

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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Contributor:

I am a qualified laboratory animal technician who has worked in the state sector with all of the commonly used species of laboratory mammals. I have taken an active interest in science and the role of animal experimentation within it for many years, including the period during which I worked as a lab technician. This has involved keeping a theoretical and historical, evidence-based interest in developments in knowledge.

Animal experiments have:

a 63% failure rate when detecting human carcinogens

a 75-95% failure rate for detecting drug side effects

a 70% failure rate for detecting drugs which cause birth defects Success rates lower than those achieved by uneducated guesswork.

This is not science!!

Recommended website: The Absurdity of vivisection <http://vivisection-absurd.org.uk/>

Information on animal research available free by EMail from [vivisectionkills@hotmail.com](mailto:vivisectionkills@hotmail.com)

### **Q1 What is your view about the use of animals in research?**

Support for animal-based research is forthcoming from many parts of the medical and pharmaceutical industry. However, it is wise to question this support as opposed to blindly accepting it as evidence that animal research is a worthwhile method of advancing medical knowledge and ensuring efficacy and safety of medical products.

This is because animal experimentation has benefit of a commercial nature for those involved financially or occupationally in the pharmaceutical sector. A major benefit is the role it plays against attempts to claim legal redress in the case of drugs which have caused adverse reactions; as the matter to prove is one of negligence (as opposed to damage to health), animal experiments provide evidence of efforts taken to ensure safety.

Another benefit is in the approval of commercial products including drugs. Animal methods are quick, and therefore enable the prospect of a shorter period before research and development costs are regained. It is also true that the results from animal experiments encompass a degree of flexibility. In choosing species, test conditions, dose levels and periods and other factors, it has been established (see below) that a spectrum of results may

be obtained. By selecting the favourable ones to present to regulating authorities, data appearing to support requests for approval can be assembled.

It is noteworthy that a multinational manufacturer of household products was discovered to be lobbying MEPs recently in an attempt to avoid a ban on animal testing for cosmetics in Europe.<sup>i</sup>

In the case of academic and fundamental research, the benefits of animal research lie chiefly in their speed and the ease with which they can be conducted. Clinical research is considered much more complex and time consuming, and requires more input on the part of the researchers. For the scientist over whom the words 'publish or perish' hang heavily, the cliché "a rat is an animal which when injected produces a paper" is a relief. Scientists risk their income and tenure if they do not publish.

It is not, therefore, prudent to accept the assertions that animal experiments are beneficial to humanity from a medical perspective, without first assessing the relevance of the method.

#### Detection of adverse reactions in man

Claims that animal experiments are absolute predictors of the human reaction have been retracted over recent years to the claim that they are reasonably good predictors, which cannot yet be replaced by non-animal methods.

Non-animal methods include the four-step CADD (Computer Aided Drug Design) process, a range of in-vitro tests, patient monitoring to detect serendipitous beneficial effects in humans, self-experimentation, clinical trials, and others. An emerging technique is DNA microarray technology, which considers the interaction between a potential drug and a patient's individual genes. Another is the use of technology to scan the brain of a patient after a tiny dose of a potential drug has been taken, in order to trace its path and destination, and determine its psychological effect. QSARs (quantitative structure-activity relationships) have been used since the 1960s to enable computers to consider the effect of chemicals on the molecular level. It is therefore established that there are highly informative methods of research available to today's researcher.

Animal-based toxicity testing has been employed since the 1960s and the tests have not been improved since that time, according to a leading toxicologist who (works in and supports animal testing) in a public report.<sup>ii</sup> Since that time the accumulation of available data and the investigation by evaluation has enabled the accuracy of the method to be assessed.

Anecdotal estimates have been made within the industry. One stated: "*As a very approximate estimate, for any individual drug, up to twenty-five per cent of the toxic effects observed in animal studies might be expected to occur as adverse reactions in man.*"<sup>iii</sup> This estimate was endorsed: "*...the best guess for the correlation of adverse reactions in man and animal toxicity data is somewhere between 5% and 25%.*"<sup>iv</sup> Less quantitative estimates exist: "*Most adverse reactions which occur in man cannot be demonstrated, anticipated or avoided by the routine subacute and chronic toxicity experiment*"<sup>v</sup>, and "*the predictive value of studies carried out on animals is uncertain.*"<sup>vi</sup>

However, tests have identified the level of accuracy for animal experiments.

