



25 November 2008

Director  
Health and Research Ethics Section  
National Health and Medical Research Council  
GPO Box 1421  
Canberra  
ACT 2601

Dear Sir,

### **Alternatives for the use of animals for scientific purposes – call for comments**

The Australian Association for Humane Research Inc. considers the development and use of alternatives to animal experiments to be crucial if Australia is to make a serious contribution to real medical progress. We welcome the opportunity to respond to your invitation for comments and advise that our submission focuses on the areas where we feel the NHMRC should play a lead role.

#### **Leadership**

The NMHRC has a unique opportunity to create a vision and strategy for the 21st Century in which reliance on animals for research is significantly reduced with better outcomes for human health.

Current scientific methods were developed incrementally over the past 50 to 60 years and have developed a conventional over-reliance on the use of laboratory animals for most research. Using the results of animal tests to predict human health effects involves a number of assumptions and extrapolations that remain controversial and the medical industry itself is questioning the validity and safety of such testing<sup>1</sup>. In the UK, the opinions of 500 general practitioners were surveyed, commissioned by Europeans for Medical Progress (now known as Safer Medicines Campaign) in 2004. The results show a “staggering level of distrust in results obtained from animal experiments” and the web-site [www.curedisease.net](http://www.curedisease.net) quotes some of the results as follows:

- 82% were concerned that animal data can be misleading when applied to humans
- only 21% would have more confidence in animal tests for new drugs than in a battery of human-based safety tests
- 83% would support an independent scientific evaluation of the clinical relevance of animal experimentation

There are many reasons for this distrust, much of which is empirical evidence<sup>2</sup>. Other factors are time and expense, besides the ethical issues which arise.

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<sup>1</sup> <http://www.curedisease.net/news/040903.shtml>

<sup>2</sup> <http://www.curedisease.net/>

The state of scientific evaluation today is ideally placed to take advantage of the on-going revolution in biology and biotechnology. More specifically scientific evaluations can use human cells and tissues to better effect and with better results than when using whole animals.

We recommend that the NMHRC take this space and lead in this important area of human health.

### **Funding incentives – overseas.**

Most developed nations have established institutions which promote the use of alternatives and these are largely funded and supported by their governments.

Therefore, in contrast to Australia, far greater opportunities exist overseas to develop and validate alternatives to animal experiments. The following lists those institutions.

#### ***United Kingdom***

*The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)* is an independent UK organisation, established in 2004, that reports to the Science Minister.

The Centre's mission is to advance and promote the 3Rs (reduction, refinement and replacement) in research and testing using animals.<sup>3</sup> It brings together members of academia, industry, government and animal welfare organisations for workshops and symposia in order to facilitate the exchange of information and ideas, and the translation of research findings into practice that will benefit both animals and science.

The Centre has a government budget of GBP 5 million per annum for the next three years.<sup>4</sup> In 2009 they are making available up to GBP 2.5 million for research grants.<sup>5</sup>

#### ***Europe***

*The European Centre for the Validation of Alternative Methods (ECVAM)* was established 1991.

Its mission is to promote the scientific and regulatory acceptance of non-animal tests which are of importance to biomedical sciences, through research, test development and validation and the establishment of a specialised database service.

ECVAM has completely validated 17 alternatives with nine more being in the last stage of peer review and another 25 undergoing final trials or analysis.<sup>6</sup>

#### ***United States***

In the United States, the *Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)* was established in 1997. The committee consists of representatives of 15 federal agencies and appoints panels of independent experts to review the available literature to assess the validity of a test.

The ultimate goal of ICCVAM is the validation and regulatory acceptance of test methods that are more predictive of adverse human and ecological effects than currently available methods.<sup>7</sup>

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<sup>3</sup> <http://www.nc3rs.org.uk>

<sup>4</sup> Dr Hadwen Trust media release 10/12/07 <http://www.drhadwentrust.org/news/government-funding-for-nc3rs-increases-but-still-not-enough>.

