Home Office

NON-TECHNICAL SUMMARY

Identification of endocrine disrupting chemicals in fish for regulatory purposes

Project duration

Years **5**
Months **0**

Project purpose

- (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 aims mentioned in purpose (b)
- (d) Protection of the natural environment in the interests of the health or welfare of man or animals.

Key words

chemicals, hormones, sexual disruption, regulation, wildlife

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?

The aim of this licence application is to safeguard wildlife (and humans) from the effects of certain type of chemicals.

Some man-made chemicals interfere with the endocrine (hormonal) system that controls, amongst other functions, reproduction. These chemicals are called Endocrine Disrupting Chemicals (EDCs). As well as posing potential risks to humans (there are several studies that attempt to link exposure to EDCs with the decline in sperm counts, the increased incidence of certain cancers, diabetes, obesity and developmental abnormalities), EDCs are of particular concern for fish. This is because the aquatic environment is often an important sink for man-made chemicals and sewage waste.

Field studies during the 1990's revealed an extensive feminisation of wildlife. In the UK both roach from rivers and flounder from estuaries were heavily affected. Factors contributing to this include large population size, small geographic area, heavy industrialisation, low riverine flow and inefficient effluent treatment. Importantly in the 1990s there was no information on the ability of certain chemicals to interfere with the hormonal system of fish and other aquatic wildlife.

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?

Chemicals are essential to life on Earth. Humans have developed chemicals to use for sanitation, preserving foods, treating diseases, and increasing crop yields to allow food security. Chemicals are also produced for less essential to life activities (i.e. recreational, travelling, communication and for personal care products); these chemicals add value to human life by increasing welfare and the sense of well-being. Although many chemicals are simply beneficial, others are harmful to humans and wildlife or present both benefits and risks.
The benefit therefore derived from this project is to provide the regulatory evidence needed for discriminating between harmful and not harmful chemicals. In this way we can enjoy the benefits from the use of not harmful chemicals and prevent the harmful chemicals entering our environment. Once harmful chemicals enter the environment, they can harm both wildlife and humans.

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?

In the 1990's there was no information on the impact of chemicals with endocrine disrupting properties. This led to the development of internationally standardised tests under the management of the OECD, all aimed at assessing the hazard and/or the risk of old and new chemicals in terms of endocrine disrupting potential. These tests have now been validated and are used to assess the chemicals to avoid further harm to wildlife and indirectly to humans. The validated species (each to a different degree for different protocols) include the Fathead minnow, the Japanese Medaka, the Zebrafish and the Three-spined Stickleback. The numbers we will use depends largely on the requested we receive from the relevant stakeholders (in this case primarily the chemical industry). To avoid licence amendments, the numbers requested are most likely overestimated in relation to the numbers we will use. In total, we request the authority to use 18,000 fish during a five year period.

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?

There is a regulatory need to assess chemicals properties in terms of endocrine potential in order to protect both wildlife and humans from their potentially harmful effects. When regulators suspect endocrine disrupting activity they can ask for these highly specific tests to be conducted. Suspicion is usually raised by a series of relevant non animal tests. Chemicals with endocrine disrupting activity are not toxic, so they don't present adversity from this point of view. The harm they can do is very different; they can completely prevent for example sexual maturation or they can block spawning. These are not perceived as effects of high severity because they don't involve any suffering; yet, their endocrine modulating activity can result in population level effects via impaired growth and reproduction.
All fish will be humanely killed at the end of each experiment. All protocols are of mild severity.

Application of the three Rs

1. Replacement

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

The regulatory requirement is currently involving vertebrate (fish) testing which can confirm the endocrine activity beyond *in vitro* (non animal) tests. If regulation was based solely on *in vitro* tests then many useful chemicals would have to be either removed from the market or never allowed to be placed in the market. This is because the false positive rate of most relevant in vitro tests is particularly high.

Nevertheless, we believe that the collection of more data from the exposed fish (as we plan to do) may allow in the future replacement (via computational modelling techniques).

2. Reduction

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

The tests relevant to this licence application have been validated following international efforts and interlaboratory testing; as such the number of animals needed and the number of treatments have been determined in a robust manner and are highly descriptive.

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.

Like in any testing involving a protected vertebrate, there is plenty of scope for refinement, even if the test conditions and aquaria housing are highly descriptive. There are four species involve in this particular test guideline programme, namely, Fathead Minnow, Japanese Medaka, Zebrafish and three-spined stickleback.

The procedures are mild (i.e. we don't expect mortalities or long and lasting suffering) but we have controls in place, should it happen unexpectedly. The main tool we will is close monitoring.

The fish are sourced from our own breeding establishment to ensure disease-free, high quality animals acclimated to experimental tank conditions and being in the right stage of age and sexual maturity. We have a dedicated, high-tech aquarium facility, with monitoring and call-out alarms. Named persons oversee staff training and performance, care of fish, and dissemination of information. Close links with the international fish research and regulatory community ensures we are aware of any developments. Consideration is given to all aspects of the environment including husbandry where a dedicated team of specialist aquarists complemented by long-standing experience operate. We believe we have a strong institutional culture of care and have review processes to identify where further improvements in care can be made.