

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.

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Question One.

The question is not whether research involving animals provides information that is not available by any other methods, but *whether research involving animals is useful in terms of contributing to the treatment of human disease.*

At present the ethical position in relation to using animals in research is, crudely, that if it benefits humans and if it cannot be done in any other way, then it is ethical. This ethical position is unstable because it rests on the assumption of that animal research benefits humans. However, there is a lack of systematic scientific evidence that animal research contributes to clinical medicine.

By systematic scientific evidence I mean systematic reviews or meta-analyses of the available evidence. These are the gold standard for evidence in clinical medicine but the same standards are very rarely applied in basic research using animals. Thus judgements are made on the basis of single experiments rather than a systematic appraisal of all the relevant experiments in a particular field. This has led to significant mistakes, for example, several clinical trials of nimodipine (1) for stroke were conducted on the basis of 'promising' results of single animal experiments. The clinical trials suggested that nimodipine was ineffective and sometimes dangerous in humans. A retrospective systematic review of the animal studies was then conducted and it was found, having weighed all the available evidence, that the animal studies had not been so promising after all (2). If a systematic review of these studies had been conducted prior to the clinical trial then many humans would have been spared the inconvenience and risk of participating in the clinical trials (3). There are other examples to show that when the animal studies are reviewed systematically the evidence suggests that benefit to humans is not as great as might have been assumed (4,5,6,7).

My point is that most of the time, single animal studies are usually cited as evidence that animal studies 'work'. It is not good scientific practice to select certain studies as 'evidence' because invariably the selection will be biased to suit the argument being made. Only when all the available studies have been appraised can we talk about evidence. It is of prime importance to establish whether or not animal research benefits humans. We do not have the answer to this question at present and because of this the current ethical basis for using animals is unstable.

Can results from research using animals be transferred to humans?

We cannot answer this question yet. First of all, the poor methodology of animal studies has to be ruled out as a confounding factor. If this is possible, and if then enough high quality systematic reviews of enough high quality animal experiments consistently find evidence of a beneficial effect of

various treatments in animals, but no evidence of a beneficial effect of the treatments when clinical trials are conducted, this would suggest that findings from animal experiments cannot be generalised to human beings and would support the theory (based on evolutionary biology) that argues that animals cannot be used to predict outcome in humans (8).

However, if enough high quality systematic reviews of enough high quality animal experiments consistently find evidence of a beneficial effect of various treatments in animals, and evidence of a beneficial effect of the treatments when clinical trials are conducted, this would suggest that findings from animal experiments can be generalised to human beings.

Acceptability of using animals

As noted above, our society only accepts the use of animals in research if there is evidence that the use of animals will benefit humans. There is not sufficient evidence of this (see above).

The suffering of animals

Any level of suffering is unacceptable given that the lack of systematic scientific evidence of the benefit of using animals.

Question Two

The issues surrounding the use of genetically modified animals in research are the same as those for all animal research. There is no ethical basis for using them because there is not sufficient scientific evidence that the research benefits humans.

Question Three

The term 'alternatives' implies that animal research is the gold standard, which it is not. As your document notes, there are many valid and reliable research methods, such as epidemiological studies, that have been used for decades in their own right and which have produced valuable data of direct relevance to humans. More funding should be directed at clinical and epidemiological studies. These methods are directly relevant to humans, have a track record of providing valuable data and are in dire need of funding (9). Ethically, they are much sounder than animal studies.

Sharing of information

There is much duplication of animal research. The best way of reducing this is to conduct systematic reviews of studies in each field. This highlights areas of duplication, establishes the evidence base in a particular field and will reduce further, unnecessary experiments.

The way animal research is reported in scientific journals

Details about the experiments, for e.g. specific surgical procedures, are disguised beneath scientific jargon. This means that the suffering that animals may experience is not revealed in the papers. This 'editing' of the research process is to make the research appear more palatable to readers but it has a 'sanitising' effect (10).

Publication bias: negative results are less likely to be published, giving the overall impression that animal research leads to positive and significant findings.

The way animal research is reported in the media is also a cause for concern. 'Promising' findings from single animal studies are quoted widely, often before the full findings are known and usually before we know the relevance – if any - to humans. This gives the sustained impression that animal research is useful, but it is misleading.

Question Four

The current ethical position regarding the use of animals in research is predicated upon the assumption that animal research is necessary to the advancement of clinical medicine, i.e. animal research is considered ethical because there is a belief that it benefits humans. However, the use of animals cannot be ethical because there is not enough systematic evidence that animal research contributes to human medicine, nor that it is the best way for clinical medicine to advance. It is also possible to argue that the use of animals in research is unethical for humans too, because there are many tried and tested research methods that are safer and more beneficial in terms of producing data of direct relevance and benefit to humans (see Q on 'alternatives').

How can we know how much animals suffer

The only research that should be undertaken to investigate how animals experience the world is observation of animals in their natural settings. Invasive research would be unethical.

Question Five

The current system whereby project licences are granted is flawed. Unless there is an available systematic review or meta-analysis on the topic in question it is difficult for the person granting the licence to judge whether further research is necessary, or to make a cost-benefit analysis. Thus a subjective judgement is made rather than one relying on an objective appraisal of the available evidence.

As to whether or not the research can be done without animals, those working within the scientific paradigm of basic animal research are unlikely to be aware of other scientific methods available for answering the question

and are therefore highly likely to give the opinion that the research could only be done using animals.

Question Six

Given that the current ethical position assumes that animal research benefits humans, one of the first things to establish when making judgements about the acceptability of research involving animals is *whether or not it works, i.e. is there good evidence that research using animals benefits humans.*

Labelling medicines

It would be uninformative and misleading to label medicines that were developed using research with animals; most medicines involve research using animals, however, this does not mean that such research was actually *necessary* or the best way of developing that medicine.

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