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Report of the International Consensus Meeting on Carbon Dioxide Euthanasia of Laboratory Animals

Preamble:

Earlier this year, I was fortunate enough to be invited to attend a meeting in Newcastle - upon –Tyne, UK, that was set up to try and form an international consensus on the use of CO_2 for the euthanasia of laboratory animals. This meeting was hosted by Dr Matt Leach, Dr Huw Golledge and Prof. Paul Flecknell from the Comparative Biology Centre at the University of Newcastle – Upon - Tyne and involved 32 delegates from around the world that included researchers, representatives of animal welfare organizations, animal care staff, regulators and journal editors.

One particularly gratifying feature of this workshop was the presentation of high quality scientific data from studies designed to test the welfare implications of CO_2 exposure at various concentrations and conditions commensurate with standard euthanasia methods. Such scientific validation of techniques that are commonly used and / or questioned is clearly a very important and positive step and one which will hopefully be a part of future debates in this and related areas.

It is possibly worth noting that at this meeting, all data presented was (necessarily) interpreted in a rather conservative manner, e.g. clear loss of consciousness was taken as the point beyond which animals would not be subject to pain or distress. Lesser states, such as drowsiness or cognitive dissociation, which are know to occur in humans suffering hypoxic / anoxic events were not considered as there was no clear evidence to support changes in “awareness” of this kind occurring in rodent species.

The following information is largely extracted from the Final report prepared by Hawkins, P. Playle, L., Golledge, H., Leach, M., Banzett, R., Coenen, A., Cooper, J., Danneman, P., Flecknell, P., Kirkden, R., Neil, L. and Raj, M. A copy of the full report is available at: www.nc3rs.org.uk/CO2ConsensusReport and I would suggest that it is worth reading.

Dr Geoff Dandie, CEO, ANZCCART

Introduction:

Laboratory euthanasia methods are obviously going to be closely scrutinized and CO_2 is one of the most commonly used methods for rodent euthanasia. It can be the most suitable method for euthanasia of large numbers of rodents (easier and less time-consuming than alternatives) and there has been a widely held belief that if used appropriately, CO_2 may also be less stressful than manipulations required for injections or physical methods. It is also highly reproducible and safe for operators when the appropriate equipment is used. However, questions have regularly been asked about the potential for CO_2 to cause pain as it is known to be painful to humans when breathed at high concentrations, so it is assumed that at certain concentrations CO_2 can cause rodents pain and/or

distress. This has lead to disagreement between those who believe the use of CO_2 may be acceptable if used appropriately and those who believe it is inhumane.

In February 2006 a 'consensus meeting' was held at the University of Newcastle (UK) which had the following aims:

- To bring together scientists who have examined CO_2 as a euthanasia agent, in order to share data and views and to inform best practice in the use of CO_2 euthanasia of rodents
- To establish where there are areas of disagreement and to identify what research needs to be done to address these
- To identify what further research needs to be done relating to CO_2 euthanasia in general and to identify potential alternative gaseous agents
- To meet the immediate need for guidance on the humane use of CO_2 euthanasia within research establishments

As indicated above, the meeting included a number of presentations from key researchers around the world that became a framework for discussions on the use of CO_2 as a euthanasia agent and how it might best be administered. There were also a number of key areas for future research in this field that were identified during these discussions that will hopefully form the basis for subsequent meetings of this group. The major limitation on this meeting was that it focussed primarily on rats and mice, which reflected both time constraints and more importantly, that lack of appropriate data relating to other species (in fact the great majority of data presented related to rats). Accordingly, the final report from the meeting limits itself to those species with the caveat that the conclusions from this meeting cannot necessarily be applied to other species at this stage.

Consensus Recommendations:

While the aim of the meeting was to try and establish a number of consensus recommendations if possible. This was not always possible and so in some instances the following recommendations were formed on the basis of a clear majority view of those present.

1. ***There is no ideal method for killing animals with CO_2 as the use of both pre-filled and progressively filled chambers can result in welfare concerns.***

The use of any method to kill animals may require a trade off between achieving a rapid death (in order to minimize stress) and not causing pain or distress. CO_2 is no exception. Exposing an animal to CO_2 can cause distress because sensitive CO_2 chemoreceptors and pH receptors have evolved in vertebrates so that elevated CO_2 levels are a potent stimulus for respiratory effort. CO_2 may also cause discomfort or pain as a result of its conversion to carbonic acid on mucosal surfaces.

