APVMA
Comments on animal welfare policy

Dangers of relying on animal experiments to determine human reactions.

It has already been widely acknowledged that extrapolation from animals to humans can and does result in dangerously misleading outcomes. Species differences occur in respect of anatomy, the structure and function of organs, metabolism of toxins, rates of detoxification and protein binding, absorption of chemicals, mechanisms of DNA repair and lifespan, and more. So if such differences can occur between similar species then it's negligent to extrapolate from say a rat to a human – two totally different species with a totally different genetic make-up.

Another major difference is in the regulation of our genes. A mouse and a human for example, may share 99% of the same genes, however they are regulated differently. Both a mouse and a human have the same gene that enables us to grow a tail. In the case of a mouse that gene is "turned on", but in humans that gene is "turned off." The argument that we share a large proportion of genes with another species cannot therefore be used as a reason for selecting a particular animal model to predict human responses.

Researchers often claim that animals are used because they need to test in a living system rather than on isolated cells or tissue, however an entire living system creates more variables which can further affect the outcome of any results.

A point of interest is that most animal models used in toxicity testing have never been formally validated.[1] Regulatory bodies often argue that alternative non-animal tests cannot be relied upon due to them not having been validated. This of course raises the question of why animal experiments (tests that are unreliable as they have been conducted on a different species) should be accepted while the humane alternatives (which are based on human data) are not?

We note that the APVMA toxicology testing requirements (APVMA 2005) encourage applicants to submit data obtained from in vitro assay systems or from alternative non-animal methods, however still permit the use of rabbits for eye irritation tests. They also require that acute oral toxicity studies should be performed on at least one mammalian species. Internationally recognized Dr Gill Langley has suggested that alternatives in toxicology have evolved rapidly in the last ten years and that the method of development, pre-validation, and validation has reached the level of international consensus.[2]

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[1] NHMRC draft document *Minimising pain distress and suffering in animals in research.* First round of public consultation 2006.

[2] Langley G (2000). Replacing animals in medical research. In *Progress in the Reduction, Refinement and Replacement of Animal Experimentation,* Balls M, van Zeller AM and Halder M (eds), Elsevier Science BV, 39-50.

Species differences mean that no other species is a suitable model for human disease/research. Several studies support this claim that animal tests are poor predictors of carcinogenicity and teratogenicity (causing birth defects) in humans.[3][4][5]

Animal ethics committees.

The presence of ethics committees, and in particular inclusion of a category C member (animal welfare representative) is often used by researchers to promote a 'clean' image of the industry to the public - as an assurance that the care and use of animals is sanctioned by those with a concern for their welfare and/or rights. However this is not the case. Many category C persons serving on an ethics committee are opposed to the use of animals in research. Their presence is to ensure that the animals are protected as much as possible but only within the scope of the Code of Practice. The committees are dominated by institutional members.

In 1998 a survey of category C members was conducted by Animals Australia. The responses received revealed that:

- One third of respondents are "not happy with the way decisions are made" on their AEC;
- Half stated that "researchers failed to adequately answer the most crucial questions on the proposal forms, particularly those dealing with justification for the research and the availability of alternatives or refinements";
- Half the respondents indicated that they had experienced "animosity or aggression from researchers on the AEC during decision making"; and
- Almost that number also indicated that "pressure is brought to bear on them to go with the status quo".

The category C representative is the only person that represents the interests of animals on an animal ethics committee. While this person may make minor suggestions to improve the welfare of individual animals (in terms of improved housing or use of analgesics), generally speaking they are not sufficiently qualified to challenge the justification of the research protocol itself. This alone is a major concern.

Several category C's have also informed the author (in confidence) that in many cases they do not fully understand the protocol, nor the actual impact it will have on animals. Often this is due to them receiving a large number of protocols just prior to an ethics meeting without sufficient time to analyse them sufficiently, or their inability to understand the scientific explanations provided to them.

Considering these points, AAHR does not consider that animal ethics committees serve their intended purpose. This has been reiterated in the Medical Journal of Australia(6)

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[3] Bailey J, Knight A, Balcolmbe J. The future of teratology research is in vitro. *Biogenic Amines* 2005:19(2): 97-145

[4] Knight A, Bailey J, Balcolme J. Animal carcinogenicity studies 1. poor human predictivity. *Alternatives to Laboratory Animals*. 2006;34

[5] Knight A, Bailey J, Balcolmbe J. Animal carcinogenicity studies 2. obstacles to extrapolation of data to humans. *Alternatives to Laboratory Animals.* 2006;34.

[6] Loff Bebe and Black, Jim, Research Ethics Committees: what is their contribution? MJA 2004; 181 (8): 440-441

which states: “One or two of the most senior members know they can nearly always sway the committee to their point of view.”

The 3R’s.

The three R’s – replacement, reduction and refinement were proposed by William Russell and Rex Burch in their manuscript *The principles of humane experimental technique*, published in 1959. The recommendations, which have been universally accepted, were intended to reduce the overall amount of suffering caused to animals during research.

Replacement
The replacement of animals in scientific research eliminates the need to subject them to any scientific procedure. They can be replaced by using less (or non) sentient animals, usually in order to study basic cellular events; by using in vitro techniques – cell and tissue cultures to test drug effects; by using non-biological techniques, such as mathematical modeling, computer simulation, electronic animals and film and studio aids; and by using humans. This may involve obtaining tissue samples from post mortems or human volunteers providing consent to undergo scientific procedures.

Reduction
This does not eliminate the use of animals, but by reducing the number of animals used can also reduce the overall amount of suffering. Animal use can be reduced by pooling available resources and sharing information so that procedures will not be repeated unnecessarily, and by using appropriate statistical techniques so that the smallest number of animals may be used.

Refinement
This involves the modification of procedures wherever possible to minimize the level of animal suffering. This may be through the use of anaesthesia or analgesia and the improvement of animal husbandry and housing, such as adding environmental enrichment, to reduce the stress factors.

Together the replacement, reduction and refinement of animal use are intended to tighten the regulation of animal research and lessen the overall level of animal suffering. Unfortunately however, reduction and refinement do not address the fact that results from animal experiments can be dangerously misleading when applied to human health. It is therefore pointless to use fewer animals or refine the procedure when it is the wrong procedure to follow. Replacement is therefore the only one of the R’s that remains a credible objective.

Threat of environmental degradation.

The AVPA policy identifies “pests” as causing environmental degradation. It must be recognized however that some of the greatest causes of such degradation are our current agricultural practices – the land damage caused by hard-hoofed animals, the effluent produced from factory farmed animals and the massive use of water to produce food animals. While this topic is not within the scope of AAHR work, we do believe that a more holistic approach be taken to this problem.

Conclusion.

AAHR acknowledges the importance of evaluating the safety of chemicals for humans, animals and the environment, however we are strongly opposed to the testing of these substances through animal experiments. There is a wide range of toxicity tests available that are more humane and scientifically-valid than relying on animal tests. We urge the APVMA to pursue these alternatives.

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