Submission No 249

INQUIRY INTO USE OF PRIMATES AND OTHER ANIMALS IN MEDICAL RESEARCH IN NEW SOUTH WALES

Name: Dr Malcolm France

Date Received: 31 March 2022

Malcolm France
BVSc PhD MANZCVS (Pathology)
Consultant in Laboratory Animal Care and Management

31 March 2022

Hon. Greg Donnelly MLC
Chair, Portfolio Committee No. 2 – Health
Parliament of New South Wales
6 Macquarie Street
Sydney NSW 2000

Dear Mr Donnelly

Inquiry into the use of primates and other animals in medical research in New South Wales

Thank you for the opportunity to make a submission to the above inquiry.

My submission is now attached and includes recommendations to which I would like to draw attention:

> ***Recommendation 1***: That a coordinated strategy is developed to identify practical opportunities for advancement of the 3Rs in a manner that would optimise returns in terms of ethical and animal welfare outcomes.
>
> ***Recommendation 2:*** That resourcing for the NSW regulator be reviewed to ensure it retains the capacity to implement animal research regulations effectively and provide leadership in promoting best practice.
>
> ***Recommendation 3:*** That government regulators in Australia develop a nationally consistent process for reporting animal use data in a manner that is meaningful for the general public and would help inform animal welfare priorities and longer-term planning of research expenditure.
>
> ***Recommendation 4:*** That all stakeholders be encouraged to promote greater openness in animal research so that public understanding and informed discourse can be enhanced.

Thank you again for this opportunity. I am willing to be contacted for further discussion on any matters relating to the inquiry if required.

Yours sincerely

Malcolm France

Submission to Portfolio Committee No. 2 – Health

Inquiry into the use of primates and other animals in medical research in New South Wales

Malcolm France
Consultant in Laboratory Animal Care and Management

Introduction

Background

I am veterinarian with experience in various aspects of animal research over the last 30 years. This has included a PhD project based on an animal model, publishing papers on disease diagnosis and pathology of laboratory rodents, serving as director of animal facilities at two major universities, member of several Animal Ethics Committees including Chair of two, and conducting external reviews of animal research programs as an independent consultant.

I have also served as inaugural president of the Australian and New Zealand Laboratory Animal Association (ANZLAA), board member of the Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART), secretary of the laboratory animal chapter of the Australian and New Zealand College of Veterinary Scientists, *ad hoc* site visitor for the accreditation organisation AAALAC International, and reviewer for the international journal *Laboratory Animals*.

Declaration of interests

- ANZCCART: I am a board member of ANZCCART. Although this position is entirely honorary, I am involved with projects relevant to this submission, particularly the openness agreement.
- UNSW: I am currently employed as Director of Animal Services at UNSW. The views expressed in this submission are entirely my own and are not intended to represent or imply any views held by UNSW.

Responses to the Terms of Reference

(a) The nature, purpose and effectiveness of medical research being conducted on animals in New South Wales, and the potential public health risks and benefits posed by this research;

As with most other areas of research, the path from basic discovery to practical application of medical research is usually long and tortuous. This makes objectively **assessing the effectiveness** of animal research extremely difficult.

This point is illustrated well in a commentary published in the highly ranked journal *Cell* which describes an investigation of the relationship between basic research and new therapies using network analysis of

publication databases. In one example, it was found that US FDA approval of a single new drug could be linked to publications involving more than 7,000 scientists extending over 104 years[1].

Another example is the development of the reagents now used widely in diagnostic tests (including the COVID RAT test), many research applications and more recently as drugs. Known as monoclonal antibodies, their origin lies in curiosity-driven animal research conducted in the 1970s for which no particular clinical outcome was being sought at the time[2].

While assessing the effectiveness of animal research in the longer term can be challenging, there is now widespread recognition of a more immediate problem in which the potential benefits of animal research can be easily compromised by poor experimental design. Various initiatives have been introduced to address this including guidelines produced by the NHMRC[3]. Because of the complex and somewhat insidious nature of this problem, the solution should be seen as a shared responsibility by all stakeholders.

(b) The costs associated with animal research, and the extent to which the New South Wales and Federal Government is commissioning and funding the importing, breeding and use of animals in medical research in New South Wales;

In addition to direct research costs such as researcher salaries, purchase of animals and equipment etc, conducting animal research to a high standard requires significant investment in support frameworks. These include:

- Veterinary and animal care staff who provide routine daily care (including weekends and public holidays)
- Infrastructure for housing animals under exceptionally clean and standardised conditions to prevent disease and other variables that might compromise research data
- Administrative support for Animal Ethics Committees and compliance with quarantine and gene technology regulations.