<sup>5</sup> NC3R's website <http://www.nc3rs.org.uk/landing.asp?id=27>

<sup>6</sup> "Reducing animal suffering often has the unexpected benefit of yielding more rigorous safety tests" Alan M. Goldberg and Thomas Hartung, *Scientific American*, Jan 2006.

<sup>7</sup> <http://iccvam.niehs.nih.gov/>

Since its inception, ICCVAM has evaluated 16 alternative methods. Six have been adopted by regulatory authorities and others are undergoing recommended improvements.

### **Germany**

**ZEBET**, established in 1989, is the Centre for Documentation and Evaluation of Alternatives to Animal Experiments, which forms part of the German Federal Institute for Risk Management, Berlin.

The goal of this scientific institution is to bring about the replacement particularly of legally prescribed animal experiments with alternative test methods, to reduce the number of test animals to (what they consider is) the absolutely necessary level and to alleviate the pain and suffering of animals used in experiments. ZEBET is responsible for the documentation and assessment of alternatives to animal experiments, and recommending them for legislative acceptance both nationally and internationally.

ZEBET undertakes its own research and has a separate budget to promote specific projects on the development of alternative methods by other institutions.

In Germany, \$96 million was invested in developing alternative models to the use of animals in scientific procedures over a 17 year period (1980 to 1997).<sup>8</sup>

### **Japan**

The Japanese Centre for the Validation of Alternative Methods (JaCVAM), within the National Institute of Health Sciences, coordinates validation studies on proposed alternative methods, coordinates the peer review of test methods, and provides recommendations to regulatory authorities.

### **Australia**

Few opportunities exist in Australia to support the development of alternatives.

- In 2008, the NHMRC awarded a total of \$338.2 million for project grants representing 671 separate research projects. Roughly half of these projects involved the use of animals. This does not mean however that the remainder used alternatives but rather that the research simply did not involve animals.
- The direction of NMHRC funds towards the development of non-animal alternatives is vague in this regard, stating “The development of non-animal alternatives will be undertaken with a number of our grants, as part of the requirements of local animal ethics committees, but we do not collect statistics on this.”<sup>9</sup>
- NHMRC lists a number of “funding types” but none are directed to the development of non-animal alternatives.<sup>10</sup>

Unfortunately, in Australia there are no bodies dedicated to the funding and finding of more ethical and scientifically valid research. Progress in this regard relies on organizations like AAHR, which have minimal resources, while animal-based research continues to receive vast amounts of government funding. To quote the CEO of the Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART), “unfortunately this is still an area where we are doing exceptionally poorly.”<sup>11</sup>

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<sup>8</sup> Lawyers For Animals Submission to the Senate Rural and Regional Affairs and Transport Committee, National Animal Welfare Bill 2005, 15 January 2006.

<sup>9</sup> Personal correspondence from NHMRC dated 29 Feb 2008.

<sup>10</sup> Lawyers For Animals Submission to the Senate Rural and Regional Affairs and Transport Committee, National Animal Welfare Bill 2005, 15 January 2006.

<sup>11</sup> Personal email 16/4/08

If Australia is truly committed to advancing the 3R's concept we recommend the establishment of a government-funded centre dedicated to replacing animals in research with budgets at least on a par with its counterparts in other developed nations. Until this is addressed, Australia will never be at the forefront of medical research.

**The need to forge alliances.**

ICCVAM-NICEATM, ECVAM, JaCVAM and Health Canada have recently developed a framework for International Cooperation on Alternative Test Methods (ICATM) to increase international cooperation, collaboration and communication on alternative test methods.<sup>12</sup> It is highly recommended that Australia seeks representation on this coalition with the aim of being able to access significant research and capability with which these organisations are forging. In this way Australia can keep abreast of alternative research techniques and avoiding costly research (re)validation.

