

RSPCA Australia and RSPCA WA Submission

INQUIRY INTO SUPPORT FOR HEALTH AND MEDICAL RESEARCH FUNDING AND PRIORITIES

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1. Introduction

The RSPCA welcomes this inquiry and the opportunity to provide comment. This is a joint submission on behalf of RSPCA Australia and RSPCA WA and it focuses on the following terms of reference:

#2 - How the state's health and medical research priorities are determined

#3 - The impact on specific types of research and areas of need.

This submission outlines the benefits for the WA government to strongly support a transition from animal-based research to that utilising and developing non-animal based methods.

2. Background

Western Australia is uniquely positioned in Australia's medical research community as hosting one of Australia's largest central repositories and suppliers of animals for biomedical research in Ozgene ARC. Ozgene ARC (previously the Animal Resource Centres – ARC) provide research groups with background strains and genetically modified mouse models for research into human disease.

Many of Western Australia's leading universities are engaged in biomedical research and therefore, consideration of the most effective and sustainable models to use in the future is crucial to the future success of Western Australia's research.

Given the home of Ozgene ARC is in WA and the prominent research profile of WA's universities, WA has a significant opportunity and responsibility to be an Australian leader in advancing the quality and translatability of medical research and to drive a transition to greater use of non-animal models of disease.

The replacement of animals in research is enshrined in *WA Animal Welfare Act 2002* (the Act) – Part 2 Use of Animals for Scientific Purposes:

S11. Condition on licences

(3) It is also a condition of each licence to use animals for scientific purposes that animals must not be used for scientific purposes unless they are used in accordance with the scientific use code.

Under the Act, the scientific use code is the term used for the prescribed code of practice for the care and use of animals for scientific purposes. This is the [Australian Code of Practice for the Care and Use of Animals for Scientific Purposes](#) (National Health and Medical Research Council, 2013).

The scientific use code contains governing principles which includes reference to replacing the use of animals in research with other methods as per 1.1(v):

1.1 Respect for animals must underpin all decisions and actions involving the care and use of animals for scientific purposes.

This respect is demonstrated by:

- (i) using animals only when it is justified
- (ii) supporting the wellbeing of the animals involved
- (iii) avoiding or minimising harm, including pain and distress, to those animals

- (iv) applying high standards of scientific integrity
- (v) applying Replacement, Reduction and Refinement (the 3Rs) at all stages of animal care and use:
 - (a) the Replacement of animals with other methods
 - (b) the Reduction in the number of animals used
 - (c) the Refinement of techniques used to minimise the adverse impact on animals
- (vi) knowing and accepting one's responsibilities.

Furthermore, the community and research funders expect research to be conducted in a responsible and ethical manner. An integral aspect of best practice includes the use of non-animal alternatives. This is highlighted by best practice guidelines in the use of animals for scientific purposes (NHMRC, 2017). High standards of research quality cannot be achieved without substantial and demonstrated commitment to the use of non-animal alternatives.

3. The case for non-animal alternatives

3.1 Questioning the efficacy of animal models

Biomedical research continues to rely on the use of animals. However, there are many reasons why this should discontinue in the future. Firstly, there are increasing reports of 'translational' failure from animal studies to human clinical trials and beyond, particularly in critical health areas such as cancer and dementia (Pound et al 2018; Mak et al 2014; Pistollato 2020; Atkins et al 2020). The review conducted by Marshall et al 2023 reports a translation failure rate of more than 92% for drugs from animal testing to human treatments with most of these due to unexpected toxicity or lack of efficacy. This review also looks at several examples of human diseases, namely Parkinson's disease, Alzheimer's disease, respiratory tract diseases and rheumatoid arthritis.

In terms of Alzheimer's Disease, which is reported to be the leading cause of death amongst all diseases, the failure rate for effective drug development remains very high at 99% (Cummings et al 2019).

3.2 Growing interest in use of non-animal alternatives

It is noted that the NHMRC has stated that funding can be applied for to assist with the development and validation of models that help achieve the 3Rs, which obviously includes funding to replace animals with non-animal alternatives (NHMRC 2024).

Furthermore, some pharmaceutical companies are showing keen interest in this area and investing heavily in non animal models. This transition should act as a driver to guide future research priorities as companies seek to ensure consistency in methodology of fundamental research conducted by research institutions. In addition, regulators in overseas countries are also adopting a considered approach to safety and efficacy testing in relation to the use of validated non-animal alternatives.

