



Code of Practice for the Supply and Use of Aquatic Species in Research

Introduction and MRC Policy

The MRC has developed a policy on the supply of animals with the overall aim of avoiding the breeding, maintenance or culling of excess numbers of animals whilst meeting scientists' reasonable expectations for a ready supply of appropriate animals. This policy is directed at the MRC's own staff, but will also be relevant to those working in Universities. This is the second Code of Practice in this series and follows the same principles as those outlined in the previous rodent code.

The MRC's position is that the avoidable production of surplus animals that have no assigned use is not ethical, nor is it in line with good scientific management practice.

A specific research project may require tightly specified animals in terms of appropriate species, genetic variety, sex, weight, pathogen status or other relevant characteristic. Meeting reasonable, fully justified requirements of this type may result in the unavoidable breeding and maintenance of animals that have no scientific use, but the scientific benefits of using the highly specified animals should be expected to outweigh the ethical costs.

However, scientists must avoid making their specifications for animals excessively narrow in relation to what is required scientifically, and to manage their requirements with foresight.

Animals identified as being surplus to scientific need will be killed humanely, in accordance with the law. Numbers are recorded in each Institute/Unit.

Many strategies exist within MRC Institutes and Units to meet the scientific requirements for the supply of aquatic species whilst minimising the production of animals that are not required for scientific use or the maintenance of breeding colonies. This Code of Practice draws these strategies together, setting out the issues which Institutes and Units should consider to ensure the production and use of aquatic animals that are not subsequently used for research purposes, breeding or archiving models are minimised.

Use of Aquatic Species

Fish and amphibians have become popular 'model' organisms in which to study gene function during embryo development. The most popular species are zebrafish (*Danio rerio*), medaka (*Oryzias latipes*), the African Claw-toed frogs *Xenopus laevis* and *Xenopus tropicalis*, and axolotls (*Ambystoma mexicanum*). All of these species are amenable to a wide range of embryonic and genetic techniques.

The use of non-mammalian vertebrates can in its own right contribute directly to the 3Rs¹. Due to their rapid external development these species can be used at unlicensed stages [Animals (Scientific Procedures) Act 1986] to gain a wealth of data that may replace the use of mammals that for similar information may be required to be used at more sentient licensed stages. Similarly, the relative size and/or transparency of eggs and embryos from these species allows for easy observation using less invasive procedures than those required when using mammals – this constitutes refinement. Use of aquatic species can provide a first step in genetic analysis and thereby reduce numbers of overall animals used for studying a variety of different processes.

¹ Replacement, Refinement and Reduction

The Home Office Codes of Practice are not prescriptive in recommending environmental parameters for fish and amphibians. However, it is extremely important that environmental conditions are kept stable and monitored regularly. Any change in water quality, hardness, temperature, feeding regimes and stocking densities must be managed through a carefully controlled husbandry experiment as aquatic animals generally respond slowly to changing environmental conditions.

Although 'core' facilities exist to maintain aquatic species, the main production requirements are driven by individual scientists from a variety of disciplines.

A variety of mechanisms exist to identify individual aquatic animals, but many are invasive and not considered 'welfare friendly'. Animals should not be subject to an invasive identification process unnecessarily. The actual need for identification should first be established. Not marking animals leads to difficulties in tracking animals individually throughout their lives, but can be considered a refinement. If identification is necessary, then the most humane method should be used (i.e. that likely to cause the least pain or distress, and which minimises the risk of secondary health problems, whilst also being effective over the required period of use – further guidance is available from the RSPCA²). Records and reports should specify how animals are identified.

Records & Reporting

The Certificate Holders at MRC Institutes and Units that breed, supply and use both conventional and genetically-altered animals for experimental use are responsible for the maintenance of definitive, contemporary records of the source, use and disposal of all protected animals bred or obtained for use, supplied for use, or used in regulated procedures. Such records account for each protected animal and provide full and accurate details of the type of animal, age, the numbers and types of animals allocated as breeding stock, held for supply or use, and the project licence to which the animal was issued. The records also include details of disposal – whether an animal was killed by an appropriate method listed in Schedule 1 or other method authorised in the Certificate of Designation; whether on welfare grounds; for harvesting tissues for experimental or other scientific purposes; as surplus to requirements; due to death from other causes; or supplied to another designated establishment. All of the records above are retained for at least five years after the death of an animal and are available for scrutiny by a Home Office Inspector on request. The information contained in these records is also used by establishments to monitor and continuously improve standards and practices – for example, to allow the prompt identification and early resolution of incidental welfare problems and to minimise animal wastage by better matching breeding programmes to likely demand.

