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HUMANE SCIENCE

Proceedings of the 2013 ANZCCART Conference

"Can we do better?"

Novotel Sydney Manly Pacific Hotel

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23rd - 25th July 2013

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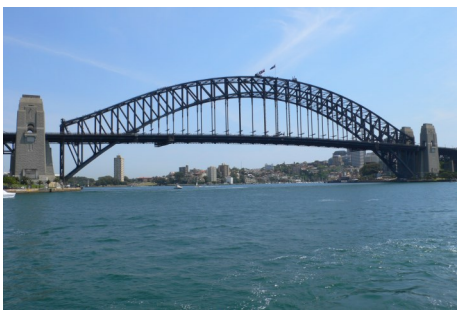

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Dr Geoff Dandie
Ms Sally Bannerman
Dr Malcolm France
Ms Lucie Nedved
Ms Jenny Kingham
Ms Chris Wadey

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2013 ANZCCART Conference Programme

Tuesday 23rd July 2013

8.30am Conference Registration Desk Opens

10.00am Conference Opening

Session Chair *Geoff Dandie (CEO, ANZCCART)*

10.15am **Margaret Rose**- Ethical decision making - do we need to reset the GPS?

10.45am **Morning Tea Break**

11.00am Discussion by AEC Categories

11.30am **Jane Johnson** – Some challenges with Animal Ethics Committees – Can greater transparency help?

12.00noon **Simon Bain** – Australian Scientific Animal Use Statistics: A History of Fragmentation, a Future of Hope

12.30pm – 1.30pm **Lunch**

Session Chair *Mandy Paterson (ANZCCART Board Member)*

1.30pm **Jenny Kingham** – Transporting embryos or sperm instead of live mice – Animal welfare gains for the future?

2.00pm **Peter Banks** – The animal ethics process for wildlife researchers: a survey of practitioner perspectives

2.30pm **Erika Vercuiel** - Highlights and challenges of the NSPCA Animal Ethics Unit, South Africa

3.00 – 3.30pm **Afternoon Tea Break**

Session Chair *Malcolm France (Member, Local Organizing Committee)*

3.30pm **Kevin Taylor** - Cryopreservation– cheaper than maintenance?

Short Presentations:

4.00pm **Paul Sou** Sydney Animal Research Ethics Group (SAREG): a multi-institute collaboration

4.15pm **Tim Tan** Can cognitive bias be used to assess affective state and welfare in captive reptiles and fish?

4.30pm **Richard Walton** Ethics and statistics in plain English (without the maths)

4.35pm **Mark Oliver** Managing ethical obligations and veterinary interactions in commercially funded livestock trials: pitfalls and solutions

5.00pm – 7.30pm **Cocktail Function**

Wednesday 24th July

Session Chair *Simon Bain (ANU)*

9.00am **Tim Karl** – The Effects of New Requirements for Laboratory Housing on Laboratory Mice

9.30am **Robyn Gentle** – Training and competency assessment of researchers

10.00am **Deb Kelly** – Comparison between rounds of external triennial reviews of AECs

10.30am **Morning Tea**

Session Chair *Jenny Kingham (Member, Local Organizing Committee)*

11.00am **Carl Power** – Imaging of small animals for research: Implications for animal welfare

11.30am **Tim Kuchel** – The animal welfare and scientific advantages of large animal imaging technologies a happy Rs win

12.00noon **Ted Rohr** - Dealing with Deviations from the Approved Protocol

12.30 – 1.30pm **Lunch**

Session Chair *Lucie Nedved (Member, Local Organizing Committee)*

1.30pm **Sanaa Zaki** – Improving the welfare of research animals: An evidence – based approach to assessing and managing pain, underpinned by a better understanding of how pain, distress and analgesic impact experimental outcomes

2.00pm **Chris Little** – Analgesic use in models of arthritis – reconciling the balance between pain relief and modifying the disease process being investigated

3.30pm **Ali Cullum** - Can We Do Better? Responding to unexpected changes during the life of a project.

3.00pm **Afternoon Tea**

Session Chair *Geoff Dandie (CEO, ANZCCART)*

3.30pm Transport of all delegates to Toronga Zoo

4.30pm **Paul Maguire** – Wild connections – using live animals for education outcomes

5.00 pm **Erna Walraven** – Ethical decision making around animal welfare

5.30pm **Paul Andrews** – A zoo's responsibilities to animals in its care

6.00pm Session Close with a stroll down to the Taronga Function Centre

7.00pm – 11.00pm **Conference Dinner** - Harbourview Room

Thursday 25th July

Session *Sally Bannerman (ANZCCART Board Member and Member Local Organizing Committee)*

9.00am **Chris Degeling** – Categorising Animal Models: Taxonomies and their implications for evaluation

9.30am **Clive Richardson** – Changing the attitudes and proficiency of livestock handlers in the meat processing sector through structured training programs

10.00am **Tony Butler** – Rural Youth Cattle Enrichment program – a strategic partnership for education

10.30am Morning Tea

Session Chair *Geoff Dandie (CEO, ANZCCART)*

11.00am **Greg Neely** – New approaches to find human disease genes

11.30am **Sharyn Watson** – Developing Alternative Methodologies to Animal Research (Paper withdrawn due to illness)

12.00pm **Tim Dyke** - The Australian Code for the Care and Use of Animals for Scientific Purposes. Launch of the 8th Edition 2013

12.30 – 1.30pm **Lunch**

Session Chair *Tim Kuchel (SAHMRI)*

1.30pm **Peter Croucher** - Small animal imaging to study cancer models

2.00pm **John Schofield** – How Anthropomorphic is the end, and will it be humane?

2.30pm **Malcolm France** – The anti-vivisection movement 150 years on: A tribute to its founder and some thoughts for the future.

3.00pm **Conference Ends**

3.30 – 4.00pm **Afternoon Tea**

Presentations given on

Tuesday 23rd July

Ethical decision making: do we need to re-set the GPS?

Margaret Rose
Prince of Wales Clinical School, University of NSW and
Centre for Values, Ethics and Law in Medicine, University of Sydney.

Abstract

Following the earlier development of ethical review committees for human research, in the 1970's Canada, Sweden and Australia were the first countries to introduce a process for ethical review of animal research through the establishment of similar committees. The establishment of such committees for animal research was in response to the growing recognition that these activities presented ethical challenges and that, given the level of concerns expressed about such activities in the wider community, scientists needed to be accountable for why and how animals were being used.

The *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* (2004) details the ethical principles and framework within which decisions as to the ethical acceptability of any proposed use of animals for these purposes should be judged. Although various editions of the Code since 1978, when the establishment of an Animal Experimentation Ethics Review Committee was first mooted, have included additional details notably as to the operation of these committees (now termed Animal Ethics Committees), the fundamental ethical principles and responsibilities have not changed significantly.

Animal ethics committees (AEC), or their equivalent, have now been established in many countries albeit with differences in their charter and standing. Never the less, the 2010 publication by the International Council for Laboratory Animal Science of the guideline *Ethical Review of Proposals to Use Animals in Science* is indicative of the level of international consensus as to the need for an ethical review process and the underlying principles and supports the approach developed in Australia.

Given the time since ethical review committees were first established, despite a substantive body of literature concerning the operation of committees which review the ethics of human research, few reports provide empirical evidence into the workings of AECs. Although these studies do not concern the operation of AECs in Australia, their findings highlight key issues which are worth consideration in the Australian context. Notably the available evidence shows that the process is supporting and informing awareness and implementation of the 3Rs, but raises important questions as to the foundations and effectiveness of the ethical review process[(1).]

The possible implications of these studies will be discussed and the case made that the ethical review process would be strengthened by a reflection upon the broader context within which AECs operate.

Introduction

Following the earlier development of ethical review committees for human research, in the 1970's Canada, Sweden and Australia were the first countries to introduce a process for ethical review of animal research through the establishment of similar committees. The establishment of such committees for animal research was in response to the growing recognition that these activities presented ethical challenges and that, given the level of concerns expressed about such activities in the wider community, scientists needed to be accountable for why and how animals were being used.

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Given the time since ethical review committees were first established, despite a substantive body of literature concerning the operation of committees which review the ethics of human research, few reports provide empirical evidence into the workings of AECs. Although these studies do not concern the operation of AECs in Australia, their findings highlight key issues which are worth consideration in the Australian context. Notably the available evidence shows that the process is supporting and informing awareness and implementation of the 3Rs, but raises important questions as to the foundations and effectiveness of the ethical review process.

The possible implications of these studies will be discussed and the case made that the ethical review process would be strengthened by a reflection upon the broader context within which AECs operate.

Development of an ethical framework

Under the auspices of the Canadian Council on Animal Care (CCAC), Canada was the first country to require institutions to establish a local animal care committee charged with the responsibility of reviewing ethical aspects of research protocols (CCAC, 1980). The establishment of these institutional committees was the cornerstone of the program of voluntary self-regulation that was developed in Canada, the other key component being the Assessment Program undertaken by the CCAC. It is of note that from the early stages the importance of public input to all aspects of this program was acknowledged and incorporated into the development and implementation of various components including committee membership (Rowsell, 1986).

The placement of the animal care committee within the broader context of the way in which an institution conducts the business of animal research was integral to how the program in Canada was conceived. The intention was that by placing these committees within an institution they would act as the 'conscience' of that institution in the ethical use of animals and further, that through the processes established, contentious issues could not be avoided (Rowsell, 1981).

Moreover, an effective working relationship between the committee and researchers was key not only in terms of deciding the ethical acceptability of a research proposal but also in the day to day conduct of research; the educational role of these committees was seen as paramount (Rowsell, 1984). Thus the AEC was not only embedded into the operation of the organisation but, through public involvement provided an outreach to the wider community; the AEC process was accountable to the wider community and able to respond to changing community views.

Sweden took a different approach. Following a three-year, voluntary pilot program, committees were established by law in 1979 to review the ethical acceptability of animal research. Six regional committees were established, external to research organizations, with the mandate to review experiments involving animals that were likely to cause pain or suffering; the researcher being responsible for so classifying proposed experiments prior to committee review. Committee membership comprised equal numbers of researchers, technical staff and laymen. Subsequently this system was reviewed and the law amended in 1988 requiring that all experiments were reviewed by a committee that was chaired by a judge with equal representation of research interests and laymen (including animal welfare representatives). Although these committees were designated 'ethics' committees, as noted by Forsman (1993) the ethical principles that were applied were not explicitly stated in legislation although the weighing of costs and benefits was implicated in associated guidelines.

Australia took a similar approach to Canada. Since 1969 the use of animals for scientific purposes has been governed by the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* (the Code) and based on a system of self-regulation with the underlying principle that "*the lives of animals, especially vertebrates, should be treated with respect and care and their welfare catered for at all times*".

The second edition of the Code in 1978 required institutions to establish an Animal Experimentation Ethics Review Committee the role and functions of which were further developed in subsequent editions of the Code (Rose & Grant, 2013). As detailed in the 1990 edition, the Code established an ethical framework for the review of animal research by setting out the guiding principles which informed the deliberations of the institutional AEC and experiments using animals could only be performed if it was determined that they were justified weighing the scientific or educational value against the effects on the welfare of the animals involved. To bring a diversity of views to the AEC determinations, the 1990 edition of the Code required AEC membership to include representatives of both animal welfare interests and the wider community, both being external to the institution. Subsequently, the 1997 edition required these categories to comprise at least a third of the total membership.

As in Canada, the effective implementation of the Code in Australia necessitates a good working relationship between the committee and researchers noting that in this way the committee would raise awareness of the ethical issues involved and assist researchers in fulfilling their responsibilities for the welfare of animals involved in their work (Anderson, 1990). It is notable that the Australian Code also has seen both the AEC and researchers as having mutual, reciprocal responsibilities. Whilst the role of the AEC is to be satisfied that there is sufficient evidence to support justification for the proposed use of animals, the researcher has ultimate responsibility for all matters related to the welfare of the animals involved in a project and must, in the planning stages, be satisfied that a case can be made that any proposed use of animals is justified weighing the predicted benefit against the suffering that may be imposed on the animals involved.

Australia and Canada have continued to develop and refine their processes for self-regulation through institutional AECs. Importantly in both countries the regular revision of policies and the publication of science-based guidelines have enabled the AEC process to develop and respond to emerging ethical issues and to be informed by scientific advances. Moreover, public

participation remains a key element and processes to strengthen this involvement have been introduced in both countries (Gauthier & Griffin, 2007; Rose, 2007).

In Australia, ethical issues in relation to the use of animals in science were considered as part of a national enquiry into animal welfare that was undertaken by a Senate Select Committee in the 1980s. Their Report on Animal Experimentation (SSCAW, 1989) identified the need to ensure that the use of animals is justified through ethical review and the application of the principles of the 3Rs (Replacement, Reduction and Refinement of animal use). Transparency of process, public participation in ethical decision-making and mechanisms for accountability were all seen as important.

This Report is notable for the in-depth consideration it gave to the role of the AEC. It was concluded that AECs were the 'lynch pin' in any system of ethical review arguing that it was the collective wisdom of a committee with each member bringing their own expertise and values to bear on deliberations that would enable broadly-based, collective judgments to be made. The Senate Committee argued that AECs served a major societal benefit by bringing together people of differing views and saw a pivotal role for lay/non-scientist members. Further, the Committee supported the self-regulatory approach that had been developed in Australia under the Code noting the AEC process provided an opportunity for researchers to demonstrate responsibility for why and how animals were used and be publically accountable for doing so. Placing responsibility on researchers, the Committee concluded, would achieve better animal welfare outcomes.

Thus today, the ethical framework which has been developed under the Code is principle based but recognises that ethical decisions involve a value judgement where, as argued by Smith and Boyd in their in depth analysis of the ethics of animal research, 'universally applicable rules' cannot be applied (Smith & Boyd, 1991).

International benchmarks

Recent changes to the US *Guide for the Care and Use of Laboratory Animals* (National Research Council, 2011) and the introduction of the new Directive by the European Union indicate significant developments in recognising the need for a process for ethical review of animal research. Whilst not requiring this to be undertaken by a committee, the new Directive on the Protection of Animals Used for Scientific Purposes (European Commission, 2010), mandates comprehensive project evaluation prior to authorisation to commence, noting that on both moral and scientific grounds, the likely harm to the animals should be balanced against expected benefits.

In anticipation of these amendments to the Directive of the European Union, in 2006 the Federation of European Laboratory Animal Science Associations (FELASA) undertook a review of then current practices in twenty (20) member countries (FELASA, 2006). Sixteen (16) were identified as having in place a mandatory requirement for ethical review although the mechanisms to do so and the scope of activities covered varied. In this detailed review, FELASA recommended that "*ethical review should aim to ensure that, at all stages in scientific work involving animals, there is adequate, clearly explained 'ethical justification' for using animals".* Further, such a review needed to take into consideration the balance of the predicted (or actual) benefits over harms caused and the likelihood that such benefits would be achieved. FELASA concluded that the ethical review process needed to reflect a diversity of views.

The publication in 2010 by the International Council for Laboratory Animal Science (ICLAS) of the guideline "*Ethical Review of Proposals to Use Animals in Science*, indicates the level of international consensus that has been reached on the need for an ethical review process and the

underlying principles. Whilst recognising that countries will approach this in different ways, the need to weigh expected benefits against the likely harms to the animals involved is cited as a foundation principle (ICLAS, 2010). This principle also underpins the recently released revised edition of the *International Guiding Principles for biomedical Research Involving Animals* (CIOMS/ICLAS, 2012) which have been adopted by the National Institutes of Health (USA) as a requirement for funding. Notably these revised guidelines recognise that such use of animals is a privilege that carries moral obligations and responsibilities and that both individuals and institutions have an obligation to respect animals and to be accountable for decisions and actions.

Evidence of effectiveness

Although there are few published studies providing empirical evidence on the operation of AECs, those available do show that the process is supporting and informing awareness and the implementation of the principles of the 3Rs. However, evidence 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.

An extensive search of Medline, PsycINFO, CAB Abstracts and Reviews, Biosis, Sociology Abstracts and Philosopher's Index databases was undertaken to identify publications which reported an evaluation of the operation of or outcomes from the ethical review of animal research including AECs (Rose, 2012).

Unlike the situation for human research ethics committees where there is a substantive body of literature (Abbott & Grady, 2011), very few publications that provided empirical evidence of the workings of AECs were found. Most of these reports concerned the operation of the AEC either in terms of the outcomes or the process and although these studies involved committees in Sweden, Canada, the UK and the US, the findings are relevant to the workings of AECs in Australia.

Forsman (1993) reviewed the outcomes of the ethical review process from 1979 to 1989 in Sweden. Based on her analysis of documentation relating to the day to day working of these committees including applications for ethical approval, minutes of committee meetings and associated correspondence, Forsman noted that what was understood as the basis for the ethical review process was unclear and that, unlike the situation with human research ethics committees, there was not a clear ethical code. However, she concluded that the introduction of AECs had been beneficial in raising awareness of the issues, in facilitating discourse and in enabling people of differing views to find common ground. Importantly, she cited substantive evidence that AECs had increased ethical consciousness and awareness of responsibilities on the part of researchers. Nevertheless, she also concluded that AECs acted, in the main, as technical committees - refinement of procedures being the predominant focus of AEC deliberations – and, in the main, weighing the balance of the predicted benefits and harms could not be substantiated.

Hagelin and colleagues reviewed the minutes of AECs in Sweden but in a later period (1989 - 2000) with the purpose of evaluating how the AECs modified applications (Hagelin et al., 2002). They found that approximately 18% of applications were approved without modification and classified the majority of modifications as addressing the goals of Refinement and concluded that AECs were being effective in improving animal welfare.

An ethnographic study of AEC members in Sweden found that different views were held on what the term 'ethics' meant and that there was no consensus on what constitutes an ethical problem in relation to animal research (Ideland, 2009). Ethical considerations within the AEC meetings were found to be situated in the committee culture and characterised by the personal views of members and hierarchies within the committee; the committee culture significantly influenced

the outcomes. Although the mix of views should provide the basis for an exploration of the complexity of ethical issues, this study showed that AECs focused on technical questions one reason being, it is suggested, that this is an area where committee members can reach consensus. The limitations to this ethical evaluation were noted and it was argued that an AEC process that recognises and evaluates differences would be a better basis for ethical review.

A twelve-month observational study of AECs at three Canadian institutions aimed to provide empirical data which the authors concluded had not been provided in previous publications (Houde et al., 2003). Based on an analysis of the type of protocol, the final decision and a verbatim record of the committee's discussions in relation to a specific protocol, data indicated that most comment was of a technical nature with 16% related to what had been defined as the 'explicit ethical categories' of the 3Rs. The complexity of the ethical review process in relation to animal research was noted and the authors concluded that on further analysis ethical concerns were implicit in both scientific and technical comments. Schuppli and Fraser (2005) investigated the interpretation and implementation of the 3Rs through in-depth, open-ended interviews of committee members at four Canadian universities. Although they found few mentioned the 3Rs *per se*, there was substantive evidence that the underlying principles were applied. However, they noted a lack of consensus as to the nature and ethical significance of pain and suffering.

In a further ethnographic study Shuppli and Fraser (2007) sought to examine the effectiveness of the committee process at four Canadian universities and to identify factors which may influence outcomes such as the possible influence of committee composition and meeting dynamics. The limitations to this study in the number of committees involved was recognised but it was concluded that there was evidence of bias towards institutional and scientific members and the dynamics within a committee prevented full participation by all members particularly community members. Various strategies to do so were discussed and reference to the wider literature on group deliberations suggested.

Purchase and Nedeva (2001) evaluated the impact of the introduction of the ethical review process in the UK through a postal survey of the various institutional stakeholders e.g. Licence Holders and Named Veterinarians, from the perspective of their attitudes to alternatives. They concluded that the ethical review process had had a positive effect in particular on the culture of institutions with the establishment of formal mechanisms to review the application of alternatives. Notably, they found a high level of awareness of the importance of alternatives with 80% of respondents of the view that alternatives should be used on moral and ethical grounds.

Two reports in relation to US committees investigated the reproducibility of the institutional committee review process. Dresser (1985) surveyed the responses of thirty two (32) IACUCs when asked to review four hypothetical protocols. Whilst there was broad agreement on the need to refine particular procedures, she concluded that assessing the justification for using animals was problematic and presented major difficulties for committees. Plous and Herzog (2001) assessed the reliability of decision-making between fifty (50) randomly selected IACUCs by comparing the evaluation by each committee member of three protocols each of which were reviewed by two committees. Their analysis revealed significant variability in the determination both between and within IACUC members. Notably, this variability related to key components of the protocol review process such as justification for the type and number of animals; the authors argued that such variability challenged the credibility of the IACUC review process.

Comment

Evidence suggests that consideration of the ethical justification for a particular project based on a full consideration of expected benefits and predicted harms is problematic and supports the contention that ethical justification is neglected by AECs where the primary focus is the 3Rs

(Kolar, 2006). The reasons for this have not been extensively explored but contributing factors could be a pervasive view that there is a fundamental justification to use animals to benefit human or animal health and welfare, a committee culture which seeks to find consensus and avoid differences, the attraction of dealing with 'practical' outcomes e.g. 3Rs rather than exploring questions of value, a view that the AEC members do not have the necessary expertise to assess the scientific merit of a proposal or a lack of agreed ethical principles upon which to base broader consideration of ethical questions.

The limitations of the current framework for ethical review of animal research have been argued by several commentators (for example, Forsmann 1993; Delpire et al., 2000). Further, within the context of a process which focuses on technical and scientific issues, there is the risk of a cost/benefit analysis (as often this is described) being utilised in a formulaic manner and so avoiding ethical considerations.

Reiss (2003) has argued that for there to be confidence in the validity of an ethical decision by a committee a number of criteria need to be met. Namely, that conclusions are supported by reason, arguments have been conducted within an established ethical framework and there is a degree of consensus arising from genuine debate.

Delpire and colleagues (2000) reviewed extant guidelines for the cost-benefit analysis of research involving transgenic animals and concluded that these did not provide adequate guidance for ethical review. Rather, they argued, there was a need for a framework that guided a broad and systematic assessment of ethical issues such as the ethical matrix developed by Mepham (2000). Such a framework would provide a practical procedural tool to support sound ethical considerations by inclusion of all values at stake, engagement with a multiplicity of viewpoints, supporting discussion of case-relevant ethically relevant aspects, allowing inclusion of ethical argument and enabling transparency of process (Kaiser et al., 2007). Thus, the adoption of this broader framework would strengthen the ethical review process, avoid the pitfalls of a simplistic cost/benefit approach and align the outcomes to the criteria proposed by Reiss.

The lack of agreed ethical principles underlying the ethical review of animal research is likely to be a major contributing factor in the difficulties identified (Rollin & Loew, 2001). This is the significant difference between the ethical review of research involving humans and that concerned with animals (Forsmann, 1993; Mepham et al., 1998; Houde et al., 2003). The basic ethical principles applied in the ethical evaluation of human research, as detailed in the Belmont Report (1979), being respect for persons, beneficence and justice; respect for persons being paramount as a necessary component of the other two (Gillon, 2003). The development of comparable ethical principles for animal research has been suggested by Mepham et al., (1998). Such a proposal was developed by van Hoosier (2000) but has not to date received further attention.

One of the obstacles, which has long been recognised, is the lack of a consensus as to the ethical basis for such principles (Tannenbaum & Rowan, 1985; Donnelley & Nolan, 1990) and the consequences of applying different ethical positions to decisions concerning animal research are well argued in the 2005 report of the Nuffield Council on *The Ethics of Research Involving Animals* (Nuffield Council, 2005).

Respect is a term frequently found in discussions about our responsibilities towards other animals but to date exploring this as an ethical principle has been argued against on the basis that as such the notion of respect requires reciprocity and thus recognition of and based upon reciprocal rights.

However, Markie (2004) has argued the case for an alternative approach. He reasons that adopting 'respect for animals' as an ethical principle would recognise that an animal has inherent value and would provide an ethical benchmark against which a proposal to use animals for

research could be tested. The interests of the animal would not be considered as equal to those of human beings but would need to be considered and argument to override their interests carefully considered. Further, taking Markie's argument that respect is a form of duty, fits well with Jonas's claim for responsibility in an ethical context (Jonas, 1976). Jonas argued that in the context of human relationships, responsibility arose when the well-being, interests or fate of others came under the control of another person and that this disparity in power carries an ethical obligation on the part of the person who is in control and because of that superiority is responsible. Further, he argued that responsibility is a function of power and knowledge where the responsible person has control over their actions and can, to some extent, foresee the consequences of their actions in terms of how that would affect others. It is notable that there are striking parallels between the circumstances outlined by Jonas and the notion of responsibility towards animals as it is widely represented in policies and guidelines concerning animal research.

If we take the ethical principles of respect for animals and responsibility as the basis for consideration of the ethical justification to use animals for research this allows the development of agreed criteria against which the outcomes of the application of these principles can be judged. Notably it is in this way agreed ethical principles outlined in the Belmont Report (1979) have underpinned ethical review of human research.

In relation to animal research that these principles underpin any decision to use animals and how they are used would be evident by (1) animals being only considered for such use when a proposal has scientific merit, is designed to achieve realistic outcomes that have potential benefit and the goals cannot be achieved in any other way, (2) in consideration of the impact on animals of any proposal, promotion of their wellbeing is the benchmark so that any factors likely to cause pain, suffering or lasting harm have to be justified and (3) in reaching a determination as to ethical acceptability there is evidence of a broad consideration of the ethical issues. Further, high standards of research integrity must be evident in the conduct of such research.*

In this way, respect for animals and pursuant responsibilities are demonstrated and there would be evidence that a thorough assessment of the breadth of ethical issues has informed the ethical review process; the principles of the 3Rs are embedded in the outcomes achieved. Further, through this approach there would be better engagement of all members in committee deliberations and the involvement of researchers would be integral to demonstrable outcomes. Nevertheless, recent reports have highlighted the need to pay attention to the quality of evidence that is taken into consideration in the ethical review process. For example, evidence as to how the quality of the experimental design may be affecting the validity and reliability of animal studies (Kilkenny et al., 2009: Krauth, Woodruff & Bero, 2013; Muhlhausler, Bloomfield & Gillman, 2013) and that a more rigorous assessment of the available literature can provide opportunities to achieve better refinement of animal models (for example, Balcombe, Ferdowsian & Briese, 2013; Franco & Olsson, 2012; Franco, Correia-Neves & Olsson, 2012) highlight the importance of an evidence-based approach in the application of the 3Rs. Further, questions as to the transferability of the results of studies in animal models to clinical research which have been the subject of commentary in the press as well as in the scientific literature (for example, Knight, 2008; Perel et al., 2007; Roberts et al., 2002) are a timely reminder of the need to carefully consider the evidence for a claim of benefit in a particular study.

Questions also are raised in the available literature as to the role of community members on AECs. Although community involvement is held to be fundamental to the ethical review of human research (Warnock, 1984), similar issues to those identified by Schuppli and Fraser (2007) have been evident in studies of human research ethics committees. A common theme in all these studies has been an identified need to clarify the role of community/lay members (for example, Webler & Tuler, 2002; White & Bourne, 2007). In a detailed consideration of these questions, Dyer (2004) supported the conclusions of Schuppli and Fraser of the need to better

define and understand the role of community/lay members on ethical review committees so as to fully realise the potential value from their involvement.

One of the arguments put forward for the diversity of AEC membership is to bring a broader perspective to committee deliberations. In his discussion of the potential difficulties of using a committee for ethical review of animal research, Caplan (1987) argued that some inconsistency in determinations was inevitable when participants bring a diversity of values to such discussions. Differences in the outcomes of the ethical review process also have been reported in a number of studies of human research ethics committees (Edwards, Stone & Swift, 2007) and there is an argument that such differences should be expected if the ethical review process is effective and not simply endorsing the *status quo*. Ideland's study importantly illustrated that this diversity of values and views is maintained and the opportunity to harness these difference in the deliberations of the AEC could be beneficial to the ethical review process (Ideland, 2009).

Conclusions

Deciding if and how we use animals for research purposes presents significant ethical challenges. Placing the principle of respect for animals with our pursuant responsibilities as the ethical basis for our reflections upon and analysis of these questions will strengthen the ethical review process, inform the identification of outcomes against which the application of these principles can be affirmed and influence a broader consideration of issues. Animal ethical review committees are integral to achieving these outcomes. By bringing a diversity of views to these deliberations these committees can be agents for change and fulfil an important societal role by challenging the *status quo* and prompting us to critically evaluate our views and values in relation to our responsibilities towards other animals.

* This is a governing principle in the 8th Edition of the *Australian Code for the Care and Use of Animals for Scientific Purposes (2013)* which was published subsequent to this presentation.

Acknowledgement

This paper includes data that was included in a presentation made at the 8th World Congress on Alternatives and the Use of Animals in the Life Sciences, Montreal, 2011 and published in the proceedings of that meeting with the approval of the Editors. Cited below as Rose MA (2012).

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Some challenges with Animal Ethics Committees – Can greater transparency help?

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Abstract

Recent media reports have suggested that Animal Ethics Committees (AECs) in Australia are in crisis, with dissatisfaction rife amongst both researchers and animal advocates. Frequently in the context of these debates about animal research, greater transparency is proposed as a remedy.

This paper will examine some of the common criticisms levelled against AECs, and show that these criticisms generally fall into one of two categories – either they relate to structural failings within the system of AECs or they relate to the way committees function within particular institutions. The idea of transparency as a mechanism to address these shortcomings will then be explored and it will be argued that in and of itself transparency can achieve little, rather what is required to improve animal research in Australia is fundamental systemic change.

Introduction

Recent media reports have suggested that Animal Ethics Committees (AECs) in Australia are in crisis, with dissatisfaction rife amongst both researchers and animal advocates. Frequently in the context of these debates about animal research, greater transparency is proposed as a remedy. However it appears different groups hold out different expectations for what transparency will deliver. According to some researchers, such transparency will help educate the public and secure their support for research, while animal activists believe transparency will reveal the cruelty underlying animal research and will ultimately end the practice (O'Sullivan 2006).

This paper will briefly examine some of the common criticisms levelled against AECs, which generally fall into one of two categories – either they relate to structural failings within the system of AECs or they relate to the way committees function within particular institutions. The idea of transparency as a mechanism to address these shortcomings will then be explored and it will be suggested that although transparency may form part of an answer to some of these problems, in and of itself transparency is no panacea to issues around animal research ethics in Australia.

Structural Challenges

The constrained brief and composition of AECs, in addition to their late placement in the process of facilitating animal research, contribute to shortcomings in their functioning.

In spite of their title, Animal *Ethics* Committees generally do not discuss ethical issues in research *per se* (Johnson 2013), rather the ethical justification of research is assumed and AECs are effectively limited to applying the 3Rs – to Reduce, Refine and Replace the use of animals in research. In reality however, this translates to applying just 2Rs - mainly Refinement (Rose 2013) and some Reduction - since on the whole, committees lack the expertise to pursue Replacement (Russell 2012). The deliberations of committees are therefore limited in ways that significantly restrict what they can achieve.

Although the membership of committees is intended to represent a range of views and expertise with respect to animals, the reality of how they function undermines the possibility that all views are adequately represented. For instance 'scientific' members (being composed of veterinarians through Category A and researchers through Category B) frequently dominate discussions so that their views and judgments tend to prevail at the expense of the views and judgments of those intended to represent the interests of animals in research (Category C members) and those charged with representing the views of the community (Category D members) (Groling 2013, Schuppli and Fraser 2007).

The composition of committees can also create conflicts of interest. Category A and B members are not required to be independent of the institution on whose committee they sit and may therefore be considered to be conflicted. Institutions have an interest in ensuring funded projects proceed and this can figure into the deliberations of institutional members, either consciously or unconsciously. Researchers are also conflicted by virtue of their chosen career – they are individuals committed to the routine use of animals in research.

Finally, in Australia the formal animal ethics process does not kick in until after funding has been approved. By this stage, many decisions regarding how animals will be used in the research have already been made, such that it is practically and strategically difficult for the committee to reject the project outright or even to suggest significant amendments (Russell).

Challenges that Vary Across Committees

Some of the criticisms levelled at AECs relate to the functioning and processes of specific committees. Researchers at certain institutions complain that AECs effectively impede their attempts to undertake legitimate research. One major concern hinges on the burdensome nature of the approval process and the complaint that it is unnecessarily onerous, intimidating and time consuming. Another concern expressed by wildlife researchers is that the process is unsuited to the kind of research they do, since approval processes were developed with laboratory rather than wildlife research in mind.

Applying Transparency to Animal Research

Transparency is sometimes put forward as if it were a universal panacea to all the ethical issues in animal research, in a way akin to how informed consent is occasionally deployed in the human research ethics literature. However transparency is, at most, a first step which exposes issues which then need to be addressed; in and of itself it does little work.

To function effectively, transparency would have to be limited since unless it were carefully managed, transparency could have unintended effects. Rather than acting to reveal how animal research ethics operates, radically open access could effectively obscure and bamboozle those interested in understanding research and how it is undertaken. Without some translation or mediation the information, language and level of detail in animal ethics applications and deliberations could overwhelm those keen to come to grips with the process.

With respect to the structural shortcomings of AECs, transparency could go some way to exposing their constrained brief and functioning. For instance, making abstracts of proposals publicly available (in a form to ensure intellectual property concerns are not created), in addition to AEC minutes, would reveal how committees deliberate and how the 3Rs are applied. If the empirical research regarding decision making within AECs is correct, greater transparency will reveal insufficient attention is directed toward Replacement. This is significant, since public support for animal experimentation depends, in part, on such experimentation minimizing animal suffering and avoiding animal use when alternatives are available (Hobson-West 2009, MORI 2008). A more informed public debate could be facilitated by bringing committee decision making and its bases to light. Exposure of the conflicts of interest of institutional committee members might also motivate change in the requirements around affiliation so that all members and their decisions would be seen to be genuinely independent of the institution within which they are made.

Transparency, however, does not speak to the late placement of ethics review in the process of animal research. This issue would be more readily addressed by instituting some requirement for the preliminary ethics review of all research.

Complaints about committee specific issues such as the time consuming and onerous nature of the process as well as its unsuitability to certain types of research could reach a wider audience through transparency and perhaps this could prompt institutions to alter their processes.

Conclusion

Greater transparency in animal research ethics should be encouraged; after all, inadequate transparency fosters a lack of trust and raises suspicions that people and organizations have something to hide. However transparency should be construed as a *first step* in addressing *some* of the issues and challenges identified with AECs, rather than the sole move required to improve animal research in Australia.

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Australian Scientific Animal Use Statistics:
A History of Fragmentation, a Future of Hope

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Australia does not have a nationwide compilation of statistics relative to the use of animals used for scientific purposes. Statistics are compiled by each state and territory, but only four states currently make the relevant statistics available to the public.

National facts and figures allow for informed debate and discussion and for planning and investment for Australia's education and research effort. They are also scrutinised by animal lobby groups concerned over unjustifiable welfare impacts on the animals involved. Cooperation for the progressive improvement of humane animal care and use, as embodied in the 3Rs, can be hindered by the absence of reliable and contemporary statistics. It is apparent that there is an Australian public general lack of knowledge of the true legislative situation regard animals in research and teaching, and such knowledge could be readily expanded by the publication of a national statistical report which emphasises AEC function, the 3Rs and the Code.

This presentation outlines the findings of a study funded by the Australian Animal Welfare Strategy. It examines systems in place elsewhere in the world, with regard to national harmonisation and cogent 'severity' grades and it reviews scientific animal use statistics currently collated by the Australian states and territories.

Central to scientific animal use statistical analysis are categories of invasiveness. AECs, researchers, legislators and the public all share concerns about pain and distress. As well as the level of pain and distress it is important that severity or invasiveness criteria take into account the duration of that pain and distress. Accurately assessing severity levels enables 3Rs education to target the areas of greatest need. Ideally to facilitate accuracy, assessments of severity should be made retrospectively i.e. it should be assessed at the end of each project for each animal. Currently in Australia severity assessment is made by the researcher at the time of the proposal being presented to the AEC, and may be modified by the AEC. New Zealand Animal Use Statistics take into account duration in severity assessments and also incorporate retrospective assessment of severity. The Directive 2010/63/EU, applicable to all EU member nations, came into effect January 1 2013 and have severity levels that take into account duration and determination is also made retrospectively. The presentation also makes recommendations relative to a uniform Australia-wide collection of statistics relative to purpose of use.

It is recognised that the 3Rs are key strategies to provide a systematic framework to achieve the goal of humane animal based research. We have been unable to find a national statistics compilation that systematically reports on the degree of 3Rs implementation. In complying with the Code, AECs already ask a number of questions that directly

reflect implementation of the 3Rs. The presentation will outline how institutions could collect this information quantitatively. Were Australia to incorporate this quantitative information in a national scientific animal statistical compilation it would reinforce the ideals of the Code, it would encourage institutional increase in implementation of the 3Rs, and it would be a statistic that could demonstrate to the public the degree of institutional engagement with animal welfare ideals.

