December 2016

Project title	**Modulating inflammation in the GI tract**		
Key words	Inflammation, intestine, experimental therapeutics		
Expected duration of the project (years)	5		
Purpose of the project (as in section 5C(3)[1]	Basic research	Yes	
	Translational and applied research	**Yes**	
	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[2]		**No**

[1] Delete Yes or No as appropriate.
[2] At least one additional purpose must be selected with this option.

Objectives of the project	To assess the effectiveness of experimental therapeutics in animal models of inflammatory bowel disease, for the purpose of determining their potential for treating inflammatory bowel disease (IBD) in humans. Methods of investigation will be improved and developed within the philosophy of the 3Rs.
Potential benefits likely to derive from this project	These data obtained will be used by Sponsors, to determine whether the drugs are suitable for the treatment of human inflammatory bowel disease.
Species and approximate numbers of animals expected to be used, and approximate period of time	Mice 7,500 Rats 250
Expected adverse effects and the likely/expected level of severity. What will happen to the animals at the end.	Animals may experience body weight loss and diarrhoea. In some instances, they may pass a small amount of blood in their stool. The expected level of severity is moderate and humane end points will be applied to all protocols in order to maintain this. All animals are euthanised at the end of a study so that changes in the structure and function of the bowel can be analysed.

Application of the 3Rs	

1. Replacement Why animals need to be used, and why non-animal alternatives cannot be used.	The gastrointestinal tract is perhaps the most complex organ system in the body. In addition to food metabolism, it is a major organ of the immune system and is home to several hundred species of microorganisms. Producing a non-animal model in a lab, which accurately replicates all aspects of gut function and dysfunction, is currently not possible. We have a range of in vitro laboratory techniques that are able to address some of the individual aspects of gut and immune system function. Such in vitro experiments will have been performed by us or our Sponsors prior to any research on animal models.
2. Reduction How the use of minimum numbers of animals will be assured	All experiments are conducted according to current best practice. Statisticians from academia and from independent companies are consulted to ensure the rigour of our experimental design and analyses. We are promoting multi-user studies to improve both the efficiency of animal usage and the robustness of individual studies.

3. Refinement Reasons for the choice of species and why the animal model(s) to be uses are the most refined, having regard to the objectives. General measures to be taken to minimise welfare costs (harms) to the animals.	Mice are the least sentient species most suitable for these studies. In some instances, a rat model may be more appropriate. Rodent models of inflammatory bowel disease are well-characterised and demonstrate broad similarities with human disease, in regard to symptoms and pathological changes within the intestine. Also, the models are responsive to agents that are used to treat human IBD. We have refined many aspects of running the models, including the optimisation of dosing protocols for different therapeutic drugs; increasing the number of different data read-outs that can be obtained from a single study; built up an historical data base that allows more accurate experimental design. Studies run for the minimum period of time sufficient to achieve their objective(s) and appropriate humane end points are employed.