National Animal Ethics Advisory Committee

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Avoiding duplication of research involving animals

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FOREWORD

It is an essential tenet of New Zealand's system for governing the use of animals in research, testing and teaching that animals are not used unnecessarily. As Chair of the National Animal Ethics Advisory Committee (NAEAC), I am therefore very happy to introduce the seventh in the committee's series of occasional papers, Avoiding duplication of research involving animals by the our Deputy Chairperson, Dr David Morgan.

In this paper, Dr Morgan defines the scientific and regulatory reasons that legitimate replication or repetition of research, and differentiates these from the undesirable issue of duplication of experiments. In acknowledging that such duplication can involve the unnecessary use of animals in research, Dr Morgan goes further to give strategies to avoid or minimise the chance of this happening. There is valuable information here for both researchers and animal ethics committee members.

NAEAC is very grateful to Dr Morgan for preparing this paper, and acknowledges the amount of work involved in its preparation.

Virginia Williams

Chair, NAEAC

March 2011

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Avoiding duplication of research involving animals

Dr Dave Morgan, National Animal Ethics Advisory Committee, 17 January 2011

Introduction

From time to time, claims are made that animals are used wastefully in research work that duplicates work already undertaken. A cursory internet search suggests that such claims have been made mainly by animal rights' organisations, and that, perhaps partly in response, many animal research organisations and regulatory agencies have policies in place to avoid duplicative research.

Typifying this conflict, Budkie (2009) claimed that duplication had occurred no less than 57 times in projects in the USA involving monitoring the functioning of the visual centres of the brain in non-human primates. While his analysis may have appeared as being objective and therefore reliable to some readers, others have pointed out that Budkie's claim rests purely on the repeated use of the same animal model and manipulations, while overlooking the important differences in focus (i.e. the research objectives) and measurement that rendered studies unique. As one respondent stated: "Budkie's criticism is equivalent to claiming that blood-sampling of humans is wastefully repetitive, while ignoring the medical condition under examination and the clinical parameters being assessed". Clearly Budkie's claims were founded on a poor understanding of how science is conducted, leading him to an erroneous conclusion.

This analysis was undertaken with the aim of clarifying what is meant by "duplication", to what extent it occurs, and measures that can be taken to minimise the likelihood that it occurs.

What is meant by "duplication" of animal research?

It is immediately apparent when reading some of the views presented on the internet on this topic, that clarification of the term duplication is needed to avoid confusion. Scientific experiments involving animals are sometimes repeated by the same or other research groups. In considering whether the repetition of experiments is desirable, it is essential to distinguish between "replication", "repetition", and "duplication":

- Replication refers to repetition of experiments or tests to increase the reliability (by replication within experiments) and generality (by replication of entire experiments) of the findings. Replication is a fundamental component of the scientific method. The degree of replication required will depend on the level of scientific precision demanded, the natural variation in the variables measured, and the range of circumstances in which findings are to be applied. The level of replication required to achieve the desired statistical precision can be predicted by power analyses of pilot data.
- Repetition of product testing is sometimes required by regulatory agencies. Such repeat testing may occur, (i) where routine testing of different batches of products are required, (ii) where "generic" companies commence manufacture of products coming "off-patent" and are required by regulators to provide evidence of efficacy and safety using animal models, and (iii) where the claimed efficacy of products is extended (e.g. an existing parasiticide is shown to be effective against an additional parasite). All cases entail, either or both, novelty and uncertainty. Therefore, repetition of the animal tests is necessary to ensure that products are fit for purpose (i.e. both efficacious and acceptably safe).
- Duplication of animal experiments, where neither replication nor repetition (as defined above) are being carried out, would be pointless. If the outcomes are predictable from previous experiments, such duplication is unacceptable because animals are needlessly manipulated. However, it could occur when a researcher (and those scrutinising the researcher's proposal – see below) is unaware that the experiment or test has already been done because results have not been published. This may be because:
  - the research "failed" and was not considered worth publishing;
  - the research findings were commercially sensitive;
  - the research is still in progress.

The Animal Welfare Act (1999) permits "duplication" only where the original experiment was found to be flawed, or for confirmation (i.e. as replication or repetition).

How much duplication occurs?

As the main possible cause of duplicated animal-based research (as defined above) is lack of awareness of previous research, it would be extremely difficult to reliably assess the extent of duplication because it is unlikely to be declared as such. However, it is considered likely to comprise an extremely small proportion of all research undertaken in any field. This is due, firstly, to the fundamental inclination (and requirement by funders) of researchers to investigate the unknown and to avoid wasting time and investment in pointless research: there is no incentive such as academic recognition or commercial success to be gained. Reinforcing this natural tendency are the formal checks and scrutiny that exist ("peer review" – discussed below) to ensure that researchers are knowledgeable about the background context and originality of proposed work.

Conventional ways in which duplication is minimised or avoided

Scientific research progresses by the accumulation of related information into a body of knowledge which then provides the foundation for new hypotheses and experimentation. To be competitive within their own field, researchers must keep up to date with these developments, and consequently they are able to largely avoid any risk of unwitting duplication. Researchers keep abreast of developments by:

a) Literature reviews

The most common and effective means of avoiding unintentional duplication of animal experiments (indeed, as for any form of research) is for researchers to ensure that they are familiar with the published literature in the particular research field. Reviewing the literature in even very large fields of science is now easier and quicker than ever before as electronic publication databases have been developed to incorporate most of the scientific literature ever published. Thousands of specialised databases now exist summarising current knowledge in all fields of animal-based research. Finding the most relevant databases has been simplified through the use of portals such as BioMed Central (2010), CABI (2010) and State University of New York (2010).

