

Animal Procedures Committee:

CONSULTATION PAPER ON THE COST/BENEFIT ASSESSMENT
and the
Animals (Scientific Procedures) Act 1986

Response from the National Anti-Vivisection Society

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Introduction

The Animal Procedures Committee (APC) has invited input from the NAVS on their consultation paper on the cost/benefit assessment, a process central to the granting of project licences under the **Animals (Scientific Procedures) Act 1986 (the Act)**.

These are the elements of the Act that we have addressed in our response:-

Permissible Purposes:

Section 5(3) of the Act states that: A project licence shall not be granted for any programme of work unless the Secretary of State is satisfied that it is undertaken for one or more of the following purposes-

- (a) the prevention (whether by the testing of any product or otherwise) or the diagnosis or treatment of disease, illhealth or abnormality, or their effects, in man, animals or plants;
- (b) the assessment, detection, regulation or modification of physiological conditions in man, animals or plants;
- (c) the protection of the natural environment in the interests of the health or welfare of man or animals;
- (d) the advancement of knowledge in biological or behavioural sciences;
- (e) education or training otherwise than in primary or secondary schools;
- (f) forensic enquiries;
- (g) the breeding of animals for experimental or other scientific use.

The Cost/Benefit Assessment:

Section 5(4) of the Act states that: In determining whether and on what terms to grant a project licence the Secretary of State shall weigh the likely adverse effects on the animals concerned against the benefit likely to accrue as a result of the programme to be specified in the licence.

(The Act does not describe how this is to be achieved, or provide a list of criteria; the criteria below have been developed by the Animals Scientific Procedures Inspectorate (ASPI, or Inspectorate).

The Use of alternatives:

Section 5(5) of the Act states that: The Secretary of State shall not grant a project licence unless he is satisfied that the applicant has given adequate consideration to the feasibility of achieving the purpose of the programme to be specified in the licence by means not involving the use of protected animals.

Question 1

Can the validity of experiments on animals be argued in absolute terms as set out in paragraph 7 or should this be considered on a case by case basis taking into account the factors such as those in para 8 above? It would be helpful if you could explain the criteria you believe should be used to assess the scientific validity of animal experiments.

The NAVS believes that the similarities between humans and other animals are frequently overstated by pro-vivisection scientists and concentrate on superficial similarities. The crucial differences between species are from the cellular level upwards. It is these differences that result in misleading information from animal experiments.

Therefore we would say, yes, animal experimentation can be argued against in absolute terms. However, there is neither the political will nor the legislative framework to proceed on this basis as present.

On the other hand the current Act already provides for scrutiny of animal research on a case by case basis. This could be used to facilitate a wider scientific and informed public scrutiny of project licence applications to allow a valuable debate and better science.

Thus, overall, the NAVS is in favour of the approach described in para 8 of the consultation document, but the cost/benefit assessment needs to be applied with greater effect, using an expanded version of the criteria currently used by the ASPI. This would include greater emphasis on whether others are conducting similar work elsewhere, especially without the use of animals; whether human data is available; whether a non-animal alternative is available; whether there are other sources of the information required. There needs to be emphasis on whether a combination of resources and methods could produce the information required. The licence application should:-

- Demonstrate the relevance of the proposed work in relation to current knowledge and the subject to be addressed.
- Demonstrate that the knowledge to be acquired by the animal studies is not already available or may be concluded from previous results.
- Demonstrate that the non-sentient methods currently available could not produce similar results.
- Indicate how the scientific quality of the proposal is assessed (for example, by periodical independent peer review).
- Demonstrate adequacy and security of funding in relation to time-scale of proposed work (prevent preliminary results not being taken further due to lack of funding).
- Demonstrate quality of experimental design, including statistical aspects.
- Demonstrate validity of working hypotheses and suitability of protocols in relation to general purpose of the work.
- Summarise the results of any pilot studies.
- Demonstrate that the research team has all the necessary experience and competence, to maximise scientific quality and animal welfare (beyond local inspector's 'personal knowledge').

Additionally:

Current legislation does not permit animal experiments to be carried out when there is an alternative method available. However, attention should additionally be given to the possibility of the researcher developing a new non-sentient technique that could be used for the proposed purpose if an applicable method is currently not available.

The possibility of **fortuitous disco very** cannot be accurately estimated and should therefore not be used as a benefit in a cost/benefit analysis. Benefits can only be meaningfully estimated from pre-calculated, well planned experiments with definite end points. If there is any possibility that the benefit could be zero, such as with 'try it and see' experiments, it is not a valid benefit to be used in the analysis.

A clear checklist needs to be built up.

Information Provided by Chief Inspector

In his 'Cost/Benefit Assessment', (*1997 APC Report, Chapter 2, Annex 1*), the ASPI Chief Inspector listed criteria and information used to form judgements made during the cost/benefit assessment of a project licence applications. These criteria need to be expanded upon, and clarified, to form a structure of rigorous checks:-

- Important of objectives

- Probability of achievement

- Cost of animals

- Likelihood of success

- How data (or other product) will be used

- Resources and track record of the research group

- Minimising costs, maximising benefits

- Costs- nature of the adverse effects;

 - the action to be taken to mitigate these effects;

 - the endpoints applying to the procedure;

 - Severity Limit – the maximum severity expected to be experienced by any animal (i.e. single worst case);

 - Severity Band – the degree of suffering expected to be experienced by the average animal; *this is the 'cost' used in the cost/benefit assessment* (the overall severity of

 - the project – the likely adverse effects on all animals, weighed against the benefits likely to accrue);

- stresses of capture and transport, e.g. when non-human primates are to be taken from the wild or transported from overseas, and for some 'field studies' the incidental effects on the local ecology.

