Contemporary Perspectives on the Development of Australia's Animal Research Regulation

Karina Monique Burns
Bachelor of Psychological Science (Hons.)

Department of History
University of Adelaide

A Thesis Submitted in Fulfilment of the Requirement of the Degree of Doctor of Philosophy (PhD)

April 2022

Abstract

This thesis considers historical and current practices in Australian animal research. I address: (i) considerations in animal model choice; (ii) Australian regulatory structures in animal research; (iii) transparency in Australian animal research; and (iv) transnational comparisons of these themes.

I review the literature on Australian animal research regulation from historical and contemporary perspectives and then situate my research questions within their global and historical context by reviewing the history of animal use in experimentation.

In a case study considering animal model choice, I review research in psychology using Australian marsupials in the place of standard model organisms. The primary aim is to evaluate the nature of studies choosing to use marsupial species. I am interested in how animal model choice is influenced by different factors such as the research question, the suitability of the animal to a research environment, and how the animal is framed in broader society. This discussion demonstrates that there are useful experimental models amongst Australia's marsupial species.

I address changes in Australian regulatory structures around animal research through the framework of The Code[1], which guides Australian legislation on animal research. Replacement as a construct is considered here as a vehicle of change, with regulation and practice moving away from traditional animal models and exploring alternatives, motivated by ethical concerns and the need for better translation to human clinical outcomes. I emphasise the importance of the Australian Government and public supporting the development of alternatives to animal models.

I argue that transparency is a vital element of the scientific process, and this is particularly true for research that makes instrumental use of animals. I appraise the processes Animal Ethics Committees (AECs) undertake in reviewing and approving applications for animal research. I respond to a claim that these committees do not reject projects by conducting a quantitative analysis of application outcomes in a sample of Australian AECs. I conclude, based on this research, that changes relating to transparency should be implemented within the AEC process to ensure public trust.

[1] The Australian Code for the Care and Use of Animals for Scientific Purposes

A transnational comparison of the themes that emerged through the discussion of historical and current practices in Australian animal research frames the discussion around how Australia may be different. I discuss the state of transparency in the US, the UK, Canada and Europe, comparing the extent to which this has been made a priority. I then evaluate and compare the processes and structures in place for the review and approval of animal research in these jurisdictions. Australia has fallen behind other countries in implementing transparency within the regulatory structures of animal research, and in supporting the development and validation of alternative non-animal models.

I present concluding statements in relation to Australia's current regulation of animal research and the state of animal research transparency. I also discuss the future of animal research in light of claims that the translation of animal research to human outcomes is poor; emerging non-animal research models become crucial from a practical standpoint, and there is a need for greater government investment.

HDR Thesis Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

Signed, Karina Burns

Acknowledgements

I would like to thank my supervisors Rachel Ankeny and Michael Dietrich for their support and the amazing opportunities I was given over the course of my PhD. Presenting and networking at conferences all over the world was a massive highlight, and one I have come to appreciate even more since international travel stopped during the pandemic.

Thank you to my family, Loretta, Nick, Errol, Maisie, Liam, Catman, and even Maku, for your ongoing support throughout this process. I feel lucky to have all of you. Special mention to Dad who never let me give up, but also reminded me that there are two kinds of theses, perfect ones and submitted ones. Thank you for reading my work, giving feedback and being a sounding board for my ideas over the last six years.

Thank you to Liam for being your calm and practical self and always offering a refuge from the academic world. I am so grateful to have had you by my side throughout this entire process.

Thank you to my dear Napier crew who were the only ones who understood what it felt like doing a PhD at the same time as a long-distance relationship and were always there for Bachelor and pizza nights, Friday wines and real talk. Emily, David and Yvette, you were the best thing that came out of this PhD. Special mention to Yvette who survived level 9 of Napier and the cockroach invasion with me and has been by my side since day 1.

Conference papers

2017:

International Society for the History, Philosophy and Social Sciences of Biology: Sao Paolo, Brazil, July 2017, **How much can a koala bear?** Based on Chapter 2

2018:

Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART): Canberra, Australia, July 2018, **Using 'The Code' to trace policy change in animal research practices in Australia 1969 – 2013** Based on Chapter 3 and Chapter 4

History of Science Society: Seattle, United States, November 2018, **The Function and Value of Animal Ethics Committees in Australia: Historical Perspectives and Current Practices** Based on Chapter 4

2019:

International Society for the History, Philosophy and Social Sciences of Biology: Oslo, Norway, July 2019, **Keeping animal research practices in Australia honest: A discussion of transparency, translation and replacement in animal research** Based on Chapter 4

Animal Research Unbound: Exeter, United Kingdom, July 2019, **Keeping animal research practices in Australia honest: A discussion of transparency, translation and replacement in animal research** Based on Chapter 4

Chapter 1: Introduction

This thesis considers historical and current practices in Australian animal research. Within this broad spectrum there are four key focal points. I will address: (i) considerations in animal model choice; (ii) Australian regulatory structures in animal research; (iii) transparency in Australian animal research; and (iv) transnational comparisons of these themes. Noting the broad scope within the animal research ethics space covered by the four body chapters of this thesis, the sparse literature within an Australian context around these issues necessitated this broad lens of investigation. The present introductory chapter will provide a background to some of the topics that will be discussed throughout this thesis. Primarily, I will address the timeline of animal use in experimentation, the history and development of animal protection movements, and the development of Australia's animal research regulations. I will also briefly consider alternate narratives which are not centred around moral or ethical arguments that contest the validity of animal use in research. A preliminary review of existing literature in the area of animal research in Australia will be provided but a focussed review on the literature will be integrated into each of the main chapters.

Current discussions in the values in science literature also provide a link between the four independent body chapters together. There has been ongoing debate on the relationship between science and values. The value-free ideal, which was widely accepted by philosophers of science from the 1960s onwards, proposes that science should be kept separate from its broader social context: "science is (or should be) a value-free enterprise, and that scientists should not consider the broader implications of their work when conducting research" (Douglas, 2009, p. 44). Contemporary discussions in philosophy of science however, question if and how values can be separated from science. Elliott and Steel (2017, p. 3) write: "values can be a serious threat to the objectivity of science, but they can also play an essential role in responsible scientific research". One example they provide to support this notion is the public expectation that scientists will value the lives of animals they use in research: "we want them [scientists] to value the health and safety of the laboratory animals and humans that participate in research experiments" (Elliott & Steel, 2017, p. 3). The idea that values are deeply rooted in the history of animal experimentation - with public opinion often shaping the regulations which have been implemented for the purpose of protecting research animals - is pivotal to the current thesis. The way that science and values are entangled is particularly visible when considering the contemporary history of animal

experimentation. Each of the following discussions will consider the role of values and public opinion in the determination of scientific practices.

Chapter 2 considers animal model choice using a case study on Australian marsupials in psychology research. This identifies marsupials as native iconic species which may be uniquely valued within Australian culture, and consequently may be controversial research subjects. In this chapter, I argue that the narrow scope of much animal research, with its focus on standardization, may contribute to the arguably poor translation of animal studies to human outcomes.

Chapter 3 provides a historical overview of Australia's regulatory structures around animal research based on an analysis of Australia's national regulatory document, the Australian Code for the Care and Use of Animals for Scientific Purposes (hereafter: 'the Code'). I combine an analysis across its eight editions from 1969 to 2013 with a literature review of animal research related search terms within an Australian periodical database. I focus on the period from 1983 to 1996 as a time of heightened discussion on topics surrounding animal research, contemplating different interacting factors which influenced the Australian public's perception of animal research. This chapter also addresses arguments concerning the replacement of animals in research and the development of non-animal models, particularly in light of claims that animal models do not translate well to human clinical outcomes. Overall, this chapter argues that the trajectory of animal research regulations in Australia, and the conversations both in the public domain and amongst the decision makers, was both a reflection of global trends, as well as unique, due to Australia's comparatively short history of animal research.

Chapter 4 discusses transparency in Australian animal research and analyses the Australian system of reviewing applications for animal research through institutional Animal Ethics Committees (AECs). The analysis of AECs is in the format of a quantitative inquiry into application outcomes, responding to a claim that no applications are rejected by these committees (Russell, 2012). In this chapter I argue that we need more uniform policy implementation directly relating to the communication of process, husbandry, and outcomes of animal research. One key element of this is the annual reporting of animal use statistics from every Australian State and Territory, which can then be translated to a nation-wide figure for the purposes of international comparisons. Another element of this relates to Australia's regulatory bodies: Animal Ethics Committees (AECs). Frameworks within animal

research regulation in this country continue to inhibit information sharing and openness and changes relating to transparency should be implemented within the AEC process to ensure trust from the wider public.

Chapter 5 provides a transnational comparison between Australia, the US, Canada, the UK, and Europe, providing an overview of the ideas that emerged in the preceding chapters. I argue that Australia has fallen behind other countries both in the area of implementing transparency within the regulatory structures of animal research, and in supporting the development and validation of alternative non-animal models.

Chapter 6 identifies important overarching themes and proposes future directions in this field. I argue that as a country with a short post-colonial history of animal experimentation, Australia should be leading the way in progressive thinking on these issues and engaging in debate on how we can achieve scientific goals with less harm to sentient creatures. Ultimately, I argue that across the various avenues I have explored in this thesis, Australia is not the progressive nation it could be in the area of re-thinking animal research, and I hope we can rise to the challenge.

A brief history

The use of animals in experimental research is in no way a modern practice; there are examples across history of animals being used in an attempt to understand the intricacies and complexities of the human condition. Here I will be considering the history of animal experimentation from a perspective based upon Western history and philosophy. Experimentation using animals arose at different times in different parts of the world, but the scope of this thesis only allows for capturing those countries particularly relevant to the development of Australia's own use and regulation of animals in research. When considering the historical development of human knowledge, one thing that becomes apparent is that it does not follow a linear trajectory. That is, often, a commonly held but erroneous belief or understanding may be perpetuated for decades or even centuries unchanged, with potential advancement often met with scepticism or outright opposition. This is particularly evident when tracing scientific technique from its origins through to the present day. Relevant to the discussion of the history of animal use in research are the concepts of *animal welfare* versus *animal rights*, these concepts are discussed in detail below.

Some of the earliest documentation of animal experimentation dates back to the beginnings of scientific investigation, as early as 6th-5th century BCE (e.g. see Franco, 2013;

Rupke, 1987); these early records come from Roman and Greek physicians undertaking methods of investigation resembling what is now known as dissection and vivisection[2]. In this time the human body and its functions were not well understood, but it was recognised that seeing organs in their living state gave a more accurate indication of their function. In spite of its early beginnings, experimentation using animals remained largely dormant for the duration of the middle-ages, only re-emerging in Europe around the 16th century with the cultural and intellectual movement of the Renaissance. This is a clear example of another phenomenon which emerges when examining the development of human knowledge across time: the cultural climate greatly influences the potential for advancement. The middle-ages, rife with religious explanations for both prosperity and suffering, left little room for the growth and progression of science.

Animal experimentation came back into common practice in Europe around the 16th century, with scientific inquiry snowballing over the proceeding centuries in a pursuit of knowledge. In early experimental procedures, animal suffering was rarely acknowledged due to the commonly held beliefs in the 16th and 17th centuries about animals' capacity for suffering: an experience believed to be uniquely human. This understanding was perpetuated by such writings as *Animals are Machines* by French philosopher René Descartes. Descartes likened animals to machines and wrote that the ability to produce and comprehend speech separated man from 'beast' arguing that "this does not merely show that the brutes have less reason than men, but that they have none at all" (Descartes, reproduced in *Animal Rights and Human Obligations*, 1976, p. 62). From this conceptualisation it was inferred that animals were not capable of suffering, or indeed any other human experience such as pleasure or boredom, "the metaphor of body-as-machine had enormous implications for medical inquiries, and especially for the use of animals as research subjects" (Shanks & Greek, 2009, p. 40). Part of the need to separate humans from animals at this time was based upon the strong religious underpinnings of society, specifically, the concept that humans are made in the image of god, with a soul "entirely independent of body" (Descartes, reproduced in *Animal Rights and Human Obligations*, 1976, p. 63). Despite the modern incompatibility between science and religion, in the time of the mechanical metaphor, "God, as the designer of the natural machine, was just one of the ways in which science and religion came to enjoy

[2] Vivisection is a term used for experimenting on live animals, historically in the absence of anaesthetics or analgesics.

a cooperative relationship" (Shanks & Greek, 2009, p. 40). Another common conceptualisation which still abounds today is that the human life has greater value due to superior mental faculties, and therefore humans are entitled to use animals instrumentally, irrespective of current understandings of the animal cognition. This notion has been labelled as 'speciesism', a term first used by Richard Ryder in 1970, which appeared in an independent publication in 1971 in the book *Animals, Men and Morals: An Inquiry into the Maltreatment of Non-humans* (Godlovitch, Harris, & Godlovitch, 1971). The term was popularised by Peter Singer - a key player in the modern animal rights movement – from 1975 onwards. Speciesism, like racism or sexism, is described as being discrimination towards one group based on perceived differences, in this case, non-human animals are considered as belonging to 'lower' species than humans. This view, unlike that of Descartes, does not deny that animals can feel pain and suffer, but that human gain takes precedence over this suffering. In modern science it is still believed that if the human gain is great enough it will justify the cost of animal suffering. This view is defended by Wesley Smith (2012) in *A Rat is a Pig is a Dog is a Boy*, who in a discussion on the difference between the animal welfare and animal rights movements, states that "human beings stand uniquely at the pinnacle of moral worth" (p.3). This argument will be considered further below in a discussion of the development of the animal movements and what they stand for.

Increasingly, society moved away from religious explanations for various phenomena, and instead searched for scientific ones. This began largely with the acceptance of the germ theory of disease towards the end of the 17th century. A significant implication of this was the search to understand disease processes, from their antecedents and constituents to the way they function in the body including what parts of the body they inhabit. New ways of studying these processes were continually developing, providing more exact and scientifically useful findings. A large part of these investigations involved animal experimentation, from the early processes of studying the disease and its functions, to the eventual development of vaccines and the testing of these: "[t]he germ theory of disease represents one of the places where non-human animals came to play an important role in medicine" (Shanks & Greek, 2009, p. 57). The more legitimacy science gained, the more trust was put in the scientific methods used, including the use of animals. A key example of the weight of the public and government being thrown behind the scientific community was in the polio outbreak which peaked in the first half of the 20th century and rapidly declined following the introduction of inactivated polio vaccine in 1955 and the introduction of oral

polio vaccine in 1961 (Centers for Disease Control and Prevention, 2021, p. 301). The development of the polio vaccine was also significant in its implications for animal research. In particular, non-human primates were used as test subjects on a larger scale than had been seen previously, and their use in scientific research escalated from this point onwards. Primates were imported to the research institutes in the United States working on developing a vaccine, causing significant controversy in the animal welfare community and the wider public based on the conditions under which they were transported. Deborah Blum in her book *The Monkey Wars* suggested "at least a million monkeys died in the race to halt polio; by some estimates the toll reaches five times that" (Blum, 1995, p. 46). Rowan (1984, p. 110), called the development of the polio vaccine "[t]he main event leading to the expansion of primate research". Other sources have suggested additional reasons for the increase in primate research; primarily the increased use of plane travel for importing the animals as a replacement for ships and trains. This more efficient mode of transport in combination with availability of sedatives to calm the animals for the duration of the transit, resulted in a reduction of mortality during the journey (Blum, 1995). Laboratory animal use in the 20th century peaked in the 1970s, both in the context of animal numbers being used in research up until this point, and in the public sentiment towards animal research: "In an age of heroic science … the vast majority of the public respected and trusted scientists and seemed not to question their need or right to experiment on animals" (Rudacille, 2000, pp. 123-124). This sentiment continued until the late 1970's and into the 1980's when a minority of the public began to protest the assumed use of animals in both experimental and other settings.

Modern research utilizing animals falls under regulations and restrictions based on the nature of the investigation and its utility, the animal model it proposes to use, and the degree of anticipated suffering to the animals. When suffering is anticipated, researchers are required to use the appropriate anaesthetics and analgesics to minimise this suffering. Regulations around animal use in research differ depending on where the research is based, these differences will be explored in Chapter 5 as part of a transnational comparison. One framework for animal welfare in research has come to play an important role in defining the regulations which govern animal research throughout the world. This model is referred to as 'The 3Rs' and was the culmination of an investigation conducted by William Russell and Rex Burch for the Universities Federation for Animal Welfare in the United Kingdom (Hubrecht & Carter, 2019). The findings of this investigation were published under the title *The Principles of Humane Experimental Technique* in 1959. Russell and Burch were strong

advocates of a framework which minimised unnecessary suffering in animal research subjects; in outlining the scope of their study they stated: “It has sometimes seemed that there is an irreconcilable conflict between the claims of science and medicine and those of humanity in our treatment of lower animals” (Russell & Burch, 1959, p. 3). Even this quote from Russell and Burch demonstrates the assumption that humans hold ultimate power over other animals. Their model is made up of three independent but aligned processes which are aimed at improving the welfare of animals in research settings. These are ‘Reduction’, ‘Refinement’ and ‘Replacement’. Reduction means to use methods which obtain the same amount of data using fewer animals and is described by the authors as being achieved through “the right choice of *strategies*” (p. 105; emphasis in original). Refinement means “to reduce to a minimum the amount of distress imposed on the animals that are still used” (p. 134). Replacement is described by the authors as “any scientific method employing non-sentient material which may in the history of experimentation replace methods which use conscious living vertebrates” (p. 69). These three processes are not mutually exclusive and can be implemented concurrently in an overall framework which aims to decrease animal use in research and reduce the suffering felt by those animals still used.

The contribution to scientific development provided by the laboratory animal in early Scientific discovery was substantive. The brightest minds of each century posed questions and pursued urgent problems, often aided by the use of animal experimentation. While many of these investigations were ground breaking, changing the conceptualisation of the human body and mind and ultimately the course of history, they often involved great suffering for their animal subjects. Science has progressed from unsophisticated experimental methods to the complex methods of inquiry employed today; concurrently, our understanding of animals’ capacity for suffering has grown, as has our advocacy for their humane treatment. The complexity of research techniques in modern scientific inquiry using animal models are largely believed to offer answers in disease prevention, detection and treatment.

Some in the scientific community would argue that there will never be a time when animals will not be useful to scientific inquiry; however, others suggest that as knowledge continues to grow and alternatives become available, the practice of animal experimentation will continue to decline: “the growth of alternatives has gained momentum during the last fifty years, and it is by no means clear that alternatives have been fully utilized or funded” (Linzey, 2013, p. 185). If the global weight of science and governmental policy could be put behind the development of alternatives to animal models, the future could see scientific

advancement with a reduction of animal suffering, and potentially a more valid model for human outcomes. The position I take on this debate has been continually developing throughout my research and I do not yet have a fully formed argument supporting my convictions. My perspective is that the use of animals in research has been a fundamental tool to scientific development throughout the twentieth century. Animals are not a perfect model but this is something that has been acknowledged as a challenge to be overcome by the scientific community. The ever-growing reliance of the modern world on technology in every area of life leads me to believe that this is the direction for scientific research too. While technology has been integrated into the scientific method to support the use of animal models, it is my strong feeling that technology will overtake the use of the animal model in its predictivity and efficiency in modelling human outcomes.

A timeline of animal advocacy movements and their catalysts

From the re-emergence of animal experimentation in the 16th century, to the present day, a level of opposition to this practice has existed. This opposition has come and gone over the intervening years, at times receiving criticism and triggering controversy, in some cases being discredited or feared because of its 'terrorist' activities. There have been many movements against the use of animals in experimental, and other, practices. These movements despite advocating for the humane treatment of animals are divergent in their ideologies, goals and tactics. An early movement which found its primary success in Britain was the so-called anti-vivisectionist movement. From the 16th century onwards, vivisection was popularised as a research method and teaching tool in Europe, attracting researchers from America who returned home to implement and develop its use. Vivisection was seen as integral to scientific inquiry due to its utility in understanding different functions such as the beating of the heart and the expanding and contracting of the lungs; and later in the deconstruction of disease processes and development of vaccines. Concurrently, opposition to it grew too, building momentum rapidly as the use of animal experimentation expanded and gained legitimacy: "around the middle of the eighteenth century a differentiation in attitudes towards animal experiments had developed, ranging from scientific enthusiasm about the method to critical doubt about its usefulness or even to outspoken indignation at the cruelty involved" (Rupke, 1987, p. 30). Anti-vivisectionists were the precursor to modern movements, namely the animal welfare and animal rights movements.

Peter Singer's book *Animal Liberation,* published in 1975 is often viewed as the primary catalyst for the opposition to the human use of animals in science, and agriculture

and by the fashion, pharmaceutical and cosmetic industries. While today many would argue that Singer's views diverge distinctly from that of modern animal movements (e.g. see, Smith, 2012), it is certain that many of his ideas were instrumental in the emergence of large-scale public opposition to animal industries. While this book is often recognised as a major catalyst for the modern Animal Rights movement, it should also be acknowledged that its ideological position is not one of animal rights but of a utilitarian/consequentialist stance. Singer presents a well defended argument which questions the superior position of humans above other species. He begins by addressing the concept of equality in humans, considering what the basis of equality should depend on, writing: "[e]quality is a moral idea, not an assertion or a fact. There is no logically compelling reason for assuming that a factual difference in ability between two people justifies any difference in the amount of consideration we give their needs or interests" (Singer, 2009, pp. 4-5)[3]. Following a deconstruction of equality in modern society and where we have gone wrong historically, he questions our assumed position above other species. The term 'speciesism' was introduced above and is used by Singer to draw a parallel, conceptually, between injustices and atrocities committed on groups of people based upon race or gender, with the instrumental use of animals by humans justified by difference in species. He defines speciesism as "a prejudice or attitude of bias in favour of the interests of members of one's own species" (Singer, 2009, p. 6). Singer's argument implies lifting the barrier between humans and animals, he justifies this by saying that some animals have greater mental capacity than some humans (he refers in this argument to infants and to the intellectually disabled in comparison, say, to chimpanzees).

A critic, Wesley Smith argues however, that "[m]oral value should not be based on the *capacities of each individual,* since that standard would obliterate universal human rights, but upon the *intrinsic nature* of species" (Smith, 2012, pp. 241, emphasis in original). He continues, saying that "[r]easoning, using language, inventing, projecting out into the future, creating … are capacities that flow from the *nature* of humans and are absent from the natures of all animals" (Smith, 2012, pp. 241, emphasis in original). This view is rather limited however, as research continues to demonstrate the remarkable capabilities of animal species; some, if not all, of the previously mentioned capacities that Smith claims to be

[3] These quotations are taken from *Animal Liberation: The Definitive Classic of the Animal Movement* which is a re-release of the original 1975 publication of *Animal Liberation.*

'uniquely human', have in fact been observed in animals (e.g., see Zentall, 2013). Singer outlines the contradiction of experimenting on animals to learn something about humans: "either the animal is not like us, in which case there is no reason for performing the experiment; or else the animal is like us, in which case we ought not to perform on the animal an experiment that would be considered outrageous if performed on one of us (Singer, 2009, p. 52)[4].

There is no single person, publication or event that can be credited for the rise of the animal rights movement, but rather a cumulative effect of many actors and actions. Moreover, it is likely that the antecedents were somewhat different from country to country, despite the global feeling of discontent over animal treatment which grew throughout the 1970's and 80's. One event which has been repeatedly referenced as a catalyst for the movement in the US is the Silver Spring monkey case which arose from the removal by police of seventeen monkeys from the laboratory of Edward Taub in September 1981. The police raid was prompted by the 'whistle blowing' of a young laboratory assistant Alex Pacheco, who was in fact an animal rights activist infiltrating the laboratory. The case has been one of huge controversy, initiating "the most bitter 10 years in the history of relations between lab animal researchers and animal advocate groups" (Blum, 1995, p. 106). Pacheco co-founded the animal rights group People for the Ethical Treatment of Animals (PETA) which was in its infancy at the time that Pacheco started volunteering for Taub in the Institute for Behavioral Research. Taub's research was interested in teaching monkeys to use limbs which had suffered nerve damage mimicking the loss of function caused by stroke. These experiments had the outcome of self-mutilation in their animal subjects due to the animals not identifying nerve damaged limbs as their own. Pacheco was able to obtain photographic evidence of the poor condition of the monkeys and their housing, he was also able to give access to veterinarians to see the conditions for themselves. The images in particular sparked horror and anger in the public at the dismal conditions of the monkeys. It has been argued however, that "the real story of the Silver Spring monkeys bears little resemblance to the myth spun by PETA propaganda" (Smith, 2012, p. 73).

Following the release of *Animal Liberation* there was a change in the opposition to the use of animals for human benefit. Over the late 1970's and especially during the 1980's the

[4] This phenomenon is known anectdotally as 'the experimenter's bind'.

climate of animal protection intensified. The pre-existing animal welfare movement was rendered moderate next to new animal rights groups whose tactics were more direct and more forceful. While the welfare movement focussed on campaigning for research methods which minimised any suffering in the animal subjects used, the rights movement did not believe animals should be treated as the property of humans and therefore were focussed on abolition of any such practices which exploited an animal's right to freedom. Gary Francione, a Professor of Law known for his animal rights advocacy and writings on the abolitionist position of animal rights, describes this ideological distinction between the two movements, saying, "[t]he rights view reflects a shift from a vague obligation to act "humanely" to a theory of justice that rejects the status of animals as property and the corresponding hegemony of humans over nonhumans" (Francione, 1996, p. 1).

Within the rights movement there are a number of branches and it has been debated whether they collectively make up a single movement or if the more radical groups define something different again. Broadly, there are two streams within the rights movement: the *political* stream, which involves itself in campaigns and boycotts against industries, groups or individuals involved in animal exploitation; and, the *direct-action* stream which involves itself in sabotaging animal industries, including vandalism, property damage and often threats to individuals working within these industries. The second group has often been labelled as terrorists due to their unrelenting violent actions 'on behalf' of animals. PETA is a primary example of a political group. PETA was formed in the United States in 1980 by Ingrid Newkirk and the aforementioned Alex Pacheco and has since grown into an international organisation. While PETA is not directly involved in said 'terrorist' activities, some critics have drawn links between this group and other more action-oriented groups, including overlaps in group membership as well as public support of the actions of these groups and sometimes financial support for their members (Smith, 2012). The Animal Liberation Front (ALF) is an example of a group involved in direct and sometimes violent action on behalf of animals. The ALF was founded in 1976 by Ronnie Lee in the United Kingdom and soon expanded to become an international movement. Because of its illegal activities the ALF is a more underground movement with counterparts all over the world who target businesses and individuals that have been highlighted by the organisation. One source stated "[m]any scientists regard the front as a barely disguised division of PETA … [although the founders Newkirk and Pacheco] firmly deny any connection" (Blum, 1995, p. 115).

The ALF and similar organisations have claimed responsibility for a great number of illegal activities including laboratory break-ins, property theft, property destruction and terrorising of individuals, especially scientists involved in animal research, by way of threatening letters and defamation on public forums. These extreme actions have been thought to give a negative image to the animal rights movement, "[t]he ALF has been destructive enough to gain a place on the FBI's terrorist list" (Blum, 1995, p. 115). Smith (2012, p. 127) writes that: "[c]riminal attacks and threats against research facilities and businesses that use animals have infected animal rights advocacy like a low-grade fever over the last twenty years". Similarly, Rudacille (2000, pp. 204-205) argues that "[l]ike their nineteenth-century antivivisectionist forebears, these activists have alienated potential supporters with absolutist rhetoric and behaviour that has greatly diminished the moral legitimacy of their cause in the eyes of the public". For these reasons the animal rights movement has gained a number of critics, Smith argues "[o]ne of the primary threats posed by the animal rights movement to society is its unremitting campaign to thwart the advance of science and medicine by means of animal research" (Smith, 2012, p. 7). Further, he attacks the popular term in animal rights activism 'speciesism': "[a]nimals are not people. Any movement that seriously believes eating meat and raising domestic animals are equivalent to our most potent examples of barbarism and evil has no business preaching morality to anyone" (Smith, 2012, p. 40). These so-called 'potent examples of barbarism and evil' likely refer to the PETA campaign launched in 2004 which equated factory farming to the holocaust; its slogan 'holocaust on your plate' was banned in Germany following an outcry in response to the insensitive content. Although the stance taken by Smith is critical of the extremism of the animal rights movement, he posits that "[s]urely we can find a middle ground that doesn't grant unwarranted rights to animals but does permit robust protection of their welfare" (Smith, 2012, p. 232). He argues that "[w]e as humans – *and we alone* – have moral agency, which means that we have not only rights, *but also duties*" (Smith, 2012, p. 232; emphasis in original).

As is the case in any debate with strongly held opinions on both sides, it can appear from the outside that the individuals on the polar extremes of the argument are unable to rationalise or see the perspective of their opponent. On the scientific side, the far extreme can seem cold and uncompassionate, while on the animal rights side, the far extreme can seem 'anti-human' in their actions. Within the middle ground there are certainly some

contradictions in human behaviour when it comes to animals[5]. In the same way that humans place themselves atop the species ladder, other species are also ranked according to arbitrary factors such as their perceived intelligence or sentience, and their domestic relationship to humans. For an example, both historically and in modern science, the public is less averse to the use of rodents in experimental research over other animals such as great apes which are perceived to have higher intelligence and sentience, or domestic pets such as cats and dogs: "the toning down of the opposition to animal use in the life sciences had … something to do with the emergence of rodent species as a recurrent animal model in research … rodents like mice and rates were seen as despicable creatures by most of the public, and therefore less worthy of moral consideration" (Franco, 2013, p. 256). This is a blatant example of human preference for some animals over others, with no regard for the animal's capacity for suffering, ability to feel fear or recall past trauma. Comparable contradictions in human value judgements are seen in the animals we choose to eat, as an example, some Western cultures have caused uproar over the consumption of horse meat while being perfectly happy to eat a steak that comes from a cow. These ideas will be developed further in Chapter 2, where I will use the case of marsupial models in psychology research to consider the way value judgements around the roles of different animals modulates public response.

Rudacille (2000, p. 8) used the analogy of Frankenstein to discuss how we have become the mad scientist who tries to play god, manipulating the human body and its functions to extend its natural capacities and essentially cheat death:

> [o]ver one hundred years ago, Charles Darwin showed that humans are a kind of animal. But we are the animal that is not content with the pleasures and limits of animal life. Instead, we push beyond the limits imposed by nature and seek to remake the world, our bodies, and our fates. We seek the powers of gods - and science has given us those powers

She continues to look at the darker side of science and considers instances where scientific authority has been used to justify crimes against humanity. An example of this is the way in which Nazi ideology in Germany during the 1930's and 1940's used science to blur the lines

[5] My view is grounded in a capacities-based approach to animals taken in the tradition of Singer and Regan. I acknowledge that other approaches (e.g., relational) would not conceive of these differences as contradictions as such, but as many in society do hold capacities-based approaches, it is sufficient for my argument that these judgments often do create tensions or even contradictions.

between human and non-human - elevating the status of some animals above the status of some humans - with disastrous consequences. It is important to consider these times in history because science cannot always be heralded as the ultimate truth and not only is science continually being disproved or made redundant by new findings but can be used in harmful and immoral ways.

Peter Singer and Paola Cavalieri in 1993 edited and compiled a series of essays to form the book *The Great Ape Project: Equality Beyond Humanity.* The book had the intention of presenting a case for great apes (gorillas, chimpanzees, bonobos and orangutans) to be given equal moral status to humans (who are also part of the great ape family), the editors outline their objective: "We seek an extension of equality that will embrace not only our own species, but also the species that are our closest relatives and that most resemble us in their capacities and their ways of living" (Cavalieri & Singer, 1993, p. 1). This is a contentious subject, and many have strong opinions both for and against such an idea. Smith (2012, p. 59) concluded his argument against the Great Ape Project saying "Peter Singer and Paola Cavalieri gave a big boost to the animal rights movement's ultimate goal of subverting the unique status of human life". The book presents writings from a collection of individuals who have studied or had experiences with great apes and from these experiences pledge support for the project. These writings include findings on the genetic similarity between humans and other great apes, descriptions of the remarkably human-like behaviour displayed by great apes in the wild, as well as how some in captivity have learnt sign language, and thus a means of communicating with humans. Jared Diamond, a Professor in Physiology at the University of California describes the work of Charles Sibley and Jon Ahlquist on the 'DNA clock', an attempt to determine the degree of similarity between the great apes. Diamond discusses the findings that our closest genetic relatives are the chimpanzee and pygmy chimpanzee (bonobo), sharing about 98.4 percent of our DNA: "[o]ur important visible distinctions from the other chimps - our upright posture, large brains, ability to speak, sparse body hair, and peculiar sexual lives- must be concentrated in a mere 1.6 per cent of our genes" (1993, p. 95). In one passage Roger and Deborah Fouts, founders of the Chimpanzee and Human Communication Institute at Central Washington University, argue: "much of the biomedical research on chimpanzees assumes a kind of schizophrenic position: it justifies the use of chimpanzees as a medical model because of Darwinian continuity, and yet at the same time it claims moral immunity with regard to the physical and mental damage done to the chimpanzees on the basis that humans are different from other animals" (Cavalieri & Singer,

1993, p. 39). Roger Fouts has spent his career fighting against the standard treatment of chimpanzees in scientific research, fighting against the system he works within as a psychologist. The founding of the Great Ape Project has had still resonating impacts on animal experimentation legislation, and these continuing changes indicate just how far the animal rights movement has progressed in the last 50 years. In 2008, the Spanish Parliament passed a resolution to grant legal rights to great apes, in line with the Great Ape Project. Similar actions are being undertaken elsewhere, with outright bans or a tightening of research restrictions for studies using chimpanzees or great apes more generally.

Relevant to Chapter 2, consideration of animal research in psychology will be briefly considered here. According to Singer (2009, p. 42) "Many of the most painful experiments are performed in the field of psychology". Largely a study of mind and behaviour, the use of animal models in psychological research often involves a different kind of demand on the animal. Psychology often uses methods which tap into the emotional lives of the animal or how they learn and make decisions. Behavioural training for example is a repetitive, lengthy process which can involve fear or pain stimuli. These types of studies are potentially more burdensome on animals than other research because of the psychological distress they produce. Psychology is interested in the complex processes of human decision making, social relationships and family bonds, learning and perception, among others. These processes are difficult to study and can be considered unethical to study in humans, thus animal models are used in an attempt to replicate and ultimately give insights into these areas of psychological investigation. This is not without controversy, however: "Animal models in experimental psychology … have been strongly criticized in part because human psychological problems reflect familial, social and cultural factors that cannot be modelled in nonhumans" (Medical Research Modernization Committee, 2006, p. 5). Attempts in the past to study complex human experiences such as depression, alcohol and drug addiction and maternal attachment, have surprisingly been undertaken using animal models with varying results. Linzey (2013, pp. 182,) argues: "[t]he practice of creating animal addicts to study as models for human behavior is particularly unsound, given the dramatic physiological and metabolic differences between humans and animals. Further, there is no shortage of human addicts who could participate in these clinical studies". Unlike some disciplines in which replacements for animals may be developed, psychology (which often considers behaviour) requires a living observable research subject. While psychology has favoured the rodent species in research, "[a]pes and monkeys are favourite subjects … [o]f all nonhuman species, they are the ones

whose behaviour most closely resembles that of humans" (Linzey, 2013, p. 182). With growing controversy over the use of primates in research, the only alternatives to animals in these studies are humans. While this is a viable option, it presents a greater resistance to reform and it is likely that psychology will be a discipline which carries animal experimentation into the future. Psychology and animal research will be considered as a case study in Chapter 2, with a discussion of the development of this discipline and its use of animals, as well as a review of psychology research using Australian marsupials.

Other opponents to animal experimentation

It is not just animal rights activists who have something to say about the utility of animal experimentation. Shanks and Greek (2009, p. 20) in their book *Animal Models in light of Evolution* write, "we hope to show that standard uses of animals in biomedical research raise a host of issues in the philosophy and methodology of science that have nothing to do with the ethical confines of traditional philosophical interest". This argument, unlike the animal rights angle which bases its argument on ethics, takes a scientific stance on the question of whether animals should be used as predictive models for humans. It is clear that ethical and epistemological arguments are not stand alone, and if animal research cannot be justified on a scientific level this also has implications for the ethics of conducting research. However, it can be valuable to consider these two perspectives independently as often the ethical view is perceived to be emotion-driven, while this argument, based upon the failings of science, may be perceived as being more evidence-based. This perspective questions the application of findings from animal studies to humans, based on the differences between species, even those closely related like humans and primates. The authors discuss one case which is usually heralded as a great success of animal research, that is the development of the polio vaccine, and which has already been discussed above. While the authors acknowledge that animal models were instrumental in this process, they also led to false conclusions in the initial vaccine development. This was due to the assumption that the disease functions in the same way in both animals and humans. In this case, both the way the disease entered the body, and the parts of the body it inhabited differed between humans and the rhesus monkey model used, "[t]he animal model of polio … resulted in a misunderstanding of the mechanism of infection" (Medical Research Modernization Committee, 2006, p. 2). Ultimately, this disparity was identified and overcome, but it is a reminder that it cannot be assumed that animals can be used to perfectly model human disease processes, even the seemingly most insignificant differences can have complex and significant implications.

Shanks and Greek (2009, p. 59) suggest that "[w]hile it is often possible to find animals that are susceptible to human diseases, they may not be susceptible in the same way". These issues have also been discussed by Andrew Knight (2011), who systematically reviewed the translation of animal studies to human outcomes, finding worryingly low levels of translation. These arguments will be revisited in Chapter 3.

Overview of relevant literature

A number of scholars have discussed animal research within an Australian context; however, there is a considerable gap in terms of a broad overview that addresses current practices in Australian animal research regulation while retrospectively considering the progression of these regulations and the social and political context they developed within. The following will introduce some of the key literature in this area. This has been organised chronologically and further thematic analyses appear in subsequent chapters.

Although the Code was first articulated in 1969, discussions of uniquely Australian approaches to animal ethics began in 1989 with a report published following an inquiry into Australia's animal welfare standards in a number of domains including animal experimentation (Australia Parliament Senate Select Committee on Animal Welfare, 1989). The report on animal experimentation gave eleven recommendations regarding the practice and regulation of animal research. Significantly, one recommendation was to report animal use statistics to improve transparency: "The Committee RECOMMENDS that the Commonwealth, State and Territory Governments publish annually accurate and comprehensive information on the extent and forms of animal experimentation conducted within their respective jurisdictions" (Australia Parliament Senate Select Committee on Animal Welfare, 1989, p. xv, emphasis in original). There was also a recommendation regarding the development of alternatives to animal models through government funding: "The Committee RECOMMENDS that the Commonwealth Government establish a separate fund for research into the use of alternatives to animal experimentation and that grants be disbursed from this fund by a board composed of representatives of the scientific community, animal welfare organisations, ACCART [now ANZCCART] and government authorities" (Australia Parliament Senate Select Committee on Animal Welfare, 1989, p. xv). It is disappointing to note that thirty years after the publication of this report, there is still not accurate or consistent reporting of animal use statistics, contributing to poor transparency from within the scientific community, and still no government support for the development of

alternative non-animal models for research. The inaction on a national policy level has led to ongoing hesitancy with respect to information sharing from animal research institutions and their affiliates. This is directly demonstrated in the current work where many institutions I approached for data on applications for animal use in research declined to participate. This will be discussed in greater depth in Chapter 4.

Anderson and Perry (1999) in a paper 'Australian Animal Ethics Committees: We Have Come a Long Way' evaluate the development and progression of Australian AECs. The authors of this text were directly involved in the 1990 and 1996 revisions of the Code and both work within the scientific community. Their paper gives an overview of the regulatory structures in place at the time of its publication, and details the AEC system including its roles, the roles of its members, and its strengths and weaknesses. Given the position of the authors on the debate around the use of animals in research, the sentiment is sympathetic to the endeavors of the scientific community and does not therefore provide any meaningful critique of the AEC system.

In a paper in the *Journal of Animal Law*: 'Opening the Laboratory Door: National and International Legal Responsibilities for the Use of Animals in Scientific Research--An Australian Perspective', Sharman (2006) evaluates Australia's legal system around animal research and conducts a case study on the legislation in place in New South Wales. In a discussion of the role of AECs, Sharman (2006, p. 74) writes: "Notwithstanding the importance and scope of their functions, AECs remain largely unaccountable to the public due to the secret nature of much of their business and the sanctions that apply for breach of confidentiality. This creates a real likelihood of experiments being duplicated. It also makes the system more translucent than transparent as it means that only certain trusted members of the public are permitted to participate in the decision-making processes that affect so many lives". These critically important themes will be explored further in Chapter 4.

O'Sullivan (2008) in 'Transparency in Australian Animal Research Regulation - How Are We Doing?' unpacks issues around transparency in Australian animal research, considering the recommendations given in the Senate Select Committee report (Australia Parliament Senate Select Committee on Animal Welfare, 1989), and whether these have been implemented in the time since its publication. This paper also provides an indication of the state of transparency at the time of publication by surveying a number of prominent Sydney newspapers over the month of May in 2004. The findings of this media analysis demonstrated

that compared to other categories of animals such as wildlife and companion animals, animals in research were discussed infrequently and usually in a positive light. O'Sullivan (2008) discusses the different stake-holders in the issue of transparency in research, and notes that researchers, policy makers and animal advocates all support the idea of greater transparency, despite having different views on why this is important. AECs are also discussed in relation to transparency and the recommendations of the Senate Select Committee, O'Sullivan (2008, p. 28) notes that "although the AEC system has developed strongly, it is not self- evident that it facilitates transparency in significant ways … the extent to which AECs provides the wider community with a timely and detailed understanding of animal research practices is questionable. Indeed, the link between AECs and enhanced transparency is difficult to interpret". This link between AECs and transparency will be discussed further in Chapter 4.

Russell (2012) in a paper 'Why Animal Ethics Committees Don't Work', evaluates Australia's system of review for approving animal research, and identifies weaknesses. This paper outlines seven reasons why AECs may not work. One of these reasons is that the confidentiality built into these committees makes it difficult to assess objectively if they are indeed functioning correctly. Another reason is that the review of research proposals occurs at the end of the approval process, including after funding has been granted, creating pressure to approve projects. Considerable attention is given to the issue of replacing animals in research and the way this is considered within the AEC review process. This responsibility falls to the researcher, who needs to state in their application that no alternatives were found for considering their research question. Russell (2012) argues that lack of knowledge around alternatives developing in unfamiliar fields means that both the researcher applying to use animals, and the scientific member on the AEC may be unqualified to comment on the availability of alternatives.

Rose and Grant (2013) in a paper 'Australia's ethical framework for when animals are used for scientific purposes' evaluate changes in Australia's animal research regulation. This paper discusses changes in the Code against a backdrop of relevant events both within and outside Australia and considers the important role of AECs. The authors identify that for the Code to function successfully it needs to be supported by an ethical framework and effective governance, concluding that: "[u]nder the Code, Australia has developed a strong ethical

framework based on a system of institutional ethics' committees and supported by effective governance arrangements" (Rose & Grant, 2013, p. 321).

Villanueva (2015) in the book *"In the Corridors of Power": How the Animal Movement Changed Australian Politics, 1979–1991* considers the animal movement within Australia. While this text is a useful point of reference for the animal movement within an Australian context, the discussion largely centres on the animal agriculture industry. This does provide a picture of the degree of activism that occurred in Australia with a direct focus on the animal research industry, given that this is a minor focus of this text.

Whittaker (2014) in a paper 'Animal Research Regulation in Australia – Does it Pass the Test of Robustness', critiques the Australian system of animal research regulation with discussion of existing literature and comparison with international systems. The author then offers suggestions for reform, these include to give the Code greater legal power by enforcing it under State and Territory animal welfare acts, and to include a statistician on AECs. Another useful suggestion which I also reiterate in Chapter 4 is "[m]andating a pre-review of applications for scientific validity by a well-constituted committee of expert scientists" (Whittaker, 2014, p. 14).

Timoshanko, Marston, and Lidbury (2016) in a paper 'Australian Regulation of Animal Use in Science and Education: A Critical Appraisal' evaluate Australia's animal research regulatory framework. This paper provides an overview of the system used in Australia to regulate animal research with a comparison to both the US and Europe. Timoshanko et al. (2016) discuss four ways that Australia's regulatory system could be improved, importantly these include suggestions for improved transparency, the implementation of a national authority to oversee the approval process for research as well as the reporting of nation-wide animal use statistics, and government investment in the development of non-animal alternatives in research.

Paytas (2018) in an article for *The Conversation* discusses the need for greater openness in Australian animal research, calling for a similar commitment to transparency upheld by the Concordat for Openness on Animal Research in the UK, which currently has 122 signatories. While this article does not appear in a peer reviewed journal as many of the papers discussed here do, I use this article as a way of considering discussion happening in the public domain around these issues.

An article published on the European Animal Research Association's website 'Call for Australia and New Zealand biomedical sector to follow Europe and be more open about animal research' (European Animal Research Association, 2019) reports on a survey of Australian and New Zealand animal care workers calling for greater transparency in animal research. This survey showed that 87% of respondents believed animal research institutions should be more open. This article also points towards Australia developing a similar commitment to openness as is seen in the UK and other European countries.

