Home Office

NON-TECHNICAL SUMMARY

Assessment of agrochemical residues in livestock

Project duration

5 years 0 months

Project purpose

- (b) Translational or applied research with one of the following aims:
  - (iii) Improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes
  - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants
- (c) Development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the following aims mentioned in paragraph (b)

Key words

Agrochemicals, Pesticides, Residues, Livestock, Food-producing animals

Animal types	Life stages
Domestic fowl (Gallus gallus domesticus)	Juvenile, Adult

Retrospective assessment

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

Objectives and benefits

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

What's the aim of this project?

The purpose of this project is to determine how agrochemical materials are absorbed by the body of food-producing animals, how they may be changed by the animals (metabolised) and excreted, and to specifically understand what residues remain, if any.

Residues in Livestock studies are conducted in order to quantify levels of residues in meat, eggs and edible meat by-products following the use of an agrochemical such as a pesticide. The situations to which such studies apply include application of an agrochemical to crops for the feeding of livestock, agrochemicals that may be directly applied to livestock and those that are used in livestock premises.

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.

Why is it important to undertake this work?

Agrochemicals: primarily insecticides (substances used for killing insects), herbicides (substances that are toxic to plants and that are used to destroy unwanted vegetation), fungicides (substances used for killing fungus) and other materials designed to kill crop pests, are essential for the prevention and treatment of diseases that commonly occur in food crops. However after use, a residue of the material may remain in the foodstuff and be eaten by animals. It is therefore important to determine that these materials are not toxic to the animals and that any parts or products of the animal (eggs and meat) are then safe for humans to eat.

Without these studies, it is not legally permissible to manufacture and sell these materials in the UK, Europe, or into other worldwide markets.

What outputs do you think you will see at the end of this project?

Information on the absorption of various agrochemical materials by food producing animals, how the body changes and excretes these materials, and what residues may remain in products which contribute to human food (eggs and meat) will be collected from these studies.

Preliminary studies will provide information to enable appropriate internal decision making regarding formulation selection and refinement. Pivotal studies will be conducted in accordance with regulatory guidelines and to the required quality standard (Good Laboratory Practice) to ensure acceptance by government regulators worldwide who will make decisions on whether these materials can be safely marketed and used in society.

Who or what will benefit from these outputs, and how?

This is a service licence whereby external clients, typically commercial agrochemical companies, will benefit from the provision of high quality data. The information provided to them will facilitate internal decision making and will enable them to gain regulatory acceptance to market safer and more effective agrochemical materials. Clients are ready to initiate these studies now so it is likely that testing could start as soon as this licence is granted.

Enabling the development of safer and more effective agrochemical materials will benefit society by enabling improved crop yields in multiple regions of the world, which are exposed to a range of environmental and biological challenges, and also by reducing the health risks to animals and to human consumers of animal-based food. It is anticipated that the environment as a whole will benefit from the development of safer agrochemical materials as the health of waterways is likely to be improved as is the health of wild animals that could come into accidental contact with the agrochemicals.

How will you look to maximise the outputs of this work?

By conducting the work to the required quality standard (Good Laboratory Practice), the data provided should be readily accepted by regulatory authorities representing all markets of the world. Where confidentiality is not breached, information will be shared across clients and published where possible to facilitate the development of a greater number of agrochemical products.

Species and numbers of animals expected to be used

- Domestic fowl (Gallus gallus domesticus): 600

Predicted harms

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

Explain why you are using these types of animals and your choice of life stages.

This project will use species generally regarded as farm livestock, i.e. chickens, which are likely to come into contact with the agrochemical materials being tested. This species appears in the food chain and it is important to understand the extent to which humans may be exposed to the types of materials being tested. Most studies are expected to be conducted in adult animals; juveniles will be used for specific purposes where juvenile animals would be routinely used in the human food chain.

Typically, what will be done to an animal used in your project?

Animals will be given an agrochemical material orally (via the mouth), which is the method by which they would naturally be exposed to them, and eggs will be collected during the studies to check for signs of the agrochemical within the eggs.

The oral dosing will be conducted for a minimum of 28 days (which is typically expected) or until residues of the agrochemical plateau in eggs, if they have not done so in 28 days. The maximum number of doses given will be 35.

Following completion of dosing, the collection of eggs in some animals may continue in order to assess the time it takes for the agrochemical to be removed from the eggs. This will typically last up to 20 days but could last up to 30 days.

The animals will be humanely killed after the collection period when edible and other tissues, including liver, kidney, muscle and fat, will be taken from the animals and analysed.

What are the expected impacts and/or adverse effects for the animals during your project?

The process of dosing animals may cause mild discomfort although no lasting effects are expected, this is because implements such as a pipette or flexible gavage needle are expected to be used for the dosing to ensure an exact, measured dose is administered. The agrochemical materials will have been tested in the laboratory prior to the conduct of these studies so are not expected to cause any significant harm to the animals themselves.

Hens will be housed in groups throughout each study. Whilst on study they may experience a degree of anxiety, reduced food consumption, fever, and/or weight loss. None of these issues are expected to happen very often, but if they do the hens will be regularly monitored and treated appropriately.

