Submission No 222

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

Organisation: RSPCA

Date Received: 31 March 2022

RSPCA AUSTRALIA AND RSPCA NSW

JOINT SUBMISSION

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

31st March 2022

The RSPCA commends the NSW Government for conducting a review in this important area and we appreciate the opportunity to provide a submission to this inquiry into the use of primates and other animals in medical research in New South Wales.

The RSPCA would be happy to provide further context and discussion on the points made in this document should there be opportunity to meet with the committee.

Introduction

The RSPCA is opposed to the use of animals for research where there is injury, pain or suffering that cannot be prevented or adequately controlled and if the use of animals is not clearly justified. The RSPCA is also opposed to the use of animals which involves unnecessary repetition, the production or use of more animals than required and where there is a lack of scientific robustness of biomedical research. We support the use of non-animal alternatives and believe that greater opportunity and resources must be provided to allow for non-animal alternatives in Australia to be more accessible, considered and utilized by research groups.

The RSPCA is particularly concerned about the use of 'high impact' experimental animal models where there are inherent and insurmountable welfare risks, or where the tests or procedures have questionable scientific validity. The RSPCA is also opposed to the use of non-human primates for laboratory-based research due to the extreme difficulty in meeting their physical and behavioural needs in a research environment.

The RSPCA acknowledges that in Australia, all states and territories have adopted the **Australian code for the care and use of animals for scientific purposes 8th edition**[i] ("The Code") in relevant legislation. This provides strong guidance on the responsibilities and requirements around approving animal-based research, however, there is still more that can be achieved to replace, reduce and improve the welfare outcomes for animals used for research.

We explain our reasoning further under each section of the terms of reference below.

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

Animal use statistics

It is difficult to clearly comment on the effectiveness of the current medical research being conducted with the use of animals due to the lack of transparency and reporting of animal use statistics. It is expected that animal use statistics are to be released within six months of the end of each calendar year, however, the NSW 2019 report[ii] is the most recent publicly available source of data. In addition, there is limited publicly available and accessible information regarding the outcomes of animal-based research and its effectiveness. Published papers provide a limited insight into a subsection of research outcomes that are selected by researchers for publication and sharing. Not all projects end in successful publication, and it is impossible to gather the information in a meaningful way to determine the number of animals used in NSW or Australia and determine the outcome of the research and the impact on the animal(s). This needs to be addressed to improve the transparency of and justification of animal based medical research activities.

Whilst there are sometimes media reports of successful biomedical research findings, there are no publicly available data on the number of animals used to achieve these results, nor the type of procedures they are exposed to during the research. Thus, the emphasis on the human benefits is prioritized above the impacts on the animals with no ability to quantify the cost to the animals to achieve these benefits. As a key stakeholder, the community has a right to know what happens to these animals.

Recommendation 1: The animal use statistics should be made publicly available within six months of the end of the preceding calendar year and include information on the number of animals used for medical research, their species and the relative impact on animal welfare of each study.

Improved transparency

RSPCA recommends that all animal studies should be pre-registered on a central database, of which there are already many available, to ensure full reporting of study details and to encourage reporting of negative results to ensure this information becomes available at the end of the study[iii]. Most registries have an option to place an embargo on the pre-registered study for up to five years, after which time the details of the study become automatically publicly accessible[iv].

There is currently little incentive in Australia for researchers to publish negative findings. This leads to the risk of replication of studies by various researchers which could be avoided if there was a requirement to publish negative findings and make this data widely available. Without this requirement, there is likely to be publication bias[v].

Scientific rigour and accountability

To improve both the scientific validity and transparency of biomedical research in Australia, in addition to pre-registration of biomedical research planning, adherence to the ARRIVE 2.0 Guidelines, which were published in 2020[vi] should also be mandatory

The ARRIVE 2.0 Guidelines provide a clear outline for the reportable features of any biomedical research program to ensure reproducibility can be achieved and encourage researchers to review common factors that can affect research outcomes. Whilst many journals have agreed to require authors to adopt these guidelines there has been limited effectiveness in leading to widespread uptake to date[vi]. Their use should be linked to the provision of and reporting on grant funding and other modes of funding including institutional funding provided and philanthropic donations. The implementation of these processes should be done such that they can be referred to in any animal ethics application to allow the ethical review process to include confirmation of pre-registration and/or adherence to the ARRIVE 2.0 Guidelines.