Animals will generally try to avoid or escape from an atmosphere containing CO_2 levels above a certain threshold limit. Any method that involves exposing animals to elevated or increasing levels of CO_2 will therefore have welfare implications because exposure to levels of CO_2 that will induce anaesthesia or cause death will result in a degree of aversion. The essential goal of work presented was therefore to determine if (a) CO_2 should be used at all and (b) if its use is to continue, how can it be administered so as to cause the least possible pain and distress.

Assuming that CO_2 will continue to be used for laboratory euthanasia for the foreseeable future, the majority of delegates believed that it was important to recommend the best possible administration protocol on the basis of current knowledge (See point 5). While the recommended protocol is consistent with ANZCCART policy and therefore something we can be comfortable endorsing, it must be acknowledged that refinements may be likely, so some leeway should be considered. The key points to consider with any attempt to refine this protocol are:

(a) How long does it take for the animal to lose consciousness?
(b) Do animals experience adverse effects before they lose consciousness?

Much of the rest of this article will attempt to address these issues in the light of currently available information.

2. ***If animals are placed into a chamber containing high concentrations of CO_2 (above 50%), they will experience at least 10 – 15 seconds of pain prior to losing consciousness. This is obviously a significant welfare concern.***

It was unanimously agreed by delegates that placing animals into chambers that had been pre-filled with high concentrations of CO_2 (above 50%) was a serious welfare issue as it would cause a high degree of pain before animals lose consciousness.

The innervation of nasal, ocular and respiratory mucosae as well as the associated sensory processing

pathways is highly conserved between species. In particular, rats and humans share similar cerebral event – related potentials and the same response threshold for nociceptors. These would all suggest that rats and humans perceive CO_2 stimulation in the same way (Danneman *et al*, 1997).

Studies with human volunteers have shown that inhaling CO_2 (single breath through the nose) result in a variety of unpleasant sensations (see Table 1). All concentrations were frequently described as "burning".

Gas	Not un-pleasant	Un-pleasant	Un-comfortable	Painful
O_2	40			
50% CO_2	4	15	14	7
60% CO_2	3	7	18	12
70% CO_2	1	8	18	13
80% CO_2			13	27
100% CO_2			2	38

Table 1: Human Subjects' rating of different concentrations of CO_2 inhaled in a single breath through the nose (From Danneman *et al*, 1997).

Other human studies have also reported that CO_2 inhalation is painful at concentrations of around 50% (Wise *et al*, 2003). Assuming that the experience of inhaling similar concentrations of CO_2 is comparable in rats and mice, pain may be experienced if they are placed into CO_2 concentration of 50% or greater.

Work undertaken by Golledge *et al* (2005) at the University of Newcastle with rats (Charles River CD rats) using electroencephalogram (EEG) and cardiovascular monitoring by telemetry found that exposure to an atmosphere of 100% CO_2 caused:

- An almost immediate bradycardia (in less than 3 seconds), indicating marked nasal irritation or nociceptor activation;
- Relatively rapid loss of consciousness (in approximately 15 seconds), but with the potential for at least 10 – 15 seconds of pain and distress;
- EEG silence at 38 ± 2 seconds (range 23 – 50 seconds).

3. If animals are placed into a chamber with a rising concentration of CO_2 they will find it aversive once it reaches a certain concentration and may experience dyspnoea or "air hunger" which to humans can be very distressing.

As the concentration of atmospheric CO_2 rises in a chamber, it will first reach a level that is aversive, presumably associated with dyspnoea, before finally reaching levels that are associated with adverse effects such as haemorrhage and seizures. As CO_2 is a respiratory stimulant, it causes a progressive increase in breathing frequency and depth which is followed by a decline as respiratory centres are depressed. In humans, dyspnoea may be caused by CO_2 concentrations as low as 7% and become severe at around 15% CO_2 (Liotti *et al*, 2001; Hill & Flack, 1908). It is possible that rats and mice may experience similar effects at the same concentrations, but as dyspnoeic responses are fairly subjective, this will probably vary and be difficult to assess. While breathing changes are commonly used as a diagnostic sign, they are not entirely reliable as dyspnoea can occur in the absence of obviously disturbed breathing (Lush *et al*, 1988) and heavy breathing does not necessarily imply the presence of dyspnoea. However, in light of it's known distressing effects in humans, the possibility that rodents may be experiencing dyspnoea should be taken seriously (See Banzett & Moosavi, 2001).