Hens will have physical, visual, olfactory, and auditory contact with others within the facility, and physical contact with humans where this does not interfere with the aims of the study. Opportunities for exercise will be provided appropriate to the species.

Expected severity categories and the proportion of animals in each category, per species.

What are the expected severities and the proportion of animals in each category (per animal type)?

Any adverse effects are expected to be associated with the application route and are expected to be no more than mild and transient. However, as the dosing will be repeated on a daily basis, this may cause long-lasting mild pain, suffering or distress. Therefore, all animals are expected to experience a moderate severity banding.

What will happen to animals used in this project?

- Killed

Replacement

State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.

Why do you need to use animals to achieve the aim of your project?

There is currently no regulatory or scientifically acceptable alternative to the use of animals in these types of tests. Such tests are conducted to satisfy the legal and regulatory requirements of governments around the world to ensure that agrochemicals, that humans and other animals may be exposed to in the food chain, are safe. The testing will be in compliance with the relevant Organisation for Economic Co-operation and Development (OECD) guidance on the testing of Residues in Livestock.

An awareness of regulatory guidance will be maintained and where non-animal alternatives exist that are approved by regulatory authorities, these will be used in preference to animal models.

Which non-animal alternatives did you consider for use in this project?

In vitro (lab based) methods to assess preliminary safety data, as well as preliminary in-vivo (animal based) tests to determine how chemicals are absorbed, distributed, metabolised and excreted, will be used as required prior to the testing of residuals. These studies determine product safety and appropriate dose levels to ensure those used in this work do not cause unnecessary harm and suffering to the animals.

However, there are currently no non-animal alternatives for the testing of residuals in livestock. Regulatory Authorities will not make decisions regarding public safety on non-animal systems alone as these do not replicate the complexity of a whole-body system.

Why were they not suitable?

Regulatory Authorities will not make decisions regarding public safety on non-animal systems alone as these do not replicate the complexity of a whole-body system.

Reduction

Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.

How have you estimated the numbers of animals you will use?

The total number of animals has been estimated based on typical study sizes, designed in accordance with the relevant Organisation for Economic Co-operation and Development (OECD) guidance on the testing of Residues in Livestock, and the expected numbers of studies required for the duration of the project.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?

As this is a service licence the experimental design phase for each required study has not yet happened.

When it does, the testing will be compliant with the relevant Organisation for Economic Co-operation and Development (OECD) guidance on the testing of Residues in Livestock. This details the minimum requirements for these studies, including the required dose levels, numbers of animals, use of control animals and duration of studies.

Statisticians may be consulted in the planning stages of studies to maximise the value of each particular study whilst still complying with the OECD requirements.

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

Pilot studies may be utilised to inform the design of subsequent pivotal studies. Control items will be used as advised by the relevant Organisation for Economic Co-operation and Development (OECD) guidance for comparative purposes and blinding methods will be used for analysis where possible as this reduces potential bias towards test groups.

Animal variability will be reduced as far as possible through the sourcing of a consistent and reproducible supply and by incorporating acceptance criteria and weight ranges into study designs.

Refinement

Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.

Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

The models and methods are defined in the relevant Organisation for Economic Co-operation and Development (OECD) guidance on the testing of Residues in Livestock. Specifically, chickens will be used in this project as the results of laying hen feeding studies may be extrapolated to other types of poultry (turkey, goose, duck and others).

The materials being tested will be given to the animals in the same way in which they would be exposed in the environment, typically by mouth, either through the eating of animal feeds or via a bolus dose (e.g. capsule). The dosing methods are well established and common for the animals to be used, and widely accepted to cause minimal discomfort.

Why can’t you use animals that are less sentient?

The models and methods are defined in the relevant Organisation for Economic Co-operation and Development (OECD) guidance on the testing of Residues in Livestock. OECD 505 states that Residues in Livestock studies are typically conducted in ruminants (cattle) and poultry (laying hen). In general the results of cattle feeding studies may be extrapolated to other domestic animals (ruminants, horses, pigs, rabbits and others) and laying hen feeding studies may be extrapolated to other types of poultry (turkey, goose, duck and others).

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?

Acclimatisation periods and refinements in animal care and pain management will be utilised where these are proven to reduce harms to the animals.

Refinements to dosing methods will be considered, such as dosing within foodstuffs, as long as it can be confirmed that the full dose has been ingested.

Hens will be housed in groups throughout each study. They will also have visual, olfactory, and auditory contact with others within the facility, and physical contact with both animals and humans where this does not interfere with the aims of the study.

Environmental enrichment methods will be utilised as appropriate. For chickens, provision of physical objects and varied environments to stimulate natural behaviors like perching, foraging, and dust bathing may be used where these do not compromise the outputs of studies.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?

NC3Rs, Replacing Animal Research, ARRIVE and PREPARE guidelines will be followed where appropriate.

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?

Through general literature review, review of NC3Rs website, OECD guidance documents, dialogue with the Named Information Officer and Named Training and Competency Officer as well as other establishments.