Submission No 212

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

Organisation: Western Sydney University

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WESTERN SYDNEY
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Office of the Deputy Vice-Chancellor and Vice-President (Research, Enterprise and International)

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30 March 2022

The Hon. Gregory Donnelly, BEc MIR MLC
Chair, Portfolio Committee No. 2 – Health
NSW Parliament House
SYDNEY NSW 2000

Dear Mr Donnelly,

On behalf of Western Sydney University (WSU), we thank you for the opportunity to provide a submission to the *Inquiry into the Use of Primates and Other Animals in Medical Research in New South Wales*.

Research involving animals, especially for medical research purposes is a cost-intensive and long-term endeavour. WSU believes in the importance of ensuring animal research is upheld at a high standard and adhering to the principles of the 3Rs (replacement, reduction and refinement) and the *Australian Code for the Care and Use of Animals for Scientific Purposes (2013; the Code)*. The *Code*, together with the *Animal Research Act (the Act - 1985, NSW)*, provides a robust regulatory framework to oversee and authorise animal research, and to prevent the misuse of animals in NSW. The current legal framework as set out by the *Act* guarantees the assessment of the benefits, costs, and scientific validity of animal research in line with what is done internationally. The assessment includes perspectives from veterinary experts, animal welfare representatives, and members from the wider community. A cooperative approach between investigators, animal facility management, the Animal Ethics Committee (AEC), and the University can also support the integrity of the research conducted.

Please find our responses to the issues raised in 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 research allows to study aspects of human diseases in a highly controlled and standardised environment, including the evaluation of disease risk factors (genes or environmental factors) as well as the testing of new therapeutic compounds. Currently, medical scientists at WSU focus on research into Alzheimer's disease, muscular dystrophy, epilepsy diabetes, cancer, and cardiovascular diseases. Please find examples of advancements made in our understanding and treatment of human diseases in the following:

- Animal models have increased our understanding of how specific proteins have roles in cancer development, regulation of RNA metabolism and immunity. These insights have wide reaching implications that may improve treatments for cancer patients[1].
- Animal research has allowed researchers to assess the tolerability (i.e. side effect profile) of novel brain cancer treatments that are more effective than the current therapeutic approach in Australia (i.e. relying on neurosurgery, followed by radiotherapy and treatment with temozolomide).

[1] Lai et al., 2021. Regulation of RNA degradation pathways during the LPS response in macrophages. *Journal of Leukocyte Biology*. 109(3):593-603.

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- Mouse research has provided first evidence for beneficial effects of medicinal cannabis in dementia therapy. These results have initiated a first human trial into the therapeutic value of cannabis constituents for patients with mild cognitive impairments[2].

There is no/very low risk to public health as all animal work (including with genetically modified organisms (GMOs) is regulated and contained according to legislative requirements. Facilities are inspected regularly by both animal ethics as well as biosafety officers to ensure compliance with *the Code* and the Office of the Gene Technology Regulator (OGTR).

(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;

The majority of costs involved in medical research (e.g., staff salaries, housing costs, laboratory consumables) is covered by grant funding obtained competitively from government bodies (e.g., *National Health and Medical Research Council*) or philanthropic foundations. Sometimes industry partners fund particular projects as well (within a rigorous Conflict of Interest framework). The scientific rationale of such grant proposals is assessed by independent expert panels, ensuring the scientific validity of proposed projects. WSU provides the facilities in which the animals are housed and tested and employs full-time animal technicians to care for and monitor the health of research animals. As an internal safeguard and in line with the *Code*, review and approval of animal research projects is conducted by the AEC prior to commencing work. Researchers provide annual updates to the AEC and notify the AEC of any adverse events that may occur. A WSU Animal Welfare Officer and a WSU Animal Ethics Officer are also employed to support animal researchers and the AEC, and to further ensure that animal research projects are conducted in line with the *Code*.

(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 a lack of funding opportunities in NSW and Australia to support research into the 3Rs. In other countries (such as the UK), national bodies have been established to provide funding into this type of research to encourage researchers to adopt a more proactive and innovative approach to directly address the 3Rs (e.g. the National Centre for the Replacement, Refinement and Reduction [NC3Rs] provide project grants to support the development of new 3Rs approaches and technologies). Nonetheless, WSU researchers have directly addressed the 3R's concept in a number of ways, examples are listed in the following:

- Replacement of animals through the use of audio-visual material, training models (e.g. latex rat for injection of substances), and use of plant tissue instead of animal tissue for enzymatic assays.
- Research into the effects of newly developed housing systems on laboratory mice suggest using these cage systems more selectively than in the recent past as they can change experimental test outcomes. These insights are nowadays covered by animal ethics training modules at several universities including WSU and UNSW[3].
- WSU researchers developed a device called the *Braincubator* to prolong the life/usability of neuronal tissue for electrophysiology and imaging. This device reduces the overall number of animals needed

[2] Reviewed in Karl et al., 2017. The therapeutic potential of the phytocannabinoid cannabidiol for Alzheimer's disease. *Behavioural Pharmacology* 28(2 and 3 – Special Issue). 142-60.
[3] Logge et al., 2014. Do individually ventilated cage systems (IVC) generate a problem for genetic mouse model research? *Genes, Brain and Behavior* 13(7). 713-20.

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(up to half the required animals) to address research questions, for example in the field of motor neuron disease therapy[4].

- Refinement has been achieved by replacing a stressful spatial memory task (where mice are required to swim to find a submerged platform) with a dry-land alternative that is more relevant to the species and dementia research. This task that has now been adopted by other Australian Universities[5].