Recommendation 2: All animal-based research should be pre-registered with specific experimental design parameters recorded including justification for the statistical methods used, to ensure robustness of results and transparency.

Recommendation 3: There should be mechanisms in place to encourage the publication of negative findings.

Recommendation 4: All animal-based research should be conducted and published in accordance with the ARRIVE 2.0 Guidelines or a similar standard of reporting to ensure transparency and reproducibility of findings.

Risks to human health

There are various risks to human health when using animals for research purposes. These include the inherent risk to those working directly with the animals due to injuries (e.g., bites, scratches etc) or disease but there may also be a risk to public health due to potential biosecurity breaches arising from working with highly transmissable and poorly understood infectious agents.

Another important risk is that to the mental wellbeing of laboratory animal workers, where it has been reported in the literature that over two thirds of laboratory workers in one study reported experiencing compassion fatigue[vii]. Furthermore, adverse animal welfare may result from poor containment practices within laboratories using infectious agents which may be transferred to other onsite animals or cause increased risk of zoonotic transfer of pathogens. For this reason, the RSPCA supports competency-based assessment of all staff working in research laboratories to ensure they understand the requirements and consequences to personal and public health of working in high risk laboratory areas.

Recommendation 5: All staff working in animal research laboratories must receive theory and practical training and demonstrate competency in all procedures and personal and public safety aspects of working with research animals prior to working unsupervised.

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

There is limited information pertaining to the total amount of funding that is provided from either federal or state governments for biomedical research.

There is significant funding that goes into providing infrastructure for research practices including the facilities used to breed and supply animals for biomedical research. Whilst the use of animals for medical research may be justified in some circumstance, the RSPCA supports the provision of adequate funding and resources to ensure facilities operate to the highest standards of animal care and welfare and of research quality.

Recommendation 6: Whilst the use of animals for medical research is still necessary and their need is adequately justified, animal research facilities must be well resourced to provide the highest standards of animal care.

C. The availability, effectiveness and funding for alternative approaches to animal research methods and technologies, and the ability of researchers to meet the 3Rs of Replacement, Reduction and Refinement.

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[viii] 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[ix] 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)[x] is coordinated by the highly regarded John Hopkins University.

In Australia, two universities have demonstrated a commitment to support the 3Rs. In 2021, it was announced by the University of New South Wales that they would provide up to $250,000 in grant funds for supporting science-based projects with a primary goal of meeting the 3Rs[xi]. The University of Wollongong also announced a $5,000 grant to promote animal welfare in small-scale projects or pilot studies[xii]. 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.

We note that a number of opportunities were identified in the 2019 NHMRC Review of the 3Rs[xiii]. 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.

Recommendation 7: A national centre, funded by the Federal Government, supporting research in the 3Rs and supporting researchers who wish to perform pilot studies to validate refinements and non-animal alternatives, should be established to reduce reliance on animal-based research in Australia.

Recommendation 8: Funding opportunities should be targeted at early to mid-career researchers with a focus on improving the perception of investing time and resourcing to 3Rs initiatives to encourage 3Rs uptake.

Animal ethics review

The RSPCA acknowledges that it can be difficult to assess discovery-based research without the use of whole animal models. However, this is too often used as a fall-back argument without provision of sufficient evidence for the reasoning and adequate research being undertaken to ensure there are no alternatives.

Animal Ethics Committees (AEC) also need to be provided with greater support, training and resources to be able to reject projects that use animals where there is not significant reasoning or evidence provided to discount the use of non-animal alternatives.

Recommendation 9: Training of AEC members should include how to assess the opportunity for non-animal alternatives and AECs should be further encouraged to require researchers to further assess alternatives through the institution providing of more resources to support this.

Recommendation 10: Institutions should be encouraged, wherever possible, to have access to a person with knowledge in non-animal alternatives that can provide advice to researchers, students and AECs. It is expected that with further resourcing in the 3Rs, more experts will become available into the future.

D. The ethical and animal welfare issues surrounding the importing, breeding and use of animals in medical research

Breeding and importation of animals for research

In relation to the breeding of animals for research, the RSPCA believes that animals should only be sourced from licensed breeding or animal supply establishments, in accordance with current NSW law. These facilities must adhere to high mandatory welfare standards and that there are stringent controls to ensure that overbreeding does not occur.

