Submission No 228

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

Organisation: Children's Medical Research Institute

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

in New South Wales

TERMS OF REFERENCE

Portfolio Committee No. 2 - Health inquire into and report on the use of primates and other animals in medical research in New South Wales, and in particular:

(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

The purpose of biomedical research is to discover underlying mechanisms in health and disease with the aim of disease-prevention and/or the development of novel treatments and cures for diseases that would otherwise me intractable, and to improve medical technologies. The outcomes are improved health care delivery and health and wellbeing benefits for sick children and adults and their families.

The research involved in developing, say, a new cancer treatment, or new technology often spans several decades – it involves building on past scientific discovery, testing new ideas and working with different types of model systems culminating eventually in animal models – before a drug or an intervention is considered safe to be tested in humans. This pre-clinical proof-of-concept work is fundamental to the ethical conduct of research in humans and relies where needed, on the use of animal models. Although every effort is made to minimise the need for research involving animals through the use of novel pre-clinical model systems, it remains a pillar of biomedical research which cannot be removed without jeopardising many of the research efforts that the community is relying on to deliver treatments for serious diseases.

The health benefits of this type of research are well documented and understood and any risks to public health from animal use are shown to be well mitigated through stringent control measures and regulations already in place.

Children's Medical Research Institute (CMRI) at Westmead investigates biological mechanisms in serious diseases affecting children, including cancer, inherited eye diseases causing blindness, neurological diseases such as epilepsy, metabolic diseases affecting the kidney and liver, and genetic immunodeficiencies. In Australia and worldwide, 1 in 20 children are born with a birth defect or genetic disease, and genetic diseases contribute to more than 30% of admissions to children's hospitals. CMRI is a member of the Australian Association of Medical Research Institutes (AAMRI) and endorses the submission being made by AAMRI.

CMRI researchers have developed novel approaches to improve or even correct genetic diseases and work is being undertaken to develop gene-based cures for life-threatening diseases in children (such as Propionic Acidaemia, a genetic metabolic liver disease that can lead to brain damage, coma and death in children and for whom the only recourse currently is a liver transplant). However, before any potentially life-saving novel gene therapy can be tested or used routinely in children, ethical standards require that it is rigorously tested in other model systems that predict its safety and effectiveness in humans.

This helps to minimise potential health risks posed by this research and to avoid the human tragedies that have occurred in the past when new treatments were undertaken in humans without first testing in appropriate animal models.

(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 costs of medical research are funded primarily by grants and donations made by hundreds of thousands of Australians which demonstrate the strong support of the community for research which leads to improvements in health. Grants received by CMRI are predominantly from the Federal and NSW Government. The provision of sufficient financial support and capacity to meet all regulatory requirements is an investment that CMRI makes in the ethical conduct of research. The use of animals is always minimised to avoid unnecessary/excess use, which is important both ethically and for reducing the cost of animal research, with all efforts made to find affordable alternatives.

(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

Scientific progress necessitates choosing the best system available to answer research questions and to generate robust evidence needed to promote discovery and lead to new advances, including new treatments for previously incurable diseases. Research involving animals, although usually unavoidable at some point in the progression from laboratory discoveries through to the introduction of new treatments into the clinic is relatively slow, expensive, and subject to stringent regulatory restrictions, so there are many other drivers of the use of alternative approaches to animal research in addition to the ethical considerations. These approaches include human cell lines or human tissues and new biotechnologies such as laboratory-developed mini-organ structures called organoids –use of which are governed by the National Statement on Ethical Conduct in Human Research (2007)[1] and the Human Tissue Act, 1983[2].

CMRI has been providing cell lines, predominantly human in origin, to Australian life sciences researchers through CellBank Australia which was established for this purpose in 2005 and supported by agencies such as Cure Cancer Australia Foundation, National Breast Cancer Foundation, the National Health and Medical Research Council of Australia and Cancer Institute NSW (an agency of the NSW Government). Cell lines are a critically important alternative to animal research.

In addition, in recent years CMRI has set up a Stem Cell and Organoid Facility, partly funded by the NSW Government through a grant to the Luminesce Alliance. This facility is able to generate mini-organoids from cells provided by patients that allow the testing of investigational drugs or gene therapies. This not only provides an alternative to animal research in some circumstances, but it is highly complementary in that it can provide research data that is essentially impossible to obtain from animal research in a timely manner. We are currently considering how to fund a major scale-up of this Facility so that its benefits can extend to many more disease indications.

Complementing these ex-vivo models are bioinformatic and computational tools that collate and analyse research data to determine the molecular pathways which govern the behaviour of cells, tissues and organs in health and disease states.