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

WSU acknowledges the need for stringent management of importing and breeding of animals and to make sure no excess animals are produced. The breeding and importation of mice needs to be approved by the WSU AEC. At all times, certified animal resource companies and courier services are employed. Furthermore, WSU provides enriched laboratory housing conditions whenever possible, and the health of laboratory animals held at WSU is managed and controlled for by the use of "sentinel" mice (sentinels are non-experimental mice that are exposed to the same housing conditions as experimental mice for a set period of time, then sent to a diagnostic laboratory for testing) that allow the monitoring of the overall health status of the laboratory animals and prevent the outbreak of diseases. The use of animals in medical research at WSU is guarded and supervised by the WSU AEC, which follows the regulations as outlined in the *Code* and the *Act*.

As mentioned earlier, researchers are required to report unexpected adverse events related to their animal research. At WSU, there were 20 adverse events reported in 2020 (96 active projects), and 33 adverse events reported in 2021 (80 active projects) for all research and teaching activities that involved animals. Of these, 30% were linked to procedural or experimental issues and involved <1% of all animals reported to be used in animal research and teaching activities across WSU in these years. Researchers were asked to perform post-mortem examinations (and, where necessary, carry out histopathological analysis) to determine the cause of death and inform mitigating actions to prevent recurring incidents and ensure the welfare of all animals used in WSU's research.

Within the research community in NSW, there is growing consensus that the current method used by the NSW Department of Primary Industries (DPI) to collect data on animal usage statistics in research and teaching activities requires revision. WSU would advocate for changes in the way the animal usage statistics are calculated for clarity. For example, the current method does not currently differentiate between wildlife research and medical research. A wildlife project may observe 20,000 flying foxes, whereas a medical research project may use 300 mice. The levels of human intervention are dramatically different. When tabled together, the numbers become conflated and inflate the sense of risk and impact on animal welfare. This could lead to misinterpretation amongst the wider community as these statistics are published by the DPI and easily accessible (for transparency). WSU advises that a review of the reporting methodology is warranted and should be consistent across the states of Australia.

(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*, together with the *Act* currently provide a robust regulatory framework to oversee and authorise animal research. WSU is currently also working on a draft proposal to join an 'Openness Agreement on Animal Research in Australia', which is coordinated by the *Australian and New Zealand Council for the Care of Animals in Research and Teaching*. WSU believes openness is an important aspect of using animals in research and teaching activities, and key to fostering engagement with the wider community and building

[4] Buskila et al., 2014. Extending the viability of acute brain slices. *Scientific Reports*. 4: 5309
[5] Karl et al. 2012. Cognitive phenotyping of amyloid precursor protein transgenic J20 mice. *Behavioural Brain Research* 228(2). 392-7.

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trust. Research is reported annually through the internal and external regulatory channels including the response to and management of adverse events. These reports are provided in summary form through the DPI annual reporting mechanisms, including of numbers of animals used.

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

Various countries (including the European Union) have made provisions to recognise sentience and have directly referred to animals as sentient beings in their legislation (e.g. Article 13 of the Treaty on the Functioning of the European Union, 2016; France, Code rural et de la pêche maritime, 2016 – "all animals that are sentient shall be placed by the owner under conditions compatible with the biological requirements of their species"; Greece, Nomos Gia Ta Deopozomena Kai Ta Adeopota, 2012, article 1[a] - "an animal is every living organism that has the capacity to experience feelings (sentient being) that lives on the land, air and sea or in any other aquatic ecosystem or wetland"). This is an important step for the welfare of animals, as it means that animals would be afforded moral and legal protection. However, the definition of the concept varies greatly across societies and has been intensively debated in fields dealing with animal ethics and the science and policy of animal welfare[6]. The *Code* mentions 'sentience' alongside the ability to experience pain and distress, but there is currently no universally accepted definition of 'sentience' concerning animal welfare. Should a clear and operable definition of "sentience" arise in the future that can be incorporated in the *Code* and NSW animal welfare laws, the inclusion of the term would be greatly encouraged but sufficient conceptual work, legal operationalisation and consultation would need to be undertaken[7]. This would put NSW at the forefront of Animal Welfare legislation globally.

(g) any other related matters.

The National Institutes of Health developed a report on enhancing rigor, transparency, reproducibility and translatability in animal research. The recommendations put forward by the report that could be applied to animal research conducted in Australia, include:

- Education of investigators in statistics, or fostering collaborations with statisticians
- Emphasis on the selection, design and relevance of animal models during the grant application/funding process
- Changes to the funding process to include additional emphasis on research experimental design to maximise the application of the 3R's, and directly address animal welfare-related issues
- Education of investigators on appropriate animal data recording and reporting; and,
- Addressing ARRIVE 2.0 Essential 10 during the publication stage of any animal research[8]. The Essential 10 are the minimum information to include in a manuscript, without which, readers and reviewers would not be able to confidently assess the reliability of the findings presented.
- The recent creation of re-homing guidelines in NSW jurisdictions is welcomed, and WSU will work with this option where possible.

WSU would like to indicate we would welcome an opportunity to discuss our views further at a Parliamentary hearing.

[6] Browning and Birch., 2022. Animal sentience. *Philosophy Compass*, e12822.
[7] Blattner, 2019. The recognition of animal sentience by the law. *Journal of Animal Ethics*, 9(2), pp.121-136.
[8] Percie du Sert, et al., 2020. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *J Cereb Blood Flow Metab*, 40(9): 1769-1777.

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Yours sincerely

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