Where animal breeding is undertaken within institutions this must be well managed by highly trained and competent staff. The risk of overbreeding is significant with students often tasked with managing their own breeding colonies with minimal training and oversight in doing so. Well run facilities have their own breeding manager who is tasked with ensuring overbreeding does not occur and that best practice is undertaken to avoid wastage of animals. Wastage occurs when animals are bred in numbers in excess of need, and then not utilized but killed and disposed. To prevent wastage, institutions must be required to track and report breeding and usage statistics relevant to individual strains of animals and the reasons for any wastage.

Recommendation 11: Whilst the use of animals for research purposes continues, stringent controls must be maintained to ensure overbreeding does not occur and the production of animals for research purposes meets the highest welfare standards.

Recommendation 12: Where animals are bred for research, procedures must be implemented to prevent overbreeding and unjustified killing of animals.

Recommendation 13: The use of animals for breeding must be reported accurately to ensure transparency of animal usage and wastage.

Australia faces unique challenges given the biosecurity restrictions on the import of reproductive material and live animals. For example, the current restrictions for importation of rodent sperm or embryos, require importers to verify that animals have been tested for Hantavirus prior to being killed for collection of reproductive material. This is not a common practice overseas as there haven't been any reports of infections in rodents or humans originating in a medical research facility. Therefore, sperm and embryos are not automatically approved for import and the process to import them can be complicated. As a result, to efficiently meet Australian Government requirements, most institutions will import live animals rather than sperm or embryos. The import of live animals leads to greater impact on individual animal welfare and should be avoided where possible.[xiv]

Recommendation 14: The Australian Government should review the justification for the restrictions on import of sperm and embryos of laboratory animals (in particular rodents), with the view to result in less reliance on importation of live animals.

Welfare considerations

Animals in a research setting are generally maintained in controlled and contained environments. Most species used, including dogs, cats, rodents and primates, are social animals and their needs and natural behaviours are best supported when housed with others of the same species. In many circumstances, research requires animals to be isolated which can restrict the opportunities for them to engage in positive natural behaviours[xv]. Other aspects of the research environment restrict natural behaviour including the opportunity to forage, exercise and meet other highly motivated biological needs which can impact on their ability to live a good life. It has also been proven that maintaining good animal welfare leads to better quality scientific outcomes[xvi]

In NSW it is current practice by the regulator to require, as a condition of holding a research authority, the compliance with a series of available guidelines, such as for the housing of specific species[xvii]. Although the guidelines are now given mandatory effect by way of license conditions, to create regulatory certainty, the practice guidelines should be given force by being prescribed as a code or standard by the regulation. Many of these guidelines have not been reviewed in more than 20 years. They should be reviewed in the process of being prescribed.

Recommendation 15: Whilst the use of animals for medical research continues, species specific care and welfare standards must be mandated to help ensure appropriate husbandry and environmental conditions to meet physical and behavioural needs to facilitate a good quality of life.

Primates stand out among other taxa for their flexibility in how they respond to the world around them and their highly sophisticated and complex social and cognitive capacities. Therefore, meeting their needs in the research setting with the consequent spatial and social restrictions and limitations on choice and control is inevitably fraught. Therefore, it is difficult to ensure that these animals in a research setting can experience a good quality of life. It is on this basis that the RSPCA opposes the use of primates for research. However, where the use of primates for research continues, this should be rigorously challenged and there must be a significant burden of proof on the researcher to justify their use for any medical research purpose.

Recommendation 16: Introduce a mandatory requirement that researchers and institutions demonstrate that animals in their care experience a good quality of life. This should be specifically assessed using welfare assessment tools and independent audits.

Recommendation 17: Prohibit non-human primates being imported to or exported from Australia for breeding or use in research.

Animal welfare officers and veterinarians are a critical component of the management and assessment of animal welfare. They should be independent of influence of research and be able to assess individual animals' welfare and provide advice on the welfare risks of proposed projects.

Recommendation 18: All institutions must have a suitably qualified and experienced AWO to monitor the welfare of the animals in terms of general care as well as experimental procedures

The breeding and use of non-human primates for medical research continues in NSW. Whilst there are specific guidelines for the use of non-human primates for research[xviii], there is no specific authority overseeing the need for improvements and the availability of alternatives in non-human primate research. The challenges associated with the breeding, care and use of baboons warrants a specific authority that oversees their management and looks to the future to plan for a phase out of the use of non-human primates.