In September 2019 the NHMRC published an information paper on the implementation of the 3Rs of Reduction, Refinement and Replacement in Australian animal research (National Health and Medical Research Council, 2019). This paper is based on a survey commissioned by the NHMRC on this topic (ORIMA Research, 2018). The paper states: "Despite the importance of the 3Rs, there is limited documented evidence about the use of the 3Rs in Australia. To address this information gap, NHMRC's Animal Welfare Committee has overseen a project to obtain current information about how the 3Rs are being implemented in Australia and factors that enable or hinder their development and adoption" (National Health and Medical Research Council, 2019, p. 5). The survey asked a sample of Investigators, AEC members and Institutional Representatives to share their understandings and attitudes on the 3Rs and their implementation. A "lack of appropriate scientific or technological innovation" was identified by all responding groups as a barrier to successful implementation of the 3Rs in Australian animal research (National Health and Medical Research Council, 2019, p. 18). The 3Rs are discussed further in both Chapter 3 and Chapter 4.

The publications form the groundwork for the current thesis, providing critique and discussion around Australia's regulatory system for animal research. Importantly many of the recommendations made over the last thirty years for improving the regulatory system for Australian animal research have not been implemented, and I reemphasise these suggestions throughout this thesis. The following section will situate this discussion within its historical context, considering the progression of animal research and the development of animal rights movements from a more global perspective.

A timeline on legislation in animal research

It is interesting to note which countries have had the greatest reforms in animal protection and those which lag behind. For example, after experiencing some of the most

extreme activism related to animal research, the UK is amongst the most progressive countries with respect to animal protection in the research space. The United States, similarly, experienced extreme activism related to animal research, but animal protection through legislation in the United States has lagged behind its counterparts. I am interested in characteristics of the reforming countries in contrast to those slow to reform. I am also interested in how the history of Australian legislation fits within a global perspective; especially given its short history of animal experimentation, particularly when compared to European countries. I will consider elements of the Australian cultural climate which may have had unique impacts upon what animal models are used in research, how regulations were implemented and what degree of animal activism was experienced. In *The Global Guide to Animal Protection* (2013, p. 3), editor Andrew Linzey posits that "there needs to be recognition that animal abuse transcends national boundaries and should therefore be a matter of international concern". This angle identifies that the state of communication and technology in the modern world could allow for greater cooperation and collaboration on the standards of animal protection. Linzey (p. 3) continues, saying "[r]epresentatives of animal protection societies need to assemble regularly on a worldwide basis to consider strategies and reform. We need to create a new worldwide forum that will be a voice for animals globally". Greater collaboration and sharing of ideas when it comes to animal research reform is an important step. Moreover, this collaboration could allow for more transparency by way of sharing national statistics on animal use in research. Transparency in this context refers to the direct communication of research methods and animal husbandry, as well as the significance of research from the scientific community to the public. Siobhan O'Sullivan identified the concept of transparency in animal research as being a key requirement desired by the public, policy-makers and researchers alike. O'Sullivan evaluates the concept of transparency within an Australian context, saying "its elusiveness, and the benefits it could bring, have been at the centre of the animal research debate in Australia for the last 30 years" (O'Sullivan, 2008, p. 21).

With the objective of tracing the history of animal research regulation in Australia, a brief comparison of legislation passed in Australia and internationally will be used here to identify ways Australian regulation may have been influenced by international policy. Using this timeline as a point of reference it may be possible to identify other influencing factors which may be Australia-specific such as aspects of the cultural climate, influential figures in animal rights or politics, and important publications. This discussion will be further

developed in Chapter 5 which addresses animal research regulation and the issues that surround it from a transnational perspective.

Especially in the nineteenth and early twentieth century Australia took its influences from outside sources, the UK in particular. The first animal protection legislation 'Martins Act' - named after Richard Martin who campaigned against cruelty to animals - was passed in the UK in 1822 (Jamieson, 1990). This act offered some minor protection for a small number of farm animals, primarily cattle. The Society for the Prevention of Cruelty to Animals: SPCA (the precursor to the RSPCA) was formed in Britain in 1824. In 1876 the British Cruelty to Animals Act was passed, this was the first documented legislation which mentioned protections for animals within experimental settings; reflecting the active Antivivisection movement in Britain during this time. It has been suggested, however, that the act did not succeed in the eyes of its supporters, "they felt that cruelty had been institutionalised rather than banned" (Linzey, 2013, p. 9). That is, by laying down simple and largely inadequate guidelines, the perceived abuse to animals would continue but now be protected by the legislation implemented to protect them. The first animal cruelty legislation passed in colonial Australia was in Van Diemen's Land (Tasmania) in 1837 with other colonies following after 1850 (Jamieson, 1990; White, 2016). The Victorian Society of the Protection of Animals was established in 1871 and in the same year proposed an act which was passed in Parliament (An Act for the Protection of Animals: 24th December, 1881). This act addressed cruelty to animals generally, in fact, Section 12 of the act states an exemption for: "any experiment or vivisection performed upon any animal by any legally qualified medical or veterinary practitioner for the purposes of scientific investigation". However, it does stipulate that appropriate anaesthetics be used for pain, and that euthanasia be the end point in cases where the experiment inflicted such injury that "recovery would involve serious suffering".

It was not until the twentieth century that research-specific legislation began to be implemented; in 1966 the Laboratory Welfare Act was passed in the United States and amended as the Animal Welfare Act in 1970. In 1969 the Australian Code for the Care and Use of Animals for Scientific Purposes was established, this document applies nation-wide and is updated to reflect relevant changes, it is now in its 8th edition. In 1986 the Council of the European Union approved Directive 86/609/EEC for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes. In the same year the Animals (Scientific Procedures) Act 1986 was implemented in the UK.

The matter of animal protection in Australia is managed by jurisdiction; therefore, each State and Territory has different legislation, implemented at different times, starting from 1985 with the Animal Welfare Act in South Australia, and the Animal Research Act in New South Wales. There was legislation passed in the remaining Australian States and Territories over the following two decades, Victoria in 1986, the ACT in 1992, Tasmania in 1993, the Northern Territory in 2000, Queensland in 2001 and Western Australia in 2002. With the exception of New South Wales, the matter of animal research regulations is addressed under the broader legislation of animal welfare or animal protection. This system has its advantages as well as its disadvantages. One issue is that because each State and Territory is managed separately, there are no easily accessible statistics on nation-wide use of animals in research; an issue which may be directly linked to the lack of researcher transparency. In 1989 a report was published by the Senate Select Committee on Animal Welfare following six years reviewing "the question of animal welfare in Australia with particular reference to: (a) interstate and overseas commerce in animals; (b) wildlife protection and harvesting; (c) animal experimentation; (d) codes of practice of animal husbandry for all species; (e) the use of animals in sport" (Australia Parliament Senate Select Committee on Animal Welfare, 1989, p. 1). At the outset of the report the Committee notes that "[f]ew statistics are kept of the extent and range of animal experimentation conducted in Australia" (p. 9), indicating that only in the last 30 years has Australia started to keep records of the numbers of animals used in research, and even today these data are incomplete, with only estimates of total numbers of animals used nationally. In reference to this, the report states "[t]he Committee believes that there is a need for the Commonwealth, State and Territory Governments to publish annually details of the numbers and particular uses of animals, by species, used in experiments in research and teaching", on the grounds that "the public has the right to know" (Australia Parliament Senate Select Committee on Animal Welfare, 1989, pp. 20-21).

It appears that this concept of 'institutionalised cruelty' mentioned above in relation to early British legislation, is one which has been perpetuated in the eyes of those opposing animal research. In a paper on an 'Australian perspective' on legal responsibilities for research on animals, Katrina Sharman discusses a case study on New South Wales legislation, saying that animal welfare laws "are often used as shields to justify ongoing experimentation on animals" (Sharman, 2006, p. 67). Similarly, Linzey writes: "animal

testing has become institutionalized and that, like all institutions, it has a tendency to perpetuate itself even and especially in the light of criticism" (Linzey, 2013, p. 185).

This thesis will deal with animal research ethics in Australia using historical perspectives to appraise current practices and consider future directions. An overarching framework based upon discussions in the values and science literature ties these topics together, with each chapter grappling with the relationship between science, values, and the public. The following chapter will consider generally the field of psychology, with a special focus on research interest in Australian marsupials as model organisms. This chapter will be used to consider alternative non-standardised animal models in research, but also to evaluate the way we as a society assign value to different animals, with marsupials being a native species to Australia and therefore putatively holding a special value in the Australian psyche. Chapter 3 takes a broad look at both historical and current regulation of animal research in Australia, alongside a discussion of translation of animal research to human outcomes, and the development of alternative models in research. Chapter 4 focusses on research transparency, an important theme which has emerged relating to the regulation of animal research in Australia, as part of this discussion, the processes undertaken by Australian AECs is examined through quantitative analysis. Chapter 5 ties these discussions together by looking at themes which emerge in the preceding chapters from a transnational perspective; considering how Australia aligns or diverges from the US, Canada, the UK and Europe, and the ways in which this country may be unique in its regulatory framework and its history of animal experimentation.

This thesis has the following aims and objectives which underpin the arguments I make throughout and as outlined above:

1. To evaluate the current regulatory structures for animal research in Australia against the backdrop of their historical development and within the framework of values and science.

2. To consider and evaluate current debates around animal research in this country, specifically:

    a) The way animals are valued and the structures which surround animal model choice.

    b) Transparency in the scientific community.

c) Translation of animal research to human outcomes.

3. To consider how Australia compares to other countries and regions in the historical and current frameworks around animal research, and particularly the ways in which Australia is unique.

Chapter 2: The Role of Value Judgements and Standardisation in Animal Model Choice: A Case Study on Marsupial Models in Psychology

"Historical questions associated with the choice of nonhuman test organisms are central to understanding the development of twentieth-century experimental psychology and to understanding research traditions based on the scientific promise of generalizing from other animals to human beings" (Logan, 1999, p. 4).

The human-animal relationship is a complex one defined by needs, desires, or both, be they for food, companionship, entertainment, or science. The way animals are valued by humans is modulated by the roles they have been assigned. Certain animals, such as domestic pets and native or exotic animals are elevated in value, while others are used instrumentally for human gain, or eradicated because they have been labelled as pests. Palmer (2010) argues that our obligation to assist animals can be considered within a framework of wild versus domesticated, and that functionally psychologically equivalent animals can be treated differently based on membership of these categories. Palmer uses the example of public reactions to animal harm can be modulated by a perceived responsibility to these animals. These roles have persisted long enough that we do not actively question why we love some animals and despise others, why we eat some animals or hunt them for sport yet are outraged to see the same done to another species, or why we go to great lengths to protect some animals which have in fact become endangered through human actions such as poaching or deforestation. But what are these roles based on, and could we defend these with reasons and arguments that explain why certain animal lives are worth more than others, or is it merely they are worth more to humans based on our need? This has been well articulated recently by the moral philosopher Gary Francione (Francione, 2020) on his social media accounts in response to the Australian bushfire crisis and the animal agriculture industry, he writes "[t]here is no morally coherent distinction between the animals we love and those we eat". Francione comes from the tradition of Animal Rights and his views are grounded in the philosophy that animals should be valued in relation to their capacities, and as such that there is an inconsistency in treating animals with similar capacities differently. Chapter 1 of this thesis introduced some of the discussions in the values and science literature that are relevant to this chapter. The concept that value judgements are intertwined with the use of animals in research contradicts the longstanding 'value free ideal' which proposes that science should be kept separate from its broader social context.

This chapter presents a case study on animal choice in the field of psychological research. Here I will review research in psychology using Australian marsupials in the place of standardised model organisms such as the rat or mouse. Amongst a matrix of proposed criteria for animal model choice (Dietrich, Ankeny, Crowe, Green, & Leonelli, 2020), novelty is one factor that may play a role in the choice to study a non-standardised and lesser studied model like a marsupial species. Model organisms have been described as "a specific subgroup of organisms that have been standardized to fit an integrative and comparative mode of research" (Ankeny & Leonelli, 2011, p. 313). The broad framing of this case study is around the ethics of conducting research using species intrinsically linked with Australia's national identity. This question leads into a discussion of the subjective value placed on different animals in the context of research, in particular, why it is that purpose-bred rodents may be perceived as being more ethically viable as research models than marsupials of a similar size. The narrow focus of this case study is to consider the nature of research in the field of psychology which chooses to use Australian marsupial species. This review will evaluate the role of standardisation in contemporary research and propose that marsupial species are valuable models as experimental organisms. I argue that the restricted focus on specific species of animals that have been standardised to reduce the impact of individual variability, may contribute to the alleged poor translation of animal research to human outcomes.

The following will expand upon the aims and motivation for the current research. A brief background will detail some of the literature in this area, including from the perspective of the history and philosophy of science on the choice of both experimental and model organisms. A historical account of the development of the discipline of psychology, its adoption and, arguably, adaptation of the scientific method, and the beginnings of animal psychology will be provided to situate the current research. A discussion around the choice of animal models in psychological research will lead into a consideration of marsupials as experimental models in psychology. My research methodology will be outlined followed by an overview and analysis of the literature obtained using the search terms and databases listed in Appendix 1. Finally, a discussion of implications for marsupials as models in psychology, and conclusions around contributions to the field will be provided.

The decision to focus on marsupials was motivated by the more recent trend for research to move away from the *official* list of model organisms to consider new and developing animal models (often termed 'emerging model organisms'; for example, see, Cold

Spring Harbor Laboratory Press, 2010). Marsupials are of particular interest for their evolutionary uniqueness: “[as] a group of mammals that have evolved along distinct lines from eutherian (placental) mammals but occupy many niches similar to those of eutherians … the study of marsupial psychology can address questions about the relative importance of niche and evolutionary history in determining learning abilities” (Bonney & Wynne 2003, p. 188). Another motivation to consider marsupials as potential models in research within an Australian context is they make up a large part of the native wildlife; there are an abundance of species and they therefore as a group make for an obvious source of potential research models.

Marsupials are undeniably part of the Australian national identity: the kangaroo features on the Commonwealth Coat of Arms; the national men's Rugby Union and Rugby League teams are the Wallabies and the Kangaroos, respectively; and there are numerous other such examples. Moreover, the majority of Australians are reluctant to eat marsupial meat, consumption by non-indigenous Australians is limited almost exclusively to kangaroo meat. In an anthropological report on kangaroo meat in the Australian diet, Pearce (2011, p. 1) writes: “I am concerned to explain in cultural terms why kangaroo meat remains such a modest, indeed minor, presence on the Australian culinary landscape”. Pearce’s paper focusses on responses to The Garnaut Climate Change Review (Garnaut, 2008), which was a document handed to the Federal Government in 2008 with recommendations around climate change. Among these was the suggestion that the Australian meat industry should rely more heavily on kangaroo meat and reduce production of cattle and sheep. Pearce discusses a number of negative responses in the media to this suggestion, one response is around the classification of kangaroos as a pest, animals which “are to be eaten only at times of outright necessity, and even then their consumption provokes a sense of disgust”, he continues: “[w]hat distinguished kangaroos from other pests, however, was their native status, and it was this that compounded their unattractive nature as food” (Pearce, 2011, pp. 5-6). The exception to this is the use of kangaroo meat by the indigenous population of Australia, for which it has been a consistent staple in the diet long before it became available for purchase in the remote community stores where many indigenous people still reside. Outside of Australia, a bill ‘Kangaroo Protection Act’ was introduced to US congress in February 2021 to ban the importation of kangaroo skin and meat, with skins being used to make football boots. An article in the ABC rural news quotes New South Wales Animal Justice Party MP Mark Pearson’s response to the bill: "Unfortunately, this is another situation where

internationally, it's a disgrace and it's an embarrassment for Australia that we have to have overseas countries making ethical decisions for the way we treat animals" (Becker & Palmer, 2021). The Garnaut Climate Change Review stands in stark contrast to this bill, with the consumption of kangaroo meat being promoted over other livestock for the sake of the environment.

Similarly, marsupials may be somewhat controversial research subjects in the eyes of the public. This idea will be explored further in relation to the way the public makes value judgements around the roles of animals, based on factors such as perceived intelligence and sentience. In the context of research, the public often has different responses depending on whether the animal has typically been seen in the role of 'experimental model'. Based on the status of Australian native marsupials, it might be expected that the literature surveyed here will acknowledge and discuss the choice of research model and justify this choice within the cost-benefit framework used in Australian animal research ethics approval. Contrary to the predominant view in the values in science literature, that science should not interact with public opinion and should remain objective, it is plausible that research that makes use of animals, and particularly that uses species that have unique value to society, should take account of public perceptions.

The studies considered in this review primarily use a marsupial species to study a known phenomenon but with an interest in how marsupials may differ from other mammals, or how studying marsupials may build upon the current understanding of the phenomenon. Some of these studies elected to use marsupials for the purpose of studying a particular process or behavioural phenomenon thought to be unique or interesting within these species. Research such as this with marsupials does not necessarily fit within the existing parameters of model organism research: according to Ankeny and Leonelli (2011, p. 318) "[model organisms] … are not being studied because they are interesting in their own right … but primarily because of the value they can have for investigating processes in a manner that will be generalizable beyond the specific organism itself". Nonetheless, the current discussion will evaluate how marsupial species could enrich or reinvigorate existing research, either within the framework of emerging model organisms or as experimental organisms, while also considering short-comings in comparison to standardised models.

I argue that the criteria for what makes a good emerging model are still under debate and hotly contested. Moreover, I will further argue that standardisation and genetics are

increasingly less important in the discipline of psychology. Concerning the latter point, the importance of individual differences in the study of psychology is becoming much better understood (Navarro, Griffiths, Steyvers, & Lee, 2006). Previously, the average response of a representative group of individuals has been used to generalise to a wider population, even though no single individual is measured at the mean of the population (Navarro et al., 2006). Variance within a sample (in the statistical sense), much due to differences between individuals in traits and dispositions, was considered 'noise' which needed to be controlled for and minimised, both statistically and via experimental design. It is now understood that this variance describes real differences between individuals. Indeed, heritable individual differences between individuals lie at the foundation of Darwinian evolution by natural selection. In studies of human cognition and behaviour, this variance should obviously be considered important. One relevant feature of rodent-based psychology research is that most studies involving rats use rats that are outbred rather than inbred. The rationale for this has been questioned on technical grounds, but it does mean that the animals in these studies are genetically heterogenous and are therefore somewhat closer to representing the diversity of a human population.

A similar impetus underlies, for example, the US government's Precision Medicine Initiative, whereby prevention and treatment strategies take individual variability into account (Collins & Varmus, 2015). Regarding animal models Leonelli and Ankeny (2013, p. 209) highlight that "[c]ritics have … questioned the scientific validity of model organisms as research tools, pointing out that their use emphasises unity across life instead of exploring diversity". When using animals to model humans, the value of using uniformity to model diversity is raised. The value of standardisation has always been to minimise the influence of extraneous variables on the dependent variable in order to observe the singular impact of the independent variable. This can be applied in the context of observing the effect of a certain drug in an animal study which is then translated to human clinical trials if the drug passes the animal trials. The problem here is that humans cannot be standardised; within clinical trials the researcher will attempt to standardise their environment as much as possible, in fact often these human trials are studies of healthy young males (this is putatively due to avoiding effects of hormonal cycles and potential for pregnancy if females were used as well as avoiding use of much larger samples if females were included because of statistical power considerations), the findings are based on average effects and will not consider interindividual variability in response. The translation to the wider population, therefore, is

often poor, and drugs are frequently abandoned due to negative and sometimes fatal side effects.

In the development of the vaccines for COVID-19, animals have been used along the way. Challenger (2021) highlights the animal cost behind the scenes of the vaccine development, mentioning horseshoe crabs whose blood is used to screen most vaccines for bacteria, transgenic mice bred to express a similar immune response to COVID-19 to that of humans, as well as primates such as marmosets and rhesus monkeys in efficacy testing. The discomfort felt around animal use in scientific research often leads to obscuring the role of animals in even such important research as the development of the COVID-19 vaccines. Challenger (2021) calls for animal use to be recognised despite this discomfort: "[a]cknowledging the animals that have had a role in life-saving vaccines and treatments for Covid-19 is not to take a position for or against their continued use in research. It is instead to accept that there is something wrong in obscuring or forgetting their part and the price they pay".

Background

The factors relevant to choice of model organism have been discussed by various scholars (e.g., see Burian, 1993; Clause, 1993; Dietrich, Ankeny, & Chen, 2014; Dietrich et al., 2020; Leonelli & Ankeny, 2013; Logan, 1999; Rader, 2004). In a paper on the publication trends of model organisms between 1960 and 2010, Dietrich et al. (2014, p. 787) outline the most commonly cited criteria for a model organism: "a rapid life cycle that permits the growth of large populations in short periods of time and increases the likelihood of spontaneous genetic mutations, relatively simple reproductive cycles and genomes, and relatively small body sizes and physical robustness under laboratory conditions, such that large, standardized populations can be bred and maintained". Building upon this foundation, a more recent paper (Dietrich et al., 2020) constructed a matrix of 20 criteria of organismal choice, loosely fitting within five clusters: access, tractability, resourcing, economies and promise.

Historically, organism choice has depended upon the area of research and what model is typically used in this area, but this choice can be modulated by available or preferred techniques and practices. This is well articulated by Richard Burian in his discussion of the choice of experimental organism within studies of biology: "[t]he value of an organism as an

experimental tool … depends not only on various features of the organism, but also on the problem to be addressed and the available experimental … techniques" (Burian, 1993, pp. 351-352). An underlying factor that has influenced this process is the critical role of standardisation of organisms and their environments, achieved by selective breeding, gene manipulation and housing animals in uniform environments. Standardisation of animals and their environments is favoured because studies that use the same model organism are comparable and results are reproducible: "[g]enetic standardization means simply that a related group of individuals can be genetically described, are similar to each other, and can be recreated by a standard and defined breeding protocol. The value of genetically standardized models is that they can be repeatedly reproduced simply by breeding" (Davisson, 1999, pp. 63-64). According to Dietrich et al. (2020) standardisation, along with ethics and other frequently quoted criteria for animal model choice, sit within this matrix of interacting factors, and argue that "[c]hoosing organisms involves making strategic choices about which of these criteria to emphasize" (Dietrich et al., 2020, p. 11).

After 1990, the choices of research models were strongly influenced by a list of model organisms released by the National Institute of Health (NIH; National Institute of Health, 2014). Ankeny and Leonelli (2011) discuss what differentiate model organisms from experimental organisms. These differences go beyond the organisms themselves, to include the research communities which use these organisms and the overarching research goals of these communities. Model organism communities are collaborative: "the epistemic goal that is shared by researchers who pursue model organism work is that they are seeking to contribute to the construction of integrative models for whole, intact organisms, using a variety of disciplinary approaches, with the long-term hope of contributing to large-scale comparative work across these organisms" (Ankeny & Leonelli, 2011, p. 316). This should be seen in contrast to researchers using experimental organisms who do not collaborate or share data in the same way researchers in the model organism community do.

Ankeny and Leonelli (2011) discuss procedural and characteristic features of model organisms, and while some of these features describe both experimental and model organisms, it is the possession of many or all of these features, along with the characteristics of the community surrounding the organism that differentiates the two. Certain features distinguish model organisms, such as "small physical and genomic sizes, short generation times, short life cycles [and] … high fertility rates" (Ankeny & Leonelli, 2011, p. 316). These are coupled with the processes of standardisation and genetic sequencing: "these processes of

standardization are essential because model organism research hinges on (eventually) developing a detailed *genetic* account of the standard organism in terms of sequence, gene function and phenotype" (Ankeny & Leonelli, 2011, p. 316; emphasis in the original). The term 'model organism' became to function like a buzz word in the scientific community in the years that followed the release of the NIH list, due to funding preference being given to research groups using these organisms (Ankeny & Leonelli, 2011). This trend narrowed the scope of animals used in research, while also motivating a broader interpretation of the term, so that many experimental organisms were labelled model organisms to attract funding: "[m]any research groups increasingly are experiencing pressures as a result of the popularity of the term, for instance due to competitive granting systems that force researchers to focus on these organisms or to rationalize any proposed research work on a particular organism by claiming that it is, in some sense, a "model organism" " (Ankeny & Leonelli, 2011, p. 313).

In many research fields, including psychology, there has historically been a strong focus on the use of mice and rats, pigeons, cats and dogs, and primates to model human disease processes as well as behaviour (e.g., see, Harlow & Harlow, 1962; Pavlov & Gantt, 1928; Seligman, 1972; Skinner, 1938). Nelson (2013, p. 7) addresses "claims about the capacities of animal models as tools for knowledge production". In a discussion of modelling the psychological phenomenon anxiety in mice, she writes: "[e]stablishing plausible relationships between mouse experiments and human disorders is arguably especially challenging in the field of animal behavior genetics, where researchers use animals to model disorders that even they sometimes describe as 'uniquely human' " (Nelson, 2013, p. 4). There is ongoing discussion around how well animals, including model organisms, can model human outcomes in biomedical research and toxicological classification (e.g., see Knight, 2011). However, this is perhaps even more striking when considering animals as models for complex psychological phenomena found in humans, such as anxiety, as described above by Nelson (2013), or drug and alcohol addiction, which are situated within human environments. These complex phenomena are understood to have environmental, social, and genetic underpinnings, and therefore the use of rodent models may be seen to reduce these phenomena to their physical expression, while ignoring the many interacting elements that contribute to their expression. It is difficult, for example, to emulate in animals the interaction of genetic predisposition to alcoholism with stressful life events, social pressures and negative thought patterns.

Logan (2001) tries to reconcile the concepts of diversity and generality in a paper tracing the origins of the use of the rat in studies of development and sexuality. She focusses on the choice of the albino rat as a standard animal model, detailing the events and individuals that surrounded this choice. Logan discusses the pivotal role of developmental neurologist Henry Donaldson and psychiatrist Adolf Meyer in this story, contrasting their focus on diversity within experimental models, with a later focus on generality, as articulated by Norman Munn in a psychology handbook where he describes rats as 'instruments'. Norman Munn was the author of an early psychological handbook *An Introduction to Animal Psychology: The Behaviour of the Rat* (Munn, 1933) [6]. In 1915, Henry Donaldson published a book which compiled the past decade of work done on the rat (Donaldson, 1915). Clause (1993, p. 344) writes that this publication "was central to the recognition of the rat as the first "standardized" laboratory animal". Logan (2001, p. 290) discusses the evolution of this species as an experimental organism, writing: "[m]y focus is … on the assumptions about diversity and generality that were associated with scientists' choice of white rats, and on the manner in which, as new methodologies emerged in developmental biology, changes in these assumptions both contributed to and resulted from the increasingly widespread use of a few standard animals".

The rat model was developed within a framework that emphasised the need to study a range of species and the importance of considering both the similarities and differences between the model and the target species; however, this framework was abandoned in favour of standardisation which focussed only on the similarities between the model and the target species. This drive towards standardisation is credited to Milton Greenman - the director at the Wistar Institute between 1905 and 1937 (Suckow, Weisbroth, & Franklin, 2005, pp. 3-4) - who looked to standardisation in other fields such as engineering, and applied these principles to science and the conduct of research with animal models. Logan (1999, p. 15) evaluates this change: "the emphasis on standardization that accompanied the industrialization of American life sciences was a central factor in the rat's transition from an animal studied with

[6] While Munn spent the majority of his career abroad, he was originally from South Australia, and has an unlikely connection to the Psychology Department at the University of Adelaide, and with marsupial research. In 1962 Munn was invited to be a visiting Professor at the University of Adelaide where along with occasional teaching, he pursued interests in research with kangaroos, facilitated by enclosures set up at the Waite Agricultural Research Institute (Winefield & Nettelbeck, 2016).

Donaldson and Meyer's comparative regard for species differences to the generic animal model represented by Munn".

There has been no attempt to standardise any marsupial species for research purposes; in traditional animal-based research, this implied interindividual variability within a given sample of animals would be seen to translate as a lack of control and precision when it comes to analysing findings. That is, it would be seen to reduce the statistical power of studies choosing to use marsupials in preference to a standardised model species. However, the importance of standardisation has been questioned, Voelkl, Vogt, Sena, and Würbel (2018) addressed the poor reproducibility of pre-clinical animal studies by considering the pitfalls of genetic and environmental standardisation. The authors discuss the inherent variability between laboratories, in spite of standardisation, because of "phenotypic plasticity caused by gene-by-environment (G × E) interactions" (Voelkl et al., 2018, p. 2). The authors used a simulation of single and multi-laboratory studies based on published pre-clinical data in order to "assess how the heterogenization of study samples through multi-laboratory study designs affects the outcome of preclinical animal studies" (Voelkl et al., 2018, p. 3). The overall finding of this study was that "multi-laboratory designs—and possibly other means of systematic heterogenization of study samples—will increase the accuracy of results and decrease inference errors, as long as the studies are sufficiently powered" (Voelkl et al., 2018, p. 8). The ethics of animal use, particularly in relation to the 3Rs of Reduction, Refinement and Replacement (Russell & Burch, 1959) and cost-benefit analysis, is discussed here in terms of how to reconcile the possibility that using less animals through the process of standardisation, may in fact have a greater cost, because these animals "may be wasted for inconclusive research" (Voelkl et al., 2018, p. 9).

The methods used here rely on a review of the existing literature in psychology; this body of work may reveal an area of research in the field of psychology which relies less heavily on the processes of standardisation of animal models; returning to the historical discussion around the rat model presented by Logan (2001) in this case with diversity rather than generality being valued by researchers.

Development of the discipline of Psychology

Before introducing the current literature review of marsupial research in psychology it is necessary to provide a brief history of animal use in the discipline of psychology. There is

a long history of humans using animals to model human anatomy and physiology. Animals were not considered as models for human behaviour until much later, however, due to the common conceptualisations of animals as mechanical thoughtless beings that acted upon reflex not cognition (Descartes, reproduced in *Animal Rights and Human Obligations*, 1976).

Psychology is interested in the complex processes of, for example, human decision making, social relationships, family bonds, learning and perception, cognition, emotion, and behaviour. These processes are difficult to study because they are not directly observable or measurable entities and can be considered unethical to study in humans. The experimental use of animals in psychology spiked in response to the development of behaviourism, a paradigm that dominated psychological thinking for the majority of the 20th century (Skinner, 1938; Watson, 1913).

Psychology emerged as an independent discipline at the end of the 19th century, influenced by both Empiricism and German Experimental Physiology (Schultz, 1975). In 1879 Wilhelm Wundt founded the first laboratory for the systematic study of the structure of consciousness in Leipzig, Germany; and in 1891 he founded the first journal of psychology, *Philosophische Studien* (Philosophical Studies). At this time the development of scientific inquiry was accelerating; while Wundt was formally and deliberately building the foundations of the discipline of psychology, other research, which would soon have great influence on the study of psychology, was also unfolding. One name which influenced almost all disciplines of scientific inquiry was Charles Darwin and his theory on the evolution of species (Darwin, 1859).

Animals have been used in the investigation of their structural similarities with humans since the earliest scientific inquiries, but it had previously been supposed that animals did not have a conscious mind and therefore were disregarded as comparative tools for the complex and largely mysterious human mind: “the evolutionary theory of Darwin provided the impetus for animal psychology. Prior to Darwinian theory, there was no reason for scientific interest in the mind because animals were considered to be soulless automata with no point of similarity to or commonality with man” (Schultz, 1975, p. 124). As psychology emerged and developed as a discipline it underwent continuous structural change. The following discussion will trace the modern development of psychology, paying particular attention to those fields of psychology that utilized animals. Landmark studies, theories and individuals will be flagged to draw attention to the contribution of animal research to the

advancement of psychology as a discipline, retrospectively considering the ethical soundness of these studies and how they were perceived at the time.

The beginnings of animal psychology have been described as "an outgrowth of the excitement and controversy engendered by Darwin's notion of continuity" (Schultz, 1975, p. 25). Initial studies with animals were more observational in nature, slowly becoming more experimental. These began with the work of George Romanes, a personal friend of Darwin, on the evolution of the mind through observation of animal behaviour. Romanes documented in great detail behaviours of many animals, from insects through to non-human primates in his book *Animal Intelligence* (1883). Despite sitting on the observational side of the spectrum, Romanes has been described as "[greatly influencing] the subsequent development of animal psychology" (Boakes, 1984, p. 25). The work of Edward Thorndike was the first to consider animal behaviour under true experimental conditions. Thorndike applied the scientific methodology, which had developed in psychology since Wundt, to the previous work in animal psychology which had lacked the scientific rigour of other work being conducted in psychology at the same time. Thorndike took the examples of animal learning described by previous researchers such as Romanes and applied them in a setting whereby he could record elements such as speed of learning and memory and present them in scientific terms. These early studies involved a contraption called a 'puzzle box', which was a wooden crate with a door and latch; using the puzzle box he studied the ability of different animals to learn to escape the box and receive the food reward outside. Boakes (1984, p. 82) describes his work as "[representing] the point in psychology when the German physiological tradition and the Anglo-American mixture of associationist philosophy and evolutionary thought began to combine". In 1905, Thorndike proposed his 'law of effect' stating that responses followed by positive stimuli are more likely to be repeated, while responses followed by negative stimuli are less likely to be repeated. Thorndike's law of effect predates the current concept in operant conditioning of positive and negative reinforcement. Behaviourism is the field of psychology which was most intrigued with animal behaviour and subsequently was responsible for the largest proportion of animal use in the field at the time, "Thorndike was obviously the behaviourists' most important predecessor" (Boakes, 1984, p. 76). Another predecessor to behaviourism was Ivan Pavlov who conducted his famous studies on conditioned reflexes in dogs at a similar time to Thorndike's studies using puzzle boxes, albeit in Russia rather than the United States. Pavlov was not a psychologist but a physiologist. His studies on the physiology of digestion involved developing means to

observe “the digestive glands … under normal conditions, without disturbing the processes taking place within them” (Asratyan, 1953, p. 60); these studies subsequently lead him into a field which was of great interest to psychologists. Pavlov’s famous classical conditioning studies grew out of discoveries around the production of saliva to aid in the digestive process. Pavlov found that his dogs would salivate not just when food was provided but also to cues which preceded the delivery of food, such as the tone of a bell. This concept of reflexive responses being paired with other stimuli became important within the behaviourist tradition.

Behaviourism was established by John Watson in 1913 with the publication of a paper entitled ‘Psychology as the behaviourist views it’ where he states that from the behaviourist standpoint “[psychology] is a purely objective experimental branch of natural science … [where the] theoretical goal is the prediction and control of behavior” (Watson, 1913, p. 158). Watson set out to replace the prominent frameworks in psychology at the time, of structuralism and functionalism, with methods based purely on that which can be observed: “he objected strongly to the introspectionists’ pretensions of reporting on occurrences within an organism which could not be verified through objective observation” (Schultz, 1975, p. 208). The rise of Behaviourism marked a turning point in psychology, away from introspection and towards objectivity, and with this change came animal experimentation on a larger scale than had been seen in the field previously.

Some valuable and impactful contributions to the psychological literature, and to the development of the understanding of human behaviour, have also been some of the most ethically questionable by modern standards. One important name in the field of developmental psychology is Harry Harlow, known for his study of social and maternal bonds using monkeys. These experiments involved what Harlow described as either partial or total social isolation, the latter involving “housing monkeys from a few hours after birth until 3, 6, or 12 months of age in [a] stainless-steel chamber … during the prescribed sentence in this apparatus, the monkey has no contact with any animal, human or subhuman” (Harlow, Dodsworth, & Harlow, 1965, p. 90). The psychological distress at the time of maternal separation was a key finding in these studies, as was the enduring psychological disturbance observed following the isolation period: “When initially removed from total social isolation … they usually go into a state of emotional shock, characterized by … autistic self-clutching and rocking” (Harlow et al., 1965, p. 92). The authors compared social adaptability following isolation between a control group and the groups of 3, 6 and 12 months of isolation, finding various degrees and patterns of behaviour in the groups and noting that “12 months of

isolation almost obliterated the animals socially" (Harlow et al., 1965, p. 94). Subsequent studies into psychopathology in monkey models were pursued after having incidentally created these states in their maternal deprivation studies: "It became clear that early deprivation of social interaction was an enormously effective procedure for the development of psychopathological behaviour patterns" (Harlow & Mears, 1979, p. 222). These descriptions come directly from the original published works, indicating the reality of both the experimental conditions as well as the researchers' indifference towards their animal subjects.

Martin Seligman, now best known for his work in the field of positive psychology, began his career researching a concept called 'learned-helplessness' in dogs. His studies applied the concepts of behavioural conditioning, using electric shocks on dogs and in doing so, teaching them to escape the shocks by jumping over a barrier. These experiments were in themselves objectively cruel: Seligman describes the behavioural responses of the dogs in this passage: "at the onset of the first painful electric shock, the dog runs frantically about, defecating, urinating, and howling, until it accidentally scrambles over the barrier and so escapes the shock" (Seligman, 1972, p. 407). His following studies - which have had substantial influence in the study of depression in humans - made the electric shocks inescapable. The design of these experiments created a conditioned state of helplessness by restraining the dogs and thus making it impossible for them to escape the shocks. Seligman found that dogs which had been previously trained with the inescapable shocks, showed reduced escaping behaviour when placed in a condition where escape was possible, "[the dog] seems to give up and passively accepts the shock" (Seligman, 1972, p. 407). In a later publication Seligman discusses the paradigm of learned-helplessness saying: "[l]aboratory evidence shows that when an organism has experienced trauma it cannot control, its motivation to respond in the face of later trauma wanes" (Seligman, 1975, p. 22).

Animal Models in Psychology

Certain animal models were used in psychology for either their convenience as research models or their putative similarity with humans. Mice and rats were favoured in many fields of research, including psychology, for their small size, easy temperament, fast population turnover, and later, for their known genetic sequencing (e.g. see Logan, 1999; Rader, 2004). Primates were also popular in psychology research for their evolutionary closeness and striking behavioural resemblances to humans. However, these animal models

also presented problems. The idea of generalising findings from rats and mice to humans has been criticized because these organisms do not demonstrate the complexity of humans (at either a structural or cognitive level) and therefore extrapolating findings from one to the other is prima facie problematic. Primates are problematic for the same reason they are favoured: their similarity to humans. Ethical concerns are elevated when an animal demonstrates obvious capacity for thought, problem solving, communication, and emotion and potentially theory of mind (e.g. see Cavalieri & Singer, 1993; De Waal, 2016). However, primates are still not a perfect model for humans, and reports suggest findings using primates in research are also inconclusive (Knight, 2007b). In addition, primates are expensive to use as they require more space and a higher level of care than rodents.

Marsupials have been discussed in the scientific literature over the last four decades as viable experimental organisms in psychology. There have been three previous reviews of the use of marsupials in psychological research, the most recent published over two decades ago. 'The Comparative Psychology of Marsupials' was published in 1999 in the *Australian Journal of Psychology* (Wynne & McLean, 1999). The two earlier reviews were those of Kirkby (1977) and Papini (1986). In his review 'Learning and Problem-Solving Behaviour in Marsupials', Kirkby pointed out that the majority of research on marsupials had been conducted with the American marsupial the Opossum, despite the abundance and diversity of Australian marsupials. Kirkby suggested that the insufficient consideration of Australian marsupial species be addressed.

There has also been growth in the use of marsupials as research models in other fields. A chapter on the tammar wallaby (*Macropus eugenii*) as a potential model for the study of developmental and reproductive biology appeared in the second volume of *Emerging Model Organisms a Laboratory Manual* (Cold Spring Harbor Laboratory Press, 2010). For an overview of some of the marsupial research outside of psychology see 'Marsupials as Models for Research' (Selwood & Coulson, 2006).

Methodology

The current review takes as its starting point the framework of the previous review of marsupial psychology (Wynne & McLean, 1999) in the development of a broader and more inclusive review of psychological research using Australian marsupials over the past two decades. The 1999 review identified 13 publications, 2 theses, and 1 unpublished manuscript that fit their search criteria and that were published since the review by Papini (1986). Wynne

and McLean's definition of psychological research was: "any work relating to the modification of behaviour by exposure to experimenter-induced stimuli or contingencies" (1999, p. 111). Therefore, their review had a relatively narrow and behaviouristic view of what constituted the subject matter of psychology. The authors organised their analysis of marsupial research by the type of study; some of the categories they used to organise the studies included in their review were 'Pavlovian conditioning', 'stimulus discrimination' and 'response to novel stimuli'. While I am narrowing the search criteria to include only research using Australian marsupial species, the search criteria relating to the study of psychology are broadened. Psychology is defined here as any study of cognition, behaviour, or perception and therefore captures various cognate and cross-disciplinary studies in fields such as psychiatry, neuroscience, and physiology.

This review considers research published since the review by Wynne & McLean (1999). Some of the criteria used to narrow down the final selection were based on the nature of the study. Having some measure of behaviour was an important criterion when filtering the results of the search. Out of a number of studies concerning marsupial vision, only a few studies were selected for this review; the methodologies of the rejected studies predominantly involved euthanizing the animals and examining the retina of the eye in order to draw their conclusions, therefore fitting more appropriately into the area of visual neuroscience rather than psychology. A body of research on wildlife conservation was also excluded because it did not fit into the broader framework of this paper. However, this conservation work does appear to make up a considerable proportion of the literature around Australian marsupial research. The exception to this exclusion criterion was the inclusion of a review paper by McAllan (2006), which considered a number of marsupial species as potential models for human ageing without the inclusion of measures of behaviour. The literature search returned twenty-one papers that are classified into four broad categories: 'sensory abilities', 'learning abilities', 'social behaviour and personality', and 'developmental neurobiology' (see Appendix 1 for table of search terms). Often there is an overlap between the categories of research I employ and I have tried to classify the paper based upon its key aims rather than the procedure; for this reason, several papers that have been classified under 'sensory abilities' have learning tasks as part of the experimental design.

Here I will briefly define the categories listed above which are being used to structure this review, I will also outline the animal models historically used in each area of research. First, the study of sensory abilities in psychology has used various animal models to consider

questions around visual perception and auditory thresholds as well as other sensory abilities such as tactile and olfactory perception. Along with the mouse and rat models commonly used in psychology, primates and cats have often been used in studies of sensory abilities. Second, the study of learning considers the acquisition of new behaviours, and traditionally involved learned associations between stimuli, or used certain schedules of reinforcement producing different patterns of learning and strengths of associations. The study of learning abilities has been dominated by the rat model, but many other models have been used including mice, cats and dogs, pigeons and primates, to name a few. Third, the study of social behaviour and personality has been undertaken under observational and experimental conditions, with interests in areas such as attachment and communication. These areas have been studied with various animal models but probably with the most interest in primate species, which demonstrate social behaviours closely comparable to those of humans. The study of developmental neurobiology considers the structure and function of the brain; disfunction of the brain can be either result of physical insult or disease processes. Fourth, developmental neurobiology has been studied in a range of animal models, the mouse is probably the most common model for the purpose of studying degenerative diseases of the brain such as Alzheimer's disease. Other models such as rats and primates have also been commonly used in neurobiology. Primates were particularly favoured for their genetic closeness to humans but ethical questions surround this choice and the use of chimpanzees in invasive research is no longer commonplace. Nonetheless, some argue that the continued use of primates in neuroscience is fundamental to the field (e.g. see, Mitchell et al., 2018). Complex behaviours in humans with neurobiological markers such as alcohol or drug addiction have been studied in rodents by creating dependence in these animal models (e.g see, Lynch, Nicholson, Dance, Morgan, & Foley, 2010).

In my analysis, I will summarise the literature that I am reviewing before analysing how ethical considerations figure in their research and choice of organisms. In addressing the question of how useful marsupials are as models in psychological research, I consider how the authors have evaluated the suitability of their chosen animal(s) to a laboratory environment and as subjects of an experiment (this is obviously less applicable in field studies). The value of the findings based upon impact on the field will be considered using the number of citations during the first five years after publication as an indication of the impact of the research (See Appendix 2 for table of citations).

Sensory Abilities

Summary of literature

Hemmi (1999) used a behavioural design to address the question of the nature of colour vision in the tammar wallaby. There was some interest at this time as to whether some marsupials, contrary to common belief, have trichromatic vision. This question had been posed in the past by this, and other, research groups; however, few of these studies considered this question using behavioural paradigms. Trichromatic vision is the more complex visual system based on three cones which allow broader differentiation between light wavelengths, and therefore the ability to see a wider range of colours. Dichromatic vision is based on two cones, allowing differentiation between greens and blues but not reds. Hemmi used an operant conditioning apparatus with a forced choice between two visual stimuli. The visual stimuli were coloured lights that were projected onto panels; the wallabies indicated their choice by pressing on one of the two panels. Correct choices were followed by an auditory stimulus and the animals were rewarded with food pellets; incorrect choices resulted in a ten second time out and repetition of the same stimulus. There were three experiments used to determine if these animals have colour vision, and subsequently to clarify if they have dichromatic or trichromatic colour vision. Subjects were two tammar wallabies, one male and one female, the small sample size could be seen as a weakness of the study. The author concluded that based on the three behavioural experiments, tammar wallabies have dichromatic colour vision.

In light of more recent findings that most of the Australian marsupials tested have trichromatic colour vision, Ebeling and Hemmi (2014) reassessed the question of whether the tammar wallaby has dichromatic or trichromatic colour vision based on behavioural tests. All experiments used an operant conditioning apparatus, which again incorporated a forced choice between two visual stimuli, with positive reinforcement for correct choices. The animals were originally trained to choose a white stimulus over a black stimulus. Following pre-training the tammar wallabies completed three different experiments based on three behavioural paradigms (LCD colour-mixing, wavelength discrimination, and neutral point). These experiments were designed to determine if tammar wallabies could discriminate between different wavelengths and intensities, which would demonstrate whether their vision was based upon two or three visual cones. The results of these behavioural experiments reconfirmed that tammar wallabies have dichromatic colour vision.