Finally we make a recommendation concerning an Australian Commonwealth agency that would ideally collate the national statistics. Statistics would continue to be collected by states and territories, but to a uniform system. It is essential that the resulting figures subsequently be astutely used to promote the ideals of the Code and present information in an informative and transparent manner.

Introduction

Australia does not have a nationwide compilation of statistics relative to the use of animals used for scientific purposes. Statistics are compiled by each state and territory, but only four states currently make the relevant statistics available to the public. This could be compared to 27 member nations of the EU who currently each assemble their national scientific animal statistics according to a mutually agreed format. Canada has 10 provinces, each with their own legislature, with scientific animal statistic collation compiled by one agency, the Canadian Council of Animal Care.

National facts and figures allow for informed debate and discussion and for planning and investment for Australia's education and research effort. They are also scrutinised by animal lobby groups concerned over unjustifiable welfare impacts on the animals involved. Cooperation for the progressive improvement of humane animal care and use, as embodied in the 3Rs, can be hindered by the absence of reliable and contemporary statistics. It is apparent that there is a general lack of knowledge among members of the Australian public, of the true legislative situation regarding the use of animals in research and teaching, and such knowledge could be readily expanded by the publication of a national statistical report which emphasises AEC function, the 3Rs and the Code.

This study, funded by the Australian Animal Welfare Strategy, examined systems in place elsewhere in the world with regard to national harmonisation and cogent 'severity' grades, examining particularly systems in Canada, New Zealand and the EU, also reviewing scientific animal use statistics currently collated by the Australian states.

Central to scientific animal use statistical analyses are categories of invasiveness (Fenwick et al. 2010, Williams et al 2006). AECs, researchers, legislators and the public all share concerns about pain and distress. As well as the level of pain and distress, it is important that severity or invasiveness criteria take into account the duration of that pain and distress. Accurately assessing severity levels enables 3Rs education to target the areas of greatest need. Ideally to facilitate accuracy, assessments of severity should be made retrospectively i.e. it should be assessed at the end of each project for each animal. New Zealand Animal Use Statistics take into account duration in severity assessments and also incorporate retrospective assessment of severity. The Directive 2010/63/EU, applicable to all EU member nations, came into effect January 1, 2013 and factor in severity levels, that take into account duration and determination that is also made

retrospectively. The nearest thing to severity grades the Australian states currently have are procedures that don't give an accurate determination of the degree of severity, don't take into account the duration of that severity impact and, in so much as they are determined by the researcher's appraisal of the proposal that goes to the AEC and the AEC's review, are assessed prospectively rather than retrospectively. This study recommends that Australia use the New Zealand system for severity assessment. The New Zealand system has five levels of impact based on the five domains of potential animal welfare compromise introduced by Mellor and Reid (1994).

Ten purposes of use are recommended. These were gathered from purposes of use currently included within Australian jurisdictions and are reflective of the purposes relevant to the Australian scientific animal use scene. Four of the six states currently list the same 5 purposes. WA lists 8 purposes, and NSW lists 10 purposes. In proposing categories of use, those listed within the Canadian, New Zealand, and EU systems were also examined to ensure that all relevant purposes had been included in the proposed Australian system.

The 10 purposes of use proposed are:

1) **Education and training**: On a global scale animals used for education and training have been significantly replaced by non-animal alternatives. There are still some situations where replacements are not an option, such as veterinary training and training in wildlife research and this category of purpose must be included.
2) **Stockbreeding**: Animals will need to continue to be bred for biomedical research on the one hand and agricultural research on another. This only includes animals used to produce progeny, not the final progeny which are subsequently allocated for other purposes.
3) **Genetically altered animal production**: This must include genetically modified animals (Recombinant DNA technology) and also must include those produced by chemical mutagenesis. The numbers of genetically modified rodents currently used in Australian biomedical research are significant and come with their own animal welfare considerations.
4) **Environmental/species conservation research**: Includes all wildlife research, often with implication for species conservation. This type of research has the potential to draw public attention in a positive manner.
5) **Basic biological research**: Studies of a fundamental nature in sciences relating to essential structure or function, and may contribute to the foundations of medical research. The list is not comprehensive, but includes for example behavioural studies, physiological studies, studies on development, and genetic studies.
6) **Human and/or animal health and welfare research**: Animal based studies that directly relate to human or animal diseases and disorders.
7) **Production of biological products**: These may be used in man or animals. Examples include the production of vaccines and antisera and serum gonadotropin, and diagnostic products developed from animals.
8) **Protection of man, animals and the environment**: Broadly known as toxicological or toxicity testing, this is often regarded as the most controversial use of animals for scientific purposes and therefore has a propensity to attract the attention of a section of the public who push strongly for methods that use alternatives to animals.
9) **Animal management or production research**: Research to achieve improvement in production technologies in livestock enterprises.

10) **Diagnostic/forensic research**: Includes animals used in research of diagnostic procedures and also forensic research, with an example of the latter using purpose killed pigs to study organ deterioration as a model for human decomposition.

The study proposes the presentation of statistics in terms of combinations of degrees of impact and purposes of use against category of animal.

There are perceived advantages in presenting information that demonstrates the positive aspects of ethical oversight. That can be achieved by assessing the number of animal proposals that are positively modified as a result of Animal Ethics Committee review relative to the total number of proposals reviewed per annum. It can also be assessed by measuring the degree of 3Rs implementation. The 3Rs are key strategies to provide a systematic framework to achieve the goal of humane animal based research. We have been unable to find a national statistics compilation that systematically reports on the degree of 3Rs implementation. Indeed, the NC3Rs (NC3Rs Evaluation Framework 2012) organisation felt that the UK national annual statistics figures in their current form do not make manifest the impact of 3Rs efforts. In complying with the Code, Australian AECs already ask a number of questions that directly reflect implementation of the 3Rs. Were Australia to incorporate this quantitative information in a national scientific animal statistical compilation, it would reinforce the ideals of the Code, it would further encourage institutional increase in implementation of the 3Rs, and it would be a statistic that could demonstrate to the public the degree of institutional engagement with animal welfare ideals. Per approved proposal the information would be collected once, at the conclusion of the protocol, and would take into account 3Rs measures included in that approved proposal. A question included in the Final Report for a protocol would ascertain 3Rs measures included since the proposals approval. Collation of these figures at an institutional level sounds like a significant workload. With small institutions this may have to be done manually. The continuing evolution of IT research management systems relative to animal ethics management in Australia has considerable potential to facilitate this process in many institutions.

Re collation of scientific animal use statistics two Commonwealth agencies that undertake national statistics compilations are identified. They are the Australian Bureau of Agricultural and Resource Economics and Sciences (ABARES) and the Australian Bureau of Statistics (ABS). Conversations with state administrators at the ANZCCART Conference identified that they are often currently under-powered in relevant human resources re scientific animal statistical collection and changes to their current state practices could present considerable challenge. It is felt that a preferred system would be the direct collection of relevant statistics by the Commonwealth agency from the institutions according to the format proposed here and subsequent return of respective figures to each state.

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Transporting embryos or sperm instead of live mice-
Animal welfare gains for the future?

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The transport of mice within Australia and internationally is an integral part of current animal based research. The proliferation of genetically modified mouse lines has led to a growing need to transport mouse lines between breeding facilities, as research focus changes or new collaborations are formed.

Welfare during transport can be improved by using specialized couriers, and by providing mice with quality nutrient gels and environment enrichment. Despite best practice, occasional deaths still occur when mice are exposed to extreme temperatures on airport tarmacs. All mice will suffer stress from strange noises, movement and smells, and mice exposed to long international journeys often lose weight and many arrive dehydrated. Post arrival care is critical to ensure mice adjust to a new cage environment and different watering system.

The Australian BioResources (ABR) facility, imports and exports large numbers of mice both nationally and internationally to establish new breeding colonies. At ABR we are beginning to import embryos or sperm instead of live mice. By importing embryos or sperm unwanted pathogens are removed during the importation process, allowing the establishment of disease free breeding colonies without additional rederivation.

With the Australian Quarantine (AQIS) requirements for the importation of mouse embryos under review, the importation of frozen embryos from international sources may soon become a viable alternative. Given the extended periods in transit, and the additional risks associated with connecting international flights, the animal welfare gains would be significant.

Currently such technology is limited to animal facilities that have the ability to collect, store and ship mouse embryos or sperm. Given the animal welfare benefits, the challenge remains how to expand this alternative to make it more accessible.

An international campaign to stop the transport of laboratory animals is underway supported by a coalition of antivivisectionist groups (http://www.gatewaytohell.net). While the campaign focuses on the international transport of primates for use in research, it has resulted in a total ban on all laboratory animal transport on ferries between the European mainland and the UK, and several airlines have agreed to ban the transport of all laboratory animals.

For an island nation such as Australia, depending entirely on air transport for the exchange of laboratory animals with the rest of the world, a total ban would have a significant impact on

biomedical research. In this context the questions must be posed – Can we do more to improve the welfare of animals during transport and what, if any, are the alternatives to the shipment of live animals?

In a case study on laboratory mice, the species used predominantly in biomedical research in Australia, the reasons for transporting mice, the potential animal welfare issues and the alternatives are examined.

The international transport of mice into Australia is primarily aimed at establishing new breeding colonies. Genetically modified mice are an important tool for examining the role of specific genes or gene combinations in disease. The type of mouse lines needed in research often changes as the research develops. While it is possible to generate new genetically modified mouse lines in Australia the process is costly, time consuming and uses significant numbers of mice. If the mouse line is not available in Australia, but can be sourced internationally, researchers will choose to import the line rather than generate it within Australia. The bulk of mice arriving in Australia come from Europe or the USA. In both cases transport involves long haul flights, often with one or more connecting flights.

What is the impact of this transport on live laboratory mice? The conditions of mouse transport have improved significantly over the last 20 years. The design of transport shippers allows better ventilation and minimizes the risk that mice will pick up infections in transit. New diet gels provide complete nutrition and fully replace the need for water during shipment. There are dedicated transport companies with air-conditioned vehicles that ensure, at least during road transport, that mice are not exposed to temperature extremes.

However, even with short, land based transport mice are stressed by the strange environment, noise and movement. If they are going to a facility with different housing conditions there is a period of acclimatization. Researchers are generally advised to allow mice to acclimatize before beginning research [1]. Air transport, particularly long haul flights presents additional dangers [2]. Mice can be exposed to extremes of temperature, either heat or cold, while on the tarmac. Occasional deaths occur due to *hyperthermia* (extreme heat) or *hypothermia* (extreme cold). The duration of transport prolongs the stress and if connecting flights are delayed or missed, the transport gel food can be exhausted.

As technology improves for embryo and sperm handling, the potential to transport embryos or sperm instead of live mice is becoming a reality[3, 4]. The collection of embryos and sperm from mice currently involves sacrificing the donor animals and surgically implanting recovered embryos into recipient females, so the process does have an ethical cost. However when live mice are moved from one breeding facility to another, the mouse line is often *rederived* to remove unwanted disease causing organisms. In *rederivation* embryos are collected from the disease-carrying female (sacrificing the female) and are surgically implanted into the disease free recipient female. This process is done to prevent infectious diseases being inadvertently introduced into a breeding facility with imported mice. Receiving embryos or sperm instead of live mice can in effect become another way of *rederiving* a mouse line. When mice are bred in one facility and transported to another for experimentation mice are not generally culled and *rederived*, so transporting embryos or sperm instead of live mice in this context would introduce an unacceptable ethical cost.

Some obstacles remain to replacing the international transport of mice with the shipment of embryos or sperm. The Australian Quarantine (AQIS) conditions for the import of mouse embryos and sperm impose practical limitations that make it difficult to use this promising

alternative. AQIS are however currently reviewing the conditions for the import of mouse embryos and a change to existing conditions is imminent.

In some countries, such as the UK, the transport of mouse embryos or sperm is becoming commonplace however both the exporting and importing facility need to have a degree of technical expertise. Special vapour phase nitrogen transport containers are available to ship frozen embryos and sperm however they remain bulky, adding to the cost of transport.

At the Australian BioResources facility, Garvan's centralized breeding facility located at Moss Vale, we have begun to receive embryos or sperm instead of live mice from other facilities in Australia. In addition to removing diseases from the imported lines there are additional advantages to the researcher in terms of cost and time- savings. Transporting embryos or sperm saves the time and cost associated with establishing a breeding colony prior to *rederivation* into the recipient facility. If the transport between facilities can be completed in less than 24 hours, freshly collected, unfrozen embryos can be sent instead of frozen material, reducing the cost of transport. For international shipments both embryos and sperm need to be frozen. When AQIS modifies the conditions for the import of mouse embryos into Australia we intend to import mouse embryos to replace the shipment of live mice whenever possible.

Most animal facilities will not have the equipment or skilled staff to receive and recover mouse lines from imported embryos or sperm, but centralized facilities in each state could perform this role. Facilities that are able to freeze mouse embryos or sperm are capable of receiving and handling imported embryos and sperm.

The collection of embryos or sperm is relatively simple in comparison, not requiring any special equipment. To allow more animal facilities to send embryos or sperm, some minimal training is required. Jackson laboratories, for example, have recently developed a sperm collection kit with simple instructions allowing anyone to collect mouse sperm. A similar approach may be possible for the collection of fresh embryos.

Replacing live mouse transport with embryos on long haul international flights would significantly reduce the risk of animal welfare problems, while the transport of embryos or sperm between breeding facilities in Australia may provide both cost and time savings for researchers. The transport of live mice within Australia from centralized breeding facilities to experimental facilities cannot be replaced by embryos or sperm without the unnecessary sacrifice of animals, so live mouse transport cannot be completely replaced.

The challenge to improving animal welfare is to make embryo and sperm transport between breeding facilities more accessible, especially for international shipments, while continuing to improve the conditions for live mouse transport within Australia.

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The animal ethics process for wildlife researchers: a survey of practitioner perspectives

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Gaining animal ethics approval is a generic requirement of any animal-based research in Australasia, but the costs and benefits of the approval process for wildlife management is poorly known. Approval should protect researchers from public criticism because it comes from an independent ethical assessment of whether research aims justify any impacts on animal welfare. Yet the process adds to the bureaucratic burden facing wildlife researchers, often through committees and requirements that are designed for animal use in medical research with little reference to the specifics of wild animals.

In this paper, we report on a web-based survey of more than 200 wildlife biologists on their perspectives of the animal ethics process. We asked researchers questions relating to three key issues: 1) their background, research interests and exposure to the animal ethics process; 2) their annual investment in gaining approval, the nature of their current approval system and the utility of codes of practice; and 3) their perspectives on the integrity of the approval process, whether they feel the system improves welfare or conservation outcomes, and whether the system facilitates or hinders research. We interpret the results as a cost-benefit analysis to guide future systems of ethical assessment for wildlife research.

No manuscript was received from this presenter

Highlights and challenges of the NSPCA Animal Ethics Unit, South Africa

Erika Vercuiel
Manager of the Animal Ethics Unit, NSPCA

The National Council of SPCAs (NSPCA) is the largest animal welfare organisation in South Africa. One of its units, the Animal Ethics Unit (AEU), is the only of its kind in South Africa, focusing on the improvement of welfare of the animals used in research. The AEU's objectives include the implementation of the 3 Rs principle: replacement, reduction and refinement of animals used in research. We achieve our objectives by carrying out inspections at research facilities, serving on Animal Ethics Committees (AECs) (currently serving on 34 AECs), reviewing research protocols (between 100 to 150 per month) and working towards improving South African legislation, which protects animals used in research and enforcing this legislation.

A highlight for our unit was organizing and facilitating the first ever "Alternatives Workshop" which assessed alternatives to the use of animals in research, teaching and education. The success from the workshop was expanded into six road shows at Universities around the country. Hundreds of frogs, pigeons, rats and pigs will be replaced by alternative methods such as manikins, models and DVDs.
Another exciting step forward towards improving welfare of animals, was the requirement for registration of Animal Ethics Committees with a National Statutory Body, the National Health Research Ethics Council, Department of Health (NHREC). This initiative will go a long way in improving the welfare of animals used in human health research. The first ever assembly of most of the major University AEC Chairpersons took place. The NHREC will audit committees to ensure standardization throughout the country.
With hard work and constant dedication the AEU managed to not get only Universities but also zoos to establish and develop Animal Ethics Committees, proving that ethics around all spheres of animal use is being taken seriously.
The AEU requested a meeting with the South African Bureau of Standards which resulted in a call for a second edition of the South African National Standards (SANS 10386) for the care and use of animals for scientific purposes.

One of the challenges with which the AEU is faced is the difficulty in enforcement of animal welfare legislation on researchers using animals to the benefit of animals, et al conservation. The lack of legislation allows anyone from any country to conduct research using South African animal resources without acquiring the necessary ethical approval.
Increase of workload and the lack of sufficient funding to carry out the necessary duties poses complicated challenges for the unit. South Africa is experiencing an increase in pre clinical research, resulting significantly to the unit's responsibility and workload.

In conclusion, the skills and expertise of AEU staff has increased dramatically over the years. We have also broadened the scope of our knowledge due to the wide range of species used in research in South Africa. Attendance of research-related conferences and closer communication with nature conservation bodies has contributed to the successful running of the unit. As the forerunner of animal welfare organisations in the country our mission is to ensure that the welfare of animals used in research, teaching and education is upheld and constantly improved.

No manuscript was received from this presenter

Cryopreservation – Cheaper than Maintenance?

Kevin Taylor
Australian BioResources, Moss Vale, NSW.

The techniques used to cryopreserve reproductive material from mice have been established for a long time, and recent developments have improved the outcome considerably. 'Freezing down' a mouse line that is no longer required for experimental purposes is not only feasible; it actually offers numerous benefits for researchers.

There will come a point where the ongoing costs of keeping a line breeding past its useful life will exceed what would have been paid to cryopreserve the line and store the frozen material. Cryopreservation can be cheaper than maintenance.

No manuscript was received from this presenter

Sydney Animal Research Ethics Group (SAREG): a multi-institute collaboration

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Animal research in NSW is legislated/governed under the *Animal Research Act 1985* and the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes – 7th Edition (the Code)*. These documents stipulate that approval must be sought from an Animal Ethics Committee (AEC) before research involving animals can commence. AECs and researchers are supported by Animal Ethics Secretariats including Animal Welfare Officers (AWO) and Animal Ethics Managers; and Animal Facility Managers. It is generally accepted that the Code is a set of principles which is open to interpretation. As such, individual institutes operate in slightly different manners.

The aim in forming SAREG was so that AWO, Ethics Managers and Facility Managers from different institutes within the Sydney metropolitan area could meet on a regular basis. These meetings would allow members to share experiences, discuss matters related to animal research, and the approach that is taken at each member's own institute.

AWO, Ethics Managers and Facility Managers meet bimonthly, with communication conducted via an online group discussion forum. Meetings are divided into three discussion topics: Animal Welfare; Policy and Procedures; and AEC administration. Topics for discussion are proposed by members for the following meeting.

SAREG has met 4 times, with the first meeting held in October 2012. At present, SAREG comprises of over 15 active members, representing more than 10 different organisations. The group has discussed the following topics: Animal use policy, Procedures to cater for ulcerative dermatitis in aging C57Bl/6 mice, Benchmarking AEC processes, 'AVMA Euthanasia guidelines', Breach of the Code/Research Misconduct, 'EU severity assessment framework', Researcher training, Asepsis for rodent survival surgery, Permissible weight loss in research animals, Tissues obtained from external sources, and Schedule 4 & 8 drugs.

The meetings have been very informative and helpful. In sharing our knowledge, we have been able to receive advice from other members who have had first-hand experience of issues our respective institutes are currently facing.

I highly encourage that you start similar groups within your local area. By sharing this wealth of knowledge with our colleagues, the animals we use in research are ultimately "better off".

***Should you wish to join SAREG, please contact Paul Sou via paul.sou@uts.edu.au*

Paper

The definition of collaboration is "the action of working with someone to produce something". Many of us are occupied with various commitments that leave little time for us to notice or care about what our colleagues are doing. However, most of us are in our field of work because we care about animals, especially those animals that are used in research. That being the case, we ultimately want the best for these animals.

One method to achieve this is through collaboration. There is a wealth of information, knowledge and expertise amongst us, but it is all confined to each of our respective institutes. When we encounter "new" issues at our own institutes, the chances are that another institute has already faced something similar, if not the same and in all likelihood have already dealt with it. As a result, the Sydney Animal Research Ethics Group (SAREG) was created.

SAREG is a group where animal welfare officers, ethics managers and facility managers can meet on a regular basis, share experiences and knowledge, and discuss things all related to animal research. Since our first meeting in October last year, we currently have over 15 active members representing more than 10 different organisations.

Format of the group

The format of the group is based on an online discussion forum using Google groups as a platform. This allows members to post topics for discussion and other members to provide input as reply threads. One benefit is that all discussion topics and documents are kept in the one location. Additionally, the group meets every 2 months at one of the hosting institutes, with the representative from that institute chairing the meeting. Meetings typically run for approximately 2 hours and are broken down into 3 broad discussion categories based on: Animal Welfare, Policy & procedures & AEC administration. Minutes of each meeting are documented and confirmed at the following meeting.

Example of topics discussed include:

Animal welfare:

- Controversial techniques, such as retro-orbital eye bleeds, administration of adjuvants like CFA and footpad injections.
- Co-housing of rats and mice in the same room.
- Single housing of animals.
- Amount of permissible weight loss in an animal before euthanasia is required.
- Aseptic rodent survival surgery.
- Caring for mice with ulcerative dermatitis.

Policies and procedures:

- Dealing with animal tissues obtained from external sources.
- Researcher training.
- Committee member training.
- Institute's animal use policy.
- Dealing with breach of the code and research misconduct.

AEC administration:

- Online application systems and data management.
- Acquisition and administration of Schedule 4 and 8 drugs
- Benchmarking committees to each other, details like committee size and workloads etc.

Advantages

Conferences such as ANZCCART, ANZLAA and the ARRP forum are great, but occur infrequently (once a year or every other year). The advantage of SAREG is that meetings occur on a regular basis - bimonthly, and members can devote time to face-to-face discussion of issues that currently affect them. Members suggest topics for upcoming meetings, thereby making it directly relevant and practical. At times, topics and issues can be sensitive and contentious, so it is preferable not to have these topics discussed in the public domain. Its incidents like these that mean direct face-to-face discussion in a private group like SAREG are ideal.

By sharing experiences, members are able to learn from each other's mistakes and potentially avoid repeating them. Some of the advice provided by members is not documented in policies and guidelines and can only be learnt through direct experience. Occasionally it is these intricate details that can significant influence the ultimate outcome of a situation.

Difficulties experienced

Initially there were some technical issues experienced in establishing the discussion forum. Some members were unable to login to the discussion forum, as google groups did not permit members to use their work emails as a login. This has been overcome with members providing more generic email addresses such as gmail, hotmail, or yahoo, or by using google chrome as a browser.

Another issue was establishing a time that suited all members. For the first few meetings, the meeting time of SAREG clashed with one of the institute's AEC meeting, however, this has been subsequently rectified.

Another point of discussion was determining the eligibility criteria for membership of the group. The question of whether SAREG should be restricted to manager and executive levels within the institute, or whether administrators, technicians or people generally interested in animal welfare should be allowed to join. Due to the sensitive nature of some of the discussion topics, SARG members have agreed to restrict it to the former.

Where we are currently

As SAREG has started to grow, we are in the process of developing formal terms of reference and a mission statement for the group.

Personally, I hope the group grows to the point where we have representation from most of the research institutes within Sydney. Once this is achieved, potentially the group can become a body that represents Sydney's research institutes in terms of animal ethics and welfare; and potentially have influence on the development of policies and procedures that affect animals used in research. As a minimum, the group can develop documents and/or training programs that are consistent and can be shared amongst all members within the group.

Summary

Through the creation of SAREG, we have helped each other both directly and indirectly to improve animal welfare by sharing our experiences and knowledge, whether it is how to cater to aging C57Bl/6 mice with ulcerative dermatitis or dealing with researchers that have breached the Code, so that they do not re-offend. By understanding why others before us do things a certain way, we are not required to reinvent the wheel, and ultimately it is the animals the benefit. That being the case, I encourage all of you to start mingling and start something similar in your local areas - share your knowledge with the world. That way, we can do better.

Can cognitive bias be used to assess affective state and welfare in captive reptiles and fish?

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Concerns regarding animal welfare are generally based on the assumption that animals can experience subjective emotions, and hence can experience suffering or pleasure. Although animal welfare science has increasingly acknowledged the importance of emotional (affective) states in determining the overall well-being of animals, our understanding of these states remains poor. This is primarily due to the lack of reliable tests to measure affective states in animals. Thus, decisions about welfare are sometimes made on the basis of anthropomorphic projection, which is not ideal because intuition is often unreliable. The development of better methods of assessing animal emotion is therefore an important topic in contemporary animal welfare science.

Recently, a novel approach for measuring the affective state of animals has been developed based on research in human psychology which shows that individuals in a negative emotional state tend to interpret ambiguous stimuli or situations more negatively (pessimistically) than individuals in a positive state. Thus, biases in decision-making under ambiguity appear to be good indicators of an individual's emotional state. These affect-induced 'cognitive biases' in decision-making have now been demonstrated in some mammals and birds. This represents a breakthrough in animal welfare science because it enables researchers to objectively assess the valence (positivity or negativity) of animal emotional states, although whether such states are experienced consciously, or in similar ways to how we experience happiness or sadness for example, cannot be known for sure. To date, however, no studies have been conducted on other vertebrate groups. This study will investigate whether affect-induced cognitive biases also occur in reptiles and fish, and validate a method for measuring such biases against other indicators commonly used to assess welfare.

Selected species of reptiles and fish will be trained to associate one cue with a high-value reward and a second cue with a comparatively lower-value reward. Once animals are trained to both cues, a third, unknown (ambiguous) cue will be presented. Response to this cue will indicate whether the animal interprets it as predicting a high or low value reward and hence whether it shows an 'optimistic' or 'pessimistic' cognitive bias, indicative of a positive or negative affective state respectively. To validate the approach, subjects will be exposed to physiological or environmental stimuli known from previous work to induce stress and a putative negative emotional state. If animals exposed to these treatments show a negative judgment of ambiguous stimuli relative to those in a control group, this will support the hypothesis that cognitive bias tests reflect affective state in lizards and fishes, and that these taxa also possess

affective systems that may be influenced by how they are managed in captivity.

Around the world, millions of animals are held in captivity for research and in zoos. We now know that appropriate animal welfare for these animals is influenced not only by physical, but also emotional factors. In fact, concerns for animal welfare are generally based on the assumption that animals can experience subjective feelings, which means that they can feel pain, suffering and pleasure (Dawkins, 1990; Mendl *et al*., 2009; Veissier *et al*., 2009). Because we recognize that many animals appear to be sentient (Webster, 2006), much of what we do in animal welfare science seeks to understand and reduce suffering, as well as promote pleasure in animals.

However, psychological well-being is not something that can be easily measured. It is not possible to directly understand what another person is feeling, let alone what a non-human animal is experiencing, because conscious experiences are essentially private and not directly accessible to others. There are however, a range of indicators that we think will provide us with some idea of what the animal is actually feeling. These include physiological indicators such as stress hormone concentrations in the blood (e.g. Mathies *et al*., 2001), concentrations of stress hormone metabolites in faeces (e.g. Berkeley *et al.*, 1997) and blood leucocyte profiles (e.g. Bennett and Gaudio Neville, 1975). In addition, behavioural indicators can be used, including distress vocalisations (e.g. Weary and Fraser, 1997) and stereotypies (e.g. Barnett and Hemsworth, 1990).

While these measures provide useful data that may act as proxies for emotional well-being, there are often problems associated with using them to inform our understanding of welfare issues. For example, physiological indicators, such as an increase in concentrations of stress hormone in blood, may occur due to a stressful event, such as the presence of a predator, or in response to an emotionally positive event, such as sexual arousal (Mendl *et al*., 2009). Similarly, it is difficult to interpret behavioural data. For example, during open field tests (where an animal is placed on a flat surface in an enclosed arena), do high levels of activity reflect motivation to explore (positive welfare implications) or escape (negative welfare implications) (Archer, 1973; Paul *et al*., 2005)?

There is a clear need for better methods of objectively assessing emotional (affective) states and welfare in animals. Recently, a novel method of assessing emotional states has been developed based on research in human psychology, known as cognitive bias. Cognitive bias, simply put, refers to how our emotions affect our decision-making. People in a more negative state of mind (for example, when they are unhappy, anxious or depressed), have been shown to interpret situations more negatively, (especially when the situation is ambiguous) compared to happy people; they see the glass as half empty instead of half full. This link between emotional state and 'optimistic' or 'pessimistic' - like decision-making in ambiguous situations can also be investigated in animals (Harding *et al*., 2004; Mendl *et al*., 2009, see below).

Cognitive bias offers a number of advantages over the current methods of animal welfare assessment that were described earlier. Firstly, this technique could potentially be an objective measure of animal emotions across taxonomic groups, because hypotheses for how decision-making should alter according to affective state are likely to hold across taxa (Mendl *et al.*, 2010b). This makes it a potentially powerful tool for animal emotion and welfare assessment. Cognitive bias also focuses on evaluating emotional valence (i.e. whether the emotional state of

the animal is positive or negative) rather than emotional intensity (i.e. how strong the emotion is), which overcomes a major disadvantage of many physiological measures of welfare such as analysis of stress hormones (Mendl *et al*., 2009). Thirdly, cognitive bias assesses both positive and negative emotional states, which fits very well with our goal of enhancing good welfare, rather than simply minimizing poor welfare. Failure to identify positive emotional states is currently a major limitation of many physiological and behavioural welfare assessment techniques (Boissy *et al*., 2007).

The emergence of the study of cognitive bias in humans triggered research into whether animals might respond in a similar way. Cognitive bias has now been recorded in a number of mammal and bird species, including rats (Harding *et al*., 2004; Burman *et al*., 2009; Enkel *et al*., 2009; Brydges *et al*., 2011), pigs (Douglas *et al*., 2012), dogs (Mendl *et al*., 2010a; Burman *et al*., 2011), sheep (Doyle *et al*., 2010; Doyle *et al*., 2011; Destrez *et al*., 2012), rhesus macaques (Bethell *et al*., 2012) and starlings (Bateson and Matheson, 2007; Matheson *et al*., 2008). However we still do not know whether other taxonomic groups are capable of cognitive bias. Our research aims to investigate whether reptiles and fish are also capable of displaying cognitive bias and whether this technique can be used to assess emotional (affective) state in these taxonomic groups.

In this project, selected species of reptiles and fish will be trained to make one type of response (e.g. turn left) to a cue associated with a high-value reward and a different type of response (e.g. turn right) to a different cue associated with a comparatively lower-value reward. Once animals are trained to both cues, a third, unknown (ambiguous) cue will be presented. Response to this cue (e.g. left or right turning) will indicate whether the animal interprets it as predicting a high or low value reward and hence whether it shows an 'optimistic' or 'pessimistic' cognitive bias, indicative of a positive or negative affective state respectively. To validate this approach, subjects will also subsequently be exposed to physiological or environmental stimuli, known from previous work to induce mild stress/distress and a putative negative emotional state. If animals exposed to these treatments demonstrate a negative cognitive bias of ambiguous stimuli relative to those in a control group, this will support the hypothesis that cognitive bias tests reflect affective state in reptiles and fishes, and that these taxa also possess affective systems that may be influenced by how they are managed in captivity. This will provide an opportunity to develop better management and welfare protocols for captive reptiles and fish.

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Ethics and Statistics in Plain English (without the mathematics)

Richard Walton
Animal Care & Ethics Committee (ACEC) University of Technology of Sydney (UTS)

The aim of any trialist is to design a fair and competent experiment in order to glimpse the truth. An animal experiment that is neither fair nor competent cannot be considered an ethical one.

A persistent statistical and ethical issue in designing animal experiments is estimating the number of animals required. A formal sample size calculation as part of an ethics application requires the researcher to think deeply about their planned experiment and forces them to walk the ethical tightrope with futility on one side (sample size too small) and needless waste (sample size too large) on the other. Arguments and justifications resting on practicality, previous experience, precedence, guesswork or cost & time constraints are commonly used to arrive at convenient and completely unethical sample size estimates.

Most researchers have neither the time nor inclination to study statistics in depth however the concepts involved in sample size estimation are simple and intuitive. This presentation discusses the basic statistical issues involved in plain English and how they intertwine with ethical aspects of an experiment along with tips and examples.

Embracing (not avoiding) statistics and experimental design allows confidence to prosecute your research agenda with the maximum chance of grasping the truth using the minimum number of animal subjects.

No manuscript was received from this presenter

Managing ethical obligations and veterinary interactions in commercially funded livestock trials: pitfalls and solutions.

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UniServices Ltd, Ngapouri Research Farm Laboratory, University of Auckland, New Zealand.

Abstract:

The great majority of large animal researchers involved in production based research work in Australasia have developed their career within a research organisation framework that involves purpose designed facilities, standard operating procedures and Animal Welfare Officers (AWO). In this environment all staff should have a good idea of their responsibilities and obligations demanded by the adherence to Animal Welfare legislation and associated codes. In this situation it is easier for the AWO and institutional AEC to keep on experimental progress and ideally help researchers optimise measureable outcomes while ensuring animal welfare cost is minimised. Even in a remote situation like Ngapouri Research Farm Laboratory (250+km from Auckland) a lot of effort goes into keeping contact and dialogue with the AEC and AWO.

While the majority of research at Ngapouri is based on biomedical funding over the last 2-3 years there has been a rapid increase in demand for research from Agri-Business interests for research provision involving, feedstuffs, nutraceuticals and pharmaceuticals. While much of this work involves experimental work at the feedlot facility (especially in the case of pharmaceuticals) or adjoining grazing other trials involve evaluation of products at 3rd party farms where livestock are owned by farmers/farming businesses.

In the situation where a trial is conducted at a third party site there are wealth of new challenges and considerations that must be dealt with to maximise the chance of a "successful" trial to be performed. These include interaction with veterinarians not used to working on experimental trials, their client obligations, and unfamiliarity of the client, owner and staff with animal welfare legislation, sub optimal practices and nutrition management etc. and commercial imperative of the client. Not the right place to go into scientific commercial conflicts but this is clearly also an issue.

In this talk I will go over the process of getting these projects off the ground and relate what lessons have been learnt in terms of familiarising clients, veterinarians, farmers and their staff with the demands of ethical and effective experimentation. Another important area is institutional support for the researcher in terms of formulating effective research contracts between the researcher client and third parties that insure as best as possible that all obligations of the parties involved a fully described and understood. I will attempt illustrate problems our team have encountered and what we have come up with to overcome them.

Overview:
The great majority of large animal researchers involved in production based research work have developed their career within a research organisation framework that involves purpose-designed facilities, standard operating procedures and institutional Animal Welfare Officer (AWO) inputs. In this formal environment all staff must have a good idea of their responsibilities and obligations demanded by adherence to Animal Welfare legislation and associated codes. In this situation it is easier for the AWO and institutional AEC to keep an eye on experimental progress and ideally help researchers optimise measurable outcomes while ensuring animal welfare costs are minimised. In a remote situation like Ngapouri Research Farm Laboratory (260km from Auckland), a lot of effort goes into maintaining regular contact and an on-going dialogue with the AEC and AWO.

While the majority of research at Ngapouri is based on biomedical funding, over the last 2-3 years there has been a rapid increase in demand for research from Agri-Business interests for research provision involving feedstuffs, neutraceuticals and pharmaceuticals. While much of this work involves experimental work at a feedlot facility - particularly in the case of pharmaceuticals – or on adjoining grazing lands, other trials involve evaluation of products at third party farms where livestock are owned by farmers/farming businesses. In the situation where a trial is conducted at a third party site, there are a range of new challenges and considerations that must be dealt with to maximise the chance of performing a "successful" trial. These include interactions with veterinarians unaccustomed to working on experimental trials, their client obligations, and a general lack of familiarity of the client, owner and staff with animal welfare legislation. There are also often sub-optimal practices and nutrition management etc. that will need to be addressed as well as the commercial imperative of the client which need to be considered. While this not the right forum to address scientific versus commercial conflicts, this is clearly another issue to consider.

In this paper we will cover the process of getting these projects off the ground and relate what lessons have been learnt in terms of familiarising clients, veterinarians, farmers and the staff with the demands of ethical and effective experimentation. Another important area is institutional support for the researcher in terms of formulating effective research contracts between the researcher client and third parties that ensure that all obligations of the parties involved are fully described and understood. We will attempt to illustrate problems we have encountered and what solutions we have come up with in an attempt to overcome them.