- Benefits include-

 - human, animal and ecological benefits – improved health or welfare, plant production, food hygiene, safeguarding of the environment;

 - scientific benefit – resolution of controversies, increasing scientific knowledge;

 - educational benefits – meeting educational objectives which cannot be satisfied by using non-animal models;

 - economic benefits – profitability, employment, conservation of natural resources;

 - Forensic enquiries

The factors and documentation informing the ASPI judgement are stated as-

- the information on the application form;

- knowledge of the research group, its track record, facilities, resources and published work;

- specialist knowledge of the area of science and other work being conducted in the same field;

- the likely adverse effects;

- knowledge of policy, precedent, practice and refinements.

Question 2

Do you consider that the cost-benefit assessment adequately addresses the scientific validity of projects and individual experiments within these? Who do you consider has/should have responsibility for assessing validity (e.g. the researcher, the funding body, the Animal Scientific Procedures Inspectorate, Ethical Review Process, regulators, other)?

There is evidence that, to date, the cost/benefit assessment has failed to adequately address the scientific validity of animal experiments. Only the widest possible scrutiny befits a proposals to deliberately inflict pain and suffering on any living being.

Responsibility for assessing validity needs to be a combination of the applicant, the funding body, the ASPI, the APC, and outside scrutineers – informed public, interested bodies such as the NAVS. At present, those with the objective of preventing animal experiments are excluded from the process.

The NAVS does not believe that the current assessment adequately addresses all of the necessary issues and factors. The Home Office produces reports outlining the theory, but it is difficult, from outside, to judge how assessment works in practice when we do not see specific examples of the process.

Blocking public access to technical details of project licence applications prevents outside input and wider scientific scrutiny, which is detrimental to science, to open government, and to the public interest.

NAVS investigations of UK laboratories, and our reviews of published research papers, has uncovered numerous examples of animal use when the results could have been predicted as the relevant data was already available elsewhere, or where the species differences were already known, or human data was, or could have been made available, or the information required was available from other sources.

For example:

The Medical Research Council's report of their inquiry into the Feldberg case noted that the ASPI had known about the problems with Feldberg, but that the ASPI did not consider it to be their role to seek out and report upon improper laboratory practice. This is at odds with the impression given to the public by ministers, and furthermore, means that there is not a body performing a basic 'policing' role within the administration of the Act (*Report of the Inquiry, MRC, 1991*).

We reported on the use of cats in migraine research, using a theory about an event in lab animal brains called 'spreading depression'; these animals were used despite that the theory had been discredited a decade earlier, with data from human studies (*1996, Access Denied, NAVS*).

We reported on animal tests of a weedkiller which had already previously been tested on animals, and which had been on the market for decades and so its effect on humans and the environment was (or should have been) already known (*1993, Labs Unlocked, NAVS*).

We have attached to this document (NAVS Cost/Benefit Response, Annex 1), assessments of research on animals at the government establishment at Porton Down.

Scrutiny, Accountability:

In order to make the cost/benefit assessment more effective, scrutiny of proposals and involvement in assessment must be as wide as possible – organisations with an interest and contribution to make (the NAVS, the Lord Dowding Fund); informed public; Animal Procedures Committee; the ASPI.

The following parties should be involved, as a matter of course, in addition to the APC:-

- Peer review process, whereby experts in the relevant field can accurately assess for the probability of success and repetition.
- Consultation with alternative experts to ensure that applicable techniques without the use of animals are not being overlooked. This could involve consulting external experts or establishing an 'alternatives' committee to advise the APC (see below).

- If Freedom of Information is applied to licence applications the pending applications could be available for public inspection (names of researchers and institutions need not be detailed) for a certain time period. Any interested individuals could offer informed opinions. The licence would only be approved providing that there is no relevant opposition offered within the set time period.
- There needs to be a thorough, open, ongoing, review process. At the Institute of Neurology, cats were suffering severely, and the staff appeared unsure what to do about it. Only when the NAVS uncovered the incident during an investigation, was the project suspended.

The Animal Procedures Committee needs to be strengthened, and provided with powers. There needs to be an overall authority over the ASPI, to act as both a policing and review body. Such a body would provide public accountability in a way that is not possible with the current arrangement, i.e. where civil servants (the ASPI) report to and advise a minister. This is not to do with any particular issue with the ASPI; it is a matter of public accountability and that the process is *seen* to be open and balanced.

Outside Advisory Body

Technical details of project licence applications need to be laid open to general public review, or, a separate scientific advisory body could be brought together to review proposals to use animals and make recommendations to the Animal Procedures Committee. Such a body would provide a structure to input from organisations whose remit prevents them from playing a role in the APC. Costs to be borne by participants.

Repeal Section 24

The NAVS strongly advocates that section 24 of the 1986 Act should be repealed, enabling wider scientific scrutiny of technical details of project licence applications (no personal or business details), before a licence is granted, and information in the administrative and licensing process be placed in the public domain. Information to be placed in the public domain to include:-

- details of licence applications
- contents of ASPI files
- scientific and factual advice from ASPI to Secretary of State
- results of research
- compliance monitoring and enforcement
- proceedings/recommendations of local ethical review committees
- application of alternative methodologies and compliance with principles of reduction, refinement and replacement

Informal Applications:

The NAVS is firmly of the view that the practice of “informal” and unrecorded applications should cease. This is an issue we have raised previously in a follow-up to a complaint (*Institute of Neurology, 'Access Denied', NAVS, 1996*).

In his ‘Cost/Benefit Assessment’ (*1997 APC report, Chapter 2, Annex 1*), the Chief Inspector describes how discussions with applicants take place on an informal basis, prior to an official application. Unrecorded applications and discussions in this way pose an enormous problem to any commitment to public accountability. Informal applications do not facilitate wider public scrutiny; informal applications make it difficult to identify areas where prospective applicants need education and advice in other methods and other sources of information; informal applications make it impossible to get a proper view of the number of applications made and refused. The ASPI informs us that ‘many’ applications are refused before they get to the formal application system. A list of reasons for refusal

are given, but we are given no idea of the numbers of refusals, because these are, apparently, not recorded.