There is no obligation under the Therapeutic Goods Act 1989 to conduct scientific research on animals. We understand however, that many products are developed for an international market and must therefore adhere to legislative requirements that in some countries specify animal tests (eg United States Food and Drug Administration requirements).

**Cap the number of animals used each year.**

Australia uses *more than twice* the number of animals in research than the United Kingdom, despite having 1/3 of the population. It uses more animals on a per capita basis than the EU, UK or NZ.

We assert that the poor comparison in funding availability referred to above is reflected in the numbers of animals used. Approximately 7 million animals were used in research and teaching in the last recorded year (2006) in Australia – a staggering increase of 23.2% (or approx. 1.6 million animals) from the previous year.

	Human population (July 07)	No. of animals used	Animals used per capita
Australia	20,440,000	6.9 million (2006)	0.338
New Zealand	4,116,000	318,489 (2006)	0.077
United Kingdom	60,776,000	3.20 million (2007)	0.052
European Union	490,426,000	12.1 million (2005)	0.025

A recent report by UK groups Dr Hadwen Trust and British Union Against Vivisection has revealed that the United Kingdom's statistics have reached 3 million animals for the first time in 16 years. While British campaigners have called the increase "an appalling failure" they would be horrified to learn of Australia's shameful record.

A reduction in animal usage must be achieved every year. This could be accomplished by putting a cap on the number of animals used and licenses issued, thereby enabling only those protocols that are deemed most justified. This would further result in a reduction of wasted resources – time and funding spent on futile experiments that are unlikely to be of any real benefit.

**Animals in teaching.**

This is an area which requires immediate addressing by NMHRC.

<sup>12</sup> [http://ec.europa.eu/enterprise/cosmetics/doc/icatm\\_200810.pdf](http://ec.europa.eu/enterprise/cosmetics/doc/icatm_200810.pdf)

1. *Legislative requirements are not being adhered to in Australia*

The Australian code of practice for the care and use of animals for scientific purposes clearly states

- “Scientific and teaching activities using animals may be performed only when they are essential.” (1.1) and;
- “Techniques that totally or partially replace the use of animals for scientific purposes must be sought and used wherever possible” (1.8).

The Code is a legally enforceable document, yet is clearly not being adhered to in Australia.

2. *Non-essential use of animals is prevalent in teaching institutions, some examples are*

*Example 1* - Footage obtained from Animal Liberation (and available on the AAHR website) shows live rabbits being used in cardiovascular physiology classes at Monash University, despite a non-animal alternative being available. The live rabbits are anaesthetised, tied down by their legs and teeth and have their throats slit in order to insert a catheter to administer drugs that raise and lower their heart rates. After completion of the experiment the rabbits are killed.

In a response received from Monash University, the Chair of its Animal Welfare Committee has confirmed that students have the option of attending a video based alternative class.

*Example 2* - Further footage obtained from a psychology student (also on the AAHR website) shows rats at Sydney University that have received 2 days ad libitum access to beer and water. They were observed over several days in small glass cages. They were separated into two groups - 50% could press a lever to receive beer (40 calories/100ml beer), and the other 50% could press a lever for access to sucrose water (10% sugar, 41 calories/100ml water). At the end of the tutorial students presented their data to see how many lever pressings occurred to obtain each substance. The aim of the experiment was to observe behavioural patterns – an objective that can easily be achieved by using a number of non-animal alternatives.

Teaching is the process of passing on knowledge to others and not the discovery of new knowledge. Clearly the use of animals in teaching is one of the most unjustified uses of animals, particularly in light of the many alternatives that are now available. There should therefore be an outright ban on the use of animals for this purpose.