Much of the funding for this work comes from public sources and therefore supports a case for openness, public understanding and consideration of social licence.

(c) The availability, effectiveness and funding for alternative approaches to animal research methods and technologies, and the ability of researchers to meet the 3 R's of Replacement, Reduction and Refinement;

There is very little funding in Australia directed primarily towards the 3Rs. Exceptions include:

- The not-for-profit Medical Advances Without Animals Trust
- A 3Rs grants scheme run by UNSW which had a total budget of $250,000 in its 2021 round

[1] Williams RS et al (2015) From Scientific Discovery to Cures: Bright Stars within a Galaxy. Cell 163:1, pp21-23
[2] France, MP (2014) The tortuous journey from bench to bedside: exploring the contribution of animal research. ANZCCART 2014 conference proceedings p75
[3] NHMRC (2018) Best Practice Methodology in the Use of Animals for Scientific Purposes

- A small grant scheme run by University of Wollongong

In 1989, a Senate Select Committee report on animal research contained 20 recommendations, the second of which was that the Commonwealth Government establish a fund for research into the use of alternatives[4]. This has never been implemented.

Notwithstanding the general lack of funding for the 3Rs, it is encouraging to see that the Commonwealth Government has recently conducted reviews into this area. For example:

- An information paper on the implementation of the 3Rs in Australia;
- A review to identify non-animal methods for safety testing of chemicals (awaiting publication)

The 3Rs concept was first articulated over 60 years ago and would be universally accepted. Nevertheless, major challenges remain. Some of these are technical, some involve regulatory considerations while others may just require greater awareness of new opportunities.

The ultimate goal of replacing animal research with other methods is one for which we all should be striving, but it is important to be realistic about the technical challenges this presents. Efforts to replace animal research with non-animal methodologies should therefore involve strategies that set achievable targets while aiming to maximise return on the resources required.

> ***Recommendation 1***: That a coordinated strategy is developed to identify and target opportunities for practical advancement of the 3Rs in a manner that would optimise returns in terms of ethical and animal welfare outcomes.

(d) The ethical and animal welfare issues surrounding the importing, breeding and use of animals in medical research;

Ethical considerations:

Under the Australian regulatory framework (and indeed that of all other jurisdictions), approval to conduct animal research involves a **harm-benefit analysis** which requires an ethical judgement that balances impact on animal wellbeing against the potential benefits of the research. Considerations such as scientific quality and social licence are often implicit in these analyses although they are sometimes given particular focus.

Systems have been developed to assist with harm-benefit analysis in animal research. These include the so-called Bateson's cube which is a 3-dimensional representation that incorporates scientific quality as well as harms and benefits. In the UK, a formal harm-benefit analysis of animal research applications must be conducted by the regulator. A 2017 review of this process included 27 recommendations which not only sought to enhance the assessment of harms and benefits but also improve consideration of societal concerns[5].

[4] Parliament of the Commonwealth of Australia (1989) Animal Experimentation. Report by the Senate Select Committee on Animal Welfare Preface, page xv

[5] UK Animals in Science Committee (2017) Review of Harm-Benefit Analysis in the Use of Animals in Research.

While I know that some Animal Ethics Committees in Australia have incorporated ethical decision-making guidelines into their procedures, my impression is that this is not widespread.

Australia's ethics-based regulatory framework for animal research has been firmly in place for decades yet it has received surprisingly little formal study or review. There would seem to be a case for such study given the overall investment in animal research.

Animal breeding:

In mid-2021, the Australian biomedical research community received notification that the country's largest breeder of mice and rats for research, the Animal Resources Centre (ARC) in Perth, was to close.

This was unexpected and raised major concerns in the research community because mice and rats represent by far the highest proportion of animals used in biomedical research.

Adding to these concerns is the fact that the ARC is renowned for meeting high standards of quality control that would be difficult to replicate – a particularly important consideration to ensure scientific rigour and avoid potential wastage of animals through compromised research.

