Response to the Parliamentary inquiry into the use of primates and other animals in medical research in New South Wales, March 2022

Introduction

The Australian Academy of Health and Medical Sciences is the impartial, authoritative, cross-sector voice of health and medical science in Australia. We advance health and medical research in Australia and its translation into benefits for all, by fostering leadership within our sector, providing expert advice to decision makers, and engaging patients and the public.

The Academy is an independent, interdisciplinary body of 451 Fellows – elected by their peers for their outstanding achievements and exceptional contributions to health and medical science in Australia. Collectively, our Fellows are a representative an independent voice, through which we engage with the community, industry and governments.

We are pleased to provide a submission to this inquiry, which has been prepared in consultation with the Fellows in our NSW State Branch.

AAHMS response

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*

Health and medical research is essential to addressing pressing health issues and improving the nation's health. Discoveries and innovations here in Australia have had profound impacts on health at home and across the world, and successive NSW governments have rightly recognised the value of health and medical research in driving economic growth, creating jobs and delivering societal benefits.

The use of animals is crucial in many areas of health and medical research – including research undertaken in NSW – and has contributed to important advances in human and animal health. This work is essential for scientists to better understand disease and to translate research into health advances, ultimately enabling the conquest of severe and potentially fatal diseases. The most commonly used are small animal models (e.g. mice and rats) but nonhuman primates remain essential in some settings.

However, while recognising the critical nature of animal studies to these advances we are in complete agreement that such use must be judicious, minimise the number of animals involved and that researchers must ensure that handling of these animals is humane.

These species are used across a range of diseases and health conditions, including the development of cures and treatment strategies for patients suffering a range of major acute and chronic conditions, including heart and vascular diseases; kidney and liver conditions; diabetes and endocrine diseases; brain, spinal cord and peripheral nervous system diseases;

obstetric and gynaecologic conditions; infectious diseases; respiratory conditions; musculoskeletal diseases; cancer and birth defects.

Valuable case studies can be drawn from the ongoing development of vaccines, immunotherapy and other forms of therapy for infectious diseases such as COVID-19, HIV, influenza and herpes. Other examples exist in the development of new treatment options for potentially fatal infections with resistant bacteria in Australia (i.e. antimicrobial resistance) and novel therapeutic approaches (including immunotherapy) for a range of cancers and ageing.

The rapid development of vaccines and drugs for COVID-19 would not have been possible without initial testing in small and large animals for efficacy, side effects and optimal dosing. The US Food and Drug Administration mandates that all promising vaccine candidates must be tested for safety and efficacy in animals before they enter human trials and it is worth noting that Australia's Therapeutic Goods Administration "closely aligns its regulatory approaches to therapeutic products with those of comparable international regulatory counterparts wherever possible".[1,2] Small animals, for instance mice, were first used to test for an appropriate and safe immune response. Researchers were then able to develop animal models in hamsters and ferrets that expressed disease closely resembling that in humans, enabling important insights into the disease and the potential effectiveness of vaccines and drug treatments.[3]

However, testing vaccines in nonhuman primates in the later stages was also essential as they resemble humans more closely, particularly with respect to their immune responses and the targets for multiplication of SARS-CoV-2 in the lungs and elsewhere.[4] Studies with the Moderna vaccine, for example, showed induction of robust protective antibody levels and rapid protection in the upper and lower airways – this demonstration of an appropriate immune response and safety in these animals allowed a rapid transition to human trials.[5] The rapid progression of COVID-19 vaccines through animal models and into humans is an accelerated example of the process through which most vaccines are developed prior to human trials. A similar process was followed during the outbreak of Zika virus in 2016.

In Australia, in the early stages of the COVID-19 pandemic, some research groups had to send their vaccine candidates overseas for animal testing because no appropriate small animals or nonhuman primates were available in Australia. Eventually hamsters were imported into Australia for our own COVID-19 vaccine development.[6] The Australian and NSW governments have now committed their own research programs to the new mRNA vaccine development approaches – this is welcome because they are much quicker than traditional methods, but small animal models and in some cases nonhuman primates will be essential for our research in this field to be internationally competitive.[7] These requirements have been included in plans developed in preparation for the next wave and the next pandemic by the Australian Infectious Diseases Network, which includes many of Australia's most eminent infectious diseases and vaccine researchers.

