



Home Office

NON-TECHNICAL SUMMARY

Pharmacology of colistin in chicken

Project duration

Years **5**

Months **0**

Project purpose

- (b) Translational or applied research with one of the following aims:
 - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants.

Retrospective assessment

The Secretary of State has determined that a retrospective assessment of this licence is not required.

Objectives and benefits

Description of the project's objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.

What is the aim of this project?

Colistin is an antibiotic used in both human and veterinary medicine for the treatment of *E. coli* and other bacterial species. This old antibiotic has not been used much in human medicine due to toxicity until recently where it has become a last resort antibiotic in where it is used to treat multidrug resistant bacteria. Colistin, however, is routinely used to treat infections in the gut of poultry in veterinary practice. The discovery of colistin resistance in bacteria from animal species and, less commonly, in humans has led to concerns that there is a link between the use of colistin in animals and the spread of resistance across host species. To ensure that colistin can continue to be used in both human and animal medicine without increasing the prevalence of resistance, we need to acquire good quality scientific

data to optimise dosage regimens based on measured effective concentrations. There are currently crucial knowledge gaps regarding how colistin use in chickens affects resistance in gut bacteria, and what effective dosage levels are most suitable to ensure efficacious treatment whilst also limiting the spread of resistance.

This project aims are:

1. To measure Colistin concentration within the gut to understand how the administered dose transits through the digestive system.
2. To describe how the movement of colistin through the gut impacts on bacterial flora.
3. To monitor the numbers of and species of bacteria within the gut and faeces. Including the prevalence (if any) of resistance.
4. To determine effective concentrations for colistin use that would increase its sustainability in both human and animal medicine.

Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.

What are the potential benefits that will derive from this project?

The knowledge derived from this study will inform regulatory bodies, veterinary practitioners and veterinary drug companies regarding the optimal dosing of colistin to poultry. This will improve animal health and welfare, and potentially help reduce the spread of resistant bacteria.

This will also have benefits for human medicine, ensuring the sustainability of colistin usage as a 'last resort' antibiotic to treat resistant infections.

Species and numbers of animals expected to be used

What types and approximate numbers of animals will you use over the course of this project?

This project will use broiler chickens sourced in the UK. Approx. 400 chickens will be used over the 4-year study period. Chickens will be used in separate study groups for each facet of the study with each group being study reared for around 40-45 days

Predicted harms

Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.

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 animals will be kept in conditions compliant with welfare guidelines, provided with enrichment, and trained to cope with human interaction. This will ensure that adverse effects are minimal and that severity remains mild. Dosing procedures may cause coughing or choking, although this is extremely rare, as all investigator will be trained to handle the chicken appropriately. Any animals showing considerably signs of distress or illness will be euthanized.

Application of the three Rs

1. Replacement

State why you need to use animals and why you cannot use non-animal alternatives.

Although models can be used that allow some aspects of drug dosing to be studied accurate determination of drug action relies on understanding the specifics in the target species.

Because of the administration of antibiotic through the feed, it is important to monitor how feeding affects dosage, how the antibiotic transits through the gut, what bacteria are present and how they are effected, and how this influences gut infection which can only be accurately assessed in the target animal

2. Reduction

Explain how you will assure the use of minimum numbers of animals.

Computer simulation and modelling of previously published data coupled with laboratory based dosage experiments will reduce the number of animals required to explore multiple different doses

The pilot study will ensure that all methods are valid to reduce negative impact throughout the project.

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.

Poultry farming is an important aspect of food production worldwide and with Colistin being one of the most commonly used antibiotics for their welfare it is important that chickens and studied to ensure optimal use and benefits

To minimise any harm to the animals taking part in the study, they will be trained and familiarised with the persons and procedures involved to prevent undue stress. They will be provided with enrichment materials including perches for roosting and litter for foraging behaviour. All animals will be observed on a daily basis to identify any illness so that it can be treated swiftly and appropriately.

All animals will be housed in a controlled environment where ventilation, humidity, temperature and light are controlled to ensure they are maintained in a comfortable and healthy environment.