Remote Operations:
Ngapouri Research Farm Laboratory is situated some 260km from the University of Auckland. The prime research focus is biomedical research using sheep as a model. Despite this distance, there are regular audit and training visits conducted by the University's AWO. New staff are trained and supervised in animal welfare and ethics by experienced staff and are supported by thorough and detailed SOPs. An important aspect to the successful running of this remote facility is a close functional relationship with a local production animal veterinarian. The local veterinarian's role extends beyond provision of veterinary care; advice is sought with regards to protocol development and at times ethics applications. Conducting commercially funded research brings new challenges to the research arena.

Commercial Research:
Our team has been involved with commercially funded projects for the last 2-3 years. In that time we have covered a broad range of research paradigms, including: fertility, lamb and calf

growth, maternal health, dietary supplements, Facial Eczema and other diseases. In years gone by, we have also been involved in commercial human drug development and testing, which in itself is a completely different kettle of fish. In reality, there is little public money available for animal health/welfare/production research in New Zealand. Commercially funded research can bring co-funding benefits for other work or equipment. For commercially funded research to be successful, institutional contracts and resources must be used in a well thought out manner. Always be mindful of perceptions: not only of the client and how they may regard 'scientist' stereotypes, but also of their attitude to the 'amazing' research service you will provide. While it is important to listen to the client and identify want they hope to get out of the project, be mindful and balance what they want with what is achievable and real. At this stage it may also be worthwhile performing a thorough literature search before committing to a large scale trial: can animal use be justified? Try not to fall into the trap of thinking about sneaking funding to do 'other stuff'. Be very clear to the client regarding risks: identify risks along with whose risk? It's also worth reminding your client that paying for research doesn't always equate with getting the results they may desire. Watch for clients who may have invested many years of blood sweat and tears developing their products: they will likely be quite sentimental about their products and believe^{x3} and know^{x3} that they work. A good idea is to have a fairly neutral attitude to this sort of thing: allow the data and numbers to speak for themselves.

Many clients are not familiar with animal welfare considerations including legislative obligations and cost, often 'best practice' may not be in line with welfare legislation. Introduction of these concepts at an early stage will save misunderstandings and frustrations further down the line. It's also a good idea to make use of flow charts to illustrate inputs, timelines and expectations. These can be used as a reference at any stage during a project. Most important of all, engaging in a formal contract is paramount. Take the time to use protocols and even AEC applications as appendices to the contract and clearly state objectives and responsibilities as well as including a disputes clause. A formal contract will assist you in ending a commercial relationship if necessary. A successful 'divorce' is a rare but important necessity of commercial research agreements.

Experimental Design:

Some commercial clients have run their 'own' trials in the past and are now ready to engage a recognised research provider to give their product credibility against their competitors. Some of these commercial clients have well-intentioned but rigid ideas about how their trials should run. Be firm and use your research experience as a means to guide them towards the best way forward. They are most likely inexperienced at protocol design, numbers required, randomisation methods and statistical analyses.

Be straight with your clients about the power and validity of the conclusions from the research. It's useful to ensure that the basics of statistical tests you use will be understood in lay terms, likewise basic understanding of how to interpret data including graphs should be discussed early on. There's nothing quite like getting a bunch of graphs together for a client, only to discover that they aren't able to interpret them.

Some philosophical discussions regarding animal use should be introduced early on as well. The 3Rs is a foreign concept to many people outside of animal research and a 'stop-go' approach can be suggested to limit needless animal use if a dead end in the trial eventuates. Always keep forefront of your mind, that the animals you will likely use are a farmer client's livelihood. While there are always ethical considerations when using animals for research, adding in a farm's prize heifer herd into the mix can add further risks. If the commercial trial involves the testing of

products (for example feed sources or supplements), ensure you have open discussions with your client about QC limitations of the product before committing to a project. Insist that there is a clause in your contract that will cover any QC issues. This should include either insisting on testing before starting or clearly describe what will need to happen if the QC tests fall short of what you were guaranteed. Most important of all, seek advice from the research staff that will actually be running the project on a day to day basis. They are your eyes and ears and being on the ground, will mean they will often have a different perspective to that of a Principle Investigator/Scientist. They should be involved in all discussions with the clients and it should also be impressed on the clients that the day to day research staff is/are the first point of contact for any discussions. We recommend that the research staff you have are experienced and are able to think on their feet. We have found that even with the best planning and intentions, commercial projects have a habit of throwing real curve balls at you. Experienced staff are able to work their way through any sticky scenario and ensure that they still adhere to the approved protocols.

Veterinarian Input:

Before undertaking a project, brief your institutional AWO and local veterinarian and seek advice before making an AEC application. As a part of this you should ask the following questions:

- Does your production veterinarian think the research is worth any welfare costs?
- Can they suggest any improvements to your hypothesis/design?
- Are they comfortable with client conflicts if the research is performed on a third party property?

If you are working with the client farmer's veterinarian, ask your client to set up a meeting that will allow you to introduce yourself and your team. A good relationship with a client farmer's vet can make or break a commercial project. Be aware they may have their own ideas and biases, so be clear about what you hope to achieve and be open to suggestions. At this stage you should encourage the veterinarian to interact with your research staff, as it's likely that they will be doing the bulk of the work. It's worthwhile getting the vet to assist with instructing the client farmer about their animal health and welfare responsibilities. All parties need to be reminded that it is essential they follow the approved protocol to the very best of their abilities. Even the smallest deviations can mean data interpretation becomes difficult or even impossible.

Ethics Application:

Check with your institutional AWO whether or not AEC approvals are required (Editor's Note: In Australia, the answer will always be yes, AEC approval will be required). Most commercial clients have no idea about ethics and what it means in the context of a trial, they will talk about 'best practice' which will vary from property to property and is often not best practice! If AEC approval is not required, always refer to Animal Welfare Codes and associated legislation in your protocols and contract. Clients should read and understand the AEC application, which should also be appended to your contract. All staff involved in a commercial trial should read the ethics application. Your clients have to understand the professional and legal responsibilities undertaken by your research team on their behalf. Deviations from protocol should be discussed ahead of time – worst case scenario – along with the ramifications of modifying the protocol, both ethically as well as from a data analysis point of view. The client needs to understand the amendment process, if one or more change is required.

We recommend a meeting of all staff involved in a project prior to starting, so that these issues can be discussed.

The Trial:
Establish resourcing responsibilities within the contract framework. This can include everything from feed supply, animal supply, importation of test substances or other requirements. Animal health and welfare standards - as set by your home institution AEC, must remain consistent throughout and be understood by all. Always stick to the approved trial design unless contingencies have been discussed thoroughly and are agreed to within the approved protocol. If necessary seek advice from either your AWO or your production veterinarian. Clear lines of communication must be established early on and should identify who is the first point of contact day to day? Remember that the PI is likely to be snowed under, juggling other work already. Watch for over enthusiastic clients. You may have to remind them that you are there to run an independent research trial as some can veer towards interference. Establish regular meetings or lines of communication. Some clients like regular progress meetings; some prefer a regular email outlining what's happening. A good idea is to think about keeping a laboratory style journal for the duration of a long trial, by the time it's completed you have got a detailed journal of what happened when, which will be invaluable for writing up! If the trial becomes compromised due to adverse events e.g., feed palatability issues, it should be stopped and so you must be be prepared to do so. Do not compromise your professional integrity in an attempt to salvage the unsalvageable. It can be a tough call to make, but use your experience and seek advice from your AWO or production veterinarian if need be.

The Results and Report:
The same professional ethics that apply in any research must apply in commercial research. You should always be critical of any hypothesis under test. Both your contracts and reports should have a waiver included that allows you to approve further dissemination or potential misuse of results. Your report should be written bearing the audience it is intended for in mind. If it's for a small company, don't weigh it down with too much jargon and complicated statistical analysis. At the same time, report what happened and don't sugar coat it, if the product didn't work – it didn't work. In other words, watch for clients who may cherry pick out parts of a report to their advantage or take quotes out of context. Any subsequent issues arising from intellectual property (who owns it?) should have been identified during contract negotiations. Try to encourage further publication if possible so that if the work is repeated, it is in a refined form (3Rs).

The Good News!
Commercial research is often relevant and applicable. You will get out of your Ivory Tower, learn new skills and get involved with the community. For researchers that are primarily focussed on biomedical research, it is refreshing to be able to meet and talk to farmers about your research. They are generally open to new ideas and are interested in new applications. The chance to communicate science to a different audience is very worthwhile and rewarding. We have found perceptions from both sides to be quite a hurdle, but make an effort and you won't be disappointed. Depending on your project, you could be involved in improving outcomes with regards to animal health and welfare.

The overriding thing we have learnt is to be proactive. Anticipate worst case scenarios, have contingencies in place and most of all never lose your professional integrity.

Presentations given

on

Wednesday 24th July

The Effects of New Requirements for Laboratory Housing on Laboratory Mice

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Abstract

Background: Over recent years, the requirements for laboratory housing have changed. Nowadays, ethical as well as hygienic and WHS demands must be considered when housing laboratory animals in research facilities. These changes have generated two new housing conditions: a) minimally enriched (ME) cages (i.e. cages with domes and other cage structures) and b) individually ventilated cage (IVC) systems. Compared to classic standard laboratory housing conditions (i.e. filter top cages with no enriched structures), ME cages and IVC systems potentially provide quite different environments for laboratory mice. However, the impact these new housing forms might have on laboratory mice and mouse model research in general is poorly understood.

Objectives: Here we present data on how ME cages and IVC systems impact on the behavioural phenotype of laboratory mice and a mouse model of schizophrenia [i.e. germline knockout mice for the schizophrenia candidate gene neuregulin 1 (Nrg1 mice)].

Methods: Male Nrg1 mice and their wild type-like control littermates (all on pure C57BL/6J background) were bred and raised in either classic standard laboratory housing conditions, in ME cages, or in IVC systems. Once animals had reached adulthood (>90 days of age), mice were tested behaviourally in a comprehensive test battery for locomotion, exploration, anxiety, social interaction, cognition and sensorimotor gating.

Results: Both new housing systems altered the behavioural phenotype of laboratory mice and more specifically of a mouse model commonly used in preclinical schizophrenia research. ME cages shifted the onset of schizophrenia-relevant behavioural characteristics of Nrg1 mice and IVC systems suppressed some of these behavioural abnormalities completely. Furthermore, other phenotypic features of Nrg1 mice were not as pronounced when mice had been raised in IVC systems instead of classic laboratory housing conditions. Finally, IVC modified the behavioural effects of a drug, which is commonly used in pharmacological mouse research.

Conclusions: These data reveal for the first time the significant impact of ME housing and IVC systems on laboratory mice and pharmacological as well as genetic mouse model research. These findings have implications for data comparability across research institutes, data reliability, and animal welfare issues (i.e. animal numbers used in medical research).

Differences in laboratory housing conditions across research institutions

An increasing number of research studies provide strong evidence that laboratory mice are sensitive to the housing conditions in which they live[1-3]. New international hygienic and ethical requirements have exposed laboratory mice to two new housing conditions: 1) individually ventilated cages (IVC) and 2) minimally enriched cages (ME; moderate level of environmental complexity compared to classic "standard" laboratory housing). Surprisingly little is known about the impact of these cage types on laboratory mice. Data generated in our laboratory suggest that IVC and ME alter brain development and behaviour of mouse models for brain disorders and influence the response of laboratory mice to pharmacological interventions[4-6]. This causes issues for the scientific validity of experimental mouse models as well as data comparability and reliability across research centres, as not all research institutions use IVCs or MEs.

Individually ventilated cage (IVC) systems:

Over the past decade, technology for housing laboratory mice has evolved. Initially, filter covers were introduced on open cages to provide partial protection of mice and workers from infections (i.e. filter-top cages). More recent developments have resulted in the employment of individually ventilated cage (IVC) systems as a measure to improve hygienic standards and space capacities of large animal facilities. Importantly, IVCs generate a cage environment different to filter-top cages:

- Noise levels and the frequency of cage changes are decreased in IVCs[7]
- IVCs block out the interchange of olfactory and acoustic cues between group-housed mice across cages and therefore represent a form of isolation housing (i.e. deprivation) [8]
- Air changing rates are increased in IVCs and induce place aversion in laboratory rodents[9]
- IVCs provide less climbing opportunities than filter-top cages[10]
- Lowered ambient oxygen concentration and increased humidity in IVC cages has been suggested to represent a potential confounder of test outcomes[11]

It is currently not known in any detail if/how these differences impact on baseline and drug-induced behaviours, which were established in laboratory mice kept in filter-top cages. Two studies have investigated the consequences of IVC systems on wild type mouse behaviours in some detail and reported strain- and sex-specific effects on motor activity, anxiety-related behaviours, spatial memory and anhedonia[7, 10]. Both research articles warned that a switch to IVC systems has the potential to bias preclinical research results in a serious manner. Importantly, our team recently published a study showing for the first time that male C57BL/6J mice raised in IVC systems were more susceptible to pharmacological manipulations (i.e. acute MK-801 treatment) compared to males kept in filter-top cages. This effect of IVCs was long-lasting as it was evident even after housing 'IVC males' in open cages for 4 weeks before testing commenced[6].

Preclinical neuroscience research relies not only on pharmacological but also on genetic mouse models (e.g. for brain disorders such as Alzheimer's disease and schizophrenia). Thus, in preliminary work, our team has also determined how mice mutant for the validated schizophrenia risk gene *neuregulin 1* (*Nrg1*)[12] respond to IVC housing. Importantly, ***core*** features of the behavioural phenotype of *Nrg1* mutant mice (i.e. deficits in prepulse inhibition, hyper-locomotion, deficits in contextual fear conditioning (See Figure 1A-C), which had been established and published for mice raised in filter-top cages[5, 13-16], could not be replicated in mice kept in IVC systems.

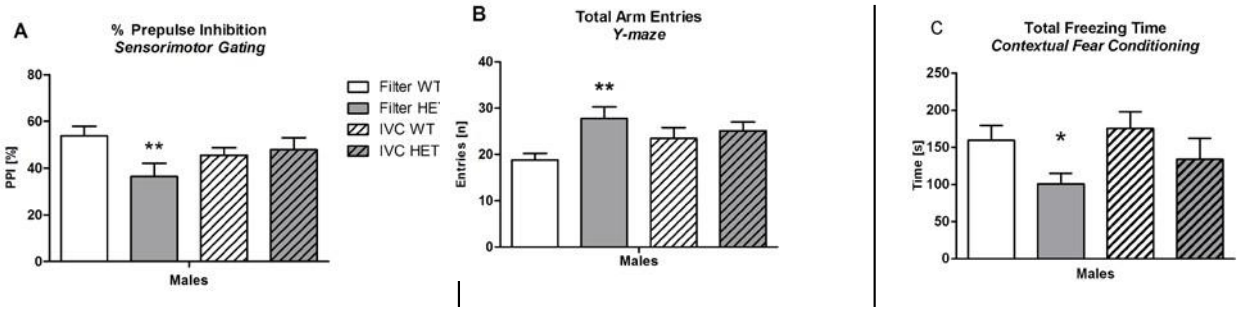

Fig. 1A-C: A) Prepulse inhibition [%] **B)** Locomotion (i.e. arm entries: [n]), and **C)** contextual fear conditioning [s] of wild type (WT) and *Nrg1* mutant (HET) mice raised in IVC or filter-top cages (Filter) are shown. ANOVA effects of 'genotype' vs. WTs are indicated as $^{*}p < .05$ and $^{**}p < .01$.

Our findings are significant to neuroscientist working with pharmacological and/or genetic mouse models, as they suggest a significant impact of IVC housing on mouse model phenotypes. In contrast to large animal facilities, most small research facilities still rely on filter-top cages.

Minimally enriched cages (ME):

Research has shown that enriched environments can shift phenotypes of disease models dramatically[2, 17]. Importantly, an increasing number of animal ethics committees worldwide demand the use of limited forms of environmental enrichment (i.e. minimal enrichment) as part of standard housing for laboratory mice and governmental guidelines have been changed accordingly (e.g. European legislation: 2007/526/CE). Therefore, "standard" laboratory housing conditions vary widely across research institutions and are dependent on local animal ethics regulations[18]. Housing conditions range from the classic standard form (i.e. cages provided with bedding, food and water *ad libitum* but no other cage structures) to more complex, minimally enriched forms where animals have access to nesting material, shelter (e.g. toilet rolls or plastic domes) and/or other cage structures (e.g. steel rings or wooden blocks).

Our team found that small cage variations can impact significantly on the outcome of experimental mouse studies. For example, the cage size influences object recognition memory of C57BL/6J mice: animals kept in small cages failed to developed an intact object recognition memory (i.e. a preference for a novel over a familiar object: See Figure 2). Also, an established age-dependent anxiolytic-like phenotype of *Nrg1* mutant mice kept in standard housing was absent when animals had been raised in ME as requested by the local animal ethics committee [5]. Subsequent studies confirmed the significant impact of ME on the neuro-behavioural phenotype of *Nrg1* mouse mutants further: initially described changes to cortical NMDA receptor levels of *Nrg1* mutant mice kept in standard laboratory housing [12] could not be replicated in mouse mutants raised in ME [4].

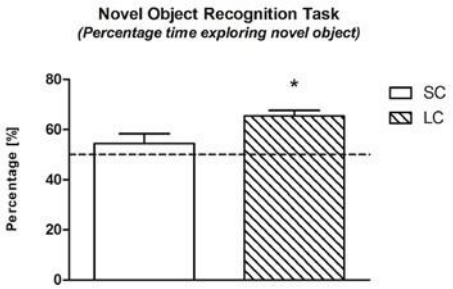

Fig. 2: Recognition memory of C57BL/6J mice housed in small (SC) or large (LC) cages (ANOVA: $^{*}p < .05$ vs. SC).

In summary, recent requirements in hygiene and animal ethics have confronted animal researchers with new housing conditions (IVC, ME), which are employed without any detailed understanding of their impact on mouse model research. Our own published studies and preliminary data from our research laboratory suggest that IVC and ME have the potential to challenge the reproducibility of phenotypic data and the validity of genetic and pharmacological mouse models across institutes, which utilise different housing conditions. Importantly, the degree of implementation of these new housing requirements differs across countries and research institutions. Nevertheless, IVCs have become an alternative animal husbandry system for an increasing number of commercial animal suppliers as well as large research institutes and universities and this despite the knowledge that physiological, neurological and behavioural phenotypes are affected by even minor environmental factors [5, 19-22]. Surprisingly, apart from our own work, nothing is known about the effects of IVCs or MEs on mutant mouse models. Those models are commonly housed in IVC facilities or exposed to ME. Researchers have also started using IVCs as a control housing condition [23] although most small research facilities are still using filter-top cages. Furthermore, ME has nowadays often replaced "standard" laboratory housing to address ethical considerations and improve animal welfare. Unfortunately, both IVC and ME conditions are not always specified or even mentioned in animal research publications. This generates significant problems for data comparability and reproducibility across research facilities. A detailed understanding of the effects of IVC and ME on mouse model phenotypes and the mechanisms involved is absolutely necessary to minimize these problems across research sites. Thus, future research should systematically define the disconcerting effects of IVC and ME housing in laboratory mice and specifically in mouse mutants for brain disorders.

There is a common understanding among animal researchers that *good welfare is better science*. Compared to enriched housing conditions, standard laboratory housing represents a negative environmental factor (i.e. sensorimotor deprivation) as it results in impaired brain development, stereotypies and anxiety [24]. Furthermore, mice themselves prefer a more complex environment [25]. Understanding the impact of particular housing elements such as ME in detail will enable researchers to provide a well-characterized alternative to standard laboratory housing [24], which will guarantee that phenotypes of transgenic animals are medically relevant and not a result of stress or deprived housing. This will also help to address some of the welfare concerns expressed by the wider community towards animal research.

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Training and Competency Assessment of Researchers.

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The 'Australian code of practice for the care and use of animals for scientific purposes' (the 'Code') requires that: 'Investigators and teachers who use animals for scientific purposes must employ the best available scientific and educational techniques and be competent in the procedures they perform or must be under the direct supervision of a person competent in the procedure.' Furthermore the Code requires that humane killing, euthanasia, anaesthesia and surgery must be performed only by personnel 'approved as competent' by the AEC'.

How does an Animal Ethics Committee ensure that researchers are trained so that both their competency and attitude to animal use is to the standard required by legislation and that the public expects?

A multifactorial approach will be described that combines recognition of prior learning, general and targeted training, and competency assessment with informal and formal inspections and analysis of adverse events.

This approach is most effective when the AEC and institution manage to establish and maintain an environment where researchers and animal care staff do not feel threatened by the animal ethics approval process, understand the advantages of ethical animal research and are happy to seek assistance when necessary.

Methods of fostering such a cooperative environment will be discussed, along with some of the challenges associated with the process.

Introduction

The legislation requires and the public expects that personnel working with research animals are competent in the procedures being carried out so that impact on animal welfare is minimised. However determining competency is not a simple process especially when animal research techniques are specialised and few people, including members of the Animal Ethics Committee have the skills to assess competency in these techniques.

At the University of Newcastle a multifactorial approach to training and competency in animal research personnel is based on gathering information about training and competency of particular personnel in specific techniques, identifying deficiencies, providing general and targeted training and arranging formal competency assessments where required.

Identifying Deficiencies in Training and Competency.

A lack of training and experience is often first identified when an investigator completes an application to the University of Newcastle Animal Care and Ethics committee (ACEC) and lists as limited or nil their experience in particular techniques to be carried out. Personnel whose experience is limited must identify a supervisor who has a high level of experience in that technique. This supervisor is then expected to supervise the inexperienced person until they become competent in the technique. Personnel who are new to the institution or who have no experience in animal research are asked by the ACEC to undertake an online training programs covering animal research legislation and ethics, hazards of working with animals, the operation of the ACEC, the steps to obtaining ACEC approval, monitoring animal welfare and pain management.

A lack of competency in animal research procedures often results in poor animal welfare and lack or research outcomes. Specific signs that animal research personnel are lacking competency include problems with animals detected during routine inspections, adverse events either self-reported or detected by animal services and veterinary staff, the use of animals without outcomes- usually detected through lack of progress identified in annual progress reports and complaints to the institution or ACEC about problems with animal welfare or lack of competency.

One Approach to Training and Competency Assessment.

The University of Newcastle ACEC monitors training and competence of animal research personnel by:

- Asking investigators to declare training and experience in each technique they will carry out in a project (Fig 1.).
- Asking investigators to undergo training via an ACEC endorsed training program and include this information in their applications.
- Inspecting procedures- particularly where a procedure is new to a group or investigator or where it has raised concerns among ACEC members.
- Inspecting the outcomes of procedures through inspections of animals in animal holding areas.
- Monitoring adverse event reports.

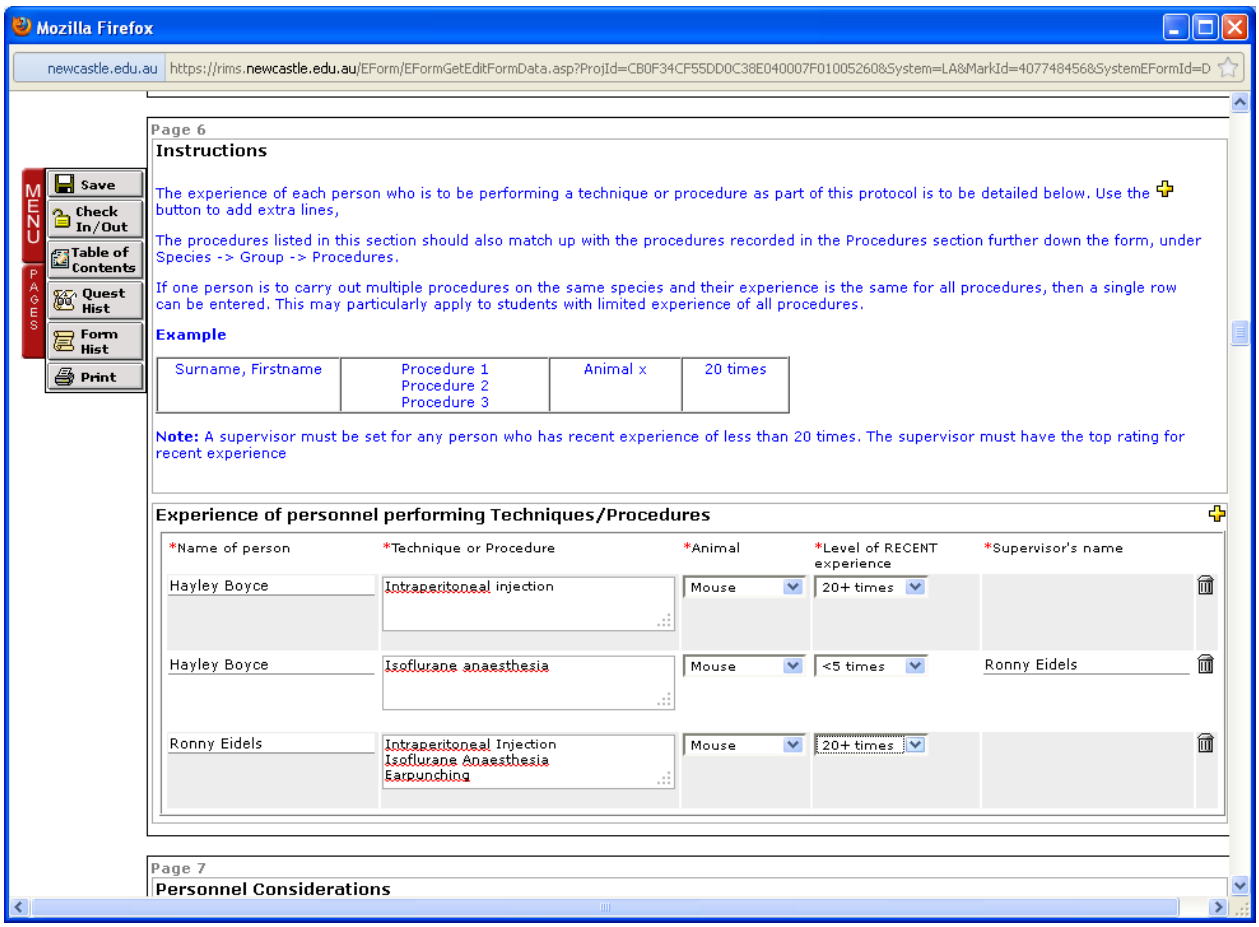


Fig 1. Declaration of Experience in particular techniques in application form to ACEC

Where deficiencies have been identified in training or competency the ACEC will require that the affected personnel undertake additional training and a formal competency assessment.

The University of Newcastle has established an "Animal Welfare and Training Unit (AWTU)" responsible for training and competency assessment of animal research personnel, veterinary clinical care for research animals, providing assistance to research personnel in the development of animal research protocols and "best practice" SOPs, and assisting the ACEC to develop guidelines for implementation of the 3R's and to monitor animal welfare through formal and informal inspections.

The ACEC and AWTU cooperate to assist animal research personnel to obtain the training they need to be competent in the techniques they use in their research protocols (Fig 2).
RPL: Recognition of Prior Learning Training-RATS (Research Animal Training Scheme) - Cert II Animal Technology Issues Identified? - Self Assessment (Declaration on ACEC application) - ACEC project inspections - ACEC facility inspections - Analysis of adverse events - informal AWTU inspections Yes/No Competent? ACEC requires additional training and formal competency assessment Competency Assessment (Optional)

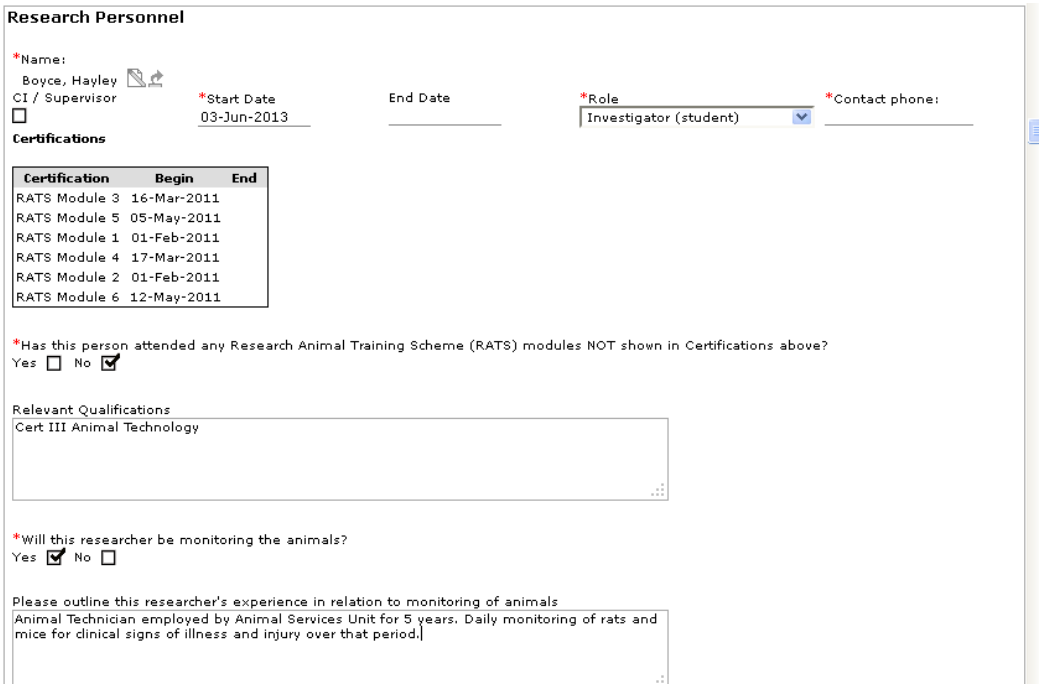


Fig. 2. ACEC /AWTU interactions in training and competency assessment.

Training Program

The Research Animal Training Scheme (RATS) is the training program offered by the AWTU to animal research personnel at the University of Newcastle. It consists of a combination of online learning and face to face seminars, tutorials and practical sessions in 7 Modules. The standard modules are supported by targeted small group and one-on-one training.
Personnel completing any combination of the modules have this information entered into the online ACEC application system (fig 3.) and receive a statement of attendance/completion for the appropriate modules.

The formal program includes:

Module 1- 'Introduction to the use of animals in Research'. This is an online course covering the legislative and institutional requirements governing the use of animals for research and teaching at the University of Newcastle, the principles and practice of animal care and welfare and the hazards of working with animals.

Module 2- 'Monitoring, pain management and anaesthesia'. An online course covering the monitoring of animal well-being, the assessment and management of pain and distress in animals, and the principles of anaesthesia.

Module 3-' Developing and using a monitoring checklist'. A seminar on how to develop and use an effective tool for monitoring the health and welfare of research animals. Includes an online learning component.

Module 4- 'Animal care, monitoring, handling and basic research procedures'. A practical session on basic animal care and handling, administration of substances (including injection techniques and gavage, blood collection, and post mortem. An online learning component is included.

Module 5- "Principles of anaesthesia in rodents'. A practical session demonstrating the principles and techniques involved in rodent anaesthesia. Topics covered include gaseous and injectable anaesthesia; pre-anaesthetic assessment, monitoring and assessment of anaesthetic depth, and OHS issues associated with anaesthesia. All participants have the opportunity to obtain "hands-on" experience with the basic techniques. Includes an online learning component.

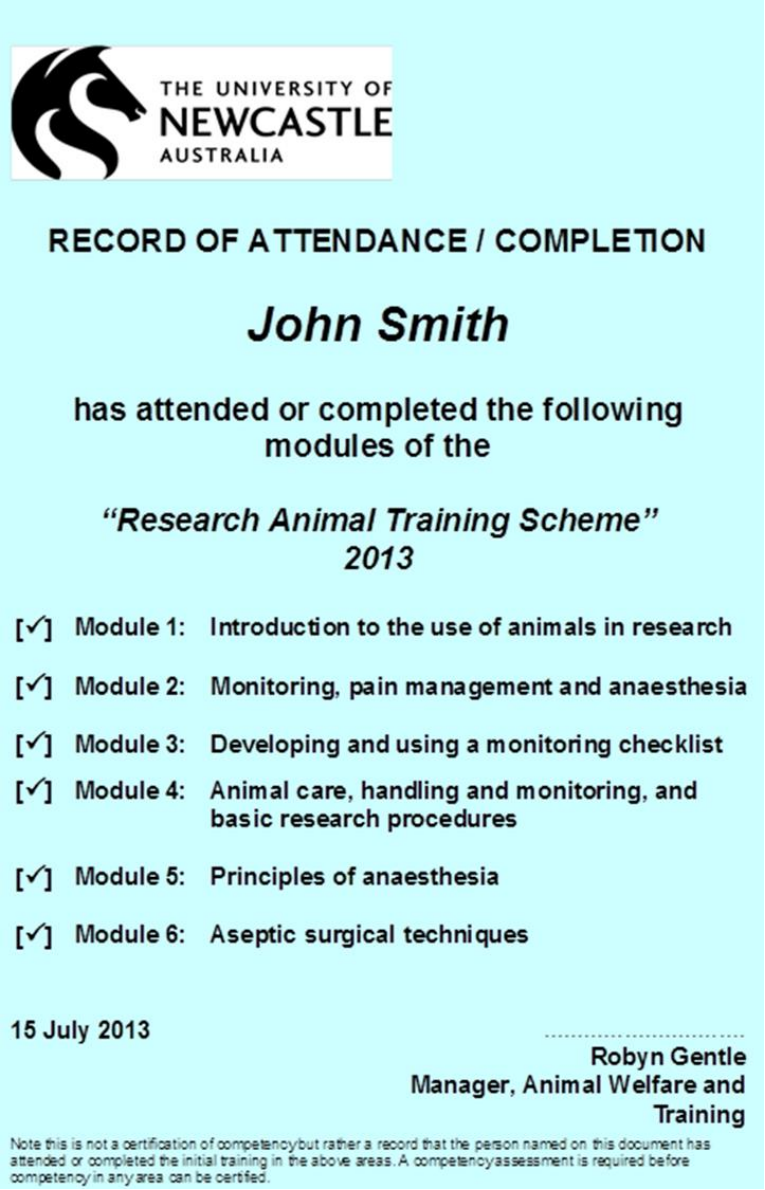
Module 6- 'Surgery and aseptic surgical techniques'. A practical session for personnel who will be performing surgery on research animals. Areas covered include instrument identification and use, aseptic technique, preparation of the environment, surgeon, instruments and animal, making incisions, handling tissues, haemostasis, choosing needles and suture material, suturing techniques. Includes an online learning component.

Module 7- 'Applications to an animal ethics committee'. A tutorial covering the composition and operation of the University of Newcastle Animal Care and Ethics Committee (ACEC), the principles underlying the questions on the application form and completion of an application to the ACEC . This session includes role playing by the participants as an ACEC where participants act as one of the membership categories and assess "Mock" ACEC applications. Includes an online learning component.

Assesments: All modules have an associated online quiz in which participants must achieve 100% correct to have completed the module. Completion of a RATS module does **not** indicate competency in that area. The RATS program modules offer an introduction to techniques used in animal research. Participants are then expected to undergo further supervised training in the laboratory and can request a formal competency assessment when they feel ready.

Additional training options are available. Animal Services Unit staff undertake, as a minimum, Certificate III in Animal Technology through an external service provider, most animal service staff, some ACEC members and some researchers are enrolled in the ANZLAA/ AALAS learning library scheme in 2013 and are self-pacing their learning through this option.

Prior training and experience is recognised but is not considered a guarantee of competency. A competency assessment may be requested without prior attendance at the RATS program. If a lack of competency is identified through assessment additional training is provided.



THE UNIVERSITY OF NEWCASTLE AUSTRALIA

RECORD OF ATTENDANCE / COMPLETION

John Smith

has attended or completed the following modules of the

"Research Animal Training Scheme" 2013

[✓] Module 1: Introduction to the use of animals in research

[✓] Module 2: Monitoring, pain management and anaesthesia

[✓] Module 3: Developing and using a monitoring checklist

[✓] Module 4: Animal care, handling and monitoring, and basic research procedures

[✓] Module 5: Principles of anaesthesia

[✓] Module 6: Aseptic surgical techniques

15 July 2013

.....

Robyn Gentle
Manager, Animal Welfare and Training

Note this is not a certification of competency but rather a record that the person named on this document has attended or completed the initial training in the above areas. A competency assessment is required before competency in any area can be certified.

Fig. 3. RATS Certifications in online application form.

Assessment of Competency.