All discussions between the ASPI and applicants should be documented, and open to scrutiny. This is helpful for both the Inspectorate, and for those with concerns about the use of animals in research, and the decisions being made. The process has to be *seen* to be working.

Confidence in Inspectorate:

“... A strength of the UK system is that those making this essentially subjective judgement for most applications have the mix of expertise required to make simultaneous assessments on clinical, welfare, scientific, and ethical aspects of research proposals. Inspectors have the clinical experience and skills to make informed judgements concerning the likely severity of adverse effects, the scientific experience and skills to enable sensible questioning of scientific quality and they are well placed to take a balanced view of ethical extremes” (1997 APC Report, Chapter 2, Annex 1,p.50).

This is unacceptable. Even for a body which works openly amongst the public, with a system of direct public accountability (e.g. the police), this request would not be well-received, i.e. ‘trust us, we know what we are doing’. There is no public, *independent*, information about the Inspectorate. Nothing is known of the background, attitudes, or diligence of individual inspectors; inspectors’ work is protected from outside scrutiny not only by a clause in the 1986 Act, but also by many of the conventions in relation to public scrutiny of the work of civil servants.

The NAVS holds the view that the background of Home Office ASP Inspectors should be subject to full public disclosure. Given the current policy of secrecy within the Home Office, it is not possible to properly ascertain the impartiality of the Inspectorate, the diligence of a particular inspection, or question decisions made.

Moreover, the NAVS notes that, for 3481 project licences in force at the end of 1999, only 21 inspectors were employed. (*HO Statistics, 1999*).

“A unique strength of the Inspectorate is that it deals nationally on a regular basis with a large number of diverse proposals. Inspectors have considerable ‘local knowledge’ of individual research groups and UK research activity in general. In addition to a breadth of knowledge of science and welfare, the Inspectorate has a unique, contemporary, specialist knowledge of biomedical and welfare issues.” (1997 APC Report, Chapter 2, Annex 1,p.59).

Nothing in the above should justify refusal of a wider scientific scrutiny of project licence applications.

Combined Database of non-animal alternatives:

NAVS recommends that a joint centralised database of non-animal alternatives be established; combined efforts and resources of non-animal research groups, anti-vivisection groups, and the Home Office could establish this.

Local Ethical Review

The NAVS has never favoured the local ethical review panel system. Our view remains that it is not feasible to provide the circa 300 outside experts needed to sit on local ethical review panel in order to provide a truly independent evaluation of any proposed animal work. Local committees of this type are inevitably made up of colleagues of applicants, and their personal knowledge and perceptions of the expertise of their colleague(s), all colour judgement.

Furthermore, we take the view that the most important aspect of the review must be a database check: is the work being duplicated elsewhere? Is there a non-animal alternative available? Is there human data available? Is the information required available from other sources? Again, we do not believe that

it is feasible for all of these questions to be addressed by 300 local bodies.

Whereas, all applications are already submitted to the Home Office via the ASPI; the information is already centralised, and a wider scientific scrutiny can be better organised through a centralised system, where experts, resources, and databases, can be shared.

Finally, we would point out that the MRC's inquiry into the Feldberg affair exposed the failures in a system where reputation and standing within an establishment can leave animals exposed to unlimited suffering. The MRC's report established that the excessive animal suffering was known about; that Feldberg had been warned twice; that Feldberg had deliberately ignored the terms of his personal and project licences; that the ASPI had expressed concern, as had the Designated Certificate holder. This was a case where the reputation of the person concerned was used to deliberately flout all of the rules, and the ASPI felt unable to take action.

There could not be a better case for full disclosure and an open, completely independent, review of all applications to use animals.

Question 3

Are there additional categories of uses of animals, or particular types of procedure, which should be viewed as unacceptable either in terms of the level of suffering involved or the species of animal that is used regardless of the benefit that comes from such use or procedures?

There are additional categories of uses of animals, and various types of procedure, in which costs in terms of suffering far outweigh any benefits the research may be expected to produce:-

- Any procedures involving **surgery on animals without the use of anaesthesia** during the operation and analgesia or anaesthesia afterwards are completely unacceptable. Procedures requiring this as part of their methods are not an exception, and alternative methods should be sought. There is no benefit to justify this barbaric practice.
- Experiments involving the **constant recording of data** from an animal, or any part of an animal, involving them being restrained or immobilised for extended periods of time. Restriction of movement is known to cause stress to many animals, and this may be increased when associated with insertion of recording devices, or other machinery.
- **Psychology experiments** involving manipulation, injections into, or recordings from the brain or central nervous system of conscious animals are unacceptable, on any species. It is possible that due to the nature of the species, or the manipulation performed, the animal may not be able to react outwardly to pain or discomfort, and no signs of distress would be visible to experimenters. Any brain manipulation can have undesired consequences, resulting in a procedure more severe than originally believed. Any procedure involving the manipulation of a conscious animal's nervous system is likely to be severe, and beyond the 'substantial' category.
- **Maternal deprivation** is unacceptable in any species, and has no relevance to the study of human infants.
- **Malnutrition:** the effects of malnutrition on body development – a wealth of human data is available.
- Breeding of animals with **harmful genetic defects**, and **genetically modified animals** and xenotransplantation, (see our notes on question 7).
- **Warfare and 'defence':** Chemical or biological agents, conventional (ballistic) wounding experiments.
- Effects of **nicotine, tobacco, alcohol**.
- **Recreational** (e.g. ecstasy); abuse of such drugs is by choice and human data is available.
- **Lifestyle drugs** (e.g. slimming, smoking, hair loss, erectile dysfunction, fertility).
- **Household products** and toiletries; the market is flooded with such products, including a substantial number containing ingredients for which there is already a wealth of human and environmental data available. Databanks of known chemicals, and advanced non-animal testing methods provide all the necessary information for re-formulations of 'new' products.
- Extra careful scrutiny should take place of experiments which involve possible **repetition**, or for the acquisition of general **scientific knowledge**.
- **Me too, or copycat drugs:** An understanding of the effectiveness of a 'new' medicine, which provides treatment, for which there are already suitable medicines available. Databanks of known effects of substances are available; a wealth of human data is available.

