EDITORIAL

Principles and standards for reporting animal experiments in *The Journal of Physiology* and *Experimental Physiology*

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Introduction

The Physiological Society publishes two leading scientific journals, *The Journal of Physiology* and *Experimental Physiology*. (A third journal, *Physiological Reports*, is published jointly with the American Physiological Society and has a separate ethics policy http://physreports.physiology.org/author-guidelines.) The journals publish papers describing the research outcomes from experiments that may use animals. Current journal policy is that for such a paper to be acceptable for publication it must comply with the home country's own legislation/guidelines, and should also conform to the principles outlined in UK legislation. However, because UK legislation involves a dialogue between investigator on the one hand and institution/inspectorate on the other there may be a lack of clarity regarding these principles, particularly when viewed from outside the UK.

Every journal is obliged to ensure that in any paper describing experiments on animals, the findings were obtained without unnecessary pain and suffering. Journals also have a responsibility to ensure that the reporting of such studies is of sufficient detail that the scientific value and ethical implications can be critically evaluated.

There is a view that the reporting of biomedical research has often been inadequate, which has led to a call for improvements (Kilkenny *et al.* 2009). Raising the standard of statistical reporting has been a major focus of *The Journal of Physiology* and *Experimental Physiology* through a series of editorials by their former Statistics Editor, Gordon Drummond (Drummond *et al.* 2011).

These editorials are a cornerstone of the ARRIVE guidelines (http://onlinelibrary.wiley.com/doi/10.1113/jphysiol.2010.192278/full) on animal research that, along with the majority of bioscience journals, *The Journal of Physiology* and *Experimental Physiology* have endorsed. Another editorial (Drummond *et al.* 2010) expounds the use of the guidelines to improve scientific reporting and ethical standards in animal research.

In May 2014 The Physiological Society signed the Concordat on Openness on Animal Research. http://www.physoc.org/sites/default/files/concordat-on-openness.pdf

This commits The Society and, by implication, its journals to:

- Be clear about when, how and why animals are used in research
- Enhance communication with the media and public
- Be proactive in encouraging public discussion
- Monitor and report on progress

Principles of these Journal guidelines

Our policy does not require all authors to operate precisely according to UK or EU law (unless they are governed by those laws by virtue of residence) but sets exacting standards, based on the principles of UK legislation and the ARRIVE guidelines, and in line with our editorials. These guidelines are designed to clarify the principles with which papers must conform, and how these can be applied within an international framework.

Best practice in research involving animals will embody the principles of the 3Rs (replacement, reduction and refinement) and a paper must also demonstrate that the study has adhered to these. Further details of these principles can be found on the National Centre for the Replacement, Refinement and Reduction of Animals in Research website (https://www.nc3rs.org.uk/the-3rs).

The Methods section of all papers must provide sufficient details (see checklist) to allow the reader to assess the life-time experience of the animals used in experiments.

The checklist

The following checklist aids authors, referees and editors in making an ethical assessment of papers describing animal studies. Papers failing to comply with the checklist will be referred to the Senior Ethics Editor and may be rejected on ethical grounds without further review.

Experiments must follow national legislation/guidelines and have had approval from an appropriate ethical body, must follow current best practice and use the most appropriate species for the study. Animals should not be used if there are alternative approaches that provide comparable results. If the research has used cats, dogs or primates, the Methods section should make the case for their use explicit.

Why clarify the journals' policy?

The UK regulations on ethics in research on animals apply to vertebrates and cephalopods. The guidelines "Operation of the Animals (Scientific Procedures) Act" (ASPA) extend to over 100 pages and cover the procedures for licensing individuals (personal licence), the project (project licence) and the establishment (certificates of designation or establishment licence). UK legislation has been recently been amended following adoption of European Directive 2010/63 of the European Parliament and of the Council.

While UK law sets out the principles behind the way animal experiments must be conducted, it is the responsibility of each scientific establishment to make suitable local provisions. This adds a further level of complexity because of the unique role played by the Home Office Inspectorate in implementing UK legislation through advising on licence applications and periodic visits to research establishments to ensure compliance with the ASPA. The Inspectorate works with the Named Veterinary Surgeon (NVS) and Named

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Table 1. Animal ethics checklist