Arrese, Beazley, and Neumeyer (2006) considered the question of trichromatic vision in the fat-tailed dunnart. They had established the existence of three types of cones in this marsupial using physiological methods and then tested for trichromacy via a behavioural study. The dimensionality of colour vision was addressed using additive colour mixture experiments. Thus, the dunnarts ($N = 3$) were trained to discriminate lights of various wavelengths in the colour space defined by the three cone types and were then tested on their ability to discriminate between the trained wavelengths and mixtures of primary wavelengths. The goal was to identify mixtures such that the dunnarts were no longer able to discriminate between the lights and hence to establish whether these marsupials were indeed trichromatic. The authors concluded that the fat tailed dunnart has "functional trichromacy … [that] differs from that of primates with the contribution of a UVS [ultraviolet-sensitive] cone" (Arrese et al., 2006, p. R194). They also contrasted this with results suggesting tammar wallabies were dichromatic (see below) and called for behavioural experiments across a range of marsupial species to establish whether trichromacy is the general colour system of Australian marsupials.

Descovich, Reints Bok, Lisle, and Phillips (2013) were interested in the question of audio laterality in the wombat. Laterality is a preference to the left or right side of the body. The authors highlight the lack of research on laterality in marsupials, despite the fact that marsupials lack a corpus callosum (the brain structure that connects the left and right cerebral hemispheres in other mammals and therefore is implicated in laterality). The study presented bilateral auditory stimuli to twelve wombats, the context of the auditory stimuli have been described as being either: (i) neutral; or (ii) associated with a threat or (iii) associated with food. The wombat's behaviour was recorded at baseline, response, and post-sound. It was clear from the nature of responses to the audio stimuli that the wombats could distinguish between the different sounds. The results suggest a right auditory bias in response to auditory stimuli: "the southern hairy-nosed wombats exhibited lateralised behaviour in response to sound presentation, although the expression was unaffected by different types of auditory stimuli. Further studies using this species are recommended to clarify the functional drivers of this hemispheric specialisation in marsupials" (Descovich et al., 2013, p. 41).

Lippolis, Westman, McAllan, and Rogers (2005) considered whether there was lateralisation in behavioural response to predator approach in the stripe-faced dunnart. A mechanical snake was presented in the left, or right visual field, or binocularly, to 30 stripe-faced dunnarts. Behavioural responses were recorded and classified into the categories

‘retreat’, ‘startle’, ‘ears back’, ‘orientation’ (changing the position of the head so that the stimulus is in binocular vision), and ‘no response’. The study found greater reactivity in striped-face dunnarts when the predator was presented in the left visual field, indicating a right hemisphere specialisation for predator detection and escape response. The most common response across all visual fields was, in fact, ‘no response’ which the authors explain may be adaptive in this species because remaining still may be the most advantageous response to danger.

Signal, Foster, and Temple (2001a) trained possums in a conditional auditory discrimination between the presence and absence of a tone (880Hz at 80bD). The study design required the possums to respond to the presence of a tone by pressing a lever, working for food reinforcers. The study found that this discrimination was learned rapidly by the six subjects, with an average threshold of 65dB reported using a threshold value of 75% correct responses.

Signal, Foster, and Temple (2001b) considered the ability of possums to discriminate a steady light from a flickering one. Therefore, the interest of this paper was in what the authors describe as the critical flicker fusion frequency (CFF) of possums: “the highest frequency at which a flickering light is still perceived as flickering” (Signal et al., 2001b, p. 152). Reinforcement for correct responses was delivered on a random interval schedule of 10 seconds. The interest in studying discrimination learning in brushtail possums has been described as a response to claims that the area of marsupial learning abilities and sensory capabilities is under-researched. In concluding remarks, the authors suggested that the abundance of these species as well as their resilience in captivity, make them a good laboratory animal. The key finding of this paper was that possums can detect flicker and thus detect movement.

Analysis

In his study on colour vision in tammar wallabies, Hemmi (1999) discusses the absence of work on colour vision in marsupial species. He suggests that this gap reflects the reputation of marsupials as difficult experimental subjects, further hindered by their nocturnal/crepuscular cycles. Hemmi however disputes these barriers; his experimental design used a fully automated apparatus which ran throughout the night (in the wallabies waking hours). In terms of suitability as research models, Hemmi (1999, p. 511) commented that “the wallabies took avidly to these tasks”. There was no mention of ethics within the

body of the paper in Hemmi's 1999 study (ethics approval is stated within the acknowledgements); however, when Ebeling and Hemmi (2014), re-addressed the question of dichromatic vs. trichromatic colour vision in the tammar wallaby, they detail the ethics approval within the method section, which may reflect a tightening of regulations for research practices over the intervening fifteen-year period.

In a study investigating lateralisation of escape routes in the stripe-faced dunnart, the authors state that a lack of knowledge about how marsupials perform in this area was a key motivator for the research: "little is known about lateralisation of brain function in marsupials" (Lippolis et al., 2005, p. 457). The authors discuss ethical considerations briefly in the method section, outlining that their experiment met the requirements of the Australian Code for the Responsible Conduct of Research. There is no direct evaluation of the stripe-faced dunnart as a research model in this study but there appeared to be no procedural issues throughout, which indicates that the dunnart performed well under the experimental conditions. Signal et al. (2001a) in their study determining the auditory threshold in brushtail possums state that "[t]he need for more studies of marsupial abilities has been highlighted" and they briefly evaluate the brushtail possum as "a marsupial that can be successfully kept in captivity" (Signal et al., 2001a, p. 200). Ethics is not discussed throughout the paper, something that may be associated with the study being conducted in New Zealand where the brushtail possum is considered a pest.

Learning abilities

Summary of literature

Cameron, Clarke, Bizo, and Starkey (2016) considered demand for food in brushtail possums with different schedules of reinforcement under geometric and arithmetic progressions. Twelve possums took part in sixteen conditions with a concurrent design, that is, where two schedules of reinforcement are presented concurrently. The study hoped to "establish if different schedule and progression types used in demand experiments provide the same determination of demand for two food types in possums" (Cameron et al., 2016, p. 98). The schedules of reinforcement were fixed ratio (FR), progressive ratio (PR) and progressive fixed ratio (PFR). FR refers to a reinforcer being earned after a fixed number of responses, PR is where the number of responses required increases following each reinforcer, and PFR is where the number of repsonses is fixed within each session and increases in each subsequent session. The study was particularly interested in whether "the PR FR procedure

provides similar accounts of demand for foods as the commonly used FR FR and PRF [*sic*] FR procedures" (Cameron et al., 2016, p. 95). The study compared PR FR and PFR FR schedules under which each condition was also exposed to arithmetic and geometric progressions. Arithmetic and geometric progressions are different calculations for increasing ratios under incrementing schedules of reinforcement. The authors reported similar response rates under the arithmetic and geometric progressions, and note that "[t]he PR FR schedule appears to be more robust in identifying a preferred food across progressions for individual animals" (Cameron et al., 2016, p. 99). The authors conclude: "Our recommendation for future use of this procedure is to use PR FR schedules and an arithmetic progression for measuring relative demand as it is time-efficient procedure that produces similar conclusions regarding the demand for food as the more timely and effort-intensive PFR FR schedule procedure" (Cameron et al., 2016, p. 100).

Bonney and Wynne (2003), compared the abilities of quokkas and fat-tailed dunnarts in two tasks of configural learning. Configural learning means to learn that different combinations of the same stimuli signal different outcomes. The two tasks were traverse patterning and negative patterning. Traverse patterning requires the animal to solve three overlapping discrimination problems, while negative patterning requires a conditioned response to two stimuli when presented together but not separately. Fat-tailed dunnarts were more successful across the experiment; however, the different environmental demands of the animals were emphasized in explaining these findings. Quokkas dwell in an environment with few predators and feed only on plants, while dunnarts, on the other hand, live in open desert areas with no consistent territory. Moreover, dunnarts are both predators and prey and therefore the demands of their environment are plausibly higher and more complex.

Bron, Sumpter, Foster, and Temple (2003) considered the utility of the contingency discriminability model and the generalised matching law for possums responding under concurrent variable-interval (VI VI) schedules of reinforcement. The generalised matching law has typically been used to analyse VI VI schedules of reinforcement, and the contingency discriminability model was proposed as an alternative. The authors wanted to consider how suitable these models were "for describing concurrent VI VI schedule performance" (Bron et al., 2003, p. 291). The authors findings with possums were similar to those found in other animals responding on the same schedule of reinforcement. It was concluded that both models were good predictors of behaviour in this reinforcement schedule but "[i]t may well be worthwhile retaining the generalized matching law" (Bron et al., 2003, p. 305).

Hudson, Foster, and Temple (1999) considered the performance of possums under fixed ratio schedules of reinforcement. The authors found a relationship between the fixed ratio size and the response patterns in the possums and these results were comparable to previous studies with other species. From these findings the authors conclude that "it is possible to use operant methods to study possum learning" (Hudson et al., 1999, p. 85).

Bonney and Wynne (2002a) considered the behavioural flexibility of quokkas using a concurrent operant discrimination task for tactile and visual stimuli. There were three phases: a pre-training task; discrimination training; and a reversal learning set. Over four twenty-trial sessions, the quokkas were able to perform the tactile discrimination task; however, neither of the two subjects were able to successfully complete visual discrimination tasks. The authors suggested that this may reflect findings that quokkas have good long-distance vision but that perhaps their environmental demands do not require acute close-range vision.

Bonney and Wynne (2002b) aimed to test if the fat-tailed dunnart could acquire a visual discrimination strategy. A Y-maze was used for the four discrimination tasks, with an entrance tunnel leading to two arms in which the visual stimuli were presented. The authors discuss the abilities of fat-tailed dunnarts in relation to the demands of their environment. Fast adaptation and behavioural flexibility are likely important skills for these small mouse-like marsupials who do not have permanent territory and are preyed upon by various predators as well as needing to hunt for their food. The authors highlighted that the success of the dunnarts in the reversal and learning sets as well as the ability to perform at a high rate in tasks of delayed spatial reversal learning is important to note in relation to the proportionally small brain size of these species relative to their bodies (about 3% - 4% of body weight).

Wynne and Leguet (2004) were interested in the ability of quokkas to reach a food goal when their path is blocked by an obstacle (detour behaviour). The authors distinguish between spatial reasoning and spatial learning in this context, where spatial reasoning means to solve the problem (choosing the shortest route) instinctively based only on previous experience with a similar problem and a visual assessment of the route. Spatial learning is the solving of the problem based upon repeated exposure and trial-and-error learning. Three of the four quokkas demonstrated laterality (a preference to choose left or right at the first presentation of the problem) and the same three demonstrated spatial learning.

Bonney and Wynne (2004) reviewed their work on marsupial cognition, focussing particularly on the quokka and the fat-tailed dunnart. This review responds to the original

review paper (Wynne & McLean, 1999) to which the first author of this paper had contributed. Wynne and McLean's review of research in psychology using marsupials had pointed to the scant body of work in this area, which the authors of this paper hoped to add to and enrich. The reported studies took place between 1998 and 2001. The authors used this review to demonstrate a range of cognitive and learning abilities in these species while highlighting the many environmental and physiological differences between them.

Analysis

In the studies of leaning surveyed here there are a number of reports that the marsupial species used were useful laboratory subjects under these conditions and provided results comparable to those found using common laboratory animals. In a study of configural learning in the fat-tailed dunnart and the quokka, Bonney and Wynne (2003) stated that the motivation for the study was the considerable gap in comparative psychology using Australian marsupial species. The authors found substantial differences between the two species and made the observation that "any differences between marsupials and eutherians are no greater than those between two marsupial species" (Bonney & Wynne, 2003, p. 199). The authors concluded that fat-tailed dunnarts may be a particularly useful model for work on comparative learning and cognition "as they are easy to train and manage and seem to possess a wide array of learning abilities" (Bonney & Wynne, 2003, p. 198). Ethics approval is mentioned in a footnote on the first page, but not discussed at any point throughout the body of the paper.

In a review of learning and problem solving in the fat-tailed dunnart and the quokka from the same authors (Bonney & Wynne, 2004), the previous assumption that marsupials are not well suited to a laboratory environment is addressed: "It seems … that marsupials are no more difficult to test than any other group of animals, and respond well to learning tasks as long as correct husbandry, rewards, and testing modalities are used" (Bonney & Wynne, 2004, p. 592).

Wynne and Leguet (2004) in a study of detour behaviour in quokkas concluded that their findings contribute "to the evidence that marsupials can match or even exceed the performance of more familiar eutherian mammals and other animals on tests used by comparative psychologists" (pp. 285-286).

Bron et al. (2003) considered the suitability of two different models for analysing VI VI schedules of reinforcement in possums. This paper does not mention ethics approval,

Bron et al. (2003, p. 291) do state however, “Possums are marsupials that, although a protected species in their native Australia, are a major pest species in New Zealand”, where the study was conducted. Therefore, while the study undoubtedly passed ethics approval, the pest status of the research model may have made reporting this in the publication unnecessary. In the discussion of motivation for the study the authors state: “One reason for using brushtail possums … was that little is known about their behavioral abilities, and it has been suggested that such knowledge would be beneficial in attempts to control their population in both Australia and New Zealand” (Bron et al., 2003, p. 291).

Social behaviours and personality

Summary of literature

Runcie (2000) considered where the rock-haunting possum sits on the monogamy-polygyny continuum, as well as the degree of paternal care in this marsupial species. Secondary aims were to determine if there is a sex difference in the degree of behaviours to maintain the pair bond, and in decision making behaviours for changing group activity. Four adult possums were caught and fitted with a radio-collar with a two-stage radio transmitter. The captured possums allowed for the identification of other possums and determination of different family groups, which inhabited different territories. Behaviours of possums were categorised into three classes: (1) pair bond maintenance; (2) initiation of changes in group activity; and (3) parental care (direct or indirect). It was concluded that the rock-haunting possum shows social obligate monogamy, unlike facultative monogamy (where the male will mate with other females and provide only limited parental care), obligate monogamy involves a high degree of paternal care. Both sexes maintained the pair bond but males participated in these behaviours more than females, and both sexes initiated changes in group activity.

Martin, Handasyde, Taylor, and Coulson (2007) studied the mating system of mountain brushtail possums. The authors discuss sexual size dimorphism which is the difference in the average body size between males and females of a species. The authors were interested in mountain brushtail possums because in this species, there is no sexual size dimorphism. Typically, in polygynous mammals the male of the species is larger, which indicates the mountain brushtail possum may be unique in its pair bonds. The study comprised of behavioural observation as well as paternity analysis to determine the patterns of social bonds as well as mating patterns. There was an indication of social monogamy based on den-sharing, overlap of home range between pairs, and proximity of pair members.

The authors suggest that this population of possums exhibit facultative monogamy, this relates to minimal paternal care despite a long-term pair bond with one female.

Fisher, Double, Blomberg, Jennions, and Cockburn (2006) studied the effect of polyandry on the survival of offspring in the brown antechinus. Polyandry is where a female animal has more than one male mate. It was observed that polyandrous females were more likely to have young attached to every teat than monandrous females and additionally that the offspring of polyandrous females were more likely to survive until weaning. The authors suggested that their findings support the good sperm hypothesis: "polyandry confers genetic benefits because paternity is biased towards sires that generally produce more viable offspring" (p.90).

Mella et al. (2016) aimed to develop measures of personality in the brushtail possum for use in naturalistic settings. While the majority of testing was conducted in field-based settings, initial trapping and tagging was required to identify the possums. One test of docility was conducted prior to the animal being released, the remainder of the tests were conducted in the field. The field tests involved man-made apparatus, which the possum would interact with and researchers would record the behaviours to quantify personality traits. The key traits being considered were docility, boldness, and activity/exploration in the field. The authors reported that their tests in the initial trapping, field-based, and release settings were able to provide reliable measures of personality that could also be adapted for other species.

Analysis

Under the category of social behaviour and personality there were more field-based studies than experimental studies. While the ethics application process for studies conducted under observational or minimally invasive conditions in Australia is the same as that for experimental studies, the assumed impact from an ethical perspective is thought to be less. With this in mind, it is unsurprising that the studies of this nature surveyed here did not discuss the ethics of using a marsupial species. Many of these studies were interested in marsupials for their uniqueness in social or mating characteristics. One study considered the mountain brushtail possum because it did not demonstrate sexual size dimorphism, which is often an indicator of monogamy in pair bonds (Martin et al., 2007). The authors found that this species demonstrates facultative monogamy, which strengthens the link between monogamy and a lack of sexual size dimorphism. On a similar line of research, Fisher et al. (2006) compared monandry and polyandry in the brown antechinus as an indicator of life

fitness in the female of the species. In terms of evaluating the suitability of marsupials to laboratory conditions, the majority of these papers did not hold their subjects in captivity, and therefore there was little discussion of how these species adapted to such conditions. It is clear, however, that valuable information can be gained through field studies in this area of social and mating behaviour in marsupial species.

Developmental Neurobiology

Summary of literature

McAllan (2006) reviewed the marsupials of the family Dasyuridae, in particular the Dunnart (*Sminthopsis*; 21 species) and the Antechinus (*Antechinus*; 15 species), both small mouse-like marsupials. The primary interest of this paper was the utility of some of these species as models of human ageing, including the pathologies of ageing such as Alzheimer's disease. The author discusses the various ways in which these species may be more appropriate models of ageing than the commonly used model, the mouse. One advantage of these marsupials as research models is their relative longevity and life history in comparison to the common mouse. The author discusses the concept of 'life history strategies', which is a theory that considers factors such as growth pattern, age and size at maturity, and lifespan of different species. McAllan draws parallels between Dasyuridae marsupials and humans in their life history strategies saying that while mice continue to grow throughout life, these marsupial species experience a stability of growth upon sexual maturity, similar to humans. The dunnart and antechinus also have a predictable reproductive cycle, which facilitates the study of sex hormones in relation to ageing. Many of the species in the family Dasyuridae demonstrate a phenomenon called 'male die-off' following the synchronised mating period. This die-off is caused by a spike in the circulation of the stress hormone cortisol in interaction with sex hormones, which leads to 'stress related' illnesses. The author focusses on two species of the genus *Antechinus* to consider this phenomenon, which is of interest as a comparison to the dementias of ageing such as Alzheimer's. McAllan suggested that *Antechinus Stuartii* and *Antechinus Agilis* may be more suitable than models such as the mouse, which are genetically modified to express genes that cause Alzheimer's disease.

Harman, Meyer, and Ahmat (2003) challenged the previous claims that marsupials do not have adult neurogenesis in the dentate gyrus as is found in eutherian mammals. Neurogenesis is the growth and development of new neurons in the brain. The rate of neurogenesis in eutherian mammals has been found to be impacted by external factors such

as stress and environmental enrichment. The experimental design in this study therefore exposed mature-aged dunnarts to one of three conditions for one week: control; stress; and environmental enrichment. Following the experimental phase, a ^{3}H-thymidine injection was administered (^{3}H-thymidine is used to label new cells in the brain). In each group one animal was euthanised 24 hours later and one animal was euthanised 1 month later. After this process was repeated four times with new subjects, the researchers had eight animals per experimental condition. The brains of the euthanised dunnarts were examined to determine the extent of neurogenesis according to the condition to which they were exposed. The authors found that neurogenesis does occur in the brain of mature dunnarts but noted that while the enriched environment did not appear to impact the extent of neurogenesis in the brain, "[s]tress and old age resulted in significantly lower numbers of new cells being generated" (Harman et al., 2003, p. 1). This paper uses the fat-tailed dunnart as an exemplar model for other marsupials, but further research is required to determine if these findings apply across other marsupial species.

Analysis

In the review paper on the value of Dasyuridae species as models of human ageing, the author discussed how predictable reproduction and longer lifespans in the genera *Antechinus* and *Sminthopsis* may make them more suitable models of ageing than the mouse (McAllan, 2006). The stress related deaths that occur in males of the genera *Antechinus* may additionally give interesting insight into the interaction between stress and sex hormones, which may have implications for research on ageing in humans. While the rapidity of population turnover in mice makes them ideal laboratory models, this life history strategy does not map on to that of humans, making them less than ideal as models of human ageing. McAllan discussed the longer lifespan as well as the stability of growth upon maturity in some of these species as more appropriate to model ageing in humans.

Implications: Could Marsupials be Good Models in Psychology?

There are some explicit defences of use of marsupials in psychological research in the available literature. On the basis of the foregoing review, several species stand out as being particularly good models for psychological research. This conclusion is based upon the observations of the researchers along with how these studies have contributed to the knowledge base in the particular field of research. Several species of the dunnart (*Sminthopsis*) have been used across the categories discussed in this review. The fat-tailed

dunnart has been described as “exceptionally adept at solving configural learning problems” (Bonney & Wynne, 2003, p. 198). The dunnart has also been highlighted as a potentially good model for “the role of sex hormones in physiological changes as ageing progresses” as outlined by McAllan (2006, p. 159). In a comparative review of learning and problem solving in the quokka and the fat-tailed dunnart (Bonney & Wynne, 2004), the authors stated that “[d]unnarts may be particularly useful subjects in future studies of brain-behaviour relationships, since these animals have some interesting neuroanatomical features, demonstrate a wide range of fast learning abilities, and as pouch young, can be accessed during early developmental stages” (Bonney & Wynne, 2004, p. 583). In a study of neurogenesis in the hippocampus of the fat tailed dunnart, the authors describe the dunnart as “a useful laboratory animal” (Harman et al., 2003, p. 2) discussing population turnover, lifespan and small size as benefits to this model. As detailed in the category of sensory abilities, the tammar wallaby appears to be a useful model in vision research and a suitable candidate in laboratory experiments, being able to respond appropriately within an operant conditioning design. The brown antechinus (*Antechinus Stuartii*) has also been used across more than one of the categories used in this review. Most prominently, however, as a model of the pathologies of human ageing in a review paper by McAllan (2006).

Based on the success of researchers using marsupials in experimental settings, it can be argued that perceived shortcomings of these models should be re-evaluated. Many of the qualities that have been outlined above as justification for the use of model organisms, such as small size, rapid population turnover, “simple reproductive cycles [and] … robustness under laboratory conditions” (Dietrich et al., 2014, p. 787) are fulfilled by the marsupial models discussed here. However, it is not just these qualities that make them suitable models, but their more atypical or unique features. One example of this is the success of Bonney and Wynne (2004, p. 592) in demonstrating various learning abilities in the fat-tailed dunnart: “[s]ince many of these behavioral tasks are often used to look at effects of various manipulations to the brains of eutherian laboratory animals, it is clear that dunnarts in particular would be of great use to researchers of brain and behavior interactions and the effects of brain damage … Marsupials can be accessed as embryos without killing them and so are particularly useful in developmental studies”. Another particularly unique and potentially useful feature is the male die-off pattern observed in the Antechinus species, which demonstrates similar pathologies to those observed in human ageing and particularly dementias such as Alzheimer’s disease. These irregularities or peculiarities offer more to the

study of psychology than a genetically identical and standardised rodent model when considering human behaviour and cognition.

In spite of some useful suggestions in the studies presented as part of this review, there is little evidence that these findings have been developed or taken further, especially regarding those studies which used marsupials to model human disease processes. It is unclear why there are not more contemporary published studies in these areas; it may demonstrate the phenomenon of funding preference being given primarily to research groups using standard model organisms; however, it may also suggest that these findings were unable to be substantiated in follow-up studies if any had been conducted. Appendix 2. summarises the total number of citations for all reviewed papers as well as the number of citations in the first five years after publication. A five-year impact factor is calculated by dividing the number of citations in the first five years after publication by five. An impact factor above five is considered good, and therefore based on the figures in Appendix 2 the impact factor was not substantial in the majority of the papers surveyed here. Three publications out of 21 had an impact factor over five in the first five years after publication. This indicates that largely these studies haven't had far reaching impacts.

The discussion around Australian marsupial species as potential 'emerging model organisms' raises a number of questions. Above I suggested that what makes a good emerging model is still under debate, and certainly in the context of the species discussed here, it is unclear how to evaluate the fit to the prescribed criteria, or if this label would be useful or necessary. Ankeny and Leonelli (2011) outline the integrative and collective framework of the research community that works with model organisms; both this collaborative agenda, along with the overarching research goal of this community to model entire organisms, rather than singular processes within these organisms, differentiates model organisms from experimental organisms. It may be the case that the communities working with marsupials are too distinct to fit within this pre-existing framework.

The above review is also used to consider the importance of standardisation and genetics in psychology. As has been discussed above, the value of standardisation in pre-clinical animal studies may be overestimated, and perhaps this process will become less important in the future (Voelkl et al., 2018). Based on these studies using marsupial species, it is evident that standardisation is not a requirement to consider research questions using these species. This does not demonstrate that psychology in Australia has moved away from

standardisation in traditional studies using mice and rats, but rather that some researchers are branching out beyond these models and techniques. Similarly, in work with marsupials, genetics is not discussed as important in the conduct of this research.

Value Judgements and Community Attitudes Relating to Model Choices

Historically, reactions from the public to animal research differ depending on the animal used, and these inconsistencies are based on factors such as perceived sentience or intelligence, domestic status (i.e., if they are a common household pet), as well as factors such as whether the animal is considered a pest (people are, for example, often much less concerned about research being conducted on rodents than on dogs or cats). Due to these differing judgements by the public on the suitability of certain animals to be research animals and others not, it intuitively seems that the use of Australian marsupials in research would spark a stronger reaction than the common mouse or rat model. Ormandy and Schuppli (2014) evaluate public attitudes to animal research in a review of literature organised by three categories: personal and cultural characteristics, animal characteristics, and characteristics of the research. These three factors are described as influencing public attitudes. Personal characteristics explored in this paper include demographics such as age, gender identity, rural versus urban background, as well as experience with animals, religion and other more specific individual elements such as vegetarianism. Animal characteristics explored include the appeal of the species to humans, the animal's perceived sentience, and whether the animal is genetically modified. Research characteristics explored include elements such as the type of research, if alternatives to animals are available, and the perceived level of harm. The paper also critiques methods of surveying public opinion, highlighting the use of samples of convenience, how questions are framed, and the limits of both Likert-scale or yes/no questionnaire types which do not allow participants to elaborate on their attitudes. A solution presented to the shortcomings of surveying public attitudes to animal research is through public engagement and improving transparency around animal research. The authors note that "current mechanisms for including public opinion in animal research policy may be lacking" (p. 401) and advocate further empirical research on public aptitudes to animal research taking into account the limitations of existing literature in this space.

In Chapter 1, I introduced the 'value-free ideal', a theory in the values in sciences literature which asserts that science should be produced in a silo, separate from its social context, including the wider public attitudes surrounding it. While the literature considered in

this chapter appeared to conform to this value-free ideal by not considering the value placed on the marsupial species they were studying, I maintain that in the context of animal research, it is impossible to separate animal model choice from public values and attitudes.

Thus, while it was anticipated that studies using Australian marsupials would provide a greater level of detail around the ethical validity of using the chosen species, this was not found here. There is minimal discussion in these papers of the ethical underpinnings of using Australian marsupial species in research due to their unique meaning within Australian culture. Ultimately, while there is a body of research using marsupials in psychology, this is currently a small research area which appears to be dominated by a small number of research groups interested in a specific species or group of species, either from a comparative perspective or because of a unique quality of interest. Because this research is not highly publicised and for the most part highly esoteric, it is unlikely that the Australian public have any knowledge of marsupials being used as experimental models in research. Without a means to measure public reactions to marsupials used as experimental subjects within the scope of the current research, and no discussion of this within the publications reviewed here, I can only speculate that there might be a stronger reaction to the use of a marsupial model in research than a standardised laboratory animal bred specifically for that purpose. Australian attitudes around native animals generally is towards their conservation and protection, and this would likely hold in the case of experimental research. Indeed, Australian native animal species (except dingoes) are generally protected (e.g., see "New South Wales Biodiversity Conversation Act," 2016). It is interesting to consider how the use of Australian marsupial as research animals would be managed if this knowledge of this was more widespread in the public domain. I anticipate the AECs would need to carefully manage the use of these species to align with public expectations concerning these animals. Finally, another issue to consider is the special significance some native animals have for particular Australian First Nations peoples. Again, it is plausible that some animals may be off-limits if they are of special significance to indigenous peoples.

Conclusion

This discussion has combined a review of literature around marsupial use in psychology research, and evaluation of the suitability of these animals as experimental models in future research, with a broad consideration of how animals are valued based on human perceptions of their correct role. Given the relative paucity of literature in this area,

my conclusions are necessarily tentative. Furthermore, many of the studies reviewed had small sample sizes, again limiting their generalisability.

In Chapter 3, I will discuss the broader ethical implications of instrumental use of animals in research, particularly in reference to the cost-benefit analysis used to determine if it is ethical to use an animal in scientific research. Knight (2011) argues that the benefit to humans rarely outweighs the cost to animals and supports this with a systematic review which indicates the value of animal models in predicting human outcomes is significantly overestimated.

The long-established rat and mouse models in psychology have remained the predominant choice of researchers to the present day. The suitability of these models to a laboratory environment and success as subjects of a broad range of experimental tasks has left little room for alternate models. While some marsupials have shown promise in terms of their ability to perform well in experimental tasks and their comparable suitability to a laboratory environment, these qualities alone will not be sufficient to compete with or replace the existing models. I propose that standardisation and genetics may continue to have less importance in the study of human behaviour and cognition in the future. The atypical characteristics, which some of these marsupial species offer, make them promising alternatives to the standardised rat and mouse models. The current paradigm of valuing one animal over another based on the societally prescribed roles of these animals is inherently contradictory and, as such, animal research shouldn't discriminate in model choice based on these roles. Ultimately, however, as will be developed in the succeeding chapters, the overall value of research using animals is on unstable ground, and research communities, policy makers and the broader community need to collaboratively look towards alternative solutions in the near future.

Appendices

Appendix 1: Literature Review Search Terms

The table below details the search methods used, PubMed, PsychInfo and Scopus were the primary databases used. The search included a broad inclusion of search terms for 'marsupial' along with search terms for 'Australia' to limit the papers to Australian marsupial species. Search terms for 'psychology' were also included to limit irrelevant results.

Database	Marsupials	Australia
PubMed	"Potoroidae"[Mesh] OR "Phalangeridae"[Mesh] OR "Trichosurus"[Mesh] OR "Phascolarctidae"[Mesh] OR "Marsupialia"[Mesh] AND psychol* **OR** marsupial*[tw] OR kangaroo*[tw] OR wallaby*[tw] OR wallabies[tw] OR possum*[tw] OR dunnart*[tw] OR wombat*[tw] OR koala*[tw] OR quokka*[tw] OR bilby*[tw] OR bilbies[tw] AND psychol*[tw]	**.au[ad] OR australia*[ad] OR Australia[mh] OR Australia*[tiab] OR Northern Territory[tiab] OR Northern Territory[ad] OR Tasmania*[tiab] OR Tasmania[ad] OR New South Wales[tiab] OR New South Wales[ad] OR Victoria*[tiab] OR Victoria[ad] OR Queensland[tiab] OR Queensland[ad]**
PsychInfo	Marsupials.sh. or marsupial*.mp. or kangaroos.sh. or kangaroo*.mp. or possum*.mp. or wallaby*.mp. or wallabies or dunnart*.mp. or wombat*.mp. or koala*.mp. or quokka*.mp. or bilby*.mp or bilbies	**australia.mp OR australia*.mp OR Northern Territory.mp OR Tasmania*.mp OR New South Wales.mp OR Victoria*.mp OR Queensland.mp**
Scopus	TITLE-ABS-KEY (marsupial* OR kangaroo* OR wallaby* OR wallabies OR possum* OR dunnart* OR wombat*	**TITLE-ABS-KEY (australia* OR Northern Territory OR Tasmania* OR New South Wales OR Victoria OR Queensland)**

	OR koala* OR quokka* OR bilby* OR bilbies AND psychol*)	

Appendix 2: Table of Citations and Impact for Review Papers

Title	Author	Year of Publication	Total Citations	Citations in first 5yrs	5 year Impact Factor
Dichromatic colour vision in an Australian marsupial, the tammar wallaby'	Hemmi	1999	44	13	2.6
Dichromatic Colour Vision in Wallabies as Characterised by Three Behavioural Paradigms	Ebeling & Hemmi	2014	1	1	.2
Behavioural evidence for marsupial trichomacy	Arrese, Beazley & Neumeyer	2006	47	27	5.4
Auditory laterality in a nocturnal, fossorial marsupial (Lasiorhinus latifrons) in response to bilateral stimuli	Descovich et al.	2013	6	6	1.2
Lateralisation of escape responses in the stripe-faced dunnart, Sminthopsis macroura (Dasyuridae: Marsupialia)	Lippolis et al.	2005	72	34	6.8
'Determination of auditory thresholds in the brushtail possum	Signal, Tania, Foster & Temple	2001	9	3	.6

(Trichosurus vulpecula)					
Visual Discrimination in the Brushtail Possum (Trichosurus Vulpecula)	Signal, TD, Temple & Foster	2001	6	2	.4
Concurrent progressive-ratio and fixed ratio schedule performance under geometric and arithmetic progressions by brushtail possums	Cameron et al.	2016	0	0	0
Configural Learning in Two Species of Marsupial (Setonix brachyurus and Sminthopsis crassicaudata)	Bonney, KR & Wynne	2003	5	3	.6
Contingency Discriminability, Matching and Bias in the Concurrent-Schedule Responding of Possums (Trichosurus Vulpecula)	Bron et al.	2003	18	8	1.6
Fixed-Ratio Schedule Performance of Possum (Trichosurus vulpecula)	Hudson, Foster & Temple	1999	16	3	.6

Visual Discrimination Learning and Strategy Behavior in the Fat-Tailed Dunnart (Sminthopis crassicaudata)	Bonney, KR & Wynne	2002	11	3	.6
Studies of learning and problem solving in two species of Australian marsupials	Bonney, K & Wynne	2004	4	1	.2
Quokkas (Setonix brachyurus) Demonstrate Tactile Discrimination Learning and Serial-Reversal Learning	Bonney, KR & Wynne	2002	7	5	1
Detour behavior in the Quokka	Wynne, C & Leguet	2004	3	2	.4
Biparental care and obligate monogamy in the rock-haunting possum, Petropseudes dahli, from tropical Australia	Runcie	2000	39	9	1.8
Long-term pair-bonds without mating fidelity in a mammal	Martin et al.	2007	23	14	2.8
Post-mating sexual selection increases lifetime fitness of polyandrous	Fisher et al.	2006	170	85	17

females in the wild					
Effective field-based methods to quantify personality in brushtail possums (Trichosurus vulpecula)	Mella et al.	2016	3	3	.6
Dasyurid marsupials as models for the physiology of ageing in humans	McAllan	2006	8	5	1
Neurogenesis in the Hippocampus of an Adult Marsupial	Harman, Meyer & Ahmat	2003	22	6	1.2

Chapter 3: Regulatory Structures and Catalysts of Change

This chapter deals broadly with changes in Australian regulatory structures around animal research. Throughout this chapter I develop the argument that there is a deficit in Governmental oversight to Australian animal research, particularly in terms of adapting to change and promoting progressive attitudes in research that embrace transparency and invest in the development of non-animal alternatives to animals in research.

The theme of change in attitudes and understanding toward animal research is considered here through the framework of The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (the Code) which guides Australian State and Territory legislation for animal research. The Code was first published in 1969 and is in its eighth edition (published in 2013). Changes in the aims outlined in each edition of the Code are used here to trace the changing attitudes towards research animals over the period of 1969-to-2013. The language used in the Code can be seen as a reflection of each time-period in the history of animal research regulation in Australia. I argue that we can use documents such as these to capture different attitudes and conceptualisations around animals in research and how these developed and evolved. Patterns in frequency of relevant search terms in an Australian database will be explored as a way of tracking the discussion around animal research in the public domain. Replacement[7] as a construct will be considered here as a vehicle of change, with regulation and practice moving away from traditional animal models and exploring alternatives, motivated both by ethical concerns and the need for better translation to human clinical outcomes. A discussion of Australian organisations dedicated to developing alternatives to animal models, and individuals who argue that animal models are not good predictors of human clinical outcomes will be outlined here. I argue that there needs to be Australian Government initiatives supporting the development of alternatives to animal models.

[7] Replacement from the framework the 3Rs (Russell & Burch, 1959) suggests replacing, where possible, animal models in research with non-sentient alternative models. This framework also includes Reduction, which involves reducing animals used in research while still obtaining statistically significant results, and Refinement, which involves refining husbandry, housing and experimental techniques to minimise pain, stress and suffering.

Exploring attitudes to research animals through 'the Code' 1969-2013

This inquiry uses the development of the regulatory document 'the Code' as a framework for understanding progressive changes in attitudes towards research animals, and how these changes filtered down to animal research practices. Specifically, I consider how the aims outlined at the outset of each of the eight editions of the Code represented the current animal welfare standards at the time of publication. The changes identified in each set of aims are used here as way of considering how attitudes towards research animals evolved over the period of 1969-to-2013 in Australia. These changes are subtle but can be discerned in the wording of the overarching aims of each edition. I argue that changes in this regulatory document were made in response to the broader social and political climate surrounding the issue of animal welfare in research at the time the changes were introduced. I develop this argument further in the following section where I report a search of publications over the lifespan of the Code to identify patterns in publication frequency and examine themes within these publications which may give an indication of what motivated increased public discourse around animal research. I will now consider each edition chronologically, and from each list of aims I will identify those which demonstrate change and progression, or exemplify a certain attitude at the time of publication. I will not discuss each of the aims because often there is repetition from one edition to the next.

The first edition of the Code was published in 1969 and it outlined that "the aim is to define a code of conduct which will promote humane behaviour towards experimental animals, the use of which is vital to the growth of biological knowledge as well as to biologists". (National Health and Medical Research Council, 1969, p. 1). From an animal welfare perspective, this aim is problematic because it frames the humane treatment of animals in the context of the growth of scientific knowledge for human gain. Nonetheless, this aim gives insight into the value placed on animals as merely tools of research at this time, while also demonstrating the beginnings of tighter regulations to protect animal welfare.

In the second edition, published in 1979, one of the aims was "to emphasise the responsibilities associated with experiments involving the use of animals" (National Health and Medical Research Council, 1979, p. 1); it can be seen that this statement introduces a greater degree of accountability for those involved in animal research. Another aim was "to promote an attitude which will encourage the efficient and considerate treatment of animals so that the degree of stress or discomfort produced is no greater than would be accepted as

reasonable and tolerable by community standards" (National Health and Medical Research Council, 1979, p. 1). As in the first edition, the sentiment here is relatively detached from the experience of the animal, again conceptualising the animal as a tool of research. However, it also suggests that the views and opinions of the wider public are valued in the decision making around animal research regulation. This inference reinforces my argument that changes within the Code were made in response to public discourse and particularly discontent in the media around animal use in research.

In the third edition, published in 1983, one of the aims was "to encourage the considerate treatment of animals used for research purposes" (National Health and Medical Research Council, 1983, p. 1). This aim is adjusted in the fourth edition published in 1985, to "ensure the considerate treatment of these animals" (National Health and Medical Research Council, 1985, p. 1). The change in terminology from 'encourage' to 'ensure' demonstrates the beginnings of change in attitudes towards research animals; that is, the welfare of animals was being made a priority rather than just a suggestion. However, it should be noted that it was also considered good research practice to make sure animals were suffering as little as possible, because this change in physiology could invalidate the results. The fourth edition also includes the aim: "to promote the development and use of techniques which replace or complement animal experiments and so reduce the numbers of animals used" (National Health and Medical Research Council, 1985, p. 1). This is the first time the concepts of 'Reduction' and 'Replacement', from the framework 'the 3Rs' (Russell & Burch, 1959) are directly introduced into the aims of the Code. As I will discuss in Chapter 4, according to the authors, this framework started to gain international attention and use within regulation during the 1980s and, in line with this, was first referenced in the Code in its second edition in 1979.

In 1983, an Australian Government Senate Select Committee was established for the purpose of conducting an enquiry into animal welfare within Australia, the culmination being a report which was released in 1989. According to Rose and Grant (2013, p. 316) "[t]his Report identified the need to ensure that the use of animals is justified through ethical review and the application of the principles of the 3Rs". The fifth edition of the Code was published in 1990 and, perhaps in response to the suggestions of the Senate Select Committee's report, puts greater emphasis on the principles of the 3Rs in its aims. This edition aims to "minimize the number of animals used in projects and limit or avoid pain or distress" and to "promote the development and use of techniques which replace animal experiments" (National Health

and Medical Research Council, 1990, p. 1). This edition shows the transition to a review system that actively seeks to minimize the numbers of animals in research and minimize pain and distress. Four of the eight editions of the Code were published in the eleven-year period between 1979 and 1990 which I suggest may reflect increased public pressure on these issues during this time in particular, an idea I will discuss in the following section. According to Villanueva (2015, p. 556) "the frequency of revisions reflected a rapid pace change in both scientific practice and knowledge, and in shifting community attitudes to animal experimentation".

In the sixth edition, published in 1997, one of the aims was to "ensure the use of animals is justified" (National Health and Medical Research Council, 1997, p. 1). This represents the beginnings of the cost-benefit thinking that asks the question: do the potential benefits of the experiment outweigh the potential harm inflicted upon the animals? This paradigm is now established within the review process undertaken by Animal Ethics Committees (AECs) (e.g. see National Health and Medical Research Council, 1990, p. 6). This cost-benefit thinking aims to identify and reject research that does not contribute significantly to improving the wellbeing of humans, animals, or the environment; an issue which I will discuss further below in relation to arguments that animal research does not translate well to human clinical and toxicological outcomes (Knight, 2011). Another aim of the sixth edition was to "avoid pain or distress for each animal used in scientific and teaching activities" (National Health and Medical Research Council, 1997, p. 1). The use of the phrase 'each animal' could be taken to reflect a change in attitude from seeing the animal as a tool of research, to an individual life that should be given consideration.

In the seventh edition, published in 2004, the cost-benefit analysis was fleshed out in the aim to "ensure that the use of animals is justified, taking into consideration the scientific or educational benefits and the potential effects on the welfare of the animals" (National Health and Medical Research Council, 2004, p. 1). The 'Refinement' principle of the 3Rs is also stated more plainly here in the aim to "refine methods and procedures to avoid pain or distress in animals used in scientific and teaching activities" (National Health and Medical Research Council, 2004, p. 1). These aims demonstrate a more proactive system of animal research regulation which reflects changes in thinking about animal suffering, which has become better understood in recent decades in terms of the capacity of animals to experience both physical and psychological distress and pain.

The eighth, and most recent edition, published in 2013, states that "An obligation to respect animals underpins the Code. This obligation brings with it a responsibility to ensure that the care and use of animals for scientific purposes is ethically acceptable, balancing whether the potential effects on the wellbeing of the animals involved is justified by the potential benefits to humans, animals or the environment" (National Health and Medical Research Council, 2013, p. 1). This is the first time the term 'respect' appears within the aims of the code in relation to the treatment of research animals and reflects the overall transformation of the research animal over this time period in the eyes of the Australian public and the scientific community.

This timeline of aims of the Code spanning from 1969-to-2013, shows a progression of the understanding of the capacity for animals to suffer, with the changing terminology demonstrating this progression. The approach I have used here is limited in its assumption that the attitudes towards animals outlined in the Code reflected the attitudes being voiced by the wider public. There is no direct causal link between public discourse and decision making by policy makers regarding animal research, but it is likely that there is some degree of influence. I also consider the social and political climate of the time as a catalyst for changes in the Code, when this is only one potential element which influenced changes to this document. Other influences could be specific events either within Australia or overseas, changes in thinking within the scientific community, or government led initiatives. This inquiry has presented a way of observing the evolution of attitudes towards research animals in an Australian context, by analysing the aims of each edition of the Code. The changing terminology in this document could be seen to represent both the attitudes of the scientific community and the wider public through the influence that public opinion may have had upon the regulation of animal research. The following section develops this thinking further by identifying times of increased discourse around animal research within an Australian database that I believe captures a broad range of publication types and, therefore, a more representative readership. Using this timeframe of increased discourse, I analyse the content of publications falling within this time period to draw out themes and identify various catalysts of discussion within an Australian context.

Media Analysis: Australian Public Affairs-Full Text

The themes presented above are clarified with a media analysis from the period 1967-to-2013 (following the trajectory of the Code but allowing two years leading up to the first

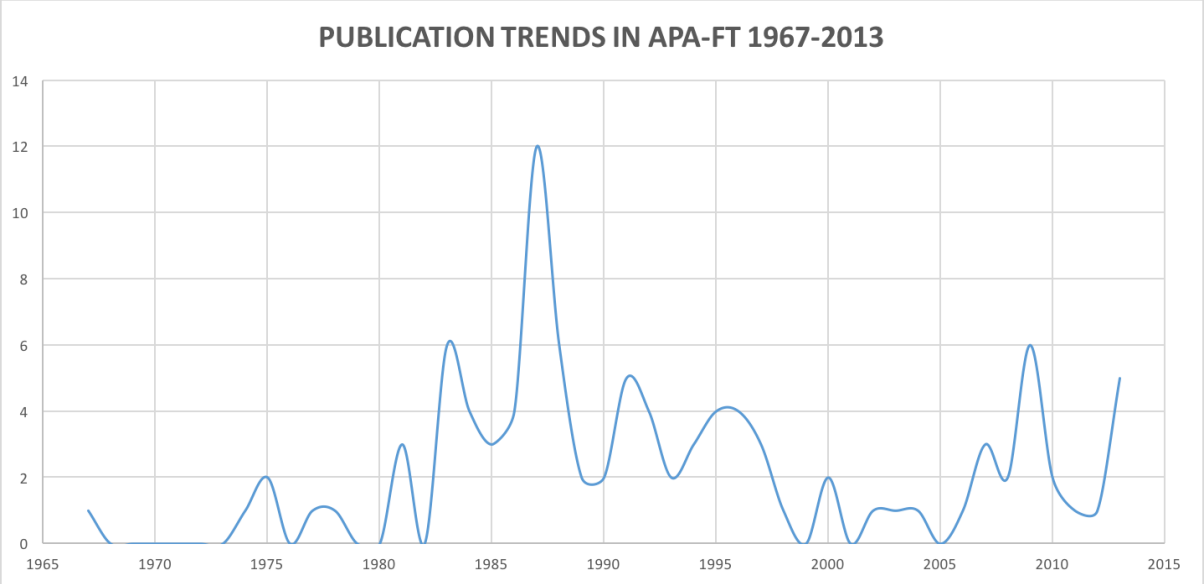
edition to capture discourse surrounding this first publication) using the database Australian Public Affairs-Full Text (APA-FT). This database is made up of a collection of journals, newspapers, magazines, books, and conference proceedings on Australia's political, economic and social affairs, providing a comprehensive picture of the kinds of issues that were being discussed in a broad range of media outlets, including within the animal rights community. The search terms used in APA-FT can be found in Table 1, below. The online database is available from 1978 onwards, and a search using this database obtained 107 records, of which twelve were eliminated from this list for not fitting the criteria of the search. The hardcopy indexes of APA-FT for the period 1967-to-1977 produced an additional five records, bringing the total to 100 records. The small contribution of the hard copy indexes may indicate that these years had minimal public discussion of these issues. The themes emerging from these articles will paint a picture of the kind of discussions happening within the public sphere regarding animal research in Australia.