No licence to use animals should be awarded where there is a non-animal alternative, or if the information is available from other sources.

Question 4

Are there some types of benefit (the overall purpose of the experiment) that might be held as not justifying the use of animals or justifying it only in exceptional circumstances regardless of whether or not the animals would suffer?

All proposed animal experiments should be rigorously challenged, whatever the reputation of the team making the application, or the perceived benefits, or overall purpose, or perceptions of the relatively 'mild' nature of the project or experiments.

There must be a thorough, exhaustive, search for potential alternatives and for potential alternative sources of the information required, as well as checking for possible repetition.

Please refer to our comments under question 3 –

Psychology experiments

Maternal deprivation

Malnutrition

Genetically modified/breeding with harmful defects/xenotransplantation

Warfare and 'defence'

Effects of nicotine, tobacco, alcohol

Recreational drugs

Lifestyle drugs

Household products and toiletries

Me too/copycat drugs

In Chapter 2, Annex I of the 1997 APC Report, the Chief Inspector notes in section 5.20 that profitability of the company applying for a licence is not a suitable benefit to be considered. Applications should therefore be closely scrutinised to ensure that profits are not the overriding benefit achievable from the proposed animal procedure.

This should preclude any animal research in the development of 'me too' drugs or other products (such as washing powders), although it may not be possible in all cases to prevent legally required tests. However, such experiments should not be manipulated into more laudable categories: For example, performing an LC50 on fish might be presented as 'protecting the environment' when it is just a step towards marketing a new washing powder.

Other areas requiring similar levels of scrutiny include the 'benefit' of breeding animals for scientific use, i.e. welfare or profit 'benefits', and research aimed at improving animal testing methods for the welfare of the animals and for greater efficiency of the trial and therefore lower financial costs, e.g. work on implantation of transmitters into mice is described as *"more efficient, reliable, and less labour intensive than thus far"* (Kramer k, Voss H-P, Grimbergen JA, Mills PA, Huetteman D, Zwiers L, Brockway B. Telemetric monitoring of blood pressure in freely moving mice: a preliminary study, *Laboratory Animals* 2000, 34: 272-280).

Question 5

Are all relevant harms and benefits identified by current HO practice? Even if, by its nature, the weighing of costs and benefits always has to be a matter of opinion, is there need for further clarification of the criteria which have been or should be employed in particular cases?

Some relevant harms are identified by the ASPI, but clarity is required on both harms, the weight accorded to each, and the list needs to be expanded.

A process which deliberately excludes those with a genuine determination to curb animal research, and restricts the breadth of the scientific search for alternatives cannot be regarded as truly exhaustive. Only fully access to the decision-making process will allow the public to ascertain the facts.

The APC should emphasise that the accommodation, handling, and husbandry of animals used for research is always stressful, and always causes a certain level of suffering. More weight should be added to these factors.

Laboratory animals suffer close confinement, lack of exercise, lack of stimulation, lack of dietary variety, minimal or abnormal interactions with their own species, and deprivation of opportunity for normal behavioural repertoire. The laboratory environment does not provide the environmental enrichment considered a minimum requirement for captive animals in other industries.

The experience of NAVS Field Officers in a variety of laboratories in the UK indicates that some projects are nodded through, simply because the specific experimental procedure involved is regarded as not being particularly stressful in itself.

The section of the cost/benefit assessment on the cost 'of' animals is brief, general and gives no guidelines as to what would be considered an adverse effect. A detailed breakdown of all the possible costs to animals arising from any licensed procedures is required to perform a meaningful assessment of justification.

This breakdown would include all harms caused before, during and after the experiment–

Psychological stress caused by, for example:

- confinement
- capture (wild caught animals only)
- restriction of movement, or normal behaviour
- deprivation (of basic physical needs, socialisation, maternal care etc.)
- forced association with conspecifics
- lack of a stimulating environment
- departure from natural living conditions (including all variants differing from conditions the animal would experience if in the wild)
- human handling, habituation to procedures or taming
- expectation of pain or discomfort; fear or lack of security
- unfamiliar surroundings/people/conspecifics/other animals
- transportation
- temporary or permanent change to the animal's body, e.g. dressing of wounds or amputation

Physical harms, for example:

- pain (including momentary)
- physiological stress as a result of anaesthesia
- restraint
- lack of veterinary care
- lack of exercise/space
- hunger, thirst or inappropriate or contaminated food

- lack of environmental conditions general or specific to the species, such as submersible
- water for amphibians etc.
- death (including incidental and that due to overbreeding)

Discomfort caused by for example:

- insertion or continued use of needles, catheters etc.
- induction of nausea or vomiting through radiation or toxicity testing
- changes to normal breathing by chemical means, or any physical manipulation
- obstruction or manipulation of bodily functions such as excretion, circulation etc.
- lack of appropriate cage cleaning or maintenance
- handling

Question 6

Are costs other than those involved in, or consequent upon, the actual procedures given their due weight? These include the physical and psychological harms/sufferings associated with capture, confinement, transportation, social isolation, husbandry systems and general handling of animals. Should death in itself be considered a harm and what weight should be given to this in the cost-benefit assessment.