One such study selected a group of drugs for which seventy-eight side effects were known to affect humans and would be detectable in animals, should they occur. Undetectable effects (e.g. depression, headaches) were disregarded. Over half (54%) were undetected<sup>vii</sup>.

Another trial examined the animal test data for a year and compared it with human experience. Seventy-five percent of side effects predicted by animals did not occur in humans.

A leading drug company evaluated standard tests to identify carcinogens by using known human carcinogens in the routine tests. Around two-thirds (67%) of the carcinogens were passed as safe, and the researchers concluded that flipping a coin would have been more effective.<sup>viii</sup> An American study of a similar type used standard animal tests and compounds known to cause oral cancer. Seventy-three percent were passed as safe.<sup>ix</sup> Warnings from experts of this misleading effect include the following: "*In monkeys none of the power carcinogens [to humans] has been shown to produce cancers.*"<sup>x</sup>

As with side effects, in carcinogenicity screening animal experiments have a tendency to compound the problem of false negatives by contributing false positives. A test of compounds known not to cause cancer in humans, discovered that ninety-five percent **did** cause cancer in the laboratory animal, indicating a 95% failure rate.<sup>xi</sup>

Unfortunately the dominance of animal testing means that the method is accepted despite clear evidence that, for scientific reasons, it should not. The implications are notable. An American study of drugs released over ten years showed that over half (52%) were re-labelled or withdrawn due to unpredicted adverse reactions in humans.<sup>xii</sup> All had passed mandatory animal tests.

The problem of adverse drug reactions (ADRs) is considered significant. In America it is estimated by a medical journal that medical drugs correctly prescribed and correctly administered cause 106,000 deaths annually. The incidence of ADRs was estimated to have remained level for three decades.<sup>xiii</sup> It was also estimated that 1,500,000 people are injured by ADRs with sufficient severity to be hospitalised.<sup>xiv</sup>

In the UK the House of Lords has considered the implications of the discovery that ADRs are the third largest cause of death, ahead of cancer.<sup>xv</sup> A medical journal estimated that "*In England, an estimated 70,000 deaths and cases of severe disability occur each year because of adverse reactions to prescription drugs, making this the third most common cause of death (after heart attack and stroke).*"<sup>xvi</sup> All these drugs are tested on animals prior to release, and pass.

In addition, medical drugs are implicated in a large proportion of cases where babies have been injured prior to birth. The rate of these events was measured at three per 100,000 live births in 1948<sup>xvii</sup>. In 1999 The Lancet estimated that serious abnormalities at birth affected over 800 per 100,000,<sup>xviii</sup> and the Congenital Anomalies Register figures for 2001 recorded 1170 serious defects per 100,00 live births.<sup>xix</sup> A detailed study into this serious problem concluded that for sixty-one percent of all birth defects and eighty-eight percent of stillbirths, drugs taken during pregnancy were directly responsible.<sup>xx</sup>

Certainly claims that animal experiments have instilled a misplaced sense of the relative danger of a drug are supported by the incidences of false negatives and false positives known to be attached to such tests. Testing known human teratogens on pregnant monkeys yielded the result that seventy percent were passed as safe.<sup>xxi</sup> Conversely, around 1,200 chemicals have been identified as dangerous to the unborn child by animal studies, yet over ninety-seven percent have no link to birth defects among humans.<sup>xxii</sup>

### Drug efficacy

In identifying beneficial effects of drugs, the success levels of animal methods are identified by a low level of success between animal trials and phase one clinical trials. The failure rate is considered to be around 92%<sup>xxiii</sup>, indicating a low level of correlation between effects identified from animal studies, and human experience. Research into certain areas has yielded further data on correlation, such as the study into twenty-five drugs identified by animal studies to be effective in treating stroke. None are used in humans.<sup>xxiv</sup>

In identifying cancer drugs, the low level of accuracy achieved by the animal model is acknowledged by experts such as National Cancer Institute (USA)

director Richard Klausner: "*We have cured mice of cancer for decades, and it simply didn't work in humans.*"<sup>xxv</sup> Thomas E Wagner, a long-serving cancer researcher stated: "*God knows we've cured mice of all sorts of tumours. But that isn't medical research.*"<sup>xxvi</sup> The Handbook of Laboratory Animal Science states: "*despite 25 years of intensive research and positive results in animal models, not a single anti-tumour drug emerged from this work.*"<sup>xxvii</sup> While this can be attributed largely to species difference with respect to the tumour, again there is evidence for direct comparison with data when considering drug action against human tumours implanted in laboratory animals. Drugs known to be effective in humans failed in sixty-three percent of cases.<sup>xxviii</sup>

