Submission No 244

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

Name: Ms Paula Wallace

Date Received: 30 March 2022

Tuesday 29 March 2022

Portfolio Committee No. 2 – Health

Legislative Council

NSW Parliament

6 Macquarie St, Sydney NSW 2000

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

Dear committee members,

I am writing in my own capacity to highlight an area of research that I believe goes to the heart of your inquiry and its terms of reference.

The research in question is smoke inhalation, which may involve any species, but which is currently known to be taking place at least at two research establishments in NSW using mice – the University of Newcastle and the Centenary Institute.

While my comments relate to all smoke inhalation procedures, I am most concerned with the use of the chronic nose-only method, sometimes referred to as smoking towers. This method delivers smoke, under pressure, directly to the noses of mice through a restraining device.

In a typical nose-only protocol, exposure consists of puffs of smoke for a minimum of one hour, twice a day, five days per week for 8 to 12 weeks. Mice remain in the restraining device throughout each exposure period.

The nose-only method differs from other procedures in which mice are exposed without restraint in a chamber to which smoke is introduced – a procedure known as whole-body exposure.

Image: Mice in restraining devices attached to a "smoking tower". Source: Humane Research Australia

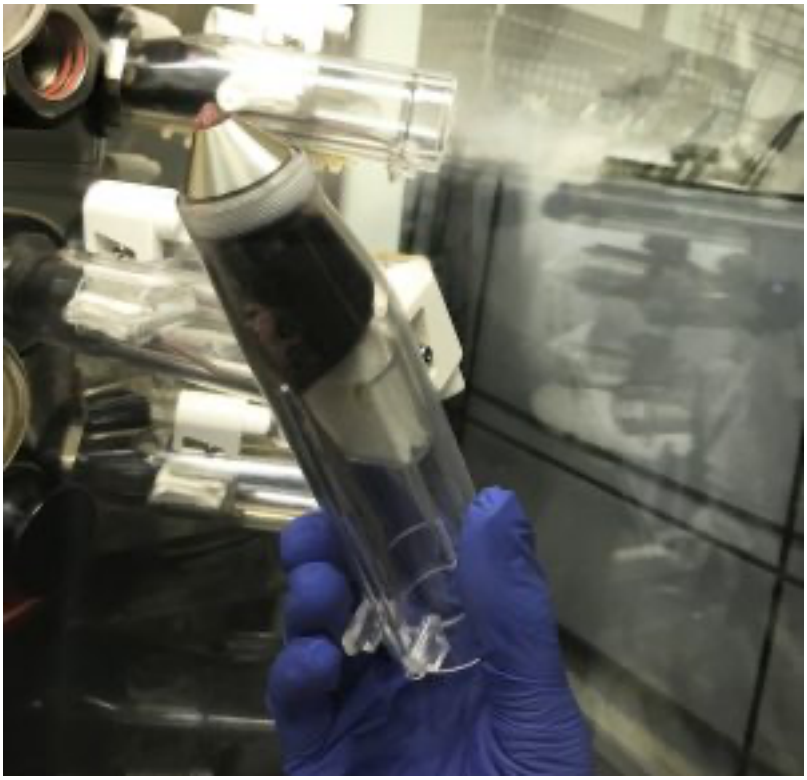

Image: Mouse in a restraining device that attaches to a smoking tower. The nose of the mouse can be seen protruding from the hole at the top, which is where the tube attaches to the tower and through which smoke is delivered directly to the nose. Source: Humane Research Australia

If your inquiry is to look at the ethical and welfare issues surrounding the use of animals in medical research and the effectiveness and funding of this research, then you must consider this area of research. The reasons for this are as follows:

1/ Welfare - Smoke inhalation procedures, in particular the chronic nose-only smoke exposure method, cause high levels of suffering and stress to the animals subjected to these procedures, both through the procedures themselves and the conditions/diseases that they induce. They are considered high impact procedures, which also result in adverse or unexpected events involving the death of animals directly related to the methods being employed.