A representation of the publication trends for the search terms shown below within the database APA-FT is shown in Figure 1. It is interesting in itself to see the way the trend for these search terms peaked and troughed over the period from 1967-to-2013. The 100 records came from 73 different sources from diverse publishing locations such as the Melbourne Age newspaper, the Australian newspaper, and magazines and journals including Women's Day, the Sydney Bulletin, Animal Liberation, Animals Today, Australian Veterinary Journal and Medical Journal of Australia. This diversity is important because it represents a wide area of interests, in support of and opposed to animal research, as well as the middle ground between. The full list of retrieved documents can be found: at https://osf.io/tjz5u/.

Table 1: Search terms used in the database APA-FT

(animal* AND (experiment* OR vivisection OR research)	AND	(rights OR ethic*))	OR	(animal AND research AND experiment*)

Figure 1. Publication trends in APA-FT 1967-2013



The analysis here will consider the frequency of publications generated annually within this database using these search terms. This will be done by calculating the mean number of publications per year and the standard deviation for this figure. These numbers will be used to identify any years which have a publication total that sits more than one standard deviation from the mean (this is a conservative criterion which mitigates against the effect of a potential increase in the numbers of publications over succeeding years). This identifies years which have substantially more publications than the average over this timeframe. The papers published within these years will be evaluated to formulate theories to explain what may have triggered greater public discourse on animal research at this time. I will present a number of theories to explain the patterns in the data.

The mean annual number of publications is 2.13 (SD = 2.35). Eleven years over the forty-seven-year period surveyed had a higher-than-average number of publications (as defined above). When considering these eleven years it was recognised that nine of the eleven years fell within a thirteen-year period from 1983-to-1996. Using the same calculations applied to the entire data set for this thirteen-year period, the mean number of publications was 4.36 (SD = 2.56). Because the majority of these higher publication years fell in a cluster, this time period will be examined as a way of identifying factors that triggered increased public discourse around animal research.

There are a number of both broader international and local reasons that could explain increased public discourse over this time period in Australia. Discussion of animal welfare

and rights began to gain momentum on a global scale in the middle of the twentieth century. The 1975 publication of *Animal Liberation* by Australian philosopher Peter Singer has often been identified as an important catalyst to the rise in attention and awareness given to this issue within the public sphere. The 1980's saw a rise in animal activism, and particularly in the mid-to-late 80's the animal activism was described as involving more direct action, and often violence. While this kind of activism was primarily occurring in the US and the UK, this influence may have caused an increase in discussion of these topics in Australia. At a more local level the enquiries of the Senate Select Committee referred to above culminated in the publication of its report in 1989. Debate and discussion around this investigation and its findings may explain the spike in publications during this time. To consider these theories, all papers identified with the search terms outlined above, and published in the period between 1983 and 1996 were examined to determine the subject matter and any motivation for the publication, in order to draw links between the publications and any possible social and political catalysts. Where relevant this will include a consideration of the source of the publication and its author(s). The survey may draw out other causes for increased discussion of animal research which have not been identified here. Important and relevant papers will be discussed to support the theories I have presented or to help inform the development of new theories.

When evaluating the content of the published material over this time period, one thing that becomes immediately apparent is that it was a time of polarized opinions. It is worth noting that media interest in issues is frequently linked to controversy, real perceived or even confected. There are publications that are both strongly in support of the animal rights cause, and strongly against it. The language used in many of the publications indicates the discord between these two points of view, and often the distain felt for the opposing view, for example, "[t]hese lunatics who call themselves the Animal Liberation Front" (Ruoff, 1985, p. 1). This was a time of transition and of questioning prevailing standards. By considering some of the article titles surveyed here, this upheaval, and the types of questions being asked by both parties at this time are elucidated: for example, 'Facing the Challenge of Animal Liberation', 'Animal Experimentation: Whose Life is in the Balance?', 'Animal Welfare: A Movement in Transition', 'Animal Welfare: How Science Can Help Us' 'Animal Rights and Wrongs', and 'Topical Issues in Animal Experimentation'. This sample of titles illustrates how salient these issues were at this time and the conflict and controversy they were creating in both mainstream media and specialist journals, conference proceedings, and newsletters. I

loosely categorised the surveyed publications based on themes emerging from the titles. These categories ranged from regulatory issues in animal research, discussion of animal welfare and rights (both in positive and negative framing), discussion around 'ethics' in animal research, animal research in agriculture, animal use in medical and biomedical research, cosmetic testing on animals, animal use in Schools and Universities for teaching purposes, and discussion pieces which present the state of animal research (often from a more neutral perspective).

One publication that sheds light on the tensions and conflict that existed particularly in this time period is 'Animal Rights and Wrongs' by Mike Safe, which was published in the magazine section of the Weekend Australian newspaper in 1991. Safe was permitted entrance into the University of Sydney's animal research facilities and his article outlines the animals, their housing, and the research they were being used for. Safe's language is emotive, and while he presents a balanced view of the issues, he is clearly aiming to capture the imagination of his readers, for example, "[a]cross the corridor are mice and rats – hundreds, thousands of little white foot soldiers for research. Bred to die in laboratories" (Safe, 1991, p. 18). Safe discusses the controversy and secrecy that surrounds animal research, he goes on to consider the animal rights movement within Australia. There is limited information on the actions of the animal rights movement during this time in Australia, and this article gives some insight on this, Safe writes:

> Australia has yet to see the violent side of this debate. In Britain, Europe and the US, bombs have been planted, researchers terrorized, laboratories raided, equipment smashed and animals taken. But local researchers have been intimidated, their cars and homes paint bombed and daubed with slogans. Their families, including children, have also been threatened. As well, there are activists who sanction laboratory break-ins and the "liberation" of animals – if not direct attacks on researchers. All this has the effect of throwing an even longer shadow of silence and secrecy over animal research. Most holding facilities in universities and teaching hospitals are anonymous - at Sydney University's Bosch animal house, names are not emblazoned on front doors. The Australian Magazine was allowed into the Bosch facility … when it was agreed none of the staff would be photographed or identified (Safe, 1991, p. 19).

Short passages like this published during this time period are the best record of the state of animal research activism in Australia, drawing a parallel with activism that was occurring elsewhere. It also gives some idea into how the state of transparency in Australian animal research developed to become how it is today, with researchers reluctant to share their research process with the wider public. This topic will be considered at length in Chapter 4. Based on some of the articles surveyed here, there is some indication that a low level of activism was occurring during this time period in Australia but that has been retrospectively overshadowed by the more extreme activism, especially in the US and the UK.

Many of the papers published in this time were defending the use of animals in scientific research, a practice that had gone largely unquestioned since the antivivisection movement in 19th century England[8]. One publication from this survey entitled 'The Case for the Use of Animals in Biomedical Research' by Carl Cohen, published in the Proceedings of the Australian Physiological and Pharmacological Society in 1987, is a good example of this defensive attitude. This paper strongly criticizes the primary arguments at the time against animal use in scientific research. Cohen dismisses the claim that animals have rights, he also criticises the concept of speciesism. In opposition to the animal rights argument he states, "[a]nimals … lack this capacity for free moral judgement. They are not beings of a kind capable of exercising or responding to moral claims … [i]n conducting research on animal subjects, therefore, we do not violate their rights, because they have none to violate" (Cohen, 1987, p. 39). He argues against speciesism saying "[b]etween species of animate life … the morally relevant differences are enormous, and almost universally appreciated … [r]efusing to recognize the moral differences among species is a sure path to calamity" (Cohen, 1987, pp. 41-42). In this paper, the animal rights group People for the Ethical Treatment of Animals (PETA) is strongly criticized, indicating that the motivation for this publication is responding to the rise in animal rights activism and the threat this was perceived to pose to the putatively productive functioning of science. Cohen (1987, p. 42) defends the past and future use of animals in scientific research saying, "virtually every modern medical therapy is due, in part or in whole, to experimentation using animals …[n]or may we ignore … the predictable gains in human (and animal) well-being that are probably achievable in the future". My position on

[8] The antivivisection movement was the predecessor of the modern animal welfare and rights movements which saw a resurgence in the late 1970s and continued to gain momentum thereafter. Vivisection originally referred to the practice of experimenting on live animals, at a time when the use of anaesthetics or analgesics was not yet common practice.

this argument is that while I wholeheartedly agree that animal research has contributed to knowledge production, particularly in disease detection and prevention, the future of animal research is on less stable ground now there is the potential for technologies to be developed which more accurately and humanely predict human outcomes.

PETA is also discussed in a positive light in an article 'Call of the Wild' published in Cosmopolitan magazine in 1995. Next to an image of one of PETA's ad campaigns, the caption reads: "while some people claim PETA's campaign tactics are too strong, the results have been undeniably positive" (Cox, 1995, p. 26). Cosmopolitan magazine has typically been targeted towards a teenage and young-adult female audience. The author of the article, Tracy Cox, gives a very broad overview of a range of ethical issues relating to animal use in various human industries including cosmetic testing, the fur industry, factory farming, entertainment such as zoos and circuses, and in scientific research. The motivation behind the article seems to be raising of awareness in the lay population, which is evident in the choice of the publication source, the non-specialised language, and the wide scope of topics discussed relating to this issue. The discussion around the beauty and fashion industries is particularly emphasised, probably because of the interests of the primary audience of this magazine. The article touches on some of the themes identified above as catalysts for increased discussion around animal research, including Peter Singer and *Animal Liberation*, animal rights groups such as PETA and the Animal Liberation Front (ALF), and the influence of more extreme actions by these groups outside of Australia. Specifically relating to animal research, the article discusses the construct of replacement, stating: "[d]espite the fact that sophisticated research methods such as computer models, cell cultures and human clinical and epidemiological studies are often more accurate, less expensive and less time-consuming than animal experiments, animal testing still continues" (Cox, 1995, p. 24).

One publication which exemplifies the influence of other western nations - in this case the UK – on Australian public discourse, is a letter published in a regular column in the Australian Law Journal called 'Links with London'. This column, written by former Chief Land Registrar in the UK, Theo Ruoff, offered a commentary on UK law for Australian lawyers. In this particular letter, published in 1985, Ruoff criticizes the actions of the animal rights movement in the UK, with particular reference to the ALF. The letter describes the negative consequences of the actions of the ALF, discussing topics such as the previous and future value animal research offers to scientific discovery, and particularly to human clinical intervention. Ruoff also mentions the fear instilled in researchers by these activist groups:

"many scientists are prevented from carrying out their valuable work for fear, not only that their laboratories may be recklessly destroyed and their homes put in jeopardy, but also that they and their wives and children may be threatened by vicious personal violence on the part of people who purport to think that a live dog is (albeit ever so slightly) more sacrosanct than a live man, woman or child" (Ruoff, 1985, pp. 1-2). Publications such as this demonstrate one of the ways in which the fear instilled in the public by activist groups in the UK and the US may have travelled to Australia, and impacted the attitudes held by researchers and policy makers in animal research. This publication also supports the theory that there was a spike in Australian publications in the period between 1983 and 1996 because of increased awareness of direct-action activism targeting animal research institutions in the US and the UK. One 1987 publication 'Animals in Medical and Surgical Research – In Crisis' by Warwick Anderson, gives some indication that direct action activism targeting animal research was also experienced within Australia: "[t]o date, the actions of radical animal rights groups in Australasia have included the theft of animals from at least two research establishments in Australia and one in New Zealand, the serious harassment of at least two research workers, and murder threats against at least another six research workers and their families. In some of these cases the threats were very explicit" (Anderson, 1987, p. 797). As I suggested above, the occurrence of violent activism in Australia may have been overshadowed by the more extreme actions overseas, because it is difficult to find substantial documentation of these occurrences in Australia.

The influence of Australian philosopher Peter Singer and his book *Animal Liberation* (1975) on the discussion of animal use across various industries - including agriculture, cosmetic testing and scientific research – cannot be disputed. This publication has been influential both within Australia and on a global scale. The impact of *Animal Liberation* on the discussion of ethical issues surrounding animal use in research is demonstrated in this survey of literature between 1983 and 1996. Peter Singer and *Animal Liberation* are referred to in a number of the published materials over this time, again both in praise and criticism of the animal rights movement. For example, (Safe, 1991, p. 19) states "No-one in Australia, and perhaps the world, has influenced the debate on what humans do to animals like Peter Singer". Similarly, a paper published in 1987 in the Australia and New Zealand Journal of Surgery by Warwick Anderson states: "The ideas of Professor Peter Singer … have been particularly influential because they have provided a new philosophical framework for the opposition to experiments on animals" (Anderson, 1987, p. 797). To provide some context,

this latter paper provided an overview of recent threats to the medical research industry, discussing the animal rights movement as well as newly implemented government policies which limited the freedom of researchers. At the time of this publication Anderson was the Chair of the NHMRC's (National Health and Medical Research Council) Animal Ethics Committee and head of the Renal Laboratory at Melbourne's Baker Institute. The motivation behind this publication was to reinforce the value of animal research and to identify the primary threats to its continuation. The tone of the article was not persuasive because its anticipated readership (subscribers to an academic journal of surgery) would have held similar views on the value of animal research.

One interesting article details an interview with Peter Singer, published in the journal *Animals Today* in 1995. This interview focusses on the two decades which had passed since the publication of *Animal Liberation* in 1975, and what changes have occurred in this time. Relevant to my survey of publications from this time, Singer is asked: "How does media coverage now compare with 1975?", his response: "It seems to me that we've had declining media coverage in print media in the last decade [between 1985 and 1995]. I live in Melbourne so I see Melbourne newspapers more than others and in the last five years *The Age* for instance, has given less attention to animal protection issues" (Singer, 1995, p. 10). This is not consistent with my findings, which saw the highest number of publications on these issues between 1983 and 1996; however, my survey is retrospective and considers a wider frame of time. Moreover, my survey includes a range of sources, including academic journal and, animal rights magazines as well as the more widely accessible print media such as the daily newspapers and magazines that Singer refers to.

The investigation and report by the Federal Government Senate Select Committee, initiated at the end of 1983 and culminating in 1989, is a likely cause for increased public discourse on animal welfare generally in Australia over this time period. The inquiry is mentioned in a number of the publications surveyed here, and therefore could be considered to be one of the primary contributors to increased discussion of animal welfare from 1983 onwards. One paper published in the *Australian Journal of Medical Laboratory Science* 'Topical issues in animal experimentation' (Blackshaw & Allan, 1987) discusses the Senate Select Committee inquiry into animal experimentation which commenced in 1987. The authors outline the steps the committee would be taking including "to call up representatives of many institutions in which animal experimentation takes place … inspect a wide range of animal housing in various institutions … [and] examine in detail the standards and guidelines

which apply to animal experimentation and animal housing, the use of animals, the sources of animals used in experiments, the training of people experimenting with and caring for animals, the lines of authority and responsibility for animals within institutions and the composition and operations of ethics committees" (Blackshaw & Allan, 1987, pp. 51-52). The authors go on to defend the continued use of animals in experimentation saying "[i]t is incontestable that animal experiments have greatly benefitted human and animal health and wellbeing and will continue to be the basis of further improvements" (Blackshaw & Allan, 1987, p. 52). The article, however, does discuss the topics of 'responsibilities involved with animal use' and 'alternatives to animal experimentation'. This publication overall reads as a relatively balanced consideration of the issues associated with animal research.

In the paper by Warwick Anderson (1987, p. 798), referred to above, he discusses the impetus for the Senate Select inquiry:

> The philosophy of rights for animals and liberation of animals from human exploitation has fallen on fertile political grounds in the 1970s and 80s. In Australia, concern for animals … has exploded in the last 15 years. In response to growing concern … the Senate of the Federal Parliament set up a Select Committee on Animal Welfare which has produced reports on the live sheep export trade and the keeping of whales, dolphins etc in captivity. In 1987, it is examining the use of animals in experiments, commencing its work in 1985 by sending a 130-part questionnaire to institutions, asking detailed questions regarding experimentation within the institution.

Anderson goes on to defend animal research from the tightening of regulations enforced by governments in Australia. He argues: "It is not appropriate that detailed scientific and medical decisions be made by government. To successfully resist this encroachment by government, however, the research community must be able to demonstrate that it is capable of effective self-regulation" (Anderson, 1987, p. 798). Anderson is evidently motivated by a felt threat from animal rights movements which may have been influential on governmental policy making, and subsequently on the practice of animal research. He calls for solidarity amongst fellow researchers in responding to this threat. Safe (1991) also discusses the animal rights movement in Australia at this time and briefly mentions the report by the Senate Select Committee (Australia Parliament Senate Select Committee on Animal Welfare, 1989), saying "In best bureaucratic understatement, the Australian Government Senate Select Committee

on Animal Welfare, which produced a 290-page report on local experimentation two years ago, noted that the issue had been at the "forefront of the animal welfare debate for a long time". And in the way this battle is fought, the committee's report was dismissed by even the more moderate animal-rights groups as accomplishing little while pandering to the wishes of scientists and the research establishment" (Safe, 1991, p. 19). This statement suggests that the committee's report did not satisfy the animal rights community and thus did not quell the discord between the scientific community and animal rights groups.

A report published in the Laboratory Information Bulletin (McKay, 1988) entitled 'Alternatives to Animals in Testing Therapeutic Goods' presents a balanced view on the need for development of non-animal models for research. McKay (1988, p. 2) states that "[t]he scientists who use animals have a substantial interest in the development of alternative test procedures. There are of course the humane reasons and the desire to limit the use of animals and the distress which may be caused. However even without these reasons there would be motivation to find alternatives". Factors such as speed, simplicity, reliability, economy and logistics are listed as "experimental advantages" of non-animal tests (McKay, 1988, p. 3). Concluding the report McKay (p. 6) states that "[t]he change to non-animal tests may never be complete and certainly cannot be fully replaced at this time … If animal tests were abandoned at this time the results would be considerable economic loss, and disease and death for both man and animals". This view echoes many others surveyed here, that while it is desirable to reduce animal use in research and seek alternative models to replace animal use, at this time it was not conceivable to discontinue animal research.

Another potential catalyst for increased public discourse around animal research is the implementation of new editions of the Code and updated animal welfare legislation. However, the influence of public discourse on new editions of the Code, or updated legislation, was likely bi-directional. In the period surveyed here, from 1983-to-1996, there were a disproportionate number of new editions of the Code published, compared to the overall time period. New editions were released in 1983, 1985 and 1990 (editions three, four and five). There were significant adjustments made in these editions including the introduction of the 3Rs (Russell & Burch, 1959) into the regulatory framework; and, after being introduced in the second edition in 1979, further development of AECs. The increased awareness and discussion around animal research in the public sphere would have put pressure on regulatory bodies to implement tighter regulation around research. This is also reflected in the inquiry and report by the Senate Select Committee. At the same time, the

rapid publication of new editions of the Code and the publication of the Senate Select Committee's report would have added fuel to the fire in terms of public discussion on these topics; there would, therefore, have been a reciprocal interaction between the publication of new editions and increased public discourse.

At this time there was also updated legislation around animal research practices enacted in several Australian States. In 1985 New South Wales passed the Animal Research Act; in the same year South Australia passed the Animal Welfare Act. In 1986 Victoria passed the Prevention of Cruelty to Animals Act. In 1992 the Australian Capital Territory passed the Animal Welfare Act; and in 1993 Tasmania passed the Animal Welfare Act. Safe (1991, p. 21) discussed the increased awareness and concern in new science graduates for animal welfare in research and explains this saying: "Much of this has been brought about by the NHMRC code coupled with revised and toughened laws in at least three States – NSW, Victoria and South Australia". A number of the papers surveyed mention new editions of the Code, new legislation, or both, usually briefly as part of a broader discussion. My interpretation is that while some of these articles comment on new editions of the Code or newly implemented legislation, they do not appear to have directly motivated their publication.

Collectively, this survey of publications over the time period from 1983-to-1996 aimed to identify factors that appeared to motivate increased discourse in the public sphere around animal research. I presented a range of theories for why this time period in particular had a higher number of publications, indicating greater public discourse. These theories were then explored by analysing the content of the publications to determine what appeared to motivate each publication, as well as factors such as the choice of publishing location and the background and interests of the author(s). It seems that within an Australian context, the role of activist groups both within Australia and internationally encouraged discussion of animal research. The Australian philosopher Peter Singer was clearly influential in sparking conversation; *Animal Liberation* was a provocative publication at the time and continues to be so. Singer's views encouraged passionate discussion both criticizing and supporting the animal rights movement. The 1983 inquiry and subsequent report published in 1989 by the Senate Select Committee appears to have triggered conversation around the state of Australia's animal welfare standards. Publication of several new editions of the Code in this time as well as new animal welfare legislation may also have played a part. My interpretation, however, is that it was the increased public discourse at this time that had a

stronger impact upon the implementation of animal protection legislation, and the publication of new editions of the Code, rather than the reverse.

Conceptually, the following section moves away from the regulatory frameworks that have shaped recent Australian history in animal research. Intstead, I focus on the construct of replacement, one facet of the framework the 3Rs (Russell & Burch, 1959), which has formed the basis of the animal research review and approval process undertaken by AECs, as mandated by the Code. Replacement within regulatory structures represents efforts of the scientific community and regulatory bodies to adhere to calls for animal models to be replaced in research with non-animal alternatives. Ultimately, benign as this construct may appear, it embodies change and progression, a move away from traditional scientific procedures. However, the power of this construct lies in its execution within regulatory structures and, as will be addressed in Chapter 4, it has been suggested that replacement is not appropriately enacted within Australian AECs (Russell, 2012). The following section will provide an overview of the body of literature which contradicts the assumed utility of animal models for predicting human outcomes. This argument sits apart from the ethical argument against animal use in research, proposing that animal use in research cannot be justified because it does not reliably translate to human outcomes. Finally, I will discuss the development of non-animal alternatives within an Australian context.

Replacement and the Development of Non-animal Alternatives

Besides the Code, and as already noted, another framework relevant to animal research regulation in Australia is the 3Rs of *Refinement, Reduction* and *Replacement* (Russell & Burch, 1959). Refinement refers to updating practices in animal research to improve welfare standards, reduction means ensuring that correct power calculations are applied so no more or fewer animals are used than necessary to obtain statistically significant results; replacement means to search for non-animal alternatives to replace animals in research. This framework is considered in Chapter 4 in relation to research transparency, but here I will focus on replacement. Specifically, what the process of replacement looks like in the context of scientific research, with the development of alternative non-animal models for research. In this chapter replacement will be considered in two related discussions. The first discussion will consider the need for alternative models in light of arguments that animal models are not highly predictive of human clinical and toxicological outcomes. This discussion will be facilitated by reference to publications by Andrew Knight (2011), and

Niall Shanks and Ray Greek (2009) and Shanks, Greek, and Greek (2009). I will also discuss the factor mediating between animal models and human outcomes, methodological quality, which has been criticised (e.g., see Hackam, 2007; Hackam & Redelmeier, 2006). The second discussion is around the development of non-animal models for research within an Australian context. This will be addressed by identifying current mechanisms in place in Australia to develop alternatives to animal models in research.

The overall argument I will make as part of this discussion is that the use of animals in scientific research has been an important tool historically but may not have a place in the contemporary context, where more precise and efficient methods are currently being developed and made available. This argument is based on research conducted by Knight (2011) which builds a body of evidence that challenges the assumption that animals are relatively good models for human disease processes and toxicity classification. Knight states that "[t]he historical and contemporary paradigm that animals are reasonably predictive of human outcomes provides the basis for such widespread use in toxicity testing and biomedical research aimed at combatting human diseases. However, their use persists for historical and cultural reasons, rather than because it has been demonstrated to be scientifically valid" (Knight, 2011, pp. 182-183). It cannot be disputed that historically, animal research has been instrumental in advancing human knowledge, particularly in relation to understanding the manifestation and progression of different diseases, and as a tool for developing vaccines[9]. As human knowledge has continued to grow, and technology has been introduced into all aspects of life, it follows that the technology being developed to replace animal models is potentially more accurate, more sophisticated, and self-evidently more humane. I argue that we are moving out of the age where it is ethically or methodologically sound to experiment on animals. While animal research is a well-oiled machine, it may be time to invest in the future of scientific research using alternative models. This is a complex and continually developing discussion, but it is not so simple to end all animal testing and medical research when it is so deeply ingrained in scientific inquiry, and surely continues to have value in some domains. The discussion on methodology adds to this complexity because it remains unclear if correcting the widespread methodological problems

[9] This claim would be disputed by many animal rights advocates such as Knight, LaFolette, and Shanks, among others, but I disagree with these views as indicated by how I phrase the claim.

evident in animal-based research would improve translation, or further confirm the arguments that animal models are not good tools for predicting human outcomes.

The argument against animal use in research has historically come from an animal rights or animal welfare perspective. While this argument is valid, it has not always been well received, particularly in the aftermath of the violent activism that surrounded the animal rights movement in the mid-to-late 1980's. There have been other voices, unrelated to the ethics of animal experimentation that have criticized the utility of animal research. For example, Shanks and Greek (2009) and Knight (2011) have critically evaluated the translation of findings from animal experiments, to human outcomes. These arguments have articulated in detail the problems associated with using animals as models for human disease and for toxicity classification on the basis of their poor application. Even within humans, there are vast variations between individuals. From a clinical perspective, genetics, environment, co-morbidities, and physiology are some of the factors that can determine how our bodies respond to both disease processes, and any medical intervention. With this in mind, even drugs which pass human clinical trials (often conducted on a young healthy male sample), can have unexpected effects in the broader population. Extrapolating further, the differences between humans and our closest primate relatives are still substantial. Because of the ethical issues and cost associated with housing and experimenting on primates, the most commonly used models in medical research are rodents, which have substantially less genetic similarity to humans. There have been attempts to bridge this gap using genetic modification, but I question the generalisability of results from these highly standardised models, when considering the importance of variation in humans.

I will begin my discussion by outlining the primary findings and arguments of Andrew Knight (2011) and Shanks and Greek (2009). I will also outline any critiques of these publications and discuss any conflicting or contrasting views on this subject. In his book *The Costs and Benefits of Animal Experimentation* Andrew Knight writes: "[t]he core principle underpinning animal experimentation regulation and policy is that the likely benefits of such research must outweigh its expected costs" (Knight, 2011, p. 3). He addresses this paradigm by discussing four themes: animal costs, human benefits, alternative strategies, and educational animal use and student impacts. I will discuss both costs and benefits here and consider Knight's discussion of alternative strategies further below. In relation to animal costs, Knight outlines the difficulties in estimating worldwide animal use in research and toxicity testing because of inconsistencies in definitions and protocols in animal research. As

an example, despite these species making up over of 90% of animals used in research, the US "excludes, mice, rats, birds, fish, reptiles and amphibians from official statistics" (Knight, 2011, p. 9). Knight also discusses worldwide inconsistencies in protocols for animal use reporting, and states that categories such as animals killed for the provision of organs or tissues, animals bred to maintain genetically modified (GM) colonies, or animals subsequently killed as surplus to requirements for laboratory use, are often excluded from reporting. Knight states that current worldwide estimates are conservative, he also suggests that there is evidence that the previously declining numbers of animals used in research are now steadily rising. There are two primary reasons he gives for this pertaining to the US and EU, these are large scale chemical testing programs using animals, and the increase in use of GM animals[10].

As a way of considering animal costs, Knight looked at the invasiveness of animal research procedures, the use of anaesthetics, and the impacts (both physical and psychological) of stressors in the laboratory. Knight classifies markedly invasive procedures as "those resulting in death … surgical procedures … major physiological challenges, and the production of GM animals" (Knight, 2011, p. 23). In his discussion of invasiveness, he looks at data from Australia, which he describes as being incomplete because under half of Australia's States and Territories are represented (this comes back to his discussion of consistency of animal use reporting). For the States with data available between 2005 and 2008, markedly invasive procedures made up 23.3 to 39.6 percent of the total. Related to the invasiveness of procedures, is the use of anaesthetics. Britain's data on use of anaesthetics were available from 1988-to-2009 (current at the time of writing), and these data showed that between 59-to-69 percent of procedures did not use anaesthetics. Knight comments that there are no data identifying the proportion of markedly invasive procedures that use anaesthetics; this interaction would more accurately represent animal cost. Another animal cost is the impact of stress in research animals. This is twofold, because stress negatively impacts the animal, but it can also distort physiological parameters and invalidate the research outcomes.

[10] Ormandy, E, Dale, J & Griffin, G (2011, p. 544) outline the definition provided by the Canadian Council on Animal Care of genetically engineered animals as "an animal that has had a change in its nuclear or mitochondrial DNA (addition, deletion, or substitution of some part of the animal's genetic material or insertion of foreign DNA) achieved through a deliberate human technological intervention." The authors add "[t]hose animals that have undergone induced mutations (for example, by chemicals or radiation —as distinct from spontaneous mutations that naturally occur in populations) and cloned animals are also considered to be genetically engineered due to the direct intervention and planning involved in creation of these animals."

In the discussion of cost-benefit analysis, the 'cost' of the stress caused to the animal may also nullify the 'benefit' to humans if the research is invalidated by the impacts of this stress. Knight outlines various stressors which impact research animals, including capture from the wild, transportation, standardised housing lacking environmental enrichment and natural light, and oftentimes diminished opportunities to experience normal species-specific behaviours, including social behaviours when separated from conspecifics. He also details research procedures which are likely to cause stress, including handling and both routine and invasive procedures. Knight additionally outlines psychological distress, indicated in many research animals by various 'stereotypical' repetitive behaviours caused by isolation and boredom. These behaviours and their evidence of psychological distress are particularly recognisable in primate species, and in fact there is discussion around psychiatric treatment for primates retired from research (e.g., see, Brüne, Brüne-Cohrs, & McGrew, 2004).

In his discussion of human benefits, Knight uses the findings of his 2007 publication 'Animal Experiments Scrutinised: Systematic Reviews Demonstrate Poor Human Clinical and Toxicological Utility' (Knight, 2007c), his consolidated findings (Knight, 2011), however, provide greater detail than the earlier publication. In the initial paper Knight collates the findings of systematic reviews "of the human clinical or toxicological utility of animal experiments" (Knight, 2007c, p. 644). Here he identified 27 such reviews, 20 which looked at human clinical applications of animal research, and seven which used animal data to identify human toxins. In his book section on human benefits, Knight categorised these systematic reviews based on what he identified as "approaches which sought to determine the maximum human clinical utility" (Knight, 2011, p. 42). These approaches included chimpanzee studies, studies approved on the basis of evidence they would lead to medical advances, and highly cited studies published in seven leading scientific journals. There are numerous examples provided based on these and other approaches, but I will discuss some important and relevant ones here.

Because of genetic closeness, chimpanzee studies are believed to be a highly translatable category of research, Knight (2011, p. 42) writes: "[c]himpanzees are the species most closely related to humans, and consequently mostly likely to be predictive of human outcomes". In order to determine which disciplines used invasive chimpanzee research, Knight (2007b) searched three major databases to "assess the value of research on captive chimpanzees … because such research raises the greatest bioethical and social concerns" (Knight, 2011, p. 43). This survey identified 749 studies which Knight analysed to gain an

understanding of the proportions of this research which fit into different disciplines and the primary interests of this research. In a sub-sample of 95 experiments on chimpanzees, Knight conducted citation analysis to determine the impact of these studies on future research, and ultimately human clinical outcomes. This review found that 49.5% of randomly selected chimpanzee studies had not been cited in any subsequent studies. The 14.7% of studies which did appear to translate to human diagnostic or therapeutic methods, had been primarily contributed to by alternative, non-animal methods (Knight, 2007c). In a discussion of why chimpanzees seem to be poor models for human disease processes and toxicity classification, Knight explains:

> Despite nucleotide difference between chimpanzees and humans of only 1-2%, this effect results in differences of around 20%, in terms of protein expression, representing a marked phenotypic differences between the species. These differences manifest as: altered susceptibility to the aetiology and progression of various diseases; differences in the absorption, tissue distribution, metabolism, and excretion of chemotherapeutic agents; and differences in the toxicity and efficacy of pharmaceuticals and other agents (Knight, 2007c, p. 650).

In short, despite genetic similarity, chimpanzees are not humans, and it should be unsurprising that differences exist in the disease progression and response between species.

Under the approach of selecting studies based on the expectation they would lead to medical advances, Knight discusses one systematic review (Lindl, Voelkel, & Kolar, 2005) which used number of citations to determine the impact of these studies over a 12-year period. In this particular review, only 0.3% "demonstrated a direct correlation between the results of animal experiments and human outcomes [and] … [n]one ... led to any new therapies, or had any beneficial clinical impact" (Knight, 2011, p. 50). Under the approach of selecting studies based on number of citations, Knight discussed a systematic review (Hackam & Redelmeier, 2006) where studies were selected if they had over 500 citations and were published in one of seven leading scientific journals. Of the studies identified, 44.7% did not translate to clinical trials, 36.8% were replicated in human trials, 18.4% were contradicted by human trials, and only 10.5% passed human trials. Knight argues that even those interventions that do reach the public are often recalled due to adverse and sometimes fatal reactions in the wider human population. In fact, adverse reactions to approved drugs is

so significant Knight states it has been identified as between the fourth and sixth leading cause of death in US hospitals (Knight, 2007a).

Animal use in human toxicity classification is a time-consuming process with high animal and fiscal costs. Knight outlines that carcinogenicity testing is the most important in terms of cost, because, "[c]ompared to most other diseases, the human and economic costs of cancer are very high" (Knight, 2011, p. 61). The assessment and classification of human carcinogens by different US agencies are evaluated by Knight (2011) who finds disparities between different agencies depending on their motivations. One agency for example, was likely to over-classify human carcinogens based on their risk-adverse policies. Knight explains the difficulties arising from using animals to classify human toxins: "Animal studies are often reasonably sensitive for human toxins. However, their positive predictivity is markedly limited by poor specificity for human toxins, resulting in high false positive rates and a lack of toxicological reliability" (Knight, 2011, p. 73). The size and complexity of the human system compared particularly to that of smaller animals is a crude way of understanding why many human toxins will also be toxins for smaller animals, but the converse may not always be true. In addition, the dose of the toxin given to the animal model is often so high it that it will overwhelm the capacity of the animal to remove the toxin from the body. Moreover, there are many important structural and systemic differences between species in terms of toxicity: "differences in rates of absorption, and transport mechanisms between test routes of administration and other important human routes of exposure, and the considerable variability of organ systems in response to toxic insults, between and within species, strains, and genders, render profoundly difficult any attempt to predict human hazard accurately on the basis of animal toxicity data" (Knight, 2011, p. 78).

Collectively, based on the 27 systematic reviews Knight evaluated, translation from both clinical interventions and toxicity classifications in animal studies were poor. Knight identified a number of factors contributing to poor translation. Across the 27 systematic reviews poor methodological quality was a common problem, even those published in leading scientific journals lacked basic methodologies such as randomisation of animals to test groups or blinding of assessment outcomes. Another issue was publication bias, where findings are only published when they support the hypotheses, which in this case skews the available information in support of animal studies being efficacious. Knight observes:

> The likely causes of the poor human clinical and toxicological utility of animal models include inherent genotypic and phenotypic differences between human and non-human species, the distortion of experimental outcomes arising from stressful experimental environments and protocols, and the poor methodological quality of many animal experiments, which is apparent from numerous systematic reviews of experimental utility … limitations resulting from interspecies differences are likely to be technically and theoretically impossible to overcome (Knight, 2011, pp. 83-84).

Upon weighing animal costs against human benefits, he concludes that "the evidence indicates that actual human benefit is rarely – if ever – sufficient to justify such costs" (Knight, 2011, p. 185). Knight, however, has been accused of bias in his book *The Costs and Benefits of Animal Experiments* (2011). Susanne Prankel, a veterinarian and senior lecturer at the University of Worcester in the United States with an interest in animal welfare and ethics, wrote a response to Knight's book: 'The Costs and Benefits of Animal Experiments: An Evaluation with Bias' (Prankel, 2012). She states, "The book is very successful as an organised accumulation of data on animal experimentation, though the interpretation thereof is debatable" (Prankel, 2012, p. 25). Her primary concern is that the degree of scrutiny applied to animal models, is not applied in his discussion of alternative models, which will be considered in greater detail below. Prankel (2012, p. 25) writes, "his approach to alternatives is less rigorous and credit is given for the mere potential of being beneficial, such that even readers sympathetic to the author's view will get the impression of bias". She also notes that "there is little mention of examples where transferability was good, which one might have expected" (Prankel, 2012, p. 26). Knight (2012, p. 86) contests these claims of bias, writing: "During more than a decade of researching and publishing in this field, on rare occasion I've been similarly challenged by others. Yet neither Dr. Prankel nor any of those other have ever provided any substantive evidence to refute my conclusions, let alone evidence of similar weight to that on which they are based".

In another review, France (2013) raises a number of weaknesses of Knight's book. These include: selectively citing reviews, with the main focus on the use of animals in translational research; and, specifically omitting discussion of fundamental biological research. He also criticises the framing of Knight's discussion of alternatives, falsely giving the impression that these are widely applicable across many fields of research whereas France (2013, p. 23) asserts that "most are limited to applications in either toxicology or drug

development". While the review acknowledges the contribution of Knight's book, he states that "there are too many gaps to fundamentally challenge the scientific validity of animal research and, without this, a major shift in the cost-benefit analysis still seems some way off" (France, 2013, p. 23).

I will briefly discuss poor methodology in animal studies and the implications of this in the context of translation of animal models to human outcomes. The issue of poor methodology is mentioned by Knight (2011), but perhaps not given sufficient attention. It has long been recognised that assessment of published studies via quality assessment (QA) tools is questionable (Greenland, 1994) and that the important issue is bias and specifically the magnitude and direction of any bias (Lash et al., 2014). Where these are not taken into account, assessments of quality and bias often do not relate to published effect sizes. When they are taken into account it is often found that bias scores are positively related to effect sizes – that is, biases tend to inflate reported effect sizes. Lash et al. identified three main sources of bias: (1) uncontrolled confounding, (2) selection bias and (3) measurement error (including misclassification). A confounder is a variable that correlates with both the exposure variable and the outcome variable and thereby causes a spurious (amount of) correlation between the exposure and outcome variables. Selection biases relate to the way that the inappropriate selection of cases and/or controls can affect the outcome of interest. Measurement errors include the inappropriate measurement of either or both of the treatment variable and the outcome variable. I now consider a specific example.

(Macleod, O'Collins, Horky, Howells, & Donnan, 2005) conducted a systematic review and meta-analysis of animal studies investigating the neuroprotective properties of the drug FK506 for stroke. Concurrently the authors investigated the methodological quality of the studies they identified using a scoring system, alongside the reported effect size. Out of a possible score of 10, methodological quality scores ranged from 0-7 with a median score of 4. It was determined that studies of higher methodological quality reported lower effect size which could reflect, for example, researcher biases introduced when studies are not blinded. The link between this finding and the translation of animal studies to human outcomes is at this time unclear, and this finding is specific to studies investigating the drug FK506 for stroke. However, if improving methodological quality in animal studies more broadly reduced the likelihood of finding a significant effect, this would have implications for the utility of animal models. The use of stroke data to investigate translation in animal studies is explained in a later publication: "[t]he presence of bias in animal studies has been tested most

extensively in studies of acute ischemic stroke, probably because in this field the gap between the laboratory and the clinic is both very large and well recognised" (Van der Worp et al., 2010, p. 4).

Van der Worp et al. (2010) give an overview of the translation discussion and identify a number of reasons that animal models are not reliably predicting human outcomes. In addition to methodological issues in animal studies, the authors indicate that human clinical trials may also be contributing to poor translation. The example of underpowered studies (i.e., insufficient numbers of participants) is given to explain discordance between human and animal outcomes. Poor external validity and generalisability are discussed, whereby animal models do not predict human outcomes because they cannot sufficiently model the human disease process. Finally, publication bias is mentioned, and bias more generally is highlighted as being a central interest of the current article. The authors breakdown the discussion of bias under three broad headings, internal validity, external validity and publication bias. The internal validity of animal studies refers to the outcome of the experiment truly reflecting the manipulation of the independent variable, and not other confounding extraneous variables which can be introduced to the environment of the experiment; essentially, the quality of the study. Van der Worp et al. (2010) describe four types of bias that can be introduced to an animal study, and their solutions. These are selection bias, performance bias, detection bias and attrition bias. Selection bias refers to the distribution of animals to treatment groups and can be avoided by using randomisation when allocating animals to groups. Performance bias is introduced when the researcher treats the animals in different treatment groups with different levels of care, this can be introduced implicitly. Detection bias relates to the outcomes of the study and is introduced when the researcher either knowingly or unknowingly alters study outcomes. Attrition bias refers to the loss of animals from treatment groups, either through researcher decisions to remove the animal or through death. This bias can be introduced when researchers are not blinded to treatment groups and this may impact decisions to withdraw an animal from a particular group. Blinding of researchers, animal technicians, and any other involved parties to treatment groups across the entire experiment from allocation to analysis of outcomes, can overcome performance, detection and attrition bias. The authors do note that blinding is not always achievable in all stages of the study. When the treatment group is noticeably distinguishable from control groups, for example in cases of surgical procedure, or when there are telling behavioural or physical characteristics which the researcher can identify.

In a discussion of external validity, the authors state: "[e]ven if the design and conduct of an animal study are sound and eliminate the possibility of bias, the translation of its results to the clinic may fail because of disparities between the model and the clinical trials testing the treatment strategy" (Van der Worp et al., 2010, p. 5). In this discussion, as detailed above the authors primarily focus on the outcomes of stroke research in animal models, "[a]s there is also no other animal model of disease that has been more rigorously subjected to systematic review and meta-analysis, stroke serves as a good example of where difficulties in translation might arise" (Van der Worp et al., 2010, p. 5). This justification is sound, but it also raises the possibility that animal models have particularly poor translation in stroke research because of various factors associated with the trajectory and context surrounding this disease. Comorbidities is one issue that is prevalent in stroke patients and is often not accounted for in animal models, another problem is the timing in administering neuroprotective drugs varies significantly from animal models to clinical settings, where it is not possible to administer these drugs as rapidly following stroke. While these are stroke specific problems, which may explain translation problems in animal models of stroke, these or similar issues are likely common in other disease models, and it is important that a stronger body of research on the translation of a wider range of animal models is developed. Finally, the issue of publication bias is outlined, that statistically significant results are more likely to be published. While this has been demonstrated in clinical studies, the authors note that it has not been extensively considered in animal studies. Nonetheless, the authors relay the findings of a small number of studies and meta-analyses that indicate the impact of publication bias in animal studies may be significant. Van der Worp et al. (2010, p. 6) state that "[n]onpublication of the results of animal studies is unethical not only because it deprives researchers of the accurate data they need to estimate the potential of novel therapies in clinical trials, but also because the included animals are wasted because they do not contribute to accumulating knowledge". In an analysis of opinion papers relating to the poor translation of stroke research, Pound and Ram (2020)found that despite researchers in the field acknowledging the widespread translation issues in the field of stroke research, there was a reluctance to consider moving away from using animal models all together, and instead the refinement of animal research was the most commonly proposed solution.