Competency assessments are carried out by the AWTU. Assessors have a Certificate IV in Assessment and Workplace Training. Competency assessment may be ordered by the ACEC or requested by animal research personnel.

Assessment tools are developed on an 'as needed' basis. It is important to define the procedure is being assessed, to divide this procedure into elements of competency, and to set performance criteria for each element. The primary assessment tool used is the "Observation Guide" (appendix I). The observation guide clearly sets out the elements of competency and performance criteria and is used during the assessment process.

A copy of the completed observation guide is provided to the assessed personnel. Where the ACEC has ordered a competency assessment it receives a report on the assessment and a copy of the completed observation guide. This assists ACEC to make an informed decision when

approving personnel as competent to carry out particular procedures.

Ongoing Issues.

Training and competency assessments require significant resources in terms of personnel and funding. The AWTU at University of Newcastle currently consists of one full time person plus a casual staff member working, on average, one day per week. With the other duties of the unit this is sufficient only to run the formal training program modules twice each year with very limited competency assessment. Competency assessment for all research personnel in all basic techniques would require a significant increase in resource commitment in this area.

Training is not compulsory and there is no requirement update training and knowledge. The ACEC asks that all animal research personnel undertake at least the two online RATS modules however this is not currently enforced.

To be effective animal research personnel must embrace the training and competency assessment process. This can be difficult when research personnel are often suspicious of the animal ethics approval process, concerned by inspections and affronted if their competency is questioned. An ACEC and institution need to establish and maintain an environment where researchers and animal care staff do not feel threatened by the animal ethics approval process, understand the advantages of ethical animal research and are happy to seek assistance when necessary. At University of Newcastle this has been a gradual and ongoing process. Much effort has been invested over the past years into fostering a cooperative attitude where animal research personnel, the AWTU and the ACEC work in unison to improve animal welfare outcomes. I believe we are making progress!

Appendix I Example of an Observation Guide used in competency assessment.

Research Animal Training Scheme
Module 4- Animal Handling and Basic Research Procedures.

Observation Guide- Administration of Substances by injection.

This observation guide will be used by your assessor to gather evidence that you have gained sufficient skills and knowledge to be considered competent in the administration of substances to animals.

Competencies

This guide gathers evidence for the following elements of competency:

1. Select animal
2. Catch and restrain animal
3. Administer substance by injection
4. Return animal to housing
5. Monitor animal
6. Record details of injection

Assessment Details

Name of candidate:

Name of assessor:

Venue for assessment:

Date of assessment:

Description of Assessment Activity

The candidate will administer a substance to an animal. .

Administration of substances will be performed as part of a research protocol that has approval from the Animal Care and Ethics Committee; hence the substance to be administered and the route of administration, will be determined by the approved protocol.

Administration of substances will be expected to be carried out in accordance with any Animal Care and Ethics Committee approved Standard Operating Procedures covering the substance and/ or route used.

Species Substance Route of Administration

Critical Aspects of the activity

Animal welfare obligations and the requirements of the Animal Research Act and Work Health and Safety legislation mean that the assessment will be halted if:

- The animal is put at risk of harm
- If the candidate or assessor are likely to be exposed to harmful conditions.

Resources Required

The following resources are required. These will generally be supplied by the candidate when the handling/ restraint is performed is part of an approved research protocol. If the handling and restraint are carried out under an ACEC approved training protocol, the resources may be provided by the trainer/ assessor:

- **Animal-** housed in appropriate caging/ pen/ yard for the species.
- **Species specific handling/ restraint equipment.**
- **Personal Protective Equipment-** gown, gloves, mask, goggles and footwear as required.
- **Substance to be administered**
- **Antiseptic-** eg Chlorhexidine in 70% ethanol,
- **Syringe**
- **Hypodermic needle**
- **Monitoring records**.
- **Pen**

The candidate should contact the assessor well before the assessment date if there are any others items they require for the assessment.

Observation Guide: Administration of substance by injection

Element of Competency	Performance Criteria	Observed/ discussed	Comments
Select animal	□ Animal Identification is checked □ Records are checked to confirm that the correct animal has been selected. □ Correct animal located in cage/pen/yard		
Catch and restrain animal	□ Animal is caught in a manner that minimises stress to the animal and the chance of injury to the handler. □ Animal is correctly restrained in a manner that minimises stress to the animal and the chance of injury to the handler. □ Animal is correctly restrained for the procedure to be carried out.		
Administer substance by injection	□ Calculate correct dose to be administered □ Correctly assemble syringe and needle with attention to safety □ Draw up drug with attention to aseptic technique and accuracy of dose □ Correctly identify the landmarks for the route of injection □ Handle syringe and needle correctly □ Perform injection with attention to the safety of the animal and the operator. □ Correctly dispose of the syringe and needle.		
Return animal to housing	□ Animal is safely and correctly returned to cage/ pen/ yard		

 Access to food and water is confirmed

 Integrity of identification cards/labels is checked.

Monitor animal

 Animal is monitored after return for any adverse effects.

 Monitoring records are correctly completed.

Record details of injection

 Written records are correctly completed.

General comments and feedback to the candidate:

Assessment decision: Competent ❑ Not Yet Competent ❑

Agreed further actions:

This document is an accurate record of the assessment procedure:

Assessor: Signed:…… Date:……

Candidate: Signed:…… Date:……

Comparison Between Rounds of External Triennial Reviews of AEC's

Deb Kelly
Manager, Animal Welfare Department of Environment, Water and Natural Resources, South Australia

The 7th edition of the *Australian Code of Practice for the Use of Animals for Scientific Purposes* (the Code) recommends that all animal ethics committees undergo an external review every three years. This recommendation has been implemented in South Australia since 2006. By 2012, all ten animal ethics committees (AEC's) and their institutions had undergone two external reviews.

The reviews were undertaken in accordance with the *Guidelines for the Review of Animal Ethics Committees and their Institutions* which was initially developed as a South Australian document and subsequently modified with a view to it potentially being applicable nationally. AEC's and their institutions were reviewed against the requirements of the Code rather than the legal requirements for undertaking research and teaching using animals in South Australia. The legal requirements differ in some respects to the Code – for example, fish are not protected by the *Animal Welfare Act 1985* so there is no head of power to enforce the Code provisions relating to fish. Conversely, in South Australia, animal ethics committees are required to have a "Category E" member who is responsible for the day to day care of animals whereas this is a recommendation, not a requirement of the Code.

Undertaking the reviews requires a significant effort on the part of the institutions, Government and the Review Panel. Therefore, it is sensible to maximise the value of the process. By reviewing against the Code rather than the legislation, value is enhanced in the following ways:

- Many funding bodies require evidence of compliance with the Code to accompany funding applications. The External Review Reports can be used for this purpose rather than undertaking a separate verification process or review;
- The Code is more specific than the legislation so its use results in more tailored recommendations;
- Legislation is the minimum standard. One of the aims of the reviews is to encourage best practice so the Code is a more appropriate tool.

A summary of the findings of the External Review Panel over those two rounds of review was prepared and provided to the AEC's. In addition, each AEC was provided with a summary of the findings of their first review and their second. This allowed the committees to clearly see the areas of improvement, areas which required further attention and to benchmark their performance against the other South Australian AEC's. It also provides a mechanism for them to see the broad areas in which other committees excel or struggle. It is worth noting that all the recommendations of the Review Panel have been implemented or are in the process of being implemented.

This paper provides a summary of the findings of those first two rounds of external reviews. Although it directly relates to the South Australian AEC's, the strengths and weaknesses and improvements made have national application.

Introduction

The 7th edition of the *Australian Code of Practice for the Use of Animals for Scientific Purposes* (the Code) recommends that all animal ethics committees undergo an external review every three years. This recommendation has been implemented in South Australia since 2006. By 2012, all ten animal ethics committees (AEC's) and their institutions had undergone two external reviews.

The reviews were undertaken in accordance with the *Guidelines for the Review of Animal Ethics Committees and their Institutions* which was initially developed as a South Australian document then later modified with a view to potentially applying it nationally in conjunction with the 8th edition of the Code. The AEC's and their institutions were reviewed against the requirements of the Code rather than the legal requirements for undertaking research and teaching using animals in South Australia. The legal requirements differ in some respects to the Code – for example, fish are not protected by the South Australian *Animal Welfare Act 1985* so there is no head of power to enforce the Code provisions relating to fish. Conversely, in South Australia, animal ethics committees are required to have a "Category E" member who is responsible for the day to day care of animals whereas this is a recommendation, not a requirement of the Code.

Undertaking the reviews requires a significant effort on the part of the institutions, Government and the Review Panel. Reviews are undertaken by a team of four people and can take up to a week to conduct. The panel reflects the composition of an animal ethics committee and includes a person from interstate to ensure independence. The review includes:

- Examination of the paperwork (operating procedures, terms of reference, minutes of meetings since the previous review etc)
- In depth examination of half a dozen protocols chosen at random. These are followed through:
    - the initial application,
    - reports and communication with the committee,
    - annual reports
    - adverse event notifications
    - interviewing the principle researcher
    - if possible, seeing the research or teaching and animals involved in the protocol
    - examining clinical and research records derived from the animal use.

Given the work involved for both the review team and the animal ethics committee, it is sensible to maximise the value of the process. By reviewing against the Code rather than the legislation value is enhanced in the following ways:

- Many funding bodies require evidence of compliance with the Code to accompany funding applications. The External Review Reports can be used for this purpose rather than undertaking a separate verification process or review;
- The Code is more specific than the legislation so its use results in more tailored recommendations;
- Legislation is the minimum standard. One of the aims of the reviews is to encourage best practice so the Code is a more appropriate tool.

At the conclusion of each review, a draft report is prepared and provided to the Chair of the animal ethics committee concerned for comment. This is to ensure that the review team did not misconstrue anything, or make an error of fact. Once the Chair has provided comment, the report is finalised and submitted to the licence holder.

A summary of the findings of the External Review Panel over those two rounds of review was prepared and provided to the AEC's. In addition, each AEC was provided with a comparison of the findings of their first review and their second. This allowed the committees to clearly see the areas of improvement, areas which required further attention and to benchmark their performance against the other South Australian AEC's. It also provides a mechanism for them to see the broad areas in which other committees excel or struggle.

This paper provides a summary of the most significant findings of those first two rounds of external reviews. Although it directly relates to the South Australian AEC's, the strengths and weaknesses and improvements may have national application.

The conduct of the reviews

Each of the AEC's and the institutions were cooperative, welcoming and supportive in the conduct of the reviews. This assistance included:

- Making local arrangements such as provision of a meeting room;
- Collation and provision of paperwork prior to the review;
- Organising meetings with researchers, teachers, senior personnel within the institution and members of the AEC;
- Organising site visits including inspections of animal housing facilities;
- Access to AEC files and records;
- Welcoming Panel members to the AEC meeting and allowing them to observe the meeting;

Without this level of support, the reviews could not have been undertaken. In particular, the Executive Officers of each of the AEC's provided exceptional assistance.

The dedication of the members of External Review Panel should also be acknowledged. The process is time consuming and hard work. Every person invited to join a Panel has accepted, worked collaboratively with other Panel members, and made a significant contribution. Their commitment made the system work.

Review Administration

Without exception, the Chairs, Executive Officers, Animal care staff and research and teaching personnel were helpful and courteous to the Review Panel. Initially, nobody knew quite what we were doing – there was no established process. Therefore the first couple of reviews were rather haphazard and not as organised as they should have been. By the second round, the process was established and the system was far more efficient. The Guide to External Reviews greatly assisted in ensuring that everyone knew what they had to do and when it had to be finished. In both rounds, all of those interviewed were genuinely interested and seeking to improve. An overall pride was evident in all those involved.

The Animal Ethics Committee - membership and procedures

All AEC members were invited to address the Review Panel either individually or as a group. In all cases the members interviewed were supportive of their AEC and the processes undertaken. They felt they were valued and that the committee listened to their concerns and opinions.

Many of the committees required additional members to provide flexibility. In-quorate meetings were very rare but sometimes meetings were deferred due to the inability of a member to attend. Although most AEC's said that it was difficult to find lay members, researchers and animal care personnel were equally in demand. The Review panel suggested to several committees that an annual meeting schedule be produced so members of the AEC and applicants would be aware of meeting dates well in advance. Those AEC's which had a statistician as a member found their input extremely useful.

During the first round it was noted that, in some cases, administrative procedures and information management systems had evolved rather than had been developed and consequently were just coping. These systems were more efficient by the second round. In the first round, many of the committees lacked comprehensive terms of reference. It was recommended by the review panel that the terms of reference address confidentiality, roles and responsibilities, executive role, dispute resolution, subcommittees and suspension or removal of approval. By the second round, these issues had been largely addressed.

AEC meetings were always inclusive, professional and frank discussions. Participation from all categories of membership was actively sought by the Chair. Members clearly dedicated considerable time to preparing for meetings. This highlighted the importance of giving advance meeting dates and providing agenda papers in plenty of time to allow members to prepare.

There was initial confusion over the role of the Executive with some committees not establishing or using an Executive effectively and others giving the Executive powers beyond those envisaged by the Code.

The Animal Ethics Committee – consideration and approval of applications

Some committees tended to focus on the animal impact of applications more than the ethical basis of the work or the 3 R's. Similarly, researchers tended to focus on procedures rather than justification of animal use. Most committees had an appropriate focus on animal welfare impacts but some focussed more on the scientific value of the work. The review panel was not critical of committees and applicants considering these issues but felt that the focus should be slightly moved.

While most applications were considered thoroughly and on their merits, on some occasions there was a tendency to approve something because it was similar to a project already approved by the committee, or to "bulk approve" protocols without individual consideration.

Category B members who were involved in a project under consideration by the committee often took part in discussion relating to that project. Often this was helpful – it was almost interviewing the researcher, but sometimes the roles of interviewee and committee member became blurred and the researcher became part of the decision making process.

Many researchers had developed their own standard operating procedure to undertake their work in a consistent manner. These were often very good. It was recommended that the committees formally consider and adopt them.

Teaching protocols tended to be considered at the beginning of the academic year and approved for twelve months. This resulted in the first meeting being extremely full and placing excessive pressure on committee members. If an application were not approved, a whole course would

have to be cancelled or modified on little or no notice. It was recommended that approval be given for eighteen months so next year the pressure is removed and members can seek clarification, modification etc and the applications can be spread over several meetings.

Communication

In all cases communication was adequate and usually it was very good. Each of the AEC's had good communication with senior management of the institutions and were committees of standing. Researchers and teachers were, without exception proud of their work and extremely willing to explain it to the review panel. Although the committees are busy, it would benefit both sides if time could be allocated for applicants to give occasional presentations on their work to the AEC.

Some school teachers had little understanding of the role of the AEC and considered it a rather bureaucratic burden. This is difficult to address but the committees are trying to improve their perception by providing useful resources and become an asset not merely a legal necessity.

Applications which were considered by two or more committees require those committees to share any conditions they have imposed and to ensure that the conditions are not contradictory. This does not always occur. The whole issue of multiple approvals is currently under discussion in South Australia.

Monitoring and site visits

Overall, the AEC's of institutions which have animal houses and/or research or teaching facilities do monitor the housing, care and use of animals well. This incorporates regular site inspections. However, it isn't as easy when animals are used in numerous locations, such as schools or in remote locations, as occurs in field studies. This was problematic in both rounds of external review; however by the end of the second round, more committees were using photos, videos, phone interviews, meetings at different locations and other mechanisms to undertake some level of monitoring.

In most cases, issues noted during site inspections were followed up by the committees and corrected by animal house management. By the second round, this system had become more formalised with improved records and reporting arrangements and more frequent site visits. A recurrent weakness found was that although the site inspections were undertaken, there was no reference them in the minutes of meetings.

It is worth mentioning that the review team visited the Royal Show to inspect school exhibits. The comment made in the review report was:

"The standard of animal preparation and the unbridled enthusiasm of the students was a rewarding experience. This component of animal use in schools is a key demonstration of the value of managing student involvement with the animals. The panel strongly recommends that the AEC should spend time reviewing the Show exhibits of school animals as it is the clear end-point of many applications it approves and a visit would sponsor substantial face to face meeting with the enthusiastic teachers and students."

This provided the panel with a first-hand view of the importance of animals in schools. The school focus person plays a crucial role in ensuring the welfare or animals and the educational outcomes in schools.

Administration of the Animal Ethics Committees

Without exception, the review team considered that the executive officers of the committees were doing an exceptional job. In many cases, the executive officer would have benefited by additional administrative support and in some cases, because systems had evolved rather than being developed, there was some inefficiency. Where these were pointed out by the panel, steps have been taken to rectify the situation. Of some concern is that the workload on the executive officers and the committees themselves is continually increasing to the point where it may not be sustainable. The Review Panel recommended a "pre-committee" screening process to reduce the workload and to minimise delays in approval. Many of the committees had developed standard operating procedures which could be referenced in the applications they received and they also had procedural guidelines on how the committee itself operates. These processes reduce the workload. It was recommended that these be shared between committees. Mechanisms to reduce workloads are now being investigated on a state-wide basis in an effort to streamline processes.

Modifications to existing approvals were sometimes confusing. A project may have been approved several years ago and the committee membership may have changed in the meantime. Researchers and teachers, who are intimately familiar with the original application, assume that the committee will be as well so the modification is written on the assumption that the context will be obvious to them. This isn't always the case. This can be addressed by providing members with the original application (or at least the lay summary) with the modification application. The standard of the minutes of meetings improved dramatically between the first and second round of reviews. In some cases, although the decision of the committee was recorded, there was no record of the discussions or considerations which led to that decision.

Reporting to, and by, the Animal Ethics Committee

In most cases, annual reports were received by the AEC's. The manner in which they were managed varied according to the number of reports and the timing of their submission. In some cases all reports were due on a single date resulting in a huge amount of paperwork for the committee to consider. In some cases, this was divided between members who gave a brief verbal summary of the reports allocated to them, in some the committee was advised that the annual reports were received but they were not distributed and in others the reports were provided to all members and discussed in detail by the committee as a whole. If annual reports were staggered (for example due a years after the application was approved) committees were more likely to consider them in detail. The review panel considered that it was important that the annual reports were considered by the committee and that their deliberations were minuted.

The reporting of unexpected adverse events was generally timely and comprehensive. The management of such events, both by researchers and the animal ethics committees improved between the first and second round of reviews. There was an interesting inconsistency, where on one hand a researcher reported any deaths in a wild population, not impacted by the research, as unexpected adverse events; while on the other hand, another researcher did not report predation on lambs as an adverse event because any sheep farmer would expect it. The review panel stressed that if deaths are predicted in the application, those deaths are not unexpected to the

committee but, if they are not included in the application, they are unexpected so must be reported.

All the committees submitted annual reports to the Minister as required by legislation. The Code requires an annual internal review of the AEC itself. In some cases, this did not occur, in others it was done, and recorded, exceptionally well.

Competency and Training

In general, there was a lack of training for new members of animal ethics committees and no clear induction process. In contrast, over the two rounds of reviews, the training of researchers and teachers increased markedly. The panel noted that most committees now require researchers and teachers to attend animal ethics training days every few years. In addition, some committees have instituted skills training days and familiarisation with animal house facilities, capabilities and expectations.

In most cases, applicants did list their qualifications and experience in their application but often this did not necessarily relate to the tasks being undertaken. For example, a person with half a dozen PhD's may not know how to bleed a mouse properly, or anaesthetise an animal. This should either be stated in the application or lodged in a skill register held by the committee. Without exception, animal house staff were well trained and competent or were working under the supervision of a competent person.

Applications to the committee

There is a huge variety of the work being undertaken, so comments in relation to applications were specific to that application and difficult to generalise. It was pleasing that the recommendations of the review panel from the first round, relating to both the application form and the applications themselves, had been largely implemented by the second round and that the overall quality of applications had improved considerably. Many researchers still struggle to describe their work in lay terms. This would be assisted by the use of flow charts.

Some teaching protocols had been repeated annually with little justification in terms of educational outcomes.

Between the first and second round, there were two major changes in the animal ethics system in South Australia. The first was the adoption of the NSW system for ethics approval and oversight in schools and the second was the development of common application forms which would be accepted by most of the AEC's. These changes contributed to the overall improvement seen.

A few applications failed to specify the fate of animals when the project was complete. Similarly, in some cases, breeding projects provided minimal detail and it was difficult to define a point in time when the projects changed from being a breeding protocol to research protocol. Most of the committees require phenotype reports for breeding colonies. These are very useful.

Approvals

The largest single issue was clarity in approvals. Some committees approved work "subject to additional information being received", Others gave "provisional approval". Terms such as these make it unclear to researchers if the approval has been given or not. It was recommended that all applications receive one of four responses:

- APPROVED (with or without conditions)
- APPROVED (with or without conditions). The AEC would appreciate further advice on the following …
- CONSIDERED and will be approved subject to the Executive being satisfied with your response to the following issues … (with or without conditions)
- NOT APPROVED resubmit after addressing the following issues …

All approvals must specify start and finish dates, the species and number of animals which can be used and any conditions imposed. The applicant should be advised of the outcome of the application as quickly as possible.

Animal facilities and record keeping

In general, clinical record sheets were specific to the work being undertaken and had a good system of assessing the animals and deciding when intervention was required. Often these were completed by exception – i.e. if everything was fine, no record was made. The review panel recommended that there should at least be a sign off point to show that the animals were checked. The clinical records must be kept with the animals so anyone who checks them can record their findings and should include any interventions such as anaesthetic monitoring, drug administration and anything else which happens to them. Euthanasia should also be recorded, including the method used and the person undertaking the procedure.

Standard operating procedures are frequently used for routine management tasks (such as cleaning, feeding and general maintenance) and for research procedures (such as bleeding, euthanasia etc). These were often very good. Institutions would benefit by sharing their procedures and building on each other's work.

On some occasions, animals were returned to a general flock at the end of the protocol. There should be a mechanism to ensure that these animals are not used repeatedly (for example for a practical class handling the animals). Recording of ear tags would address this issue. A relatively common finding in the first round was that neither the animal ethics committee nor the person undertaking the research or teaching using privately owned animals gave them the same level of scrutiny as they would if they had been owned by the institution. It was assumed that the owners would oversee the use of their animals. This was corrected as soon as it was highlighted.

The review panel visited dozens of animal holding facilities including schools and satellite research stations. By far the majority in good condition and very well managed. Some needed money spent on them, but through good management, this did not result in animal welfare issues. Virtually all indoor facilities had excellent temperature and humidity monitoring, control and recording systems and suitable lighting regimes. On one occasion, this system had failed so the backup split system air conditioner set up was being used and working well. There were individual situations which the panel considered required address:

- A livestock facility lacked scales, a race and a crush which imposed a risk to humans and animals
- One piggery had old style stalls which required updating

- One facility lacked step over barriers to enter rooms
- One facility used tape to seal rodent lids to their cages. These required replacing
- One facility used wire floor cages for mice which required replacement or justification.

On the first round, several facilities were using low top rat housing. On the recommendation of the panel, these were replaced by high tops by the time the second round was undertaken.

All facilities had appropriate security commensurate with the type of work being undertaken and the likelihood of theft or interference. All but one had an emergency alarm system which would alert senior management if something was wrong. The panel recommended that this be instituted.

Animal housing was generally extremely good and well maintained. At two sites, the panel considered that animals were overcrowded; on one occasion the panel considered that the sheep off shears and new born lambs should have more shelter; and in one case the pen floor was wet and conducive to foot problems. On several occasions, cage labels did not include an AEC approval number and in one case there was no emergency contact listed. These issues were all addressed.

Food and water provision met the needs of the animals. In one yard, hay was fed from the ground rather than in a feeder; in another, the hay was mouldy; and in a third the water had been knocked over. These issues too have been addressed.

By far the majority of facilities had excellent record systems. This applied to breeding, research and teaching animals. It was clear that there is good communication between researchers/teachers, animal care staff, the animal welfare officer (if there is one) and the animal ethics committee. In some cases, this could be as simple as a white board in the shed or as complex as a computerised integrated system – but in all cases it was appropriate for the facility, purpose and animals involved. The panel was particularly complimentary about a "counting down to zero" system for monitoring the use of allocated animals.

Isolated criticisms were:

- Documentation of specific procedures for the acquisition quarantine and health status of animals being introduced into the facility should be completed
- researchers should be have their own record system to track animal use rather than depending on animal house staff to provide this information.
- A yearly planner of animal use would assist in preparing and conducting a cycle of animal care
- Research animals were identified by red ear tag, with no additional identification labels or information provided with the animal.
- "Better practice" would involve the keeping of separate species records for animals.
- A lack of cleaning records
- Poor records of mortalities and fecundity in a breeding colony
- Very specific records on the science of the project but observations on behaviour and welfare were not as impressive.
- Researchers failed to supply animal care staff with updated numbers of animals used in order to keep accurate records.
- A lack of a record system of the allocation animals to projects

Most facilities had environmental enrichment to varying degrees, particularly in the second round. This varied from rotating toys, providing floor pens or exercise time for rabbits, hides and

furniture in cages and AEC policies restricting the time animal could be retained in metabolic cages. However, this was highly variable. Overall, environmental enrichment is an area of animal housing which could be improved.

The health, care and husbandry of animals was good or excellent in all but one of the sites visited. On this one occasion, sheep kept in a remote site were scouring and in need of veterinary attention. The delineation of responsibilities between animal care staff and teachers and researchers was the underlying cause of this issue. There needs to be a clear chain of responsibility for animals particularly those held in sites other than the central animal facility.

Summary – the highlights and the low lights of the first two rounds of reviews

Many things were learned by everyone involved in the first two rounds of the external reviews. The core members of the panel agree that the highlights of the first two rounds were:

- There is an incredible diversity of work being undertaken providing significant benefits to people and animals.
- The overall pride of animal managers, researchers and teachers and their willingness to share information was impressive.
- The committees are really trying to abide by the Code and to ensure animal welfare.
- All the recommendations of the reviews have been, or are in the process of being, adopted.
- The AECs have dramatically increased their emphasis on training of researchers in animal ethics and appropriate experimental techniques.
- Most of the committees have very good communication with researchers. A number of Executive Officers in particular are excellent in this regard.
- The external review process has brought uniformity and enhanced communication across all South Australian committees.

Of course there are areas which still require addressing, namely:

- Monitoring of remote and multiple sites is problematic and most committees have not found a mechanism to manage this every time it comes up.
- The workload is increasing and in some cases is unsustainable.
- Teaching and research records are well maintained, but in many cases day to day clinical monitoring records are not.
- The standard of applications is improving but there is room for further improvement particularly in lay summaries and addressing the 3R's.
- There is a lack of adequate resources for AECs and animal welfare secretariats in many institutions.
- AEC's need to give clear consideration of potential impact on animals and how this can be best managed.
- Lack of clarity in when and if an application is approved.
- Understanding of what constitutes an unexpected adverse event.

Acknowledgement

I would like to acknowledge the cooperation and hospitality of all the institutions, their staff, researchers and teachers and the animal ethics committees during the external reviews. Although the process is hard work, you made it a pleasure and very rewarding. I would also like to thank everyone who was a member of a review panel team but particularly our "core" members, Mary Barton, Brigitt Hines and of course our review panel chair, Peter Penson. We couldn't have done it without you – thank you team!

Imaging of small animals for research: Implications for animal welfare.

Carl Power
Biological Resources Imaging Lab, Mark Wainwright Analytical Centre, University of New South Wales

In the last decade imaging of research animals has become a standard practice in many animal research facilities to support preclinical research. Imaging modalities for preclinical research include MRI, PET, SPECT, CT, ultrasound, bioluminescence and fluorescence imaging and intravital microscopy. These systems have the capacity to dramatically improve our ability to assess experimental outcomes by providing not only a means to visualize but also to quantify structural properties and physiological, metabolic and molecular processes in living animals. Concomitant with these experimental benefits, the technologies collectively grouped under imaging have great potential to facilitate improved welfare of research animals. Imaging technology has significant positive potential for the three R's of animal research by providing a means to reduce the number of animals used in experiments, reduce the impact of experimental interventions on animals and potentially provide an alternative to animal research. However, animal imaging procedures *per se* are not without impact on the animal and these influences must be balanced against the potential benefits to both the research and animals' wellbeing. The animal welfare benefits of imaging are not inherent to the instrumentation, but must be realised through careful experimental planning. Knowledge of each imaging modality, its capabilities and limitations is thus a necessity not only for ensuring optimal research results but also to capitalize on the potential benefits for animal welfare.

No manuscript was provided by the authors for this presentation

The animal welfare and scientific advantages of Large Animal imaging technologies - a happy Rs win.

Tim Kuchel & Raj Perumal
SAHMRI- South Australian Health and Medical Research Institute
Preclinical, Imaging and Research Laboratories (PIRL)

There is general acceptance that animals are still central to the conduct of experiments to expand/extend our understanding of biology and potential human (and animal) therapies. However, we must remain ever vigilant to the express need to respond to the 3Rs principle so that we can continue to act upon the privileged mandate we are given regarding the use of animals in science.

The relatively rapid adoption of imaging technologies in small animal research has not been matched until relatively recently in the 'large animal models of human disease' arena.

The National Imaging Facility (NIF), administered out of UQ and funded by a series of Federal and State Government research infrastructure strategies, is making available a whole suite of small and large animal imaging modalities to the research community in Australia. NIF has helped fund the Large Animal Research & Imaging Facility (LARIF), now administered by SAHMRI, to bring dedicated modern equipment to large animal users. This avoids sneaking sheep and pigs into human hospitals after hours, and allows for better experimental designs to be contemplated.

This presentation will demonstrate some examples of the new ability to track the progression of disease (using the same animal), track the healing process under study (using the same animal) and how new important scientific questions can be constructed and asked.

Whilst there is an obvious opportunity to replace serial humane killing of animals to enable histopathology to be used to describe a disease process, there is an important improvement in the quality of the science available to us.

An added benefit of using clinically available imaging technologies is the fact that the translation of the data or insight to the clinical environment is enhanced. Clinically relevant questions are more easily asked, and answers found.

The funding environment in which expensive imaging equipment finds itself is a challenge. There are cost recovery models which we all need to follow, and funding bodies need to understand what the real cost is to provide a comprehensive imaging service. Highly skilled staff need to drive these machines to extract their full capacity, and access to data files and post-acquisition data analysis must both be dialled into the service.

Large Animal imaging has opened up new opportunities to improve Animal Welfare by attending to two of the 3Rs, and imaging can also enhance the sophistication of the scientific approach adopted.

No manuscript was provided by the authors for this presentation

Dealing with Deviations from the Approved Protocol

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Monitoring of research is becoming an increasing priority for those involved in setting the goal posts for research practice, from regulators, to funding bodies, and to the institutions themselves. As a result, incidents where deviations from the protocol approved by an Animal Ethics Committee are reported are likely to become more frequent, at least until awareness has been raised through professional development. The Australian code of practice for the care and use of animals for scientific purposes is quite clear in stating that institutions and their AECs need to have in place written procedures to deal with non-compliance in a fair and effective manner. At the same time institutions in Australia are obliged to comply with the Australian Code for the Responsible Conduct of Research that recognises that activities non-compliant with the conditions of the AEC, in particular if the result involves serious harm to animals, are potential research misconduct. It also provides the framework for dealing with breaches and research misconduct, in particular by prescribing that institutions nominate a Designated Person who conducts an initial investigation whether a *prima facie* case of research misconduct exists. Who then deals with allegations of breaches and research misconduct? Is there one process for all research, regardless whether it involves humans, animals or poetry? Do we end up with the possibility of multiple investigations and therefore multiple findings? Do we treat research involving animals differently by developing separate procedures? Who should collect evidence and report it to whom? Who are the experts in deciding that there may have been a breach as opposed to research misconduct? Who decides on when an experiment needs to be stopped and what the appropriate preventative measures are? These are some of the questions that need to be considered at a time when institutions are working through the complex web of interactions among multiple parties to develop research misconduct procedures. This presentation will outline the pathways in light of the relevant legislation and codes and identify possible roles for the Designated Person, the Animal Ethics Committee, the Animal Welfare Officer and Animal Facility Managers.

Why do we need to talk about deviations:

Monitoring of research is becoming an increasing priority for those involved in setting the goal posts for standards of research practice, from regulators, to funding bodies, and to the institutions themselves. As a result, incidents where deviations from the protocol approved by an Animal Ethics Committee (AEC) are reported are likely to become more frequent, at least until awareness of standards has been raised through professional development. The *Australian code of practice for the care and use of animals for scientific purposes* [1] (Code of practice) is quite clear in stating that institutions and their AECs need to have in place written procedures to deal with non-compliance in a fair and effective manner. At the same time institutions in Australia are obliged to comply with the *Australian Code for the Responsible Conduct of Research* (Code of

[1] At the time of the presentation the 7th Edition of this publication was the current version. Since then the National Health and Medical Research Council has released the 8th Edition. The references to the 7th edition are still valid and do not change the roles or responsibilities as outlined in this paper.

conduct) that recognises that activities non-compliant with the conditions of the AEC, in particular if the result involves serious harm to animals, are potential research misconduct. It also provides the framework for dealing with breaches and research misconduct, in particular by prescribing that institutions nominate a Designated Person who conducts an initial investigation into whether a *prima facie* case of research misconduct exists.

Consequently there are multiple roles that need to be aligned and defined to ensure a sound, fair and efficient investigation is conducted where appropriate. A number of questions need to be considered, including: Who deals with allegations of breaches and research misconduct? Is there one process for all research, regardless whether it involves humans, animals or poetry? Do we end up with the possibility of multiple investigations and therefore multiple and potentially different findings? Do we treat research involving animals differently by developing separate procedures? Who should collect evidence and report it to whom? Who are the experts in deciding that there may have been a breach as opposed to research misconduct? Who decides on when an experiment needs to be stopped and what the appropriate preventative measures are? These are some of the questions that need to be considered at a time when institutions are working through the complex web of interactions among multiple parties to develop research misconduct procedures. This paper outlines the potential pathways in light of the relevant legislation and codes and identifies possible roles for the Designated Person, the Animal Ethics Committee, the Animal Welfare Officer and Animal Facility Managers.

What are the institution's responsibilities and expectations?

The Institution and individual members involved in managing animal welfare and animal research have a responsibility to ensure that the standards of care, as outlined in the Code of practice and the Code of Conduct, are maintained. One measure that institutions implement (as outlined above) is to monitor the activities of research involving animals to ensure compliance with the institutional published standards and the AEC-approved animal research protocols. There are some important definitions we need to consider on this topic. The Code of practice defines monitoring as:

> "…measures undertaken to assess the wellbeing of animals in accordance with the Code [of practice]. This occurs at different levels. For example, at the level of the researcher and animal facility manager, monitoring is undertaken to assess the wellbeing of animals that are used and cared for, and at the level of the AEC, monitoring is undertaken to assess the adequacy of standards of animal care and use."[2]

This short paragraph already identifies three parties involved in the monitoring process. Researchers monitor their animals and may need to report on adverse events. Animal facility managers monitor animals in their facility and may need to raise awareness on animal welfare issues, often urgently. The AEC itself monitors facilities and animal care, both the researchers and the facilities, and may need to inform the institution it reports to if care is found wanting. Across an institution there are various levels of monitoring and thus multiple opportunities to identify and address practices or processes that may compromise animal welfare and fall below accepted standards of care and use of animals. The three parties highlighted above may have different levels of responsibility and functions when it comes to dealing with animal welfare issues. How and to whom do these three parties report instances of suspected breach or research misconduct involving animals in research?

[2] National Health and Medical Research Council (2004), Australian code of practice for the care and use of animals for scientific purposes, 7th edition. Canberra: National Health and Medical Research Council p 4

Standards of research conduct, deviations from standards and institutional responsibility

The standards of research, and for research involving animals the standards of care, are well documented in the Code of practice. The Code of conduct requires that all research comply with these standards of care indicating that "researchers must respect the animals they use in research, in accordance with the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes"[3]. Further, where a researcher does not meet those standards it may be considered research misconduct.

> Research misconduct may "…include… avoidable failure to follow research proposals as approved by a research ethics committee, particularly where this failure may result in unreasonable risk or harm to humans, animals or the environment"[4] and "conducting research without ethics approval as required by the *National Statement on Ethical Conduct in Research involving Humans* and the *Australian Code of Practice for the Care and use of Animals for Scientific Purposes*"[5].

Between the two regulating documents it is clear that the standards of care must be followed and where deviations from these standards occur it may be considered a breach or research misconduct that may attract disciplinary actions with serious consequences for a researcher's career.