Recommendation 19: Establish a national advisory authority that reviews all breeding and research projects involving non-human primates, conducts inspections and develops mandatory standards for the care and management of non-human primates. This body should also have responsibility to monitor and develop a pathway to phase out breeding and use of non-human primates.

Prohibiting certain unjustifiable, high impact research activities

Two key experimental models have attracted significant attention over recent years as their efficacy is questionable and they are known to cause severe distress to animals. This includes the use of forced swim tests and inhalational or smoke exposure studies.

The forced swim test has historically been used in a number of research protocols related to neurobiology and drug studies including to evaluate anti-depressants for humans[xix]. This test involves placing a rodent in a transparent cylinder of water where they will swim and/or attempt to climb the walls of the cylinder for a period of time before becoming immobile. Animals who spend more time floating (i.e., less time swimming) are considered to be more 'depressed'. In the first

instance, depression in humans is a very complex condition which is influenced by many diverse factors including those associated with lifestyle. On a scientific basis, it is difficult to justify the relevance of exposing 'anti-depressant' drug treated and untreated mice to a single stressor in order to evaluate the potential effect on humans. Furthermore, despite the test being developed in 1978 and used over many decades, acknowledgement of its limitations regarding mouse response were reported in 2013 by Bogdanova et al[xx]. It has been proven that these tests cause a significant stress response[xxi]. Factors identified as influencing animal behaviours, and therefore confounding these studies, included biological factors (strain, age, body weight, gender), individual animal experiences (handling, social isolation, enrichment, food manipulations) as well as schedule and routes of treatment etc. Also, interobserver variability has been noted as a significant issue in relation to correct identification of bona fide mobility[xxii].

We also know that stress from confinement and feelings of panic from asphyxiation are likely outcomes for rodents being exposed to smoking and inhalational studies, in particular nose only chambers. In addition, the use of nose-only smoke exposure chambers leads to isolation from cage mates.

There are clear inherent and insurmountable animal welfare risks to the use of these tests.

Recommendation 20: The high impact studies with questionable scientific validity be reviewed to consider the justification for their continued use.

Staff training and competency assessment

Training of individuals working in the biomedical research sector is pivotal to the welfare of animals and the quality of research outcomes. All staff ranging from junior wash up and animal care staff through to senior research academics must receive regular training which must be competency based and reflective of current international best practices. This training must include animal care, recognition of signs of good health and behaviour indicating good welfare, identification of signs of animal pain and distress/illness, appropriate scientific methods, genetic management of breeding colonies and animal welfare and ethical decision making in the use of animals. Standardisation of training requirements and competency assessment across NSW and indeed, Australia, would improve the outcomes and expectations between facilities and remove any variability in the standards of ethical and high welfare practices[xxiii].

RSPCA notes the positive move towards consistent national training by the development of the Australian and New Zealand Council for the Care of Animals used in Research and Teaching (ANZCCART) ComPass course which provides modules for research students, experienced researchers, animal care staff and veterinarians in the theoretical aspects of working with animals in research. However, we feel additional resourcing is needed to ensure truly consistent national training and ensure competency training in a practical sense is developed and used by all institutions.

It is essential that institutions record training and competency assessment of all staff to demonstrate that procedures are being performed to best practice standards and to help identify deficiencies.

Recommendation 21: All staff working in animal research laboratories must receive theory and practical training and demonstrate competency in all procedures prior to working unsupervised.

Recommendation 22: All institutions must maintain a comprehensive skills competency register for all staff undertaking general husbandry and experimental procedures.

Recommendation 23: National training and competency assessment framework be established for all husbandry and experimental procedures and that this is complied with by all institutions and individuals conducting research.

Ethically, the use of animals for medical research is often justified on a cost benefit analysis*. Is there enough evidence that the use of the animals will result in a significant enough benefit to humans to justify the extent of any harm caused?* In this utilitarian perspective, animals are to be considered as sentient beings and the impact on the animal(s) must be considered relative to the proposed benefit. It is this proposed benefit that needs more robust argument and a stronger scientific footing than is often provided. Research groups may claim to be trying to 'cure cancer' or 'identify mechanisms of disease' without providing further detail to define exactly how the use of the animal(s) in this perspective will help achieve the stated goal and identify the potential risks of using animals for human disease research. This can be especially true in the case of discovery-based research whereby the basic mechanisms of biology are studied to create opportunities for further research pathways.

