EDITORIAL

Guidelines for reporting experiments involving animals: the ARRIVE guidelines

JC McGrath¹, GB Drummond², EM McLachlan³*, C Kilkenny⁴ and CL Wainwright⁵

¹Autonomic Physiology Unit, Integrative and Systems Biology, Faculty of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK, ²Department of Anaesthesia, Critical Care and Pain Medicine, Royal Infirmary, Edinburgh, UK, ³Spinal Injuries Research Centre, Prince of Wales Medical Research Institute, University of New South Wales, NSW, Australia, ⁴National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), London, UK, and ⁵Animal Welfare & Integrative Pharmacology Panel, British Pharmacological Society, Institute for Health & Welfare Research, The Robert Gordon University, Schoolhill, Aberdeen, UK

Correspondence
JC McGrath, Autonomic Physiology Unit, Integrative and Systems Biology, Faculty of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK. E-mail: i.megrath@bio.gla.ac.uk

*Present address: Autonomic Physiology Unit, Integrative and Systems Biology, Faculty of Biomedical and Life Sciences, West Medical Building, University of Glasgow, Glasgow G12 8QX, UK.

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British Journal of Pharmacology (BJP) is pleased to publish a new set of guidelines for reporting research involving animals, simultaneously with several other journals; the ‘ARRIVE’ guidelines (Animals in Research: Reporting In Vivo Experiments). This editorial summarizes the background to the guidelines, gives our view of their significance, considers aspects of specific relevance to pharmacology, re-states BJP’s guidelines for authors on animal experiments and indicates our commitment to carrying on discussion of this important topic. We also invite feedback via the British Pharmacological Society website.

Background

In the last 20 years, several factors have stimulated a more structured approach to reporting medical science. These include more exact standards of conduct for studies to be used to support drug approval, greater stringency regarding the ethical conduct of experiments and the popularity of ‘evidence-based’ practice. A satisfactory evidence base requires structured review and meta-analysis, and this cannot be performed without full experimental details. Such a structured approach to reporting was generated in the CONSORT statement, designed to allow a formal reporting on randomized clinical trials. (Altman et al., 2001; Begg et al., 1996; Moher et al., 2001; Schulz et al., 2010).

For animal research, a comprehensive set of guidelines on reporting studies has thus far been lacking. This gap has now been filled following the generation of a set of guidelines referred to as ARRIVE (Animals in Research: Reporting In Vivo Experiments) (Kilkenny et al., 2010) by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), a UK government-sponsored organization. The guidelines recommend the format and content of details relating to animals in a typical scientific report.

Our view

Several organizations support the case for improved reporting and recommend the use of reporting guidelines, including the International Committee of Medical Journal Editors (2008), the Council of Science Editors – Editorial Policy Committee (2009), the Committee on Publication Ethics (COPE) (2010) and the Nuffield Council on Bioethics (2005). BJP together with its parent organization the British Pharmacological Society (BPS) is pleased to add its name to this list and we urge other
journals to similarly publish these guidelines and incorporate them into their Instructions to Authors. Already, several journals have agreed to publish these guidelines simultaneously and/or to provide accompanying editorial settings the guidelines in the context of their specialized field (Kilkenny et al., 2010a,b,c,d,e).

Scientific reports should always be clear and explicit, so that their content can be judged properly and incorporated into our knowledge. A number of features are relevant, such as adequate ethical standards and statistical treatment. Crucially, the details provided must allow another researcher to be able to replicate the study, so that the study could be independently verified.

These guidelines are designed to be comprehensive and some of the content will not immediately appear relevant to pharmacology and related areas of research. However, what is relevant changes with time and science continually develops in new directions. Therefore we must be mindful of new audiences, unfamiliar with the traditions of current practice, who may be interested in particular articles and, in order to further their own understanding, require information that is not often included as detailed protocols at the present time. Thus adherence to a comprehensive set of rules for inclusion of detail that is consistent across all articles has many advantages.

Specific relevance to pharmacology

In terms of this journal, there are undoubtedly some pharmacology-specific aspects within these guidelines to which we would give greater emphasis.

While the guidelines were devised in relation to reporting of in vivo experiments, these same principles apply equally to in vitro experiments conducted on tissues derived from animals killed for the purpose, irrespective of whether or not the source animal previously underwent an in vivo procedure. The guidelines use the qualitative term ‘euthanasia’, i.e. ‘good death’, whereas we prefer the plain English term ‘killing’, whether this is the final step in a terminal in vivo procedure or a method of killing for tissue harvest. The details of the method of killing are essential in order for us to understand what influence this may have had on either the data obtained from in vivo experiments or from experiments performed on tissue obtained post mortem.