### **Develop a national Animal Ethics Committee.**

There are several major concerns about the Animal Ethics Committee system, in particular

- They are heavily weighted in favour of the researchers. Consider for example, the following quotes:

*“...those who oppose the use of animals in research may also argue that animal ethics committees are stacked against the animals and in favour of the research. They may argue that a Category C person is unlikely to effectively make their voice heard for three reasons. First, they are often outnumbered; secondly, they may not be confident to speak up when in conference with doctors and professors, and finally, they are unlikely to have the scientific ability to understand the detail of the protocol before them and come up with an effective counter argument.” - Siobhan O’Sullivan<sup>13</sup>*

*“I and the other animal welfare representative have never succeeded alone in stopping an experiment. Recently, for example, we challenged on ethical grounds, the provision by our institution of transgenic pigs for research into organ transplantation. We did this on the*

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<sup>13</sup> “Introduction to the Politics of Animal Protection”, anzccart news, Volume 18, Number 1, 2005.

*grounds that the NH&MRC has placed a five-year moratorium on animal to human organ transplantation. The remainder of the committee opposed us and the experiments went ahead.” – (Category C member, name withheld.)*

- Another major concern is lack of expertise. AEC members are able to insist on more bedding, more appropriate food and cage sizes. Those with a greater understanding may also insist on higher dosage of analgesic, but do they have the scientific knowledge to challenge the legitimacy of the actual protocol itself?

*“I certainly don’t understand all the protocols. The scientists who develop the experiments are often specialists and have advanced knowledge in specific fields. Sometimes all members of the committee, even the scientists, admit that they don’t fully grasp what the experiment is about. I tend to concentrate on specific areas such as animal housing, monitoring and pain relief..... I am certain that my lack of knowledge prevents me fully comprehending what the animals involved in experiments are going through.” – (Category C member, name withheld.)*

- Further concerns:
  - Are AEC members capable of being able to question the design of the protocol?
  - Can they critically evaluate the number of animals used in order to reduce that number, but to ensure that a sufficient number is used in order to statistically justify the research and not cause it to be repeated?
  - Can they be assured that the right species has been chosen to validate the work? This is particularly important because different species can produce vastly different outcomes.
  - Is there an over-reliance on researchers to have sought alternatives?

Clearly these concerns indicate an inconsistency across the ethics committee system which could be addressed by the establishment of a national committee. Such a committee would consist of experts in the fields of ethics and alternatives and thus be in a position to ensure there is no repetition of experiments by different institutions, and have adequate knowledge about the appropriate alternatives that are available.

This centralised activity could be assisted by the administration of databases listing what experiments have been conducted and what alternatives are available. For example, a German-developed online database was launched in April 2008 as an easy to use search engine for alternative methods to animal experiments. [www.GO3R.org](http://www.GO3R.org) draws on millions of articles and research papers. It is funded by the German Federal Institute for Risk Management and its service is free of charge.

### **Stricter policing of protocols**

The development of a national ethics committee would also ensure stricter policing of protocols that currently “slip through” institutional committees with no justification. Some examples follow:

*Example 1* - In an attempt to recreate the effects of the party drugs methylenedioxymethamphetamine, MDMA (ecstasy) and methamphetamine (speed) in animals, researchers at the University of Sydney and Macquarie University tried to replicate the lasting social behavioural effects of repeated doses of these drugs in rats. After 7 weeks of drug inducement the researchers noted a decrease in social interaction in the chronically drug-treated rats. Then to induce stress and depression in these animals they forced them to swim for extended lengths of time.

The researchers claimed the purpose of this study was to compare the results of this repeated weekly exposure to these drugs with experiments previously carried out in which they had studied the effects of a single day of dosing in rats. In their publication, the experimenters acknowledge the already well-known results of using both drugs (ecstasy and speed together) in humans and

the severe long- term cognitive behavioural and neurological changes. National Health & Medical Research Council funding was provided for this experiment.

*Example 2* - In another project published this year, 59 male rats were trained to self administer speed from a lever in a high temperature enclosure in an attempt to recreate the heat in dance parties or nightclubs where the drug is often consumed and the ambient temperature is high. In order to self administer intravenously the rats underwent surgery to implant an indwelling catheter into the jugular vein and a screw assembly heat mount so that the number of drug infusions and lever presses could be recorded. The results of this experiment included hyperthermia being observed and that high ambient temperatures encourage higher levels of drug intake in rats. An NHMRC grant was given to the researchers to conduct this experiment.