Although anecdotal, the history of drug discovery is punctuated with examples of discoveries made by accident, such as when the drug has been administered for a different cause and found to affect a different ailment. Conversely, there are few cases where a reliable chain of discovery can be described where the effect has been discovered in animals and successfully translated to humans. Indeed, while the House of Lords Select Committee on Animals in Scientific Procedures were compiling their report in 2001, it was notable how little evidence in support of vivisection was forthcoming, and how the claims made in its favour were anecdotal and unreferenced.

## **Q2 What are your views about the use of genetically modified animals in research?**

It has been difficult for me on a personal level to identify genuinely held beliefs underpinning the increase in genetically modified animal use. It may appear cynical to suggest that researchers are attempting to identify a less understood area in which to work with less opposition, but the claimed benefits of these models is not realistic.

Whilst working in a London medical school I worked for over a year with a colony of 'mdx' mice numbering, on average around one hundred. They are used as a model for muscular dystrophy due to gene alterations. I have also been in contact with human patients of this illness, which is irreversible, and fatal in most cases by the mid 20s.

For several months as the sole charge of this colony, I was unaware of their genetic profile, and was not told of any special needs compared with the other seven strains of mice for which I was responsible. I have since learned that their comparison is impractical.

*"The animal (mdx mouse) was not noticeably weak or clinically compromised. In fact, after an early transient phase of slight weakness, its*

*muscles grow larger and stronger than normal and the animals remain healthy and active throughout a more or less normal lifespan.*"<sup>xxxix</sup>

A higher profile genetically altered model is the genetically altered mouse used for researching cystic fibrosis. In ninety-five percent of human patients death is caused by excessive fluid on the lungs,<sup>xxx</sup> yet in the mouse model this symptom is never seen.<sup>xxxi</sup> In humans, the mucus is secreted by the serous glands, which do not exist in the mouse<sup>xxxii</sup>, highlighting the limitations of relying on a single gene in an entirely different biological system.

About eighty-five per cent of human patients are unable to properly secrete pancreatic digestive enzymes<sup>xxxiii</sup>, and around a third have a liver disorder (focal biliary cirrhosis)<sup>xxxiv</sup>. In the mouse model occasional pancreatic changes have unreliably been produced, and no liver effects have been detected.<sup>xxxv</sup>

Intestinal health problems are a feature of the mouse model, claiming up to half the lives of the mice within thirty days from birth, yet this is unparalleled in human patients.<sup>xxxvi</sup> Human male patients are infertile in eighty-five to ninety-five percent of cases, yet there are infertility trends among the mouse model<sup>xxxvii</sup>. These differences identify the fact that altering a gene or even a range of genes is an inexact science, as the role of the gene depends on many factors including the interaction with other genes, the biology of the animal, environmental factors, and others.

The genetic uniqueness of man is underlined by the admittance by a laboratory animal manual that although many human diseases are known to be caused by a defect in a single gene, no illnesses caused by single genes have ever been shown in any monkey species.<sup>xxxviii</sup> This underlines the limits to which genetic comparisons are subject.

I am unable to suggest a scientific reason for the continuation of research using genetically manipulated laboratory animals.

### **Q3 What is your view about the use of alternatives**

The work of organisations such as Interniche has been invaluable in highlighting the range of scientific methods available to individuals and organisations still using animals. The range of techniques and technology available is always a matter for interest and a testament to the scientific ingenuity of researchers who hold scientific progress in mind. However, the use of these methods will always be neglected while:

- there is insufficient political effort to put into action stated but neglected demands that non-animal methods will be used in preference to animals unless good reason can be stated;
- there exists scope within the legal framework for the use of animals to be used as a defence against drug-injured patients.

While much of this will be expanded in the later section on legislation, it remains to be noted that there is severe neglect on the part of commercial organisations, the government, scientific researchers and especially the Home Office to ensure the limitations of animal experiments are recognised and medically superior methods are used instead wherever possible.