Consistent with the "3Rs" as defined in the Australian Code for the Care and Use of Animals for Scientific Purposes (8th Edition 2013)[3], the above alternative approaches *Reduce* the number of animals used in medical research and assist in *Replacing* the use of animals.

The *Refinement* of techniques to reduce the impact on animals is achieved by all research projects requiring the use of animals being examined by the Animal Ethics Committee (AEC) to ensure the use

of animals is ethically appropriate, have scientific merit and compliant with the Australian Code for the Care and Use of Animals for Scientific Purposes (8th Edition 2013), the Animal Research Act 1985[4] and the Animal Research Regulation 2010[5]. Compliance is strictly enforced. CMRI staff undertake mandatory training on the use of animals prior to commencement and at appropriate intervals thereafter.

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

These issues are well covered by current stringent governance systems. The Animal Welfare Unit of the NSW Department of Primary Industries (DPI) authorises the supply of research animals in accordance with the legislation and Code of Practice and institutions conducting animal research are required to be accredited as an animal research establishment. Accreditation site visits and inspection of animal research facilities holding an animal supply licence are carried out every three years by the Animal Research Review Panel set up by the DPI.

At CMRI, additional welfare procedures have been put in place. The Animal Ethics Committee (AEC), which is a joint committee with the Children's Hospital at Westmead, inspects CMRI animal research facilities on a 4-monthly basis. The AEC is responsible for ensuring that the research considers first and foremost, the ethical, humane and responsible care and use of animals used for scientific purposes.

Additionally, CMRI's animal facility is overseen by a certified laboratory animal veterinarian and all animal technical staff hold college- or TAFE-level qualifications.

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

We consider the current regulatory regime to be highly stringent with sufficient safeguards relating to animal welfare in medical research, and to transparency and accountability, as noted below.

To meet the requirements of the NSW Animal Research Act, 1985, the NSW Department of Primary Industries (DPI) publishes the statistics around use of animals in research on an annual basis. These data are collected from accredited animal research facilities across NSW. This ensures public transparency on the use of animals in medical research.

In terms of accountability, the Australian Code for the Care and Use of Animals for Scientific Purposes (8th Edition 2013) is enforceable in NSW, and is incorporated into the Animal Research Act, 1985. In response, CMRI has implemented policies, procedures and training to ensure its staff abide by this Code. Training on the Code is also provided to members of the CMRI/CHW Animal Ethics Committee to ensure they can review and oversee animal research protocols effectively.

Care needs to be taken not to introduce regulations that make it so difficult to undertake essential animal research in Australia that it will have the effect of increasing animal research in jurisdictions that may not have the same high standards regarding animal welfare.

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

Internationally, the 3Rs are the recognised approach towards the use of animals in medical research. An example of how this is being implemented is the National Centre for the Replacement, Refinement and Reduction in Animals in Research. This is a UK-based scientific organisation that works nationally and internationally with the research community to replace, refine and reduce the use of animals in research and testing (https://www.nc3rs.org.uk/who-we-are). Funding for this initiative is provided

by UK's two core research funding organisations: Medical Research Council, equivalent to Australia's NHMRC, and the Biotechnology and Biological Sciences Research Council. They also receive funding from charitable and commercial sectors. While their mission is to support the discovery and adoption of predictive, reproducible and cost-effective alternatives to the use of animals, they also work to improve the standards where animal use is necessary.

A similar approach is being undertaken in Norway with "Narecopa", Norway's National Consensus Platform for the advancement of "the 3Rs" in connection with animal experiments: https://norecopa.no/about-norecopa.

In Australia, NSW is leading the way in educating the public on the state of animal research and supporting the 3Rs: "Animal Ethics Infolink": https://www.animalethics.org.au/three-rs . Similar to the UK, Phenomics Australia (https://phenomicsaustralia.org.au/) is working with Australian medical research organisations on the development of a roadmap for non-animal technologies (invitro/cell-based models).

Source:

1. National Statement on Ethical Conduct in Human Research 2007 (Updated 2018). The National Health and Medical Research Council, the Australian Research Council and Universities Australia. Commonwealth of Australia, Canberra.
2. Human Tissue Act, 1983. NSW Legislation: https://legislation.nsw.gov.au/view/html/inforce/current/act-1983-164
3. National Health and Medical Research Council (2013) Australian code for the care and use of animals for scientific purposes, 8th edition. Canberra: National Health and Medical Research Council.
4. Animal Research Act 1985. NSW Legislation: https://legislation.nsw.gov.au/view/html/inforce/current/act-1985-123
5. Animal Research Regulation 2010. NSW legislation: https://legislation.nsw.gov.au/view/pdf/asmade/sl-2010-425