

The response reproduced below was submitted to the consultation held by the Nuffield Council on Bioethics on the ethics of research involving animals during October-December 2003. The views expressed are solely those of the respondent(s) and not those of the Council.

Anonymous #11

## **QUESTIONS ANSWERED:**

### **1. Background: the use of animals in research**

#### **ANSWER:**

It is considered that animal research is a very important and necessary forerunner to the application of new medicines in humans. In vivo experiments in animals help to provide very valuable answers to many questions in science that other techniques such as in vitro tissue culture cannot. The response of the whole mammalian body to various agents or drugs for example is an important reason for undertaking animal experiments prior to undertaking human clinical trials since the issues of safety and toxicity in humans is extremely important for any new medication. In general scientists believe that the results from such animal studies are largely transferable to the human situation, however they recognise that there may exist species differences in reactions between for example a rodent and a human. At present for many studies requiring whole body responses there does not appear to be other viable alternatives to well controlled animal research. The use of animals for research purposes should however be dependent on the purpose of the research and it is therefore important to have approval for all animal work and safeguards provided through specific project and personal licences as well as consideration of ethical issues by a suitable committee. This protection is offered by the 1986 Animals Scientific Procedures Act. Different types of research do require the use of different animal species. For example for veterinary medicine research on BSE it is best to use cattle, which are the affected species. In humans the use of experimental procedures or new drugs is not acceptable without having first completed extensive laboratory studies as well as animal studies to advance the likelihood of success as far as possible before the stage of human testing using volunteers. A lot of these studies will begin in rodents and may move to pigs since this latter animal is thought to more closely resemble human physiology. Also a lot of animal work will begin with small rodent experiments since many more sites in the UK will be eligible to participate in this type of work because of physical restraints. Whether rodents are the best animal to study for research related to human disease is debatable but practicalities dictate that these are often used and related results in the scientific literature are likely to focus on rodents. In relation to the suffering of animals in research this will depend largely upon the type of procedures involved (mild, moderate or substantial) and we have a relatively poor idea of how to measure pain or distress in animals, as signs may not be obvious (at least for less severe instances). For animal procedures regarded as "substantial" it would not be acceptable to perform these (e.g. surgery) without pain relief or anaesthesia since this approach will be eventually be used in human surgical procedures. There may be very exceptional procedures, which may require no anaesthesia, but every effort should be made to keep such procedures to an absolute minimum. Furthermore, good statistical advice at the planning stages in such cases should cut down on the unnecessary use of animals. Obvious stress or pain as judged by a veterinary surgeon or inspectorate without pain relief for procedures will not be permitted for procedures rated as causing "substantial" distress under the 1986 Animals Scientific Procedures act.

## **2. Genetically modified animals**

### **ANSWER:**

Genetically modified (GM) animals potentially do raise different ethical issues in relation to for example to wastage of animals in the process of development such a strain due to the inefficiencies of the techniques involved. Also cloning may have implications for the normal aging process in the cloned animal (e.g. Dolly the Sheep was thought by some to have aged prematurely and died earlier than expected). In general GM animals do not appear to the scientific community as particular unnatural. They are not vastly different to specialised strains of animals bred to portray a particular trait. Although the genetic modification of GM animals (e.g. knock-out receptor) is unlikely to occur in the normal environment the end result may well be similar to an animal with characteristics similar to the phenomenon of an animal with a defect in the same receptor, which displays a non-active receptor phenotype. GM animals allow scientists to focus specifically on the action of a particular gene and assess its importance in a disease process. It will often aid scientists in understanding the related physiology or biochemistry and the opportunity to assess the significance of a gene or its protein product in the development of a disease. GM animals may in fact lead to the more rapid development of targeted drugs for relief of human suffering. GM animals may well compensate for a deficiency in one gene by up-regulation of another gene and allow scientists to assess gene interactions. GM animals which have severe defect such as missing a limb or which are models of continuous suffering without any form of analgesic pain relief would generally be unacceptable to the scientific community. For example animals, which suffer from a degenerative disorder such as Parkinson's disease, should not be expected to survive without pain relief since humans with this disorder would not be left unaided in these circumstances. However, in certain limited circumstances it may be justifiable to produce such GM modified animals as a model to assist in human disease therapy but the breeding of such animals should be controlled to combat the unnecessary suffering of animals. Issues that are likely to be controversial in the future are cloning of animals with particular traits (e.g. racehorses). Further controversy will be found in the production and experimentation of GM animals, which do not have the potential at least for relief of human or other animal suffering. Also research into xenotransplantation of tissues into animals or humans will be controversial. However, for example there will never be enough human pancreatic tissue available for Type 1 diabetes therapy and such options may well have to be investigated in future once the issues of prevention of graft rejection are better understood.