Aversive responses are another potential welfare problem as they may indicate that animals are experiencing discomfort or distress and may well lead to negative emotional states if an animal cannot escape from the aversive stimulus. The strength of an aversive response may also be an important factor as low levels may be tolerable while higher levels may cause significant distress. However, it should be noted that a lack of obvious distress behaviours such as escape attempts or vocalization during forced exposure to CO_2 or any other gas does not necessarily indicate good welfare outcomes.

Experiments have also been done to test the degree of CO_2 aversion in rats where food rewards are placed in chambers with a CO_2 enriched atmosphere. At static CO_2 levels of 5% and 10%, the rats ate more quickly and then left the chamber, but the quantity they ate was unchanged (Niel & Weary, In Press). When the CO_2 content of the chamber was 15%, consumption of food rewards was reduced and animals were unwilling to remain in the chamber for food reward at levels above 15%. This indicates that CO_2 concentrations of 15% and above are aversive to rats, but this would appear to be associated with dyspnoea rather than pain. A further study in which rats were provided with food reward in a chamber being filled with CO_2 at a rate of between 3 – 27% of the chamber volume per minute, found that they find the gas sufficiently aversive to leave the chamber at a mean concentration of about 15% CO_2 (Kirkden et al, 2005; Niel et al, In Press). Again, this is consistent with the aversive reaction being associated with dyspnoea rather than pain and would remain a factor until the

animals are anaesthetised by chamber CO_2 concentrations of 30 – 40%.

Currently available evidence would indicate that adverse physical effects of exposure to high concentrations of CO_2 such as laboured breathing, seizures or haemorrhaging may or may not be welfare problems, depending on the level of consciousness at which they occur. Since CO_2 is an anaesthetic gas that results in a loss of consciousness at concentrations of 30 – 40% for rats (Niel & Weary, In Press; Smith & Happap, 1997; Gollege – unpublished data presented to the meeting), animals may be unconscious before the onset of adverse physical effects, but not necessarily before the onset of aversion or dyspnoea. The rather compelling data presented to the meeting by Huw Gollege included a time matched compilation of CO_2 concentration, video observation of the rats behaviour, EEG monitoring, heart rate, blood pressure and electromyograph (EMG) recording (taken from electrodes placed on neck muscles), provided strong support for the notion of animals losing consciousness before the onset of physical signs of aversion during the progressive increase in CO_2 concentration. In these experiments, CO_2 was introduced to the chamber at a rate of approximately 20% of the chamber volume per minute and resulted in:

- Loss of consciousness before autonomic signs of nasal irritation (bradycardia) (see table 2);
- Gasping and seizures, which occurred during deep anaesthesia and so were not considered welfare concerns.

Pre-treatment of nasal mucosae with lignocaine (local anaesthetic) or acetazolamide (which slows carbonic acid formation) had little effect on cardiovascular and EEG parameters, suggesting that acute pain due to acid formation was not a significant factor when using this filling rate and method of exposure.

Event	Time (seconds; mean and SE)	CO_2 Concentration (%)
Recumbency (n = 11)	110 ± 6	30
EMG Silence (n = 6)	110 ± 5	30
Loss of Consciousness (behavioural)(n = 11)	156 ± 5	39
Bardycardia	242 ± 85	47
Brain Death (isoelectric EEG)(n= 6)	327 ± 8	72

Table 2: Sequence of events in Charles River CD Rats during exposure to a rising concentration of CO_2 at a fill rate of 0% chamber volume per minute.

There was no evidence from heart rate or blood pressure data of marked arousal or stress seen in this study (Table 3), but the anaesthetic and other physiological effects of CO_2 may have confounded this. It is also important to note that the fill rate used in this study was significantly less than may be used in many facilities. It may still therefore be possible that faster fill rates may lead to nociceptor activation before loss of consciousness.

