clinically silent process, so many patients present at an advanced stage (cirrhosis) when treatment of the underlying cause is ineffective. Currently, there are no drugs licensed for use in humans for the treatment of liver fibrosis and there is a shortage of donor organs for liver transplant. New and effective treatments for liver fibrosis and the complications associated with cirrhosis (such as bleeding from the gut, kidney failure etc) are urgently needed to reduce the number of patients dying prematurely from liver disease. Once treatments are identified we need reliable methods (that are acceptable to patients) to measure their effects. Therefore, the major objectives of this project are to evaluate potential new treatments and to develop new diagnostic tests in animal models of liver disease that mimic, as close as possible, the humah condition.	
What are the potential benefits	The principal beneficiaries of our research will be:	

likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	Patients - through access to better treatments and, potentially, earlier detection of disease due to improved diagnostic tests. Researchers - interested in the study of liver fibrosis and fibrosis in other organs (where discovery of new treatment targets would have relevance) and chronic kidney disease (where, like in patients with cirrhosis, abnormal control of the blood supply in the kidney has been implicated). Pharmaceutical/Biotech sectors - where new insights into the causes of cirrhosis and its complications will help in the design of new diagnostic tests and stimulate interest in drug development. Animals: through developing new 'non-invasive' methods to monitor disease (e.g. magnetic resonance imaging, ultrasound scans or special blood tests) we will reduce the number of animals used for research.
What species and approximate numbers of animals do you expect to use over what period of time?	We plan to use rats, and possibly mice, to achieve our research objectives. Over the next 5 years, we will use on average less than 600 animals per year. It is anticipated that usage will be much lower than this, if our new non- invasive techniques prove successful and if there is no reason to use mice (mice are sometimes needed for experiments where the importance of a particular gene or protein is investigated — so called gene 'knock-out' mice).
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	To replicate human cirrhosis and complications in animals requires models designated as moderate or severe, where animals may display signs of liver disease such as jaundice, ascites or weight loss. However, we have used these models for many years and have learned how to minimize the chances of any unnecessary suffering or harm. Animals are very closely monitored for signs of distress and killed in a humane manner if necessary.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	Animal models are necessary to study complex biological processes such as organ fibrosis (scarring) and regeneration, and to study the circulation in a clinically meaningful fashion. As yet, laboratory culture dish ('in vitro') experiments simply cannot

	model this complexity. Furthermore, animal models are critical to demonstrate proof that new drugs have a good chance of working in humans and to obtain information about the likely dose required and any safety issues. Where possible, we are increasingly using in vitro experiments that mimic processes that occur in a living animal, and also studying human liver tissue specimens. For example, we anticipate that a new technique using small slices of humar liver which are kept alive in an incubator for several days might prove very useful in studying the effects of new drugs.
2. Reduction Explain how you will assure the use of minimum numbers of animals	Our group has many years of experience in the design and conduct of rodent liver disease models. We will use data from our previous published studies to estimate the minimum number of animals needed to show a true effect from a treatment whilst at the same time maintaining sufficient numbers for the experiment to be meaningful. Advice from biomedical statisticians will be sought when appropriate. New non-invasive techniques (such as magnetic resonance imaging) may enable us to track disease in an individual animal over time and will help to reduce the numbers of animals required. We will continue to ensure that any tissues generated from our work are archived and stored appropriately, therefore preventing unnecessary repetition of experiments.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	We have published numerous papers in the scientific literature using these rodent models of liver fibrosis, which are well-established and provide a reliable system to understand how liver scarring is caused and to determine the effectiveness of new treatments. It is important to use models that reflect the different types of liver disease in humans (e.g. carbon tetrachioride most closely mimics human liver injury due to alcohol or toxins, whereas dietary models mimic human fatty liver disease). Therefore, the observations we make in these species can be directly translated to the human condition. The clinical complications of cirrhosis only occur at the more advanced end of the disease spectrum. Therefore, models of at least moderate severity are often required. We will minimize any potential suffering by

	using the least injury required for each model and the earliest possible study endpoints. A major component of our research programme is the development of non-invasive techniques (imaging, blood tests) which may refine our approach — for example, by allowing experimental models to be stopped sooner if these tests give an earlier indication of response to a drug. We will regularly consult the NC3Rs website to ensure best practice.