## **3. Alternatives**

### **ANSWER:**

The scientific community generally believe that research into alternatives to animal experiments would be a positive development. Ultimately alternative strategies may require the used of smaller groups of animals in targeted studies but such refinement would reduce overall animal number used. The Government should fund studies into looking for alternative approaches (e.g. artificial organs or tissue research) and grant money should be made available to research councils specifically for this purpose to encourage applications from researchers to change practice. Even with alternative approaches it may well be the case that the "proof of concept" will have to be confirmed in smaller targeted studies in animals in vivo but this should help reduce overall animal

experiments. It may be possible to reduce for example toxicity testing of potential skin irritants using artificial systems. Also human volunteer studies incorporating informed consent and consideration of ethical issues might help reduce animal experimentation. However, the environment for such human studies is getting much more problematic with new EU guidelines and regulations governing such procedures due to change in 2004. This factor may have the knock on effect of driving researchers to use animal models of disease more widely. Furthermore, only the very largest NHS facilities or drug companies may soon have the capability of performing such studies in humans forcing smaller groups to move away from clinical trials with associated liability risks. It is reasonably difficult for researchers to get an idea of the amount of duplication in animal experiments apart from the published literature since many drug trials will remain within the pharmaceutical industry. Also very often a procedure will not be performed in exactly the same way (e.g. the route of drug administration may vary) and thus related studies will be repeated on the same compound. The appearance of experimental animal result data in good quality peer-reviewed journals is the best way of disseminating information to other scientists. (However, one must remember that negative results will rarely be published). Drug companies involved in animal studies will not be willing to share their findings with the wider scientific community due their own IP and drug development issues. It would be difficult to see how dissemination could occur in these circumstances unless there was some sort of legislation, which protected the interests of such companies in these circumstances.

#### **4. Ethical issues**

##### **ANSWER:**

The suffering of animals for the benefit of humans this is often regarded as acceptable if there is the potential for medical science to progress in combating human diseases. However, all scientists would agree that animals should be used in a regulated manner and often as a last resort if no alternative exists. The issue of extending matters of pain, suffering and distress from the human perspective to animals is very difficult. It is likely that all animals with a well-developed nervous system will feel pain but the issue of psychological stress is impossible to appreciate in animals. It may be possible to monitor brain activity at sites of pain detection in animals but we were unsure on this issue. This type of procedure is likely to be in its infancy. Two factors, which should be considered in relation to the justification of animal suffering, would be the following. (1) Does the research have a possibility of improving the likelihood of human disease prevention or therapy? (i.e. benefit) (2) What will be the overall cost in terms of animal numbers (cost) and is the potential improvement worth the effort. The issue of improving other animal health by performing animal experiments would need similar assessment. The environment is likely to be a relatively important issue in terms of assessing the wellbeing of animals. Some animals will prefer contact with others of the species and are gregarious by nature. Also animals should not be exposed to unnecessary viewing procedures or suffering of other animals since this may well cause unwarranted psychological stress and raise anxiety within the experimental group.

#### **5. The regulations**

##### **ANSWER:**

The regulations governing the use of animals since 1986 and also the training of those

involved in these procedures is very thorough in the opinion of research scientists involved in this field. There is a trained NACWO (named animal care welfare officer) looking after animal welfare issues and this is backed up by a named veterinary surgeon plus animal inspectorate. The welfare assessment should be carried out throughout (during) a project. The welfare assessment is well catered for but this procedure by its nature may be a little subjective and depend on the experience of the NACWO or personal/project licence holder. It is appropriate to perform a cost-benefit analysis of the animal work performed in the light of the results of the research and the results of research should be published if possible to inform the wider scientific community. Again negative research findings are often difficult to publish in scientific journals. If regulation on animal work is increased further than the existing 1986 Act then this may well be off putting for researchers. This may well result in UK researchers losing a competitive edge if animal work is carried out elsewhere. Researchers may choose to move abroad where research is less restrictive, but it is more likely they would try to collaborate with others in overseas institutes.

## **6: Providing information to the public**

### **ANSWER:**

We have the impression that researchers would rather have the details of clinical trials performance in humans than any animal work involved in drug development. However, some may wish to be informed of the numbers any type of animals used in the development of for example a drug. Information would need to be succinct on labelling. Perhaps information could be provided by researchers of published work in layman's terms of how the work was conducted and numbers involved. Researchers would choose to remain anonymous in the respect because of possible risk of animal's rights activists.