Niall Shanks and Ray Greek published *Animal Models in Light of Evolution* in 2009 (Shanks & Greek, 2009), which presents similar arguments to Knight (2011) but with a focus on evolutionary perspectives. In the same year Shanks et al. (2009) published the paper 'Are

Animal Models Predictive for Humans?', which has more utility for the current discussion. This paper puts an emphasis on the term 'predict' and its meaning within Science. Shanks et al. (2009) unpack what prediction means in the context of animal research, with a focus on toxicology and pathophysiology. The authors argue that for something to be predictive it needs to consistently and reliably predict a certain outcome, in the case of animal models, they need to consistently and reliably predict human outcomes. In light of this, they criticise the manner in which the term predictive is used as relating to animal models and set out to outline the disparities between animal models and human outcomes. First, the authors identify arguments which contradict the concordance between animal models and human outcomes, then they critique a case which is said to confirm the predictivity of animal models. A primary argument made in this discussion is the difference between prediction of human outcomes using animal models and taking a known human outcome and cherry-picking data to find an animal model which demonstrates the same outcome. Animal models inconsistently predict human outcomes, and while different species can show predictivity for different disease processes or responses to chemicals in humans, no one species will consistently predict human outcomes; the authors add that "evolutionary closeness does not increase the predictive value of the model" (Shanks et al., 2009, p. 10). Shanks et al. (2009, pp. 7-8) make a similar argument to Knight, saying: "Sensitivity is not the same as prediction. While it is true that all known human carcinogens that have been adequately studied have been shown to be carcinogenic in at least one animal species … [n]onetheless, this is meaningless without also knowing specificity, positive prediction value, and negative predictive value". Shanks et al. (2009, p. 13) identify ten useful reasons as to why different species have varied responses to drugs and toxins or have different disease progressions and trajectories:

> Vertebrates are evolved complex systems. Such systems may manifest different responses to the same stimuli due to: (1) differences with respect to genes/alleles present; (2) differences with respect to mutations in the same gene …. (3) differences with respect to proteins and protein activity; (4) differences with respect to gene regulation; (5) differences in gene expression; (6) differences in protein-protein interactions; (7) differences in genetic networks; (8) differences with respect to organismal organization … (9) differences in environmental exposures … [and] (10) differences with respect to evolutionary histories

The authors critique a regularly cited paper which has been used to argue for the predictivity of animal models. This paper 'Concordance of the toxicity of pharmaceuticals in humans and in animals' (Olson et al., 2000), as suggested by the title, demonstrates predictivity of animal data for human toxicity. The survey found a human toxicity concordance rate of 71% for rodent and nonrodent species. Shanks and Greek provide a commentary on the methodology and findings of this study, identifying a number of problems which weaken the case being made. The pharmaceutical industry was responsible for this publication which is troubling because "the study was put together by parties with a vested interest in the outcome" (Shanks et al., 2009, p. 16). Despite often being used as evidence of animal model predictivity, the authors weaken their case by stating within the paper that "the data could not answer completely the question of how well animal studies predict overall the responses of humans" (Olson et al., 2000, p. 58). Shanks et al. (2009, p. 16) argue that "The Olson Study was concerned primarily not with prediction, but with retroactive simulation of antecedently known human results", this refers to the study counting concordance between human toxicity and any animal model as a positive result, which discounts discordance between human toxicity and any number of other animal models. The study only considered clinical trials, which excludes the majority of drugs which did not make it beyond animal studies. This is important because the small proportion of pharmaceuticals that proceed beyond animal studies are more likely to have concordance with human toxicity because of what Knight (2011) described as the high-sensitivity low-specificity problem, where animals are often sensitive to human toxins but are also likely to produce false positives. This is reiterated by Shanks et al. (2009, p. 16) where they state, "In carcinogenicity studies, the sensitivity rate using rodents may well be 100%, the specificity, however, is another story". Many substances may be incorrectly classified as a toxin or carcinogen because of the low specificity problem in both toxicity and carcinogenicity testing in animals.

Shanks and Greek return to the consideration of the term 'predict', they state "Prediction does not mean retrospectively finding one animal that responded to stimuli like humans and therefore saying that the animal predicted human response nor does it mean cherry picking data nor does it mean occasionally getting the right answer" (Shanks et al., 2009, p. 18). The authors also reiterate the sensitivity versus specificity argument saying that "[a]dvocates who maintain animals are predictive confuse sensitivity with prediction" (Shanks et al., 2009, p. 18). The book published in the same year by the authors presents the same arguments as their paper but has a strong focus on evolution as the basis for species

differences. This book is more specialist reading and has also been criticised for the evolutionary argument they make. Lewis Wolpert, an evolutionary biologist states bluntly, "The case that Shanks and Greek make about animal models is important and persuasive. Their arguments based on evolution contribute very little" (Wolpert 2010 p. 2).

Collectively, the arguments presented by Andrew Knight (2011) and Shanks and Greek (2009) provide evidence that animal models have less utility than is widely believed. The discussion of translation from animal models to humans leads into a discussion of alternative non-animal models in research. This is a global initiative and there are organisations worldwide which are currently developing alternatives to animals in research. The following discussion will primarily focus on the development of alternatives within an Australian context.

Non-animal Alternative Models within an Australian Context

Andrew Knight (2011) dedicates a section of his book The Costs and Benefits of Animal Experimentation to discussing alternative non-animal models in research. As detailed above, one critic (Prankel, 2012) argued that he did not apply the same level of scrutiny in his discussion of alternatives as he did in his discussion of traditional animal models. Knight also published a paper 'Non-Animal Methodologies within Biomedical Research and Toxicity Testing' (Knight, 2008b) which details the scope of these alternative methodologies by discussing select examples. It should be noted that toxicology is more adaptable to the use of non-animal models that many other areas of research. It should be further acknowledged toxicology research is limited within Australia, thus opportunities to replace animals in research are correspondingly less. Here I will overview these two publications where Knight discusses non-animal methodologies and consider the accusation of bias in terms of the degree of scrutiny Knight applies to these methodologies compared to animal-based studies. Knight (2008b) evaluates a number of examples of non-animal methodologies including the sharing of existing data to avoid duplication of studies, computational modelling, the use of minimally sentient animals, the use of tissue cultures and *in vitro* assays, human clinical trials using micro-dosing and the use of epidemiological[11], sociological and psychological research among a number of other examples.

[11] Epidemiological research makes use of population-based studies to identify toxic agents and possible risk factors.

Knight discusses the importance of sharing of toxicity data in order to reduce animal testing and study duplication. He states that: “to maximise commercial competitiveness, much existing data remains excluded from the public domain within pharmaceutical and chemical company files. However, such exclusion is contrary to the public interest when toxicity data regarding the components of new pharmaceutical or consumer products are not disclosed, when animal experiments are repeated, and when product development is slowed, as a result” (Knight, 2008b, p. 216).

From considering the two publications (Knight, 2008b, 2011) I can appreciate the interpretation that Knight has not been as rigorous in his evaluation of non-animal methodologies as in his evaluation of the translation of animal models to human outcomes. I believe the difference is not due to bias but to the purpose of these evaluations and where each type of methodology sits in terms of its historical trajectory. Animal models are well established as the accepted methodology in biomedical research and toxicity testing. The consideration of animal models and their utility is an entirely different conversation to the consideration of developing alternative models. These new models have shown promise and utility but have not yet been used on the scale to which animal models have. The purpose of an evaluation of non-animal methodologies is to continue to raise awareness of their existence in place of animal models and to encourage investment in their development and validation. In support of this notion Knight (2008b, p. 226) states that: “it remains clearly apparent from this limited review that a broad range of investigative tools exists, with the potential to replace animal use within biomedical research and toxicity testing”. Knight merely claims here that these alternatives exist and have the potential to replace animals. He continues that: “Non-animal investigative methods cannot, of course, provide answers to all questions about humans, particularly given present technological limitations. However, the same is certainly true of animal models, which have a more limited capacity for further development” (Knight, 2008b, p. 226). Undoubtedly as non-animal methodologies continue to develop and are selected in place of animal models, the data available on their use and validity will be able to be evaluated with the same scrutiny that Knight (2011) has applied to animal studies.

The development of alternatives to animals in research is a fast-growing initiative involving various disciplines. While in many countries there has been strong support for the continued development of alternatives, evidenced by the establishment of organisations with

this focus, Australia lags behind in this domain. On the Royal Society for the Prevention of Cruelty to Animals (RSPCA) website it states: “there is currently no dedicated government funding for developing alternatives to animals … Australia urgently needs a national, coordinated approach to reduce animal use and to investigate, develop and validate alternatives to animals in research and testing … The RSPCA has been asking the government to develop a national strategy for alternatives and the establishment of a national centre to implement the three 'R's” (RSPCA Australia, 2019). As is discussed further in Chapter 4, there appears to be a degree of resistance to the replacement of animals in research ingrained in the regulatory system of institutional AECs. While these committees operate on a framework developed around the 3Rs, there has been the suggestion that in the approval process of animal research, replacement is not enacted as strongly as refinement and reduction. The responsibility of finding alternatives to the animal model proposed in the application process is given to the researcher. Russell (2012) argues that both the researcher and members of the committee reviewing the application will not have the appropriate background to identify new and developing alternatives from different fields. This system may reflect the reluctance of the Australian government to invest in developing alternatives to animal models.

Despite the lack of government initiatives towards replacing animals in research, one Australian organisation is committed to this goal, Medical Advances Without Animals Trust (MAWA) was established in 2000. The organisation states its aim is “to advance medical science and improve human health and therapeutic interventions without using animals or animal products for biomedical research” (MAWA brochure 1704). In 2010 MAWA partnered with the Australian National University (ANU). MAWA functions as a grant funding provider to Australian researchers developing and using non-animal models. The development of alternatives from a transnational perspective will be addressed in Chapter 5. However, it should be noted here that while MAWA is the only Australian organisation directly promoting the development of alternatives through funding incentives, it is also one of the only replacement-only organisations worldwide. Overwhelmingly, the organisations developing alternatives internationally are promoting the 3Rs of Refinement, Reduction and Replacement, and therefore are still supporting the use of animals in research. MAWA only funds projects that do not use animals or their products in any way. The organisation’s brochure on conditions of financial support states:

> MAWA will not support the use of animals with potential for sentiency, including animals from lower phylogenetic orders or early developmental vertebral stages. Proposed studies using micro-organisms will be considered on a case-by-case basis … The Trust does not offer funding for research which uses (non-human) animal cells, animal tissues, animal cell lines, animal derived antibodies (monoclonal and polyclonal), animal derived stains or reagents. This reflects recent progress in the culture and availability of human cells and tissues, as well as concerns about the problems of species variation (MAWA Scientific Policies and Conditions of Support).

MAWA is currently developing The Australian Centre for Alternatives to Animal Research at ANU (MAWA, 2019), which will be an important development in bringing Australia forwards on a global scale, especially given its replacement focussed structure. It is vital, however, that the Australian government recognises and supports the development of alternative models with the aim of replacing animals in scientific research. This could be initiated through its major funding bodies the NHMRC and ARC by mandating a statement for the consideration of non-animal models in research proposed for funding. However current legislation does not encompass these issues.

Chapter 4: Transparency

This chapter was reworked into a paper which was submitted to the journal *Studies in History and Philosophy of Science* under the title of 'The Role and Value of Transparency in Australian Animal Research: An Appraisal of the Australian Animal Ethics Committee Process'. This paper is included here in the place of Chapter 4.

Additionally, a book chapter with similar interests to the current chapter has come to my attention following the completion of both this chapter and its paper adaptation (Merkes, Monika & Buttrose, Rob. (2019). Increasing the Transparency of Animal Experimentation: An Australian Perspective). The proof of concept for the current chapter can be found in the archive of Australian and New Zealand Council for the Care of Animals in Research and Teaching Ltd. 2018 conference "Keeping it Relevant" (see Conference Papers, p.5, above).

Statement of Authorship

Title of Paper	The Role and Value of Transparency in Australian Animal Research: An Appraisal of the Australian Animal Ethics Committee Process
Publication Status	Submitted
Publication Details	*Studies in History and Philosophy of Science*.

Principal Author

Name of Principal Author (Candidate)	Karina Burns		
Contribution to the Paper	Sole author		
Overall percentage (%)	100		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the sole author of this paper.		
Signature		Date	06/12/2021

The Role and Value of Transparency in Australian Animal Research: An Appraisal of the Australian Animal Ethics Committee Process

Key words: transparency, animal research, animal ethics committees, Australia

This paper considers the role and value of transparency in animal research within an Australian context. Historically this construct has not been well defined in Australian animal research, because, I claim, transparency has not been meaningfully operationalised within research regulation or practice in this country. I argue that there needs to be more uniform policy implemented in Australia, across all jurisdictions, for the communication of process, husbandry and outcomes of animal research. Related to this, the reporting of animal use needs to be consistent between jurisdictions with clearly defined definitions, in order to be translated to national annual statistics which can then be used to make comparisons on animal use globally. The implementation of transparency should also apply to Australia's regulatory bodies, Animal Ethics Committees (AECs). These committees should be resourced to facilitate transparency, understanding that openness can bring attention to these institutions and the resourcing should also include the tools to appropriately respond to this.

Previous research has proposed that there are three actors in the animal research debate: the scientific community, animal advocacy groups, and policy makers. O'Sullivan (2006) highlights that discourses from the three actors in this debate in Australia all conceptualise transparency as being desirable despite coming from different perspectives. Ultimately, this paper argues that until transparency is meaningfully incorporated into research practices, the construct will retain three or more contrasting definitions. Here, transparency is examined through the lens of AECs, the regulatory bodies embedded within animal research institutions and responsible for reviewing applications for animal research. Despite these committees putatively acting in the public interest to uphold ethical research practices, their deliberations and decisions are not publicly accessible. The outcomes of both qualitative and quantitative analyses considering application outcomes and perceived barriers to transparency for AECs demonstrate that more open processes need to be implemented in uniform national legislation.

Introduction

In Australia, the role and value of transparency in animal research has not been well defined and it appears that transparency is conceptualised differently by different actors in the animal research debate. However, on all sides transparency is perceived to be valuable in relation to public attitudes (O'Sullivan, 2008; O'Sullivan, 2006). This paper aims to extend an ongoing dialogue by focussing on Animal Ethics Committees (AECs), the regulatory bodies responsible for the review of applications for the use of animals in Australian research. AECs are seen to ensure the responsible and ethical conduct of animal research in the public interest; however, the processes and outputs of these committees are not publicly accessible. This inconsistency will be addressed here. Using quantitative and qualitative methods, the following will consider the processes by which these committees operate, proposing that greater transparency can be introduced to them. Drawing on previous Australian literature and the findings from the current analyses, a stronger statement on the role and value of transparency within Australia will be developed.

Transparency has been operationalised within animal research practices in a number of countries, notably in the UK. There are active efforts within these research communities to make animal research visible and accessible to the wider public. In Australia, however, transparency has remained a point of discussion without becoming formally embedded within the regulation or practice of animal research. In May 2004, Siobahn O'Sullivan conducted a media analysis of four Sydney newspapers, to assess the visibility of research animals in the public sphere (O'Sullivan, 2008). Looking at this analysis retrospectively demonstrates how the current discussions around transparency in Australian animal research have developed from conversations happening over a decade ago. Moreover, it is clear that the recommendations made at this time have not been meaningfully incorporated into Australian animal research governance. Even at the time of publication, transparency had long been a point of contention and debate, O'Sullivan (2008, p. 21) wrote:

> Different stake-holders have their own reasons for thinking transparency is important. Some people think it is a way of holding the research community accountable for their actions. Others see transparency as providing the public with the information it is rightfully entitled to because public money funds much of the research sector. Others speak of educating the public about the benefits of animal-based research, and still others think of the issue in terms of

> protecting the interests of research animals through public debate and enhanced awareness. However, regardless of the terminology employed or the perspective from which the issue is approached, transparency, its elusiveness, and the benefits it could bring, have been at the centre of the animal research debate in Australia for the last 30 years.

The concept of transparency, and 'its elusiveness' in animal research in Australia, as introduced here by O'Sullivan, will be interrogated in this paper by looking more closely at the role of AECs. Historically transparency has not been well defined in Australian animal research, because, I claim, transparency has not been meaningfully operationalised within research regulation or practice in this country.

Literature review on transparency in animal research

Transparency in animal research plays different roles for different actors, and achieves different goals (O'Sullivan, 2008). It has been conceptualised in varying and sometimes contrasting ways as different groups try to make it fit in their own objectives. In action, transparency is often equated to openness or visibility, particularly with reference to institutions sharing process or output with the wider public. Yeates and Reed define transparency in an editorial of the *Journal of Medical Ethics* as "communicating meaningful information (eg, data or details of decision-making processes) to audiences, openly and honestly, with the intention of informing, enabling understanding and meeting responsibilities of accountability" (2015, p, 504). Benjamin Worthy writes that "the concept is synonymous with openness and is rooted in the idea of letting in light or knowledge" (Benjamin Worthy in Nerlich, Hartley, Raman, & Smith, 2018, p. 23), this is a good starting point. In *The Anti-Corruption Plain Language Guide* published by Transparency International[12], transparency is defined as: "[c]haracteristic of governments, companies, organisations and individuals of being open in the clear disclosure of information, rules, plans, processes and actions" (Transparency International, 2009, p. 44). Despite there being a general understanding of the term within the literature, it is still tangled in the complexities of interpretation and its framing within a broader dialogue.

[12] Transparency International is a not-for-profit organisation founded in 1993 in Berlin, Germany with the goal of identifying and ending corruption globally.

For the purposes of this paper, I propose, consistent with the definition provided by Benjamin Worthy above, that transparency within animal research can be understood as openness of communication processes. This openness broadly refers to the flow of information from the scientific community to the public. This may include making available information on standards and practices used in animal research, the species and numbers of animals used, the husbandry and housing practices, or the aims and anticipated value of the research.

Transparency in animal research has been a contentious issue both in Australia and in the West more generally. There have been various initiatives within scientific communities outside Australia to embrace transparency. For example, in the US there has recently been a push from the scientific community in favour of greater transparency in research. On June 20, 2018 *USA Today*, an internationally distributed newspaper, published a letter signed by 592 US scientists calling for greater transparency from their colleagues in the scientific community: “We call upon our country’s research institutions — large and small — to embrace openness. We should proudly explain how animals are used for the advancement of science and medicine, in the interest of the wellbeing of humans and animals” (USA Today, 2018). Carbone (2021) provides a commentary on what he calls New Openness, the movement from scientists and research institutions towards greater openness and transparency in animal research, in line with the UK's Concordat on Openness. The framing of this essay is in considering ways forwards within the United States, where efforts toward openness in animal research are more limited. Carbone provides a series of proposals encompassing invitational openness, an openness that seeks not only to engage with a neutral public but also with animal advocates. These proposals include suggestions around inclusion of animal protectionists in consultation and drafting of guidelines, inviting a "diversity of opinion in their production" (Carbone, 2021)(Carbone, 2021 p. 14). There is also discussion of the virtual tours of select animal facilities that have been made available mostly in Europe and the UK, and how this could go further than the selective transparency in current curated virtual tours by using live stream footage. Carbone also discusses the constitution of animal ethics committees and proposes that the United States follow other models which require a proportional representation of lay members and include animal protectionists on ethics committees. The communication to the broader public of animal harms, either in high impact studies or in cases of research non-compliance, is an area that has not been well addressed in the United States, and it is recommended that this information is openly shared.

In Canada, an animal research advocacy group, Speaking of Animals, states in an article 'Canadians Support Animal Research', that transparency in animal research is responsible for the overwhelming support for animal research by the Canadian public. The author Michael Brunt writes: "The CCAC [Canadian Council on Animal Care] occupies a pivotal role of encouraging transparency in the Canadian regulatory system by ensuring that the use of animals, where necessary, for research, teaching and testing employs optimal care according to acceptable scientific standards and communicating all relevant information to the Canadian public, to whom they are accountable" (Speaking of Research, 2014). The United Kingdom has embraced animal research transparency in recent years through initiatives such as the Concordat on Openness on Animal Research (Understanding Animal Research, 2014), and online laboratory animal tours at a select number of UK research institutions (Understanding Animal Research, 2017). The Concordat on Openness on Animal Research was established by a not-for-profit organisation, vis. Understanding Animal Research, in 2014 and represents a commitment by a number of UK organisations to greater openness in animal research practices. Preceding this, in 2012, 40 organisations signed a Declaration on Openness on Animal Research which set the precedent for the Concordat. At the current time the Concordat has 122 signatories that "are all involved in carrying out, funding or supporting animal research in some way" (Understanding Animal Research, 2014, p. 5). Perhaps it is the previous experience with radical activism that has encouraged the research community in the UK to be open with the public about animal research practices.

A recent article entitled 'Is it time for Australia to be more open about research involving animals?' published on the media outlet, The Conversation, discusses the need for Australia to follow the UK and implement similar initiatives towards research transparency (Paytas, 2018). Tyler Paytas, a research fellow in Philosophy at the Australian Catholic University, writes: "[s]ecrecy only leads to more divisiveness and hostility, including possible direct action that can interfere with research. Lack of openness can also lead to a general lack of trust in scientific researchers among the general public" (Paytas, 2018). This example demonstrates just one opinion on Australia's research policies relating to transparency, outlining why following the lead of the UK on transparency would increase public trust in the research community[13].

[13] Chapter 5 will unpack these international comparisons of transparency in animal research and consider ways Australia might benchmark its own practices on those in other countries.

The discussion around transparency in Australia can be traced to 1983 when an inquiry was initiated by the Federal Government into animal welfare in Australia. A Senate Select Committee was formed to investigate this inquiry and evaluated evidence over the intervening years between 1983 and the publication of a report in 1989 (Australia Parliament Senate Select Committee on Animal Welfare, 1989). The Committee addressed animal welfare in Australia across a number of domains beginning their investigation into animal research in 1987. In 1994, an article published in *Search*[14] quoted the first Chair of the Senate Select Committee, Senator Georges saying:

> [t]here is a view prevalent among institutions that any information on animal experimentation, other than a few bland statistics will be misused by animal welfare organizations if it is released to the public … Secrecy breeds suspicion. If information is withheld from the public, it is natural for concerned members of the public to assume that what is being hidden cannot withstand public scrutiny. The more stubborn is the institution, the more determined is the animal welfare organization to obtain the information and the more concerned becomes the public about the matter (Puplick, 1994, p. 263).

It is apparent from the quote above that the tension between the scientific community and animal welfare groups was clearly visible in Australia even in the early 1980s. Senator Georges offers an evaluation on the response of the scientific community to transparency, highlighting the circular nature of the animal research debate, wherein researchers are reluctant to share their data for fear of misrepresentation and animal welfare organisations interpret this silence as a reflection of secrecy and ultimately misconduct. He reflects the view that the animal research community were doing themselves a disservice by remaining silent, leaving room for speculation and fabrication around research practices.

In the report on animal experimentation, the Senate committee made several recommendations relevant to the issue of transparency. Primarily, that there should be annual publication of statistics around the number of animals used in Australian research and their particular uses but with the proviso that the statistics are outlined and contextualised correctly so as to avoid misinterpretation. The committee stated

[14] *Search* is a journal interested in Media and Communication research.

that “the public has the right to know the extent of use of animals in experiments in Australia” (Australia Parliament Senate Select Committee on Animal Welfare, 1989, p. 21).

It is interesting to consider that these recommendations were made some three decades ago, and yet the concern within the scientific community around the repercussions of sharing information about animal research practices lingers. The construct of transparency prescribed by the committee’s report seems to be accompanied by a need to control the process of sharing information. This need to ensure the ‘correct’ interpretation of any information reported demonstrates a continued reluctance, a restricted transparency, constrained by concern around potential responses to this openness. The committee appears to advocate for transparency but also appears to support controlling the interpretation of this information.

There appears to be similar evaluations of transparency today as there were at the time of the Senate Select Committee inquiry. While today, there are statistics reported on animal use in research and teaching in Australia, there are no national statistics. Instead, statistics are reported by each individual Australian state and territory. The current system of reporting animal use in Australian research should therefore be streamlined to produce coherent, consistent and annual data for international comparison; at present the data coming out of Australia is flawed and incomplete due to inconsistent state-based reporting. Thus, according to the organisation Humane Research Australia (HRA): “Even at state/territory level, there are lengthy delays in reporting, extremely inconsistent collection and reporting methods between jurisdictions and institutions, some states collate statistics but do not publish them, and some states and territories don’t even collect statistics at all” (Humane Research Australia, 2021)[15]. The consequence of this is that nation-wide animal use statistics are merely estimates based on the available data. Humane Research Australia has been a key source for collated statistics for animal use in research in Australia. The organisation collected available data from Australian States and Territories and reported annual estimated

[15] Humane Research Australia has been a key source for collated statistics for animal use in research in Australia. The organisation collected available data from Australian States and Territories and reported annual estimated figures based on this. On their website, the organisation states the following: “Due to the difficulty in obtaining statistics from states and territories, and discrepancies in data, it is difficult to collate an accurate picture of the national use of animals in research and teaching. HRA has therefore made the decision to refuse to take on this responsibility with 2018 being the last year we will publish our data” (Humane Research Australia, 2021).

figures based on this. On their website, the organisation states the following: “Due to the difficulty in obtaining statistics from states and territories, and discrepancies in data, it is difficult to collate an accurate picture of the national use of animals in research and teaching. HRA has therefore made the decision to refuse to take on this responsibility with 2018 being the last year we will publish our data” (Humane Research Australia, 2021). On their website HRA state: “There is a critical need to set up a national framework for the collection and collation of national statistics of animals used in research” (HRA, 2021). This framework would need to account for any differences between jurisdictions to ensure that the data collected from each State and Territory reflects the same definitions of what constitutes animal research. The capacity for accurate international comparison of animal use in research is a vital step for Australia to enter the global conversation on animal research practices.

In a review of animal research data reporting in Australia, Bain and Debono (2013) evaluate Australia’s collection and reporting of animal use statistics as well as pain assessment in animal research and implementation and reporting of the 3Rs. These findings are benchmarked against structures in place elsewhere in the world, such as New Zealand, The United Kingdom and Canada. This paper recommends nation-wide collection of animal use statistics by category of use. There is a further recommendation to adopt the New Zealand model of severity assessment which considers duration in the assessment of impact and includes retrospective scoring instead of projected pain scores made by researchers at the outset of the study. Finally, there is a recommendation for institutions to be involved in the collection and reporting of statistics relating to the implementation of the 3Rs, it should be noted that since this publication, the NHMRC has released a paper on the uptake of the 3Rs in an Australian context.

The Australian literature addressing the need for greater transparency in animal research in Australia (e.g. see O'Sullivan, 2008; O’Sullivan, 2006; Sharman, 2006; Timoshanko et al., 2016; Whittaker, 2014) offers several additional recommendations concerning transparency in animal research. Sharman (2006) evaluated Australia’s legal system around animal research and conducted a case study on the legislation in place in New South Wales. In a discussion around the role of AECs and ways this system can facilitate transparency, Sharman (2006, p. 74) notes that “[n]otwithstanding the importance and scope of their functions, AECs remain largely unaccountable to the public due to the secret nature of much of their business and the sanctions that apply for breach of confidentiality”, she adds that this “makes the system more translucent than transparent as it means that only certain

trusted members of the public are permitted to participate in the decision-making processes that affect so many lives". Sharman suggests that the adoption of a global set of principles could harmonise the regulation of animal research and offer greater protection to animals used in research. However, the feasibility of a global set of principles, given the discrepancies that exist even between different States and Territories in Australia, for example, is not likely. It should be acknowledged that contrary to the above, the responsibility of implementing transparency should not fall on AECs, these committees are part of a larger system that needs fundamental changes to reflect the principles of transparency.

In her month-long media analysis, O'Sullivan (2008) evaluated the state of transparency in Australian animal research. The paper reflects upon "the extent to which the Australian research sector is in fact accountable to the public" (O'Sullivan, 2008, p. 16) through retrospective consideration of the recommendations made in the Senate Select Committee report in 1989. This analysis aimed to identify the frequency with which animals were mentioned in popular media, and the number of these articles which concerned experimental animals. Her findings demonstrated that "animals used for research and education are discussed in the media at a fraction of the rate of wildlife and companion animals, and less often than exhibited animals and animals used in agricultural production" (O'Sullivan, 2008, p. 18). Based on these findings she concludes that "to date, the animal research community has not adequately increased its level of public accountability" (O'Sullivan, 2008, p. 16). As part of this paper, O'Sullivan revisits an earlier publication (O'Sullivan, 2006) where she discusses the three stake holders in the animal research debate: researchers, animal advocates and policy makers. She argues that in Australia, there is support from all three parties for greater transparency in the animal research sector. O'Sullivan (2008) evaluates dialogues from each of these parties on the value of transparency, demonstrating that despite differing perspectives, all three groups believe transparency is in their best interest. The proposed role transparency would play for each of these groups is different, although each discusses how transparency would change the public's opinion on animal research practices. O'Sullivan concludes that without a move from within the research community, transparency will need to be enforced by policy, and only then can it be determined what role transparency will play in Australian animal research.

Whittaker (2014, p. 2), in a paper evaluating the robustness of Australia's animal research regulation, asks the question "does the current system adequately protect animal welfare, or does a cloak of intransparency hide serious underlying actual, or potential animal

welfare concerns?". This paper identifies a number of issues in the Australian regulatory system, in particular with the Code of Practice, which Whittaker critiques in terms of its practical applicability. AECs are also critiqued, with a "lack of centralised oversight" being a key concern (Whittaker, 2014, p. 9); this issue is also detailed below in relation to the current research. Finally, a number of recommendations are offered, including giving full legal power to the Code "to allow national harmonisation of the system" (Whittaker, 2014, p. 13), and mandated pre-review of applications submitted to AECs, a recommendation that will be reiterated below in response to the current research.

Timoshanko et al. (2016, p. 327) identified transparency as one of four areas in Australian animal research in which regulatory reform is required. In their paper, they critically evaluated Australia's animal research regulatory framework, identifying strengths while also highlighting areas which could be developed "to bring Australia in line with international best practice" (Timoshanko et al., 2016, p. 324). Besides transparency, Timoshanko et al. (2016, p. 324) identified "higher standards of competency, the development of a central regulatory authority, and greater incentives to encourage research and development into nonanimal alternatives" as areas that need regulatory reform. The regulatory reform proposed by the authors for higher standards of competency refers to the poorly defined competency requirements outlined in The Code for certain responsibilities involving the care of animals. The authors write: "there is no requirement under the applicable legislation or Code to appoint a veterinary surgeon to care for the health and wellbeing of the animals". The authors also point to the competencies of Category C and D members on AECs (animal welfare representatives and lay members, respectively) in this argument. The proposal by the authors for the creation of a central regulatory authority for the review of animal research suggests a streamlined and more consistent process which would ensure that inconsistencies in jurisdiction between Australian States and Territories would not impact the review of applications for animal research. Moreover, "[a] centralized authority would help ensure that decisions are made with full knowledge of the nonanimal alternatives available and whether the experiment is even necessary" (Timeshanko, 2016 p. 229).

Despite various discussions on transparency in animal research, beginning with the Senate Select Committee report in 1989, the construct has not translated from literature into policy and practice. The lack of transparency in Australian animal research appears to have stemmed from the alleged terrorist activities of animal rights activists especially during the

1980's, largely within the US and the UK. Fear is thought to perpetuate this reluctance to be open with the public about animal research practices; this concern can be identified in certain practices employed by Australian AECs. As an example, the names of committee members and the Chair are confidential: this policy was born from a time when there was a perceived fear for the safety of these individuals. While violent activism was perhaps a less real threat in Australia, there are documented occurrences of threats and harassment of Australian researchers (e.g., see 'Animals in Medical and Surgical Research – In Crisis' by Warwick Anderson, p. 797). Moreover, the occurrence of violent activism in the US and UK appears to have been influential on increased public discourse in Australian media, which may have impacted policy making in Australia at this time.

Literature review on ethics committees in animal research

One way to look at the issue of transparency in Australian animal research is through the regulatory platform used to process applications for animal use in research, AECs. These committees are responsible for the approval of any application for research using animals; however, the deliberation and decisions made by these committees are largely confidential. As part of her evaluation of transparency in Australian animal research, O'Sullivan (2008, p. 28) discusses some of the claims made by the Senate Select Committee regarding the function of AECs, she comments on the (then) current state of transparency in relation to AECs:

> … although the AEC system has developed strongly, it is not self-evident that it facilitates transparency in significant ways. The AEC system has consistently been presented as one of the pillars of enhanced dialogue between the research community and the public. Yet, the extent to which AECs provides the wider community with a timely and detailed understanding of animal research practices is questionable. Indeed, the link between AECs and enhanced transparency is difficult to interpret …

This statement is useful when considering the history and future of the relationship between AECs and research transparency. There has been the suggestion that AECs institutionalise animal use in research and allow the public to turn a blind eye (e.g. see, Johnson, 2013). The secrecy which continues to surround the AEC review process does not facilitate a transparent process and obscures the animal research process from animal welfare groups and the wider public, and animal welfare groups. The research presented here aimed

to dissect the application process conducted by AECs and to understand the proportion of applications that are approved and what this might mean in terms of the function of these committees. Do these committees simply serve the bureaucratic function of reassuring the public that there are processes in place to safeguard the welfare of animals and perhaps to turn away projects that do not add value?

In order to understand how Australia's current practices and regulations were developed in relation to the social and political backdrop they emerged within, I will provide a brief overview of the history of the regulatory structures in Australia which govern animal research and explain the role and make up of Australian AECs.

The regulatory structure that governs animal research in Australia is based on The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (the Code). This document was first published in 1969 and is now in its eighth edition. This document is not legally binding, but its content is integrated into the State and Territory legislation governing animal research: "the substantive content of the regulation is effectively national due to the legislative incorporation of the Code in each jurisdiction" (Timoshanko et al., 2016, p. 325). Grant (1995, p. 11) states: "[the Code] has been incorporated in the legislation of most States and Territories, so the requirements of the Code are law", however, any misconduct will only be dealt with as prescribed by the State and Territory legislation and therefore in terms of penalties, the Code does not carry the same weight. In Australia, any individual or group proposing to use animals in research is required to put an application to their institutional AEC for review. AECs were first incorporated and described within the Code in its second edition in 1979: "Institutions undertaking research which involves the use of animals must establish an Animal Experimentation Ethics Review Committee, whose role is to ensure that all investigations in which animals are used conform with accepted standards of animal care" (National Health and Medical Research Council, 1979, p. 2). These committees have evolved over this period and these changes are reflected in the successive editions of the Code via the description of the roles and members of these committees.

AECs are made up of at least four members; in the eighth and most recent edition of the Code, published in 2013, these members are classified as: "Category A—a person with qualifications in veterinary science … Category B—a suitably qualified person with substantial and recent experience in the use of animals for scientific purposes … Category C—a person with demonstrable commitment to, and established experience in, furthering the

welfare of animals … [and] Category D—a person not employed by or otherwise associated with the institution and who has never been involved in the use of animals in scientific or teaching activities" (National Health and Medical Research Council, 2013, p. 20). This last member is supposed to represent the lay perspective on animal research, and along with the animal welfare representative, provide a more balanced view on welfare issues that appear when evaluating proposals for animal research. There is a stipulation in place that requires in committees of over four members, for category C and D members to constitute a minimum of one-third of committee membership. In some jurisdictions there is also a Category E member who is someone responsible for the daily care of the animals within the institution. The appointment of an animal welfare officer to the committee is also recommended and this member (or members) is able to provide additional veterinary insight regarding experimental procedures as well as report on the husbandry and housing practices employed by the institution's research facilities, and closely monitor any welfare issues. The committee Chair is advised to be someone "who holds a senior position in the institution … appointed in addition to Category A to D members" (National Health and Medical Research Council, 2013, p. 20).

AECs have a number of important roles. According to the most recent edition of the Code: "[t]he primary responsibility of an AEC is to ensure, on behalf of the institution for which it acts, that all activities relating to the care and use of animals are conducted in compliance with the Code" (National Health and Medical Research Council, 2013, p. 25). According to the Code one of the primary roles of these committees is the review of applications for approval to conduct animal research (National Health and Medical Research Council, 2013, pp. 25 - 28). During a periodic meeting each application is scrutinised for any potential welfare issues, this includes, for example, reviewing statistical power calculations used to justify the number of animals requested, considering the choice of drugs and route of administration, and noting the inclusion of environmental enrichment for animals or use of social housing where appropriate. Any concerns raised by the members are discussed to reach a consensus on what action should be taken. Applications are approved, rejected, or returned to the researchers with comments asking for clarification, modification of process, or provision of additional information. Besides this role, committees also oversee the progress of the approved projects to ensure that the protocols agreed to are upheld. This role includes site visits, where AEC members oversee the husbandry and housing practices of their

institution's research projects, and by following up on any adverse events (National Health and Medical Research Council, 2013, p. 27).

A primary theoretical framework which is outlined in the Code, and which underpins the functioning of AECs, are the principles of Refinement, Reduction and Replacement (the 3Rs). *The Principles of Humane Experimental Technique* (Russell & Burch, 1959) introduced these principles in the context of animal research. Refinement refers to the refinement of research practices to minimise pain and suffering in research animals; reduction means to reduce the number of animals used in research while maintaining sufficient statistical power; replacement means to find non-animal models to consider research questions. These principles have come to be regarded as the cornerstone of animal research regulation across the international arena over the last forty years, evolving to become a prominent structural feature of many of these systems. Currently the evaluation of applications submitted to Australian AECs use guidelines that rely heavily on the 3Rs, particularly the principles of refinement and reduction.

In September 2019 the NHMRC published an information paper on the implementation of the 3Rs in Australia (National Health and Medical Research Council, 2019). This paper is based on a survey commissioned by the NHMRC on this topic (ORIMA Research, 2018). The paper states: “Despite the importance of the 3Rs, there is limited documented evidence about the use of the 3Rs in Australia. To address this information gap, NHMRC’s Animal Welfare Committee has overseen a project to obtain current information about how the 3Rs are being implemented in Australia and factors that enable or hinder their development and adoption” (National Health and Medical Research Council, 2019, p. 5). The survey asked a sample of Investigators, AEC members and Institutional Representatives to share their views on the implementation of the 3Rs. The survey report provides clear informative statistics on attitudes and understandings held by each of the respondent groups towards the 3Rs. The survey data demonstrated that 71% of investigators and 77% of AEC members “agreed that 3Rs methods are recognised throughout the Australian scientific community” (ORIMA Research, 2018, p. 21). The survey report also indicated that investigators would almost always consider the 3Rs when designing an experiment and preparing an application for the AEC (90% and 89% respectively), however were less likely to consider the 3Rs when writing a publication or attending conferences (29% and 17% respectively)(ORIMA Research, 2018, p. 27). In regards to barriers and enablers to the implementation of the 3Rs in Australia, all groups identified “increased funding to develop

replacement options … [and] help to identify replacement techniques" as key enablers to investigators achieving "their scientific/educational objectives in the future without using animals"(ORIMA Research, 2018, pp. 40-41). All groups identified "lack of appropriate scientific or technological innovation" as the primary obstacle to the 3Rs being implemented (p.49).

The value and effectiveness of the 3Rs has been challenged, however. In her paper 'Why Animal Ethics Committees Don't Work', Russell (2012) argues that the way in which these principles have been applied within AECs in Australia has perpetuated the idea that animals play indispensable and irreplaceable roles within scientific research. In this paper Russell problematises the principle of replacement and its applicability within the AEC review process. Her position is that the Category B member (someone with experience in animal experimentation) will be consulted on the matter of replacement. She highlights that "[a]lternatives to using animals in scientific research are being developed in a range of areas including *in vitro* studies, computer simulation, epidemiology, genomics, use of microorganisms and ethically sourced cadavers or human tissue" (Russell, 2012, p. 129). Due to current standards that limit interdisciplinary collaboration, the literature from these areas may not naturally flow to those working in biomedical research: "the research protocols received by the AECs are coming out of animal research dominated disciplines that at present are usually quite separate from the emerging fields" (Russell, 2012, p. 137). Based on this disciplinary divide, replacement may not be appropriately considered within the review process because of the assumption that the Category B member will have an up-to-date knowledge of the alternative models that are developing in fields outside of their own. This is equally true, Russell argues, of the researcher applying to use animals in research, who is required to state in their application that they were unable to find a suitable non-animal alternative to use in their proposed research. It is Russell's view that the principle of replacement in the context of AECs entrenches the existing paradigm of animal models in scientific research. This view is reiterated by Johnson (2013, p. 502): "AECs do not and cannot ask deeper questions about whether animal research should occur at all or what form it should take. AECs are simply charged with assessing whether a particular research proposal conforms to the 3Rs and, in effect, this reduces to a consideration of whether it complies with just 2Rs [refinement and reduction]".

The 3Rs suvey discussed above included some relevant statistics to Dr Russell's argument. Significantly:

> When asked to assess the helpfulness of their AEC in supporting the implementation of the 3Rs, investigators reported that their AEC was most helpful with regards to improving standards of animal care (72%), followed by refining animal use [53%] … Less than half of respondents found their AEC helpful with regards to reducing animal use (43%), improving/ adjusting the experimental protocol (41%), and replacing animal use (26%)" (ORIMA Research, 2018 p 24).

These statistics support the idea that replacement is not the strongest of the 3Rs within the AEC review process.

Another issue which Russell discusses in her paper is that the review by AECs is the final step in the process of obtaining approval to conduct animal research. According to Russell, because AECs review applications at the end of the approval process and, importantly, after the research has received funding, "the institutional pressures are such that there is no possibility that the research will be rejected outright" (Russell, 2012, pp. 135-136). There is a conflict here between the institution's stake in obtaining research funding, and the ethical obligations of its AEC to reject applications which cannot justify the benefits of the research to humans, animals, or the environment outweigh the costs incurred by the animals used. Ultimately these two processes of assessing the ethics and the provision of funding should be distinct, and funding should be provided only after some form of ethical pre-approval.

Reinforcing the recommendations offered initially in the report by the Senate Select Committee, which have been repeated in various publications over the subsequent decades (O'Sullivan, 2008; Sharman, 2006; Timoshanko et al., 2016; Whittaker, 2014), this paper will grapple with the inaction around transparency in Australian animal research. Looking closely at the practices undertaken by Australian AECs, this paper aims to evaluate the structures that maintain outdated attitudes around the value of openness in animal research practices. Russell (2012) claims that no projects are rejected outright by AECs; however, due to confidentiality, these claims remain untested. In spite of adhering to the same review process, every AEC will function somewhat differently; the human element of these committees inevitably

introduces variation. It is difficult, therefore, to assess blanket statements regarding the review processes undertaken by Australian AECs. This paper empirically evaluates Russell's claim that no applications for animal research are rejected outright by obtaining quantitative data on application outcomes from a sample of Australian AECs which were prepared to provide such data.

Methodology

Quantitative analyses

Data were collected from nine institutions on the outcomes of applications for use of animals in research in 2016 and 2017 (Ethics approval number H-2016-079). The categories of data requested were: number of applications received, number of applications approved without modification, number of applications approved with modification and number of applications rejected. These data are used to represent broad patterns in the review process undertaken by AECs. The analysis involved standardising the data from each institution so that the data can be combined into a single data set.

Data were collected through outreach to AEC representatives for Australian animal research institutions - varying from Universities and Medical Research Centres, to smaller agricultural research institutions - inviting them to share their AEC outcome data. This outreach was through various methods. The request for information was circulated by a third party via an email list pertaining to AECs, the research was also raised at a meeting of animal welfare officers. Some institutions were recruited at the 2018 annual ANZCCART conference after a presentation of the research proposal and preliminary findings. The outreach was not exhaustive; not every institution in every state and territory in Australia could be reached via this recruitment process. However, through the help of individuals within this community, the scope of this survey was still substantial. Because of the broad reach and snowballing that occurred through the recruitment process, it is impossible to know how many institutions were reached overall. Despite this, the proportion of institutions that elected to be involved was small compared to the number contacted.

There is limited public information on the total number of AECs in Australia. After making considerable enquiries in this area, I have been able to estimate the number of AECs in Australia but this is a rough estimate and is used here only for comparative purposes. There is no list or register which collates the number of AECs in the different States and Territories in Australia; even individuals closely involved in the regulation of animal research

at the highest levels do not have this information. After enquiring with the regulators in each State and Territory I have a figure that represents 6 of the 8 States and Territories, and importantly includes those States which I anticipated would make up a considerable proportion of the country's total number AECs: New South Wales and Victoria. I was unable to obtain data for either Northern Territory or the ACT which likely only have a small number of committees. The total number of AECs in Australia excluding the above mentioned is 181. There would likely be at least an additional 7 committees from the 5 Universities in Canberra and 2 Universities in the Northern Territory. Including this speculative data would make 188 committees in Australia. With this rough number which may still be a slight underestimation, the data I have obtained from nine committees makes up almost 5% of the total number of committees in Australia, which is quite a modest proportion.

In addition to the quantitative data, anecdotal accounts from those approached to be involved has been used to develop a more rounded picture of the functioning of AECs. These details are not necessarily methodologically robust but will be included in the discussion of outcomes below.

Qualitative analyses

Alongside the quantitative analyses, field work was conducted, which involved semi-structured interviews with individuals I understood to be involved with animal research. At the time of these interviews I was scoping out information pertaining to animal research and did not have a direct interest or focus on transparency. The interviewees have involvement with animal research across a broad spectrum, either as members of the scientific community, through involvement with AECs, or as researchers and teachers with interests in ethics in animal research. These interviews were conducted in February 2018. Consent was obtained, and interviews were recorded for review purposes. There was a total of five interviews which were largely used for information and perspective gathering purposes. Ultimately these interviews have provided greater depth to the understandings and attitudes that exist in this country towards animal experimentation, and what role transparency is perceived to play. Excerpts from these interviews as well as follow up statements on views around animal research transparency in Australia are reproduced below.

Analyses

Quantitative Analysis

The figures below represent the data obtained from these analyses. The figures show outcome categories as a percentage to protect the anonymity of the institutions. Figure 1 shows a breakdown of data received from nine institutions for the calendar year of 2016. Along the Y-axis is each institution, and along the X-axis is a breakdown of the outcome categories by percentage for each institution. Figure 2 shows the same institutions but data for 2017. Figure 3 is a representation of the data received for all nine institutions over both 2016 and 2017.