This is likely to have a substantial cumulative effect because each animal is typically subjected to the procedure up to 120 times, for a minimum of one hour while tightly restrained. Based on published accounts, it is unclear how animals are monitored to ensure the welfare impact of the procedure does not exceed a defined humane endpoint as required by the *Australian code for the care and use of animals for scientific purposes* (the Code).[1]

Furthermore, the Code states:

> *Pain and distress may be difficult to evaluate in animals. Unless there is evidence to the contrary, it must be assumed that procedures and conditions that would cause pain and distress in humans cause pain and distress in animals.*

[1] https://www.nhmrc.gov.au/about-us/publications/australian-code-care-and-use-animals-scientific-purposes

Therefore, one needs to apply the "pub test" and ask whether being attached to a smoking tower with smoke delivered under pressure directly to the nose, over consecutive days and weeks, would likely cause them pain and distress.

It is also widely accepted that people with Chronic Obstructive Pulmonary Disease or inflammation of the airway and lungs – the conditions purportedly induced in mice through the chronic nose-only smoke exposure method – experience significant pain and distress.

It is worth noting that procedures or projects that cause animals severe suffering or distress, which is likely to be long lasting, are banned in the European Union and smoke inhalation research is one of only three types of research that is subject to approval by the Chief Inspector of the UK Home Office Inspectorate. So, it has been singled out as requiring greater regulatory oversight and attention on welfare grounds.

Under the Code's governing principles, the expectation of refinement requires that any adverse animal welfare impacts of a procedure be minimised, this includes not just the initial approval of the project but while the research is underway.

The Code states:

> *The effectiveness of strategies for supporting and safeguarding animal wellbeing must be kept under review during the lifetime of activities, including projects. Where relevant and applicable, the outcome of this review must be implemented in current activities and taken into account in planning future activities, including projects.*

Furthermore, the section of the Code entitled *Review and approve new and ongoing activities*, encourages the use of pilot studies to enable the assessment of "the potential for refinement and reduction".

It is not apparent from published accounts of research using the chronic nose-only method whether any significant refinements have been implemented. It is possible that alternatives to the chronic nose-cone method are not fully being explored, or other refinements such as less intense exposure regimes or the administration of pain relief where reasonable.

Is it possible that the chronic nose-only method is simply the method that has been most explored because it's cheaper and quicker than other methods? If so, this does not reflect the Code's governing principle of respect for animals and scientific integrity, as opposed to making decisions based on utility and convenience.

2/ Ethics – The Code's governing principles require a judgement to be made on whether a proposed use of animals is ethically acceptable. Central to this is a harm-benefit analysis that must balance the potential impact on the animals' wellbeing against the potential benefits of the research.

After looking at a large number of methods and frameworks on harm/benefit analysis, they all come back to the same point, including the latest UK guidelines on this for the use of animals in science, which are arguably the most advanced in the world:

They make the point that there is no numeric formula for harm/benefit analysis, it is not a quantitative process, it's a matter of judgement which is always contestable.

This is mirrored in the Code that says each Animal Ethics Committee member is responsible for deciding whether, in their own judgement, an application or other matter under consideration by the AEC is ethically acceptable and meets the requirements of the Code.

This is especially true when it comes to work like that using the chronic nose-only method due to the wide range of opinions on its effectiveness and the high impact on the animal. Confounding this is the lack of consistency in dosing and length and method of exposure in the literature; and the lack of consensus on whether disease models for COPD and related conditions can effectively be replicated in mice using the nose cone and whole body exposure methods and the differences between the two.

Arguments on the need to do research on diseases such as COPD, do not justify the use of any particular model such as the nose-only method over whole body exposure for example.

A sound ethical review should also include consideration of replacement of animals altogether. Sources are available for this including a recently published review of non-animal alternatives in respiratory disease research by the European Commission's Joint Research Centre Chemical Safety and Alternative Methods Unit.

While research establishments may be adhering to the Code in relation to their conduct, there is a precedent for some procedures to attract greater oversight or regulation – for example, the use of non-human primates, the Draize test and LD50 testing.

Taking into account the sustained high animal welfare impact of smoke inhalation research and the difficulties in conducting a sound ethical assessment of such projects, there seems to be a strong case for placing regulatory conditions on its use.