*Example 3* –The same researchers attempted to replicate in 48 male Wistar rats the acute effects of ecstasy. They acknowledged, that in humans, regular use develops subsensitivity to the positive effects of the drug and humans thereby tended to escalate their intake over time. The researchers therefore described in this paper how they attempted to replicate ecstasy intake over 2 days to study the social interaction in male rats. Their conclusions depended in part on some assumptions about rats’ motivation, for example, classifying rearing on hind legs as “non-social behaviour”. Also in this latter publication the researchers even acknowledged that a different strain of rat could produce a different response and suggested further research to compare the results in Albino Wistar and the Dark Agouti rat strains “would be a useful exercise”.

We strongly argue that this research is certainly not useful!

We vehemently oppose this type of psychopharmacological research on the following grounds:

- the attempt to replicate in rats the results that are already known in humans is a waste of valuable resources.
- it is unscientific to base this research on animals. Humans are simply not large rats and the physiological, social, behaviours and anatomical differences are too great to attempt to extrapolate results to humans.
- notwithstanding approval of the projects by the university’s ethics committee, they were quite clearly inhumane and served no purpose.
- huge amounts of taxpayers’ money (via the NHMRC) are expended in these experiments when it could be better spent on awareness campaigns warning people of the already well-known effects of drug use.<sup>14</sup>

We consequently recommend far greater enforcement and auditing of the requirement of the Code of Practice section 1.8 : “Techniques that totally or partially replace the use of animals for scientific purposes must be sought and used wherever possible”. If institutions are found not to have rigorously conducted research on the existence of alternatives the institution should be penalised either through the withholding of licenses or some other means.

## **Summary**

AAHR maintains the following core principles:

- Extrapolation of research data obtained from animal experimentation to humans is ineffective, inconclusive and often unnecessarily dangerous.
- There are more scientifically effective ways to conduct research other than with the use of animals.
- Animal-based research and teaching represents unnecessarily cruel and unethical treatments of other sentient beings with little or no redeeming value for human or other species’ advancement.

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<sup>14</sup> [http://www.aahr.org.au/experiments/psychopharmacology\\_research.html](http://www.aahr.org.au/experiments/psychopharmacology_research.html)

Our strong recommendations pertaining to this consultation are:

- i. To develop a vision and strategy for the 21<sup>st</sup> Century
- ii. To ensure that there is sufficient funding incentive available for researchers – ideally through the establishment of an “Alternatives Research Centre”.
- iii. Forge alliances with existing funding centres internationally.
- iv. Place a cap on the number of animal experiments permitted each year.
- v. Totally eliminate the use of animals in teaching.
- vi. The establishment of a national animal ethics committee.
- vii. The establishment of a national knowledge database focussed on alternative research.
- viii. Stricter enforcement of the Code of Practice section 1.8 and penalties to apply to institutions which are found not to have conducted rigorous research on the existence of alternatives.

As quoted by medical experts:

“...alternative testing systems to studies involving animals are being developed and I expect that, in time animal studies will be largely redundant for many purposes.”

***Dr Kerri Mackay, Acting Director, Adverse Drug Reactions Unit, TGA, personal correspondence 25 January 2007***

“For good medical research we need the precision of modern technology and human-based study, not unreliable results produced by animal experiments. Non-animal techniques are faster, cheaper and more rigorous, such as by allowing for larger sample sizes and greater reproducibility.”

***Coecke S. et al. (2006)***

We therefore welcome the NHMRC’s consultation on alternatives research and consider it to be a significant development if Australia is to be considered at the forefront of international progress in medical research.

Please do not hesitate to contact the undersigned should you require us to provide any further information or clarification.

Yours sincerely,

Helen Rosser  
Chief Executive Officer