	10 sec exposure to CO_2		100 sec exposure to CO_2	
	Mean BP (mm Hg)	Heart Rate (beats / min)	Mean BP (mm Hg)	Heart Rate (beats / min)
Air	141 ± 16	405 ± 41	141 ± 17	376 ± 68
CO2	130 ± 17	415 ± 48	137 ± 24	275 ± 42

Table 3: Mean arterial blood pressure (BP) and heart rate in Charles River CD rats during exposure to rising concentrations of CO_2 and air at a fill rate of 20% chamber volume per minute.

4. ***The great majority of meeting participants agreed that it was more important to avoid or at least minimize pain and distress than it is to ensure a rapid loss of consciousness (i.e. a "gentle" death that may take longer was considered preferable to a faster but more distressing death).***

This is a general principal that the majority of delegates believed should apply to any method for euthanasia and a position that ANZCCART endorses. The central question here is whether death by CO_2 exposure can reasonably be described as "gentle".

5. ***While the optimum rate of chamber filling has not been determined, the use of 100% CO_2 at a flow rate of 20% of the chamber volume per minute has been shown to produce a loss of consciousness without evidence of pain, but not without evidence of dyspnoea. Reduced CO_2 flow rates can be increased once the animals have lost consciousness.***

The advantages and disadvantages of pre-filling chambers with 100% CO_2 versus the progressive introduction of CO_2 at a flow rate of 20% chamber volume per minute are outlined in Table 4.

	Pre-fill (100% CO_2)	Rising concentration (20% chamber volume per minute)
Adverse effects before loss of consciousness	Pain, potentially severe	No pain, but other effects unclear – possible distress, discomfort, dyspnoea
Time to onset of adverse effects	Instant	Ataxia at around 55 seconds
Time to loss of consciousness	38 ± 2 seconds (n = 6)	156 ± 5 seconds (n = 11)*
Time to cortical inactivity	45 seconds	5 – 6 minutes

Table 4: Comparison of the physiological effects of pre-fill versus rising concentration of CO_2. *This is a conservative estimate based on behavioural loss of consciousness – the true value may be 110 seconds using recumbency and EMG data as a basis. It was not clear when animals were actually unconscious.

The rising concentration technique should not cause pain, but may result in some distress by other mechanisms (as described above). The aim should be to induce unconsciousness before the animals become significantly distressed. The majority of delegates agreed that the potential for exposing animals to noxious CO_2 levels can be minimized by using slow fill rates, but the optimum CO_2 flow rate and administration protocol(s) have not yet been determined. A fill rate of 20% of the chamber volume per minute appeared to cause loss of consciousness before nociceptor activation. Note that the chamber was filled from the top, which mixes CO_2 more effectively than filling from below, but there would still be potential to improve the mixing efficiency by appropriate use of mixing baffles at the point of entry. Filling chambers from a lower point can produce localized high CO_2 concentrations at the level of an animal's face, so there may be a need to assess effects in individual chambers or make appropriate modifications. A flow rate of 20% chamber volume per minute does not solve all welfare problems, as can be seen from Table 4; however the majority of delegates agreed that a gradual fill technique was preferable to pre-fill and this is also consistent with ANZCCART guidelines.

It was recognised that there may be some practical limitations to using slow flow rates on the grounds that establishments having large numbers of animals to kill may not be able to spend up to 8 or 10 minutes on each batch, to ensure that no animals recover. This can be overcome by either having multiple euthanasia chambers available or by filling the chamber at a rate of 20% chamber volume per minute until the animals lose consciousness and then increasing the flow rate to 100% volume per minute or more.

6. ***It was considered possible that the addition of O_2 to carbon dioxide may reduce, but not overcome, welfare problems associated with the potential for dyspnoea or pain. It is also possible that high concentrations of oxygen would prolong consciousness, which may be undesirable. Currently, there is not sufficient evidence available to allow conclusions to be drawn about an appropriate level of O_2 supplementation.***

Some studies have demonstrated that the addition of oxygen to CO_2 made the gas less aversive to birds. The addition of oxygen to CO_2 has also been shown to reduce agitation and gasping in the rat (Coenen et al, 1995), but it has been suggested that the apparent lower aversiveness may have been due to the difference in CO_2 concentration and flow rate (Conlee et al, 2005). However, one study on rats at the University of British Columbia compared CO_2 with a mix of CO_2 and O_2, at a uniform CO_2 flow rate and found that the aversion to CO_2 was slightly (not completely) reduced with O_2 supplementation (R. Kirkden, pers. comm.). A number of delegates expressed the view that evidence for the benefits of O_2 supplementation was not clear. For example, haemorrhaging has been reported with the addition of O_2 in mice, but it is not known whether this occurred before or after the loss of consciousness (Ambrose *et al*, 2000). The group did not feel able to recommend protocols for the addition of O_2, but there was full agreement that more studies are needed into the effects of O_2 supplementation (see below).