To ensure that the use and care of animals in research complies with the published standards the Code of practice specifies that "institutions using animals for scientific purposes must ensure, through an AEC that all animal use conforms to the standards of the Code [of practice]".[6] That is, the Code of practice allocates the *regulatory role* around animal use to the AEC. This is by now well established in Australian institutions using animals in research. However, the Code of practice goes further and stipulates that institutional processes must include "addressing concerns by the AEC regarding non-compliance with the Code [of practice] which may include disciplinary action upon advice of the AEC".[7]

The reference to disciplinary action is significant. The Code of practice is silent on the mechanism that should be used to determine and implement disciplinary action. In this context, it should be remembered that the conduct of research in Australia is governed by the Code of conduct. In particular, Part B of the Code of conduct outlines the investigation and management pathways for institutions to manage breaches (which includes non-compliance with the standards of the Code of practice) and, if serious, with research misconduct. That is, the Code of conduct requires researchers to conduct research consistent with those standards as outlined in the Code of practice. Where it is suspected that research involving animals has deviated from accepted practice then the framework for investigating breach or research misconduct as outlined in the Code of conduct should be followed.

Understanding the different institutional responsibilities conferred by the Code of practice and the Code of conduct is essential in assisting the respective parties to contribute to the monitoring, investigation and disciplinary processes. A good understanding of these respective roles reduces the likelihood of an overlap of efforts and the risk of multiple and potentially conflicting outcomes.

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[3] National Health and Medical Research Council (2007) Australian Code for the Responsible Conduct of Research, Canberra: National Health and Medical Research Council Section 1.9

[4] National Health and Medical Research Council (2007) Australian Code for the Responsible Conduct of Research, Canberra: National Health and Medical Research Council Section 10.1

[5] National Health and Medical Research Council (2007) Australian Code for the Responsible Conduct of Research, Canberra: National Health and Medical Research Council Section 10.2

[6] National Health and Medical Research Council (2004), Australian code of practice for the care and use of animals for scientific purposes, 7th edition. Canberra: National Health and Medical Research Council S1.5

[7] National Health and Medical Research Council (2013) Australian code for the care and use of animals for scientific purposes, 8th edition. Canberra: National Health and Medical Research Council S2.1.1 (v)

Understanding breach and research misconduct and the investigation process

If a person reasonably suspects that a breach or research misconduct has occurred and formally reports this incident, the institution has a responsibility to investigate the allegation. The Code of conduct establishes the frame work for dealing with deviations from accepted research practice and requires that investigation pathways distinguish between a breach or research misconduct. The delineation between the breach and research misconduct is important and will determine the disciplinary and follow up actions that are necessary to resolve the investigation process. A breach can be defined as a less serious deviation from the Code of conduct that is appropriately remedied at the local level, through steps such as counselling, advice, supervisory action, warning, education and appraisal procedures.[8] Research misconduct includes intent and deliberation, recklessness or gross and persistent negligence and, as already mentioned, actions without or failing to follow ethics approval, in particular where they involve unreasonable risk or harm to animals[9]. Due to the serious consequences that substantiated research misconduct can have for a researcher's career it is important to follow institutional processes to ensure a sound, just process. Usually the formal investigation process is embedded in institutional employment instruments. These instruments may confer the investigation responsibilities on a person holding a particular office at the Institution or a properly constituted investigation committee. This means that the investigation of potential breach or research misconduct involving animal research cannot be solely conducted by the AEC and therefore, is not the sole responsibility of the AEC. In what capacity does the AEC then contribute to the investigation of suspected breach and research misconduct?

What constitutes an investigation:

The majority of allegations or reports coming to the attention of the institution or the AEC involve breaches of the Code of conduct rather than research misconduct and all efforts should be undertaken to make this clear to all parties involved. Usually all good will towards resolving even minor breaches is lost once the term 'research misconduct' is used, in particular if the person against whom the allegation is made feels the allegation is unjustified. Breaches should be dealt with as such and, as pointed out above, they should be handled at the local, departmental level, by a person in a supervisory relationship with the person against whom an allegation is made. Where higher-order invertebrate or vertebrate animals are involved the AEC should play an important if not leading role. Regardless of the seriousness of the allegation or complaint, however, it is important to investigate and document appropriately, to adhere to the principles of natural justice and procedural fairness, and to bear in mind that the person making an allegation may need to be protected.

As the first step, then what constitutes an investigation? There are abundant resources available on the subject, most prominently around the topics of criminal investigation and audits. In the first instance, there is the statement of the initiation of the investigation, that is, a clear communication about what happened and in what time frame[10]. This should be accompanied or followed by the identification of all parties involved and be supported by statements from these parties regarding the event. Records and other documents or materials or copies of those will need to be collected and stored together with other evidence. This material will then need to be reviewed and discrepancies or conflicts of evidence explained. Another step is to determine if existing policies or regulations were followed or not and then, finally, the determination of

[8] National Health and Medical Research Council (2007) Australian Code for the Responsible Conduct of Research, Canberra: National Health and Medical Research Council, refer to sections 10 and 11

[9] National Health and Medical Research Council (2007) Australian Code for the Responsible Conduct of Research, Canberra: National Health and Medical Research Council Section 10.2

[10] See State Government of Indiana (U.S.) Family & Social Services Administration Policy BQIS 4600316043.

findings which should include substantiations of evidence. Doing all this properly requires diligence, dedication and skill.

The Designated Person and *prima facie* investigation

In Australia we do not have a dedicated government body to investigate allegations of research misconduct such as the U.S., with its Office of Research Integrity. An ethics committee is unlikely to have the capacity time-wise or the requisite skills to undertake a thorough investigation of breach or research misconduct. For the purposes of investigating instances of alleged research misconduct, the institution is required to nominate a Designated Person to conduct a preliminary investigation of formal allegations[11]. If the Designated Person establishes that there is a *prima facie* case of research misconduct the formal investigation process is conducted through those processes usually embedded in institutional employment instruments.

For the Designated Person to commence a preliminary investigation there should be, in the first instance, a formal statement about what the alleged research misconduct is, such as the behaviour observed that is inconsistent with standards of research[12]. Where possible the complainant should be encouraged to provide as much supporting and documentary evidence to support their allegation. During the preliminary investigation the Designed Person may collect information pertaining to identification of all parties involved and supporting statements from these parties regarding the event as well as records and other documents (or copies) and materials that may be useful to ascertain a clear picture of the events surrounding the allegation. At a minimum this collected information should be examined in light of documented institutional policies, procedures or practices and whether the alleged behaviour has contravened the standards of research.

The recommendations of the preliminary investigation should include the standards that are expected, whether the person has complied with these standards, and be accompanied by documentary evidence and other supporting information to support the finding. This investigative process requires diligence, expertise and skill particular to the investigation process. Although the AEC may not conduct the investigation it is still very much needed for its expertise, such as detailing where and how the research may have deviated from the approved protocol or explaining the animal welfare implications.

Who are the parties involved:

Research involving animals can require a multitude of parties, some of which we have identified above. First of all, there are the researchers, research trainees and technical staff working on animals or supporting the process, including provision of equipment. Then there are those looking after the facilities the animals are housed in and the care of the animals, including animal facility managers, animal care staff and the suppliers of animals and equipment and materials as well as those providing transport for animals. There are Animal Welfare Officers who monitor animal welfare across an institution, often working closely with the AEC and its Chair, committee members and Executive Officer. There are Licence Holders, often the department heads, who answer to the State Regulator but also to senior institutional managers, such as the Deputy or Pro Vice-Chancellor (Research). As per requirement of the Code of conduct institutions have a Designated Person who advises the CEO or their Delegated Officer, and there are Research Integrity Advisors who can advise those thinking of making an allegation of research misconduct. Not the least there are federal funding bodies and State regulators, all of

[11] Formal allegations are those made in writing and should be compliant with the institutional procedure.

[12] See State Government of Indiana (U.S.) Family & Social Services Administration Policy BQIS 4600316043.

whom have the authority to audit research. And there are members of the public who may be against research involving animals, or who notice what they perceive to be an animal welfare issue and who then lodge a complaint. Complaints may also come to an institution via their ombudsman or the State government ombudsman under the relevant whistle blowers protect act. In short, there are many parties that may be involved in or be affected by an investigation.

Possible roles and functions:

Given the complexities of investigations and the multiple parties involved it is important to try and delineate roles and responsibilities. There are some critical functions that could be assigned to key roles, bearing in mind that the exact match depends on the characteristics of the people in a particular role and on the environment and structure within an institution.

The Animal Welfare Officer and Facility Manager are often the first, or at least the first senior personnel to come across incidents involving animals. Both are familiar with the projects that are conducted in a facility and should have access to ethics protocols but also notice if an unusual procedure was carried out; they should therefore be able to quickly recognise if there is a potential deviation from the approved protocol. Both parties are likely to be involved in emergency responses and are well suited to collect evidence around an incident, such as records and entry logs to facilities, and make photos and arrange or conduct autopsies. They are also likely to be some of the first people to talk to other parties involved, be it the investigators or animal care staff or contractors delivering animals, and could therefore record the discussions and statements. In addition, as a veterinarian the Animal Welfare Officer has the skills judge the impact of the potential deviation and associated events on animal welfare, a judgment that is important in deciding whether an event may be classified as breach or research misconduct. The Animal Welfare Officer also plays an integral part in addressing educational needs to prevent re-occurrence of non-compliance and adverse effects on animal welfare.

The AEC should be informed quickly of an event that may involve deviation from the approved protocol and receive copies of all evidence, statements and other materials that has been or is being gathered. The information can come from the Animal Welfare Officer and Facility Manager as relevant and also from the Chief Investigator of the project in question. The AEC is required by the Code of practice to decide whether a project needs to be stopped, at least until remedial actions have taken place. The AEC also needs to make the decision whether a deviation from approved protocol took place or not. In many circumstances these decisions need to be made quickly, most likely by the Chair, and it is important to convey these decisions to the members and provide the opportunity for feed-back in between meetings. The AEC should actively discuss all allegations of breaches and research misconduct at quorate meetings until it is satisfied that the matter has been dealt with and document the discussions in meeting papers and minutes.

When dealing with breaches of the Code of conduct the AEC may want to work closely with the Head of School to ensure that preventative steps are incorporated into local research culture. The Head of School, or area manager in an institute, will be aware of and is authorised to use disciplinary measures appropriate to the level of breach that has occurred. Depending on the employment instrument this may involve oral and written warnings, demotion or suspension, but also extend to directions to improving research practice through professional training. For example, the Head of School may direct a researcher to complete an accredited training course on animal handling before re-commencing procedures. In many cases the Head of School is also the licence holder with State regulators, with significant responsibilities, and should therefore play an active role in ensuring animal research under his or her care is conducted responsibly.

Allegations of research misconduct are received by the Designated Person of an institution who then conducts the initial investigation whether a *prima facie* case of research misconduct exists. Where research involving animals is concerned it is important that AEC Chairs and AWOs are

aware of the definitions of breach *versus* research misconduct and refer matters involving research misconduct to the Designated Person in the first instance. Otherwise there is the real possibility that multiple investigations are conducted, possibly leading to different findings. At the same time, however, both the AWO and the AEC have the duty to ensure animal welfare issues are addressed as soon as possible. That is where the possible functions and definitions of roles of the AWO and the AEC discussed above become relevant to ensure that a proper investigative process is followed but that animal welfare issues can be addressed effectively at the same time. In other words, the Designated Person leads the preliminary investigation, the AWO provides emergency treatment, collects evidence and judges the welfare impact on animals, and the AEC stops a project if required, determines whether there was a deviation from the approved protocol and prevents re-occurrence.

The big picture issue:

Research misconduct *per se* is serious for any researcher involved and can mean the end of a career that took years of studies and training. Tolerance levels among peers for research misconduct are low, even more so if it involves adverse outcomes for research participants or animals. Research misconduct is thought to be sufficiently rare so as to be viewed as the exception rather than the norm[13]. We need to bear this in mind when dealing with deviations from the approved protocol and ask, first up, whether the decision is likely to have been made wilfully and with intent to do other than approved by the AEC. However, experience also shows that some of the most prominent cases of research misconduct came to light because of a lack of appropriate ethics approvals[14] which leads us to the 'big picture' issue. Problems following approved protocols, whether intentional or not, may well be indicators of research quality, or more specifically a lack of. Research needs to be planned, conducted and recorded precisely following logical process, and any deviation from this approach is likely to impact on the quality of the research that is produced. Recently pharmaceutical companies found in several instances that many published results could not be verified independently[15]. For those involved in dealing with deviations from approved protocol the implication is that the matter may then not only be one of animal welfare but one that goes to the heart of the quality of research. If research is not conducted according to the highest standards, we miss out in developing benefits for mankind in the form of drugs and other treatments, novel outcomes that are used to justify the use of animals in science.

Addendum: A question was raised by the audience whether persons who are investigated by the Designated Person should be informed of their legal rights, i.e., that their statements and information/materials they provide may be used against them. Legal advice was sought afterwards and we were advised that criminal proceedings are expected to arise only rarely, as the exception rather than the rule. In such cases, the police would handle the matter themselves and would investigate and bring their own evidence quite independently of what the University may do. Therefore it would not be necessary to make specific provision for this as part of the procedures around research misconduct

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[13] See for example: Fanelli D (2009) How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data. PLoS ONE 4(5): e5738. doi:10.1371/journal.pone.0005738;

[14] See for example: Akst J (2012) Anaesthesiologist Fabricates 172 papers, The Scientist, http://www.the-scientist.com/?articles.view/articleNo/32312/title/Anesthesiologist-Fabricates-172-Papers/ and, Adam, M (2012), Retraction Watch, http://retractionwatch.wordpress.com/2012/06/18/three-more-fujii-papers-fall-for-lack-of-irb-approval/

[15] See for example, Begley C G & Ellis L M (2012) "Raise standards for preclinical cancer research", Nature, 483 p 531, and, Prinz F, Schlange T and Asadulla K (2001), "Believe it or not: how much can we rely on published data on potential drug targetes?", Nature Reviews Drug Discovery 10, p328

Improving the welfare of research animals: An evidence-based approach to assessing and managing pain, underpinned by a better understanding of how pain, distress and analgesics impact experimental outcomes.

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The principles of Replacement, Reduction and Refinement lie at the core of what the *Australian code of practice for the care and use of animals for scientific purposes* aims to achieve with respect to promoting the well being of animals and augmenting research outcomes. By investigating scientific problems using *in vitro* experiments and other methodologies first, researchers optimise their use of animal models to answer complex research questions (Replacement). By developing clearly defined experimental objectives that directly address the research question, researchers minimise the number of animal experiments and the numbers of animals used (Reduction). Similarly, by identifying how each intervention, positive or negative, impacts on both the animal and the experimental outcome, researchers can design experiments that address animal welfare issues and achieve robust experimental results (Refinement). For this to occur, researchers need to be better informed about the degree of pain caused by different interventions, how that pain manifests in different animal species, and what effect treating that pain can have on the experimental outcomes. In addition, researchers need to better understand the physiological stressors that can impact both animal welfare and experimental results when conducting live animal studies. This includes seemingly benign interventions such as the handling associated with weighing laboratory animals or the administration of injections. Veterinarians, neurophysiologists and Veterinary ethologists have an important role to play in advising researchers on these matters, if we are to move towards a more evidence-based approach to identifying and managing pain and distress in laboratory animals.

Introduction

Any organization that uses or supplies animals for research or teaching purposes must comply with the State Acts that regulate how animals are used. Put simply, there are laws that protect research animals and these should translate to a "code of conduct". The Australian code for the care and use of animals for scientific purposes (Rose and Grant, 2013), defines this code of conduct. The principles of Replacement, Reduction and Refinement lie at the core of what the Code aims to achieve with respect to promoting the wellbeing of animals and augmenting research outcomes. But what do the three R's really mean? They are as much about the research as they are about the animals. Good science should go hand in hand with good animal welfare.

Scientific Method

The investigation of complex scientific questions is carried out using a number of different methodologies (replacement). *In vitro* experiments for example, are an important foundation from which to develop clearly defined experimental objectives for animal experiments that directly address a specific research question, resulting in a reduction in the number of animal experiments and the numbers of animals used. This then ensures the design of animal model experiments where the impact of each intervention is carefully considered so as to achieve robust results and address the welfare needs of the animals (refinement). Animal models provide a 'proof of principle' from which researchers can then develop human studies.

A sound scientific approach ensures a researcher produces work that is publishable and this in turn supports the on-going funding of their future research. This approach is hardly rocket science, and yet many researchers still fail to see the important link between experimental design, animal welfare and robust publishable results.

It is often easier to focus on replacement and reduction, rather than refinement. The first two are tangible and have numbers attached to them. They appear in annual reports and impress the reader. However, reducing animal usage numbers by 20% should not be a substitute for allowing a proportion of the other 80% of animals to undergo invasive procedures without appropriate analgesia. In a research climate where the number of animals used for experimentation is increasing overall, especially in growing fields of research such as pain (Balcombe et al., 2013) and cancer, it is important that all researchers actively implement the 3R's in their scientific method.

Yet modifying a surgical approach, altering the type of anaesthesia used, or introducing analgesics into already established protocols, is considered sacrilege by many researchers; often with very little science to support their unwillingness to refine their experimental methods. If we are to improve the welfare of animals used for scientific purposes, an attitudinal change is required amongst our researchers, and Institutional Ethics Committees are best placed to drive this change.

Current Guidelines

Refinement of current animal experimentation practices requires researchers to make informed decisions about the impact of pain and other physical and physiological stressors. Researchers need to be better educated about the degree of pain caused by different interventions, how that pain manifests in different animal species, and what effect treating that pain can have on experimental outcomes. In addition, they need to better understand the physiological stressors that can impact both animal welfare and experimental results when conducting live animal studies. This includes seemingly benign interventions such as the handling associated with weighing laboratory animals or the administration of injections.

There are numerous published guidelines to aid researchers in this process (AVMA, 2013, NHMRC, 2008). They provide an informed approach for minimising pain and distress, assessing and treating pain, and selecting humane end points.

In addition, international research organisations are developing standards for conducting animal experimentation and guidelines for reporting animal research. For example, in 2006 the AO Foundation and Research Institute brought together Veterinarians, musculoskeletal researchers,

ethicists and legal experts to develop a consensus paper on the proper use and design of experimental animal models in musculoskeletal research, and published a list of 10 "golden rules" for conduction of animal experiments in fracture research (Auer et al., 2007). The ARRIVE (Animals in Research: Reporting *In Vivo* Experiments) guidelines (Kilkenny et al., 2010) were developed in consultation with scientists, statisticians, journal editors and research funding bodies, and are a checklist of 20 items describing the minimum information that all scientific publications reporting research using animals should include. The guidelines have since been adopted by a number of high impact journals.

Pain assessment

Laboratory animals eat and drink, groom to maintain a clean and shiny coat, void regularly, are active and inquisitive, and have a predictable, species specific, response to being handled (table 1). Current standard operating procedures for assessing pain in laboratory animals tell us about severe pain states. Sunken flanks, neglected grooming, piloerection, ocular and nasal discharge, and severe acute weight loss, define a moribund health status for mice. These signs are best used as indicators of endpoints rather than signs of pain. The challenge is developing standardised evaluation methods that identify mild to severe pain before these endpoint behaviours are reached.

Table 1: Pain assessment criteria for different laboratory animal species

Observation	**Species**			
	Rats/mice	**Rabbits**	**Sheep**	**Fish**
Feeding	↓	↓	↓	↓
Physical appearance	Coat condition Nasal/ocular discharge Posture	Coat condition Pale eyes Posture	Fleece condition Nasal/ocular discharge Posture	Fin/skin condition Colour change Secretion accumulation
Clinical signs (objective)	RR Temperature Blood pressure	RR Temperature Blood pressure	Panting, grunting Temperature Blood pressure	RR
Unprovoked behaviours	Activity Social interaction Burrowing Grooming Self-mutilation	Activity Jaw grinding Grooming Self-mutilation	Activity Herd seeking Jaw grinding Self-mutilation Vocalisation (bleating)	Activity Social interaction Position in water column Posture/orientation
Provoked behaviours	Avoidance response Aggression	Avoidance response Aggression	Avoidance response Reluctance to move	Avoidance response

* ACLAM Guidelines for the Assessment & Management of Pain in Rodents and Rabbits (2006)
** Policy on the Care & Use of Sheep for Scientific Purposes Based on Good Practice (2005), Workshop Recommendations, Monash University and the Animal Welfare Science Centre, Victoria
*** Canadian Council of Animal Care in Science

Defining the "pain potential" of common procedures (table 2) is one way to ensure treatment of pain is addressed even if the observable behaviours are subtle and difficult to identify. However, not all pain states are simple in nature and easy to characterize. Animal research that involves cancer models, induction of diabetes, nerve injury models or chronic pain such as arthritis, results in pain that is more complex. It manifests as hyperalgesia, allodynia and spontaneous pain, which translates to behaviours that are difficult to assess or have yet to be clearly defined in animals.

Table 2: Pain severity potential of common experimental procedures

Mild	Mild to Moderate	Moderate to severe	Severe
tail clip	ID injections	major laparotomy	thoracotomy
ear notching	vascular canulation	minor orthopaedic	major orthopaedic
venipuncture	thyroidectomy	c-section	trauma/burns models
vasectomy	minor incision	organ transplantation	Fracture models

Research has helped us to understand the complexities of the pain state (Bennett, 2012, Mogil, 2012a). Pain starts with stimulation of specialised nerve endings (nociceptors) and subsequent transmission of signals along afferent peripheral sensory nerves to the spinal cord. These sensory nerves comprise two main types; myelinated Aδ fibres that are fast conducting and localised, and the non-myelinated C fibres that are slow conducting and more diffuse. The cell bodies of these afferent neurons reside in the dorsal root ganglia (DRG). From the spinal cord this signal is then transmitted via a number of pathways to the higher brain centres for processing into what is then perceived as pain. Pain perception occurs at the level of the thalamus and the localisation of the pain occurs in the sensory cortex.

But the nervous system has an added complexity. All along this "pain pathway" are opportunities for intrinsic and extrinsic factors to influence the nature, amplitude and perceived location & duration of the original pain signal. Peripheral and central pain sensitisation is a feature of chronic and neuropathic pain. This sensitisation is mediated by a number of pro inflammatory cytokines that are released after cell injury. These include prostaglandins, bradykinin, and tumour necrosis factor (TNFα). Central pain sensitisation occurs at the level of the spinal cord or somatosensory cortex and is mediated by numerous inflammatory neuropeptides such as calcitonin gene related peptide, substance P, glutamate and vasoactive intestinal peptide (VIP). In addition, endogenous opioids and cannabinoids, also released by the body can block the pain signal. This nervous system plasticity makes diagnosis and treatment of chronic and neuropathic pain a challenge for researchers and clinicians alike (Woolf, 2011, Mease et al., 2011).

Responding to pain in experimental animals subjected to procedures that directly cause tissue injury or induce a pain state over time, requires a researcher to be able to identify and treat acute pain and to accurately assess chronic pain in order to determine humane endpoints for long-term studies.

Pain Behaviour

Prey animals such as rodents, rabbits and sheep, avoid displaying signs of pain and injury as a survival mechanism. Therefore, we need to look beyond severe signs such as rapid weight loss to identify pain in these species.

The notion that animals express emotion through facial expression is not a new one. In fact, Darwin first proposed this in 1872. However, it is only recently that researchers have started to develop standardized coding systems for facial expression changes that translate to pain in different laboratory animal species. Researchers in Canada first identified five facial features, which they attributed to acute pain in mice, after observing these same facial expressions in 14 different pain assays and reversing them with the administration of morphine (Langford et al., 2010a). Pain grimace scales have since been developed for rats (Sotocinal et al., 2011) and rabbits (Keating et al., 2012) as well.

An alteration in nest building behaviour has also been identified as an indicator of pain and distress (Jirkof et al., 2010, Jirkof et al., 2013). Researchers recorded the percentage of mice/hour that commenced burrowing after being placed in a cage and identified an increase in burrowing behaviour latency attributable to both surgery (responsive to analgesics) and anaesthesia (non - responsive to analgesics).

The significance of facial expression as a measure of pain or distress has also been demonstrated in sheep. Sheep are able to recognize, and use, face emotion cues to interact socially (Tate et al., 2006). Researchers identified four stress related facial cues; enlarged protruded eyes, pupils showing white, flared nostrils and flattened ears. Sheep also have the capacity to remember the faces of other sheep and people.

This greater understanding of how facial expressions and natural behaviours are altered when animals experience pain and distress are powerful tools for quantifying pain intensity and duration, and calculating dose response data for analgesics commonly used to treat pain in research animals (Leach et al., 2012, Matsumiya et al., 2012). Standardised behaviour changes such as those discussed above, allow researchers to evaluate common experimental procedures utilised in a range of animal models and characterise this pain and identify suitable analgesic regimens. All this can lead to a more evidence-based approach to identifying and treating pain in experimental animals.

In addition to tools that assist with identifying and quantifying pain, researchers require a suite of pharmacological (table 3) and non-pharmacological (table 4) strategies to treat pain and minimize distress in experimental animals. The better we understand normal animal behaviour patterns the better we will become at creating environments that minimise environmental and social stressors for a particular species.

Pain researchers have made interesting observations about how animal social groups respond to individuals in pain and how in turn that individual's pain levels may be altered depending on the social group they are housed with. It seems humans are not the only species that demonstrate 'empathy'(Mogil, 2012b). In one study (Langford et al., 2010b), female mice were more likely to approach a cage mate displaying pain than an unaffected but equally familiar mouse. Researchers did not observe this behaviour in male mice, or females when placed with unfamiliar mice. Even more interestingly, they were able to demonstrate a negative correlation between the proximity of a familiar cage mate to an affected mouse and the pain behaviour displayed by that mouse.

Table 3: Pharmacological pain management strategies for laboratory animals

	Rats	**Mice**	**Rabbits**	**Sheep**
Local Anaesthetics	1 or 2% Lignocaine for topical, infiltration, nerve blocks. Maximum total dose 6mg/kg 0.5% bupivacaine for nerve blocks. Maximum total dose 2mg/kg			
NSAIDs				
carprofen	5mg/kg SC q12-24	5mg/kg SC q12-24	4mgkg SC q24	1.5 – 2mg/kg SC q24
ketoprofen	2.5 – 5mg/kg SC	2.5 – 5mg/kg SC	3mg/kg SC	
meloxicam	1 – 2mg/kg SC q24	1 – 2mg/kg SC q24	0.2 – 1.5mg/kg SC q24	
Opioids				
buprenorphine	0.05 – 0.1mg/kg IM/IP q6 – 8	0.05 – 0.1 mg/kg IM/IP q6 – 8	0.02 – 0.05mg/kg IM q6 – 8	0.005 – 0.01mg/kg q4 – 6
morphine	2 – 5mg/kg SC q4	2 – 5mg/kg SC q4	0.5 – 3mg/kg SC q4	0.2 – 0.5 mg/kg IM q4
pethidine	10mg/kg SC q2	10mg/kg SC q2	5 mg/kg SC q2	2mg/kg IM q2

Table 4: Non pharmacological pain management strategies for laboratory animals

Mild to Moderate Pain	**Moderate to Severe Pain**
Rats/Mice/Rabbits	**Rats/Mice/Rabbits**
Bedding: soft, absorbent, change frequently	Bedding: soft, absorbent, change frequently
Food and water access	Food and water access
Single housing if non-ambulatory	Single housing if non-ambulatory
Heat supplementation	Heat supplementation
	Fluid & nutrition supplementation
	Food palatability

Treating Pain

Pain and distress elicits a physiological stress response that has been well described in mammalian species. This 'stress response' is driven by the autonomic nervous system, the neuro-endocrine system (hypothalamic-pituitary-adrenal axis), and the immune system, and also manifests as characteristic behaviours that are species specific. Interestingly, changes in these

systems make up the key research outcomes for pre-clinical biomedical research that utilizes animal models. Excessive pain and distress that goes untreated can confound experimental data making it difficult to interpret results. This represents one aspect of the important link between science and animal welfare.

The other aspect is the impact that the use of analgesics, especially opioids and NSAID's, can have on research outcomes. The immune-modulatory effects of opioids (both innate and adaptive) have been characterised in a number of species. However, the exact mechanisms involved and their clinical relevance is still under investigation (Sacerdote et al., 2012, Al-Hashimi et al., 2013). Opioids affect the production of pro-inflammatory cytokines by macrophages (Franchi et al., 2012); mu opioid receptors are constitutionally expressed by developing T lymphocytes in the thymus (Zhang et al., 2012); functional mu opioid and cannabinoid-1 receptors are not expressed in resting human T cells, but are induced by IL-4 and activation of T cells (Kraus, 2012).

Opioids affect both the immune and the inflammatory response. They decrease, immunoglobulin production, phagocytic activity, ADH, prolactin and somatotrophin release; and they increase histamine release. However, not all opioids induce the same immunosuppressive and anti-inflammatory effects. Therefore, opioid profiling becomes important for determining appropriate analgesic selection in different experimental models.

Conclusion

Both pain and analgesic use can alter experimental outcomes. However, the pragmatic approach of not changing outdated experimental protocols is not the answer. Instead, researchers and Ethics Committees must work together to continue to improve the welfare of research animals in a way that does not confound data or invalidate experimental outcomes. This can only happen if an evidence-based approach to assessing and managing pain and distress is implemented. Veterinarians, neurophysiologists and Veterinary ethologists have an important role to play in advising researchers and ethics committee members. Researchers must continue to refine experimental methods and introduce better standards into their analgesic and anaesthetic protocols. In the short term this refinement may impact negatively on reduction, as additional experimental animals may be required to validate data and test any perturbing effects from changes made to protocols. However, in the long term this will only benefit animals used for research purposes.

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Analgesic use in models of arthritis – reconciling the balance between pain relief and modifying the disease process being investigated

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Arthritis is the most widespread musculoskeletal disease in Australia afflicting nearly a 5th of the entire population. The total annual cost of arthritis in Australia, attributable to the burden of disease, productivity costs, and direct health expenditure is over $24 billion, and continuing to increase as the population ages. Osteoarthritis (OA) is by far the most prevalent of the joint diseases, and there are currently no registered therapies that halt OA joint structural damage, and the available symptom-modifying (analgesic) treatments have only moderate long-term effect sizes at best. In light of its enormous and growing social and economic consequences, arthritis has been designated as a National Health Priority in Australia, and improving our management of OA in particular is a critical and unmet medical research goal. Only through improved understanding of the cellular and molecular pathophysiology of OA, will disease structural- and symptom-modifying targets be identified enabling new, specific and effective therapies to be developed.

One of the cornerstones of OA research as in most other fields of medicine, is the use of preclinical animal models that mimic the human disease. OA in patients is characterised pathologically, by abnormalities in all joint tissues: cartilage erosion and loss, thickened subchondral bone of reduced mineral density, excessive marginal new bone formation (osteophytes), synovitis and joint capsule thickening/fibrosis; and clinically by varying degrees of pain and disability. The relationship between joint structural damage and clinical symptoms in OA patients is poor, and defining the specific tissue, cellular and molecular drivers of pain in this disease is a major international research focus.

It is scientifically incumbent upon us as researchers to do everything possible to make certain that our experiments are well designed, controlled, powered, analyzed and reported. In the case of research involving animal models, this is true not only from the perspective of good scientific practice but also to fulfil our responsibility for the appropriate and ethical use of animals i.e. implementing the "3Rs". These dual responsibilities can at times come into conflict, and give rise to ethically challenging dilemmas: for example if a critical clinical and research question is to define the correlation between disease pathology and pain. Perhaps this issue becomes even more difficult if pharmacologically managing the discomfort of an induced disease in an animal model alters the molecular processes/characteristics of the disorder and yet it is defining these pathways that are the primary goal/outcome of the research being done. How do we as a research community (which includes the researchers, funding bodies, ACEC members), balance the value and validity of the scientific outcome with the comfort and well being of the research animals? Does this differ with the research goal or hypothesis/question being asked? What about with the specific model and/or species being used? In this presentation these issues will be discussed with regard to preclinical models of arthritis, and OA in particular.

No manuscript was provided by the authors for this presentation

Can We Do Better? Responding to unexpected changes during the life of a project.

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The life of a research, testing or teaching project can be altered, or prematurely ended, for reasons that were unforeseen at the time of approval by an ethics committee.

These reasons, which are common everyday events, may include: a change of staff and/or their circumstances, adverse events, institutional changes, funding changes, world events and natural disasters. Such changes, in turn, alter the parameters that were evaluated during the ethical cost benefit analysis upon which the project was approved. With the changed circumstances, the ethical cost may outweigh the benefit(s) that were realised to date, or were limited by that change. This raises the question: if a project can only continue in part, should it continue at all?

This paper explores the fate of the animals on projects that have unexpected events impacting on them, and the outcomes in terms of moral and ethical justification. It also addresses when and how a project might be re-evaluated by ethics committees during its life, if changes alter the cost-benefit. How are ethics committees made aware of these changes to ensure that the animal use continues to be justified? In addition, should ethics committees require applicants to consider a wider range of project outcomes, and to detail their response in their contingency planning?

Introduction:

The idea of this presentation is to ask questions, and to provide "food for thought". I am a veterinarian and Animal Welfare Officer for an Ethics Committee in New Zealand.
I would like to start with a joke……..
What are we qualified to talk about?

An atheist was seated next to a little girl on an airplane and he turned to her and said, "Do you want to talk? Flights go quicker if you strike up a conversation with your fellow passenger."

The little girl, who had just started to read her book, replied to the total stranger, "What would you want to talk about?"

"Oh, I don't know," said the atheist.

"How about why there is no God, or no Heaven or Hell, or no life after death?" he smiled smugly.

"OK," she said. "Those could be interesting topics but let me ask you a question first.
A horse, a cow, and a deer all eat the same stuff - grass. Yet a deer excretes little pellets, while a cow turns out a flat patty, but a horse produces clumps. Why do you suppose that is?"

The atheist, visibly surprised by the little girl's intelligence, thinks about it and says,

"Hmmm, I have no idea."

To which the little girl replies,
*"Do you really feel qualified to discuss why there is no God, or no Heaven or Hell, or no life after death, when you don't even know anything about s**t?"*

And then she went back to reading her book……..!

So, am I qualified to talk about this subject? In the course of more than 30 years with direct and indirect involvement in research, I have seen a number of studies end prematurely. The reasons have been varied and all occur throughout the research world. My first experience was very unexpected when my BSc Honours thesis supervisor and study investigator, died suddenly when the six month animal trial was little more than a week underway! Fortunately he had involved a colleague and myself in the very thorough planning stages, so with our combined knowledge, the study was able to continue! That was in Scotland in 1979 and I don't think we had any Ethics approval to worry about for our work!

Today the use of animals in science is very different:

Under NZ Animal Welfare Act 1999, Section 6, *The Use of Animals in Research, Testing and Teaching*, we are allowed to use animals providing:

- that the findings of the research or testing or the results of the teaching will enhance the understanding of human beings, animals, or ecosystems; the maintenance or protection of human or animal health or welfare; the management, protection, or control of ecosystems, plants, animals, or native fauna; the production and productivity of animals; or the achievement of educational objectives; and
- that the benefits derived from the use of animals in research, testing, and teaching are not outweighed by the likely harm to the animals.

As Ethics committees, we are charged with a duty to:

- (a) to consider and determine on behalf of the code holder applications for the approval of projects:
- (b) to consider and determine, under section 84(1)(a), applications for the approval of projects:
- (c) to set, vary, and revoke conditions of project approvals:
- (d) to monitor compliance with conditions of project approvals:
- (e) to monitor animal management practices and facilities to ensure compliance with the terms of the code of ethical conduct:
- (f) to consider and determine applications for the renewal of project approvals:
- (g) to suspend or revoke, where necessary, project approvals:
- (h) to recommend to the code holder amendments to the code of ethical conduct

We are also asked to look at the following criteria:
In considering any application for the approval of a project and in setting, varying, or revoking conditions of the approval of a project, **every animal ethics committee must have regard to such of the following matters as are relevant:**

- (a) the purposes of this Part of the Animal Welfare Act (Section 6); and
- (b) any matters that the committee is required to consider by regulations made under this Act; and
- (c) the scientific or educational objectives of the project; and

- (d) the harm to, or the distress felt by, the animals as a result of the manipulation, and the extent to which that harm or distress can be alleviated by any means (including, where the pain or distress cannot be held within reasonable levels, the abandonment of the manipulation or the humane destruction of animals); and
- (e) whether the design of the experiment or demonstration is such that it is reasonable to expect that the objectives of the experiment or demonstration will be met; and
- (f) the factors that have been taken into account in the choice of animal species; and
- (g) whether the number of animals to be used is the minimum necessary to ensure a meaningful interpretation of the findings and the statistical validity of the findings; and
- (h) whether adequate measures will be taken to ensure the general health and welfare of animals before, during, and after manipulation; and
- (i) whether suitably qualified persons will be engaged in supervising and undertaking the research, testing, or teaching; and
- (j) whether any duplication of an experiment is proposed and, if so, whether any such duplication will be undertaken only if the original experiment—
- § (i) is flawed in a way that was not able to be predicted; or
- § (ii) needs to be duplicated for the purpose of confirming a result that was unexpected or has far-reaching implications; and
- (k) whether the same animals are to be used repeatedly in successive projects, and, if so, the cumulative effect of the successive projects on the welfare of the animals; and
- (l) whether there is a commitment to ensuring that findings of any experiment will be adequately used, promoted, or published; and
- (m) any other matters that the committee considers relevant.