Published literature generally reflects research that was at least partly successful in achieving its aims. However, some research is unsuccessful in demonstrating the expected outcome and often remains unpublished or unpublicised. Not only could this lead to failure by peers to recognise the possibility of alternative outcomes, but it could lead to unwarranted duplication of the research. An encouraging recent development is the establishment of journals dedicated to publishing "unsuccessful" research findings with the aim of providing scientists and physicians with responsible and balanced information (e.g. the "Journal of Negative Results in Biomedicine" and the "Journal of Negative Results (ecology and evolutionary biology)". Such journals will be encompassed by conventional literature search tools. Given the growing recognition of the importance of negative results, it is likely that more "unsuccessful" research will be published in future, further reducing the risk of unwitting duplication.

Other research findings that may not be available by literature searching arise from studies that are deliberately kept secret for commercial reasons, and from research that is ongoing and has not yet reached the stage of publication.

b) Networks

As well as maintaining familiarity with the publicly available literature and data, individual researchers typically develop personal networks of individuals and organisations that operate in the particular research field. Researchers naturally develop such networks as a consequence of the curiosity that drives their specific research interests. Internet communication has improved the ease with which such contacts can be established and developed. Nevertheless, where commercially sensitive research is undertaken, awareness of both unsuccessful research and ongoing research is not assured.

c) Peer review

Most animal-based research is undertaken only after a lengthy process of peer-review by the host institution, funding bodies (most of which have review panels of technical experts), regulatory agencies, animal ethics committees, and end-users. This stakeholder system not only ensures the scientific appropriateness and rigour of the proposed research, but it also provides another means of checking that the research is needed and that it has not already been done. Peer review greatly extends the background of experience against which a proposal is considered and therefore further reduces the likelihood that unnecessary research would be undertaken. Peer review also occurs when research papers are submitted for publication. Since journals will only publish research findings that are original, this serves as a disincentive against intentional duplication.

New ways for further minimising/avoiding duplication

The following approaches could help further reduce the likelihood of unwitting duplication of unpublished or confidential research.

a) Institutional codes and procedures

When considering applications for animal research, animal ethics committees should require evidence that the applicant is aware of previous work. While the New Zealand legislation wisely provides the flexibility needed for code holders to develop processes appropriate to the nature and scale of animal research, codes should, ideally, require demonstration that literature and perhaps patents have been searched to determine if the work has previously been done.

Additionally, since AECs maintain databases of research applications and outcomes, such information could be collated into either an institutional or national database for checking against potential duplication. However, commercial confidentiality may prohibit the incorporation of certain research projects in such databases.

b) Searching patents

Patent searches offer another means of helping to avoid duplication due to unawareness of "failures", "secrets", and "current studies". While the level of scientific detail contained in patents may often be less than that demanded by formal publication, the outline presented is usually sufficient to determine whether proposed research has been previously conducted. Checking patents is now a very simple procedure as world patents can be searched easily on-line at no cost through the European Patent Office (2010).

c) Research registers

An international system established in 2004 and operated by the World Health Organization (2010) acts as a single source for information on human clinical trials, collating information from registries operating in 14 countries. It was developed principally to counter the effects of bias in the scientific literature arising from the selective reporting of positive results that may lead to overestimation of the benefits of biomedical developments (An-Wen 2004). However, another of its aims is "improving awareness of similar or identical trials (that) will make it possible for researchers and funding agencies to avoid unnecessary duplication".

Such a model could be developed for the registration of animal-based research (as opposed to human clinical trials). However, while clinical trials typically conform to one of a small number of protocols, such as the "randomised, double-blind" trial, many other types of animal based research utilise a much wider variety of experimental designs that may prove too complex and costly to reliably categorise and sort in a database. Meeting the cost of establishing, maintaining, and encouraging use of such a system is probably not justified by the small risk that animals may be wastefully used unwittingly in research.

Conclusion and recommendations

The most likely circumstances under which animal-based experiments may be duplicated is when a researcher, and the system of stakeholders within which the research is conducted, are unaware of previous "failures", "commercial secrets", and "current studies". For the reasons given above, such duplication is believed to be rare, but in the absence of reliable information on the extent of duplicated animal research, it is impossible to define an appropriate scale of avoidance measures. It would, however, be inappropriate to pursue all possible measures suggested by this analysis, incurring substantial cost to research and testing organisations, if wasteful use of animals is extremely unlikely to occur. Nevertheless, some simple safeguards are recommended to help maintain a consistency of rigorous pre-emptive effort.

The following recommendations are made as a result of this analysis:

- AECs need to be aware of the important distinction between "replication", "repetition", and "duplication" as defined in this article.
- AECs need to avoid approving research that involves "duplication" unless previous studies were flawed.
- Researchers should be asked by AECs to provide evidence, in research applications, of the efforts made to avoid duplication of past research. Evidence could include: the literature and patent databases searched and key-words used, and reference to previous searches.
- Researchers should be asked to consider the likelihood that the research is currently being undertaken elsewhere, and if so, to seek clarification via personal networks and/or patent searches.

References

(All internet references were last sourced 19 February 2011)

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