Figure 1: Animal Ethics Committee Application Outcomes 2016

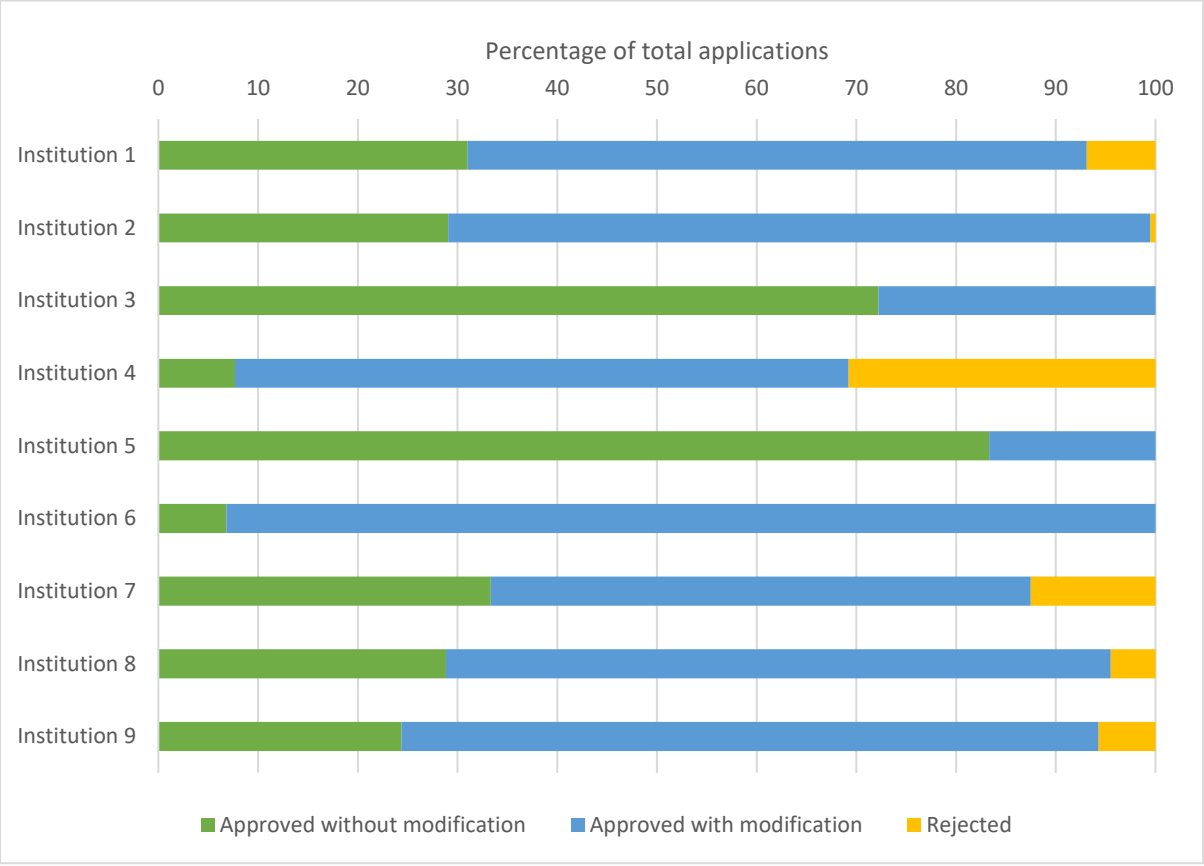


Figure 2: Animal Ethics Committee Application Outcomes 2017

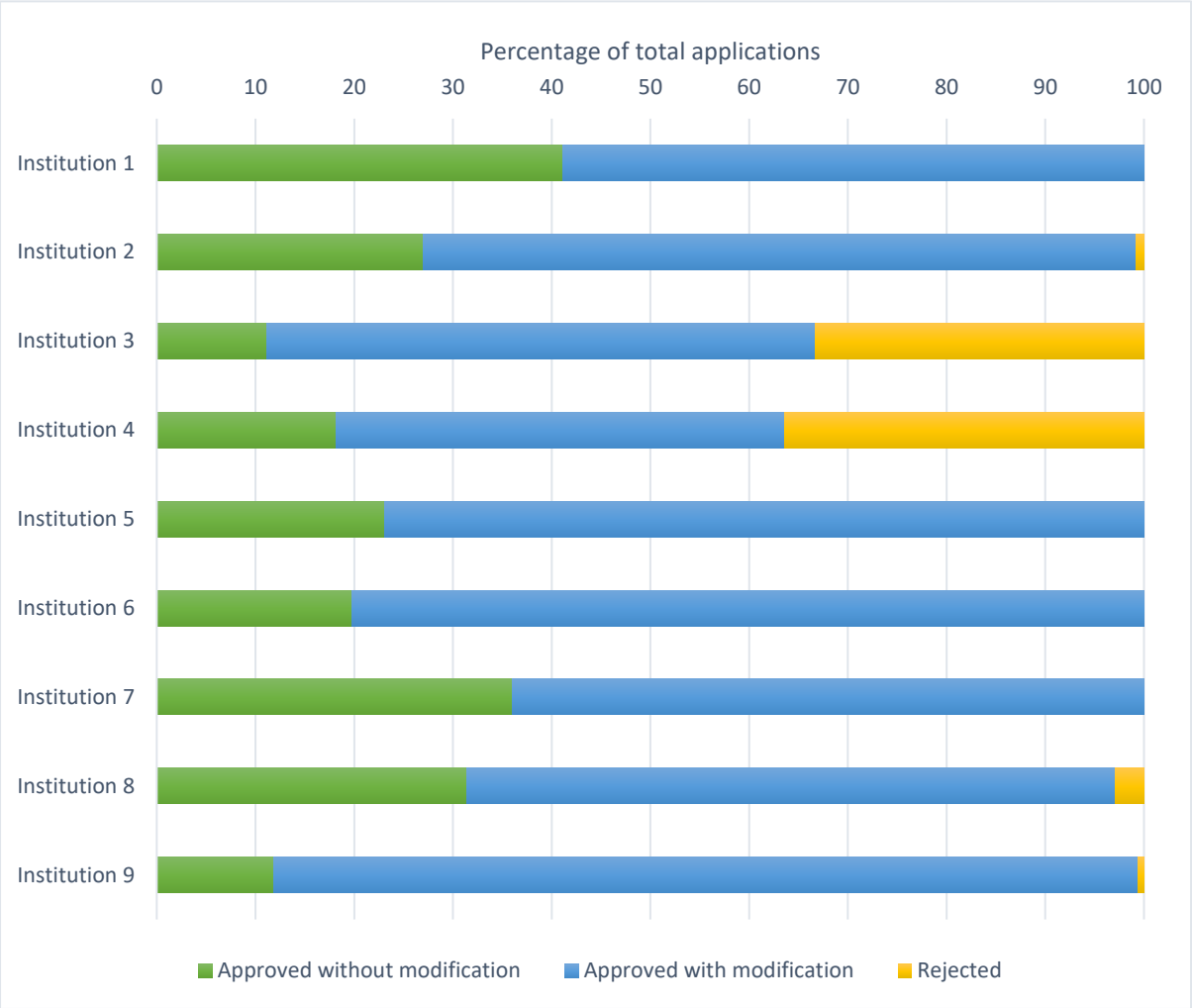
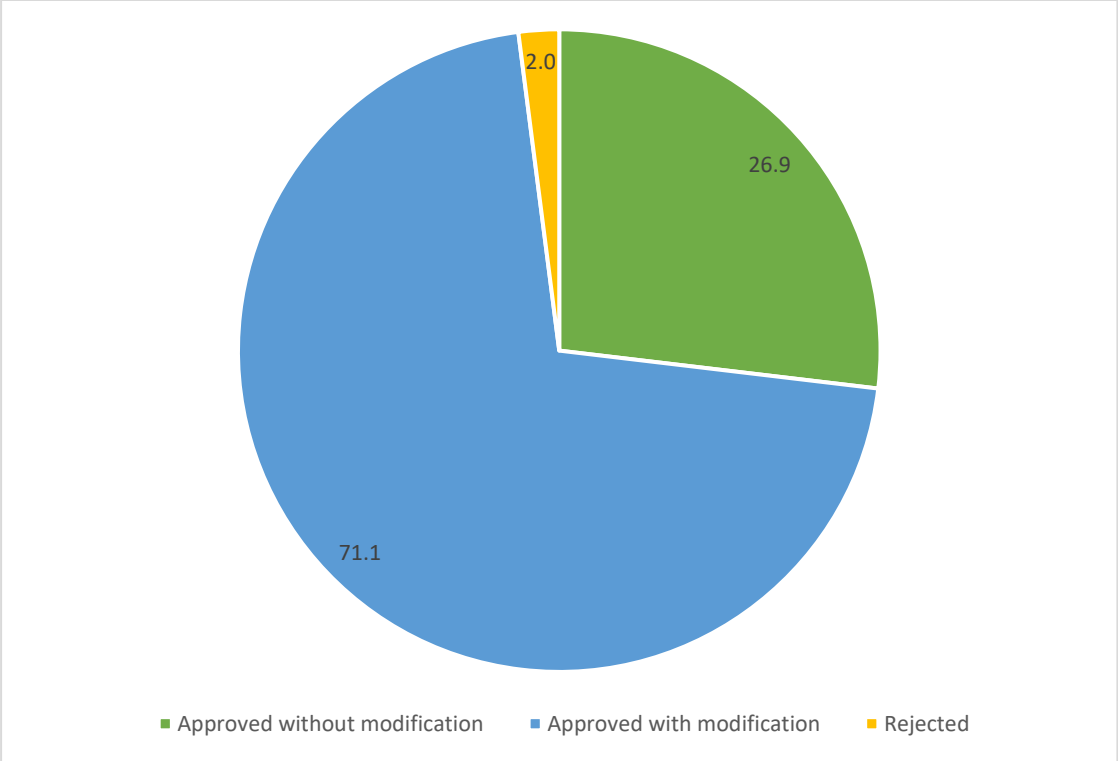


Figure 4: Outcome Trends 2016 and 2017



The primary outcome is that the claim that no projects are rejected is not supported but the data clearly demonstrate that very few projects are rejected. It should also be noted here that the definition of rejected will also likely encompass the outcome 'reject/resubmit' where the committee will invite the applicants to resubmit a new application that perhaps reconceptualises the project in a different way or makes major changes to procedure. As discussed further below, this may reflect that outright rejection is indeed an uncommon outcome for applications put to Australian AECs; or, it may in part also reflect a pre-review process that precedes formal AEC review within some institutions. A secondary finding is that a high percentage of project applications are modified prior to approval. This could be taken to demonstrate the rigorousness of the process of review and challenges the argument that AECs are just a façade to reassure the public. But clearly it also reflects the fact that even small amendments to an application will count as a modified project. Thus, this category may give the impression that these projects had to change a part of their process to adhere more strictly to welfare guidelines, but it may also reflect changes in wording, or process that are unrelated to animal welfare. The patterns demonstrated here seem robust across the participating institutions but a more substantial and representative survey of Australian AECs would be required to fully understand the outcomes of AECs.

Field Work Analysis

This section will detail relevant excerpts from the five interviews conducted in February 2018. The first section will focus on transparency. In cases where transparency was not discussed in great depth, interviewees were followed up for a written statement on their views around transparency which are detailed below. The second section will focus on the role of AECs.

Transparency

Below are statements from the original interviews, the follow up statements, or both. Not all interviewees agreed to be identified by name and in these cases I have provided a brief overview of their role as it relates to animal research. One interviewee declined to provide a follow-up statement on transparency and will be introduced below instead in the discussion of AECs.

Interviewee 1 has had a long involvement in the regulation of animal research in Australia. Their role has placed them in the crossfire between the scientific community and animal activist groups over the last forty years. I asked if they believed that the goals set out by the Senate Select Committee in their 1989 report were taken on board by the research community, especially in terms of transparency. They responded:

> There seems to be sometimes a reluctance to have that conversation [around transparency] and that's been brought about I think historically because of the problems that have occurred particularly overseas [this refers to strong public reactions in the US and UK to the treatment of animals in research, particularly during the 1980s] … There has been this movement in the UK for a much more open dialogue about animal research, and that has not occurred here because there hasn't been a push for it … and there hasn't been the leadership for it to occur … I think we have in many situations a very robust process … [but] we run a risk in this country of not having conversations about the ethics of what we do and openness around it … [there seems] to be a reluctance to do it and it's not seen to be a priority … I just don't think we should close the doors.

Interviewee 2, Dr Malcolm France, is a consultant veterinarian specializing in the care and management of animals used in research. I asked Dr France how important he believes

transparency is to the relationship between scientists and the public. His response was: “transparency is one area where the scientific community has a lot of work to do … I just want the community to be better informed … [transparency] would help the community make an informed decision”. His follow-up statement expands and articulates his view on this:

> While occasional researchers and institutions have taken steps to improve transparency, the overall research community in Australia seems to be a long way off any sort of broader effort towards this goal and is certainly well behind other countries with whom we like to benchmark in relation to research activity. I have often found quite strong "grass roots" support for greater transparency, especially among animal care staff and vets, but senior managers are reluctant to take the initiative. This lack of high level support can often be attributed to unfounded security fears. The result is that public discourse over the ethics of animal research in Australia is one-sided and poorly informed.

Interviewee 3, Dr Denise Russell, is an Honorary Research Fellow in the Department of Philosophy at the University of Wollongong, New South Wales. Dr Russell’s follow up statement on transparency in Australian animal research is:

> It is almost impossible for the public to find out about what research is being conducted especially research which uses animals. The organisation Humane Research Australia has been very important in drawing attention to particularly problematic examples of research using animals such as the research on Macaque monkeys into Parkinson's disease. I have worked at the University of Sydney, including on their Animal Ethics Committee, and the University of Wollongong. I have not been even able to find out which animals are used and what is done to these animals at these institutions despite asking questions. On the AEC I found out about particular protocols but got absolutely no picture of how widespread the use of animals was. It is a terrible situation when public money is used to fund the research that the public cannot find out about. In fact it is an abuse of our trust.

Interviewee 4, Dr Jane Johnson, is a research fellow at the Centre for Values, Ethics and the Law in Medicine in the School of Public Health at the University of Sydney. Dr Johnson’s follow up statement on research transparency in Australia is:

> Transparency in animal research is important, but sometimes it is spoken of misleadingly, as if it were an end in itself – if only we had transparency, ethical issues in animal research would instantly be resolved! However most of the time transparency is only a first step; it is what transparency enables and what we do with what we learn through transparency that is significant. Personally, I'm interested in the kind of transparency that could facilitate an independent assessment of the claims made linking animal research and human clinical outcomes, as well as of the ethical justifications given for research. I think transparency also has an important role to play in signalling a preparedness on the part of researchers and animal ethics committees to be accountable for what they do. I think it is reasonable for the public to be suspicious of practices that are not visible or open to some measure of outside scrutiny. There are however reservations expressed about transparency. For instance, there are suggestions that transparency poses a physical threat to researchers, but in Australia (unlike some other parts of the world) there is no real history of violence against researchers. There are also worries expressed that transparency could mean researchers have their ideas appropriated by others. But the kind of transparency I'm interested in doesn't have to be simultaneous with the research, it could actually be even more effective if occurred after the protocols are completed.

Animal Ethics Committees

In a discussion of the role of AECs in regulating animal research and ways this system could be improved upon, Dr Malcolm France, stated: "I think their role is absolutely crucial, but I think there is more they could do". Similarly, in discussion with Interviewee 5, Dr Vaughan Monamy, author of *Animal Experimentation: A Guide to the Issues* (Monamy, 2000) he stated, "I think their role is invaluable but flawed". These statements speak of the importance of AECs in the regulation of animal research, as being 'crucial' and 'invaluable', while also highlighting a need for development and change. This need is taken up by the community itself reflected, for example, in the 2018 ANZCCART conference theme of 'keeping it relevant'. This conference has a majority attendance by AEC members, which reflects the community's engagement with change and development. These conferences bring together the AEC community and challenge them to question the roles they play and ways that they as a community can continue to grow and learn. It is ultimately the lack of

government initiative, not an unwillingness from the animal research community, that restricts Australia from keeping up with the global momentum on thoughtful and transparent animal research practices.

A theme that emerged out of this fieldwork regarding AECs was the use of the word ethics in the title of these committees. In a paper on the vulnerability of research animals Johnson (2013, p. 502) writes: "[p]erhaps perversely given their title, Animal Ethics Committees rarely consider or discuss ethical issues regarding animals and experimentation per se; rather, they are focused on moderating harm within predetermined constraints. The existence of AECs and the 3Rs that guide them are predicated on the assumption that the practice of experimentation is already morally justified". Moderating harm is an important part of ethical consideration in animal research but the more complex implicit assumptions around the instrumental use of animals are largely not considered.

Dr Monamy discussed the use of the word ethics in AECs. He stated, "I think they should be called either animal welfare and ethics committees or animal welfare committees, because they are dealing with day-to-day welfare; whether the experiment should proceed from an ethical point of view I'm not sure they're fully qualified to decide". AECs have a framework they use when reviewing applications for animal use in research, this framework is based on a cost/benefit analysis using the 3Rs, and while useful in identifying welfare issues, it is ultimately working on the assumption that human life is hierarchically superior to all other species. On the basis of their title, should AECs be better equipped to deal with ethical questions? Or, conversely, should they be renamed to reflect the role they primarily play, in assessing the animal welfare implications of proposed research protocols by way of the 3Rs.

Dr Russell also addressed the concept of ethics within these committees:

> At the moment, we've got it in writing that the NHMRC [National Health and Medical Research Council] does not consider ethical questions, it's considering only what they call 'scientific questions' … and that's something that has to change, the ethics has to come in at the starting point.

I asked Dr Russell, given her criticisms of AECs, how would she would change the review process. The crux of her response was that "until we get out of this web of connections where the finances get mixed up with the ethics, I think that there isn't going to

be a significant step forward and that's why I think there has to be some assessment prior to the funding".

Discussion

Using both quantitative and qualitative methods, I have examined processes conducted by Australian AECs which are not normally publicly accessible. Exploring the ill-defined construct of transparency within the Australian research community was the primary motivation for this inquiry. Johnson suggests that AECs are a regulatory platform which simply exists to reassure the community that a process exists in Australia to regulate animal research: "With the existence of AECs the public may be falsely comforted that ethical issues are being handled and that they need not be concerned" (Johnson, 2013, p. 502). These suggestions raise the further question of whether these committees deal with the ethical issue of why animals are used in research at all, or if they only assess the animal welfare aspects of research. By considering Dr Russell's suggestion that no applications for research with animals are rejected, this research attempted to clarify these questions.

The primary finding from the quantitative analyses was that while it is uncommon for projects to be rejected (2% of total application outcomes from nine Australian institutions over 2016 – 2017), the claim that no projects are rejected was not supported. Furthermore, there may be a greater degree of complexity in the AEC approval process that cannot be demonstrated through the methodology of this study (see below). There is also a high proportion of projects that require modification prior to approval (71.1% of total applications) and this does suggest an active role of AECs in the approval of animal research. However, the grounds for and nature of any required modifications is not known. Outcomes from the 3Rs survey conducted by the NHMRC provides some insight on these patterns: "In relation to their approval process, one-in-five AEC members (19%) reported that their AEC *frequently* or *very frequently* approves applications without modification. Around two-in-five indicated that their AEC *sometimes* (41%) or *rarely* (39%) approves applications without modification, while just 1% indicated that their AEC *never* approves applications without modification" (ORIMA Research, 2018, p. 37).

The primary finding of the qualitative analyses is that irrespective of the position of the interviewee on the animal research debate, themes on transparency from the five field work interviews converged. The impression formed was that transparency is seen as

important to various stake-holders in the transparency debate, whether that is from the perspective of the scientific community, from a regulatory standpoint, or in opposition to animal research. These findings supported earlier claims made by O'Sullivan (2008). Largely, my interviewees believed that more could be done to implement a transparent process, and some pointed to a lack of government leadership on this issue.

Throughout the collection of data, some members of the AEC community raised the concern that my specific interest in application outcomes may not give an accurate representation of the role of AECs. In particular, it was highlighted that in many AECs, it is common practice for there to be some form of pre-screening process which precedes the application process. This is not a requirement in all committees, and the process may often be relatively informal in nature, meaning that there may not be documentation of it, or records kept. Nonetheless, such processes should be considered in the interpretation of the data obtained. Any research proposals which are screened out before making it to an AEC will not be reflected in these data. If any of the institutions represented in these data have a pre-screening process, the number of rejected projects may be artificially low due to early detection and rejection of unfit projects prior to being put to an AEC. If true, this therefore would misrepresent the overall AEC process. The other aspect in which AECs are involved is the continued review of approved projects, including the monitoring of husbandry standards by site visits and continued review of research outcomes and adherence to stipulated welfare standards. Any projects which are subsequently discontinued after approval based on this process will also not be reflected in these data. The only way that this limitation can be addressed in the current research is to acknowledge its potential impact and suggest that a formalized pre-screening or pre-review process be implemented across all institutional AECs which would not only reduce the substantial time commitment of those AEC members who take on these roles voluntarily but would also streamline the AEC review process.

Considering the output of this research, the question arises as to how representative these data are. First, given the small sample size (N=9 participating institutions), the patterns identified in the data are merely an indicator of potential broader national patterns in AEC application outcomes. Second, the representativeness of the institutions that elected to share their data is also questionable given the majority of institutions contacted declined to provide data, or did not respond at all. Many of the institutions that did share data also shared comprehensive descriptions of the processes that their AEC uses in the review of applications for animal research. One interpretation of this is that these more transparent institutions have

less to hide or have other characteristics that do not generalise to other research institutions in Australia. Another possible limitation is that the animal research institutions represented here are varied, ranging from large medical research institutes and Universities, to smaller more specific research institutes; consequently, the number of applications received annually by each institution range substantially and the percentage represented in each outcome category may be distorted by this – nonetheless, the summary data are useful but the context qualified their interpretation.

An important way this research informs the discussion on transparency in Australian animal research is through the responses received from the scientific community to my initial research proposal. The data being requested were to be de-identified before publication, with no risk of individual institutions being recognizable; nonetheless, institutions were largely wary and unwilling to be involved. In one case, I was blinded to the identity of a contributing institution to assure them of the confidentiality of their data. This was achieved by a trusted third party receiving this institution's data and passing it on to me in a de-identified format. The research proposal was met with responses ranging from enthusiasm to scepticism and criticism. Some institutions were immediately enthusiastic (e.g., "The project sounds positive and hopefully will aid in promoting a positive light on animal research"), while others requested further information and clarification before providing data (e.g., "I would need to make sure the AEC members are comfortable before it can be authorised"), and yet others declined to participate (e.g., "At this stage I would be reluctant to provide our information as I believe the outcomes will not be an accurate reflection of reality"). The majority of institutions contacted did not even engage or respond to the invitation to participate. This in itself illustrates the problem of lack of transparency. I faced similar challenges when trying to obtain data on the number of committees in each State and Territory in an attempt to piece together a complete picture of Australia's AECs. While almost all the regulators I contacted for information eventually provided a figure for me, I was shunted between departments in some cases and told on one occasion initially that the data could not be provided for me. The challenge I faced trying to obtain this data indicates that there is a widespread reluctance to share even the most benign details of the regulatory process in Australian animal research.

The broad reluctance to share data indicates sustained issues around information sharing in animal research in Australia. When AECs were first implemented and described in the Code in 1979, there was a degree of fear around the threat posed to animal researchers from animal rights activists. The confidentiality around members, and the proceedings of

meetings, therefore, was likely to have been written into guidelines at this time to protect researchers and committee members from potential threat from animal activists. This degree of secrecy within the current social climate, however, further entrenches the distrust between the scientific community and both activist groups and the general public. Moreover, it facilitates the dissemination of potentially inaccurate statistics around animal use.

Based on this evaluation of the process undertaken by AECs, the following suggestions for increased transparency are offered. The use of the term ethics has the implication that these committees deal with the greater ethical questions which surround instrumental animal use in research. To avoid confusion or misrepresentation, these committees should adopt the membership category of 'Ethics Advisor' which could be filled by a member of the local Department of Philosophy or someone with training in bioethics. This member would have the added role of considering the moral underpinnings of proposed research rather than just the welfare of the animals. This role may cause greater conflict and difficulty in the approval process, so an alternative recommendation would be to rename the committees to 'Animal Research Welfare Committee' to more honestly represent the role they play. Another recommended amendment to AEC membership categories would be on the affiliation of the Chair. While some institutions appoint an external Chair, this is not universal. Formalising this requirement would ensure that personal agenda and collegial ties will not impact the role in any way. Finally, incorporating an official pre-screening process for animal research review (as opposed to the current inconsistent use of pre-screening which is not always documented and not consistent across all Committees in Australia). This process would minimise the number of rejected projects by screening out underdeveloped projects (ethically or otherwise) prior to the official application process. In order to dismantle the association between funding and ethics, this pre-screening process should precede awarding of funding, with the consideration of ethics as a starting point. This process would ensure that there is no conflict between ethics and funding and, moreover, would ensure that there is a consistent review process across all animal research institutions in this country. However, a counter argument to ethical review preceeding funding is that this will likely increase the workload on ethics committees and their administrative teams who will have to review applications that may not even take place if funding is not secured.

At the outset of this paper, I claimed that the role and value of transparency is poorly defined within an Australian context. While a stronger definition would be valuable, it is not feasible to define the role and value of transparency in Australian animal research at this

time. There are a number of interacting factors blocking this conceptual refinement. First and foremost, there has been no dedicated attempt to implement transparency at any stage within the animal research process despite repeated suggestions over the decades (Australia Parliament Senate Select Committee on Animal Welfare, 1989; O'Sullivan, 2008; Timoshanko et al., 2016). As a result, the state of transparency practices is in constant flux as it is often merely an idea rather than an active process. The three major stake-holders in the animal research debate: the scientific community, animal welfare organisations, and policy makers, perceive transparency as positively impacting the attitudes of the wider public in favour of their contrasting views. Various, ultimately incongruent conceptualisations of transparency exist in parallel. These differing conceptualisations are able to co-exist because transparency has not been actioned in Australian animal research as it has been elsewhere. Transparency may not be well defined within an Australian context historically, or at the present time, but it is this state of flux that should encourage action. When transparency is formally implemented within Australian animal research practices and governance, its role and value will be determined, and from this place, a stronger definition will be developed.

Conclusion

Here I considered application outcomes submitted to a sample of AECs in Australia as a way of evaluating the process of review for animal research. This inquiry fits within the broader discussion in this paper around animal research transparency and the benefits of Australian research institutions adopting a more transparent process. Based on quantitative analyses I was able to tentatively suggest that outright rejection, while rare, is not unheard of within the AEC review process. Looking forward, I offer some recommendations and suggestions to researchers, institutions, AECs, government and funding bodies. Through the adoption of some of these strategies it is my hope that Australia can make productive steps towards greater transparency, and both more productive and more ethical animal research practices.

To fellow researchers: pick up this topic for further investigation on a larger scale. The more we encourage institutions to share their data on animal research, the sooner we will obtain data with sufficient statistical power and representativeness to draw meaningful conclusions and further the discussion around transparency. To institutions: share your data. There is nothing to fear from an open process, this is the natural way forward and the most productive way to have an informed public in order to both develop alternatives to animal

models and to continue important research that at this time requires animal models. To government and funding bodies: invest in the development of alternatives. Any area which is supported will thrive, and more successful models which do not require the use of sentient life will be discovered. Develop frameworks that facilitate transparency and encourage information sharing, moreover, fund the resourcing of AECs to implement processes built around transparency and openness. There is a global movement towards transparency in animal research, as will be discussed in Chapter 5, this is particularly evident in Europe and the UK, where various initiatives from both governments, not-for profits, and private organisations are emerging. Australia should join this movement.

Work Cited

Australia Parliament Senate Select Committee on Animal Welfare. (1989). *Animal experimentation / report by the Senate Select Committee on Animal Welfare*. Retrieved from https://catalogue.nla.gov.au/Record/1162665

Grant, E. (1995). Monitoring Ethics in Medical Research. *Wisenet : journal of the Women in Science Enquiry Network*(38).

Humane Research Australia. (2021). Statistics of Animal Use in Research and Teaching in Australia. Retrieved from http://www.humaneresearch.org.au/statistics/

Johnson, J. (2013). Vulnerable subjects? The case of nonhuman animals in experimentation. *Journal of bioethical inquiry, 10*(4), 497-504.

Monamy, V. (2000). Animal Experimentation: A Guide to the Issues (Vol. 1). Caimbridge: Caimbridge University Press.

National Health and Medical Research Council. (1979). *Code of practice for the care and use of animals in research in Australia*: Australian Government Publishing Service.

National Health and Medical Research Council. (2013). Australian Code for the Care and use of Animals for Scientific Purposes. In: Canberra: National health and medical research council.

National Health and Medical Research Council. (2019). *Information paper: The implementation of the 3Rs in Australia*.

Nerlich, B., Hartley, S., Raman, S., & Smith, A. (2018). *Science and the politics of openness: Here be monsters*: Manchester University Press.

O'Sullivan, S. (2008). Transparency in Australian Animal Research Regulation-How Are We Doing. *Austl. Animal Protection LJ, 1*, 15.

O'Sullivan, S. (2006). Transparency and animal research regulation: an Australian case study. *Animal Liberation Philosophy and Policy Journal, 4*(1), 1-25.

ORIMA Research. (2018). Survey on the replacement, reduction and refinement of the use of animals for scientific purposes in Australia. Survey Findings Report. NHMRC. Retrieved from https://www.nhmrc.gov.au/file/14584/download?token=X_aCRhKq

Paytas, T. (2018). Is it time for Australia to be more open about research involving animals? Retrieved from http://theconversation.com/is-it-time-for-australia-to-be-more-open-about-research-involving-animals-103439

Puplick, C. (1994). Animal welfare and scientific research: an opportunity to shape public health policy' *Search, 25*(9).

Russell, D. (2012). Why animal ethics committees don't work. Between the Species: an online journal for the study of philosophy and animals, 15 (1), 127-142.

Russell, W., & Burch, R. (1959). The principles of humane experimental technique. London: London: Methuen & Co. Limited.

Sharman, K. (2006). Opening the Laboratory Door: National and International Legal Responsibilities for the Use of Animals in Scientific Research--An Australian Perspective. *J. Animal L., 2*, 67.

Speaking of Research. (2014, 06/01/2014). Canadians Support Animal Research. Retrieved from https://speakingofresearch.com/2014/01/06/canadians-support-animal-research/

Timoshanko, A. C., Marston, H., & Lidbury, B. A. (2016). Australian Regulation of Animal Use in Science and Education: A Critical Appraisal. *ILAR Journal, 57*(3), 324-332. doi:10.1093/ilar/ilw015

Transparency International. (2009). *The Anti-Corruption Plain Language Guide*. Berlin, Germany: Transparency International.

Understanding Animal Research. (2014). Concordat on Openness on Animal Research. Retrieved from http://concordatopenness.org.uk/wp-content/uploads/2017/04/Concordat-Final-Digital.pdf

Understanding Animal Research. (2017). 360° LABORATORY ANIMAL TOURS. Retrieved from http://www.labanimaltour.org/

USA Today. (2018, 20/06/2018). Let's continue animal testing: America's scientific community. Retrieved from https://www.usatoday.com/story/opinion/2018/06/20/lets-continue-animal-testing-americas-scientific-community/718331002/

Whittaker, A. (2014). Animal research regulation in Australia-does it pass the test of robustness? Global Journal of Animal Law(1).

Chapter 5: Transnational Comparisons

This chapter will bring together three themes which have emerged from the preceding chapters: the relevance of value judgements and public perception in animal model choice in research, changes in regulatory systems for animal welfare, and the state of animal research transparency. This thesis has primarily considered animal research within an Australian context, this chapter aims to consider each of these themes from a transnational perspective as a means of identifying how Australia compares on these issues on a global scale. Overall, I argue that Australia has fallen behind comparable countries in the area of implementing transparency within animal research regulations and frameworks as well as in the area of supporting the development and validation of alternative non-animal research models.

In Chapter 2, I presented a case study of the use of alternative non-standardised animal models in research, considering the use of Australian marsupials in psychology research. This discussion examined the kinds of value judgements placed upon certain animals in the context of research, with the Australian marsupials as examples of iconic species that may hold special meaning within Australian culture. To consider this transnationally, I will discuss some other examples where value judgements and public perception have relevance in animal model choice in research.

In Chapter 3, I discussed the progression of Australia's regulatory system by considering the changing aims of the regulatory document The Code of Practice for the Care and Use of Animals for Scientific Purposes (the Code) over its eight editions from 1969 to 2013. I surveyed literature in the database *Australian Public Affairs-Full Text* using animal research and ethics related search terms and found that there appeared to be an increase in discourse around animal research in the period between 1983 and 1996. This survey identified social and political factors which may have motivated discussion around this issue. Finally, I considered a current debate around the translation of data from animal models to human outcomes. These discussions required the consideration of the development of alternative non-animal models, which I addressed within an Australian context.

In Chapter 4, I evaluated the state of research transparency in Australia, that is, the extent that the Australian scientific community is open with the public about its animal research practices. As part of this discussion I also considered the review process undertaken in Australia to approve applications for animal research. Here I will discuss the state of animal research transparency in the US, Canada, the UK, and Europe and any recent policy

changes aimed at improving transparency. Comparisons with the state of transparency in Australia will be made here. I will also compare the processes by which animal research is approved in these countries and regions and provide commentary on strengths and weaknesses of the different systems. This may identify a particularly fruitful approach to animal research approval that encourages transparency and the development of alternative non-animal models in research. One weakness that has been identified in the Australian Animal Ethics Committee (AEC) process is the lack of structural support for the replacement of animals in scientific research (Russell, 2012). I am interested if there are any systems which have a more active way of integrating the 3Rs, but particularly replacement, into the animal research review process.

Here I will discuss the regulatory systems that exist in the US, Canada, the UK, and Europe and consider bi-directional influences between these systems and the Australian system. The reason I have chosen a restricted number of countries and regions for this comparison is that the scope of this research does not allow for a broad and representative global comparison. The countries and regions selected are useful for my comparative purposes because they have similar trajectories in the implementation of animal research regulation, despite some having longer histories of animal experimentation. I am interested in global trends of change in animal research regulation, and what local and external factors may have influenced these changes, or if the 'zeitgeist' triggered simultaneous changes on a global scale. I will also look at government and private organisations developing alternative non-animal research models in the countries and regions outlined above, with a comparative focus on the degree to which replacing animals in research - in line with the 3Rs of Refinement, Reduction and Replacement (Russell & Burch, 1959) - has been made a priority.

Research animal value judgements

Animal model choice in research is dependent on a number of practical considerations such as how suitable the animal is to a laboratory environment and how well it appears to model the phenomenon of interest (Dietrich et al., 2020). Another consideration that may not be made consciously when selecting an animal model, is how this animal is valued by the wider public, and the role it is typically seen in. There is an interesting contradiction in the way animals are valued in modern society; some animals are adored pets, some are farmed for food, some are protected species in the wild, and - perhaps a less salient category - others are used in scientific research and toxicity or cosmetic testing. While these are not new or

even mutually exclusive categories, the dissonance has never been stronger than it is today. Moreover, the markers that delineate these categories are arbitrary and based upon subjective, sentimental, or erroneous ideas. From these indistinct categories develop value judgements, and strong ones, around the roles and place of different animals. Largely these roles are built within Western countries but particularly the core Anglo-sphere: the US, Canada, the UK, Australia and New Zealand. A broader global comparison will demonstrate disparities in the roles given to animals. When an animal appears in a role where it does not typically belong, based upon these value judgements, there are often strong public reactions. Outside of the context of research, examples of this are the reactions to dog meat in some Asian countries (e.g., see Newkey-Burden, 2018) or, the scandal that emerged when it was discovered that Ikea meatballs imported from Sweden to the Czech Republic contained horse meat (e.g., see *The Australian*, 2013). These examples are given to indicate the wide-reaching inconsistencies in the roles we assign to animals. Both these cases see an animal that is not typically conceptualised as a food within Western society, appearing as such. The reactions to these cases are often horror and disgust, and yet there is no such wide-spread reaction to cows, sheep or pigs being slaughtered for food. There is some contradiction in the public response to these cases because the animals farmed for meat are not unlike dogs and horses either in their appearance, sentience, or intelligence. Instead, it is the roles each of these animals are given within a society that dictate the level of care and concern they receive from the wider public.

In Chapter 2, I discussed this idea as it relates to research animals as part of a broader discussion on the use of Australian marsupials in psychology research. Marsupials play an important part in the Australian identity, being native to Australia and subsequently taken up as recognisable icons within and outside of Australia. This is particularly true of kangaroos and wallabies but other Australian marsupial species such as koalas, quokkas and wombats have become internationally recognisable as uniquely Australian species. Based on this, I speculated that there would be a stronger public reaction to the use of Australian marsupials in research than to purpose-bred laboratory mice, for example. While there are a number of rodent-like marsupial species not dissimilar in appearance to laboratory mice, their native status gives a special value and legal status that laboratory mice are not afforded. However, I did not find this concern reflected in the research literature with there being little discussion around the choice of a particular marsupial species or any justification for its use within an ethical context. This was not particularly surprising in hindsight; often the conduct of

research has been kept out of the public eye, and justification is usually only given in response to public outcry.

Here I want to discuss two cases outside of Australia which demonstrate the place of these value judgements within the context of animal research. The first is a good example of the idea that research is often conducted outside of the public eye and remains hidden unless relevant information becomes available to the public. The role of dogs in research has often aroused public concern and anger. Because dogs are most commonly viewed as a loyal pet, revelations around dogs in research cause public distress disproportionate to reactions to any other animal in research. There are many examples of this; the selling of impounded dogs to research institutions has historically been a common occurrence in the countries and regions I am considering here. Only more recently have there been efforts to implement legislation to prevent the use of stray or pound animals in research. A North American report entitled 'Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research' (National Research Council, 2009) deliberated on the necessity of random sourced dogs and cats in biomedical research. This report responded to public concern that these animals "are obtained from pounds and shelters and may have come from the general pet population" (National Research Council, 2009, p. 2). Following this report the National Institute of Health (NIH) in the US discontinued funding of research using random sourced dogs and cats in 2014 and 2012, respectively (Animal Alliance of Canada, 2016). Another historical case is the use of beagles in US chemical testing. Beagles have been described as a good research animal, largely because of their disposition, and have consistently been used in research. Singer (2009) in the updated edition of *Animal Liberation* discussed a case in 1973 where the use of beagles in research became known to the public and the response was immense. Singer described the case which involved the United States Air Force purchasing beagles in order to conduct chemical testing. The reason this case originally received public attentions was because Les Aspin - a member of the United States House of Representative at the time - had voiced concern over these experiments. Singer (2009, p. 29) writes: "Letters from an outraged public began pouring in … an internal Department of Defense memo released by Aspin said that the volume of mail the department had received was the greatest ever for any single event, surpassing even the mail on the bombings of North Vietnam and Cambodia". Singer was interested in the uproar caused by this single case and speculated whether it was because of the experimental animal being used. He goes on to say, "In any case, it is wrong to limit our concern to dogs. People tend to care about dogs because they generally have more

experience with dogs as companions; but other animals are as capable of suffering as dogs are" (Singer, 2009, p. 30). These examples from the US demonstrate the strength of public response when the use of dogs in experimentation comes to light, often resulting in enquiries and policy change to reassure the public.

The second case is more general; I will discuss the use of non-human primates, and specifically chimpanzees in research. Given the genetic similarity between humans and chimpanzees - "[m]olecular genetic studies over the last half-a-dozen years have shown we continue to share over ninety-eight per cent of our genes with the other two chimps [the common chimp and pygmy chimp or 'bonobo'] (Diamond, 2002, p. 2) - there has been increasing concern over recent decades around the ethics of using chimpanzees in invasive medical research, as well as in psychological research which can arguably be more damaging (e.g., see Cavalieri & Singer, 1993). This example diverges somewhat from the previous example: chimpanzees have demonstrated complex cognitive and emotional capacities, and our value judgements around using chimpanzees in research are not necessarily misplaced. However, this comes back to the framing of the instrumental use of animals. If framed as a hierarchical valuation based upon perceptions of intelligence and sentience, chimpanzees may merit greater consideration. If framed within the paradigm of animals as vulnerable subjects (Johnson, 2013) capable of pleasure, pain, and suffering, this hierarchical valuation is less useful. I will focus here on a contemporary topic of discussion: the ending of research using chimpanzees as experimental animals and on the rehoming of retired chimpanzees. This discussion is an interesting transnational comparison at the current time because already a number of countries have banned the use of chimpanzees and other great apes in research, while others, including the United States still have chimpanzees in laboratories. According to Knight (2008a), "[b]y 2008, legislative or policy bans or restrictions on invasive great ape experimentation existed in seven European countries, Japan, Australia and New Zealand".

In Australia there are strict regulations around the use of primates in research (National Health and Medical Research Council, 2013); however, there is no outright ban on the use of chimpanzees. According to the Humane Research Council: "There are no recent records of research conducted on great apes in Australia, and whilst the National Health and Medical Research Council (NHMRC) has strict guidelines on their use, it is not explicitly prohibited" (Humane Research Australia, 2015).

The United States is in a transitional period at the current time, with the retiring and rehoming of the remaining chimpanzees used in research as of 2015. In the US wild chimpanzees were classified as endangered in 1990 under the 1973 U.S Endangered Species Act ("Endangered and Threatened Wildlife and Plants - Listing All Chimpanzees as Endangered Species," 2018) but this protection did not include captive chimpanzees. In 2015 the National Institutes of Health (NIH) withdrew support for chimpanzee research, and planned retirement for its remaining chimpanzees (Kaiser, 2015). During the same year the US Fish and Wildlife Service classified US captive chimpanzees as endangered "effectively ending biomedical studies on them" (Grimm, 2017, p. 1115). Knight (2008a) reported that in 2006 there were 1,133 chimpanzees across six primate centres in the US. In 2013, according to a newspaper article published at the time (State News Service, 2013), the US had 950 chimpanzees across five laboratories, and of these, a majority were owned or funded by the government. Grimm (2017) presented some data to demonstrate the rate of retirement of both privately owned and government owned chimpanzees; while these data are not current it is still useful to demonstrate movement of chimpanzees from laboratories to sanctuaries. At the time of this publication, there were a reported 577 chimpanzees in five laboratories and 470 in eight accredited sanctuaries. It should be noted that the chimpanzees remaining in laboratories in 2017 were no longer being used in invasive research but were waiting to be moved to a sanctuary. These figures from various sources show a slow decline in chimpanzees held in laboratories in the US after 2015.

What emerged following the move to retire the remaining laboratory chimpanzees in 2015 was a discussion around what was to become of so-called 'retired' chimpanzees. Grimm (2017) outlines the issue regarding availability of chimpanzee sanctuaries compared to the number of chimpanzees waiting to be rehomed. Another issue around moving chimpanzees to sanctuaries is the stress of the journey itself followed by adjustment to a new environment, both of which can strongly impact old and sick chimpanzees, with many dying shortly after arriving in sanctuaries (Reardon, 2018). These issues are ongoing, and many chimpanzees remain in laboratories while "[t]he NIH will form a working group to develop recommendations for veterinarians to consider when determining whether or not to move a chimpanzee" (Reardon, 2018). This report, published in May 2018 and titled 'Council of Councils Working Group on Assessing the Safety of Relocating At-Risk Chimpanzees', presents figures relating specifically to NIH-owned or supported chimpanzees. As of May 2018, the NIH had chimpanzees across three research facilities and one federal sanctuary,

‘Chimp Haven’; there remained 272 chimpanzees within the three facilities and 232 in the sanctuary. This report also identified a number of chimpanzees that were over 35 years old, or which had a chronic infection or chronic disease, factors relevant to the decision whether or not to move these chimpanzees. The working group discussed these and other risk factors in relation to moving chimpanzees but ultimately recommended that “The NIH and the facilities that house NIH-owned and NIH-supported chimpanzees should relocate all of these chimpanzees to the federal sanctuary system unless relocation is extremely likely to shorten their lives” (NIH Council of Councils, 2018, p. 27).

Like Australia, Canada does not have national legislation on animal research. There is no direct ban on the use of chimpanzees in research; however, one source quotes the Canadian Council on Animal Care (CCAC) as stating that “no chimpanzee has been used for scientific purposes in Canada before or since [the CCAC’s] creation in 1968” (Canadian Broadcasting Corporation, 2017). According to the annual data reports published by the CCAC, non-human primates made up 0.1% of the total animals used in research during 2017, 6412 in total; however, the species of primates are not listed (Canadian Council On Animal Care, 2017).

In the UK, research with great apes was banned in 1997 (Thew, Bailey, Balls, & Hudson, 2012). However, this was briefly revisited in the media when Directive 2010/63/EU was implemented across all European member countries. While Directive 2010/63/EU also banned the use of great apes in research, “EU Member States can seek … a derogation from the Commission to permit such use, where this is considered essential for the preservation of the species in question or in relation to an unexpected outbreak of a life-threatening or debilitating clinical condition in human beings” (Thew et al., 2012, p. 3). Under Directive 2010/63/EU despite the 1997 ban it was now possible that researchers in the UK could request an exemption in order to use great apes in research. Although there is no indication that this has occurred in the intervening years, it did become a point of discussion in the media during the period surrounding the implementation of these new regulations.

In Europe, Directive 2010/63/EU banned the use of great apes in research. Prior to this in 2008, Spain extended some human rights to great apes in line with the Great Ape Project (Cavalieri & Singer, 1993), “becoming the first country to explicitly acknowledge the legal rights of nonhumans” (The Christian Science Monitor, 2008). Founded in 1994, the Great Ape Project set out “to fight for the basic rights to life, freedom and non-torture of the

nonhuman great apes – Chimpanzees, Gorillas, Orangutans and Bonobos, the closest relatives of man in the animal world" (Great Ape Project, 2013).

It is interesting to consider the way global discussions around the use of chimpanzees in research may have impacted decision making in these countries and regions, but particularly in the US, which lagged behind other Western countries in implementing legislation or policy restricting use of chimpanzees. The next legislative move will likely be towards limiting or banning research on all non-human primates, rather than just great apes. There are already public discussions around the continued use of primates in research, and certainly a great deal of secrecy surrounds this continued research in Australia where openness and transparency are still limited.