We, as an Ethics Committee, are ultimately concerned with making an ethical cost benefit analysis of a proposed project, and looking at whether the animals will be adequately cared for and any intended or potential harm minimised.
The critical statement is: ***"Using animals for scientific purposes is acceptable only when any harm done to the animals is very greatly outweighed by the benefits of their use".***

We do ask the proposer to provide contingency plans for adverse animal welfare outcomes, but not specifically to consider what they do with the animals if the project has to cease unexpectedly.
What is involved in the life of a research project?

- hypothesis or objective to be investigated
- principle investigator
- trial design
- *Ethics approval*
- funding
- Regulatory approvals
- facility
- staff
- animals

Setting the scene: The principle investigator has all the necessary approvals to carry out the study, and begins the animal phase. However, due to unforeseen circumstances, the life of the project is altered.

Why might a project not continue to fruition?

- researcher's personal circumstances may alter, eg. may get married, become pregnant, move jobs, die etc
- funding for the project may alter, eg. company may declare bankruptcy, company may be re-organized, may be incorporated into larger company with different needs, etc
- researcher may discover someone else has completed the work and obtained the answers they require
- other work may be published which makes the objective null and void
- adverse event involving animal welfare, eg. drug reaction
- facility problem, eg. earthquake, hurricane, flooding of facility

My question is: if the project's planned path is suddenly blocked, or altered, have we (or should we) as Ethics committees, asked the proposer to consider what they might do from an animal perspective?

What are you left with?

- project with no funding or facility to continue
- animal population brought together, or bred, specifically for the trial
- animals that have been manipulated
- animals that cannot be used for other purposes
- incomplete data sets, is any of the information useful?
- animals that have suffered, or are suffering (unnecessarily)?

How will the committee be informed?

*Investigators should inform the AEC when each project is completed or discontinued. As part of its role in monitoring manipulations the AEC should also be informed of the outcome of the project. (*Good Practice Guide for the Use of Animals in Research Testing, and Teaching; National Animal Ethics Advisory Committee September 2002*)*

- what reporting will be made?
- project staff will inform? (guidelines say they should)

What will be the report timing?

- historic – report at end?
- through routine monitoring channels?
- what action will be taken?
- what will be the timing? - before or after report?
- what assessment of the proposed outcome will be made?
- who will make the assessment?
- will the Ethics Committee be involved?

What should be the fate of these animals?

- are they reusable?
- have they suffered enough?
- what is the new ethical cost-benefit balance?
- should they be euthanased?

What does euthanasia involve?

*Debate exists about whether euthanasia appropriately describes the killing of some animals at the end of biological experiments[11] and of unwanted shelter animals. The Panel believes that evaluating the social acceptability of various uses of animals and/or the rationale for inducing death in these cases is beyond its purview; however, current AVMA policy supports the use of animals for various human purposes,[12] and also recognizes the need to euthanize animals that are unwanted or unfit for adoption. (*AVMA Guidelines for the Euthanasia of Animals: 2013 Edition)

- no more suffering
- no more living
- end of a living resource (can be "stored" eg cryopreservation)
- numbers involved – is it euthanasia, or depopulation, or slaughter?
- disposal of bodies
- justification

Discussion

As President Obama commented when referring to race relations and the recent Zimmerman case: "Can we do better? – We MUST do better – WHAT CAN WE DO ABOUT IT?"

What can we, as Ethics Committees, and people caring for and using animals, do to mitigate the effects on animals of unforeseen project outcomes?

We ask for reporting (mandatory), we ask for contingency plans and reporting of adverse events.

We monitor studies both as committees, and through our Animal Welfare Officers.

We now only approve applications for one year (maximum two years) duration. This reduces the impact of staff and career changes on projects.

Do we do enough? Do we respond to (or are we aware of?) changes in a timely fashion? Can we do better?

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Wild Connections – using live animals for education outcomes

Paul Maguire
Taronga Conservation Society Australia

Animals are at the centre of all Taronga's education and engagement programs. In most cases it is live animal interactions that are the most productive and deliver superior education and conservation outcomes. This is because animals inspire and engage all us all especially students, even students who have disengaged from formal learning environments. There is a magical connection that occurs when students get close and personal with animals that is hard to quantify.

Using live animals creates an inspiring learning environment that can be used to deliver syllabus outcomes from the different key learning areas with students of all ages and backgrounds. Balancing these experiences and encounters with the welfare of the zoo animal collection requires discipline and diligence. There needs to be clear policies and procedures to ensure the animal welfare is maintained and considered.

At Taronga Zoo live animals are used in many forms for many different outcomes. The context and the type of experience are key in motivating and delivering key student outcomes and action for conservation. Taronga education programs use animals in formal classroom workshops, Zoomobile outreach programs, immersive exhibits and in communities to inspire behaviour change. The animals are the key driver successful community conservation campaigns where they are used as ambassadors for outcomes focusing on sustainable seafood, wildlife trade and palm oil.

This paper will discuss some of the significant impacts animals have on student learning and engagement along with the benefits for conservation and sustainability. The paper will all outline how these experiences can be choreographed in an animal welfare and ethical framework to ensure best practice and highest impact.

No manuscript was provided by the authors for this presentation

Ethical decision making around Animal Welfare

Erna Walraven and Simon Duffy
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Ensuring good animal welfare is not the one and **only** goal of a zoo. Others may include contributing to the management of conservation relevant populations, education, research, and the provision of an authentic and educational biodiversity experience for visitors. These different goals are at times competing and decisions may be needed to ensure that the institution optimizes its overall contribution to both animal welfare and conservation.

For an ethical approach to such decisions, Taronga has adapted St James Ethics Centre's Ethical Decision Making Model to assess the relative merits of one option over another.

A simple example may be impacting the immediate comfort of an easily stressed individual animal to gain a long-term or future benefit for that individual. A remedial medical procedure may cause short-term negative sensations to an animal; the benefit being its own long-term health.

A more complex example may be hand-rearing an animal in such a way that inhibits some of its behavioural expression for the purpose of conditioning that animal to providing public education presentations.

Another example may be that in some species, mating behaviour places an animal at risk of injury but is at the same time an important component of natural behaviour and the future of any breeding program.

An ethical approach, using a utilitarian assessment, is required to resolve these dilemmas providing the best possible outcome for both animal welfare, the zoo's conservation goals and conservation education.

This paper describes an ethical decision model which can help zoos with the moral question of "what ought one do?"

Introduction

Ensuring good animal welfare is not the one and **only** goal of a zoo. Others may include contributing to the management of conservation relevant populations, education, research, and the provision of an authentic and educational biodiversity experience for visitors. These different goals are at times competing and decisions may be needed to ensure that the institution optimizes its overall contribution to both animal welfare and conservation.

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This paper describes an ethical decision model which can help zoos with the moral question of 'what ought one do?'.

Discussion

As a conservation organization with responsibility for the care of wildlife, we ensure that at all times the needs, interests and welfare of our animals is a primary consideration. We believe that good welfare is essential and will also assist us in achieving our conservation goals.

Taronga provides excellent husbandry, veterinary management and housing that promotes good welfare to all animals in our care.

Taronga believes that good welfare is achieved when each animal has a life experience that approximates the quality of a life experienced by an equivalent member of that species living in the wild.*

This is achieved by ensuring that our animals experience species-appropriate stimuli, which may include some stimuli that will challenge. To enrich their lives, our animals are given opportunities to react to those stimuli in a species-appropriate way.

*A member of that species born into a relatively benign environment during a period of plenty.

We're committed to providing an environment that focuses on the well-being of the animal and provides circumstances that the animal's biology has evolved to experience and expect. We acknowledge that zoos cannot truly replicate the wild but, as far as possible, we provide animals' with environments that meet their behavioural and physiological needs.

Taronga has an Animal Welfare Charter, associated policies and procedures to enable this Charter. The Charter reflects the philosophies that I have just presented and to meet the requirements of the Charter we have developed a series of Commitments. These commitments are:

- We ensure our animals have appropriate nutrition and drinking water
- We ensure that our animals have enough space to move around freely, have comfortable resting places and thermal comfort
- We strive to keep our animals free of physical injuries and disease
- We ensure our animals do not suffer pain or distress from poor management or handling
- We ensure our animals are able to express species specific behaviours

Each of these commitments have further qualifying statements to allow for interpretation, implementation and monitoring.

Optimizing decisions around animal welfare

During the implementation of the Charter and the specific Commitments it was evident that there were difficult decisions around animal welfare, where there may be competing goals, we have interpreted the St James Ethics Centre's Ethical decision making model as a template to guide our thinking.

St James Ethics Centre's Ethical Decision Making Model©
Interpreted for use in Animal Welfare Decisions

St James Ethics Centre's Model	Taronga Animal Welfare interpretation
Maximises benefit over harm	Maximises benefit over harm (i.e. conservation good or beneficial to individual animal welfare)
Would make a good general rule	Would make a good general rule
Develops and maintains a virtuous character	Develops and maintains qualities that ensure Taronga acts in a virtuous way with regards to animal welfare
Promotes common good related to defining purpose	Promotes common good related to defining purpose (defined as Taronga Vision and Role)
You could live with it if it was done to you	You could live with it (the proposed decision)
You would be prepared to support it in public	You would be prepared to support it in public
Applies espoused values and principles	Applies espoused values and principles (defined as the principles in the Taronga Animal Welfare Charter)
Protects fundamental moral rights	Protects fundamental moral rights (defined as the welfare needs outlined in the Taronga Animal Welfare Charter)
Promotes care for other/relationships	Promotes care for animals and Taronga's Vision of securing a shared future for wildlife and people

The following illustrates the kinds of optimization decisions likely to require consideration;

- **Compromising the immediate welfare of an individual to gain a long-term or future benefit for that individual.**

  Our Animal Welfare Charter aims to not have our animals suffer fear or distress, yet simple veterinary procedures to promote good heath may indeed in the short term cause the animal to be fearful or distressed. For example, a remedial medical procedure may cause short-term negative sensations to an animal, the trade-off being its own long-term health.
  The decision we then need to weigh up is impacting the immediate comfort of an individual animal to gain a long-term or future benefit for that individual. A remedial medical procedure may cause short-term negative sensations to an animal; the benefit being its own long-term health. This could be a bear requiring a full anesthetic to have a full heath check and have its teeth cleaned.

- **Compromising delivery of one of our Animal Welfare Commitments in order to satisfy another**

  Our Animal Welfare Charter aims to enable our animals to express species specific behaviour. Natural reproduction is off course an elementary component of species specific behavioural

expression. Yet, in some species, mating behaviour can place an animal at risk of injury, but is at the same time an important component of natural behaviour and essential to the zoos breeding programs. The introduction of tigers for breeding can put the animals potentially at risk of aggression from the other. However, with only 400 Sumatran Tigers remaining in the wild, breeding this species as an insurance population is an essential role of the modern zoo. The opportunity for an animal to breed and rear its young is also a significant expression of natural behaviour.

- **Compromising the welfare of an individual to further one or more of Taronga's other goals.**

  A more complex example may be hand-rearing an animal in such a way that inhibits some of its behavioural expression for the purpose of conditioning that animal to providing public education presentations. Taronga regularly admits orphaned Ring-tailed Possums and other native species at the Taronga Wildlife Hospital for rehabilitation. Rehabilitation and release to the wild is not always successful. Post release research has shown that most hand-reared Ring-tailed Possums do not survive long term after release (Augee et. al. 1996).

  The options available for this animal then are:
  - Hand-rear the animal and release, knowing that successful long term survival after release is unlikely
  - Euthanise the animal given the above
  - Hand-rear the animal as a contact animal for our education programs (acknowledging that this may impact, to a degree, the ability of the animal to express its species specific behaviours but will educate the public on why it is important to keep the cat inside at night for example)

By discussing each of the options available to an individual animal with the relevant stakeholders, against the considerations of the St James Ethical Decision Making Model we are able to make well considered decisions that optimize the individual animal's contribution to a conservation outcome and aligns with our Animal Welfare Charter.
Each option is discussed against the St James considerations and given a score of 1 to 3. One = do not agree, 2 = agree somewhat, 3 = fully agree. This way we are able to come to a decision that considers the ethical implications of our deliberations in a structured way whilst maintaining our animal welfare commitment to the individuals in our care.

Conclusion

Taronga is committed to providing excellent husbandry, veterinary management and housing that promotes good welfare to all animals in our care. Making ethical decisions about animals' lives requires us to think carefully about all the options available to achieve our broader conservation goals and our goals for the wellbeing of animals in our care. By scoring the adapted St James Ethics Centre's Ethical Decision Making Model against various options for animal husbandry, veterinary care conservation education and public presentation, we can evaluate how best the greater good of an animal's life may be achieved.

Reference:

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A zoo's responsibilities to the animals in its care

Paul Andrew
Taronga Conservation Society Australia

When talking of a zoo's responsibilities to animals in its care it is useful to recognise an animal perspective and a human perspective. To characterise these perspectives we can talk of 'interests' and 'values', the former relevant to animals as moral subjects and the latter relevant to humans as moral agents.

Interests are prudential, that is, they relate to how things are for an individual. The idea that we might talk of interests amongst sentient animals makes intuitive sense: for example, the idea that a sentient animal has an interest in whether or not it suffers or is happy seems like a reasonable thing to say. We might also ask if an animal has an interest in liberty or we might ask if an animal has an interest in continued life. We can ask these questions without inferring duties or rights: we can ask them purely in respect of whether an animal has interests that might warrant consideration when we reflect on our responsibilities as moral agents.

Interests can thus be distinguished from values which are judgements and are a human perspective. For example, it might be said that something is beautiful (of aesthetic value), rare (of conservation value) or even dignified (worthy of respect). In making such judgments, however, we need make no reference to how things are for the individual itself. The values that humans attribute to animals are the subject of this paper. Such values include dignity, respect and a right to life.
The relevance of sentience to value is questioned and it is argued that all species are equally worthy of respect. The value of the individual, however, varies between and within species: some species invest heavily in a few young, and other species produce young in large numbers and suffer high mortality. It is argued therefore that an objective measure of the value of an individual can be derived from an understanding of its species' life history. Using life history to gauge individual value is more objective than basing value on similarity, beauty, or cuteness.

No manuscript was provided by the authors for this presentation

Presentations given on

Thursday 25th July

Categorizing Animal Models: Taxonomies and their Implications for Evaluation

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Most philosophical arguments about the value of animal experimentation put ethical concerns first – they seek to interrogate and justify a particular position as to the moral status of nonhuman animals. In recent years there has been an evidentiary turn, with arguments about the value of animal experimentation more likely to include philosophical critiques as to limits of the predictive capacities animal models and the validity of extrapolating knowledge across species boundaries. Influential amongst these accounts is the HAM / CAM taxonomy developed by Hugh LaFollette and Niall Shanks which neatly collapses ethical questions into issues of evidence. While there is much to commend in LaFollette and Shanks' argument, it presents an idealized picture of the nature of model-based science that misrepresents how biomedical models are used to develop theories and promote courses of action. An alternate taxonomy is offered that captures the fluidity and unpredictability of model-based science, accounts for the 'instrumentalisation' of failure in its practice, and allows for the clear distinction of ethical and evidentiary questions in the evaluation of specific model-based studies.

Introduction

What does it mean to use a model in biomedicine? Models are used to develop, test and demonstrate theories. And yet models are essentially made up things – almost like theoretical projections. Indeed because models are always quite tightly entangled with a set of theories, philosophers of science have some difficulty in clearly articulating the difference between the two[1,2] However, most of the models used in biomedicine are also material objects. Whether they are a cell culture or an entire organism, models have a 'thingyness' about them – they can be manipulated and refined in a way that is distinct from a theory. This is because each model is the product of a set of distinct idealization procedures and practices to produce a simpler hypothetical system that resembles the model target in relevant respects - and just about anything can be a model of anything else as long as the modeller can justify a resemblance relation.

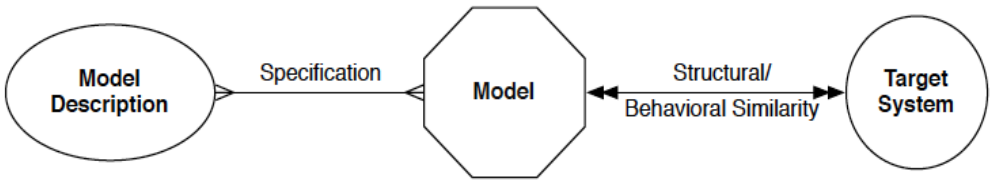

Fig 1. A model and its relations to a model description and a real-world target.[3]

The development of resemblance relations is the essential part of what it is to model. As the philosopher Michael Weisberg[4] has helpfully pointed out the difference between model-based science and non-model based science is that modelling is a two-step process based on two resemblance relations. In contrast, the defining feature of non-model based science is that it relies upon direct representation. Instead of developing a model, the scientist attempts to

describe the properties of the target system without the imposition and investigation of another representative object. Consequently, modelling is a two-step process that involves indirect representation and abstraction. The first step is always the specification of the model system. The second step is the specification of similarity of the model to the target (See fig 1). This two-step process creates ambiguity and flexibility in the development of theories in a way that direct representation does not.[5] It is arguable that this plasticity of purpose and description is actually key to the success of modelling practices.

Against this background, most philosophical accounts and arguments about the value of animal experimentation have tended to focus upon the moral status of the sentient nonhuman. In recent years there has been an evidentiary turn, with arguments about the value of animal experimentation more likely to include philosophical critiques as to limits of the predictive capacities animal models and the validity of extrapolating knowledge across species boundaries. Influential amongst these accounts is the HAM / CAM taxonomy developed by Hugh LaFollette and Niall Shanks which neatly collapses ethical questions into issues of evidence[6]. In doings so, LaFollette and Shanks have helped to reframe the debate about the value of animal experimentation. Using historical and empirical case examples they developed a theoretical account of differences in the predictive capacities of animal models in biomedicine. They make a compelling case that the role of animal models in the epidemiological transition is overstated, to the extent that animal studies may actually lead 'research' astray. Because the evidentiary benefits of modelling practices are questionable and by their account rarely useful to the progress of medicine, the traditional utilitarian justification of the use of animals in biomedical experimentation is undermined.

It does not take too much effort to find an example of the problems of extrapolation identified by Lafollete and Shanks. The case of TG 1412 is an excellent example, not least because it is also illustrative of a number of features of model-based science. In 2006 eight subjects were enrolled in a phase 1 clinical trial of the compound, which, as mandated by the Declaration of Helsinki, had been tested on two different animal models producing no reaction in mice and a mild lymphadenopathy in chimpanzees[7]. Six participants of this first-in-human trial were given the compound in quick succession (two of the eight participants were controls). All participants given the substance rapidly developed a severe and life-threatening immunological reaction, later described as a cytokine storm. Unfortunately the effects of this were devastating and although all of the effected participants survived, many of them have ongoing health problems. It was later ascertained that TG 1412 binds to a protein unique to humans – which is why it failed to produce a similar reaction during either of the animal studies.

What has become known as the "London trial" garnered worldwide attention and caused significant controversy. Yet the trial did what it was supposed to do – it identified a highly toxic compound before it was given to a larger population of patients. In philosophical terms the problem was not the model description (what we know about chimpanzees) – the problem was the incomplete description of the target system (in this case humans). For LaFollette and Shanks[8] cases like this exemplify two central problems for the use of animal models in biomedicine. The first is what they call the extrapolator's circle – which is the problem of how we can acquire additional information from a model given the limitations on what we can know about the model target. What this means, in other words, is we can never know the limitations of the model unless we test its description against the target, and our target description is always incomplete. The second problem is how can modellers justify and explain the presence of causally relevant dis-analogies between the model and the target system. Building on the conundrum presented by the incomplete description of the model target, the second problem asks modellers to provide grounds for claims that a model is predictive, which of course they cannot, given that they cannot

be sure that the model will respond in the same manner as the target system until it is actually tested on this system.

In light of historical cases such as the above, LaFollette and Shanks[9] constructed a two-part taxonomy to account for differences in the predictive capacities of animal models in biomedicine. By their reckoning models can be classified either as CAMs (Causal analogue models) or HAMs (Hypothetical analogue models). CAMs are a completely predictive model. They can predict effects of causes and causes of effects. In comparison to CAMS - HAMS are just heuristic devices. In no way predictive, HAMs are only useful to explore ideas and generate new hypotheses. Because they are predictive, CAMS are defined by strict requirements: there can be no causally relevant dis-analogies between the model and the model target. The presence of causally relevant dis-analogies exposes the experimenter to what they call the "modeller's functional fallacy". They describe this through a non-biological example - just a digital clock and a sundial both function to tell the time, the mechanisms that perform this function are completely dis-analogous – each will respond very differently to the absence of light or a pulse of electromagnetic radiation. Even though a digital clock and sundial have the same function – dis-analogies in their underlying mechanisms mean they are extremely poor models of each other. Even as many mechanisms are shared across species boundaries as a consequence of a shared evolutionary history, it is also the case that identical functions in animals can also be underpinned by different mechanisms – and these differences become more likely in complex higher order functions or the further the model and the target are separated on the phylogenic tree. So it is fallacious to assume that similar functions in different organisms will respond the same way to a specific stimulus such that we can make any useful predictions.

Assessing the HAMs / CAMs taxonomy

At first LaFollette and Shanks account looks difficult to refute philosophically. Indeed there is much to commend in L & S carefully articulated argument. But they treat predictive capacity as an ideal state – rather than a relative measure. In this regard the most successful attempt by a philosopher of science to reject this account is from Daniel Steel[10] who makes a case that the strength of extrapolations rely upon the strength of similarities between causal capacities rather than homologous mechanisms. And yet examples such as the TG1412 case indicate that most of the public and many scientists forget that any model by definition has a less than perfect resemblance relation to the target, and its theoretical utility is dependent upon the intentions and assumptions of the modeller. The inadequacy of the target description means that there is always a possibility of a causally relevant dis-analogy that will have consequences for the adequacy of any models function. In many ways the CAMs / HAMs taxonomy misrepresents how models are used in biomedicine to construct theories – and thereby promote courses of action.

Attempts at classification are not neutral, but can be better or worse. Classification systems are by their very nature political, they codify distinctions and similarities.[11] Even as the CAMs/HAMs distinction opened up debate upon the evidentiary value of animal experimentation for human benefit – it also provides compelling support for LaFollette and Shanks' ethical argument. And yet, empirically at least, the distinction does not deal with a number of other factors in experimental practice and design that can confound the predictive capacity of animal studies. Analyses of biomedical practices here are a number of other shortcomings with animal experimentation that affect the outcome of animal experiments including the practice of multiple hypothesis testing and a lack of randomization at allocation or outcome assessment which produces optimism bias.[12,13] Aside from these issues, it is possible to formulate a number of other non-empirical objections to the HAMS / CAMS taxonomy.[14]

First – the HAMS / CAMS taxonomy creates a near empty idealised class and therefore the opportunity for some sort of middle ground between researchers and those who question the scientific and ethical validity of modelling practices. And yet even LaFollette and Shanks acknowledge that for various genetic dietary and cultural reasons humans may not be CAMs for other humans. They also acknowledge that HAMs have some value but this admission is subsumed under the weight of their other causally-related philosophical arguments about the nature of evidence. This means that CAMs are portrayed as the 'gold standard' and anything that falls short is an inferior model. It seems that rather than maintaining some reflexivity within the construction and transition between their evidentiary and ethical positions, LaFollette and Shanks have focussed on overarching goals and ignored practices – what animal-based researchers are actually "doing". The consequences of L & S's approach to this issue also seem to mirror sociological debates on the role abstraction, expertise, and tacit and semantic knowledge in the scientific enterprise. Other philosophical attempts at describing modelling do not come close to the hard predictive determinism of LaFollette and Shanks description[1,2,4] - which leads to the second objection.

Second - dividing animal experimentation with the HAMs / CAMs distinction suggests animals are deemed to belong to just one of two camps, more likely the former (HAMs). Once such a determination is made this is where the model belongs and stays. Yet a specific model might be used to observe a phenomenon in one context and employed to test a plausible hypothesis in another. Both of these experiments may, or may not, have relevance to or inform the conduct and evidentiary value of the other. Rather than conforming to innate teleology scientific research has both predicted and unpredicted consequences. To attempt to pigeon hole a model for all time based on how it performs or does work in one context seems arbitrary and unnecessarily limiting. Hence, once again, it is arguable that LaFollette and Shanks' taxonomy belies the nature of the practice of biomedical experimentation and the nature of most scientific investigations. Biomedical models become valuable through the gradual accretion of species-specific and comparative knowledge. During their development, at various times, the relevant properties of the model and humans are sometimes causally and functionally homologous and at other times have been dis-analogous. Hence even if we were to accept Lafollette & Shanks taxonomy, models that have anything like the predictive capacity of a CAM must be discovered and elucidated using a variety of experimental and clinico-pathological processes and comparisons.

Finally – LaFollette and Shanks have misconstrued the nature and practice of model-based science. Davis Baird, a philosopher of instruments, provides a functionalist definition of models as knowledge creating things that do three types of work: they can represent something (ball and stick model); they can enact something (a biological function); or they can work as a hybrid between these two functions (for example a thermometer). Given the nature of current biomedical practices the instrumental description of modelling in biomedicine seems appropriate because rather than trying to attain idealised goals it acknowledge that models embody different types of knowledge production processes which are built upon a set of agreed theoretical assumptions. Mirroring the idea that models are types of knowledge creating things that do work the 'Modeller's taxonomy' I present is a more complex in that it employs another dimension of differentiation than HAMS / CAMS distinction – being comprised of two overlapping systems of differentiation: purpose and similitude. The alternate taxonomy reflects the nature of model-based science in that does not create an idealised empty class or assume an innate teleology. And more importantly, it relates to the construction and evidentiary fluidity of modelling practices.

Categories of Purpose:

Exploratory models form the largest and most general taxon of animal models. The purpose of these models is to serve the open ended goal of investigating and understanding normal or abnormal biology in terms of development and or function. They are used to discern and then manipulate biological mechanisms in order to generate hypotheses that can be tested. The type of knowledge creating work performed is as an instrument that creates novel phenomena.

Explanatory Models are a representative system that is comprised of either an isolated specific mechanism or is judged to reliably represent the complexity of multiple interacting mechanisms. The knowledge creating work performed by explanatory models is as a representative instrument.

Predictive Models are usually explanatory models subjected to quantified or qualified interference or disruption of function. In this type of model a predictable normal or abnormal biological mechanism is tinkered with to allow researchers to infer how this mechanism might react to a specific interaction with another entity or within other contexts, organisms or environments. As knowledge creating workers or things, these models are hybrids that create phenomena and then allow their measurement. Given the goals of biomedicine – predictive models are a sought after commodity.

Categories of Similitude

Homologous models – in biomedicine, homologous models are those in which aetiology, symptoms and outcome of the animal-model duplicates those of the human disorder. Theoretically a homologous model allows all aspects of a mechanism or disorder to be studied, i.e. interactions, mechanism and predictions.

Isomorphic models resemble the human disorder, but are artificially produced in the laboratory in a way that does not reflect normal human aetiology. Therefore the phenomena being used to predict the response in the target system in isomorphic models can be causally un-related. Therefore isomorphic model only allow the study of certain carefully selected mechanisms and predictions.

Partial models are neither homologous nor isomorphic but allow some isolated aspect of a biological mechanism to be studied and perhaps to generate further hypotheses.

Each of these types of models can then be evaluated on the basis of their *fidelity* and discriminating ability. The fidelity of a model described its similarity of structure to the target system. The discriminating ability of a model is a measure of the similarity of response between the model and the target system. Both qualities are highly relevant to a models predictive capacity, and models that simultaneously embody both are incredibly rare. Because biomedical researchers are interested in response they tend to put a greater weight on the *discriminating ability* of a model – and as LaFollette and Shanks highlight, this cannot be assessed until a phase 1 clinical trial. In fact, it is the unreliability of predictive models as a mechanism to translate pharmacological innovations to human clinical testing or correspond to the multiplicity and co-morbidity of disease expression in human populations, which comprises the key evidence that supports LaFollette and Shanks' argument. However, this does not mean that the HAMs / CAMs distinction is sufficiently robust to defend the type of ethical argument that LaFollette and Shanks' want to run, that collapses any ethical concerns into questions about evidence.

Advantages of the Modeller's Taxonomy

Ethnographic and socio-historical examinations of the natural sciences demonstrate that many developments in scientific theory and practice are the products of the instrumentalization' of experimental failure. This is an ongoing but essentially unpredictable interaction between model-characterisation and attempts to discern a set of theories that govern the phenomenon being modelled.[15,16] Hence it is arguable that when predictive models fail, they can in turn be converted back into an exploratory model where the mechanism of failure or its biological products becomes the object of further scientific enquiry. The alternate taxonomy presented has several advantages – especially if it is to be used as a means to evaluate specific types of models or animal studies. First it is not 'alien' to biomedical practice and therefore allows a meaningful discourse on the evidentiary validity of specific models. Second it accommodates the fluidity and unpredictability of modelling practices and therefore accounts for the 'instrumentalisation' of failure. Successful models (of any sort) require ongoing refinement of the model description and the model target and the continuous development of analogies between them. Models are part a chain through which knowledge is created, stored and transmitted. Because the evidentiary value of any particular model performing these functions is always underdetermined - the Modeller's taxonomy allows for and defends the clear distinction of ethical and evidentiary questions about animal models

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Changing the attitudes and proficiency of livestock handlers in the meat processing sector through structured training programs.

Clive Richardson
Senior Project Officer, Meat Industry National Training Advisory Council (MINTRAC)

Introduction

This presentation draws on the meat processing industry's experience of delivering competency based training to livestock handlers at slaughtering establishments. The industry has taken a strategic, structured and systematic approach to addressing animal welfare. The industry's strategy has involved research, development of industry animal welfare standards, structured training programs for management and personnel as well as ongoing professional development activities for trainers and regulators. Over the last two years regulatory audits have shown improved compliance with the industry animal welfare standard.

Yet despite these improvements there have been some disappointing and disturbing incidents which have brought the industry unwelcome publicity and indicate that improvements had not been uniform throughout the industry. In response the industry has increased its own efforts at improving animal welfare outcomes by investing more in professional development and regulators have mandated a whole range of training requirements for operators.

Animal welfare training in the meat industry

It is timely therefore to revisit the aims, structure, content and methodology of the meat industry's animal welfare training. The industry's training programs are delivered against a back drop of considerable staff turnover in some plants and a shrinking pool of competent stock handlers and slaughterers to draw on. This in itself creates difficulties in ensuring the competency of operators and these difficulties are compounded by diminishing access to state funded training and the essentially regional nature of the industry.

The industry's operator training programs aim to equip stock handlers and slaughterers with the skills and knowledge necessary to comply with the relevant work instructions, SOPs and company policies. Likewise, manager/supervisor training aims to equip staff with the ability to define good animal welfare outcomes and what impacts on animal welfare.
However, the research and the industry's own experience indicate that one of the most critical aspects of these training programs is the impact they have on staff and operator attitudes. Training has to reinforce positive attitudes to livestock and the importance of good animal welfare outcomes if the industry is to achieve long term compliance with the performance indicators that our customers and the community expect.

The industry's challenge then is to deliver training programs that result not only in operator competency but also in workplace attitudes that enable sustainable animal welfare outcomes.

Introduction

The Australian meat processing industry has taken a strategic, structured and systematic approach to addressing animal welfare. The industry's strategy has involved

- research into current practices and compliance
- development of industry animal welfare standards
- structured training programs for management and personnel
- ongoing professional development activities for trainers and regulators.

As a consequence, regulatory and commercial audits over the last two years have shown improved compliance with the industry animal welfare standard and regulatory requirements.

Animal welfare outcomes at meat processing plants are principally a function of the quality of the livestock handling in lairage and the effectiveness of the stunning and slaughtering process.

In this paper I will be focusing on the industry's efforts at developing and ensuring the competency of livestock handlers and monitoring the animal welfare outcomes achieved in lairage (ie the paddocks, yards, laneways and races used to hold and process livestock).

Drivers for improving animal welfare outcomes

Firstly I need to make it clear that in this paper when I refer to animal welfare initiatives I am not referring to just eliminating overt acts of cruelty. Such acts have been illegal and not acceptable behaviour in abattoirs for nearly a century. In addition the issue of cruelty has been systematically dealt with in training materials for the last 50 years.

Today the industry's training goal is to have workers and managers adopt positive / best practice stock handling and slaughtering techniques that optimise the animal welfare outcomes and minimise the pain and stress experienced by livestock at processing plants.

There are some very clear drivers for the industry to focus on the animal welfare outcomes at plants. There are several principle reasons why animals should be handled humanely at slaughtering plants:

- product quality
- product safety
- legal requirements
- customer expectations
- consumer expectations
- company profitability
- ethical reasons.

Product quality

Inhumane handling that stresses animals can result in an inferior meat product. Pale soft exudative pork and dark cutting beef are a direct result of stress prior to slaughter. In addition this meat is usually tougher.

Product safety

Stress of livestock can also result in a weakened immune system that can show up as a growth

of gut bacteria such as *Salmonella* and *E. coli*. These bacteria are potential food poisoning agents or pathogens and the risk of potentially dangerous contamination during dressing is greatly increased. Likewise stressed stock produce meat with a higher pH and this can result in a shorter shelf life for the product.

Legal requirement

Animal protection and its enforcement is a legislated requirement of state and territory governments. Ensuring the welfare of animals in lairage at an abattoir is the responsibility of all those working with animals. Failure to treat and manage these animals properly is against the law and each state has specific legislation dealing with the prevention of cruelty to animals.

In addition the registration/licensing of any particular abattoir is dependent on compliance with both this legislation and for export works of the Australian Meat Industry Council's (AMIC) National *Animal Welfare Standards*. Standards are currently being developed to define minimum animal welfare regulatory requirements at all slaughtering plants.

Failure to treat animals properly can cause a meat processing plant to be fined, lose its customers and/or its registration. Workers also have responsibilities and they can be dismissed for not following the company's animal welfare practice requirements. In addition, they can be fined or jailed for acts of cruelty.

Customer expectations

Customers such as the major retail chains and fast food outlets are becoming increasingly concerned about the animal welfare aspects of meat production. This is because adverse consumer perceptions can impinge on their sales of meat. For these reasons the workplace animal welfare SOPs and the relevant work instructions are written to incorporate all of the customers' requirements. These customer requirements are built into the Australian Meat Industry Council's (AMIC) *National Animal Welfare Standards* and the assurance schemes such as those by the British Retail Consortium. Animal Welfare Assurance Schemes such as Freedom Foods are also used by food processors to differentiate between products.

Countries importing our meat are also increasingly insistent on good animal welfare practices at livestock processing plants. A recently implemented EU regulation requires that all plants exporting to the EU ensure

- all stock handlers and slaughterers are competent and complete accredited training programs
- all plants have an animal welfare officer responsible for managing animal welfare on the plant.

Company profitability

There is a direct relationship between animal welfare and the profits that a processing plant makes. Livestock that is poorly handled in the yards:

- gets injured more often causing bruising and therefore decreases yield and the value of the carcase
- is more stressed and this results in a poorer eating quality of the meat
- results in hides and pelts being damaged and reduces their market value

- are stressed, more dangerous and cause more injury to other animals and stock handling staff.

Ethical reasons

What society considers right and wrong is changing all the time and animal handling practices that were considered acceptable twenty-five years ago are no longer acceptable to society as a whole. The infliction of unnecessary stress and pain to animals is now less acceptable to society and hence the regulators and the community have high expectations of slaughtering establishments. As a consequence the industry needs to demonstrate that it has measures in place to limit this pain and stress if it is to be regarded as ethical.

Yet despite the motivation and efforts the industry has made to date there have still been some disappointing, disturbing but isolated incidents which have brought the industry unwelcome publicity and indicate that improvements have not been uniform throughout the industry.

In response the industry has increased its own efforts at improving animal welfare outcomes by investing more in worker training and the professional development of management. In some jurisdictions both here and overseas regulators have mandated a whole range of training and QA requirements for operators.

Catalysts in the development and uptake of animal welfare/livestock handling training.