3/ Social licence - Another concept relevant to ethical review is that of social licence or how well an establishment is able to understand, assess and respond to stakeholder and public views on its work.

Animal welfare has been in the public spotlight in recent years, with media reports and public opinion resulting in stricter regulations globally in a number of areas related to animal welfare - namely, live export, puppy farming, farm animals, greyhound racing and the cosmetics industry.

There is also a history of campaigning, which has gained public support, around opposition to smoking related research. Humane Research Australia recently released a report on optimising inhalation research and launched its "Forced to Smoke" campaign highlighting the issues related to the nose-only method.

The research community globally has also made attempts to increase transparency and improve stakeholder engagement through initiatives such as the Concordat on openness on animal research in the UK and others. There is now a similar project underway in Australia.

Currently, taxpayers who are direct stakeholders in much of the animal-based research in Australia (including smoking inhalation research) supported by government-funded NHMRC and ARC grants, do not have sufficient information to make a reasonable assessment of the ethics of using animals in various research settings. In the absence of this, research establishments cannot claim to have a social licence to operate, which raises concerns about the ethics of ongoing research.

With greater openness, accountability and stakeholder engagement on the part of research establishments, it's likely that high-impact procedures such as smoke inhalation research, in particular chronic nose-only smoke exposure methods, would rightly come under greater scrutiny than they do currently.

4/ Regulatory regime – There is no public source of information to ascertain which research establishments in NSW are undertaking smoke inhalation procedures; how many mice are involved; how effectively their AECs are functioning; and whether the welfare of animals involved could be improved.

Is it possible that if the Minister for Primary Industries were to be asked how many licenced research establishments were using smoking towers and how many mice were being subjected to this procedure, he may also not be able to answer that question?

It is virtually impossible for a member of the public to inform themselves about this research taking place in NSW, although much of it is funded by the taxpayer through government grants.

Furthermore, it is equally difficult to raise concerns around this research, or any area of research for that matter, other than through government channels such as the Department of Primary Industries and subsequently the Animal Research Review Panel, which may or may not provide a timely or satisfactory outcome.

One therefore has to ask: where does the accountability lie for those conducting high-impact research such as smoke inhalation procedures on animals?

Conclusion and recommendations

The principles that underpin the Code that governs the use of animals in research and science nationally, are to protect the welfare of animals and to ensure such research is subject to ethical review.

For research to be ongoing using the chronic nose-only method of smoke inhalation, I don't believe that those principles of the Code have been followed. Also, some areas of research and certain procedures simply require more than the application of the Code, such as LD50 testing, and I believe smoke inhalation is in that category.

In my view smoke inhalation research is one area of research that requires greater oversight by regulators and the chronic nose-only method should be phased out, for the following reasons:

- Given the high impact nature of smoke inhalation procedures on animals and the under-development and under-utilisation of refinements and alternatives that could produce similar if not the same results.
- Given the complex nature of smoke inhalation projects and the difficulty some AECs may face in undertaking a sound ethical assessment and introducing refinements.
- Given that opportunities for lay people (and taxpayers) and others to discuss, challenge and raise concerns around smoke inhalation research are very limited, which brings into question the social licence and accountability of establishments conducting research with high animal welfare impacts.

My recommendations to the inquiry are as follows:

- Seek to phase out the use of the chronic nose-only smoke inhalation method of research as soon as possible.
- Seek to place restrictions on other forms of smoke inhalation research such as making it a condition that all smoke inhalation research:

- be assessed and approved by the government/regulator
- demonstrate efforts to use alternatives to direct smoke inhalation
- provide a detailed understanding and consideration of actual or expected harm to the animal over the full course of its life and outline actions to mitigate harm
- provide regular reporting to the government/regulator on any approved projects.

- Seek to establish an independent office of animal welfare that will, among other things, provide information to the public and others on animal-based research and respond to questions and complaints; and act as the regulator.

I commend you for undertaking this inquiry and giving your time and attention to this important issue. I have more information on this topic than what I have provided in this submission, and I would welcome the opportunity to attend a hearing of the inquiry and give evidence.

Please contact me directly should you require any further information about my submission or clarification of any kind.

Regards,

Paula Wallace