Regulatory Structures

There have been a number of publications which provide an overview on the different animal research regulatory structures worldwide (e.g., see Phillips & Sechzer, 1989; Vasbinder & Locke, 2016). Here I will briefly overview the current regulations in place in the US, Canada, the UK, and Europe, while retrospectively considering how these regulations developed. This will not be an extensive or detailed account, rather, the primary aim of this discussion is to identify differences that exist and make comparisons to the Australian regulatory system. I also want to identify times of major change or upheaval in the implementation of animal research regulation and any similarities in the timelines of these countries and regions. I will use this comparative discussion to illustrate the ways that Australia may be unique in its approach to the regulation of animal research and argue that this may reflect the shorter history of animal experimentation in Australia particularly when compared to the UK and Europe. There are also many ways that Australia has modelled its regulatory systems on pre-existing systems, and perhaps how Australia's system may be looked to in the future as a model for other countries developing or updating their animal research regulation.

The regulation of animal research in the US is multifaceted and complex. The first federal legislation in the US was the Animal Welfare Act (AWA), introduced in 1966. The AWA is the primary feature of an overlapping structure of regulation for animal research. Depending on the species used and the kind of funding received, firmer regulations may apply, with the AWA being the widest reaching and also the most moderate. Other narrower regulations will apply under different funding schemes and these may provide greater

protection for a wider range of animals used in research. The AWA has been amended a number of times, with important changes being made in the 1985 amendment. The most significant of these changes was the establishment of Institutional Animal Care and Use Committees (IACUC; National Research Council, 2004, p. 29) and the implementation of institutional registration through the United States Department of Agriculture (USDA). An amendment to the AWA in 1977 excluded mice, rats, birds and farm animals, including horses, from its protection (Phillips & Sechzer, 1989, p. 22). This remains a controversial element of the US regulatory framework and makes between-country comparison of animal use difficult due to differing definitions. The USDA is responsible for overseeing the AWA, and the Animal Plant and Health Inspection Service (APHIS) division of the USDA conducts inspections of research institutions (Phillips & Sechzer, 1989, p. 21). Another major element of the regulatory system in the US is the Public Health Service (PHS) policy which was legislated through the Health Research Extension Act in 1985. Any project receiving support from the Public Health Service needs to line its research practices up with not only the AWA but also the separate guidelines under the PHS. Additionally, the PHS policy requires use of the Guide for the Care and Use of Laboratory Animals (the Guide; National Research Council, 2010). This set of guidelines was first published in 1963 and is in its eighth edition. The primary intention for the Guide is "to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate", and additionally, "to assist investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, humane, and ethical principles" (National Research Council, 2010, p. xiii).

In Canada there is no federal legislation relating to animal research but the Canadian Council on Animal Care (CCAC) is responsible for overseeing the conduct of animal research and was established for this purpose in 1968 following an inquiry and report by the Medical Research Council (MRC; Canadian Council On Animal Care, 1993, p. 1). The structure of the CCAC is as a multi-tiered organisation with 22 member organisations and two funding bodies. The member organisations elect a board of directors which oversees four committees. These committees are responsible for governance and nominations, assessment and certification, public affairs and communication, and standards. Each institution is required to establish an Animal Care Committee (ACC) which is "responsible for overseeing all aspects of animal ethics and care at their institution" (Canadian Council On Animal Care, 2019). The self-governance of this regulatory framework with the CCAC and local ACCs

responsible for ensuring compliance to guidelines appears to be progressive and effective in engaging both individual researchers and institutions in the process.

The call for regulation around animal experimentation was most prominent in the UK and, in response to the antivivisection movement, the Cruelty to Animals Act was introduced in 1876 (Phillips & Sechzer, 1989, p. 5). This legislation was rudimentary and did not satisfy the antivivisectionists who continued to push for greater protection for animals in research. The current system of regulation in the UK is based upon the Animals (Scientific Procedures) Act (ASPA) introduced in 1986. This nation-wide legislation falls under the responsibility of the Home Office which oversees various societal matters including immigration and security. The Home Office is responsible for granting licenses to institutions and researchers, as well as conducting inspections to enforce the requirements outlined in ASPA. Any institutions using animals in research are required by the Home Office to establish an Animal Welfare and Ethical Review Body (AWERB). When Directive 2010/63/EU was implemented across all European member countries in 2010, this impacted the UK as part of the European Union; however, largely, the UK already had more stringent regulations under ASPA and these remained unchanged. Changes currently in progress after the UK left the European Union will mean the UK will no longer fall under the regulation of Directive 2010/63/EU.

In Europe animal research is regulated by Directive 2010/63/EU on the protection of animals used for scientific purposes. This Directive meant member countries had a deadline of January 2013 to make necessary changes. Previously, European animal research regulation fell under Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. Directive 86/609/EEC was proposed in 1986 to create consistency across Europe in the regulation of animal research. However, ongoing discontinuity between European countries gave rise to the development of Directive 2010/63/EU (National Research Council, 2012). While the same expectations have been implemented across Europe, each member country is responsible for overseeing them. A new requirement of Directive 2010/63/EU was “the evaluation and authorization of all research projects and training activities involving the use of animals” (Guillén, Robinson, Decelle, Exner, & Van Vlissingen, 2015, p. 23), and this mandated some form of approval process for proposed animal research.

As has been outlined in previous chapters, Australia’s animal research regulatory framework comprises one national regulatory document (the Code) which

does not have legislative power but is enacted through State-and-Territory-based legislation. The Code requires any institution using animals in research to establish an Animal Ethics Committee (AEC) which is responsible for reviewing applications for research with animals, along with monitoring by site visits the housing and husbandry practices of the institution's animal facilities. There are some similarities between this regulatory system and each of those outlined above. Australia does not have national legislation and therefore is structurally different to the US, the UK and Europe. One broad similarity between all countries and regions considered here is the use of some form of approval process for animal research that is comparable to Australian AECs. The ways these committees fit within their broader regulatory structures differ and this will be discussed further below. The significant role of funding on the degree of regulation imposed upon animal research is a unique feature of the US system, where stricter guidelines may be imposed under certain funding schemes. This may be seen as a weakness of the US system in comparison to other systems which have a more consistent frameworks that protect animals regardless of the type and source of funding.

Another difference between the US and the other systems discussed here is which animals are protected under each system. In Australia, according to the most recent edition of the Code (National Health and Medical Research Council, 2013, p. 1), "The Code applies to the care and use of all live non-human vertebrates and cephalopods". Similarly, in an updated and consolidated version of the 1986 UK legislation ASPA "Subject to the provisions of this section, "a protected animal" for the purposes of this Act means any living vertebrate other than man [and any living cephalopod]" f. In Europe, according to Directive 2010/63/EU, "In addition to vertebrate animals including cyclostomes, cephalopods should also be included in the scope of this Directive" (The European Parliment and the Council of the European Union, 2010, p. 34). Under the US revised version of the 1966 AWA:

> The term "animal" means any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal, as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes, or as a pet; but such term excludes (1) birds, rats of the genus Rattus, and mice of the genus Mus, bred for use in research, (2) horses not used for research

> purposes, and (3) other farm animals, such as, but not limited to livestock or poultry (USDA, 2019, p. 16).

In Canada, the most reliable source regarding which animals are included under regulatory guidelines is the CCAC, which publishes guidelines for the use of animals for scientific purposes. One animal welfare organisation 'World Animal Protection' ranked different countries on an index from A to G based on their animal protection policies across a number of domains including within scientific research. Canada was ranked D overall, and under the section on 'protecting animals in scientific research' it is noted that eight of Canadas ten provinces reference the CCAC guidelines within their animal welfare legislation (World Animal Protection, 2014). Based on this I will use the guidelines provided by the CCAC as representing the regulations for animal research across Canada. There is no statement which identifies which animals fall under regulatory protection in Canada but the CCAC is quite transparent and publishes animal use data annually, although this is only data from CCAC certified institutions and so may be incomplete. The 2017 document on animal use in experimentation lists fifteen categories of animals including mice, rats, birds, reptiles and fish (Canadian Council On Animal Care, 2017), indicating that these species fall under the protection of CCAC guidelines.

These differing definitions on what constitutes an animal and is thus protected under research regulation is important in the context of this transnational comparison. The UK is the strictest in its protection by regulation, with the updated and consolidated version of ASPA (GOV.UK, 2014, p. 1) reading:

> Any such vertebrate in its foetal, larval or embryonic form is a protected animal only from the stage of its development when—
>
> (a) in the case of a mammal, bird or reptile, [two-thirds of] the gestation or incubation period for the relevant species has elapsed; and
>
> (b) in any other case, it becomes capable of independent feeding

Conversely the US excludes a number of its most frequently used research animals from protection, including mice, rats, birds and farm animals. A significant implication of this is the difficulty these inconsistencies create in the comparison of different countries and regions on animal use. Because the US does not include the above listed species under legislation, data is also not collected on their use, resulting in an underestimation of total

animal use in the US. By the same token, the UK figures will be higher based on their wide reaching and inclusive definitions.

Considering the different regulatory systems, Phillips and Sechzer (1989), surveyed scientific literature in the United States with an interest in the ethics of animal research between 1966 and 1986. This publication provides a useful overview of regulation across a broad number of countries over this time period. As part of a discussion on Australia's then developing regulation of animal research, the authors state, "The Vice-Chancellors' Committee [to the Senate Select Committee] has recommended that a system of review and monitoring, developed from the Canadian model, should be implemented" (Phillips & Sechzer, 1989, p. 113). In the report by the Senate Select Committee (Australia Parliament Senate Select Committee on Animal Welfare, 1989, pp. 197-198) it states:

> For some years there has been a move to establish an Australian Council for the Care of Animals in Research and Teaching (ACCART) based on the model of the Canadian Council on Animal Care … Although ACCART was modelled to some extent on the Canadian Council on Animal Care, after lengthy deliberations among the proponents … and other interested organisations, it was decided to exclude accreditation, a major function of the Canadian Council, from the role of ACCART. It was decided that accreditation should remain the responsibility of State Governments.

ACCART is now ANZCCART so as to include New Zealand. There remain parallels between the modern Canadian and Australian systems of animal research regulation which likely stemmed from these early discussions when Australia was still developing its regulatory structures. As noted above, accreditation was not made the responsibility of ANZCCART and remains under State and Territory jurisdiction.

In comparing the different influences on the implementation of new animal research regulations in the US, Canada, the UK and Europe, considering times of parallel change is important. In Chapter 3, I considered the period between 1983 and 1996, where the discussion of animal research in a sample of Australian publications increased. Based on themes from the articles I surveyed, one possible catalyst to this increase in discourse was increased animal activism both within and outside of Australia. Activism and increased media coverage of the controversy surrounding animal research may have impacted conversations around the regulation of research. It is likely that significant changes in

regulation of animal research worldwide were in response to this time of heightened discussion in the public sphere. Phillips and Sechzer (1989, p. 19) in a discussion of regulations in the US state that "[t]actics of the animal protection movement have often been directed towards the goal of governmental regulation of animal experimentation". In Australia this time period saw a Senate Select Committee investigation into the state of animal welfare, three new editions of the Code, new State and Territory Legislation, and the implementation of institutional Animal Ethics Committees through the Code. Similarly, the UK legislation ASPA was introduced in 1986, and the important amendments to the AWA in the US were made in 1985. In Europe, Directive 86/609/EEC was introduced in 1986. With only Canada not making any significant changes to its animal regulatory system during this time. There is no doubt that during the 1980s in particular, the time was right for a shift in the perception and treatment of animals in scientific research, as well as in other domains. This was felt on a global scale. This push for change has been sustained over the intervening decades and animal research remains a topical issue but perhaps, however, lacking the intensity of the 1980s.

The role of animal movements becomes relevant in this transnational discussion of regulatory changes in animal research. Considering the simultaneous timing of new and updated animal research regulations globally, there was clearly an undercurrent of change and momentum from the 1980s onwards. According to Villanueva (2017, p. 80) "Through the interplay of lobbying, alliance building, and participation in state and industrial bodies, activists began to change and pluralise Australian politics. Activists extended the political agenda, influenced public policy, and reshaped the state bureaucracy to include new avenues for animal protection". However, this quote does not refer specifically to research; in his book *A Transnational History of the Australian Animal Movement, 1970 – 2015*, Villanueva (2017) provides an extensive discussion of the development of the Australian animal movement, and importantly for this discussion, the focus is largely on the industry of animal agriculture, and not on animal research. The reason this is so important in a transnational discussion of animal research regulation, is that the role of activism was certainly not as pertinent to research activities in Australia as it was elsewhere. If anything, the current regulatory structures in Australia still echo a fear of activism that was not felt strongly here but instead was borrowed from the aftermath of these events in the US and the UK. What is stranger still, is that the countries that actually experienced violent activism targeting the

animal research industry (particularly the UK) have developed more open practices in research than is seen in Australia.

The 3Rs of Reduction, Refinement and Replacement were first proposed in 1959 (Russell & Burch, 1959), but their global dissemination and uptake as part of regulatory frameworks in animal research did not occur until the 1980s (Russell, 2005). This is an example of the way information can be produced at one time but not be recognised until later. This concept supports this idea of the zeitgeist being what causes social movements or the recognition of certain theories and ideas at particular times. It was during the 1980s that the modern wave animal issues came to the forefront, perhaps riding the current of dissonance and outrange sparked by the civil rights movement and women's rights movement.

Non-animal model development

While the uptake of the 3Rs (Russell & Burch, 1959) has been globally promoted, and as part of this, replacement has been integrated into many animal research regulatory bodies worldwide, the development of alternative non-animal models has been inconsistent across the countries and regions discussed here. In Chapter 3 not support research that uses any animal derivatives including: "(non-human) animal cells, animal tissues, animal cell lines, animal derived antibodies (monoclonal and polyclonal), animal derived stains or reagents" (Medical Advances Without Animals, 2016). Another point of difference when looking at organisations advocating replacement is whether the organisation is replacing animals in fundamental biomedical research, in chemical and cosmetic testing, or both. A large number of the validated replacement models are used in chemical or cosmetic safety testing, and while this goal is important, it is a secondary interest of this thesis which focusses on the use (and replacement) of animals in fundamental (i.e., basic not applied) research.

In the US there are a number of organisations involved in developing and validating alternative models for research. One such organisation is the Johns Hopkins Center for Alternatives to Animal Testing (CAAT; John Hopkins Bloomberg School of Public Health, 2019b). CAAT uses the 3Rs framework in defining alternatives and, therefore, any method which refines, reduces or replaces animal use in research fits within the goals of their organisation. CAAT is a non-government funded organisation which receives funding from a number of sponsors including several companies within the cosmetic industry. Another US non-government organisation is the American Fund for Alternatives to Animal Research (AFAAR). AFAAR offers postdoctoral grants to women either developing, validating or

using alternative models in research. The US government has a body responsible for evaluating new alternative methods but this committee focusses solely on chemical toxicity testing (Interagency Coordinating Committee on the Validation of Alternative Methods; National Institute of Environmental Health Sciences, 2019).

In Canada, the CCAC established a 3Rs program in 2008. Griffin (2009) describes this program as looking towards longer standing organisations such as the Fund for the Replacement of Animals in Medical Experiments (FRAME) in the UK for direction. The Canadian Centre for Alternatives to Animal Methods (CCAAM) and the Canadian Centre for the Validation of Alternative Methods (CaCVAM) were established in 2017 and are hosted by Windsor University in Ontario, Canada. These organisations "aim to develop, validate, and promote non-animal, human biology-based platforms in biomedical research, education, and chemical safety testing" (University of Windsor, 2019). These organisations claim to be the only ones of their kind in Canada at the current time.

In the UK, the Fund for the Replacement of Animals in Medical Experiments (FRAME) was established in 1969. This organisation puts a strong emphasis on the guidelines embodied in the 3Rs and, particularly, replacement. According to Griffin (2009, p. 65) "FRAME went on to play a significant role in shaping the Animals (Scientific Procedures) Act 1986". In 2004 the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) was founded as an initiative of the British government. These are both examples of 3Rs organisations; Animal Free Research UK is an example of a replacement only organisation and their website states: "We award grants to research scientists to implement existing techniques and develop new ones which are more human-relevant and will replace animal experiments. Only those projects with the highest scientific calibre and the best potential for the replacement of animals are awarded funding" (Animal Free Research UK, 2017a). Animal Free Research UK, previously the Dr Hadwen Trust for Humane Research, was established by the British Union for the Abolition of Vivisection in 1970 but this partnership ended in 1980. The Dr Hadwen Trust for Humane Research continued as a registered charity and became an incorporated charity in 2013, before changing their name in 2017 to Animals Free Research UK (Animal Free Research UK, 2017b).

In Europe, the Johns Hopkins Center for Alternatives to Animal Testing established a European centre in 2010, called CAAT-Europe at the University of Konstanz in Germany

(John Hopkins Bloomberg School of Public Health, 2019a). The Netherlands is one of the leading countries in the world in the replacement of animals in research (particularly in chemical safety testing); according to PETA UK, the Dutch government aims to eliminate animal use in "safety tests for chemicals, food ingredients, pesticides, veterinary medicines, and vaccines" by 2025 (PETA UK, 2016). This does not include, however, animals used in fundamental research, and PETA urges the Netherlands National Committee for the protection of animals used for scientific purposes (NCad) to "also act expediently to end experiments in the areas of illnesses such as obesity, diabetes, stroke, and cancer, where there has been an overwhelming failure of animal use to benefit humans" (PETA UK, 2016). Ncad is a 3Rs organisation and therefore at this time still supports the use of animals in research.

There are a number of ways to compare the extent to which the replacement of animals in scientific research has been made a priority in the countries and regions considered here. The greatest indicator of commitment to replacement is the degree of government support, which demonstrates the overall stance of each country towards the goal of replacing animals in research. However, government policy does not necessarily represent the views of the wider population; there can often be strong support for an issue in the wider community before the government takes direct action. Regardless, the support of government behind initiatives towards replacement is vital for country-wide uptake. Another way to compare this commitment to replacement, is by looking at the number of organisations in each country but this is only useful up to a certain point because the size of the country and the scale of animal research done in each will also impact this. Finally, whether an organisation is committed solely to replacing animals in research, or if it also supports the refinement and reduction of animals in research, indicates the degree of commitment to replacement. While both types of organisation are playing a part in awareness raising, and ultimately in the replacement of animals in scientific research, the replacement-only organisations are more hard-line in their policies towards this. In Australia, while there is one organisation with a replacement-only approach, there has not yet been government support widely given to the replacement of animals in research. In the US there are a number of 3R based organisations, and the government supports the Interagency Coordinating Committee on the Validation of Alternative Methods which validates alternative methods for chemical toxicity testing. In Canada, the CCAC disseminates the use of the 3Rs through its guidelines and established a 3Rs program in 2008. There also is an alternative development and validation centre based within the Windsor University in Canada. In the UK, there are government supported 3R

organisations as well as a replacement-only organisation, the UK is probably one of the most advanced in the protection of animals in research and support for the development of non-animal alternatives. In Europe there are different degrees of uptake of policies and centres to replace animals; the Netherlands was discussed above as an example of a progressive country on these issues, with a commitment to ending animal use for toxicity testing by 2025.

Transparency

Beyond the regulation of animal research, transparency in animal research is an important part of current discussions. Transparency is seen as a key aspect of rebuilding a trusting relationship between the scientific community and both animal welfare communities and the wider public. Different countries experienced lesser or greater duress from animal rights groups and responded in different ways. I argue this is an important factor when comparing the steps taken to implement policies that foster transparency in the practice of animal research. Here I will consider transparency in the US, Canada, the UK and Europe, as compared to Australia, including any indication of the importance placed on transparency and justifications given in the literature.

In Chapter 4, I discussed the state of transparency in Australian animal research. There are no significant policies or guidelines encouraging transparency in Australian animal research, and while there are some statistics on animal use reported, these are inconsistent and there are no accurate national figures available. In a quantitative analysis I conducted in Chapter 4, looking at patterns in application outcomes submitted to Australian AECs, I noted strong apprehension from the animal research institutions I approached to participate. The reluctance to share this de-identified data demonstrated the secrecy which is ingrained within AECs and the review process they undertake. This reflects more broadly the regulatory stance of the Australian government towards openness. O'Sullivan (2008) discusses transparency in Australian animal research; her paper is discussed in some detail in Chapter 4 but will be used here in the context of a broader discussion on transparency. Her month-long media survey of four Sydney newspapers was used to demonstrate the minimal exposure the Australian public has to the realities of animal experimentation in this country through mass media. The report showed that research animals were one of the least reported on categories of animals, with wildlife and companion animals making up the large majority. O'Sullivan (2008, p. 21) writes: “[t]he tussle over transparency in animal research has engaged all three human stake-holders: those who oppose the use of animals in research; those who make their

living from animal-based research; and public policy makers who mediate between the two". This paper evaluates the recommendations handed down by the Senate Select Committee regarding transparency in animal experimentation in 1989 and finds limited progress towards adopting these recommendations. In particular O'Sullivan notes that the means by which greater openness could be facilitated, such as through AECs and animal use statistic reporting, remain ambiguous regarding transparency.

In the US there has recently been a push from the scientific community in favour of greater transparency in research. On June 20, 2018 *USA Today*, an internationally distributed newspaper, published a letter signed by 592 US scientists calling for greater transparency from their colleagues in the scientific community: "We call upon our country's research institutions — large and small — to embrace openness. We should proudly explain how animals are used for the advancement of science and medicine, in the interest of the wellbeing of humans and animals" (*USA Today*, 2018). The letter sparked a number of other publications immediately after, including an article in *Science* (Wadman, 2018), that spoke to People for the Ethical Treatment of Animals (PETA) on this development: "We urge animal experimenters to video everything they do, from inducing heart attacks in dogs to shocking the feet of mice to cutting open the skulls of monkeys, and release it to the public that funds most of it," said PETA Senior Vice President Kathy Guillermo. "We ask them to be open about the fact that 90% of animal studies fail to lead to treatment for humans and to explain why they still use animals in drug research when 95% of new drugs that test safe and effective in animals fail in human trials". Another opinion piece published in *The Scientist* in April 2019 (Buckmaster, 2019), continues the conversation around transparency as a way to defend animal research and correct false claims around its value. Buckmaster (2019), the Chair of the organisation 'Americans for Medical Progress' writes: "as a result of our collective silence, animal rights activists for the most part now own the narrative. They've convinced a large number of their fellow citizens to reject an often-irreplaceable part of the health research process".

In Canada, an animal research advocacy group, 'Speaking of Animals', state in an article 'Canadians Support Animal Research', that Canada's transparency in animal research is responsible for overwhelming support for animal research by the Canadian public. The author Michael Brunt writes: "The CCAC occupies a pivotal role of encouraging transparency in the Canadian regulatory system by ensuring that the use of animals, where necessary, for research, teaching and testing employs optimal care according to acceptable

scientific standards and communicating all relevant information to the Canadian public, to whom they are accountable" (Speaking of Research, 2014). The CCAC reports figures on animal use annually which are very extensive. The report is available on the CCAC website and includes the headings 'number and type of animals in science', 'purpose of animal use' and 'category of invasiveness'(Canadian Council On Animal Care, 2017). This openness likely reassures the public because there is no perceived secrecy surrounding the process of animal research. The narrative around animal research benefitting from greater transparency is not uncommon, it is often a message that comes from within the scientific community but is equally supported by animal welfare groups.

The UK has consistently been a beacon of change throughout animal research controversies over the last three centuries. It was the birthplace of the antivivisection movement, saw some of the most extreme reactions from the animal rights movement, has some of the most extensive regulation for animal research, and significant efforts have been made towards increasing transparency. In a recent thematic analysis, McLeod and Hobson-West (2016) looked at discourses around transparency in the UK. This paper identified three communities contributing to this discourse: animal protection groups, the animal research community and government/research funders. The way the term transparency was utilised and operationalised by these three communities in this analysis demonstrated different understandings and expectations of transparency. For animal protection groups transparency represented uncovering a hidden truth behind animal research; for the animal research community it represented correcting distorted impressions of the animal research industry which have been portrayed by those in opposition to animal research; for government/research funders transparency represented "a counter to public mistrust in science and politics" (McLeod & Hobson-West, 2016, p. 801). The authors in discussion of their methods of analysis note: "In general, debates relating to the use of animals are often characterised by polarised positions. However, in the discourse relating to openness, it is fascinating to see some similarities as well as the expected oppositional stances" (McLeod & Hobson-West, 2016, p. 802). In drawing conclusions based on this analysis McLeod and Hobson-West (2016, p. 802) write: "the current transparency agenda does provide at least the *potential* for transformation. Our analysis shows the complexity and slipperiness of the concept of transparency and confirms that no one definition exists" (McLeod & Hobson-West, 2016, p. 802; emphasis in original). This paper provides a useful way of understanding the evolving role of transparency in animal research discourse, and how various actors in this

debate can promote transparency for contradicting reasons. In the current discussion I am considering transparency from a transnational perspective, and this in-depth analysis of discourse in the UK provides insight to one country's approach to transparency, with a deconstruction of the aligned but conflicting views within society.

Some of the important ways the UK has embraced animal research transparency in recent years are the Concordat on Openness on Animal Research (Understanding Animal Research, 2014), the Freedom of Information Act (Understanding Animal Research, 2015a), the review of Section 24 of ASPA by the Home Office (Home Office, 2014b), and online laboratory animal tours at a select number of UK research institutions (Understanding Animal Research, 2017). The Concordat on Openness on Animal Research was established by a not-for-profit organisation 'Understanding Animal Research' in 2014 and represents a commitment by a number of UK organisations to greater openness in animal research practices. Preceding this, in 2012, forty organisations signed a Declaration on Openness on Animal Research which set the precedent for the Concordat. At the current time the Concordat has 128 signatories that "are all involved in carrying out, funding or supporting animal research in some way" (Understanding Animal Research, 2014, p. 5). The document reads: "the signatories to this Concordat want people to be able to find out more about animal research so that they can debate the issues from a position of knowing the facts and make up their own minds about animal research" (Understanding Animal Research, 2014, p. 4). There are four commitments which are upheld by the signatories of the Concordat, and while these have been expanded significantly within the document, the Understanding Animal Research website states these four commitments concisely:

> We will be clear about when, how and why we use animals in research … We will enhance our communications with the media and the public about our research using animals … We will be proactive in providing opportunities for the public to find out about research using animals … We will report on progress annually and share our experiences (Understanding Animal Research, 2019).

The Freedom of Information Act of 2000 came into force in 2005 and is officially described as "[a]n Act to make provision for the disclosure of information held by public authorities or by persons providing services for them" (Information Commissioners Office, 2000). In 2014, the Home Office conducted a public consultation on the review of Section 24

(Home Office, 2014a). In the consultation stage of this review, the Home Office describes Section 24 of ASPA as "a statutory prohibition on disclosure that provides for the protection of information received in confidence that is provided in connection with our regulatory activities under the 1986 Act" (Home Office, 2014b, p. 1). Essentially, Section 24 of ASPA exempts the Home Office from releasing certain confidential information that may be requested under the Freedom of Information Act. In the review it states: "The Government is reviewing Section 24 since its inflexible confidentiality requirements are now out of step with government policy on openness and transparency and with the approach taken in other legislation, such as the Freedom of Information Act 2000" (Home Office, 2014b, p. 1). The report presented a number of solutions, these were to retain Section 24, to repeal Section 24 with amended legislation around the kind of information that can be released and its intent, or to repeal Section 24 absolutely (Home Office, 2014a). From considering the current legislation however, there appears to be no change to Section 24 in ASPA following this review.

In 2017 four institutions in conjunction with the organisation Understanding Animal Research, launched virtual laboratory tours of their facilities, accessible online to the public (Understanding Animal Research, 2017). The online tool enables 'walk through' tours of each facility, with a map feature showing the purpose of each room in the building and providing additional information on the institutions research practices. These tours are not live streaming so of course these institutions are still curating the information available to the public; however, this is nonetheless an important step forwards in transparency.

In Europe transparency has been addressed differently across the region, Understanding Animal Research (2015b) reported that in France, the National Centre for Scientific Research had launched virtual tours through its facilities and that this may be a useful model for the UK in developing the Concordat on Openness on Animal Research. The virtual laboratory tours at the National Centre for Scientific Research evidently inspired the program launched two years later in the UK by Understanding Animal Research in conjunction with several institutions. There are agreements comparable to the Concordat that have been launched in both Spain and Portugal, with one source reporting that Belgium and Switzerland would soon follow suit and develop a similar commitment towards transparency (European Animal Research Association, 2019).

There has recently been a call for Australia to follow the UK and Europe in its policies around animal research transparency. This followed a survey by Australian and New Zealand Laboratory Animal Association (ANZLAA) of animal care workers including veterinarians in animal research, which demonstrated a large majority (87%) were in favour of greater openness in this sector. Dr Malcolm France who was interviewed as part of my field work in Chapter 4 on transparency, is quoted in one report as saying

> [A] sad consequence of the lack of openness is the negative impact it has on those who provide day-to-day care for the animals. Most animal technicians choose their vocation because they love animals. Even if they have mixed feelings about animal research, they are determined to see the animals receive the best possible care. Unfortunately, they are often reluctant to talk about their work because they fear a negative reaction based on public misunderstanding and outdated images in anti-vivisection campaign material (European Animal Research Association, 2019).

Animal research approval processes

As was briefly detailed above, in the countries and regions considered here, as in Australia, there is a requirement for an approval body that reviews applications for animal research. These committees may ultimately serve different purposes or hold greater importance depending upon the other regulatory structures that surround them. (Rose, 2012) reviews the history of AECs and notes that Australia was among the first countries to implement committees for the ethical review of animal research, along with Sweeden and Canada. This paper provides a systematic review of publications which empirically evaluate the processes and outcomes of AECs. The body of literature in this area is limited but this review "questions the foundations and effectiveness of the ethical review process, not only in terms of the application of a framework for ethical review but also as to the underlying ethical principles" (Rose, 2011 p, 285). Rose highlights in this evaluation that the framework underlying ethical review of animal research is not well defined and suggests that the principle of respect and responsibility should form the "basis for consideration of the ethical justification of the use of animals in research … [and the] development of agreed criteria against which the outcomes of the application of these principles can be judged" (Rose, 2011 p, 285).

In Chapter 4, I considered the roles and structure of Australian AECs in some detail, here I will briefly overview key features of the Australian system for animal research review. AECs were first established in the second edition of the Code in 1979 and were subsequently enforced through State and Territory Legislation. The proposed structure of AECs has changed and developed over the six subsequent editions of the Code, but committee member categories have remained consistent since the fourth edition published in 1985. Structured category membership was introduced in the fifth edition published in 1990, with Category A being "A person with qualifications in veterinary science" Category B, "A person with substantial recent experience in animal experimentation" Category C, "A person with demonstrable commitment to, and established experience in, furthering the welfare of animals" and Category D "An independent person who does not currently and has not previously conducted experiments using animals" (National Health and Medical Research Council, 1990, p. 11). Definitions of committee member categories have been tightened and updated over subsequent years, but the four categories remain the same. These committees are also required to have a Chair and an animal welfare officer who is directly involved in the institution's animal facilities. The committee meets periodically to review applications for animal use in research, with frequency depending on the size of the institution. Members also conduct site visits of the institution's animal facilities to ensure adherence to stipulated welfare standards, therefore continuing to monitor active projects. The 3Rs are an integral part of the AEC review process, and replacement is considered by the researcher in their application to use animals, where they must state that no alternative methods are available. Russell (2012) however, has questioned the efficacy of addressing replacement within the application process, when the researcher is unlikely to have knowledge of alternative models developing in fields outside of their own. The construct of transparency has not been integrated into these committees which continue to operate behind closed doors.

In the US, Institutional Animal Care and Use Committees (IACUC) were implemented under the 1985 revision of the AWA. The committee membership differs according to which regulations are being adhered to; according to Lamberti and Suckow (2017), the United States Department of Agriculture requires three members, while the Public Health Service requires five. These members should include a scientist with experience working with animals, a veterinarian, a non-scientist from inside or outside of the institution, and a member not associated with the institution, as a representative of community views (National Institute of Health, 2019). These committees also have a Chair, and the committee

as a whole reports to an Institutional Official who "bears the ultimate responsibility for the animal care and use program" (Lamberti & Suckow, 2017, p. 66). The primary roles of these committees are the evaluation of proposed research and teaching involving animals, the inspection of animal facilities, and following up any concerns brought to the committee regarding animal use at the institution. As discussed above, a weakness of the structure of US animal research regulation is that it is not consistent across all laboratories and projects but will vary depending on what animals are being used and subsequently which regulations are required. Similarly, the structure of the IACUC should not be impacted by the regulations being followed but should be consistent across all institutions. The 3Rs are built into the protocol review for IACUCs and replacement is part of project applications, with the requirement to consider the "availability or appropriateness of the use of less invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation" (National Research Council, 2010, p. 25). Despite recent calls from within the scientific community for greater transparency in animal research, this has not yet been implemented within IACUC protocol review.

According to the terms of reference for Canadian animal care committees: "[t]he Canadian Council on Animal Care (CCAC) requires that institutions conducting animal-based research, teaching or testing establish an animal care committee (ACC), and that it be functionally active" (Canadian Council On Animal Care, 2006, p. 1). According to the terms of reference, "ACCs may also choose to form subcommittees to work on specific areas such as protocol review or development of standard operating procedures" (Canadian Council On Animal Care, 2006, p. 1). The membership of ACCs is similar to Australian AECs, with requirement for a Chair, a scientist or teacher with experience working with animals, a veterinarian, a community representative and a technical staff representative (someone who works in the institution's animal facility). The difference between the committee membership in Canada compared to Australia is that ACCs do not require an animal welfare representative but do require a member of the institution who does not work with animals, and where students are present, a student representative. These committees also require an ACC coordinator, "the institutional employee who provides support to the ACC" (Canadian Council On Animal Care, 2006, p. 3). ACC membership can also extend where necessary to include others such as "person(s) responsible for health and safety/biosafety, biostatisticians, ethicists, public relations liaisons" (Canadian Council On Animal Care, 2019). The committee as whole reports to a senior institutional administrator responsible for animal

ethics and care. The 3Rs are considered in the terms of reference for ACCs at considerable length. Regarding the replacement of animals with alternative models, ACCs have a similar stance to Australian AECs, with the requirement to justify the use of animals falling to the researcher in their application (Canadian Council On Animal Care, 2006, p. 6). While the CCAC has a strong stance on transparency, this is not integrated into its ACCs, where transparency has not been discussed in the terms of reference for these committees.

In the UK, the Home Office requires any institution using animals in research to establish an Animal Welfare and Ethical Review Body (AWERB). This body was brought into effect on January 1st 2013, replacing the Ethical Review Process (ERP) that existed since 1998 (RSPCA and LASA, 2015). The membership requirement for an AWERB is a minimum of an animal care and welfare officer, a veterinary surgeon, and a scientific member, all from inside the institution. Additional flexible membership includes involvement of information officers and training and competence officers. Finally, as quoted in 'Guiding principles on good practice for Animal Welfare and Ethical Review Bodies', a report by the RSPCA Research Animals Department and Laboratory Animal and Science Association (RSPCA and LASA, 2015, p. 6) the institutions' licence holder is required "to arrange for their AWERBs actively to seek a wider membership, taking into account, in a transparent manner, the views of people who do not have responsibilities under ASPA, as well as one or more persons who are independent of the establishment". Despite the diverse ways that the UK has embraced transparency in animal research, one paper published in the journal *Alternatives to Laboratory Animals*, argues that "the legitimacy of animal research continues to be undermined by selective openness"; proposing that "openness could be increased through public involvement, and that this would bring about much needed improvements in animal research" (Pound & Blaug, 2016, p. 167). In this paper the authors note that: "the only opportunity for public involvement is as a mandatory lay-member on an Animal Welfare and Ethical Review Board (AWERB) … [s]uch boards, however, are dominated by scientists and do not lend themselves to equal participation by lay-members, particularly if the latter hold differing views about animal research" (Pound & Blaug, 2016, p. 170).

In Europe, Directive 2010/63/EU requires "the evaluation and authorization of all research projects and training activities involving the use of animals" (Guillén et al., 2015, p. 23). Under the previous Directive, this was not a requirement but some European countries already had a system of animal research approval in place prior to 2010. Guillén et al. (2015)

discuss the different ways this particular regulation was implemented across European member countries by considering the UK, the Netherlands, France, Germany and Spain. As has been mentioned here, the way animal research approval functions will vary depending on the system it is implemented into; in the same way that these approval bodies differ between the countries and regions I am considering here, when Directive 2010/63/EU was introduced, European countries implemented these new regulations differently to fit within pre-existing structures. This is noted in the analysis by (Guillén et al., 2015, p. 31), concluding that, "[a]fter transposition of Directive 2010/63/EU, there is still variation in approaches to project evaluation in EU, which may be partially explained by the differences in resources and experience across member states … Approaches may vary, but the outcome should be the same: animals should be used only when justified and necessary; the number of animals used should be the fewest needed to meet the scientific objectives proposed; and projects should follow animal care and use standards that minimize animal pain, suffering and distress". Directive 2010/63/EU highlights in its requirements of project evaluation "the need for transparency" (Guillén et al., 2015, p. 23). On the website of the European Commission, it states that Directive 2010/63/EU "improves transparency through measures such as publication of non-technical project summaries and retrospective assessment" (European Commission, 2019). The website also states that "[t]he development, validation and implementation of alternative methods is promoted through measures such as establishment of a Union reference laboratory for the validation of alternative methods supported by laboratories within Member States and requiring Member States to promote alternative methods at national level" (European Commission, 2019).

The review of applications for animal-based research in the countries and regions discussed above are all structured around the 3Rs. As part of this replacement is considered but the effectiveness of incorporating replacement into the application process has been questioned within the Australian system (Russell, 2012) and this criticism applies to other committees that use this approach. While transparency has been implemented to varying degrees in these locales, and often through the impetus of the scientific community, the review of applications for animal research has not yet incorporated policies to improve transparency. The composition of these committees is similar, all committees require a scientific member with experience working with animals, a veterinarian, and most either require or suggest including a member independent of the institution to represent community

views. Australia is the only country that has mandatory membership of an animal welfare representative on the committee, which is a strength of the Australian system.

Conclusion

A primary aim of the current transnational discussion of animal research regulation, and the ethical debates that surround it, was to illustrate the ways that Australia may be unique in its approach to the regulation of animal research. I postulated that any differences may reflect the shorter history of animal experimentation in Australia, particularly when compared to the UK and Europe. However, when looking at the development of Australia's regulatory system for animal research, there are also many ways that Australia has modelled its regulatory systems on pre-existing systems. One way that Australia's regulation is unique, is that its AEC membership includes an animal welfare representative, the only country of those considered here that makes this membership explicit in its terms of reference. Moreover, the combined membership of the community member and animal welfare representative must make up no less than one third of total membership of AECs when the committee has more than four members, ensuring a balanced perspective in the review of applications.

Historically, the development of animal research regulation in these countries and regions has followed a similar trajectory. Despite the UK and Europe having a significantly longer history of experimenting on animals, the implementation of regulations was relatively parallel, beginning in the twentieth century, with the notable exclusion of the Cruelty to Animals Act, which was introduced in the UK in 1876 following lobbying by the antivivisection movement and the outcome of the *Royal Commission on the practice of subjecting live animals to experiments for scientific purposes* (Great Britain Royal Commission on Vivisection, 1876). One period which saw an increase in the implementation of regulations was throughout the 1980s and early 1990s, likely in response to a rise in activism, most notably in the US and the UK. The entrenched secrecy which surrounded animal research following this period has continued into modern day practice, with efforts to implement a transparent process being a more recent development. Given the similarities evident in the regulatory systems I have considered here, there has undoubtedly been influence and sharing of information in the development of these systems. As discussed above, there was explicit discussion around Australia implementing a similar body to the CCAC but despite ANZCCART being established based on this model, there were significant

differences between the two, with the role of accreditation remaining the responsibility of State and Territory governments in Australia. The CCAC would be worth further study as a model for a more cohesive national approach to animal research regulation in Australia. The inclusion of an evaluation of the New Zealand system would have been valuable here due to the links between Australia and New Zealand, and this is a limitation of this review.

Australia's regulatory system for animal research is robust, it has one consistent set of guidelines which are legislated through the States and Territories. One way that national rather than State and Territory legislation could improve Australia's transparency would be through a streamlined reporting process of animal use statistics, which would allow more accurate between-country comparisons around animal use. Alternatively, Australia could learn from the regulatory structures used in Canada, which are similar to those in Australia but have integrated systems of reporting on animal use including on the levels of invasiveness of the research. The UK is probably the most progressive in its policies around animal research, with the widest reaching definition of 'animal' for legislative protection, the most extensive efforts to increase transparency, and both government and privately-owned organisations dedicated to developing and validating alternative non-animal models. Australia could also implement a similar commitment to transparency as is reflected in the Concordat on Openness on Animal Research in the UK, which allows individual institutions to sign an agreement to uphold a set of guidelines around openness in scientific research. This could filter down to the AEC system, integrating policies around transparency of process. Australia is also lagging behind in government support for developing alternative non-animal models. The Medical Advances Without Animals (MAWA) trust has established a strong foundation but the government needs to back this initiative in order for Australia to catch up with those countries I have considered here.

Chapter 6: Conclusion

At the outset of this thesis, I set out to do the following:

1. To evaluate the current regulatory structures for animal research in Australia against the backdrop of their historical development

2. To consider and evaluate current debates around animal research in this country, specifically:

    a) The way animals are valued and the structures which surround the choice of a particular animal model

    b) Transparency about the use of animals in research in the scientific and broader communities

    c) Translation, if any, of animal research to human outcomes

3. To consider how Australia compares to other countries and regions in both the historical and current frameworks around animal research, and particularly the ways in which Australia differs from similar jurisdictions

This concluding chapter will summarise and draw together themes from the body of the thesis. I will present concluding statements in relation to Australia's current regulation of animal research and the state of animal research transparency. I will also discuss the future of animal research in light of claims discussed in Chapter 3 that the translation of animal research to human outcomes is poor. Emerging non-animal research models become crucial from a practical standpoint, and the need for government intervention in terms of legislation and funding outcomes is critical. The following will outline the primary outcomes from each of the four body chapters along with discussion of limitations, broad implications and any future directions.

In Chapter 1, I introduced my topics and reviewed the literature on Australian animal research regulation both from historical and contemporary perspectives. I identified this enquiry as sitting against the backdrop of the values in science literature with animal research in particular sitting on the intersection of these discussions due to the active public commentary in this area. I then situated my research questions within their global and historical context, broadly reviewing the history of animal use in experimentation. I presented

an overview of the beginnings of animal experimentation and its growth in the twentieth century and beyond. I discussed the animal protection movements, beginning with the anti-vivisection movement in the UK which developed into the welfare and rights movements that grew particularly after the 1975 publication of *Animal Liberation* by the Australian philosopher Peter Singer (Singer, 1975). Finally, returning to my specific research questions, I discussed the broad timeline of legislation and regulations around animal research both in Australia and internationally.

In Chapter 2, I presented a case study considering the choice of a particular animal model for use in scientific research. Specifically, I reviewed research in psychology using Australian marsupials in the place of putative standard model organisms such as the rat or the mouse. I was especially interested in the unique value placed upon these species as being native and somehow revered or iconic within the Australian context, and how this may have modulated their perception as suitable research models. The studies I reviewed were primarily using the marsupial species to consider an already studied phenomenon but with an interest in whether and how marsupials may differ from other mammals, or how studying this phenomenon in marsupials may add novel insights. However, some of the studies chose marsupials for the purpose of studying a particular phenomenon thought to be unique or interesting in its own right within these species. The primary aim of this research was to evaluate the nature of studies choosing to use marsupial species. More broadly, I was interested in animal model choice in research and how this is influenced by different factors such as the research question, the suitability of the animal to a research environment, but also how the animal is framed in broader society and if it has commonly been conceptualised as a research animal. This chapter demonstrated that there are useful experimental models amongst Australia's marsupial species. Moreover, the narrow scope of much animal research, with its focus on standardization, may contribute to the arguably poor translation of animal studies to human outcomes.

In Chapter 3, I dealt with the changes over time in Australian regulatory structures around animal research. This was considered primarily through the framework of The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (the Code) which guides Australian State and Territory legislation on animal research. The Code was first published in 1969 and is now in its eighth edition (published in 2013). Changes in the aims outlined in each edition of the Code were used here to trace the changing attitudes towards research animals over the period of 1969 to 2013. This analysis demonstrated a clear

progression and change in the conceptualisation of research animals. Patterns in frequency of relevant search terms in an Australian database were used as a way of tracking the discussion around animal research in the public domain. This analysis indicated that there was heightened discussion of issues surrounding animal research in the period between 1983 and 1996. This period of increased discourse around animal research demonstrated the uptake of this topic for public debate and discussion from the 1980s onwards. Continuing with the theme of changes in regulation, Replacement, one pillar of the 3Rs (Russell & Burch, 1959) was considered here as a vehicle of change, with regulation and practice moving away from traditional animal models and exploring alternatives, motivated both by ethical concerns and the need for better translation to human clinical outcomes. A discussion of Australian organisations dedicated to developing alternatives to animal models, and individuals who argue that animal models are not good predictors of human outcomes were also outlined here. These discussions emphasised the importance of both the Australian Government and the wider public supporting the development of alternatives to animal models. I also advocated that the Government via its major funding bodies the NHMRC and the ARC should mandate an explicit statement of the consideration given to alternatives to using animals in research being proposed for funding.