7. ***It is not yet possible to recommend the use of any suitable alternative gases or gas mixtures that would cause death by hypoxia such as argon, nitrogen, carbon monoxide, helium or xenon for killing rats or mice. Hypoxia may be a method preferred by some for killing other non – rodent species, but there are insufficient data available in terms of the impact of these gases on rodents at this stage.***

8. ***The use of volatile anaesthetic agents may be an appropriate alternative to CO_2, but the aversive nature of these gases can vary. They can either be used as the sole euthanasia agent or they may be used to anaesthetise animals prior to completing the process by switching to CO_2.***

Possible alternative inhalation agents to CO_2 can be divided into (a) gases that cause hypoxia and (b) volatile anaesthetic agents. Each potential alternative has its own animal welfare, practical, human safety and economic issues.

In the case of gases that cause hypoxia, such as argon, nitrogen, carbon monoxide, helium or xenon, there are a number of studies in the literature that have set out to evaluate their potential as euthanasia agents. Unfortunately, the literature is currently not sufficiently comprehensive to enable judgement on the suitability of any of these agents for rats and mice. It is known that spontaneously breathing humans lose consciousness without experiencing discomfort when exposed to profound hypoxia (Luft, 1965), yet rodent studies have shown that rats are not prepared to enter chambers containing high levels of argon for reasons that are not yet understood (Niel, personal communication). Extrapolation between species is therefore difficult if not impossible.

In rodent studies published to date, protocols have employed either pre-fill or different flow rates, and it has not always been clear whether animals were conscious when adverse effects occurred. As discussed above, animals may convulse while they are conscious or unconscious, but without EEG data it is impossible to assess whether they might have been conscious at the time.

The key elements of the humane induction of anaesthesia are (i) the animal's initial perception of the anaesthetic agent and (ii) any distress associated with the induction, for example due to irritancy of the vapour. Determining whether animals find volatile agents aversive can provide important information when deciding on the most humane killing technique.

Measures of aversion include locomotory responses such as initial withdrawal times from the test chamber; re-entry times if animals go back inside; and total dwelling times, or the total amount of time animals spend in the chamber. Types of behaviour that are commonly monitored include rearing, washing, sniffing the test chamber entrance ad elimination. If gases are aversive, then these behaviours should increase, re-entry times should increase, and withdrawal and total dwelling times should decrease. Using these parameters, the least aversive euthanasia agents appear to be halothane for rats (now difficult to obtain, so Sevoflurane would be considered the next best based on aversion studies) and enflurane for mice (Leach *et al*, 2003). The use of these agents could then be followed by CO_2 after loss of consciousness if there is a need to reduce anaesthetic use or save time.

Changing from CO_2 to volatile anaesthetics can also require capital outlay as calibrated vapourisers and efficient scavenging devices are required to meet human health and safety concerns.

9. More research is needed into the physiological and affective responses to a range of gaseous agents in order to identify best practice and / or possible alternatives to CO_2. This will require a multidisciplinary approach and effective communication between researchers.

While the meeting identified a number of areas of consensus, it was also clear that there are significant gaps in current knowledge that need to be addressed in order to make definitive recommendations on humane euthanasia using gaseous agents. In particular, more research is needed to find an appropriate alternative to the use of CO_2. It is also important to study and evaluate the links between the chemistry of CO_2, its physiological effects and their significance for animal welfare – particularly mice where less work has been done. There is an inherent ethical dilemma in conducting studies that may cause animals pain and distress in order to improve the well being of other animals. However, given the large number of rats and mice killed every year using CO_2 and the uncertainty as to what they experience, further animal studies were believed to be justified by the majority of delegates.

The group provided a list of recommended study topics, which are set out below and may be broadly divided into behavioural and physiological studies.