In the experience of NAVS personnel, gained during periods of working in UK laboratories, there is not enough weight accorded to sufferings/deprivation as a result of the laboratory environment. In brief, the smaller the species, the less provision is made for space, welfare, mental stimulation, and opportunity for expression of natural behaviours.

Laboratory animals, by nature of the environment to which they have been brought, must live in barren environments; sterile caging, minimal and sterile bedding, pelleted or other specially processed food, no access to fresh air. They are frequently overcrowded and unable to avoid bullying cage mates.

The *Code of Practice for the Housing and Care of Animals used in Scientific Procedures* (COP) is routinely ignored, and not enforced. For many species, the standards laid down in the COP are rudimentary and in some respects, inadequate. Yet even these standards are not met; at the Institute of Neurology, a project licence was awarded for a project using monkeys, despite that the accommodation breached almost every recommendation in the COP. A similar situation had been found some years earlier, again with monkeys, at St. Mary's Hospital Medical School; in this instance, an undertaking had been given to improve the facilities. Despite the proximity of the two laboratories, the exposure of poor facilities at St. Mary's did not prompt workers at the Institute of Neurology to improve their own facilities.

The animal may well suffer more psychological harm through being caught, transported and kept in captivity than through the actual procedure to which it is subjected. Due consideration must be given to the psychological state of any animal used in a scientific procedure, be it small or large.

Cost benefit assessments should give a large weighting to the extra stress placed on a wild caught animal through being brought into captivity. Particularly stressful will be:-

- lack of space, own territory and freedom to roam or forage
- lack of exercise
- lack of freedom to associate with, or avoid conspecifics, including relations/mates
- presence of and handling by humans
- process of capture and transport
- change in diet and frequency of feeding
- restrictions on normal behaviour e.g. burrowing
- change in daylight cycle or climate
- change in stimuli to primary senses
- change in substrate

Captive bred animals also suffer major psychological harms before and after the procedure, due to those listed above, under question 5.

Physical harms, besides those during or due to the procedure may include:

- injury incurred in trapping or transportation
- fighting with conspecifics
- methods used to prevent fighting with conspecifics
- methods used to identify individual animals such as ear punching
- foot injury due to substrate

- debilitation due to lack of exercise
- death (including overbreeding)

These harms should be given equal weighting, along with harms occurring during the procedure. Applicants should estimate and inspectors check labs or past records as to whether and to what degree animals will experience all these harms, before the animals are acquired. Death of all animals intended to be involved in the project should be given significant weighting, and included as a cost.

Overbreeding and ‘Waste’ Animals:

In the case of genetically modified animals, vast numbers die in the process of attempting to produce animals with the required gene (only 1-10% take up the gene).

Likewise, research requiring specific weights and/or ages may require large breeding programmes, with considerable wastage. In ‘normal’ circumstances, for every animal used, two must die because they are surplus to requirements.

These factors also, should be given weight.

Non-designated suppliers:

The public are always reassured that animals for experimentation as supplied by designated suppliers. Yet, in 1998, a total of 1,120 animals (689 mice, 255 rats, 12 guinea pigs, 25 rabbits, 57 cats, and 82 dogs) were supplied by non designated sources. The NAVS has previously identified researchers requesting primates from non-designated sources abroad, simply because there were no animals of the right age available in the UK at the time. Better planning would avoid such occurrences, and secrecy allows poorly planned projects to be covered up. Current Home Office policy on confidentiality of all information concerning animal experiments prevents proper questioning of occurrences such as these.

Question 7

Are there costs to animals, for example, aspects of poor welfare or undesirable changes in animals, which could be specific to transgenic animals or animals treated with products from genetically modified organisms? Do you consider that any of these costs could never be justified by benefits?

The 'promised' benefits and uses of genetically modified animals (and in some cases those bred with a harmful genetic defect) include:-

- fundamental research
- safety testing
- 'models' of human disease (despite that there is no successful model)
- biopharming; production of pharmaceutical products in their milk, blood, eggs, urine or semen (despite that there are other methods available)
- cloning
- growing of spare body parts for humans

There are costs specific to transgenic animals, and these harms can never be outweighed by the so-called benefits. These include:-

- Unstable phenotype
- unexpected, uncontrolled and undetected suffering in transgenic animal models of human disease (*Michael Balls (1999), ATLA 27, supt.: 811-13*). Leading to licences being granted where animal suffering is unacceptably high
- choice of humane endpoints in breeding program
- increased number of animals used to produce transgenics
- specific welfare costs of animals serving different roles, e.g. donor, surrogate etc., pain or discomfort
- welfare of animals involved in unsuccessful or erroneous breeding attempts
- any suffering deviant from that of non-transgenics of the same species:
 - behavioural changes
 - effects on endocrine system and other physiological changes, including neurological
 - morphological changes to sense organs, body hair, skeletal system, skin, weight etc.
 - growth abnormality
 - immunosuppression
- decreased survival rate
- increase in number of lab animals used due to GM animal use in addition, not replacement procedures
- questionable scientific validity of the transgenic animal study
- the process of genetic modification (surgery, egg collection, egg implantation, repeated blood and tissue sampling for the offspring)
- environmental deprivation (sterile environments, lack of stimulation, confined spaces)
- severe illness when the protein is produced in the wrong part of the body

There is a danger that the costs to the animal models will be disregarded due to the expected benefits of transgenics to medical research. However, these benefits may prove illusory and *certain* suffering should be weighed against *possible*, not actual, benefit (*Michael Balls (1999), ATLA 27, supt.: 811-13*).

Animals treated with products of GM organisms may experience unexpected, uncontrolled and/or undetected suffering from disease or disruption caused by GM pathogens or products. This could result in damage to systems, causing symptoms such as vomiting, excreta problems, poor circulation, neurological malfunction etc. These symptoms cannot be predicted precisely, but must be considered likely costs when assessing the use of transgenic animals.