There is increasing evidence that animal models often do not reflect human disease and for this reason, greater ethical assessment of all animal research is necessary[xxiv].

Recommendation 24: The Code should include an obligation for the researcher to satisfactorily address the question of translatability of research findings.

Where the impact to animals is higher, the benefits and scientific validity deserve greater interrogation. Institutions should be required to openly report where high impact (significant negative effects on animals) research is undertaken. There is a lack of standardization in Australia as to the definition of high impact or high-risk research. There is plenty of ethical modelling that has been done that could help provide a framework for this. The EU and UK have a framework for severity assessment and reporting which not only assists with the assessment of expected severity but also requires reporting of actual severity occurring during and after the experiment[xxv].

Ethical decision making is generally considered only to be the remit of AECs, but this is often a difficult process with individuals varying in their knowledge and understanding of research and biology. Including additional membership categories to bring expertise on statistical modelling and on non-animal alternatives would greatly enhance the decision-making process. However, currently this would prove difficult in Australia as there are limited individuals with this expertise due to years of lack of funding and opportunities to specialize in these fields locally. A long-term strategy could be to improve resourcing and motivation to work in these areas to expand the number of subject matter experts to allow for this to be implemented in the future.

Recommendation 25: All AECs should have access to specialist advice on animal based statistical modelling practices to minimize numbers of animals used and to ensure results that are published are valid

Recommendation 26: Australia, through the NHMRC, should review the classification of animal studies to ensure consistency across Australia and ensure that high impact studies are appropriately interrogated and reviewed for opportunities to reduce animal suffering and reduce animal usage.

Rehoming

The Code supports the principle of rehoming research animals that are no longer required for research purposes and are suitable for rehoming. The RSPCA supports this prospect on the basis that research institutions can ensure appropriate controls are in place to support a 'life worth living' for the animals once rehomed. We acknowledge that some species or individual animals may not be suitable for rehoming and should be identified as such to minimize any risk to animal welfare.

Recommendation 27: Rehoming of animals after their research life must be considered by research institutions, taking into account whether the animal will have an opportunity to experience a 'life worth living' once rehomed.

E. The adequacy of the current regulatory regime regarding the use of animals in medical research, particularly in relation to transparency and accountability

The Code does state that institutions must:

> *"...consider publishing a summary of the external review report (e.g. as part of an institutional annual report or website) and making the summary report available to the relevant regulatory authority and funding bodies of the institution (see Clause 2.1.10)."*

However, this is not commonly undertaken and there is no other motivation to do so in the Australian environment.

Within NSW there is reporting required of the number of animals used however there is variability in the reporting of breeding vs experimental animals and the interpretation of the impact of the research. Further guidance and a standardisation of these interpretations across Australia would improve transparency and the public's understanding of how animals are used in research.

We appreciate the current push from ANZCCART to set up an openness agreement[xxvi] process amongst Australian institutions, however, there is concern that uptake may be slow and limited by the lack of mandated requirements to acknowledge animal-based research within institutions.

As most institutions are publicly funded, there must be transparency to ensure that the high standards set by The Code are met and the concept of continual improvement should underpin all aspects of the use of animals to benefit human life.

Recommendation 28: Institutions should be proactive and support the animal research openness agreement being developed by ANZCCART.

Peer review

The scientific quality and validity of research projects is sometimes, but not always, peer reviewed prior to proceeding. There is the possibility for researchers to use funds from sources outside the

grants system on personal projects and points of interest without significant assessment of the scientific rigor of such projects. Whilst the AEC system is established to review the welfare implications and assess projects against "The Code," there is often not sufficient academic knowledge in the field of expertise required to perform a review of the scientific methodology and statistical methods proposed for any particular project.

Recommendation 29: Research that has not been peer reviewed prior to submission to an AEC must be identified as such and should go through a peer review process managed by the institution.

Committee Review

Independent reviews of AECs can currently be performed between every 3-4 years. This will vary depending on the local legislation requirements, however in The Code, the mandatory period is every 4 years. This is a significant amount of time between reviews and could lead to delays in implementation of recommendations and poor compliance over long periods of time.