Ethical approval	At the beginning of the Methods section state the institutional ethical committee that approved the study and also the national guidelines under which the institution operates. Authors must demonstrate they have taken all steps to minimise the animals' pain and suffering.
Origin and source of the animals	Identify the animal supplier/breeder. Specify species, strain, genetic background, weight, sex, age and any genetic modification. Indicate the group size and total numbers of animals, including any animals used but subsequently excluded for any reason, specifying any unexpected events.
Access to food and water	State the feeding regime e.g. fasting, feeding *ad libitum* or on a specific diet.
Euthanasia	Animals must be killed using methods approved for that species, stage of development and size. If national or local guidance on this is not available, information on UK/European Union requirements can be found in ASPA Schedule 1 in the UK and in Annex IV in the European Directive 2010/63/EU. Methods not on Schedule 1 or Annex IV could be permissible but the onus is on the author to provide scientific evidence to support the method used and to demonstrate that it is at least as humane as those on Schedule 1 and Annex IV.
Anaesthetic protocols	Describe anaesthetic protocols in detail (premedication, anaesthetic(s) used, dose, route, supplementary dosage). These must be appropriate for the species, experimental time course and whether the procedure was terminal (in which the animal is killed without ever gaining consciousness) or required recovery. For the latter there should be appropriate post-surgical care and analgesia, which the paper must also describe. Researchers have an obligation to ensure that pain or distress, whether physical or psychological, is minimised, and steps taken to achieve this should be noted.
Surgical procedures	Provide a brief description of the operation.
Monitoring	Describe how the depth of anaesthesia was determined and maintained. This is especially important when neuromuscular blocking agents were employed. The journal website provides specific details on the use of neuromuscular blockers, see http://www.physoc.org/animal-experiments
Terminal procedures	State what happened to the animals at the end of the study and how they were killed. Animals should have been humanely killed unless reuse in another study had been specifically authorized by the ethics body. Reuse depends upon full restoration of health and well-being and on the severity of the previous and subsequent procedures, evaluated as part of an assessment of the animal's lifetime experience.
Confirmation of compliance	Include in the Methods section a statement that the investigators understand the ethical principles under which the journal operates and that their work complies with this animal ethics checklist.

Animal Care and Welfare Officers in encouraging good practice, in setting severity limits for procedures and in advising on requests for any variation from established procedures based on scientific rationale.

There are several aspects of UK legislation that are not always completely transparent, due to these potential differences in local regulation. Severity limits are a feature of UK legislation and are defined in individual project licences. Non-recovery experiments in which an animal is anaesthetized throughout the procedure and killed at the end of the experiment are unclassified. Procedures performed on non-anaesthetized animals are classified as mild, moderate or severe depending on the degree of pain and suffering that the animal is expected to experience during the course of the experiment. Since an experiment may involve more than one procedure, the severity band sets the upper level of suffering that animals can experience under a particular project and if this is exceeded the experiment must be terminated. Procedures classified as severe receive additional scrutiny before any licence is issued.

Under UK legislation investigators also need to demonstrate that they have performed a harm–benefit analysis in which distress, pain and discomfort are weighed against the benefits to human or animal health, society or environment that might follow from the research.

The journal guidelines are being clarified because this approach to licensing, on a case-by-case basis in compliance with

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exacting and strictly applied principles, is unique to the UK. It is therefore sometimes difficult for authors, reviewers and publications staff to assess the extent to which a particular study conforms with the principles of UK legislation. As a consequence, in a small number of cases, papers with potential problems in this area are sometimes not spotted early in the review process. This is potentially frustrating for authors and puts a heavy burden on the ethics editors, particularly if favourable referee comments are set aside because of a concern regarding animal ethics.

Best practice and ethical acceptability

As a consequence of this possible lack of clarity, a small number of papers are rejected because the procedures they describe would not be permitted in the UK, because they are not considered best practice, or because they are ethically unacceptable.

The most common cause of rejection on the grounds of best practice is because of the use of certain anaesthetics would not be accepted in the UK. Ether is a classic example because it is still commonly used in various laboratories around the world. However, its use as an anaesthetic has long been criticised and in the UK and elsewhere, is no longer tolerated because induction of anaesthesia is slow and potentially very unpleasant to the individual animal, causing irritation to the eyes, nasal mucosae and the upper respiratory tract and leading to excessive tracheo-bronchial secretions. Endocrine parameters indicate significant stress to the animals and a number of physiological parameters are affected by ether anaesthesia. There are therefore both ethical and scientific grounds for avoiding its use with most ethical review bodies recognizing this and advising against its use. Any paper using ether would therefore not be acceptable for publication in the journals since this no longer complies with the principle of best practice.

There have also been issues around the use of chloral hydrate as a recovery anaesthetic. Chloral hydrate is a hypnotic agent but a poor anaesthetic for surgical procedures because it does not provide analgesia. It would only be accepted in the UK under special authorization based upon experimental needs, and only then for non-recovery procedures. This agent is highly irritating to the GI tract and is therefore not accepted in the UK for recovery surgery because of the risk of post-operative complications. Again, best practice dictates therefore that the use of chloral hydrate for recovery surgery is not acceptable and is incompatible with journal policy.

These are just two examples of procedures for which some (e.g. non-UK) institutional approval would have been obtained and national guidelines followed, but because these agents no longer reflect best practice and there are cost-effective and better alternatives there are no grounds for their continued use.

By being explicit with respect to our required standards for experimental procedures involving animals, their reporting, and issues of best practice, the journals will continue to positively influence the standards of ethical review, encourage more openness and identify and therefore reduce the likelihood of publication of ethically suspect papers.

Conclusion

The Journal of Physiology and *Experimental Physiology* policy on animal ethics has been underpinned by UK legislation for over a century. These guidelines are designed to clarify the journals' requirements for the reporting of work involving animals, against this background, to maintain our exacting standards while also improving the reporting of animal studies. The outcome, we hope, will be greater transparency in a global research environment and a more thorough ethical review process as awareness improves in ethical committees, by investigators, peer reviewers and journal editors of what the journals and community expect. In adopting the new guidelines *The Journal of Physiology* and *Experimental Physiology* should continue to lead the way in standards of scientific reporting.

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