Behavioural Studies:

- The strength of aversion to argon and to volatile anaesthetics, and the associated welfare consequences in rats and mice.
- Examination of different methods to evaluate strength of aversion, as some may be limited, e.g. animals will be unable to escape if they are immobile; or flawed, e.g. CO_2 exposure might interfere with feeding motivation in an approach – avoidance test.
- Use of conditioned place preference and aversion studies to compare a variety of gaseous killing methods.
- Effects of adding supplementary oxygen to CO_2.

Physiological Studies:

- The time and concentration of a range of gaseous agents, including CO_2, required to (a) anaesthetise and (b) kill rats and mice. This should be determined using EEG and correlated with EMG data; any occurrence of adverse effects should also be evaluated.
- Studies to evaluate the physiological effects of exposure to a rising concentration of CO_2, to try to infer what mice and rats could be experiencing

between aversion and unconsciousness.
- More measurement in rats and mice of physiological parameters that are used to predict stress levels, such as heart rate and corticosterone levels.
- Studies on ventilatory patterns and their relationship to the sensation of dyspnoea in humans.

The above list shows that a multidisciplinary approach, involving different research fields, techniques and approaches will be necessary to gain a fuller understanding of animals' experiences of euthanasia. This will clearly require effective communication between researchers, with respect to practical aspects – such as agreeing protocols for evaluating the effects of gases and keeping in touch regarding research programmes and collaborations – and also free discussion on interpreting results and agreeing appropriate research directions, as occurred at the meeting. A particular point that should be emphasised is the relative lack of information on mice, which needs to be addressed because extrapolation of data from rats may not always be appropriate.

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Conflict of Interest and Independence: A Reminder.

Dr Catherine Berglund, on behalf of the NHMRC Animal Welfare Committee members

There have been occasions when membership of the Animal Ethics Committees (AECs) has been noted by the Animal Welfare Committee (AWC) to fall short of membership requirements as set down in the *Australian code of practice for the care and use of animals for scientific purposes* (2004), particularly in relation to Category D membership. This is of some concern to the AWC, and it is felt that it may be timely to remind AECs of the importance of the membership composition of the AECs.

The membership requirements are set out in Section 2.2.2 of the Code as follows:

An AEC must have a membership that will allow it to fulfil its terms of reference. It must comprise at least four persons, including a separate person appointed to each of the following categories:

Category A:
a person with qualifications in veterinary science with experience relevant to the activities of the institution. Veterinarians who lack this experience must familiarise themselves with the biology and clinical characteristics of the species of the animals used;

Category B:
a suitably qualified person with substantial recent experience in the use of animals in scientific or teaching activities. This will usually entail possession of a higher degree in research;

Category C:
a person with demonstrable commitment to, and established experience in, furthering the welfare of animals, who is not employed by or otherwise associated with the institution, and who is not involved in the care and use of animals for scientific purposes. Veterinarians with specific animal welfare interest and experience may meet the requirements of this Category. While not representing an animal welfare organisation, the person should, where possible, be selected on the basis of active membership of, and nomination by, such an organisation; and

Category D:
a person who is both independent of the institution and who has never been involved in the use of animals in scientific or teaching activities, either in their employment or beyond their under-graduate education. Category D members should be viewed by the wider community as bringing a completely independent view to the AEC, and must not fit the requirements of any other Category.

Animal ethics committee membership is diverse so as to ensure rigorous discussion and debate on the ethics and welfare elements of each proposed piece of research. The model maximises diversity of perspectives and views potentially voiced in committee deliberations, and specifically, includes members with interests that are transparently separate from those of research and the institution which hosts the research endeavour. Hence, the requirement that Category D members be independent from the institution and independent of research and teaching activities involving animals. This should largely eliminate the need to consider whether a Category D member needs to declare conflict of interest in the consideration of proposals. They should theoretically be available to bring their valuable perspective to all potential committee considerations. Their independence from research activities under their consideration should be transparent.

It is worth noting that the same cannot be assumed of Category B members, who are also valuable members of the AECs, but by definition have a vested interest in the research process. Researchers must not however take part in deliberations in which they have a direct interest. Their own research, for example, should not be deliberated by them, nor that of close colleagues or friends, nor that involving companies, in which they feel they have a strong vested interest. They should declare 'conflict of interest', and properly absent themselves from deliberations and decisions on those pieces of business. Such declarations of conflict would be expected to be routine. To be aware of such a conflict of interest is an individual responsibility primarily. The person concerned can best judge if they have interests that are in competition with the unbiased decision making they are obliged to undertake.