There are always areas of research where, due to novel developments, 'new' diseases, or simply increased social pressure, there follows a sudden rush into the field. The US government's 'war' on

cancer is one example; then in the 1980s a huge concentration of AIDS projects appeared, worldwide. The idea of anything goes as long as it was AIDS research, without vigorous and realistic appraisal of the chances of success, has left chimpanzees stranded in US labs with nothing to show for their incarceration in isolate chambers. Similarly, the advent of genetic engineering, and the human genome project have created something like a 'gold rush fever' amongst animal laboratories. An entire industry based on genetically modified animals is being allowed to develop out of public control, all on a 'promise'.

Question 8

Please give detailed examples of benefits specific to the use of transgenic animals, or to the treatment of animals with products from genetically modified organisms, which are likely to be very great. Are there, or will there be, benefits whose magnitude is too small, or whose likelihood of accruing is too remote or too distant in time, to outweigh the costs?

Please refer to our comments under question 7.

Question 9

Do you believe that this [collaboration with research abroad, where there might be less regard for animal welfare] is a significant problem? If so, what might be done to address it?

If workers develop a trend of working abroad in order to circumvent UK legislation, the licensing process should be used to bring pressure to bear upon both the workers concerned, and laboratories abroad.

An objective of a more pro-active Animal Procedures Committee could be to export new ideas on legislation, and ideas on non-animal research techniques.

UK government departments can lobby to bring other countries standards up.

If a researcher is requesting a licence, whilst working or proposing to work in an environment where the treatment of animal is substandard, the licence should not be awarded. When a licence is awarded, there is a high level of trust that the researcher will fulfill their obligations in the best interests of the animals. This is a trust that cannot be placed in someone who is prepared to work in an environment where animal welfare is substandard.

If researchers are collaborating on a project where overseas research is integral to the UK work, but is not conducted by a licensed UK researcher, then the UK researcher, and the ASPI, should ensure that UK standards are met before the project is licensed. Just as an overseas animal supplier must meet certain standards before supplying live animals.

General Comments on the Consultation

In the general introduction to the 'Consultation' document, the APC position on the use of animal experiments clear, and we would submit adds weight to our argument that the Committee is unbalanced.

In referring to its previous review of the Animals (Scientific Procedures) Act 1986, the APC notes that: *"... many believe that the cost-benefit assessment has made a contribution to animal welfare since the 1986 Act first brought it into law, but some thought that the law was not applied with sufficient rigour."*

Here is the core of this debate. Can the success or not of the Act (of which the cost/benefit assessment is central) be put to the test? There seems little to support the former point, beyond blind optimism.

The statistical decline in animal experiments shows little alteration before and after the passage of Act. Certainly nothing to indicate a great tightening up of what can be licensed. Without access to information on what is or is not licensed, and the reasons for those decisions, it would seem impossible to substantiate this view. Strange, then, that this should be the view of the *"many"* – one suspects that the *"many"* must be from within the vivisection industry.

On the other hand it is possible, to a degree, to test whether there have been inadequacies in the enforcement of the legislation, as *"some thought"*. Are there examples of experiments published or being conducted in UK laboratories where, for example, there is a non-animal method available, or the experiment has already been performed elsewhere, or the experiment has been shown to be demonstrably unreliable, the data is already available from human studies and so on? The NAVS has, on several occasions, provided clear examples of such instances.

"More generally there was some uncertainty about how the cost/benefit assessment operates in practice – uncertainty regarding the factors that are taken into account and how these are put together in coming to a judgement."

Whilst there can be guidelines on how to make such a judgement, it is how these are actually applied to each application that is crucial. Information regarding the licensing process is therefore only of real value when it can be applied to actual examples, which is why the NAVS has called for this process to be open.

We must also take issue with the assumptions made about the value of animal experiments, as outlined in the APC's guidance notes and extra information.

In para 7, outlining the arguments regarding the validity of animal experiments, the APC concludes: *"Basing the validity argument solely on the relevance of animal to humans therefore seems unsustainable."* It is claimed that this is because *"research goals can be the study of animals themselves"*. This is true, but ignores the fact that statistically, the majority of animal experimentation is purportedly for the benefit of humans. Furthermore, this is how the industry is consistently defended by its supporters, and in the context of this consultation paper is central to the cost/benefit assessment. After all, the vast majority of research is on rodents, but no-one believes that the reason for this is the welfare of rodents.

Paragraph 8 says that *"A more considered review of the issue of validity in relation to the cost-benefit assessment seems necessary which would need to take into account at least:*

the purpose and experimental design of the research / testing programme;
the reasons for believing the animal model will give insight into a problem;
what the individual experiments are designed to achieve;

*the potential and / or limitations of other approaches;
how the results will be used; and
the benefit of fortuitous discovery.”*

Whilst there are other criteria that should be added to this list (and these are contained in our detailed response), we would object to the inclusion of *“the benefit of fortuitous discovery”*. Is it really acceptable in the 21st century to allow someone to experiment on animals simply because they might get lucky?

We agree that there have been medical advances through fortuitous discovery in a number of fields over the years, and it should be stressed here that the majority of medical research does not involve animals, and many of these ‘lucky’ findings were involved with studies on humans. Also much medical research (non-animal) does not necessarily yield the result hoped. However, this does not involve the researcher conducting acts that would be criminal for anyone else. The bottom line is that animal research cannot be regarded in the same light as the rest of science, and cannot be afforded the freedoms of other areas of research – there have to be restrictions because animal research allows the deliberate infliction of pain, suffering, and environmental deprivation of other animals.

Those responsible for enforcing this legislation need to stop seeing it as an Act that is there to enable animal research, but rather to protect animals – for that is how the Act was sold to a concerned public, when it progressed through parliament.