Ethical funding groups also seek to meet the requirements of those wishing to invest in activities and initiatives which meet ethical considerations.

3.3 Advances in the development of non-animal methods

It is important to note that there has and continues to be ground-breaking advances in the use of non-animal alternatives which offer the potential to be more reliable, less expensive and more efficient options to support biomedical research. Published studies promoting the use of non-animal alternatives for disease conditions including cancer and Alzheimer's disease are increasing (Jackson & Thomas 2017; Pistollato et al 2015).

A review by Vinken 2020 focuses on international projects that address the 3Rs concept in relation to toxicity testing, chemical risk assessment and disease modelling. The following are just a couple of examples included in this review.

TOXANOID: pharmacological safety testing in human adult stem cell-derived organoids

The TOXANOID project (2017-2018; <https://www.fabiadisconzi.com/open-h2020/projects/209165/index.html>)

CryoProtect: a new cryoprotectant formulation for the next generation of high-throughput screening toxicology tests

The CryoProtect project (2016-2017; <https://environment.leeds.ac.uk/see-re-search/dir-record/research-projects/788/cryo-protect-erc-proof-of-concept>)

The European Commission's Joint Research Centre also provides a comprehensive review of available and emerging non-animal alternatives, which can be found here; (<https://publications.jrc.ec.europa.eu/repository/search?query=advanced+non-animal>) and the Non-Animal Technologies (NAT) Database (<https://nat-database.org>).

3.4 Opportunities with Non-Animal Models

On a national front, a recent CSIRO report describes exciting opportunities for innovative and committed research bodies to invest and explore the possible benefits offered by non-animal alternatives, including potentially significant economic returns in the global market (CSIRO, 2023). Various models include in silico, in vitro (2D and 3D), in vitro organ on a chip and in vitro tissue explant (e.g from patient biopsies). It is also interesting to note that the driver for this review came from a report on Australia's preparedness for future pandemics which highlights the need to consider the potential role and benefits of non-animal alternatives for understanding cellular pathogenicity of new viruses and allowing faster testing of anti-viral treatments etc (CSIRO Futures, 2022).

The CSIRO report outlined the significant investment opportunities that could be created by Australia being an early investor in the development of non-animal model technologies. Western Australia should build on recent government funding to establish the [Western Australian Organoid Innovation Hub](#) at Curtin University, the time is right for Western Australia to embrace this opportunity to become a key player in this emerging technology. Initiatives in other jurisdictions also offer an insight into the potential benefits gained by investing in non-animal alternatives. For example, in 2023, the NSW government announced funding of \$4.5M for projects to reduce and/or replace the use of animals in research.

National Centre for 3Rs

Unfortunately, Australia has made limited progress in meaningful implementation of the 3Rs over recent decades. Australia is well behind many countries in the world in the regulation of and in particular, improvements in the use of animals for biomedical research.

[NORECOPA](#) is a leading organization based in Norway with a platform encouraging the application of the 3Rs. It provides a website with links to 3Rs resources and produces the PREPARE guidelines which are designed as a supplementary tool to the ARRIVE guidelines.

In the UK, a national centre known as the [NC3Rs](#) advocates for better science to identify, develop and use 3Rs technologies. It also provides funding schemes for innovation in the 3Rs.

In the US, the Centre for Alternatives for Animal Testing ([CAAT](#)) is coordinated by the highly regarded John Hopkins University.

We note that a number of opportunities were identified in the 2019 NHMRC Review of the 3Rs (NHMRC 2019). In particular, two key barriers identified in implementing the 3Rs were the challenge of comparability of data and insufficient funding. We also note that potential enablers of 3Rs implementation include improved collaboration between institutions, and improved willingness of investigators to share their methods. By establishing a national centre for 3Rs with funding opportunities, some of these key points could be addressed to improve uptake of the 3Rs.

The availability of such a funding model needs to be high profile and seen as a career opportunity for early and mid-career researchers. Too many researchers see diverting to the use of alternatives and replacements or refinements as a risk to their research profile and a blight on their publication record if they slow in publishing due to a change in research methodology. This culture must change to incentivize the use of alternatives.

However, despite the lack of a national 3Rs centre, two Australian universities have demonstrated a commitment to support the 3Rs. In 2019, the University of New South Wales established the [3Rs grant scheme](#) with current funded projects totaling \$500,000 including:

- A 3-dimensional bioengineered organ-cultured mammalian cornea to study pathophysiological mechanisms in a dish
- A chemically defined alternative to animal-derived materials
- Using patient derived organoids to treat endometrial cancer
- A soft artificial heart system to reproduce myocardial biomechanics.