Project 5	**Development of remote controlled capsule endoscopy**	
Key Words (max. 5 words)	Remote cytology, microbiology, tissue, capsule	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)		Basic research
	X	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	To test feasibility of using a remote controlled capsule to sample and retrieve cells or fluid from the intestine and to test potential ways of improving the method prior to use in human patients.	
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	Miniature, painless, less invasive remote controlled cell and fluid collection from specific sites in the gastrointestinal tract may improve early diagnosis and treatment of cancers, inflammatory bowel disease and acute and chronic infections.	
What species and approximate numbers of animals do you expect to use over what period of time?	Adult pigs. 16 animals over 5 years	
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected	The animals will undergo two anaesthetics, one during which the device will be tested and another which will be terminal. The expectation is that adverse effects will be close to zero. Rare sore throat, and	

level of severity? What will happen to the animals at the end?	very rarely perforation or bleeding (1 in 200 to I in 400 per animal). The animals will be killed with an overdose of barbiturate while under anaesthesia.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	Tests in animals demonstrating efficacy and providing safety data are needed to support ethical committee application for the use of this method in human volunteer studies. We plan to use intestinal tissue and ex-vivo models to improve prototypes and testing methods prior to use in live animals
2. Reduction Explain how you will assure the use of minimum numbers of animals	1. Experimental methods with over-tubes allow rapid multiple tests of device reducing numbers of animals. The device to be tested can be inserted, tested and removed at the desired position quickly. 2. Because several tests of efficacy can be performed quickly and atraumatically in a single animal, fewer animals are required to allow statistically significant testing. This experimental design allows statistically valid verification of feasibility in a very small numbers of animals.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Adult pig is similar in gastrointestinal anatomy to the human and can be examined with flexible endoscopes and capsule type endoscopes avoiding the need for surgical incisions. The harms of anaesthesia will be reduced, by monitoring with pulse oximetry measurements while on a ventilator. Post operative observation and care should also help reduce morbidity during this period.

Project 6	**Dietary regulation of intestinal epithelial cells**	
Key Words (max. 5 words)	Crohn's; Dietary treatment; Intestinal inflammation	
Expected duration of the project (yrs)	5	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	x	Basic research
	x	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
	x	Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	We know that children who have a severe illness called Crohn's disease, have inflammation in the intestine. This subsides when they are treated with an exclusive liquid diet. This anti-inflammatory effect of the diet is as strong as giving high dose steroids to the children. However, we don't understand the underlying mechanisms whereby changing the diet (albeit radically) improves the inflammation. The interactions between the contents of the intestine (affected by diet), the cells lining the intestine (the epithelial cells) and the immune cells within the wall of the intestine must be central to this process. Although most of our research is with children affected by Crohn's disease (with appropriate consent) and samples collected from them, there are questions that we cannot probe using humans; these include the regulatory mechanisms within the epithelial cells that affect immune responses, and how these are modulated by diet. To do this we have to take epithelial cells in large numbers and study proteins that bind to DNA called histones, and study	

	how diet affects them. We also need to mimic the stimulatory effects of gut bacteria on the intestine, and we can do this by increasing the signals from one of the receptors in the epithelial cell. This has been done by genetically modifying the receptor in mice to be more active in the intestine – without causing any harmful effects in the mice. We will test the effects of this bacterial signalling in inflammation induced by a salt called DSS in the drinking water, which produces a moderate inflammation, without causing suffering in the mice.
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	Science can be advanced by understanding how changes in diet affect the immune responses underlying intestinal inflammation. This is an area of interest to both scientists and to the general public. Humans (children) will benefit, because if we understand how diet reduces inflammation, it will give us the scientific base by which we can design new dietary treatments for children with inflammatory bowel disease.
What species and approximate numbers of animals do you expect to use over what period of time?	We propose to use approximately 50 mice per year to maintain our breeding of transgenic mice. We propose to use approximately 120 mice per year to include testing the diets on inflammatory regulation and to measure the effects of the transgene on inflammation.
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	We expect the colitis induced to be mild to moderate. Mice with even moderate colitis show no overt signs of pain; however, we have strict criteria in place to assess pain and suffering, and if these criteria are met in a mouse, he or she will removed from the study and killed. All mice will be killed at the end.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	Animal experiments are a small part of our work. Our research group works for over 90% of the time in children or on samples taken from children (under ethical approval). We also use human cell lines in the lab. However, there are some questions which can

	only be examined in a living mammal because we need the complexity of the living intestine (which is why biopsies and cell lines are not useful), and the ability to harvest large numbers of cells on the other (which is why human studies are not useful).
2. Reduction Explain how you will assure the use of minimum numbers of animals	All studies are carefully planned. We will use the minimum numbers of mice necessary to provide consistent results. Where necessary, we will use a statistician to ensure that we have the correct number of mice to achieve a statistically valid result.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	We will use mice because they are the species whose immune system is best understood, and they can be used to give insights into the mechanisms underlying inflammation in the human intestine. I work closely with the animal care staff to ensure that the mice do not suffer or experience pain. I treat the mice with great respect, as living beings.