More balance

We also object to the annex to the Consultation document, which provides a discussion of similarities and differences between humans and other animals. To ensure balance, the opposite point of view should have been included.

January 2001

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Attached: Annex 1: Military & Psychological Research
 Annex 2: Ethical Considerations

NAVS RESPONSE TO APC COST/BENEFIT CONSULTATION

ANNEX 1: MILITARY RESEARCH ON ANIMALS

SARIN ON MARMOSET MONKEYS

Cost/Benefit analysis

The experiment example given provides an illustration of how the criteria for cost/benefit assessment have not been applied rigorously as part of the Animals (Scientific Procedures Act) 1986; specifically, the criteria for granting a project licence, as set out in section 5(3) or 5 (4), or 5(5) of the Act, have not been fulfilled:

Publication

PC Pearce *et al.* The effects of acutely administered low dose sarin on cognitive behaviour and the electroencephalogram in the common marmoset. *Journal of Psychopharmacology*, 1999; 13 (2): 128-135.

Summary & Background

The Ministry of Defence funded experiments by the Chemical and Biological Defence unit at Porton Down to test sarin, a toxic chemical used in warfare¹, on marmosets, to see if it would affect their behaviour in the long-term. It was administered by injection and electrical recordings were made of their brain activity after surgical implantation of a transmitter and electrodes, for which holes were drilled in their skulls. Regular blood tests were taken to assess the physiological effects of the poison. The acute toxicity (immediate effects) of organophosphate (OP) compounds such as sarin are well known. They exert their effects by inhibition of the action of an enzyme (a protein that precipitates a chemical reaction in the body), acetylcholinesterase, that breaks down acetylcholine, which acts as a transmitter of nerve impulses. Inhibition of the enzyme causes a build-up of acetylcholine².

The analysis follows that described for a cost/benefit assessment in the 1993/1997 APC Reports. It is, necessarily, in retrospect, owing to the fact that project licence applications are not in the public domain. Thus, scientists at the National-Anti-Vivisection Society were not allowed access to the information contained in the application before a licence was granted.

Importance of Objectives

The purpose of the study was to assess the long-term effects of an acute low-dose concentration of sarin (isopropyl methylphosphonofluoridate), synthesised at CBD Porton Down, on awareness (complex cognitive behaviour) and on measurements recorded on an EEG (electroencephalograph: an instrument used for recording the electrical activity of the brain).

Although the overall objectives of the experiment may have been considered to be important by the Inspectorate, given the perceived threat of the use of sarin during warfare, marmosets were selected for the study instead of existing human data being utilised. The use of these animals was due to their "small size and species characteristics" which according to the authors of the paper "make them particularly suitable for long-term studies", and their use for neurophysiological studies is becoming increasingly widespread².

However, the use of marmosets for the study negates:

a) The general attributes of the objectives.

In assessing the importance of the general attributes of the objectives it should have been taken into consideration that:

(i) the experiment should provide a new approach or fresh insight in relation to existing knowledge provided as “Background”.

The only new insight provided by the experiment is how sarin affects marmosets, not humans. Relevant human data is available and could be used instead. Existing knowledge from animal experiments provided as background is misleading (see below).

Relevant human data

Human testing at Porton Down

Between 1948-49, the first human trial was conducted, in which 129 servicemen were enrolled for testing of the gases tabun, soman and sarin, to assess in detail the effects of the chemicals on the human body. The volunteers were put in gas chambers for exposure, including to low doses of sarin, the most frequently and extensively tested of these nerve gasses. The resulting reports of the human trials were hailed as landmark accounts of nerve gas poisoning, containing "a wealth of information". The human experiments continued into the 1950s³. During this time, hundreds of men were tested for the effects of sarin, some of whom are still alive today⁴. It would have been more prudent if the long-term effects of sarin were assessed on these men instead of using an unsuitable species.

Other human studies

There have been many studies carried out that suggest various OPs produce effects on the central nervous system, such as anxiety, tension, poor concentration, disturbed sleep, memory loss and mental confusion, that may persist for many weeks or months. These epidemiological studies, carried out on around 500 human patients altogether, who were exposed to OPs, including a study carried out on 45 professional pesticide applicators who had received low doses of OPs and showed no clinical symptoms (as in the marmoset study). There have been differences between results in the human studies which can be explained by the differences in OPs to which people were exposed⁵. The marmoset experiment was only involved with sarin. As human studies had been carried out, there was no justification, therefore, in carrying out the tests on animals. Also, there was a sarin attack on the Tokyo underground in 1995. Studies of victims of the attack (Yokoyama et al., 1998) suggested that in some people there were long-term effects on their behaviour. The effects of OPs on acetylcholinesterase are well known - for example, that normal amounts are produced within weeks after exposure².

Existing knowledge from animal studies irrelevant due to species differences

Previous animal studies:

Similar tests to those conducted on the marmosets were carried out in 1976, by Burchfiel and others, on rhesus monkeys. The results of that study and of another, unpublished one on rhesus monkeys at CBD, Porton Down, are inconsistent with those from the present study. The researchers involved in the experiment on marmosets explain these differences by saying that the methodology was different. However, they also raise the possibility of “*a species-specific threshold for effect*”². In other words, there are species differences between different monkeys that would affect results. Species differences between humans and monkeys would be even greater.

Additionally, in the three years prior to 1948 when human trials of nerve gasses began, they were extensively tested on animals³. Repetition by conducting more animal experiments was therefore unnecessary, particularly in light of the availability of human data.

It is known that there is “*no single animal species which always reacts to behaviour-affecting substances in the same way as man*”⁶.

(ii) Is the project realistic, achievable and likely to be funded?