Chapter 4 had a broad interest in transparency in Australian animal research. Conceptually, transparency in research refers to the flow of information from the scientific community to the broader public. This may include the availability of information on standards and practices used in animal research, the species and numbers of animals used, the husbandry and housing practices employed, or the research aims and anticipated value of the research. This chapter argues that transparency is a vital element of the scientific process, and that this is particularly true for research that makes instrumental use of animals. Within an Australian context, I argue, we need more uniform policy implementation directly relating to the communication of process, husbandry, and outcomes of animal research. One key element of this is the annual reporting of animal use statistics from every Australian State and Territory, which can then be translated to a nation-wide figure for the purposes of international comparisons. Another element of this relates to Australia's regulatory bodies: Animal Ethics Committees (AECs). As part of this chapter, I appraised the process these committees undertake in reviewing and approving applications for animal research. I empirically investigated a claim that these committees do not reject projects (Russell, 2012), by conducting a quantitative analysis of application outcomes in a sample of Australian

AECs. This analysis demonstrated that projects are often modified before approval and are infrequently rejected. The primary outcome from this analysis was that this process could be streamlined to create more consistency between committees, and greater transparency needs to be introduced into the approval process. I concluded based on this research that changes relating to transparency should be implemented within the AEC process to ensure trust from the wider public. A further insight taken from the experience of collecting data from Australian AECs was observing that the frameworks within animal research regulation in this country continue to inhibit information sharing and openness. There is still widespread distrust and suspicion in response to requests for information in this area. I found this both in 2018 when I first put a call out for data for my analysis of application outcomes, and again in 2021 when I tried to reach out to State and Territory regulators for numbers of AECs within each State and Territory in order to construct a national tally of AECs. While I did eventually successfully obtain data from six of eight States and Territories, there was a degree of hoop jumping involved in obtaining data from some jurisdictions.

Chapter 5 tied together the themes from the preceding chapters with a transnational comparison of historical and current practices in Australian animal research. The theme I took from Chapter 2 was that of animal model choice in research and how this is impacted by value judgements. Bringing this theme into a transnational discussion I looked at other cases where animal model choice is impacted by the perceived value of the animal by the wider public. Taking the theme of change and disruption within animal regulatory structures and regulations from Chapter 3, I discussed the regulatory systems that exist in the US, the UK, Canada, and Europe. I also looked at organisations in these countries and regions which are developing or advocating for alternative non-animal models. From Chapter 4, I took the theme of openness as a desired construct by all stakeholders in the animal research debate and I discussed the state of transparency in the US, the UK, Canada and Europe, comparing the extent to which this has been made a priority. I then evaluated and compared the processes and structures in place for the review and approval of animal research in these countries and regions. Overall, I argue, Australia has fallen behind other countries both in the area of implementing transparency within the regulatory structures of animal research, and in supporting the development and validation of alternative non-animal models.

Broad Commentary, Limitations and Future Directions

What follows is a broad ranging commentary that synthesises themes that arose across chapters and highlights some limitations of the current research and points to directions for future research. After this, I will draw the discussion to a close with an overarching statement of the take home messages of this thesis.

Together these four chapters presented a picture of historical and current practices in Australian animal research regulation. A significant finding was that there appear to be global patterns in the development of, and change in, animal research regulation. That is, the uptake of certain reforms in regulation, the investment in developing alternatives, or the implementation of policies that support transparency have followed a trajectory globally but some nations have spearheaded these developments, with others lagging behind. These times of change may have had specific catalysts in different countries but there are underlying similarities, such as the pressure applied by animal rights groups particularly throughout the 1980s and 1990s. This shows that as the globe becomes more interconnected, the nations discussed here have, and will continue to be, influenced by broader international trends and movements regarding the regulation of animal research. In the current environment actions are held to a global standard due to rapid and widespread information sharing. There is greater pressure now than ever for Australia to keep up with the momentum of assessing and re-evaluating practices in animal research and striving to improve our standards.

Another finding arising from both the quantitative analysis in Chapter 3 and the field work in Chapter 4 is the need and desire for greater transparency in Australian animal research. Previous literature has demonstrated that transparency is framed differently by different stakeholders in this debate (McLeod & Hobson-West, 2016; O'Sullivan, 2008) despite being largely perceived as positive by all groups. For animal advocates, transparency is seen to be a means to uncover the harsh realities of research practices and to give the wider community the opportunity to form opinions based on this reality. For the scientific community, transparency is an opportunity to correct distorted opinions of the animal research industry as putatively fed to the public by animal protection groups. Within an Australian context, there has been a push for greater transparency coming from animal care staff (European Animal Research Association, 2019). Despite calls from within the scientific community for greater transparency, there has been a lack of leadership in the implementation of changes such as has been seen in the UK with the Concordat on Openness

on Animal Research (Understanding Animal Research, 2014) and the virtual laboratory tours available for a select number of research institutions (Understanding Animal Research, 2017). Similarly, Australia falls behind other countries in support for the development and validation of non-animal models for research. While the Medical Advances Without Animals Trust (MAWA) is developing the Australian Centre for Alternatives to Animal Research at the Australian National University, there is a glaring lack of government support for these endeavors.

As highlighted at the outset of this thesis, many of the topics explored in the four body chapters have a grounding in the values in science literature and raise questions on the intersection and tension between science and values. In Chapter 2 this is a distinct theme emerging from discussions of animal model choice in research and how the valuation of different animals in the broader community interacts with the animal models utilised in research. This notion directly contradicts an idea which has emerged from the values in science literature of the 'value-free ideal' which suggests that the wider social and political context of a scientist's research should not impact on their decisions and judgements around their work. I argue that in the field of animal research it is important for the broader social context to be part of the research narrative, and that the researcher should interact with this broader context in the conduct of their research, reacting and responding through their work to public attitudes and concerns. In Chapter 3, the discussion of public discourses around animal research and their impact on policy change across the history of animal research regulation are ingrained in this theme of values and science. There are many interacting elements which impact upon the evaluation and change of regulations on animal research but there is no doubt that public discourse feeds into these decisions, again creating a grey area in the conceptualisation of scientific research being conducted in a silo, uninfluenced by its surroundings. In Chapter 4 the discussion of openness and transparency in the practice of animal research directly relates to the interaction between science and values, with all interested parties agreeing that transparency is vital to this process and must be incorporated into the conduct of animal research.

The preliminary findings presented in this thesis could usefully be developed further. In particular, the discussion around the framing of animals in the context of research did not reach definitive conclusions. Evidently, public perception shapes the roles of different animals; in Chapter 2 I explored this through an evaluation of the use of Australian marsupials in psychology research. While this review provided a consideration of the ways

non-standardised experimental models could contribute to scientific enquiry, the anticipated justification for model choice on the part of researchers due to the value assigned to this group of animals was not evident. I propose that a survey of the interested general public would find concern or discomfort with these animals being used in research. Given that Australian animal research is still conducted largely outside of the public eye, any public justification for these research practices in the scientific literature is not commonplace. A future direction arising from the current research would be the conduct of public surveys on perceptions of animals in different roles, particularly in research, to determine a clearer understanding of the degree of support from the wider community for animal research. It would also be interesting to pose questions around different animals being used in research as a way to identify value judgements around different species, or the expected outcome of the research to determine a cost-benefit framework in terms of public support for animal research.

Another enquiry that could be developed with additional research is the evaluation of application outcomes submitted to Australian AECs. There were several limitations to the study reported in this thesis, which had a small and potentially unrepresentative sample and a relatively narrow scope. An additional study with a larger and more representative sample is needed, ideally reaching out to all AECs in the country in order to facilitate accurately reporting the proportion that eventually participated. This could be achieved by an anonymous survey being distributed to all Australian AECs with the first question identifying the committee's willingness to provide any further data. Assuming that all AECs engaged with this survey this would in itself produce data on transparency in Australian AECs. The foregoing proposed survey could request data not just on approval numbers but also on animal models used, numbers of animals used, outputs generated from research and any repeated studies. It would also be useful to include survey questions about the pre-screening processes in place at participating AECs to provide a clearer picture of the patterns in application outcomes and ways these committees could improve. Based on the current research I recommended the implementation of pre-screening across all Australian institutional AECs to create consistency.

Within my evaluation of AECs, I also considered the capacity of these committees to discuss fundamental ethical questions within the current framework they operate under. Based on this it could be evaluated whether it is appropriate to appoint an ethics advisor on these committees, or the renaming of these committees as Animal Welfare Committees to

more accurately represent the role they play. It was also suggested that implementing ethical review prior to receiving funding may remove institutional pressures that arise given the projects submitted to these committees have already been granted funding. The nexus between ethics approval and funding is difficult to evaluate in terms of efficiency, as it does not make sense to spend time and resources on ethical review for a project that has not yet received funding and therefore may not go ahead. Ideally, ethics could be considered through the funding bodies at an elementary level and again through institutional ethics committees more comprehensively after funding has been granted. It would also be useful to embed the consideration of non-animal models for research proposals at this funding stage. Future research could also address the transparency question by comparing processes and practices between AECs and Human Research Ethics Committees (HRECs) to identify differences in levels of transparency between the two.

One limitation of the current research was I was unable to provide a definition of transparency against the backdrop of Australian animal research. While I had set out to more clearly define this construct in an Australian context, I felt that the conflicting conceptualisations of transparency reflected the fact that this construct had not been fully operationalised in this country. That is, transparency is seen to be beneficial by both the scientific community and animal advocates, with both groups believing that transparency will enlighten the wider public on what they see as the 'truth' about animal research. It is difficult to define this construct while there are two conflicting ideas about what transparency will achieve without an outcome to resolve this conflict. In the UK and Cananda transparency has been implemented in varying ways to increase the degree of openness in animal research practices. The Canadian Council on Animal Care (CCAC) has a long history of openness, particularly in the reporting of detailed statistics on animal use which has been said to increase the trust of the public in the scientific community. The UK has implemented measures such as the concordat on openness on animal research which has been signed by 127 UK organisations pledging to implement openness into their practices. While these countries have gone further than Australia in embedding transparency into the animal research domain, one paper published in the journal *Alternatives to Laboratory Animals*, argues that "the legitimacy of animal research continues to be undermined by selective openness" (Pound & Blaug, 2016, p. 167); despite any efforts to improve transparency, there will always be questions around the motive behind this and how genuine and complete the information provided is. Nevertheless, Australia will need to implement transparency in its

regulations and practices to find out how this construct will impact the attitudes held by the wider public on animal research in this country.

Together, the four substantive chapters of this thesis present an evaluation of Australian animal research which considers the ways history has shaped the development of the current regulations and looks forward to what the next stage of scientific enquiry will look like in this country. I have questioned the way society values and 'pigeonholes' different animals, viewing some as companion animals, some as food, and others as instruments for use in research. I have discussed the way the Australian system of animal research regulation has developed and the way various social and political elements have shaped this process. I assessed whether there are global trends of change in the implementation of animal research regulation. I reviewed literature that criticised the predictivity and usefulness of animal models in contemporary biomedical inquiry and discussed organisations that are supporting the development of non-sentient models for this purpose that may be more sophisticated and more accurate. I evaluated current discussions around transparency in Australian animal research and conducted quantitative analyses to determine the patterns in application outcomes put to Australian AECs. Finally, I considered how Australia may be unique in its regulatory structures by reviewing historical and current systems in the US, Canada, the UK and Europe. Overall, this thesis has tried to continue and add to the discussion around Australian animal research practices. As a country with a short history of animal experimentation and the benefit of the experiences of other countries, we should be leading the way in progressive thinking on these issues and engaging debate on how we can achieve scientific goals with less harm to sentient creatures. Ultimately, I argue that across the various avenues I have explored in this thesis, Australia is not the progressive nation it could be in the area of re-thinking animal research, and I hope we can rise to the challenge.

References

Anderson, W. (1987). Animals in medical and surgical research—in crisis. *Australian and New Zealand Journal of Surgery, 57*(11), 797-800.

Anderson, W., & Perry, M. (1999). Australian Animal Ethics Committees: We Have Come a Long Way. *Cambridge Quarterly Healthcare of Ethics, 8*(1), 80-86.

Animal Alliance of Canada. (2016, 11/12/2018). How pet dogs and cats are acquired by research facilities. Retrieved from https://www.animalalliance.ca/campaigns/pets-research/acquired/

Animal Free Research UK. (2017a, 6/10/2017). Governance. Retrieved from https://www.animalfreeresearchuk.org/governance1/

Animal Free Research UK. (2017b, 06/10/2017). Our History. Retrieved from https://www.animalfreeresearchuk.org/our-history/

Animal Rights and Human Obligations. (1976). (T. Regan & P. Singer Eds.). Englewood Cliffs, New Jersey: Prentice-Hall Inc.

Ankeny, R. A., & Leonelli, S. (2011). What's so special about model organisms? *Studies in History and Philosophy of Science Part A, 42*(2), 313-323.

Arrese, C. A., Beazley, L. D., & Neumeyer, C. (2006). Behavioural evidence for marsupial trichromacy. *Current Biology, 16*(6), R193-R194.

Asratyan, E. (1953). *I.P. Pavlov His Life and Work*. Moscow: Foreign Languages Publishing House.

Australia Parliament Senate Select Committee on Animal Welfare. (1989). *Animal experimentation / report by the Senate Select Committee on Animal Welfare*. Retrieved from https://catalogue.nla.gov.au/Record/1162665

Bain, S., & Debono, K. (2013). *Australian Scientific Animal Use Statistics: A History of Fragmentation, a Future of Hope.* Paper presented at the Proceedings of the 2013 ANZCCART Conference “Can We Do Better.

Becker, J., & Palmer, H. (2021, 12/02/2021). US Congress to consider ban on kangaroo skin and meat, putting Australian industry at risk. *ABC News*.

Blackshaw, J., & Allan, D. (1987). Topical Issues in Animal Experimentation. *Australian Journal of Medical Laboratory Science,, 7*(2).

Blum, D. (1995). *The monkey wars*. New York: Oxford University Press.

Boakes, R. (1984). *From Darwin to behaviourism: Psychology and the minds of animals*: CUP Archive.

Bonney, K., & Wynne, C. D. L. (2002a). Quokkas (Setonix brachyurus) demonstrate tactile discrimination learning and serial-reversal learning. *Journal of Comparative Psychology, 116*(1), 51.

Bonney, K., & Wynne, C. D. L. (2002b). Visual discrimination learning and strategy behavior in the fat-tailed dunnarts (Sminthopsis crassicaudata). *Journal of Comparative Psychology, 116*(1), 55.

Bonney, K., & Wynne, C. D. L. (2003). Configural learning in two species of marsupial (Setonix brachyurus and Sminthopsis crassicaudata). *Journal of Comparative Psychology, 117*(2), 188.

Bonney, K., & Wynne, C. D. L. (2004). Studies of learning and problem solving in two species of Australian marsupials. *Neuroscience & Biobehavioral Reviews, 28*(6), 583-594.

Bron, A., Sumpter, C. E., Foster, T. M., & Temple, W. (2003). Contingency Discriminability, Matching, and Bias in the Concurrent Schedule Responding of Possums (Trichosurus Vulpecula). *Journal of the Experimental Analysis of Behavior, 79*(3), 289-306.

Brüne, M., Brüne-Cohrs, U., & McGrew, W. C. (2004). Psychiatric treatment for great apes? *Science, 306*(5704), 2039-2039.

Buckmaster, C. (2019, 11/04/2019). Opinion: Transparency Is Critical to Defend Animal Research. *The Scientist*.

Burian, R. M. (1993). How the choice of experimental organism matters: Epistemological reflections on an aspect of biological practice. *Journal of the History of Biology, 26*(2), 351-367.

Cameron, K. E., Clarke, K. H., Bizo, L. A., & Starkey, N. J. (2016). Concurrent progressive-ratio and fixed-ratio schedule performance under geometric and arithmetic progressions by brushtail possums. *Behavioural Processes, 126*, 94-100.

Canadian Broadcasting Corporation. (2017). Safe Haven for Chimps. Retrieved from https://www.cbc.ca/natureofthings/features/using-chimps-for-research-in-canada

Canadian Council On Animal Care. (1993). *Guide to the care and use of experimental animals* (2 ed. Vol. 1). Ottowa, Ontario: Canadian Council On Animal Care.

Canadian Council On Animal Care. (2006). Terms of reference for animal care committees. Retrieved from https://www.ccac.ca/Documents/Standards/Policies/Terms_of_reference_for_ACC.pdf

Canadian Council On Animal Care. (2017). CCAC Data Report. Retrieved from https://www.ccac.ca/Documents/AUD/2017-Animal-Data-Report.pdf

Canadian Council On Animal Care. (2019). Oversight System. Retrieved from https://www.ccac.ca/en/certification/about-certification/oversight-system.html

Carbone, L. (2021). Open transparent communication about animals in laboratories: Dialog for multiple voices and multiple audiences. *Animals, 11*(2), 368.

Cavalieri, P., & Singer, P. (1993). *The great ape project: Equality beyond humanity*. London: Fourth Estate.

Centers for Disease Control and Prevention (Ed.) (2021). *Epidemiology and Prevention of Vaccine-Preventable Diseases* (14 ed.). Washington D.C.: Public Health Foundation.

Challenger, M. (2021, 17/05/2021). Animals are our overlooked allies in the fight against Covid. *The Guardian*.

Clause, B. T. (1993). The Wistar rat as a right choice: Establishing mammalian standards and the ideal of a standardized mammal. *Journal of the History of Biology, 26*(2), 329-349.

Cohen, C. (1987). The case for the use of animals in biomedical research. *Proceedings of the Australian Physiological and Pharmacological Society, 18*(1), 38-45.

Cold Spring Harbor Laboratory Press. (2010). *Emerging Model Organisms: A Laboratory Manual* (Vol. 2): Cold Spring Harbor Laboratory Press.

Collins, F. S., & Varmus, H. (2015). A new initiative on precision medicine. *New England journal of medicine, 372*(9), 793-795.

Cox, T. (1995). Call of the Wild. *Cosmopolitan*.

Davisson, M. T. (1999). *Genetic and phenotypic definition of laboratory mice and rats/what constitutes an acceptable genetic-phenotypic definition.* Paper presented at the Microbial and phenotypic definition of rats and mice: proceedings of the 1998 US/Japan conference.

De Waal, F. (2016). *Are we smart enough to know how smart animals are?* London: WW Norton & Company.

Descovich, K., Reints Bok, T., Lisle, A., & Phillips, C. (2013). Auditory laterality in a nocturnal, fossorial marsupial (Lasiorhinus latifrons) in response to bilateral stimuli. *Laterality: Asymmetries of Body, Brain and Cognition, 18*(1), 32-43.

Diamond, J. (2002). *The rise and fall of the third chimpanzee: how our animal heritage affects the way we live*. London: Vintage.

Dietrich, M. R., Ankeny, R. A., & Chen, P. M. (2014). Publication trends in model organism research. *Genetics, 198*(3), 787-794.

Dietrich, M. R., Ankeny, R. A., Crowe, N., Green, S., & Leonelli, S. (2020). How to choose your research organism. *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences, 80*, 101227.

Donaldson, H. H. (1915). The rat,--data and reference tables for the Albino rat and the Norway rat. Memoirs of The Wistar Institute of Anatomy and Biology, No. 6.

Douglas, H. (2009). *Science, policy, and the value-free ideal*. Pittsburgh: University of Pittsburgh Press.

Ebeling, W., & Hemmi, J. M. (2014). Dichromatic colour vision in wallabies as characterised by three behavioural paradigms. *PLoS One, 9*(1), e86531.

Elliott, K. C., & Steel, D. (2017). *Current controversies in values and science*. London: Routledge.

Endangered and Threatened Wildlife and Plants - Listing All Chimpanzees as Endangered Species. (2018). Retrieved from https://www.federalregister.gov/documents/2015/06/16/2015-14232/endangered-and-threatened-wildlife-and-plants-listing-all-chimpanzees-as-endangered-species

European Animal Research Association. (2019). Call for Australia and New Zealand biomedical sector to follow Europe and be more open about animal research [Press release]. Retrieved from https://www.eara.eu/post/call-for-australia-and-new-zealand-biomedical-sector-to-follow-europe-and-be-more-open-about-animal

European Commission. (2019, 08/08/2019). Legislation for the protection of animals used for scientific purposes. Retrieved from https://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm

Fisher, D. O., Double, M. C., Blomberg, S. P., Jennions, M. D., & Cockburn, A. (2006). Post-mating sexual selection increases lifetime fitness of polyandrous females in the wild. *Nature*, *444*(7115), 89-92.

France, M. (2013). Book Review: The costs and benefits of animal experiments by A Knight. *Australian Veterinary Journal*, *92*(1-2).

Francione, G. (1996). *Rain Without Thunder: The Ideology of the Animal Rights Movement*. Philadelphia: Temple University Press.

Francione, G. (2020, 10/01/2020). The past twelve stories about the Australian fires that have appeared in my in-box all had pictures of, and talked primarily about, koalas. Retrieved from https://www.facebook.com/profile/100044505336684/search/?q=no%20morally%20coherent%20distinction%20between%20the%20animals%20we%20love%20and%20those%20we%20eat

Franco, N. H. (2013). Animal experiments in biomedical research: a historical perspective. *Animals*, *3*(1), 238-273.

Garnaut, R. (2008). *The Garnaut Climate Change Review: Final Report*. Port Melbourne, Vic: Cambridge University Press.

Godlovitch, S., Harris, J., & Godlovitch, R. (1971). *Animals, men and morals*. New York: Taplinger Publishing Company.

GOV.UK. (2014, 14/06/2017). Consolidated version of the Animals (Scientific Procedures) Act 1986. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/619140/ConsolidatedASPA1Jan2013.pdf

Grant, E. (1995). Monitoring Ethics in Medical Research. *Wisenet : journal of the Women in Science Enquiry Network*(38).

Great Ape Project. (2013, 13/06/2019). History of Great Ape Project. Retrieved from https://www.projetogap.org.br/en/history/

Great Britain Royal Commission on Vivisection. (1876). *Report of the Royal Commission on the Practice of Subjecting Live Animals to Experiments for Scientific Purposes*. Retrieved from

Greenland, S. (1994). Quality scores are useless and potentially misleading. *American Journal of Epidemiology, 140*(3), 300-301.

Griffin, G. (2009). Establishing a three Rs programme at the Canadian council on animal care. *Alternatives to Laboratory Animals, 37*(2_suppl), 63-67.

Grimm, D. (2017). Chimps in waiting. *Science, 356*(6). doi:10.1126/science.356.6343.111

Guillén, J., Robinson, S., Decelle, T., Exner, C., & Van Vlissingen, M. F. (2015). Approaches to animal research project evaluation in Europe after implementation of Directive 2010/63/EU. *Lab animal, 44*(1).

Hackam, D. G. (2007). Translating animal research into clinical benefit. *The British Medical Journal, 334*(7586), 163–164. .

Hackam, D. G., & Redelmeier, D. A. (2006). Translation of research evidence from animals to humans. *JAMA, 296*(14), 1727-1732.

Harlow, H., Dodsworth, R., & Harlow, M. (1965). Total social isolation in monkeys. *Proceedings of the National Academy of Sciences, 54*(1), 90-97.

Harlow, H., & Mears, C. (1979). *The human model: Primate perspectives*. New York: Vh Winston.

Harlow, H. F., & Harlow, M. K. (1962). Social deprivation in monkeys. *Scientific american, 207*(5), 136-150.

Harman, A., Meyer, P., & Ahmat, A. (2003). Neurogenesis in the hippocampus of an adult marsupial. *Brain, Behavior and Evolution*, *62*(1), 1-12.

Hemmi, J. (1999). Dichromatic colour vision in an Australian marsupial, the tammar wallaby. *Journal of Comparative Physiology A*, *185*(6), 509-515.

Home Office. (2014a). Consultation on the review of Section 24 of the Animals (Scientific Procedures) Act 1986. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/313410/Consultation_on_the_review_of_Section_24_of_ASPA.pdf

Home Office. (2014b, 07/02/2014). Review of Section 24 of the Animals (Scientific Procedures) Act 1986. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/307831/Section24IA.pdf

Hubrecht, R. C., & Carter, E. (2019). The 3Rs and humane experimental technique: implementing change. *Animals*, *9*(10), 754.

Hudson, D., Foster, T. M., & Temple, W. (1999). Fixed-ratio schedule performance of possum (Trichosurus vulpecula). *New Zealand Journal of Psychology*, *28*(2), 79.

Humane Research Australia. (2015). Ban Primate Experiments. Retrieved from http://www.banprimateexperiments.org.au/ban-primate-experiments/great_apes

Humane Research Australia. (2021). Statistics of Animal Use in Research and Teaching in Australia. Retrieved from http://www.humaneresearch.org.au/statistics/

Freedom of Information Act, § 36 (2000).

Jamieson, P. (1990). Duty and the Beast: The Movement in Reform of Animal Welfare Law. *University of Queensland Law Journal*, *16*, 238.

John Hopkins Bloomberg School of Public Health. (2019a, 28/05/2019). CAAT-Europe.

John Hopkins Bloomberg School of Public Health. (2019b, 29/07/2019). John Hopkins University Center for Alternatives to Animal Testing. Retrieved from https://caat.jhsph.edu/

Johnson, J. (2013). Vulnerable subjects? The case of nonhuman animals in experimentation. *Journal of bioethical inquiry, 10*(4), 497-504.

Kaiser, J. (2015). An end to US chimp research. *Science, 350* (6264), 1013.

Kirkby, R. J. (1977). Learning and problem-solving behaviour in marsupials. In B. Stonehouse & D. Gilmore (Eds.), *The Biology of Marsupials*. London: Palgrave.

Knight, A. (2007a). Animal experiments scrutinised: systematic reviews demonstrate poor human clinical and toxicological utility. *ALTEX-Alternatives to animal experimentation, 24*(4), 320-325.

Knight, A. (2007b). The poor contribution of chimpanzee experiments to biomedical progress. *Journal of Applied Animal Welfare Science, 10*(4), 281-308.

Knight, A. (2007c). Systematic reviews of animal experiments demonstrate poor human clinical and toxicological utility. *ATLA - Alternatives to Laboratory Animals,, 35*(6), 641–659.

Knight, A. (2008a). The beginning of the end for chimpanzee experiments? *Philosophy, Ethics, and Humanities in Medicine, 3*(1), 1.

Knight, A. (2008b). Non-animal methodologies within biomedical research and toxicity testing. *ALTEX-Alternatives to animal experimentation, 25*(3).

Knight, A. (2011). *The Costs and Benefits of Animal Experimentation*. London: Palgrave Macmillan.

Knight, A. (2012). Bias During the Evaluation of Animal Studies? *Animals, 2*(1), 85-92.

Lamberti, G. A., & Suckow, M. A. (2017). Institutional Animal Care and Use Committee. In M. A. Suckow & K. L. Stewart (Eds.), *Principles of Animal Research for Graduate and Undergraduate Students* (pp. 65-74). London: Academic Press.

Lash, T. L., Fox, M. P., MacLehose, R. F., Maldonado, G., McCandless, L. C., & Greenland, S. (2014). Good practices for quantitative bias analysis. *International journal of epidemiology*, *43*(6), 1969-1985.

Leonelli, S., & Ankeny, R. A. (2013). What makes a model organism? *Endeavour*, *37*(4), 209-212.

Lindl, T., Voelkel, M., & Kolar, R. (2005). Animal experiments in biomedical research. An evaluation of the clinical relevance of approved animal experimental projects. *Altex*, *22*(3), 143-151.

Linzey, A. (2013). *The global guide to animal protection*. Illinois: University of Illinois Press.

Lippolis, G., Westman, W., McAllan, B., & Rogers, L. (2005). Lateralisation of escape responses in the stripe-faced dunnart, Sminthopsis macroura (Dasyuridae: Marsupialia). *Laterality: Asymmetries of Body, Brain, and Cognition*, *10*(5), 457-470.

Logan, C. A. (1999). The altered rationale for the choice of a standard animal in experimental psychology: Henry H. Donaldson, Adolf Meyer, and" the" albino rat. *History of Psychology*, *2*, 3-24.

Logan, C. A. (2001). "[A] re Norway Rats... Things?": Diversity Versus Generality in the Use of Albino Rats in Experiments on Development and Sexuality. *Journal of the History of Biology*, *34*(2), 287-314.

Lynch, W. J., Nicholson, K. L., Dance, M. E., Morgan, R. W., & Foley, P. L. (2010). Animal models of substance abuse and addiction: implications for science, animal welfare, and society. *Comparative medicine*, *60*(3), 177-188.

Macleod, M. R., O'Collins, T., Horky, L. L., Howells, D. W., & Donnan, G. A. (2005). Systematic review and metaanalysis of the efficacy of FK506 in experimental stroke. *Journal of Cerebral Blood Flow & Metabolism, 25*(6), 713-721.

Martin, J. K., Handasyde, K. A., Taylor, A. C., & Coulson, G. (2007). Long-term pair-bonds without mating fidelity in a mammal. *Behaviour, 144*(11), 1419-1445.

MAWA. (2019). About the MAWA trust. Retrieved from http://www.mawa-trust.org.au/pdf/MAWA_Brochure-1704.pdf

McAllan, B. (2006). Dasyurid marsupials as models for the physiology of ageing in humans. *Australian Journal of Zoology, 54*(3), 159-172.

McKay, D. J. (1988). Alternatives to animals in testing therapeutic goods. *Laboratory Information Bulletin, 3*(1).

McLeod, C., & Hobson-West, P. (2016). Opening up animal research and science–society relations? A thematic analysis of transparency discourses in the United Kingdom. *Public Understanding of Science, 25*(7), 791-806.

Medical Advances Without Animals. (2016). The MAWA Trust - MAWA Scientific Policies and Conditions of Support. In MAWA (Ed.).

Medical Research Modernization Committee. (2006). *A Critical Look at Animal Experimentation* (A. Christopher, K. Archibald, J. Bailey, M. J. Cohen, S. R. Kaufman, & J. J. Pippin Eds.).

Mella, V. S., Krucler, J., Sunderasan, L., Hawkins, J., Herath, A. P., Johnstone, K. C., . . . McArthur, C. (2016). Effective field-based methods to quantify personality in brushtail possums (Trichosurus vulpecula). *Wildlife Research, 43*(4), 332-340.

Mitchell, A. S., Thiele, A., Petkov, C. I., Roberts, A., Robbins, T. W., Schultz, W., & Lemon, R. (2018). Continued need for non-human primate neuroscience research. *Current Biology, 28*(20), R1186-R1187.

Monamy, V. (2000). *Animal Experimentation: A Guide to the Issues* (Vol. 1). Cambridge: Cambridge University Press.

Munn, N. L. (1933). *An introduction to animal psychology: the behavior of the rat*. Boston, Massachusetts: Houghton Mifflin.

National Health and Medical Research Council. (1969). *Code of practice for the control of experiments in animals*: National Health and Medical Research Council.

National Health and Medical Research Council. (1979). *Code of practice for the care and use of animals in research in Australia*: Australian Government Publishing Service.

National Health and Medical Research Council. (1983). *Code of practice for the care and use of animals in research in Australia*: Australian Government Publishing Service.

National Health and Medical Research Council. (1985). *Code of practice for the care and use of animals for experimental purposes*: Australian Government Publishing Service.

National Health and Medical Research Council. (1990). *Australian code of practice for the care and use of animals for scientific purposes*: Australian Government Publishing Service.

National Health and Medical Research Council. (1997). *Australian code of practice for the care and use of animals for scientific purposes*: Australian Government Publishing Service.

National Health and Medical Research Council. (2004). *Australian code of practice for the care and use of animals for scientific purposes*: Australian Government Publishing Service.

National Health and Medical Research Council. (2013). Australian Code for the Care and use of Animals for Scientific Purposes. In: Canberra: National health and medical research council.

National Health and Medical Research Council. (2019). *Information paper: The implementation of the 3Rs in Australia*.

National Institute of Environmental Health Sciences. (2019, 19/08/2019). About ICCVAM. Retrieved from https://ntp.niehs.nih.gov/whatwestudy/niceatm/iccvam/index.html?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=iccvam

National Institute of Health. (2014). Model Organism Databases Supported by the National Human Genome Research Institute. Retrieved from https://www.genome.gov/10001837/model-organism-databases/

National Institute of Health. (2019, 08/11/2019). The Institutional Animal Care and Use Committee. Retrieved from https://olaw.nih.gov/resources/tutorial/iacuc.htm

National Research Council. (2004). *Science, medicine, and animals*. Washington, DC: National Academies Press.

National Research Council. (2009). *Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research*: National Academies Press.

National Research Council. (2010). *Guide for the care and use of laboratory animals*: National Academies Press.

National Research Council. (2012). *International animal research regulations: impact on neuroscience research: workshop summary*: National Academies Press.

Navarro, D. J., Griffiths, T. L., Steyvers, M., & Lee, M. D. (2006). Modeling individual differences using Dirichlet processes. *Journal of mathematical Psychology, 50*(2), 101-122.

Nelson, N. C. (2013). Modeling mouse, human, and discipline: Epistemic scaffolds in animal behavior genetics. *Social Studies of Science, 43*(1), 3-29.

Nerlich, B., Hartley, S., Raman, S., & Smith, A. (2018). *Science and the politics of openness: Here be monsters*: Manchester University Press.

New South Wales Biodiversity Conversation Act. (2016). Retrieved from https://legislation.nsw.gov.au/view/html/inforce/current/act-2016-063

Newkey-Burden, C. (2018, 15/02/2018). Offended by Koreans eating dog? I trust you've never had a bacon butty. *The Guardian*.

NIH Council of Councils. (2018). *Council of Councils Working Group on Assessing the Safety of Relocating At-Risk Chimpanzees'* Retrieved from https://dpcpsi.nih.gov/sites/default/files/CoC_May_2018_WG_Report_508.pdf

O'Sullivan, S. (2008). Transparency in Australian Animal Research Regulation-How Are We Doing. *Austl. Animal Protection LJ, 1*, 15.

O'Sullivan, S. (2006). Transparency and animal research regulation: an Australian case study. *Animal Liberation Philosophy and Policy Journal, 4*(1), 1-25.

Olson, H., Betton, G., Robinson, D., Thomas, K., Monro, A., Kolaja, G., . . . Bracken, W. (2000). Concordance of the toxicity of pharmaceuticals in humans and in animals. *Regulatory Toxicology and Pharmacology, 32*(1), 56-67.

ORIMA Research. (2018). Survey on the replacement, reduction and refinement of the use of animals for scientific purposes in Australia. Survey Findings Report. NHMRC. . Retrieved from https://www.nhmrc.gov.au/file/14584/download?token=X_aCRhKq

Ormandy, E. H., & Schuppli, C. A. (2014). Public attitudes toward animal research: a review. *Animals, 4*(3), 391-408.

Palmer, C. (2010). *Animal ethics in context.* New York: Columbia University Press.

Papini, M. R. (1986). Psicología comparada de los marsupiales. *Revista Latinoamericana de Psicología, 18*(2).

Pavlov, I. P., & Gantt, W. (1928). *Lectures on conditioned reflexes: Twenty-five years of objective study of the higher nervous activity (behaviour) of animals*. New York: Liveright.

Paytas, T. (2018). Is it time for Australia to be more open about research involving animals? Retrieved from http://theconversation.com/is-it-time-for-australia-to-be-more-open-about-research-involving-animals-103439

Pearce, A. (2011). Kill Skippy? Red Meat versus Kangaroo Meat in the Australian Diet. *Australian Humanities Review, 51*(1).

PETA UK. (2016, 20/12/2016). UPDATE: Dutch Government Announces Plan to Phase Out Animal Safety Testing by 2025! Retrieved from https://www.peta.org.uk/blog/update-dutch-government-announces-plan-phase-animal-safety-testing-2025/

Phillips, M., & Sechzer, J. (1989). *Animal research and ethical conflict: an analysis of the scientific literature, 1966-1986*. New York: Springer New York.

Pound, P., & Blaug, R. (2016). Transparency and public involvement in animal research. *Alternatives to Laboratory Animals, 44*(2), 167-173.

Pound, P., & Ram, R. (2020). Are researchers moving away from animal models as a result of poor clinical translation in the field of stroke? An analysis of opinion papers. *British Medical Journal Open Science, 4*(1), e100041-e100041.

Prankel, S. (2012). The Costs and Benefits of Animal Experiments: An Evaluation with Bias. By Andrew Knight. Palgrave Macmillan: Basingstoke, Hampshire, UK, 2011; Hardcover, 272 pp; ISBN 978-0-230-57686-5; Paperback, ISBN: 978-0-230-57687-2. In: Molecular Diversity Preservation International.

Puplick, C. (1994). Animal welfare and scientific research: an opportunity to shape public health policy' *Search, 25*(9).

Rader, K. A. (2004). *Making mice: Standardizing animals for American biomedical research, 1900-1955*. Princeton, NJ: Princeton University Press.

Reardon, S. (2018). US government rethinks how to retire research chimps. *Nature*. doi:10.1038/d41586-018-01324-7

Romanes, G. J. (1883). *Animal intelligence*. New York and London: D. Appleton and Company.

Rose, M. (2012). Ethical review of the use of animals in research: A reflection on the journey. *ALTEX Proc, 1*(12), 281-288.

Rose, M., & Grant, E. (2013). Australia's ethical framework for when animals are used for scientific purposes. *Animal Welfare, 22*(3), 315-322.

Rowan, A. N. (1984). *Of mice, models, and men: A critical evaluation of animal research*. New York: State University of New York Press.

RSPCA and LASA. (2015). Guiding principles on good practice for Animal Welfare and Ethical Review Bodies. *A report by the RSPCA Research Animals Department and LASA Education, Training and Ethics Section*.

RSPCA Australia. (2019). Animal Testing. Retrieved from https://www.rspca.org.au/campaigns/makeover-world/animal-testing-other-areas

Rudacille, D. (2000). *The scalpel and the butterfly: the war between animal research and animal protection*. New York: Macmillan.

Runcie, M. J. (2000). Biparental care and obligate monogamy in the rock-haunting possum, Petropseudes dahli, from tropical Australia. *Animal Behaviour, 59*(5), 1001-1008.

Ruoff, T. (1985). Links with London: Activities of the Animal Liberation Front. *Australian Law Journal, 59*(3).

Rupke, N. A. (1987). *Vivisection in Historical Perspective*. Kent, UK: Croom Helm.

Russell, D. (2012). Why animal ethics committees don't work. *Between the Species: an online journal for the study of philosophy and animals, , 15* (1), 127-142.

Russell, W. (2005). The three Rs: Past, present and future. *Animal Welfare, 14*, 279-286.

Russell, W., & Burch, R. (1959). *The principles of humane experimental technique*. London: Methuen & Co. Limited.

Safe, M. (1991, 17/18 August 1991). Animal Rights and Wrongs *The Australian Magazine*, 16-21.

Schultz, D. (1975). *A History of Modern Psychology* (2 ed.). New York: Academic Press.

Seligman, M. E. (1972). Learned helplessness. *Annual Review of Medicine, 23*(1), 407-412.

Seligman, M. E. (1975). *Helplessness: On depression, development, and death*: WH Freeman/Times Books/Henry Holt & Co.

Selwood, L., & Coulson, G. (2006). Marsupials as models for research. *Australian journal of zoology, 54*(3), 137-138.

Shanks, N., & Greek, C. R. (2009). *Animal models in light of evolution*. Irvine, California: Universal-Publishers.

Shanks, N., Greek, R., & Greek, J. (2009). Are animal models predictive for humans? *Philosophy, Ethics, and Humanities in Medicine, 4*(2), 20.

Sharman, K. (2006). Opening the Laboratory Door: National and International Legal Responsibilities for the Use of Animals in Scientific Research--An Australian Perspective. *J. Animal L., 2*, 67.

Signal, T., Foster, T., & Temple, W. (2001a). Determination of auditory thresholds in the brushtail possum (Trichosurus vulpecula). *Physiology & Behavior, 73*(1), 195-200.

Signal, T., Foster, T., & Temple, W. (2001b). Visual discrimination in the brushtail possum (Trichosurus vulpecula). *Australian Journal of Psychology, 53*(3), 152-154.

Singer, P. (1975). *Animal Liberation*. New York: HarperCollins Publishers.

Singer, P. (1995). Animal Liberation: the book that has changed perceptions about animals. *Animals Today*, *3*(1).

Singer, P. (2009). *Animal Liberation: The Definitive Classic of the Animal Movement*. New York: Harper Perennial.

Skinner, B. (1938). *The Behavior Of Organisms*. New York: Appleton Century.

Smith, W. J. (2012). *A rat is a pig is a dog is a boy: The human cost of the animal rights movement*. New York: Encounter Books.

Speaking of Research. (2014, 06/01/2014). Canadians Support Animal Research. Retrieved from https://speakingofresearch.com/2014/01/06/canadians-support-animal-research/

State News Service. (2013, 2013/01/22/). Expert Advisory Panel Confirms Chimpanzee Retirement from Laboratories to Sanctuary is the Way Forward, Article. *States News Service*. Retrieved from https://link.gale.com/apps/doc/A315961158/AONE?u=adelaide&sid=AONE&xid=ceaf06a4

Suckow, M. A., Weisbroth, S. H., & Franklin, C. L. (Eds.). (2005). *The laboratory rat*. Amsterda, Netherlands: Elsevier.

The Australian. (2013, 2013/02/26). Horse meat found in Ikea meatballs. *Australian, The (Australia)*, p. 009. Retrieved from https://infoweb.newsbank.com/apps/news/document-view?p=AWNB&docref=news/144AFBE0877C1F58

The Christian Science Monitor. (2008, 27/06/2008). Spain to grant some human rights to apes.

The European Parliment and the Council of the European Union. (2010). *Directive 2010/63/EU The European Parliament and the Council of 22 September 2010 on the protection of animals used for scientific purposes*. Retrieved from https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:en:PDF

Thew, M., Bailey, J., Balls, M., & Hudson, M. (2012). The ban on the use of chimpanzees in biomedical research and testing in the UK should be made permanent and legally binding. *Alternatives to Laboratory Animals, 40*(1), 3-8.

Timoshanko, A. C., Marston, H., & Lidbury, B. A. (2016). Australian Regulation of Animal Use in Science and Education: A Critical Appraisal. *ILAR Journal, 57*(3), 324-332. doi:10.1093/ilar/ilw015

Transparency International. (2009). *The Anti-Corruption Plain Language Guide*. Berlin, Germany: Transparency International.

Understanding Animal Research. (2014). Concordat on Openness on Animal Research. Retrieved from http://concordatopenness.org.uk/wp-content/uploads/2017/04/Concordat-Final-Digital.pdf

Understanding Animal Research. (2015a, 20/08/2015). Freedom of Information Act. Retrieved from http://www.understandinganimalresearch.org.uk/openness/freedom-information/

Understanding Animal Research. (2015b, 14/09/2015). Virtual lab tour. Retrieved from http://www.understandinganimalresearch.org.uk/news/video-of-the-week/virtual-lab-tour/

Understanding Animal Research. (2017). 360° LABORATORY ANIMAL TOURS. Retrieved from http://www.labanimaltour.org/

Understanding Animal Research. (2019, 23/09/2019). Concordat on Openness On Animal Research in the UK.

University of Windsor. (2019, 18/04/2019). Canadian Centre for Alternatives to Animal Methods. Retrieved from http://www.uwindsor.ca/ccaam/

USA Today. (2018, 20/06/2018). Let's continue animal testing: America's scientific community. Retrieved from https://www.usatoday.com/story/opinion/2018/06/20/lets-continue-animal-testing-americas-scientific-community/718331002/

USDA. (2019). *USDA Animal Care: Animal Welfare Act and Animal Welfare Regulations*: Department of Agriculture (USDA).

Van der Worp, H. B., Howells, D. W., Sena, E. S., Porritt, M. J., Rewell, S., O'Collins, V., & Macleod, M. R. (2010). Can animal models of disease reliably inform human studies? *PLoS medicine, 7*(3), e1000245.

Vasbinder, M. A., & Locke, P. (2016). Introduction: Global laws, regulations, and standards for animals in research. *ILAR Journal, 57*(3), 261-265.

Villanueva, G. (2015). "In the Corridors of Power": How the Animal Movement Changed Australian Politics, 1979–1991. *Australian Journal of Politics & History, 61*(4), 546-561.

Villanueva, G. (2017). *A Transnational History of the Australian Animal Movement, 1970-2015*. London: Palgrave Macmillan Cham.

Voelkl, B., Vogt, L., Sena, E. S., & Würbel, H. (2018). Reproducibility of preclinical animal research improves with heterogeneity of study samples. *PLoS biology, 16*(2), e2003693.

Wadman, M. (2018, 20/06/2018). Hundreds of U.S. scientists urge more transparency in animal research. *Science Insider*.

Watson, J. B. (1913). Psychology as the behaviorist views it. *Psychological review, 20*(2), 158.

White, S. (2016). Animal Protection Law in Australia: Bound by History. In D. Cao & S. White (Eds.), *Animal Law and Welfare-International Perspectives* (pp. 109-129). New York: Springer.

Whittaker, A. (2014). Animal research regulation in Australia-does it pass the test of robustness? *Global Journal of Animal Law*(1).

Winefield, T., & Nettelbeck, T. (2016). *A History of the Psychology Schools at Adelaide's Universities.* Adelaide, SA: University of Adelaide Press.

World Animal Protection. (2014). Animal Protection Index. Retrieved from https://api.worldanimalprotection.org/?_ga=2.230216538.759881186.1662270446-343747968.1662270446

Wynne, C. D. L., & Leguet, B. (2004). Detour behavior in the Quokka (Setonix brachyurus). *Behavioural Processes, 67*(2), 281-286.

Wynne, C. D. L., & McLean, I. G. (1999). The comparative psychology of marsupials. *Australian Journal of Psychology, 51*(2), 111-116. doi:10.1080/00049539908255344

Zentall, T. R. (2013). Animals represent the past and the future. *Evolutionary Psychology, 11*(3), 147470491301100307.