G: NON-TECHNICAL SUMMARY (NTS)

Please attach the Non-technical Summary as generated by your application in ASPeL.

This summary will be published (examples of other summaries can be viewed on the Home Office website at www.gov.uk/research-and-testing-using-animals.

(WORD LIMIT: 1000 WORDS)

Please complete the following:

Project Title, Purpose & Duration	will automatically populate from other sections of the form completed on ASPeL
Key Words (max. 5 words)	Muscular dystrophy, stem cell, pericytes, transgenic.
Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	We aim at developing a new therapy for muscular dystrophy, based upon stem cell transplantation. Muscular dystrophy affects patients' muscles and often also the heart; in its most severe forms it reduces quality and life expectancy. We conducted experiments in animal models that led to a first clinical trial, based upon transplantation of donor stem cells from a brother. The trial proved safe but only modestly efficacious. In order to reach clinical efficacy, we now plan to develop novel protocols to isolate the stem cells of the patient, genetically correct them and then re-introduce them in the same patient, after having optimized all the step of the transplantation. We will test this strategy first in cells in culture and then in dystrophic animals. The same experiments may help to develop therapies for other diseases of the muscle and to alleviate damage to the heart in muscular dystrophy.
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)?	Muscular dystrophies compromise quality and length of patient life, lack any efficacious therapy and carry a severe burden for the patients' families and for the NHS that needs to provide palliative and supportive care, often for many years. Even a partially efficacious therapy that would arrest or delay the progress of the disease would have an immense medical and socio-economical impact.
What types and approximate numbers of animals do you expect to use and over what period of time?	Mice and rats will be used. We will use the minimal number of animals to reach statistical significance, use any possible alternative method, such as cell cultures. However, by taking all the projects to be carried out be carried out, approximately 3,800 mice and 1,000 rats will be needed over a 5 years period.

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 procedures envisaged are injections, minor surgery, catheterization and therefore the level of severity will range from moderate to mild. The animals will be monitored for beneficial effect, in the absence of which, or in the presence of unforeseen complications, the animals will be humanely culled. In case of successful therapeutic outcome the animals will be monitored until one year of age, after which time they will also be humanely culled.
Application of the 3Rs	
Replacement State why you need to use animals and why you cannot use non-protected animal alternatives	The first part of the experiments will be conducted on cells in vitro, thus significantly replacing part of the work that would otherwise be conducted on animals. Moreover we will develop advanced cultures that allow muscle maturation in vitro and study of muscle function, further replacing the work in vivo. However, there is no actual surrogate method that allows measuring the outcome of cell transplantation on the animal motility.
Reduction Explain how you will ensure the use of minimum numbers of animals	The use of cell cultures will greatly reduce the number of animals employed, since many answers will be obtained in vitro. Expert advise has been obtained to reduce the number of animals to the minimum sufficient to produce statistically significant results.
Refinement Explain the choice of animals 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.	Mice are the main species that model all the genetic diseases we intend to treat. Newly created dystrophic rats will also be used. We will use power calculation to use the minimal number of animals require to reach statistical significance of results. Anaesthetic and analgesic treatments will be administered to reduce or eliminate stress and pain associated with the surgery the animals will undergo.