Much of the above paragraph is extracted from the Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 and demonstrates the legal requirement to take all practicable approaches to ensure minimum wastage. It also offers a number of practical suggestions to minimise production of surplus animals that have no assigned scientific or husbandry use.

MRC Head Office has an annual requirement for data from each Unit of numbers of animals used that are non-returnable under the Act, most of which will be non-GM animals. This data will be sought at the same time as Units make their returns to the Home Office. (Units will also be expected to be able to provide, if required, more detailed numeric breakdowns of such animals, against the categories in the Act.)

The MRC Biological Services Managers Group audit data on avoidable surplus breeding, biennially, in order to spread best practice.

² Reed B (2005) Guidance on the housing and care of the African clawed frog *Xenopus laevis*. Research Animals Department, RSPCA: Horsham, UK
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Role of the Ethical Review Process (ERP)

The local Ethical Review Process (ERP) of each MRC establishment is central to the analysis of supply and demand and monitoring trends in use. There is a legal requirement that the ERP regularly reviews an establishment's managerial systems, procedures and protocols where these bear on the proper use of animals and also to undertake retrospective project reviews and ensure application of the 3Rs to all projects requiring the use of animals. In addition, the Animal Procedures Committee (APC) reports annually on the Statistics of Scientific Procedures on Living Animals.

Approach and Rationale of this Code of Practice

This Code of Practice does not intend to be prescriptive about the approaches to ensure that supply of aquatic species does not exceed demand and use. The main elements and principles of this document are similar to the previous MRC Code of Practice for the Supply of Rodents in Research and are presented in the same style. Other papers such as the 1998 LASA Task Force Report³ and the more recent APC report⁴ identify good practices in assessing, evaluating and auditing breeding programmes which are suitable for use with aquatic species.

Key elements

1 Planning and Communication

The importance of regular communication between scientific laboratories and facility staff cannot be overemphasised. This must be inclusive of the ERP as well as an ongoing dialogue through formal and informal meetings, e.g.:

- Consult literature and local community before embarking on new projects;
- Ensure regular access to animal care staff;
- Project Planning discussions, to establish lead time(s), feasibility, costing and time scales;
- Progress discussions, to include estimated completion of project(s);
- Review discussions, to audit requirements for regular standing orders;
- Strategy discussions, to include breeding schemes, troubleshooting, ideas for sharing and archiving;
- Attendance and presentation of work in different fora.

User groups should also work towards use and application of common/standard nomenclature. Labelling on tanks should match a recognised nomenclature or use a shortened form or nickname that is recognisable to all users and animal care staff.

2 Archiving Models

Currently it is neither routine nor reliable to freeze germplasm from aquatic species although techniques do exist and are being developed. The ability to store such material would greatly aid in reduction of animal use as well as protect stocks and allow easy dissemination of strains.

3 Sharing Models and Resources

There are a number of ways in which models and resources can be shared within and between establishments to prevent unnecessary breeding and to reduce the need to specifically breed or order animals. These include:

- Coordinating the harvesting of tissues and organs to meet the needs of multiple users to ensure best and maximal use;
- Use of national and international resources/stocks;
- Communication within and between MRC Units and Institutes, and also with other breeders and holders of animals;

³ The Production and Disposition of Laboratory Rodents surplus to the Requirements for Scientific Procedures: The Report of a LASA Task Force Meeting, 12 June 1998

⁴ Report of the Animal Procedures Committee 2003 – The Control of Surplus Laboratory Animals (Overbreeding)

- Consideration of supply from other sources including other establishments and commercial breeders;
- Consideration of conducting small scale pilot studies, before breeding or using large numbers of stock.

4 Training

In addition to the statutory training requirements (Home Office modules), formal and on-the-job training are essential in the effective management of breeding stocks and coordinating scientific projects. Regular training for facility staff and scientific users should include the following:

- Good record keeping;
- Data capture and analysis;
- Basic performance statistics such as egg quality and quantity;
- Experimental planning to ensure statistical relevance.

5 Alternative Uses of Aquatic Species

Where some breeding of surpluses cannot be avoided, there may be alternative uses that should be considered to make use of these animals. Wild type animals such as fish may be suitable to be released from the Act to become pets in some circumstances although this should not be encouraged. Genetically modified animals should not be released, and no *Xenopus laevis* should be able to reach the environment as they will cause ecological harm.

Summary

There are a wide variety of reasons why animals produced may become surplus to requirements. Some surplus will be inevitable, particularly with the increasing use of genetically-altered animals, but must be justifiable within the circumstances in which it arises. The MRC therefore expects that MRC Institutes and Units will adhere to the above guidance, as well as regularly reviewing and auditing breeding numbers locally, to further reduce surplus breeding and ensure cost-benefit analysis of animals bred and maintained for possible use in research.