Recommendation 30: It should be a mandatory requirement that an independent audit is conducted for all research and teaching institutions at least every three years. The review report must be published to allow transparency and accountability.

Recommendation 31: More unannounced inspections should be performed by the regulator to monitor compliance to The Code and other relevant guidelines.

F. Overseas developments regarding the regulation and use of animals in medical research

In the UK there is a standardized assessment method to determine if the impact on animals of the research is mild, moderate or severe. This includes a clear manner for assessing cumulative impact which may result in multiple mild impact procedures being classed as moderate or severe due to the ongoing compromise to animal welfare. This has allowed for a significant focus on minimizing severe suffering to become a project whereby Animal Welfare Ethical Review Body (AWERBS -the UK equivalent of Australian Animal Ethics Committees (AECs) are better trained to identify high impact studies and determine if there are improvements that can be made to minimize severe suffering and cumulative impacts.

Recommendation 32: There should be greater standardization across Australia on the assessment of the potential impact of animal studies on the welfare of individual and groups of animals. This should include using a 5 domains model to provide guidance as to potential one off impacts and cumulative impact experiences taking into consideration the training and competency of the individual(s) undertaking the procedures.

Recommendation 33: High impact or projects that are likely to lead to severe suffering must be reviewed with the intention of reducing suffering and/or discovering and validating possible alternatives. Funding must be made available to dedicate appropriate resources to address these issues for these types of projects.

G. Any other related matters.

The Code was published in 2013 and should now be considered for review. Whilst the last revision was helpful in clarifying what obligations and responsibilities lay with which parties, further development of mandatory requirements would be beneficial to improving transparency and research quality.

Recommendation 34: The Code is reviewed and updated to address questions of research quality and transparency of animal-based research.

At present, the animal ethics process within institutions is too often seen as mandatory 'red tape' and not as a collaborative process to improve research quality and animal welfare outcomes. This is left to the individuals employed at each institution to develop relationships to ensure a cohesive effort for continual improvement. It should be made clear that improvement is mandatory and that just because a protocol was approved three years prior (the maximum approval period that can be provided in most jurisdictions), this does not mean that there will be continuing approval for the same practices. Some advancement in the 3Rs or research methodology would be expected over that time.

It is evident that investment in early and mid-career researchers is necessary to gather momentum and culture change. It is difficult to change an established research career without significant funding and provision of time to perform validity assessments of non-animal alternatives etc. However, by encouraging and rewarding such parallel and replacement activities in less established research groups, this would contribute to a culture change over time. This will also avoid early career academics from becoming indoctrinated in outdated and no longer appropriate methodologies that should be discontinued due to poor research and animal welfare outcomes.