Similarly in 2022, the University of Wollongong announced a [\\$5,000 grant](#) to promote animal welfare in small-scale projects or pilot studies. This type of institutional led change is welcomed. However, it highlights the lack of federal and state government initiatives available to support significant cultural change in the field of the 3Rs.

Despite significant investment in biomedical research each year, Australia has no centre for championing the 3Rs. Such a centre could be initiated by one of the leading universities or research institutes with dedicated individuals who would be supported to advance the adoption of the 3Rs in Australia. Whilst the progress of the University of Wollongong and UNSW are to be congratulated, a national approach to 3Rs schemes would be valuable and would do more to change the research culture within Australia.

The RSPCA urges that significant investment is committed as a priority to better encourage a cultural change from reliance on the use of animals, and to make animal alternatives and replacement initiatives more accessible to all researchers from early, mid and late career stages. In addition, National Health and Medical Research Council (NHMRC) funding should be closer tied to the principles of reproducibility and translatability of research outcomes and there should be strict requirements to meet these principles.

3.5 Benefits offered by using non-animal models

An area which is receiving increasing interest relates to the mental health of staff working in health and medical research (Ferreira et al 2022). A recent North American study by Randall et al 2021, reported that 69% of 154 laboratory personnel surveyed had feelings of compassion fatigue. A further study which surveyed over 800 personnel in Canada and the USA supports these findings as well as identifying high animal stress/pain and the use of physical euthanasia methods as important factors contributing to compassion fatigue (LaFollette et al 2020). Huge benefits in terms of safeguarding and improving the mental health of both laboratory animal technicians and researchers can be gained by replacing the use of animals where possible. Although theoretically, the need for laboratory animal technicians would decline with increasing use of non-animal alternatives, there would be scope for retraining to transition their role over time.

Replacing the use of animals with alternatives will allow funders and institutions to be better placed to meet their legal and moral obligations under the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (2013).

4. Promoting humane research

Whilst supporting the transition to increasing use of non-animal models it is also important to promote humane and ethical research practices in the meantime.

Central breeding facilities such as Ozgene ARC are important organisations that can help ensure consistency in breeding but should also have a significant responsibility in minimising overproduction of animals.

Australia is well behind many other countries in the world in terms of providing consistent, publicly available reports on animal usage for research purposes. Given the focus on production of research models in WA, it is crucial that WA are supportive of, and an integral component of any move towards creation of a national database on the use of animals and to track usage into the future.

5. Summary

It is clear that there are opportunities for Western Australia to actively explore and evaluate potential benefits of developing, promoting and using non-animal alternatives in health and medical research. This is based on many imperatives including being better prepared to respond quickly and effectively to future pandemics, being able to better meet community and funder expectations, capitalising potential financial gains and helping the research community to meet legal and ethical obligations.

In addition, current national and international trends strongly indicate that embracing development and implementation of non-animal alternatives in health and medical research is an expanding area.

However, it appears that to date, initiatives in this space are piecemeal and lacking an overarching strategy on a national level to maximise potential opportunities. Thus, Western Australia can help lead a national push thereby taking an active and pivotal role rather than a cautious and less involved approach as has happened to date. Being proactive requires strong leadership and effective

facilitation of key stakeholders. The WA Government is well placed to take on this role to support the research community, attract investment, and meet legal and ethical obligations to further advance health and medical research in this state.

6. Recommendations

1. The WA government convene a task force to oversee a review of the current status of the use of non-animal alternatives in health and medical research in Western Australia as a priority.

This would involve analysing current trends and future needs to identify gaps and opportunities.

2. The WA government to establish a steering committee to oversee recommendations accepted by government from the review as per Recommendation 1.
3. The WA government to take a leadership role in advocating for funding to establish a national 3Rs centre with a strong focus on developing and promoting non-animal alternatives in health and medical research.
4. The WA government to support the establishment of a national statistics database on the use of animals to demonstrate progress in the uptake of non-animal alternatives.
5. The WA government to establish an advisory group to support WA researchers and institutions to use non-animal alternatives in health and medical research as well as provide advice on sourcing relevant eligible funding.

This would involve establishing an accessible database, facilitating research staff training, advocating for a specialist advisory role at each institution, encouraging and recognising scientific publication of relevant studies, transitioning roles for researchers and laboratory animal technicians etc.

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