**Q4 What is your view about ethical issues relating to the use of animals in research?**

Ethics is a matter for conjecture, personal opinion, and philosophy. My personal conclusion is that animal experiments cannot be justified, as their continuation represents a conflict, which holds two beneficiaries on opposition. One is the welfare and rights of animals, the improvement of medical knowledge, the efficiency of the National Health Service, the welfare and rights of human patients, the economy (which is to benefit from a healthy population), and the preservation of human life. Opposing beneficiaries are the shareholders, directors and staff of drug manufacturers, individuals who have built their careers on the animal method who would have to re-train, and those involved commercially with the animal research industry.

Given the relative benefits and losses to be incurred by either abandoning or continuing animal experiments, the greatest amount of benefit will be achieved by abandonment.

**Q5 What is your view about the UK regulations on research involving animals in the UK?**

It is frequently stated that all animal experiments are conducted and approved subject to strict government guidelines, that experiments are only permitted if a significant benefit can be demonstrated to be likely from the experiment. My experience is entirely to the contrary, and on reflection I find it fantastic that these claims are made at all.

There is no legislation which controls the manner in which animal experiments are conducted to such a degree as to control matters which influence animal welfare and experimental results. The 1986 Animals (Scientific procedures) Act does not demand welfare standards, and in my view relies heavily on statements of 'should' when 'must' might enforce requirements. Welfare standards for animals are not demanded by the law but merely requested by a Code of Practice (COP), which is clearly voluntary. Laboratories frequently neglect these very rudimentary standards. Other than these standards there are no demands made by the law which are effective in preventing animal suffering which, by definition dictated by supporters of animal experiment, is unnecessary.

It is notable that in 2001 the government's claim that the 1986 Act was "the most rigorous piece of legislation of its type in the world" offering "a high level of protection to animals..." and with "sufficient flexibility to allow the latest ideas and technology to be taken into account when deciding whether the use of animals is justified", was challenged legally. On the 16<sup>th</sup> July that year the government backed out of the case, agreeing to pay all their opponent's costs. Clearly the argument seemed unwinnable; examination of the available evidence shows why.

I estimate that during my career I came into contact with ten thousand laboratory animals. These included mice, rats, cats, dogs, sheep, pigs, gerbils, rabbits, guinea pigs, mastomies, and three breeds of macaque. I do not believe I saw any of these live and die according to the COP.

Overcrowding was common; cages meant for three mice were routinely used for five, and in one area were routinely used for between five and ten (inclusive) adults. The problem was compounded by the inhabitants being mixed sex sibling groups, which often bred and produced unwanted offspring.

By studying documentation based on figures we kept, I ascertained that over two-thirds of all rats and mice bred were killed as surplus to requirements (and therefore not included in figures released by the Home Office. While studying the gassing technique at college I identified many transgressions by my employer from the correct method, which was also stipulated in the legislation.

Animals were gassed in an unclean chamber which was caked with blood and faeces. The smell was easily detectable by my smell, and caused panic among the animals. The inlet points for the gas were all at the bottom of the chamber when they should be at the top. The gas was compressed, cold, and noisy, in contrary to instructions, and caused further panic. There was

no way of telling (as required by the legislation) the level at which the gas was introduced.

Panic was evident: it was common for animals to fight and climb over each other trying to find breathable air, and the positions in which they died indicated they had attempted to burrow out or tear the metal bars which restricted them. Death is to be confirmed by checking for rigour mortis, neck breaking or throat slitting - it was routine to do none of these. As result animals were removed from the chamber and put in rubbish bags while still alive, and were found to recover. It is likely that others recovered but did not come to staff attention as they were buried under other bodies and died among them.

Space does not permit me to enter into all digressions from good policy and legislative requirements. An example of this was a project involving macaques to map the brain. This involved invasive, non-terminal surgery on an intelligent species of macaque (Pig-tailed macaque, *Macaca Nemestrina*). The macaque was housed in a small cage barely longer than her body, with no access to nesting, bedding, recreation, privacy, social contact, or any of the other imperatives. Reference to the COP revealed consistent breaches. The conditions were witnessed by an inspector, but continued.

A significant failure of the claimed intentions of legislation is in the prevention of experiments which cannot be justified. Experiments still continue for household cleaners, agricultural chemicals, commercially competitive products similar to existing ones, which cannot be justified. On a medical level, it is incredible that licenses are still being permitted for cancer research in mice, given the demonstrated history of failure and an established understanding of the ineffectiveness of the study of mouse cancer to add anything to the knowledge of human cancer at all.

