Submission No 232

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

Organisation: Western Sydney Local Health District

Date Received: 31 March 2022

Dear Mr Donnelly

Re: Inquiry into the use of primates and other animals in medical research in New South Wales

Please find below a submission by Western Sydney Local Health District.

About the Western Sydney Local Health District

The Western Sydney Local Health District (WSLHD) serves one of the largest Health District populations in Australia, providing tertiary health care to 1 million people in western Sydney and specialist referral services to a large proportion of rural NSW. It incorporates two of Sydney's largest teaching hospitals (Westmead Hospital and Blacktown-Mt Druitt Hospitals) and employs 15,000 health care and support staff. Through its Research and Education Network WSLHD also provides professional education to 900 doctors in training and 5000 students in nursing, medicine, dentistry and allied health disciplines, each year. Medical Research is an integral component of the work of WSLHD and spans laboratory research, clinical trials, public health and prevention, and basic sciences. Innovation and transition of discovery into patient care are the key goals of research in WSLHD. We currently have over 2000 active research projects, including >600 clinical trials of new drugs or medical devices, representing the highest involvement in clinical trials of any local health district in NSW. This program of research aligns with our mission to provide best practice and continuous quality improvement to the care of our patients. Research involving human participants is the predominant focus of research in WSLHD. However, there is also an important component of discovery and implementation research which is performed in animal models; as well as work in cell and organ preparations, molecular biology and genomics.

The following submission is oriented to the stated terms of reference of the Inquiry:

(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

Research in medical therapeutics can be viewed as a continuum from (i) dry laboratory computer modelling and hypothesis generation through to, (ii) discovery of basic mechanisms of disease and therapeutics in cell and animal models, (iii) design and refinement of potential therapies and (iv) testing of their effectiveness in clinical trials. This is later followed by translation of discoveries into routine clinical practice and re-evaluation of their impact at a population level and in a health economics framework. Every aspect of this continuum is important for the best outcome in human health. It is clearly important to balance the desire for improved human health outcomes with a parallel concern for an ethical relationship between humans and other species, care for the environment, and appropriate use of resources.

Animal research is an essential component of the continuum of research activity. Without animal research our understanding of disease would be severely diminished and our capacity to develop new therapies would be severely curtailed. The development of the greatest breakthroughs in human therapeutics and disease prevention have come through this

pathway; including treatments such as anaesthetics, antibiotics, insulin, vaccines and organ transplantation, and medical devices such as pacemakers, prostheses and surgical instruments.

At WSLHD, when considering the ethical approval of a clinical study in humans, one of the prime considerations is to balance the potential benefit versus risk for human trial participants. This will almost invariably rely on safety and efficacy data derived from pre-clinical studies performed in animal models. The design of a trial (e.g. determining dosage and administration, monitoring methods, anticipating adverse effects) will also be based on such data. Experimentation in humans – an essential requirement for all new therapies – is virtually impossible to plan and perform without prior animal research. The public health risk of being unable to effectively test new discoveries (such as a vaccine or a cancer treatment) would be vast. We would face a choice between having human medical needs unmet, or the risk of new, inadequately tested therapies being put forward into clinical practice without thorough prior evaluation.

Regarding public health risks of animal research - we presume this alludes to the notion of dangers that could "escape" from the research environment and pose a threat to the general population. Perhaps in public perception there is a notion that research animals could pose a threat? In reality this is an extremely remote possibility. Infectious organisms or genetically modified (GM) animals are strictly controlled in Physical Containment labs (PC2 for GM, PC3 or PC4 grade for infectious material). All material leaving a PC2 lab is treated as biological waste and no live animals leave a laboratory environment and enter the food chain or animal breeding pool. In PC3 and PC4 labs everything that leaves the lab is incinerated or autoclaved. A far greater threat of animal to human transmission of infection arises from the food processing industries (origins of avian influenza H5N1, SARS, and possibly COVID-19), herding and farming practices (MERS coronavirus) or from human-induced habitat loss which drives wild animals into contact with humans or human companion animals (Hendra virus in Northern NSW and Queensland).

(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 vast majority of the pre-clinical research in Australia is funded by major government sources including the NHMRC, Medical Research Future Fund, NSW Government Office of Health and Medical Research, the National Institutes of Health (USA), and non-profit organizations such as the Cancer Council of NSW, National Heart Foundation and similar NGOs. Research funding is granted for the totality of a project – with direct costs of animal management being a relatively small proportion of the overall cost (and considerably less that staff costs and major equipment). Overall use of animals has reduced considerably in the last decade. For example, on the Westmead campus there have historically been four different small animal holding facilities (Westmead Hospital, Westmead Institute for Medical Research, Children's Medical Research Institute and Children's Hospital). At the present time most of these facilities are greatly under-utilized and in 2022 all four will be consolidated into one, which will still be well below capacity.

(*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*

All researchers are looking to ways to implement the 3R's. On the Westmead Precinct all animal ethics applications are evaluated against the 3R's to avoid unnecessary duplication, and to ensure the optimal number of animals are used to achieve the research objective. Whenever possible tissue which is surplus to requirements for one project will be utilized in another to minimize the number of animals used. New technologies such as advanced imaging, advanced flow cytometry and high throughput genomics and proteomics have meant that more information can be obtained with smaller animal numbers. Cell culture methods, including the 3D printing of mixed-cell organoids can replace the use of whole animal experiments in some applications. However, cell culture can never fully replace whole animal experiments to evaluate new drug treatments. For example, cell culture experiment may allow the researcher to determine if a drug will kill cancer cells in isolation – but it cannot determine whether the drug will also damage other organs, how the drug is metabolized or excreted, which tissues it can access in a whole body model, what dosage is most effective or toxic, and many other pertinent questions which must be answered before the first trials in humans can be undertaken. Therefore, the principles of replacement and reduction have practical limits.