According to its latest update, the WA Government expects to identify a new independent provider by about mid-2022. This period of transition presents an opportunity for review of the existing model which, while effective, has been in place since the ARC was established over 30 years ago. Possible initiatives that could be incorporated into a new model that would also promote efficiency and the 3Rs include:

- Integration and enhancement of complementary services such as cryopreservation of embryos to reduce the need for maintaining large colonies of live animals
- Greater matching of supply with demand to reduce the production of surplus animals
- Establishment of local nodes to reduce stress on animals from long distance transport

(e) **the adequacy of the current regulatory regime regarding the use of animals in medical research, particularly in relation to transparency and accountability;**

Regulatory oversight and support:

The regulatory body for animal research in NSW has been recognised for leading initiatives to support key aims of animal research regulations, especially those relating to animal welfare. These have included publishing evidence-based animal care guidelines, symposiums for Animal Ethics Committee members, and inspections of institutions conducting animal research.

Unfortunately, the scale of these initiatives has diminished noticeably in recent years. Several of the animal care guidelines are long overdue for revision, there have been no symposiums for some years and, of particular concern, an inspection backlog has presented significant challenges to some institutions in meeting the Code's requirements for independent external review.

It appears to me that this decline is the result of resourcing constraints because the regulatory personnel with whom I have contact continue to provide excellent service within the scope of their availabilities.

Recommendation 2: That resourcing for the NSW regulator be reviewed to ensure it retains the capacity to implement animal research regulations effectively and provide leadership in promoting best practice.

Transparency – Reporting animal research:

The first of 20 recommendations in the 1989 Senate Select Committee report on animal experimentation called for the publishing of "accurate and comprehensive" information on animal research and for analyses that would be "meaningful to the public, and…reduce the potential for misinterpretation"[6].

While some jurisdictions in Australia make commendable efforts to provide the public with data on animal research, no nationally consistent reporting system has yet been implemented and there are significant discrepancies in reporting between jurisdictions. This situation has been criticised both from within the animal research community and by animal protection advocates[7,8], and it falls short of the consistency delivered under reporting systems in the UK, the EU, Canada and New Zealand.

Notwithstanding the widespread concerns over animal research reporting in Australia, the challenges of ensuring that such reporting is genuinely informative must be acknowledged. Presenting data without appropriate context, for example, is susceptible to misinterpretation and is unlikely to provide the public with insight into the ethical harm-benefit analyses on which animal research is based.

Far greater opportunity to provide context exists within reporting requirements of the EU. Since 2010, EU member states have been required to publish non-technical summaries of animal research projects at the time of approval. This is in addition to data that must be reported at the conclusion of studies.

The benefits of Australia implementing a nationally consistent reporting system could extend beyond meeting expectations for transparency. For example, data accumulated over time could reveal trends that might inform animal welfare priorities and decisions on research expenditure.

Recommendation 3: That government regulators in Australia develop a nationally consistent process for reporting animal use data in a manner that is meaningful for the general public and can help inform animal welfare priorities and longer-term planning of research expenditure.

Transparency – Openness Agreements:

In 2014, the UK launched a public pledge to which institutions could become signatories to show commitment to greater transparency in animal research. Known as The Concordat on Animal Research in the UK, its signatories now include over 120 institutions spanning universities, funding bodies, scientific societies and government organisations.

Similar initiatives (now usually known as 'openness agreements') have since been launched in six European countries and New Zealand, and a major effort is underway to develop one in the USA.

---

[6] Parliament of the Commonwealth of Australia (1989) Animal Experimentation. Report by the Senate Select Committee on Animal Welfare Preface, page xv

[7] Bain, S. & Debono, K. (2013) Australian Scientific Animal Use Statistics: A History of Fragmentation, a Future of Hope. ANZCCART 2013 conference proceedings page 22.

[8] Merkes, M., & Buttrose, R. (2019). Increasing the Transparency of Animal Experimentation: An Australian Perspective. In Animal Experimentation: Working Towards a Paradigm Change (pp. 224-243). Brill.

Australia does not yet have an openness agreement, but a working group convened by ANZCCART has just completed public consultation on a draft version based on that of the UK. Submissions have yet to be reviewed but informal feedback points to general – if sometimes qualified – support within the scientific community.

A common reservation expressed by the Australian scientific community regarding an openness agreement is a perception that it will incur a significant increase in workload. In my opinion, this is unlikely to be the case, especially when it can be seen that some institutions are already taking steps that significantly improve openness, seemingly within existing resources.

> ***Recommendation 4:*** That all stakeholders be encouraged to promote greater openness in animal research so that public understanding and informed discourse can be enhanced.

(f) Overseas developments regarding the regulation and use of animals in medical research;

No comments.

(g) Any other related matters.

No comments.

END OF SUBMISSION