Returning to the macaque brain experiment mentioned above, it might appear that such a controversial experiment might be subjected to rigorous scrutiny given the fact that it involved over a dozen primates, re-use of an animal (which was illegal in the UK from 1876-1987), and brain injury from which a primate will recover (twice for one animal).

Further investigation revealed that on medical grounds alone the experiment was not defensible due to noted species difference which exists between macaques and humans with respect to the brain.<sup>xxxix</sup> Furthermore, human-based techniques were available, and were declared superior.<sup>xl</sup>

Similarly, an experiment using cats involved a condition known as 'spreading depressing', which affects electrical charges on the surface of the brain. This phenomenon affects only smooth-brained animals (e.g. cat, rats, mouse,

fish) and not convoluted brained animals (e.g. monkey, human)<sup>xli</sup>. It had only been witnessed when induced. The process by which it is induced matches closely a technique used by a leading neurologist who has used the technique on an estimated 1,000 patients, in which electrical recordings were made. He and other are unanimous in stating they have not witnessed spreading depression.<sup>xlii xliii xliv xlv</sup>

In addition to my experience, I have taken an interest in the findings of people who have worked in laboratories since then and recorded their findings. The video, photographic and documentary evidence emphasises the failure of the law to achieve its stated objectives.

### **Q6 What do you think about the information that is available to the public about research involving animals?**

A continuing interest in animal experiments has been hampered continually by the refusal of the Home Office to enter into debate and the refusal of government and public bodies to acknowledge the need for discussion without prejudice.

The Home Office has responded to my letters with factually incorrect information. The letters are probably standard, and do not answer specific queries I have raised. On responding to them, I have been ignored. Suggestions for improvement in procedures have been dismissed without consideration or justification. Certainly the Home Office is either aligned directly with the most hard-line of the pro-vivisectionists, or it is satisfied to give the impression that it is.

The Home Office is perpetuating wastes of money, animals, and opportunities in refusing to release details of licences applied for. These could be then considered by organisation concerned with ethics, scientific responsibility and accuracy, before they are approved. Such a debate need not (as the Home Office has asserted) involve risk to institutions or individuals from 'animal rights fanatics'. Details of proposals need not include names of institutions or people for the debate to proceed.

A further source of disappointment in terms of information made available relates to the consultation paper issues by the Nuffield Council. An examination of the Council reveals that several members have financial interests in the continuation of animal experimentation, and one leads the main lobby group for its continuation. Despite the existence of many able and available doctors and active medical researchers who support abolition, none were included on the council. Those nearest to this point of view

include an RSPCA representative who I have heard speak at a conference, who clearly supports continuation, and one representative of animal welfare who does not enter the scientific argument.

This is reflected in the guide, which lists seven websites. Four are for organisations which support continuation, two for animal-protection groups, and one for FRAME, who claim to be working in the interests of reduction, but are essentially continuation supporters. Many websites were neglected in this list. Similarly the book list avoids the most prominent and respected of the recent medical books supporting abolition, such as those by Dr C Ray Greek.

Most people I speak to perceive animal research to be a dubious subject. They picture 'mad scientists' performing experiments of their own choice, unregulated, in underground secret chambers. This view is inevitable given the secrecy with which the licensing and legislation is conducted. In my experience, the secrecy also enables practice to tend towards this image.

If the debate is to be allowed to progress it is essential that:

- Those opposing animal experiments on scientific grounds are involved in licensing and policy decisions at a Home office and governmental level.
- The Home Office engages in dialogue with concerned members of the public and maintains standards in which it uses factual information only, responds to points, suggestions and queries, and is able to take the views of the public into account provided they are presented rationally.
- Details of experiments are presented in a way in which they may be challenged by opponents and prevented unless they can be justified.
- Independent bodies are allowed to investigate current practice and policy, evaluate it, make public value judgements and expect response on a policy level.
- Independent bodies oversee the debate and ensure that unreferenced, unsubstantiated claims regarding the benefits of animal experiments are challenged and those making them are forced to withdraw them.
- Government bodies are prohibited from taking a prejudiced view or from publishing or otherwise promulgating a view in support of vivisection.

I have concluded from my interest in this matter that the UK is running health services at a significantly compromised level of efficiency, and is lagging behind many competitors internationally in developing an incisive policy on medical research. In order to rectify this, the first priority should be to develop open lines of communication with rational interested parties.

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