Moreover, while the guidelines mention anaesthesia and analgesia, it is important also to stress the separate importance of analgesia in recovery experiments, both for ethical considerations and because of the possibility of drug interactions that might confound the experiment. Further, tissue removed under terminal anaesthesia and studied post-mortem can be affected by not only the nature, but also the timing of killing. Details of the techniques used are also necessary to satisfy ethical considerations (Drummond, 2009). Thus, while ARRIVE is a convenient acronym for the guidelines, their reach and influence might be greater if we simply considered them to be guidelines for reporting research involving animals.

It is worth commenting on some of the issues that were identified in a survey of published biological science research, carried out by the NC3Rs, and that subsequently helped to inform the guidelines (Kilkenny et al., 2009). For example, the survey found that only 59% of 271 randomly chosen articles stated the hypothesis or objective of the study and the number and characteristics of the animals used (i.e. species/strain, sex and age/weight). Moreover most papers surveyed did not report using randomization (87%) or blinding (86%) to reduce bias in animal selection and outcome assessment. This comment reflects the basis of the guidelines on the principles for randomized controlled clinical trials.

It is important, however, to recognize that experimental strategies in pharmacological and other laboratory-based disciplines are normally completely different. In studies of large uncontrolled populations, variance can be primarily ascribed to genetic, behavioural and environmental diversity. On the other hand, animals used for research in pharmacology consist of small rigorously selected groups for species, strain, age and sex and controlled for diet, temperature and light exposure, etc., in order to minimize variance and, hence, the requirement for large numbers of experiments. In many laboratory experiments, blinding may not be possible.

The survey also found that only 70% of the publications that used statistical methods fully described them and also presented the results with a measure of precision or variability. There is no doubt that the statistical methods used in pharmacology are generally simpler than those appropriate for clinical trials. Nevertheless we fully acknowledge there is room for improvement in the design and reporting of statistical analyses published in our discipline.

**BJP guidelines on ethical and animal welfare issues**

BJP requires articles to contain information that allows the journal referees and editors to be satisfied
that the conditions under which human and animal experiments are performed are consistent with prevailing standards in the UK. Our view is that our journal should abide by the legal framework of the country in which it is published. Studies on animals published in BJP must comply with the prevailing standards of animal welfare embodied in UK laws governing animal experimentation and authors are offered advice on ethical and animal welfare issues, through the British Pharmacological Society’s Animal Ethics Adviser via the BJP editorial office. Where there is a discrepancy between the author’s country’s laws and those of the UK, we would refer this to our Ethics Committee and, in general, would come down on the side of the most rigorous set of rules.

Contained within the Instructions for Authors are the following guidelines:

Authors must make it clear that the procedures they used were as humane as possible and complied with the guidelines for animal care of their institutions or with national/international guidelines. For animal studies, the species, strain and total number used must be stated, as well as conditions of maintenance (food, water, light/dark cycles and compliance with ethical guidelines). The doses (initial and subsequent) of anaesthetics and analgesics should be clearly stated; the method of assessing anaesthesia, particularly after the administration of neuromuscular blocking drugs, must be clearly stated. For animal studies performed under anaesthesia vital signs (e.g. blood pressure, heart rate and blood gases) should be monitored and these data be included in the Methods.

**BJP and ARRIVE Guidelines – the way forward**

Of course, the time of writing a manuscript is not the point to be considering the issues raised in the ARRIVE guidelines. Refining experimental approaches to minimize pain and distress to the animals, and reducing animal use based on sound ethical, scientific and statistical principles is best performed when planning and devising the project and designing experiments. However, communicating the results effectively to the scientific community, is equally important. The objective should be to obtain the maximum amount of high quality data from the minimum number of experiments that answer an important question. This is ethical, scientifically and financially efficient, and should be common sense.

The BPS/BJP is actively involved in encouraging informed debate on the strategies used in animal experiments. The BPS, together with The Physiological Society and the NC3Rs held a Symposium in London on 31 March 2010 addressing the challenge of how to ‘define a future cardiovascular research agenda with reduced reliance on the use of in vivo models’. Discussion papers arising from this will be published in BJP later in 2010. This event follows a recent review on ‘Opportunities for the replacement of animals in the study of nausea and vomiting’ (Holmes *et al.*, 2009) and an accompanying commentary (Robinson, 2009).

Through publication of the ARRIVE guidelines we aim to continue this debate. We would ask our readers that, after considering the ARRIVE guidelines, you provide us with your feedback on them: BJPguidelines@wiley.co.uk BJP will then consider the feedback and modify the guidelines appropriately for our discipline and incorporate them into our Instructions to Authors.

**References**