Nonhuman primate studies are required beyond these sudden disease outbreaks. For example, Hepatitis B has continued to be the most common bloodborne disease worldwide (killing more than 800,000 people annually). Infections remain incurable mostly due to the historical lack of available systems to develop drugs. Newly established nonhuman primate models that accurately model the disease are key to furthering therapeutic development that would benefit the 360 million people globally affected by Hepatitis B.[8]

Another potentially valuable application of research using animals is 'xenotransplantation' – through which cells, tissues, or organs are transplanted between two species, e.g. from a nonhuman animal to a human. The number of patients requiring solid organ transplants currently exceeds the number of donors, meaning individuals unfortunately die while they wait for a suitable donor. Perfecting the science of animal to human transplants could provide another source for transplantation and could help solve this organ shortage.[9]

The Academy recognises that the use of animals in research is in some cases necessary – where research is high quality (as judged by expert peer review), where it complies with all relevant regulations, and where there is no alternative to achieve the same outcomes. High standards of animal welfare are essential, including strict protocols around safety and supervision. We support and endorse the principle of the 3Rs – to refine, reduce and replace the use of animals in research (see section c below). It is important that governments and the research community are open about how animals are being used in research, and the associated outcomes and impacts.

In Australia, animal research is supervised in appropriately designated facilities. The facilities are either PC2 (Physical Containment level 2) or BC2 (Biosafety Containment Level 2) biocontainment facilities. All staff working in these facilities are trained and accredited, with strict adherence to PC2/BC2 procedures and standard operating procedures on cleaning and maintenance of the facility. Oversight is provided by Animal Ethics Committees (AECs) in each research institution. In NSW AECs report to the Animal Research Review Panel (ARRP) in the Department of Primary Industries (see below). This mechanism of regulation aims to generate an environment in which the use of animals in research is minimal and humane, and potential health risks to the wider community are minimised.

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*

Medical research in Australia is funded by grants from Commonwealth government agencies and sources such as the National Health and Medical Research Council (NHMRC), the Medical Research Future Fund (MRFF), Australian Research Council (ARC) and CSIRO, grants from state and territory governments (including NSW), and by charitable/philanthropic organisations and industry. As far as we are aware, neither the state nor federal government commissions the importing of animals for medical research.

The vast majority of the animals used in research are bred in Australia at the Australian BioResources Centre (located in NSW) and the Animal Resource Centre (in Western Australia). A suitable source of research animals, which follows the relevant protocols, regulations and standards, is important not only for animal welfare, but for ensuring that the research undertaken using those animals is of the highest quality – and therefore minimises the number of animals required and maximises the value of that research.

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*

The Academy supports and endorses the principle of the 3Rs – to refine, reduce and replace the use of animals in research. They underpin the ethical, humane and responsible care and use of animals for research purposes in Australia – and overseas.

The *Australian code for the care and use of animals for scientific purposes* – which provides guidance for investigators, institutions, animals ethics committees, animal carers and all those involved in the care and use of animals for scientific purposes – requires the application of the 3Rs at all stages of animal care and use.[10]

Replacement

Where possible, alternative methods to using animals to model diseases should be used by researchers – for instance the use of human tissues, cell lines and organoids cultured in the laboratory, and *in silico* computer simulation. At present, not all animal research can be replaced by these models because they cannot accurately mimic the whole organ systems of humans.

Reduction

Researchers should use the minimum number of animals required for sufficient statistical power to be certain of their study results – this is recommended and actively overseen by Animal Ethics Committees.

Refinement

As part of the ethical approval process, researchers agree only to use methods that minimise pain and distress, and maintain animal wellbeing. All staff handling animals are fully trained and monitored. Animals are carefully monitored by researchers, animal care technicians and the directors of animal research facilities to minimise pain and discomfort. Animal care technicians are particularly attuned to this issue.

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

Animal welfare is of the utmost importance in all instances in which animals are used for research purposes. Ethics approvals are crucial for ensuring that animals are used only where needed, that studies are appropriate designed and that the principle of the 3Rs is appropriately and properly considered. Research using animals must be done ethically, humanely and responsibly – and governments and the research community must be open about how animals are being used for such purposes.

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

Research institutions, Animal Ethics Committees (AEC) and individual researchers are bound to actively comply with the NSW Animal Research Act 1985, Animal Research Regulation 2021 and the *Australian code for the care and use of animals for scientific purposes*.[10-12]

Animal Research Facilities are inspected annually or more frequently by AEC members.

The Animal Research Review Panel (ARRP) in the NSW Department of Primary Industries mandates annual reporting, publishes animal use statistics yearly and audits institutions every three to four years, accompanied by an inspection. Instances of non-compliance are notified and rigorously followed up until rectified.

Research findings are reported in articles that include the methodology outlining the animals used, are published and accessible through peer review journals.

Australian Academy of Health and Medical Sciences, NSW Branch

This response was developed through contributions from AAHMS Fellows based in New South Wales and was approved for submission by the AAHMS Executive. We would like to thank the Academy's Fellows who contributed to this response.

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