There are four important catalysts that have helped direct and define the industry's approach to the aims and content of livestock handling training in Australia.

1. The work undertaken by the Australian Meat Industry Council (AMIC) and Michelle Edge (then with the Vic DPI) in developing national standards for animal welfare in processing plants that documented performance criteria and welfare targets.
2. The research undertaken in Australian plants by Professor Hemsworth and his Melbourne University team that investigated
   - what constitutes positive and negative stock handling behaviours in terms of its impact on livestock stress
   - the standard of stock handling in Australian plants.
3. The research undertaken by Professor Coleman in establishing that stock handler attitudes were an important predictor of stock handler behaviour.
4. The mandating of accredited stock handler, slaughterer and animal welfare officer training by the EU for companies exporting to the EU starting the 1 January 2013.

These first three catalysts have provided industry with an understanding of what has to be done to impact positively on animal welfare outcomes and some objective measurements of assessing welfare on plant. The EU initiative has provided the export sector with the impetus to rigorously embrace and implement accredited training for slaughterers and stock handlers.

Livestock handling training in the meat industry

It is timely therefore to revisit the aims, structure, content and methodology of the meat industry's livestock handling training. The industry's accredited training programs are delivered against a back drop of considerable staff turnover in some plants and a shrinking pool of competent stock handlers and slaughterers to draw on. This in itself creates difficulties in ensuring the competency of operators and these difficulties are compounded by

- diminishing access to state funded training
- the essentially regional nature of the industry.

The industry's operator training programs aim to equip stock handlers and slaughterers with the skills and knowledge necessary to comply with the relevant work instructions, SOPs and company policies. This compliance with regulations, policies and procedures as well as attaining some objective measures of good stock handling is how the industry assesses and measures competency.

Depending on their duties employees receive training in a core stock handling unit and then task specific training such as unloading stock, operating the restrainer etc. The skills component of livestock handling and the demonstration of competency in the workplace over a period of time is a vital component of the training. Stock handling skills are not innate and plants have to mentor and tutor the increasing number of employees who have had no prior stock handling experience for their own safety and the welfare of the livestock.

These training programs also focus on delivering and assessing a knowledge component relating to animal behaviour, stock stressors as well as regulatory and customer requirements.

Likewise the Animal Welfare Officer training program for managers, supervisors and QA personnel aims to equip staff with

- the ability to define good animal welfare outcomes
- identify what impacts on animal welfare
- the systems to ensure compliance with regulatory and customer requirements.

However, the research and the industry's own experience indicate that one of the most critical aspects of competency is the attitude that stock handlers bring to the job. Training has to reinforce positive attitudes to livestock and the importance of good animal welfare outcomes if the industry is to achieve long term compliance with the performance indicators that our customers and the community expect.

The industry's challenge then is to deliver training programs that result not only in operator competency but also in workplace attitudes that enable sustainable animal welfare outcomes.

Impacting on attitudes in the workplace.

If we regard attitudes as beliefs we hold about a particular issue, then shaping attitudes becomes critical to modifying and reinforcing behaviours. However we develop attitudes in a number of different ways in response to a whole range of stimuli and information and this can be problematic for training. In this instance we are looking to modify worker attitudes, specifically to get stock handler compliance with workplace, customer and regulatory requirements.

Regardless of what behaviours one is trying to influence there seems to be three broad attitudinal determinants that drive behaviour. These three drivers can be broadly described as

- compliance attitudes i.e. what do I have to do to comply with to avoid sanctions
- normal attitudes i.e. attitudes that are common round here and which if held, enable me to fit in
- intellect based attitudes i.e. attitudes based on an understanding of the situation and the logical conclusions that can be drawn.

These attitudinal determinants seem to be evolutionary and apply to society, organisations and individuals. But in this case let us just look at how this works in the meat industry at a business and individual level.

Compliance

Whenever changes in behaviour are required the industry is usually responding to a sanction or a potential sanction from regulators or customers. Let us call this the **compliance motivator or attitude**.

This initial driver is usually accompanied by a specific change of regulation or customer specification and is translated into changes to company policies and procedures. This is usually initially communicated to workers and staff in terms of "thou shalt" if "thou" does not this is what is going to happen.

The sanctions for the business might take the following forms:

- loss of business
- fines
- corrective action requests
- increased regulatory monitoring
- loss of registration.

The sanctions for the individual might take the following forms:

- workplace discipline procedures
- demotion
- loss of job
- legal action/fines/jail.

Normal

For the industry and in the workplace another powerful driver of attitudes is the perception of the "normal" and when identified this increases company and individual willingness to adopt particular practices. In these instances adoption of practices is accelerated or reinforced by the fact that "everybody" else is doing it and the majority of folks do not want to stand out from the crowd. Let us call this the **"normal" motivator**.

Intellect

Lastly there is an intellectual acceptance of the reasons for change; this acceptance motivates the adoption of new practices and reshapes attitudes. In this instance the company or individual

embraces the reasoning behind the change and this is or becomes the primary motivator for the adoption of new practices.

The industry therefore seeks to bring logic to the design of the attitudinal aspects of the stock handling training program and does this by addressing the forces that mould our work place attitudes seeking to influence workplace attitudes through :

- the design of workplace QA systems and assessment of worker competency
- outlining the nature of regulatory and customer requirements
- providing role models for best practice
- explaining the science underpinning best practice.

Shaping training programs to address the determinants of worker attitudes

The content of the stock handling courses is therefore used and designed to address these aspects of the development of workplace attitudes. Trainers are constantly reminding trainees of why good stock handling is important and thus shaping their attitudes on all three levels.

Modifying compliance based attitudes

There is a strong emphasis in the course content on the serious nature of the consequences for the individual, the business and the industry if regulatory and commercial requirements are not complied with. Individuals have been fined heavily, plants have been shut, customers have been lost and the volume of red meat sales decreased because of an incident where there was a failure to comply with animal welfare requirements. This is a vitally important issue for the industry and employees must understand that there is very little tolerance for workers who fail to comply with company and regulatory requirements.

The level of official monitoring of individual behaviour is also explained to stock handlers as is the ever present possibility of a third party filming without the company's knowledge. In most sites, slaughtering is monitored daily and livestock handling once a week by company QA staff. In export plants there is a full time on-plant government veterinary presence monitoring livestock handling. In many plants this is supplemented by CCTV of lairage and slaughtering areas which can be viewed by managers and QA staff at any time.

In addition all plants have regular regulatory audits that include the review of livestock handling practices and procedures. The majority of larger companies are also subject to third party audits as part of the maintenance of quality systems to meet corporate customer specifications.

Employee knowledge of the nature and importance of regulatory and corporate requirements and awareness of the level of monitoring and surveillance stock handling receives has helped reinforce the importance of this issue with both stock handlers and management.

Modifying attitudes based on what is "normal"

When promoting best practice in stock handling which involves low stress techniques (such as noise and contact reduction) there is often a resistance built on the rationale: "that is not the way we do things round here" and "it is not normal practice here".

What the industry has attempted to do to address this is to redefine what normal looks like and what competent or professional looks like. This is not easy but is vital for sustainable change. The initial strategy is to roll out training using preeminent and high profile trainers and advocates. The initial programs are run with trainers, supervisors and industry "champions". These initial deliveries are very intensive and quite challenging for some. This initial phase of the roll out is then reinforced with plant visits and the development of plant by plant strategies to train and assess stock handlers. Industry has funded this approach and now hundreds of animal welfare officers and stock handlers have been trained in this way.

The adoption of standardised assessment tools for competency which detail or checklist common measures of good stock handling are critical to this approach. With management support, the assessment tools help to quickly redefine what is acceptable, what is normal, what is competency and what good stock handling looks like.

Intellect

Undoubtedly at management level at least, an intellectual "buy in" is critical to maintaining good standards of stock handling because without this management commitment

- workers/supervisors lose interest in good stock handling because it is not valued
- monitoring results that record poor stock handling and slaughtering procedures go unaddressed
- trends are ignored until critical incidents occur
- training is undervalued and under resourced.

However buy in from the majority of workers at this level of attitudinal development is important and should not be ignored because ongoing changes to behaviour are most effective when supported by "peer pressure". This pressure exerted by fellow stock handlers can be most effective when supported by logical arguments as well as the usual self interest arguments.

Equally with high staff turnover, the rationale for why we maintain high standards of stock handling can easily be lost when the only motivation is to avoid "the sack". This necessity of having workers engage at higher levels of motivation and attitude also links to developing a thinking and problem solving culture in the work place where employees are encouraged to identify problems and suggest solutions.

Conclusion

In developing stock handling training programs the industry has sought to address the range of attitudes that workers and supervisors bring to the workplace. At any one time and with any one person it is necessary to engage with the nature and type of attitude that they have to the job. People's attitudes tend not to be static and may evolve over a period as a workplace's "norm" changes and as they reflect on new information relating to their job.

Just like in the meat processing industry, researchers working with animals may be closely supervised at some stages and working alone at others, so it is their own attitudes and beliefs that will determine how they care for their animals. This means that engendering the right attitude from the start of their career is essential.

Rural Youth Cattle Enrichment Program

- *STRATEGIC PARTNERSHIP FOR EDUCATION*

Tony Butler
RYCE Coordinator Tumut High School NSW
NSW Department of Education Communities

A community partnership was developed with Tumut High School in 1995, to engage local cattle producers, societies, parents, schools and students, industry representatives and local businesses.
The partnership's aim is to impart industry knowledge, skills and experiences in the cattle industry and to address the current shortage of industry skills within the agriculture sector.
In 2012, Tumut High School's community partnership was the national winner of National Australia Bank Schools First Impact Awards. The $200,000 award is for the development and expansion of the school/community partnership and improves student educational outcomes. The Rural Youth Cattle Enrichment Inc. (RYCE) was established to take the program and students to a new level within the cattle industry.
Tumut High School is a comprehensive secondary school in the rural town of Tumut on the southwest slopes of New South Wales and caters for 560 students from Year 7 to 12.
The school identified the need to provide opportunities for students to develop an interest in an agriculture career. The school recognised the significant gap in education, the level of agricultural skills and the lack of employment opportunities for children who wanted to stay in a rural community.
The development of RYCE, with the support and input of its partners, Rising Sun Rural and Weemaru Murray Grey Stud, addresses the current shortage of industry skills within the agriculture sector.
Since 1995, the success of the program has been demonstrated by the creation of 2476 competitive participant positions through local, national show and sales competitions. Participants have competed in cattle parading, cattle junior judging, national sales and breed society workshops. **The increased responsibility that the students demonstrate when showing cattle assists in the development of team work, confidence, public speaking skills and work ethics. This also increases self-esteem and self-discipline.**
The program has provided opportunities to enrich the lives of disadvantaged students and has motivated students who have been previously disengaged. The school's profile has been lifted and broadened in local and wider communities and the media attention, which has focused on the school and the cattle program, has created an awareness of and importance of the agriculture curriculum at the school.
The RYCE program has demonstrated the importance of an educational program using animals as a vehicle in developing student learning outcomes. The delivery mode of the RYCE program supports the need for the program to provide an opportunity for students to experience rural life in a positive agricultural setting.
The cattle program provides an opportunity for students to be re-focused on the animal, to provide for its needs and quality of life, be aware of its surroundings, treat animals with compassion and respect. It also helps students understand and implement 'best practice' and learn about the science of animals. Students working with cattle learn the science of animal welfare, animal behaviour and ways to communicate with livestock.
The animal and teenager work in equilibrium. This creates an atmosphere where students learn the values of respect, not only for the animal but for each other; the acceptance of responsibility to themselves, to others and the animal. Students develop life skills of honesty, trustworthiness and integrity while working with animals. These values permeate through to their education in other subject areas and their lives.

Introduction:

A community partnership was developed with Tumut High School in 1995, to engage local cattle producers, societies, parents, schools and students, industry representatives and local businesses. The partnership's aim is to impart industry knowledge, skills and experiences in the cattle industry and to address the current shortage of industry skills within the agriculture sector.
In 2012, Tumut High School's community partnership was the national winner of National Australia Bank Schools First Impact Awards. The $200,000 award is for the development and expansion of the school community partnership and improves student educational outcomes. RYCE was established to take the program and students to a new level within the cattle industry.

The School:

Tumut High School is a comprehensive secondary school in the rural town of Tumut on the southwest slopes of New South Wales and caters for 560 students from Year 7 to 12. The students come from within the town and from surrounding localities, including Adelong, Talbingo, Brungle, Bondo and Adjungbilly. Students have access to a well-rounded education that values and supports the intellectual, creative, physical, social and emotional development of each student by providing them with the knowledge, understanding, skills and values for productive and rewarding lives. Tumut High School provides many opportunities for students to develop a range of skills through a variety of quality educational activities, including sport, rural fire cadets, outdoor education, academic excursions, cattle parading and gifted and talented activities.

The Need:

The area surrounding Tumut has experienced a decline in skilled rural labour, professional agricultural expertise and agri-science and the school was aware of the absence of relevant rural career opportunities for local students. The school identified the need to provide opportunities for students to develop an interest in an agriculture career.

Bringing a Partner on Board:

The school wanted to open up possibilities for students in part time rural work, to improve and develop the practical skills and knowledge of students in the rural sector and to promote industry confidence through the demonstration of skills to prospective employers.

The school formed partnerships with organisations in the local community to address fundamental socio-economic deficiencies in the rural sector. Partnerships were formed with Rising Sun Rural and Weemaru Murray Grey Stud to create RYCE.

The school recognised the significant gap in education, the level of agricultural skills and the lack of employment opportunities for children who wanted to stay in a rural community. The development of the RYCE Program provided an opportunity for participants to experience rural life in a positive agricultural industry setting. RYCE, with the support and input of its partners, addresses the current shortage of industry skills within the agriculture sector.

The Partnership:

The partners are involved at all stages of the program and share resources and expertise.

The manager of Rising Sun Rural has worked in the cattle industry for 25 years, specialising in cattle selection, marketing, breeding, conditioning, extensive showing and judging at national levels. This partner brings skills and knowledge in rural consultancy and all aspects of cattle husbandry, as well as industry level training skills.

Weemaru Murray Grey Stud is an operational cattle stud in the local area. The owners have had extensive experience in cattle selection, breeding and showing. The Stud provides resources in the form of stock and equipment to the program, as well as expertise in cattle husbandry. Both partners provide transport, stock, feed, land and business advice.

Students participate at local and metropolitan shows and are thoroughly engaged in rural work, such as cattle management, hay carting, collection and storage of stock feed, preparation of stock for shows and the 'breaking in' of cattle.

There is a weekly cattle management program and the students are given the chance to be involved in public speaking.

Since 1995, the success of the program has been demonstrated by the creation of 2476 competitive participant positions through local, national Show and sales competitions. Participants have competed in cattle parading, cattle junior judging, national sales and breed society workshops.

Benefits of the Partnership:

There have been many individual achievements and awards won by the school but the success can also be measured by the increasing number of students who **have been inspired by the program and by those who have gained the confidence to speak publicly to their peers and when cattle judging.**

The increased responsibility that the students have to take on when showing the cattle develops team work, increases self-esteem and self-discipline. The program has provided opportunities to enrich the lives of disadvantaged students and has motivated students who have been previously disengaged.

The school's profile has been lifted and broadened in local and wider communities and the media attention which has focused on the school and the cattle program, has created an awareness of and importance of the agriculture curriculum at the school.

There have been improved outcomes for students in their increased inter personal skills such as confidence, team work, public speaking, self-esteem and work ethic. The number of students attending local and national shows in cattle competitions has increased and there is improved engagement and increased involvement in the program.

The partners have gained greater recognition and they have, among the many things that they do, been involved in committee meetings, established the RYCE Incorporation, developed the Charolais stud and contributed to the Community Festival Day. They have formulated a business and vision plan for the program, organised cattle workshops, and shown the students artificial insemination of cattle and cattle disease testing procedures. RYCE have purchased livestock for the program, developed the partnership by involving additional community members, including Visy Industries.

Over the many years the partnership has been operating, teachers have witnessed an improvement in not just student educational outcomes, but personal, emotional and social skills. There has been an improvement in students' self-confidence by working as a team, taking on individual tasks and working at the Royal Show under the guidance of cattle stud managers.

The educational outcomes can be measured by the improved performance in a range of subject areas through the demonstration of experience, knowledge and understanding.

Partnership for Education:

The RYCE program, has demonstrated the importance of an educational program using animals as a vehicle in developing student learning outcomes.

The delivery mode of the RYCE program supports the need for the program to provide an opportunity for students to experience rural life in a positive agricultural setting. The program is based on rural properties in close proximity to the school. This rural setting provides students with an authentic opportunity to be engaged and enjoy the handling of cattle in an environment that is safe and ideal for maximising student learning.

The program caters for students from year 7 to 11 from farm and non-farming background. It is this 'rural' classroom which caters for students to develop team work, confidence, and self-esteem and demonstrate students as educators.

Partnership for Education:

The members of the partnership, between the school and community have ensured that the RYCE program has a vision plan which is both student centred and focused on educational

outcomes. A business plan complements the RYCE vision and this ensures the program is sustainable.

Adolescent students can be challenging. The cattle program provides an opportunity for students to be re-focused on the animal, to provide for its needs and quality of life, be aware of its surroundings, treat animals with compassion and respect; understand and implement 'best practice' and learn about the science of animals.

Students working with cattle learn the science of animal welfare, animal behaviour and the ways to communicate with livestock.

Specifically students learn about;

A. **Animal Welfare.**

The five freedoms;

1. **hunger, thirst, malnutrition**
2. **fear and distress**
3. **physical and thermal discomfort**
4. **pain, injury and disease**
5. **expression of normal behaviour**

B. **Animal Behaviour.**

1. **Mob structure: follow each other**
2. **Flight Zones**
3. **Vision**

C. **Communication with Livestock.**

1. **Position**
2. **Pressure**
3. **Movement: pressure/release**

"School professional have linked the benefits of animal assisted therapy to a classroom setting with a belief that animals can provide many educational, emotional and physical benefits to students"

(Seigal 2004)

The animal and teenager work in equilibrium. This creates an atmosphere where students learn the values of respect not only for the animal but for each other; the acceptance of responsibility to themselves, to others and the animal. Students develop life skills of honesty, trustworthiness and integrity while working with animals. These values permeate through to their education in other subject areas and their lives.

Quote:

"It is important to provide the next generation of educationalists with the rural skills, knowledge and opportunities to maintain Australia's reputation as a country that produces clean, healthy, high quality food to world class standards. The RYCE Program, with the support of its community partners, provides the tools for today's rural youth to continue the primary production of food in an efficient, technologically advanced, environmentally aware, sustainable agricultural system."

Tony Butler, RYCE Coordinator, Tumut High School

New approaches to find human disease genes

Greg Neely
Garvan Institute of Medical Research

Research using vertebrate models has drastically improved our understanding and treatment of human disease. DNA sequencing has allowed us to identify over 20,000 genes in the human genome, and researchers are now investigating the various functions of these genes *in vivo*. While rodent models have clear value, issues with cost, breeding time, and ethical concerns limit large scale functional genomic investigation. To circumvent some of these issues, and optimise rapid progress in the discovery of new disease genes, we use high throughput functional screening in the fruit fly Drosophila melanogaster. We apply these techniques, in combination with rodent validation and human association, to rapidly identify novel genes participating in major human diseases.

No manuscript was provided by the authors for this presentation

The MAWA Trust – Developing Alternative Methodologies to Animal Research

Sharyn Watson
Executive Director, The Medical Advances Without Animals Trust (MAWA), Weston Creek, Canberra, ACT

The aim of *The Medical Advances Without Animals Trust (MAWA)* is to advance medical science and improve human health and therapeutic interventions without using animals. The Trust is taking a leading role in replacing animals in medical research in Australia and deliberately fosters dialogue with the scientific research community to discover common ground to achieve its goals. MAWA's Board and Scientific Advisory Panel includes senior scientists, academics and medical consultants. MAWA operates as an independent medical research trust fund which facilitates the development and utilisation of non-animal based experimental methodologies. The Trust provides: research, development and equipment grants; scholarships; bursaries; sponsorships; and funding for a range of other initiatives to further MAWA's goals.

To stimulate greater interest and activity in this regard, MAWA awarded funds to *The Australian National University (ANU)* for two Fellowships to provide scientific leadership in replacement research. A key objective of the partnership between ANU and MAWA is to establish *The Australian Centre for Alternatives to Animal Research (ACAAR)* to encourage and support the development of alternatives across Australia.

The ANU based research program has begun by establishing a bioinformatics research group within *The John Curtin School of Medical Research*, Australia's national medical research institution, and by supporting computational biophysics research projects in the *ANU Research School of Biological Sciences.* The ANU has also been awarded research grants, scholarships and bursaries for other alternatives projects.

MAWA is constantly being approached by animal ethics committee members, scholars, academics, researchers and organisations, for guidance and resources in regard to alternatives. In response MAWA developed an Alternatives Information and Resource Pack which has been found to be of value to its users.

The ANZCCART Conference will provide MAWA with an opportunity to introduce attendees to the Trust's initiatives, and to provide interested participants with an Alternatives Resources Pack.

This paper was not presented at the conference due to ill health.
However, the following information has been supplied by the author

MEDICAL ADVANCES WITHOUT ANIMALS

2013 ANZCCART CONFERENCE
NOVATEL SYDNEY manly pacific 23-24 JULY 2013

This folder has drawn materials from an alternatives resource kit developed (at very short notice) by MAWA for a Victorian BAW training course for animal welfare representatives and lay members of Animal Ethics Committees and animal management officers training. It includes information on MAWA and its initiatives, a journal article and poster on alternatives, examples of replacement research, and resources and information on: journals; websites; links; international organisations promoting alternatives and funding replacement research; 3Rs Centres; search engines; databases; and two step-by-step guides on how to search for alternatives with accompanying work sheets.

ALTERNATIVES INFORMATION AND RESOURCE PACK CONTENTS:

About The MAWA Trust - Many more scholarships and grants have been awarded since this publication

Initiatives for MAWA Funding - Scholarships, Grants, Bursaries, Fellowship, ACAAR etc

MAWA's Awards 2012/2013 - Additional awards for 2013 will be announced in November.

The Australian Centre for Alternatives to Animal Research (ACAAR) - Draft short statement

Alternatives to the Use of Animals for Scientific Purposes - Paper by Dr Simon Bain, Director Research Integrity, ANU, which discusses the situation in Australia and what might be done in the future to promote alternatives.

Non-Animal Methodologies within Biomedical Research and Toxicity Testing
Journal abstract & poster by
Dr Andrew Knight, Fellow of the Oxford Centre for Animal Ethics and Director Animal Consultants International

Dr Hadwen Trust Research Portfolio (UK) - Examples of Replacement Research

ATLA - Journal - Alternatives to Laboratory Animals

(FRAME UK) **ALTEX - Journal - Alternatives to Animal**

Experiments (Europe) **ALTWEB - Website - Alternatives to**

Animal Testing (CAA T USA) **AltTox - Website - Non-**

Animal Methods for Toxicity Testing (USA)

ALTWEB - Links to Resources and Organisations Promoting Alternatives (USA)

NC3Rs - National Centre for the Replacement, Refinement and Reduction of Animals in Research (UK)

CAAT - The Johns Hopkins Centre for Alternatives to Animal Testing (USA)

ICCVAM - Interagency Coordinating Committee on the Validation of Alternative Methods (USA)

ECVAM - European Centre for the Validation of Alternative Methods (Europe)

ZEBET - Centre for Documentation and Evaluation of Alternatives to Animal Experiments (Germany)

Transinsight - Go3R Internet Technology for the Replacement of Animal Experiments (ZEBET Germany)

Two examples of Step-by-Step Guides on How To Search for Alternatives and Accompanying Worksheets:

The University of California Centre for Animal Alternatives (UCCAA) developed 2005 (USA)
The Canadian Council on Animal Care (CCAC) developed 2009 & which draws from the UCCAA version (Canada)

Australian code for the care and use of animals for scientific purposes
Launch of the 8th Edition 2013

Dr Timothy Dyke
Executive Director, Strategic Policy Group
National Health and Medical Research Council

OUTLINE

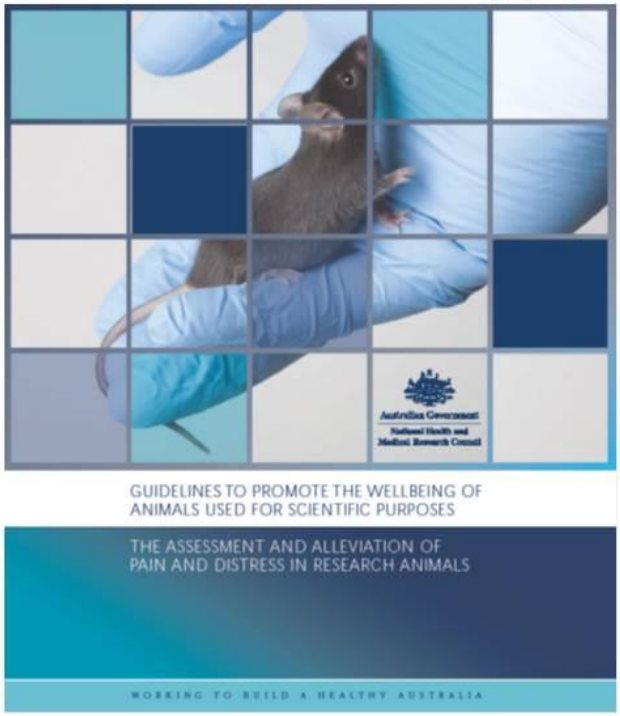
- National research frameworks
- How the 8th edition was developed
- Key issues, changes, areas that are preserved
- New structure and specific sections

The 3 national research standards

National Health and Medical Research Council
Australian Research Council
Universities Australia
CSIRO (Code only)

NHMRC

NHMRC supporting documents



- Policy on the care and use of non-human primates for scientific purposes (Under review)
- Guide to the use of Australian native mammals in biomedical research (Under review)
- Guidelines for the generation, breeding, care and use of genetically modified and cloned animals for scientific purposes
- Guidelines for monoclonal antibody production
- Guidelines on the use of animals for training interventional medical practitioners and demonstrating new medical equipment and techniques
- Guidelines on the care of cats used for scientific purposes
- Guidelines on the care of dogs used for scientific purposes

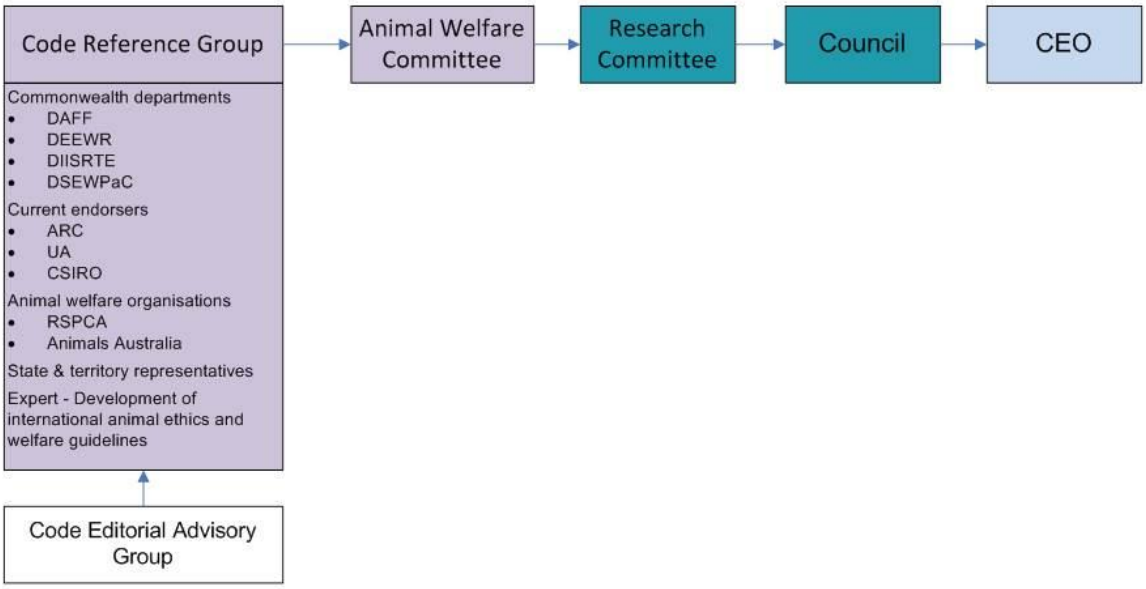
Developing the 8th edition

- NHMRC as a facilitator
- 2009 Jul-Sept: Targeted consultation. 70 submissions.
- 2009-2011 Review of submissions & preparation for public consultation by Code Editorial Advisory Group
- 2011 Oct-Dec: Public consultation. 246 submissions
- 2012-2013 Consideration of submissions & development of 8th edition by Code Reference Group
- 2013 Considered by NHMRC's AWC, Research Committee and Council, and CEO
- 2013 Endorsed by ARC, CSIRO and UA

Stakeholders involved

- Researchers
- Teachers
- Institutions
- AEC members and executive officers
- Veterinarians
- Animal technicians
- Animal facility managers
- Ethics administrators
- Animal welfare officers
- Animal welfare organisations
- State and territory governments
- Commonwealth government departments
- Australian Research Council, Universities Australia, CSIRO
- General community

Stakeholders involved



NHMRC

Key elements of the 8th edition

- Four governing principles for the care and use of animals for scientific purposes, to be applied in all situations
- Constant reference to these principles throughout the document
- Clearer guidance on responsibilities
- Clearer distinction between 'musts' (obligatory) and 'shoulds' (strongly recommended; how a person may meet obligatory requirements)

Key issues raised during development

- Principles-based *vs* detailed guidance
- Use of the terms 'should' and 'must'
- Clearer attribution of responsibilities
- Category E member of AEC
- Role of veterinarians
- Role of person managing and supervising an animal facility
- Definition of 'animal', 'activity' and 'project'
- Managing unexpected adverse events and emergencies
- Managing complaints and non-compliance
- Animals in schools

Important areas that have not changed

- Scope of the Code
- Replacement , reduction and refinement
- Assumption that procedures and conditions that would cause pain and distress in humans cause pain and distress in animals, unless there is evidence to contrary
- Institutional responsibility for compliance
- Membership of an AEC
- Ethical review and approval from an AEC
- Personal responsibility of investigators for an animal throughout the period of use approved by the AEC

Important changes

- Re-structured to reflect governing principles
- 'Must' and 'should' phrases
- *Supporting* animal wellbeing during their care and management, and *safeguarding* animal wellbeing during conduct of procedures
- Independent external review conducted at least every 4 years
- Quorum for AEC decision-making the same as the quorum for the conduct of an AEC meeting
- 'Current best practice' – to provide guidance for evaluation of acceptability of practices. Definition allows for situations where the evidence for current best practice is up-dated, or is not available

Making the Code clearer

- Separation of the governance of an AEC, and the responsibilities of an AEC for ethical review, approval and monitoring
- AEC approval for '*projects*' conducted for a scientific purpose, and '*activities*' associated with the care and management of animals in facilities
- AEC Executive may approve a 'minor amendment'; e.g. change that is not likely to cause harm to the animals, including pain and distress
- All procedures must be performed competently, by a person who is competent or under the direct supervision of a person who is competent
- Situations involving unexpected adverse events, complaints and non-compliance
- 'Teaching' - the care and use of animals for the achievement of educational outcomes in science

New Code structure

- Section 1: Governing principles
- Section 2: Responsibilities
- Section 3: Animal wellbeing
- Section 4: The care and use of animals for the achievement of educational outcomes in science
- Section 5: Complaints and non-compliance
- Section 6: Independent external review of the operation of institutions

Governing principles

- 1.1 Respect for animals must underpin all decisions and actions involving the care and use of animals for scientific purposes.
- 1.2 The care and use of animals for scientific purposes must be subject to ethical review.
- 1.3 A judgement as to whether a proposed use of animals is ethically acceptable must be based on information that demonstrates the principles in Clause 1.1, and must balance whether the potential effects on the wellbeing of the animals involved is justified by the potential benefits.
- 1.4 The obligation to respect animals applies throughout the animal's lifetime during its care and use for scientific purposes.

Governing principle 1.1

Respect for animals is demonstrated by:

- using animals only when it is justified
- supporting the wellbeing of the animals involved
- avoiding or minimising harm, including pain and distress, to those animals
- applying high standards of scientific integrity
- applying Replacement, Reduction and Refinement (the 3Rs) at all stages of animal care and use
- knowing and accepting one's responsibilities.

Responsibilities (Section 2)

- 2.1: Institutions
- 2.2: Institutions – Governance of AECs
- 2.3: AECs
- 2.4: Investigators
- 2.5: Animal carers
- 2.6: Other responsibilities: Institutions, AECs, investigators
  - Use of AECs established by other institutions
  - Investigators without access to an AEC
  - More than one institution and/or AEC
  - Projects conducted in other countries
- 2.7: Institutions – Developing AEC application forms

Animal wellbeing (Section 3)

- Applies to all situations and all species
- 3.1: How to approach supporting and safeguarding the wellbeing of animals
- 3.2: Supporting the wellbeing of animals during their care and management
- 3.3: Safeguarding the wellbeing of animals during the conduct of specific procedures
- 3.4: Provisions for animals at the conclusion of their use

The care and use of animals for the achievement of educational outcomes in science (Section 4)

- Principles that are unique to the teaching situation with reference to other sections
- As with the 7th edition:
  - Teachers are considered 'investigators' under the Code
  - Teaching institutions are considered 'institutions' under the Code

Further information:

- HTML and PDF documents only
  - Capacity to include links to clauses in HTML version in institutional documents and application forms.
- Available from NHMRC website
- Further information: ethics@nhmrc.gov.au

- National research frameworks
- How the 8th edition was developed
- Key issues, changes, areas that are preserved
- New structure and specific sections

Small animal imaging to study cancer models

Peter Croucher
Garvan Institute of Medical Research

A number of cancers either grow directly in bone, including the haematological malignancy, multiple myeloma, or metastasis preferential to bone such as breast or prostate cancers. Once resident in the skeleton these tumours cause devastating bone destruction. There are few approaches to treating tumours once present in bone making them a major cause of morbidity. As a result new approaches to preventing bone metastasis and the development of tumours that grow in bone are urgently required. The interactions between tumour cells and the cells of bone are complex and cannot be modelled *in vitro.* As a result animal models have played a pivotal role in developing new approaches to both treating tumour-induced bone disease and understanding how tumours grow in bone. Critical to the study of tumour-induced bone destruction has been the use of imaging techniques, including radiography and microCT imaging. Techniques such as bioluminescence imaging have been important in identifying tumours growing in bone and measuring tumour burden in bone. In recent years the sensitivity of these techniques has improved, extended to 3-dimensional imaging and linked directly to *in vivo* microCT imaging. This is facilitating the direct visualization of tumours in the skeleton and more accurately measuring tumour burden in bone. Finally, as we start to unravel the importance of the interdependence between tumour cells and the cells of bone new technical developments have been required to visualize these key interactions. This has including *intra-vital*, two photon microscopy. These techniques are having a direct impact on the role of animals in bone metastasis research, particularly by reducing their number and facilitating the study of early events in disease progression. This is already having an impact on our understanding of disease development, but also allowing us to develop new approaches to treatment. Ultimately, we anticipate that this will lead to approaches to prevent the development of bone metastasis entirely.

No manuscript was provided by the authors for this presentation

How anthropomorphic is the end, and will it be humane?

J C Schofield
J & L Consulting, Dunedin, New Zealand

Laboratory animals are used in wide range of studies to investigate biomedical questions. The answers derived from these animals may lead to the development of new therapies, drugs, or prosthetic devices. Despite such advances in knowledge, there is usually a significant cost to the animals involved, in terms of potential pain, distress, suffering and death.

One important strategy which can minimize such adverse effects is the implementation of scientifically and clinically relevant humane endpoints.

This paper will review some commonly utilized endpoints in biomedical science. I hope to convince the conference delegates that: (1) humane endpoints are essential for the conduct of humane science and (2) an anthropomorphic approach is essential for the successful application of humane endpoints.

A key anthropomorphic strategy in this context is to consider palliative care methodologies used to support people during their last stages of a terminal illness. And although the application of such methods are generally not directly applicable to animals in the biomedical research arena, the comparisons which can be drawn are of considerable value and I would argue, serve to strengthen the anthropomorphic approach.

A range of humane endpoints will be discussed to provide information for members of Animal Ethics Committees and animal care technicians.

Introduction

The purpose of this paper is to persuade the reader that an anthropomorphic approach to the use of animals in research, testing and teaching (RTT) has major benefits for those animals and can be applied by any person using animals, regardless of their cultural background.