[i] NHMRC (2013) Australian code for the care and use of animals for scientific purposes 8th edition
[ii] NSW Government Department of Primary Industries NSW 2019 Animal Use in Research Statistics
[iii] Bert B, Heinl C, Chmielewska J, et al. Refining animal research: The Animal Study Registry. *PLoS Biol*. 2019;17(10):e3000463. Published 2019 Oct 15. doi:10.1371/journal.pbio.3000463
[iv] German Centre for the Protection of Laboratory Animals. Animal Study Registry [Accessed 18th March 2022]
[v] Dwan K, Gamble C, Williamson PR, Kirkham JJ; Reporting Bias Group (2013) Systematic review of the empirical evidence of study publication bias and outcome reporting bias – an updated review. PLos One. 5;8(7):e66844
[vi] Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. (2020) The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLoS Biol 18(7): e3000410. https://doi.org/10.1371/journal.pbio.3000410
[vii] Randall MS, Moody CM, Turner PV. Mental Wellbeing in Laboratory Animal Professionals: A Cross-Sectional Study of Compassion Fatigue, Contributing Factors, and Coping Mechanisms. J Am Assoc Lab Anim Sci. 2021 Jan 1;60(1):54-63. doi: 10.30802/AALAS-JAALAS-20-000039. Epub 2020 Oct 7. PMID: 33028460; PMCID: PMC7831355.
[viii] NORECOPA Norecopa [Accessed 18th March 2022
[ix] National Centre for the Replacement Refinement & Reduction of Animals in Research NC3Rs [Accessed 18th March 2022
[x] John Hopkins Bloomberg School of Public Health Center for Alternatives to Animal Testing - Johns Hopkins Bloomberg School of Public Health (jhsph.edu) [Accessed 18th March 2022]
[xi] UNSW (2021) UNSW 3Rs Grant Scheme UNSW 3Rs Grant Scheme | UNSW Research [Accessed 18th March 2022]
[xii] UOW (2022) https://documents.uow.edu.au/content/groups/public/@web/@raid/documents/doc/uow272035.pdf [Accessed 18th March 2022]
[xiii] NHMRC (2019) Information paper: The implementation of the 3Rs in Australia
[xiv] National Research Council (US) Committee on Guidelines for the Humane Transportation of Laboratory Animals. Guidelines for the Humane Transportation of Research Animals. Washington (DC): National Academies Press (US); 2006. 3, Good Practices in the Transportation of Research Animals. Available from: https://www.ncbi.nlm.nih.gov/books/NBK19639/
[xv] Jennings M, Prescott MJ. Refinements in husbandry, care and common procedures for non-human primates: Ninth report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement. Laboratory Animals. 2009;43(1_suppl):1-47. doi:10.1258/la.2008.007143
[xvi] Prescott MJ, Lidster K. Improving quality of science through better animal welfare: the NC3Rs strategy. Lab Anim (NY). 2017 Mar 22;46(4):152-156. doi: 10.1038/laban.1217. PMID: 28328893.
[xvii] NSW Agriculture (1999) Guidelines for the Care and Housing of Dogs in Scientific Institutions Animal care | Animal Ethics Infolink [Accessed 25th March 2022]
[xviii] NHMRC (2016) Principles and guidelines for the care and use of non-human primates for scientific purposes. [Accessed 31st March 2022]
[xix] Molendijk ML, de Kloet ER. Immobility in the forced swim test is adaptive and does not reflect depression. Psychoneuroendocrinology. 2015 Dec;62:389-91. doi: 10.1016/j.psyneuen.2015.08.028. Epub 2015 Sep 2. PMID: 26386543.
[xx] Bogdanova OV, Kanekar S, D'Anci KE, Renshaw PF. Factors influencing behavior in the forced swim test. Physiol Behav. 2013 Jun 13;118:227-39. doi: 10.1016/j.physbeh.2013.05.012. Epub 2013 May 14. PMID: 23685235; PMCID: PMC5609482.
[xxi] Benedict CR, Fillenz M, Stanford C. Noradrenaline release in rats during prolonged cold-stress and repeated swim-stress. Br J Pharmacol. 1979;66(4):521-524. doi:10.1111/j.1476-5381.1979.tb13689.x
[xxii] Can A, Dao DT, Arad M, Terrillion CE, Piantadosi SC, Gould TD. The mouse forced swim test. J Vis Exp. 2012;(59):e3638. Published 2012 Jan 29. doi:10.3791/3638
[xxiii] Collins T, Cornish A, Hood J, Degeling C, Fisher AD, Freire R, Hazel SJ, Johnson J, Lloyd JKF, Phillips CJ, Tzioumis V, McGreevy PD. Importance of Welfare and Ethics Competence Regarding Animals Kept for Scientific Purposes to Veterinary Students in Australia and New Zealand. Vet Sci. 2018 Jul 14;5(3):66. doi: 10.3390/vetsci5030066. PMID: 30011903; PMCID: PMC6163741.

[xxiv] N. Bryce Robinson, Katherine Krieger, Faiza M. Khan, William Huffman, Michelle Chang, Ajita Naik, Ruan Yongle, Irbaz Hameed, Karl Krieger, Leonard N. Girardi, Mario Gaudino. (2019) The current state of animal models in research: A review, International Journal of Surgery. 72:9-13) https://doi.org/10.1016/j.ijsu.2019.10.015.

[xxv] European Commission. Caring for animals aiming for better science. Directive 2010/63/EU on protection of animals used for scientific purposes. Animals used for scientific purposes - Environment - European Commission (europa.eu) [Accessed 18th March 2022]

[xxvi] ANZCCART. Public Consultation for an Australian Openness Agreement on Animal Research Public Consultation for an Australian Openness Agreement on Animal Research | ANZCCART | University of Adelaide [Accessed 18th March 2022]