Date of second strand review: 26 March 2014

Project title	**Immunoregulation during parasitic helminth infection**		
Key words	Parasites, Immunity		
Expected duration of the project (years)	5		
Purpose of the project	Basic research	Yes	
	Translational and applied research		No
	Regulatory use and routine production		No
	Protection of the natural environment in the interests of the health or welfare of humans or animals		No
	Preservation of species		No
	Higher education or training		No
	Forensic enquiries		No
	Maintenance of colonies of genetically altered animals		No
Objectives of the project	The project is designed to define the underlying reasons for resistance to infection by helminth (worm) parasites. Also, because such infections are extremely common and tend to be long lived in humans and animals across the world, we also wish to understand why our defence system does not operate efficiently against them. Not only will the work increase our basic understanding of how the immune systems works against these large infectious agents but, in humans, these kinds of infection are regarded as Neglected Tropical Diseases and, therefore, address clear global clinical needs.		
Potential benefits likely to derive from this project	The project will generate a deeper understanding of how the immune system works following infection by worm parasites. Relatively little is known as to the ways in which the body protects itself following this kind of infection and such knowledge is key to development of new approaches of control such as vaccines. The project will have application to both human and animal health as worm infections are prevalent throughout the animal kingdom and responsible for considerable ill health, in children, in domestic stock and in companion animals across the world.		
Species and approximate	Mice are the mains species to be studied in conjunction with parasites that natural infect rodents in the wild. We		

numbers of animals expected to be used, and anticipated period of time	anticipate using approximately 15,000 mice over a five-year period. Smaller numbers of rats (up to 500), Gerbils (up to 100), Guinea pigs (up to 100) and rabbits (up to 25) will be used over a five year time period.
Expected adverse effects and the likely/expected level of severity. What will happen to the animals at the end.	The great majority of treatments will be of mild severity such as general discomfort following infection or transient irritation during an injection or immunisation "vaccination". Occasionally, the level of severity may increase transiently to moderate with some of the parasite infections used, which is usually associated with the immune system controlling the infection.
Application of the 3 Rs	
1. Replacement Why do animals need to be used, and why non-animal alternatives cannot be used.	The body's immune system operates as a co-ordinated response involving multiple cells and molecules at a variety of body sites. Thus, at present, isolated cell cultures or computer modelling cannot accurately model the immune response. Also, no worm parasites can complete their life cycle outside their host. In order to study the immune response to worm parasites in depth, animals are required.
2. Reduction How the use of minimum numbers of animals will be assured	We will use appropriate statistical expertise to ensure that we design experiments using the minimum numbers of animals required to generate meaningful results. We maximize the information gained from each individual animal through the use of the most advanced technologies enabling extensive analysis of cells and molecules. We will also develop new cell tissue culture methods to complement our animal studies wherever possible.
3. Refinement Reasons for the choice of species and why the animal model(s) to be used are the most refined, having regard to the objectives. General measures to be taken to minimise welfare costs (harms) to the animals.	In order to study to understand the mammalian immune system we use the mouse as a model system as it is the best understood animal in terms of how the immune systems works with remarkable similarity to other mammals including man. The mouse system also provides us with the most tools to precisely define immune responses thus ensuring clearly defined informative objectives to be met. Moreover, we primarily study parasites that are naturally found in the mouse to ensure that we are investigating the most natural system of host/parasite interactions. As such parasitic infection by worms tends not to induce severe illness as a general feature. Nevertheless sometimes infection and associated studies can be associated with ill health. Animals under our care are monitored daily by trained technicians who raise

	any concerns about animal welfare with us and the named veterinarian who decides on the course of action to be undertaken such as treatment. Our experiments are designed with clearly defined endpoints with animal welfare paramount balanced with scientific information gained.