Anthropomorphism in this context can be defined as attributing human form or emotions to animals. The concept is almost as old as the history of Homo sapiens. One of the oldest archaeological artefacts, which displays this concept, is the Lion- man of Hohlstein-Stadel. It has been carbon dated to approximately 40,000 years old. This early ivory carving of a lion's head on a human body was found in the German Alps in 1939.[1]

In more recent times, much of children's literature in the 19th century was based on many anthropomorphic characters, a few examples include A A Milne's Winnie the Pooh, and the Mad Hatter, Cheshire Cat and White Rabbit of Alice in Wonderland by Lewis Carroll. Walt Disney developed an entertainment industry, initially based on the anthropomorphic exploits of Mickey Mouse, Donald Duck and other members of his imaginary menagerie. His animation techniques gave us visible proof of instant genetic modification in the Pinocchio phenotype with impressive nasal elongation whenever the character told a lie.

It is my belief that an anthropomorphic approach and the timely application of humane endpoints are essential, if animals are to be treated according to humane principles. These two strategies offer a form of welfare insurance for animals used in research. In effect, the animal user imagines them self in the place of the animal. Once this thought experiment is accomplished, the importance and value in considering humane endpoints becomes readily apparent, as the user quickly starts to think of strategies to end the suffering.

This paper is written from the perspective of a laboratory animal veterinarian with more than 30 years' experience in biomedical research working in academia, involved with providing clinical care, training for graduate students and consulting on animal models and study design. Notwithstanding institutional policies and procedures which are directed at the humane care and use of experimental animals, it has been my experience that in a clinical crisis, an individual animal's fate all too often depends on the mind-set and knowledge of the graduate student using it. Poorly trained students usually make poor decisions and even well trained students can lose their sense of perspective when faced with clinical catastrophes.

By using a couple of case studies, I hope to demonstrate the value of these ideas.

Case study 1:

Rat #13 is used for an experiment. It is observed daily and it becomes increasingly sick. It is found dead five days later at the morning room check.

Regrettably such a scenario is all too common in research facilities. It begs several questions; why was its clinical condition not identified and treated? Why was it left to die? Why were humane endpoints not applied to this animal?

In my experience all manner of strange explanations surface when such a death is investigated. Despite an institution having documented procedures and policies for managing adverse events, the sick animal is sometimes at the mercy of inexperienced, and/or emotionally distraught individuals, who fail to apply the correct procedural steps. For example, the laboratory animal technician or the graduate student using the animal may not have identified that there was a clinical problem. Alternatively, the student might have recognized the situation, but failed to act. A strange, but not uncommon reason for inaction is the grim situation in which the student states: *"I had to wait until the supervisor came back from conference leave to check with him first, before I could call the vets and tell them that the animal was sick"*. It's regrettable that priorities could become so confused as to place the welfare of an animal secondary to the controlling influences of a supervisor.

It's interesting to reflect on the history of scientific views in this matter. An anthropomorphic approach to the study of animal behaviour has not always been widely accepted. For example the 'Oxford Companion to animal behaviour in 1987' states*: "One is well advised to study the behaviour rather than attempting to get at any underlying emotion"* Scientists were generally dismissive of others who suggested that human behaviours might explain animal behaviours. But the work of Jane Goodall on chimpanzees and Dian Fossey on gorillas has changed scientific opinion. And the new technologies which allow the brain, both human and animal, to be imaged in real- time are helping us to better understand the mysteries of thought, behaviour and emotion.

Endpoints:

Animal based studies can have several endpoints. The most common is the study endpoint. This is generally a defined period of time by which a test drug is presumed to have had a pharmacological effect. The effect might be measured by test blood, urine or other samples or techniques, either during the study, or at the termination of the study.

Major problems arise for the scientist when animals become clinically ill during the study, because such animals threaten the collection of a full set of data-points, by which the experiment is evaluated. If the experimental group consists of 8 animals and the study duration is 16 weeks, when 3 animals become unexpectedly ill at week 12, important decisions need to be made. Does the scientist allow the 3 sick animals to continue in the study in the hope that all 3 survive to the end? That option raises ethical concerns. Alternatively, does the scientist have the animals treated, in order to restore them to health? That option potentially compromises the research data, because the treatment might invalidate the science.

There is a third option; utilizing humane endpoints.[2] These are criteria, determined beforehand, which are used to judge whether an animal should be treated or euthanased. Examples include:

- 15-20% weight loss compared with controls
- 10% weight loss in 24 hours
- Cachexia (a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat)
- Self-mutilation
- Hypothermia below set point: eg: 32 C
- Skin Tumours reach a maximum size
- Hind limb paralysis in some tumour models
- Inability to rise or walk
- Convulsions
- Moribund condition (dying or in the process of dying)

Case Study #2:

Rat #15 is used for an experiment. It is observed daily and it becomes increasingly sick. It is one of a cohort of 8 animals expected to survive for another 4 weeks until the study endpoint. It is reported by the Laboratory Animal Technician (LAT) who weighs the animal and checks its state of hydration by the skin turgor test (the skin is gently raised and dehydration is determined when the fold remains tented). Simple calculations reveal that #15 has lost more than 18% of its body weight and careful physical examination confirms that it is markedly dehydrated. All other 7 rats in the cohort are increasing in weight and are observed to be bright, alert and responsive. The Animal Ethics Committee- approved protocol for this study specifies a 15% weight loss as a humane endpoint. The team managing the welfare of this cohort comprises the LAT, a graduate student (whose thesis depends on this series of experiments) and her academic supervisor. Despite the supervisor being out of town, the student and LAT decide to euthanase #15 and ask for a post-mortem.

In study #2, the institutional AEC mandated humane endpoint provided animal welfare insurance. The animal met the euthanasia criteria specified in the policy and the policy was implemented. Certainly the statistical power of the study may have been compromised, however, the welfare of the individual animal was protected.

Problems with humane endpoints:

Ideally, endpoints selected should be reliable, readily interpreted and predictive of death. However, some common sense should be used in the application of these humane endpoints. For example, a 10% weight loss in 24 hours might be recovered rapidly; depending on the clinical condition of the animal and the cause of the problem. Occasionally the cause of the dehydration is a mechanical failure of the water delivery system- which can be quickly rectified.

Hypothermia has been effectively used in some influenza murine infectious disease models as an endpoint. Pilot studies are generally used to determine the temperature set point, which is species, strain and pathogen specific. Variables in applying this system include the volume and type of cage bedding used and the methods to measure body temperature.[3]

The moribund condition is readily diagnosed by experienced personnel, but to the novice animal user, the animal may simply appear depressed. Some would argue that animals in a moribund coma are not suffering because they no longer have sensory awareness. And this argument is often used to justify leaving the animal to die. However, based on human palliative care principles, moribund patients cannot be assumed to be lacking in awareness.[4] Therefore when faced with a moribund animal, we should give it the benefit of the doubt and ensure that euthanasia is promptly performed.

The 20% weight loss criteria appear to be somewhat arbitrary. In my clinical experience, animals with such a massive loss appear emaciated with prominent ribs and pelvic bones. They resemble human victims who have suffered concentration camp conditions. The animal's fur coat can often confuse the novice when examining emaciated animals. A number of body scoring systems are available, which provide instruction in observing the physical condition of weight loss subjects. These systems focus on the bony prominences and degree of muscle wasting.[5]

Humane endpoints threaten the collection of research data:

The use of animal models for RTT is fraught with numerous technical challenges, time constraints and financial limitations. In the biomedical field, within universities, the majority of animal usage is performed by graduate students, working under the direction of their academic mentor. The level of supervision can vary considerably and is often inversely proportional to the number of students an academic is required to manage.

Research based on animals is generally regarded as the most expensive form of scientific investigation, because of the high overheads needed to support the infrastructure which provides climate controlled disease-free conditions and Specific Pathogen Free animals.

When unexpected clinical complications arise in the midst of a study, the student is under great pressure. Most studies are well designed and the numbers of animals proposed is generally based on specific statistical advice. In case study #2, the example uses 8 animals per treatment group. We can assume that this figure of eight was derived from statistical calculations; that 6 animals would not give sufficient power for the study and ten or more would be regarded as a waste of animals and money. When a study has multiple treatment groups (for example 50 different treatments) and each is paired against a control group, the size of each group is critically important to ensure that a meaningful result is obtained, while not wasting resources.

The loss of one or two animals per treatment group can threaten the study by compromising the data- set collected. In my experience over several decades, clinical problems with experimental animals typically generate the following different types of responses from students desperate to salvage the impending scientific disaster:

1. *'Please can't you do something to keep rat # 15 alive, so that it makes it to the end of the study'*
2. *'I don't see that this animal is all that bad, why do we need to do anything, it's still moving'*
3. *'Look I can't afford to lose any animals or the data won't be reliable'*
4. *'How come my rats have this problem, the student before me didn't get any sick animals?'*

And the most concerning of all statements from students, the product of a completely different cultural background is: '*I just don't see a problem here, it's only a rat, so it doesn't matter if it's sick, they don't feel pain like we do. I recommend we leave it in the cage and do nothing!'*

Clearly it's one thing to have policies on humane endpoints and quite another to ensure that they are enforced and applied.

To ensure that animal welfare is promoted, institutions should have procedures in place to ensure that every adverse event is formally reported and a system to ensure prompt delivery of adequate veterinary care. In many cases, the most appropriate treatment might be euthanasia.

Anthropomorphism can be the trump card:

When we have empathy for animals in our care, they are more likely to be appropriately managed. This is because the welfare of the animal becomes the priority, instead of data collection.

I have discovered an effective strategy when a student is resisting veterinary advice on humane euthanasia of one of their valuable experimental subjects. I ask the student; '*imagine <u>that was you</u> lying there in a pool of diarrhoea, dehydrated and barely able to move?' 'How would you feel?'* In practice, I have used far more graphic terms than these, but I am sure the reader understands the strategy.

A related technique which may be of value to the reader, is what I could label as 'the sham injection'. When observing a student attempting to inject a mouse with a large 18G needle, (when a smaller 26-27G would be more humane) it has proved very effective to pull from one's pocket, a large 12G needle (with a bore the size of matchstick) and tell the student that what they propose to inject into the mouse, is the equivalent of the 12G into their own arm! And I then proceed to attempt do just that. But stopping short of actual injection. The surprise and shock seems to change students' perceptions of pain.

Even when the student comes from a different cultural background, appealing to their sense of empathy can be remarkably successful. I like to believe that it works as an argument because the student momentarily suspends their attitude that; *'it's only a rat so I don't care about it '*.

The reader might question the notion that a veterinarian would feel the need to debate humane endpoints with resisting students? Why not simply invoke legislative controls and demand that the student comply?

The veterinarian has a key role as an animal welfare advocate and educator. These students are the next generation of scientists and the welfare of the future animals they will inevitably use can be influenced by patterns of behaviour and welfare attitudes they develop as graduates. Far better to change hearts and minds by reasoned anthropomorphics and empathy, than to berate them with legislation. One can always resort to enforced compliance if all else fails.

What can the Animal Ethics Committees do?

Legislation requires AECs to manage an institution's animal care programme. This can be accomplished in many different ways:

1. One of the most effective strategies is to implement an animal welfare insurance policy by well-defined humane endpoints. These should be part of every AEC application form to use animals. A number of internationally accepted endpoints should be included on the form and all applicants should be required to explain in writing how adverse events will be managed.

2. A policy for the mandatory reporting of all adverse events should be implemented.

3. A strategy to provide adequate veterinary care for such event reporting is essential, if welfare is to be promoted.

4. Compliance with humane endpoints should be monitored by regular site visits to laboratories by an agency of the AEC. This will enable the committee to consider whether earlier endpoints might be developed in order to limit animal suffering.

Conclusions:

The anthropomorphic approach in dealing with experimental animals experiencing adverse events, offers another strategy to limit suffering which relies on common sense and human decency. In the absence of any humane endpoints or other controls, it may the only last hope for an animal in desperate need of pain relief or permanent termination of their suffering.

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5. Hickman, D.L., M. Swan. 2010. Use of a body condition score technique to assess health status in a rat model of polycystic kidney disease. J Am Assoc Lab Anim Sci. 49(2):155-9.

The anti-vivisection movement 150 years on:
A tribute to its founder and some thoughts for the future.

Malcolm France
Consultant in laboratory animal management, Sydney.

In 1863 (exactly 150 years ago this year), a prominent English literary journal published an article entitled "The rights of man and the claims of brutes". The article had been prompted by reports of the mistreatment of horses used in veterinary training and was the first public foray by its author, Frances Power Cobbe, into the incipient animal research debate. Cobbe occupied a prominent place in the intellectual life of London in the second half of the 19th Century during which time she used her considerable talents to promote social reform. While she is perhaps more widely remembered for her advocacy of women's rights, she can also be regarded as foremost among those involved in the establishment of an organised opposition to animal research. This presentation (which is based on one presented to the Interational Society for Transgenic Technologies in February 2013) looks at her role in the early anti-vivisection movement and the broader response that followed. It can be seen that much of the polarised debate around animal research we see today has changed surprisingly little in either form or content over the past 150 years. But a more nuanced view is also possible if one reflects on Cobbe's remarkable life and the context to which she was responding. More recently, the cross-disciplinary field of Human Animal Studies has created new opportunities to consider the true complexity of the ethics of animal research by promoting dialogue between the humanities and the sciences. Participation in this process is encouraged and should be seen as an opportunity to work towards common goals and move away from the often simplistic divisions of the past.

I would like to share a story with you today. It's one that covers the events leading up to the world's first law specifically designed to control animal research. But my story is also a tribute to a remarkable person – Frances Power Cobbe – who was closely involved in the events leading up to that legislation and who is often regarded as the founder of organized opposition to animal research – the so-called anti-vivisection movement.

Presenting a tribute to Frances Cobbe I think has a place here for a couple of reasons. Firstly, her public contribution to the animal research debate began exactly 150 years ago. Coinciding as it also does with the release of the new Code, this seems a good milestone to reflect on the legacy of someone so central to the development of animal research regulation. Secondly, I feel that reflecting on Cobbe's life helps put a more human face on the animal research debate and the legitimate personal feelings of those participating in it.

I will conclude the presentation with some thoughts on what I see as an opportunity to progress the debate a little more constructively than has often been the case in the past, based especially on my own positive dialogue with animal advocates over recent years. But first, my tribute.

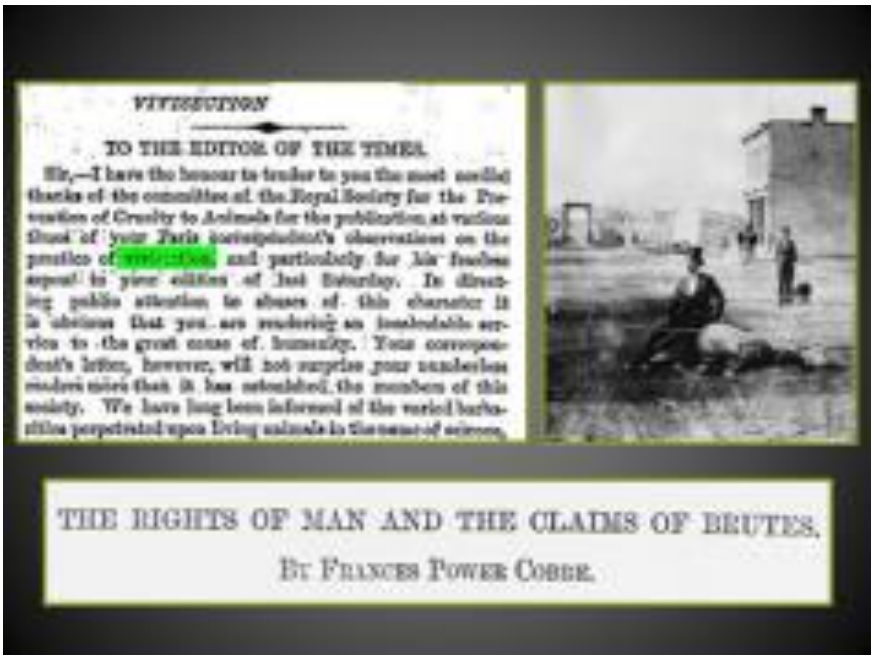
Frances Power Cobbe was born in 1822 into a wealthy Irish family of the landed gentry. A highly sociable person with a powerful intellect, she was home-schooled until the age of 16 then was sent to an expensive finishing school for young ladies. This she regarded as an interruption to her education and as one who reveled in laughter and good food, Cobbe would sometimes find herself at odds with the expectations of Victorian society. I can imagine her views on fashion, for example, would have raised some eyebrows when she asserted that women's clothing should allow "liberty of action to all organs of the body and freedom from pressure".

Today Cobbe might be branded an activist, but such stereotyping would do her an injustice. A contemporary account of a meeting with Cobbe has been left to us by Louisa May Alcott (the author of 'Little Women'). She wrote: "…the door suddenly flew open, and in rolled an immensely stout lady, with skirts kilted up, a cane in her hand, a … green bonnet on her head, and a loud laugh issuing from her lips, … she cast herself upon the sofa, exclaiming breathlessly: '*Me dear creature, if you love me,* [bring me] *a glass of sherry!*'". Not quite the stereotype of an activist.

Having the means to travel, Cobbe embarked on a year-long tour of Europe and the Middle East. Unusually for the day, she chose to travel alone and un-chaperoned. She wrote extensively of her travels including a later reflection that "I rejoice to think that I saw those … wonderful lands of Palestine and Egypt while Cook's tourists were yet unborn…and the solemn gaze of the Sphinx encountered no Golf-games on the desert sands."

She also observed that her travels had greatly expanded her appreciation of the beauty of Nature, the wondrous achievements of human Art and the enormous amount of human good-nature to be found almost everywhere. Again, not exactly the views we might expect from the single-issue activist.

Cobbe eventually settled in London where she became established as a writer with a network of influential friends. In addition to possessing great charm, she was deeply committed to helping the disadvantaged and it was this quality that often saw her as a leader in social reform, especially the feminist movement where her advocacy for women's independence and protection against domestic violence is still highly regarded.


VIVISECTION

TO THE EDITOR OF THE TIMES.

Sir,—I have the honour to tender to you the most cordial thanks of the committee of the Royal Society for the Prevention of Cruelty to Animals for the publication in various times of your Paris correspondent's observations on the practice of vivisection, and particularly for his fearless appeal in your edition of last Saturday. In directing public attention to abuses of this character it is obvious that you are rendering an inestimable service to the great cause of humanity. Your correspondent's letter, however, will not surprise your numberless readers more than it has astonished the members of this society. We have long been informed of the varied barbarities perpetrated upon living animals in the name of science,

THE RIGHTS OF MAN AND THE CLAIMS OF BRUTES.

By Frances Power Cobbe.

But it was in 1863 (exactly 150 years ago) that Cobbe came across a series of newspaper reports on the mistreatment of horses in French veterinary schools. These animals were often old or sick

military horses supplied for use in surgical training. It was reported that the horses underwent numerous procedures without anaesthesia and were then left to die. Cobbe was so angered by these accounts that she published a 12,000 word manifesto called '*The Rights of Man and the Claims of Brutes*' in which she argued that inflicting pain on animals for teaching or research was morally wrong. Interestingly, Cobbe still accepted that the limited use of animals in research was justifiable provided there was adequate pain relief. But as we shall see, her views were to change.

When Cobbe published her treatise in 1863, there was relatively little animal research conducted in Britain. There was even a view shared by Cobbe and the medical press that in contrast to the culture of continental Europe, British science would never widely embrace such ethically contentious activities. Public debate on vivisection was therefore rather sporadic at this time.

In 1873, 10 years after Cobbe's treatise, things started to change. This year saw the publication of the first manual of animal research published in the English language. Entitled 'Handbook for the Physiological Laboratory', its front page declared that it contained "no less than 853 beautifully executed illustrations". The text ran to nearly 600 pages and provided a readily accessible account of contemporary practice. Suddenly, opponents of animal research had comprehensive documentation of what really went on behind laboratory doors – and it hadn't come from infiltration or stealth, it had been placed proudly in the public domain by leaders of the scientific elite.

Barely a year later, the medical establishment again brought controversy on itself over animal use. This time, it led to an escalation which would permanently change the regulatory environment of animal research.

It was now 1874, and the British Medical Association was holding its Annual Conference in the city of Norwich. Among the speakers at the conference was a prominent scientist who was interested in the toxicological effects of alcohol on the central nervous system. In addition to delivering a lecture, arrangements had been made for him to conduct a demonstration in which two dogs would be used to demonstrate the toxic effects of the strong alcoholic drink known as absinthe. This might seem an odd choice, but as always, it must be viewed in historical context. At that time, the abuse of absinthe (also known as 'the green fairy') was a public health issue of growing concern since it had become associated with social disadvantage and its adverse effects included convulsions and hallucinations.

When the demonstration commenced, two dogs (kindly supplied by a local veterinarian) were brought in with their mouths bound and each was tied to a bench by all four legs. Without anaesthetic, an incision was made in the skin of the thigh of the first dog to expose the femoral vein and a volume of plain alcohol given intravenously. As the dog began to struggle, a member of the audience protested at what he regarded as cruelty while another came forward and cut the ropes that tied the dog to the bench. The situation started to escalate but when a vote was held on whether the demonstration should be stopped, the result was strongly in favour of it continuing.

The second dog was therefore injected in a similar fashion but with a quantity of absinthe instead of plain alcohol. This produced convulsions which lasted about 45 minutes. Although this dog recovered, the first dog, which had been in visibly poor health even before the demonstration commenced, went into a coma and died soon afterwards.

News of the incident reached Britain's largest animal welfare organisation, the RSPCA. Founded exactly 50 years earlier, the RSPCA was now a powerful body with sufficient resources to pursue hundreds of investigations into animal cruelty each year. Until now, however, it had not investigated a case of alleged cruelty relating to animal research.

Seeing this as an opportunity to test whether existing laws could be applied to animal research, the RSPCA instigated proceedings against the scientist as well as 4 local doctors who had helped arrange the demonstration. By the time the trial commenced, however, the scientist had returned to his home country so was unable to appear. The defence therefore argued that because the remaining defendants had not actually conducted any procedures on the dogs, they had not committed any act of cruelty. This was accepted by the magistrates and the RSPCA lost the case. It had, however, won an important public relations victory because the attention generated by the trial had escalated the incident into a scandal reported throughout the country.

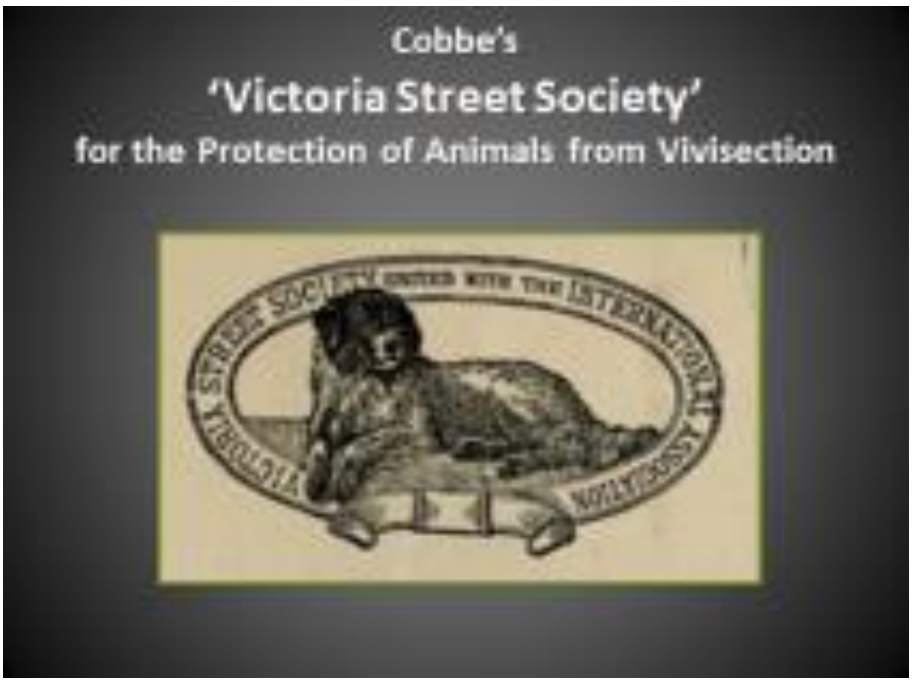
Soon after the trial, Frances Cobbe was approached to use her influence to campaign for greater control of animal research. She quickly responded with a petition to the RSPCA urging it to draft a bill for parliament to create a law that would severely restrict animal research. Her petition was signed by no less than 600 people, every one of whom she declared was "a man or woman of some social importance."

But Cobbe was soon disappointed. The huge size of the RSPCA meant that its membership covered a wide range of views and this made it difficult for the organisation to respond quickly or decisively. Cobbe subsequently withdrew from her involvement with the RSPCA and later noted rather sardonically she had heard that when the society's secretary had sought to observe some animal research, he was only "shown a painless [experiment] on a cat [then] offered a glass of sherry".

Cobbe decided a more direct approach was necessary. In a typical display of her energy and influence, and having given up on the RSPCA, she drafted her own bill and managed to have it introduced into parliament within just 3 months.

By now, however, the scientific community realised that animal research would need some regulatory protection of its own if it was to continue to progress in Britain. A select group of scientists had therefore been preparing a competing bill which was introduced to parliament only 8 days after that of Cobbe.

Now faced with the prospect of debating two bills on animal research, the government decided a more considered approach would be prudent and so announced a Royal Commission instead. Since a Royal Commission is the highest form of public inquiry in the British legal system, it gives an idea of the level of public interest now being generated by the issue.



While the Royal Commission was underway, Cobbe's disappointment with the mighty but conservative RSPCA led her to establish a new organisation specifically to campaign against animal research. It became known as the Victoria Street Society (VSS) and still operates today although under a different name, the National Anti-Vivisection Society. Cobbe selected a leadership team from among her high profile friends and the society soon became the most influential of its type.

The Royal Commission handed down its report in early 1876. In a publication running to over 350 pages (in very small font), the report includes a detailed record of interviews from both sides of the debate although in a reflection of the times, neither Cobbe nor any other women were among them.

It concluded that important advances had come from animal experiments, but recommended that in the interests of animal welfare, a law was needed to regulate such work. So once again, a bill was drafted for parliament, but this time it was passed (albeit after many amendments) and became law in August 1876. As a law solely directed to the regulation of animal research, it was the first of its kind in the world and despite a number of challenges, would remain in force for over a century.

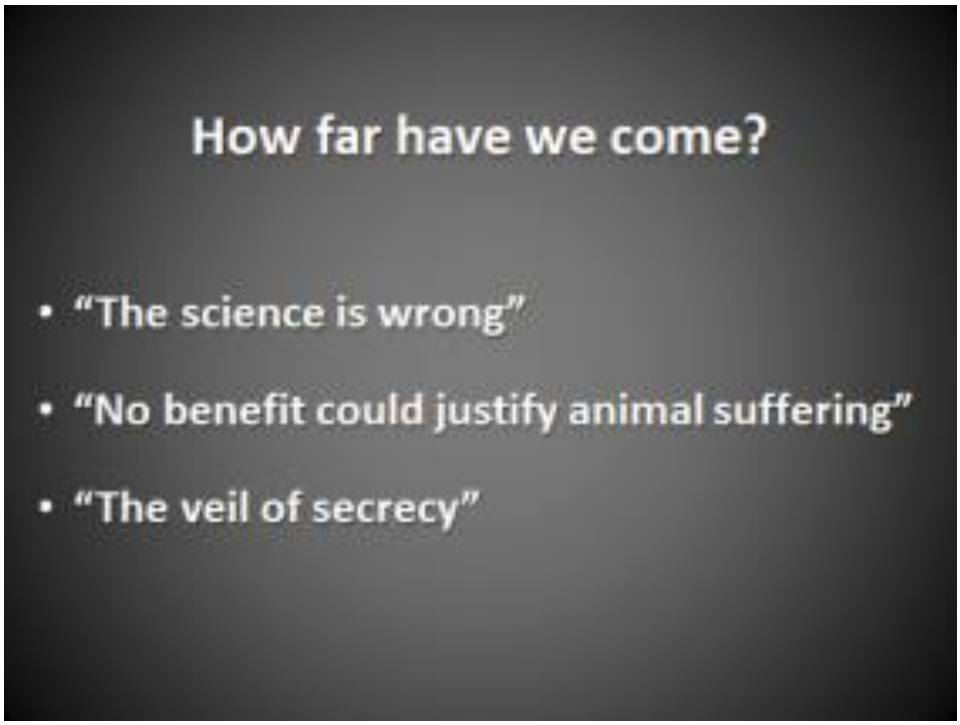
To pass a law on such a contentious issue was always going to require many compromises and it was inevitable that the end result would have critics on both sides. But it was the passionate opponents of animal research who were the most disappointed and perhaps none more so than Cobbe. She felt abandoned by her friends in parliament whom she said had "mutilated" the bill and she began cutting social ties with former supporters including the great Charles Darwin. Reflecting on events nearly 20 years later she wrote in her memoirs "The world has never seemed to me quite the same since that dreadful time."

The original policies of Cobbe's VSS had only sought to impose severe restrictions on animal research. But now, following her disappointment over the new law, Cobbe wanted to see complete abolition and with this, her tactics became more militant. For example, she suggested a 'name and shame' policy which eventually led her VSS to publish a catalogue known as 'The Vivisectors' Directory' which summarized many hundreds of animal experiments and identified the scientists responsible.

Over the next few years, Cobbe's VSS inundated London with posters and leaflets and through its journal, began publishing letters and essays attacking animal research from many angles. Cobbe estimated that she alone wrote over 400 of these. In another campaign, she wrote to 700 school masters enclosing a collection of her pamphlets. Her arguments broadened from moral reasoning to attacking the scientific validity of animal research and here, her targets included the pioneer of antiseptic surgery, Joseph Lister, and two of the most prominent names in the history of microbiology, Robert Koch and Louis Pasteur.

Cobbe's determination to now abolish (rather than just restrict) animal research and her increasingly controversial tactics eventually led to clashes with other members of the VSS. Ultimately, she could no longer reconcile her position with those around her so she resigned from the organization she had founded.

Shortly afterwards, Cobbe surprised many by announcing she was going to leave London and move with her life partner to a small village in Wales. This house became her home until her death 20 years later. The distance from London meant that her involvement in the anti-vivisection movement was diminished although she still had sufficient influence to establish a second anti-vivisection society in the 1890s. Reflecting her change in views, the new organization was committed to complete abolition rather than just restriction of animal research. As with the VSS, this organisation (the British Union for the Abolition of Vivisection) still operates today and again made headlines as recently as April this year when it released under cover video footage of animal laboratories at Imperial College London.



HOW FAR HAVE WE COME since the time of Frances Cobbe?

If we look at the anti-vivisection arguments put forward by Cobbe and her supporters, a number of recurring themes emerge. Three that I find particularly interesting are:

- Firstly, That the science of animal research is unsound;

- Secondly That no amount of human benefit could justify deliberately inflicting pain on animals (an argument that nicely pre-empts the modern philosophical doctrine of animal rights - "Better that I or my friend should die than…years of torture upon animals"); and
- And thirdly That animal research is conducted behind a veil of secrecy (in order to avoid public scrutiny).

Each of these was of course rebutted vigorously by the scientific community. But what strikes me most is how familiar these arguments and their respective rebuttals are today and it's sometimes hard not to wonder how much progress the debate has really made in the last 150 years.

Time doesn't allow discussion on the first two of these arguments, but I would like to spend a little time on the third, especially because I feel that many in this audience are in a position to make a positive contribution.

The assertion that animal research is conducted in secrecy in order to avoid public scrutiny was often made by Cobbe who once referred to "the perpetrators" who "draw a veil of secrecy over the disgusting mysteries of their operating tables". Similar sentiments have been repeated many times – this picture is from a campaign in the early 1900s – and are still heard widely today. For example, the BUAV's website featuring its expose at Imperial College London states that "…the secrecy surrounding animal research means that people are not able to judge for themselves." Interestingly, the 2003 ANZCCART conference also acknowledged this concern with its conference title being "Lifting the veil of secrecy".

Rebuttals by the scientific community usually highlight the need to protect intellectual property, the existing public participation through the AEC system and of course the fact that animal research can be scrutinized once it has been published. Less frequently, a defense is made on the grounds of concerns about research being deliberately misrepresented in anti-vivisection

propaganda or the risk of targeting by extremists. With the exception of the extremist risk – which I believe is greatly overstated in Australia – I feel these defenses are legitimate. Yet regardless of how legitimate they may be, they help sustain a perception of secrecy and leave many people feeling shut out.

I think it is fair to say that the scientific community has taken some positive steps to address this criticism in recent years. In Australia, for example, the NHMRC's "Statement on … Community Participation in …Medical Research" urges researchers to make their work accessible to the broader community rather than limiting the dissemination of their findings to scientific journals. This is also referenced in their grant application process and connects to open access data repositories operated by many Australian universities and research institutions.

Further afield, international organizations have guidelines supporting greater access to animal research data such as those of the Basel Declaration Society, and peak bodies have developed standards to promote more detailed descriptions of the methodology when animal-based research is published; a good example here is the ARRIVE (*Animal Research: Reporting In Vivo Experiments*) Guidelines prepared by the National Centre for the 3Rs in the UK.

And of course there is the voluntary but widely utilized provision of the UK Home Office for researchers to post a summary of their research proposals online.

These various initiatives should all help reassure those genuinely concerned with the perception of secrecy. But I contend that more could be done at the personal level. And this is where we come in. Just as we saw the human warmth and compassion of Frances Cobbe when we looked beyond her activism, I have found we can gain much by engaging directly with those who continue her mission today.

As one who conditionally supports animal research, I have had the opportunity over several years now to engage in discussions with activists who are strongly opposed. Despite inevitable points of difference, it has always been possible to have constructive and positive dialogue. And be assured there is no consistent stereotype on either side of the debate: just as scientists are not the white-coated monsters that some might suggest, I have yet to meet the hard line animal activist who is completely unwilling to listen. And again I turn to Frances Cobbe. Not only have we seen that she was far from being the stereotypic radical, her views on animal protection were actually quite complex: for example, in spite of her adamant opposition to animal research, she was happy to eat meat and had no problem with the sport of hunting.

A particularly good opportunity for personal discourse has emerged in academia in recent years. It is a cross-disciplinary field referred to as Human Animal Studies. An increasing number of universities support meetings and groups dedicated to HAS and in my experience, they are ready to welcome anyone willing to participate in an informed discussion. It has to be said that the prevailing philosophical position is one of animal rights, but I have always found that alternative positions are given a fair hearing. At the present time, membership of HAS studies groups is dominated by the humanities, especially the fields of law, philosophy, politics and gender studies. Clearly there is scope for greater participation by the biomedical sciences. For those interested in joining such discussions, I suggest making contact with the Australian Animal Studies Group as a starting point.

My final behest is to a stakeholder in the animal research debate from which we probably hear the least: I am referring to the research institutions. It is not uncommon for animal advocates to contact research institutions expressing concern over a specific research project. The feedback I hear regularly from animal protectionists is that they end up frustrated and with a reinforced belief that institutions have something to hide. They feel their inquiries get slow-tracked; sometimes they are not answered at all. They find their inquiries are often met with just a bland reassurance that all research has been fully approved by an AEC. In some cases their inquiries are branded as complaints and so are directed through a complaint-handling bureaucracy shrouded in assertions of confidentiality. This in my opinion is not the way to handle an inquiry from someone who clearly feels passionately about an issue and who has taken the time to put their concerns in writing. Margaret Rose in her opening presentation to this conference spoke of respect. I think respect is critical here too. Institutions must be willing to put themselves in the position of the person making the inquiry; this way, inquiries from activists change from a threat to a welcome opportunity for dialogue. This at least has always been my experience.

Frances Cobbe died in her Welsh country home in 1904 at the age of 82. Despite her enormous contribution to enforcing greater protection for laboratory animals, her failure to achieve the ultimate goal of abolition was a cause of profound disappointment until the end of her life. Even in her final days, she remarked of her campaign that "I have sacrificed everything to it and it is a failure." Such a judgment might not be totally unexpected from one of such compassion and restless intellect, but I think she was too hard on herself.

Cobbe fearlessly challenged entrenched attitudes in the establishment of which she was a part. But I suspect out of frustration at feeling she was not being heard, she moved to increasingly militant tactics – ultimately to her personal cost.

Today, everyone agrees that regulatory protection for animals used in research is essential. History shows that Frances Cobbe played an important role in initiating that protection. But I hope that today's tribute shows there is more we can draw from her legacy. By getting to know something of the person she was, we put a human face to the debate. I encourage you all to look beyond the arguments that have persisted unchanged for last 150 years and try to see the issues from the other side's point of view – whichever side you might be on.