Avoiding potential for conflict of interest is a safeguard of decisions making processes that is undertaken in many contexts. So, for instance, a consultant should not act for more than one commercial enterprise in competitive tender processes. If a consultant did so, he or she would be privy to confidential and sensitive information from both tenders, placing him or herself in direct conflict of acting in the best interests of both parties. It is usual for consultants to accept a brief from one firm, then to decline the next offer on that basis of earlier agreement to act for a competitor. Similarly, law firms should only act for one party in a dispute, no matter if the firms have separate legal officers who could take on the cases. A potential conflict of interest is therefore routinely avoided.

Yet, the standard for judicial or upper level administrative decision making is somewhat higher. In those forums, decision makers should not only be satisfied that they have no actual conflict of interest, they should also minimise potential for conflict of interest, and further, be perceived to have no potential conflict of interest. This is a very strict standard. It means guarding against the public perception of potential conflict of interest. Maintaining independence of members is a common strategy for meeting such a standard. That is the approach which is taken for Category D members. So, the independent members, Category D members, should not be perceived to have vested interest in research, nor in the objectives of the specific institution. They must not be employed by the institution. They must not be researchers, nor have ever been involved in scientific or teaching activities beyond their own under-graduate education.

News from ANZCCART New Zealand

ANZCCART (NZ) has new Chair

The Royal Society of New Zealand has appointed Mr James Battye of Palmerston North as the new Chair of ANZCCART for a 2-year term starting on 1 January 2006. Jim was born and spent the first half of his life in Perth, WA, and came to Massey University, Palmerston North, in 1971 after studying Physics and Philosophy at the University of Western Australia. In addition to Critical Thinking, his main teaching interests have been in Ethics, Applied Ethics, the Philosophy of Science and Philosophy for Children. His research interests are in Applied Ethics and Philosophy for Children. Jim's main extracurricular interests are classical music, especially singing, reading novels, travelling, and eating foreign food.

Reappointments to National Animal Ethics and Animal Welfare Committees

The New Zealand Minister of Agriculture has recently reappointed Mr John R Martin as the Chairman of the National Animal Ethics Advisory Committee for a three-year term (from 1 November 2006 to 31 October 2009). The chairperson of NAEAC is an ex officio member of the National Animal Welfare Advisory Committee. The Minister also reappointed Dr Peter O'Hara as Chairman of the National Animal Welfare Advisory Committee for the same three-year term.

International Fish Welfare

Throughout the European Union and North America there is a rapidly increasing concern for fish welfare. This is supported by 'fish welfare' sessions increasing in appearance in conferences at both European and international levels.

Fish Welfare Course

Held at the University of Insubria, Varese, Italy, September 11-17, 2005. Included: Lectures by experts and lab sessions on techniques currently used to determine fish welfare. Funded by Aqua TT (AquaTT was founded in 1992 under the EU COMETT programme as the University Enterprise Training Partnership (UETP) for the European Aquaculture Industry.) www.aquatt.ie

World Aquaculture Society and joint European Aquaculture Society Conference

AQUA 2006, 9th – 13th May, Florence, Italy. Over 3000 attendees. Session on EU projects on welfare, which included: 'Cost action 867': "wellfish" – welfare of fish in european aquaculture; 'Wealth' – welfare and health in sustainable aquaculture; 'Seafoodplus' – ethical quality traits in farmed fish; 'Fastfish' – on farm assessment of stress level in fish

www.easonline.org and www.was.org

7th International Congress on the Biology of Fish

St Johns, Newfoundland, Canada, 18th – 22nd July 2006. Welfare of fish session which included presentations on: Pain perception in rainbow trout (*Oncorhynchus mykiss*): impact of social context on behaviour and physiology; Fin erosion found in UK farmed rainbow trout (*Oncorhynchus mykiss*); Acute stress tolerance of Atlantic cod larvae fed differentially enriched live-food.