If animal experimentation is to be undertaken, a variety of species are required to be used in order to provide the most appropriate model to inform the application of that research to humans. Special requirements exist for the development and testing of medical devices. These often require testing in an intact animal model, and the choice of appropriate species is determined by biocompatability. For example, pigs may be employed in research for cardiac devices or heart surgery - because the pig heart is similar in size, structure and function to the human heart.

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

In our experience, the only animals imported from overseas for medical research are specific, genetically modified mice that are purchased from reputable research providers (e.g. Jackson Laboratories in USA). In these cases, breeding pairs are imported and a breeding colony is established in the local institution. The importation and breeding is subject to approval by the Animal Research Ethics Committee (AEC) and requires an import permit and oversight from AQIS. To our knowledge all animals used for large animal medical research, including non-human primates, are bred in Australia under strict conditions. They are from captive bred colonies and not imported.

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

We have reviewed this issue with our colleagues at the Westmead Institute for Medical Research. NSW has a strong regulatory regime for the protection and welfare of all animals used for research. Governed by legislation, all institutions using animals for research must be accredited by the Department of Primary Industries (DPI). Animal Ethics committees must contain members with veterinary experience (Category A), members representing the welfare of animals (Category C), lay members (Category D) and those with relevant scientific expertise (Category B). In addition to approving research projects, they undertake inspections and audits of research facilities, which are also audited by inspectors from the DPI. Genetically modified animals have additional regulation via the Office of the Gene Technology Regulator. Non-human Primates (NHP) have added layers of oversight and regulation, as is appropriate. All protocols for NHP are reviewed and approved by 4 separate and independent ethics committees: The AEC of Royal Prince Alfred Hospital with oversight of the state's single Baboon colony, the local AEC where the work is being undertaken, the NHMRC NHP Ethics Committee that has responsibility for NHMRC funded projects using NHP, and the DPI AEC. In our experience, all 4 ethics committees undertake inspections and audits. The current level of regulatory oversight is comprehensive, has been demonstrated to remove 'bad actors' and improve animal welfare and ensures compliance with the 3R's. In our opinion the regulatory framework does not need to be changed.

The public, rightly, have high expectations of the ethical conduct of research in animals. Previous polling of public opinion has demonstrated majority acceptance of the need for animal experimentation in certain aspects of medical research where benefit to humans is highest (such as life-saving drugs) but an increasing abhorrence of experimentation which is not high impact (such as cosmetic products). Importantly, publicly funded medical research is almost always in the former category, while the later is predominantly commercially funded. When the public has been asked what checks and regulations they would like to see in place for animal experimentation the responses overwhelmingly nominated the exact same regulations which are already in place in NSW, although the respondents often did not know what rules already existed. Studies in the UK, with similar regulatory framework to NSW identified that the public would widely support the existing regulatory system if they knew more about it (in "The ethics of animal research. Talking Point on the use of animals in scientific research" by Simon Festing and Robin Wilkinson, EMBO Rep. 2007 Jun; 8(6): 526–530. doi: 10.1038/sj.embor.7400993).

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

NSW has among the highest levels of regulation of animal research in the world. To our knowledge there have been no breeches in the conduct of research with animals that have resulted in threats to public safety. With regard to ethical research practice we would suggest that the current regulatory framework serves us well and meets the expectations of most people in NSW. Many overseas jurisdictions have more lax regulation and attempts to reduce or restrict capability for animal research in NSW is likely to drive such work into settings where the attention to animal welfare and ethical practice is considerably worse that in the local setting, while at the same time decreasing research competitiveness and impact in NSW.

(g) any other related matters

The NSW State Government has earmarked Westmead as a lighthouse precinct for biomedical commercialisation and investment. It is expected to create more than 50,000 well paid, 'knowledge' jobs in Western Sydney; based around the Westmead Health and Medical Research precinct. The success of this venture requires the creation of a "whole research ecosystem", including the necessary contribution of animal research. Animal research is a major component of a broad range of research technologies and capacities. The translation of medical research into better patient outcomes requires animal models for pre-clinical evaluation of potential therapies and a better understanding of human biology and disease. If access to appropriate use of animals for research is unreasonably curtailed or impeded, then the development of world class collaborative research will be severely impeded, with a consequent brain drain to other states and overseas.

The recent events around COVID-19 has been a classic example of the value of well developed local research expertise. The outstanding outcome in our state and nation was in large part due to our long-established research expertise in viral and vaccine research at Westmead. The development of RNA vaccines was very much dependent on animal research which meant that we witnessed a life-saving vaccine developed in record time. COVID-19 has reminded us that reliance on importation of knowledge and health technology is perilous. The next major epidemic or similar health challenge we face may not be global but rather be regional. Weakening our research infrastructure will severely inhibit our ability to urgently address these future health challenges.

Discussion on the subject of research ethics is often portrayed as being essentially between two positions that are either 'for' or 'against' the use of animals. This is unhelpful, since the matter itself is complex, as are the many views that surround it. We welcome the opportunity to engage in constructive discussion with all stake-holders and with Government regarding this important subject.

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