http://www.mun.ca/biology/icbf7/index.html

COST 867 action meeting

Arcachon, France, 9th – 11th October 2006

The main objective of the COST 867 Action was to improve the knowledge of welfare for fish and formulate a set of guidelines embodying a common and scientifically sound understanding of the concept of welfare in farmed fish and to construct a range of targeted operational welfare indicator protocols that can be used in industry. The economic dimension of activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at Euro 120 million in 2004 prices.

www.fishwelfare.com

Recent Changes to the Victorian Prevention of Cruelty to Animals Regulations

A reminder that the final parts of the Prevention of Cruelty to Animals (Amendment) 2006 Regulations came into effect on August 1st 2006. This means that:

> the seventh edition of The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (The Australian Code), and The Code of Practice for the Housing and Care of Laboratory Mice, Rats,Guinea Pigs and Rabbits (The Laboratory Animals Code of Practice)

has become a mandatory condition of each licence type.

Licence holders and persons nominated under section 26(2) of the Prevention of Cruelty to Animals Act 1986 will be responsible for ensuring that all scientific procedures are carried out in accordance with the Laboratory Animals Code in addition to the Act, associated Regulations, the Australian code of practice for the care and use of animals for scientific purposes and the Victorian Code of practice for the use of animals from municipal pounds in scientific procedures.

From 1st August 2006, monitoring compliance with these Codes has become part of the Bureau of Animal Welfare audit. The Codes are available from the Bureau website: www.dpi.vic.gov.au/animalwelfare and select Scientific Procedures from the left hand menu.

News from Overseas

Brussels, 21 March 2006

European Union approves new alternatives to animal testing of drugs and chemicals

The Scientific Advisory Committee of the European Centre for the Validation of Alternative Methods (ECVAM) has approved six new alternative testing methods that will reduce the need for certain drugs and chemicals to be tested on animals. The new tests use cell cultures rather than animals to establish the toxicity of cancer drugs and identify contaminated drugs. The tests approved will not only reduce the number of animals needed for testing, but will also increase the accuracy of the tests, thereby making the products concerned safer. The role of ECVAM, which is based at the European Commission's Joint Research Centre, is to replace, refine and reduce methods of animal testing for cosmetics, drugs and chemicals. Tests validated by ECVAM must be approved by its Scientific Advisory Committee, composed of representatives of the 25 member states, academia, industry and animal welfare organizations before they can be used in labs across Europe.

One of the tests is designed to assist the dosage of some highly toxic drugs used in chemotherapy for cancer, a disease which causes almost a million deaths in the EU every year. Using bone marrow culture from mice and cord blood cells from humans, a test has been developed that will decrease the risk of a lethal overdose in the first cohort of patients to which they are administered, a risk that cannot be identified during current preclinical testing strategies.

International studies have shown that this new test can provide more accurate predictions than testing on animals, so the new method will not only reduce the number of animals needed, but also increase the safety of patients.

Five of the new tests address the issue of bacteria. Our immune system is designed to guard us against bacteria. However it cannot distinguish between live and dead bacteria, and will react also against dead bacteria or part of them. A drug may be sterilised, but not necessarily free from all traces of bacteria and this can lead to side-effects such as fever, pain and shock. 200,000 rabbits are used every year to test the drugs before they are put on the market. The new method uses human immune cells grown in the laboratory, which can detect bacteria just as the human immune system does. This test will not only reduce the number of animals used in labs, but also the costs of testing. An added bonus is that these new tests are far more effective in finding contaminated drugs than the previous animal tests.

The work of ECVAM is funded from the EU's Research Framework Programme, with support from Member States, industry and animal welfare organisations. By using advances in scientific knowledge, ECVAM will help to increase patient safety and animal welfare Member States, industry and animal welfare organisations.

A conference in Brussels on 7 November 2005 entitled "Europe goes alternative" saw the adoption of a European Partnership with industry to promote

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Contributions to *ANZCCART NEWS* are welcome and should be sent to:
ANZCCART
C/- The University of Adelaide
South Australia 5005
Australia
Tel. 61-8-8303 7585 Fax. 61-8-8303 7587
E-mail. anzccart@adelaide.edu.au
http://www.adelaide.edu.au/ANZCCART

or

ANZCCART New Zealand
PO Box 598
Wellington
New Zealand
Tel. 64-4-472 7421 Fax. 64-4-473 1841
E-mail. anzccart@rsnz.org
http://anzccart.rsnz.org/

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