This particular criterion is not relevant to whether or not a licence should have been granted for this experiment. The fact that any known toxic substance administered to any animal is likely to affect the animal in some way should not be a reason for carrying out an experiment if it has no potential benefits.

(iii) Relevance of the project

The testing of sarin gas on the long-term behaviour of marmosets has no relevance as such research can not be linked with, or have implications for, other areas of research. This is due to the lack of relevance to humans for the reasons of species differences as outlined in (i) above.

(iv) Current in relation to issues of developing interest or concern

The threat of chemical warfare, with the related consequences to the welfare of service personnel, is perceived by some to be both current and an issue of concern. However, the granting of a licence to experiment on marmosets does not solve the perceived problem. On the contrary, results from such an experiment will merely serve to mislead and delay progress into the solution of the problem due to species differences as outlined in (i) above, and there would possibly be a delay or an omission to carry out a meta-analysis of human data.

b) Potential benefits:

(i) The experiment has no potential benefits to humans:

An attempt to justify the application for a licence to conduct this experiment on marmosets was made on the grounds that no specific doses of sarin were documented in human studies, or the degree of enzyme inhibition, or the time-course of events. However, this is not a justification as it is unlikely that specific levels for human exposure would be known as dose exposure is not measured in a real-life situation, so to give an animal a set dose is unrealistic. In addition, it is known that animals do not react to behaviour-altering substances in the same way as humans.

More importantly, it is evident from the said justification for the tests that a thorough literature search was not carried out in advance of the application. In the early 1950s, hundreds of servicemen were given escalating, measured doses of sarin via drops on their bare skin and their cholinesterase levels were measured. The details of the experiments on humans (in which one died) are contained in Porton Down technical documents, in particular *Porton Technical Paper 399*, published in 1954^{3,4}. There is no excuse for the Ethical Review Board at Porton Down having no knowledge of the human data, either.

5.21 of Chapter 2, Annex 1 of the *1997 APC Report* advises that *"No useful data should be ignored or discarded, and resources and findings should be shared with others"*.

Potential ecological, environmental, animal, food hygiene or plant protection benefits were not stated in the research.

(ii) No scientific benefits (see B (i) above)

(iii, iv & V). No other potential benefits suggested.

Probability of Achievement

(i) On the question of whether animal use was necessary at all for this experiment, whether non-sentient alternatives were considered and (ii) the choice of species:

A licence should not have been granted for the reasons outlined in 5a and 5b above, that relevant human data is available which could have been considered as a non-sentient alternative and that there is considerable species disparity between humans and monkeys. This is apparent, not only in the way various substances affect their behaviour, but monkeys even metabolise drugs at different rates from man⁷.

(iii) Choice of method. Irrelevant due to the questionable choice of project.

(iv) Number of animals

Seventeen marmosets (eight males and nine females), bred at CBD Porton Down, were used in the study. They were housed either in single sex or mixed sex (in which the males were vasectomised) pairs². The animals' lives were wasted, considering the non-viability of the project.

(v) Track record of the research group in the field

The monkeys were subjected to behavioural tests during the study into the effects of sarin. The research group have previously carried out behavioural research (cognition) on non-human primates, including on marmosets and have published a number of related papers. Such research is not relevant to humans. Results cannot be extrapolated due to species differences. It is unlikely that certain complex cognitive processes have any counterpart in other species⁸. The track record of the team is therefore not relevant to the current project. In addition to the issue of species differences related to cognition, relevant human data on the effects of sarin were available at the time of application for a licence. That the team have published prolifically does not automatically guarantee that a continuance of similar research is necessary or deserved.

Cost to the animals

The suffering of the animals was far greater than the potential for any benefits as outlined in 5a and 5b, above, due to the severity limit being substantial (see below) and the invalidity of the experiment.

Severity limit

The Home Office *Guidance on the Operation of the Animals (Scientific Procedures) Act* gives examples for each of four severity limits. Although the judgement of severity is considered subjective, this particular experiment is likely to have been categorised under the 'substantial' level. The following protocol indicates "*a major departure from the animals' usual state of health or wellbeing*" as well as involving major surgery.

The animals were premedicated with diazepam, anaesthetised with alphaxalone/alphadolone and a radiotelemetry transmitter device was implanted into the abdomen. Holes were drilled in their skulls and sensing wires from the device were tunnelled under the skin to the top of the skull where they were placed in each hole and cemented into position, so that EEG measurements could be recorded remotely, at intervals throughout the study. Painkillers were given during recovery. The monkeys were subjected to behavioural tests, including one test sequence before surgery. After the third test, an intramuscular injection of sarin was given to nine animals and saline was injected into eight control animals (non-test, for comparison)².

EEG recordings were taken over a period of 15 months and blood samples were taken from a leg vein of the animals while they were conscious, at approximately monthly intervals. Marmosets' EEG recordings and cognitive behaviour were not significantly different after sarin administration and measurement of acetylcholinesterase in the blood was normal after 3 months².

Conclusion

A project licence for "*The effects of acutely administered low dose sarin on cognitive behaviour and the electroencephalogram in the common marmoset*" by PC Pearce *et al* should not have been awarded because:

- Relevant human data was available and the literature should have been scrutinised.
- There are species differences between monkeys and humans in the way substances affect behaviour and in the rate of metabolism of substances
- Repetition. Similar work had been carried out in rhesus monkeys and other animals

- There were no potential benefits
- The costs to the animals in terms of suffering was high

This is an example of an experiment where the National Anti-Vivisection Society believes a licence should not have been granted. We would therefore seek to have the cost/benefit analysis process not only rigorously enforced, but open to public scrutiny.

According to the *Fourth Report of the Animal Welfare Committee*, November 1999, the use of marmosets in research at Porton Down will remain high for some time. The report gives the reason for this as that they are being “used to investigate the effects of organophosphorous [similar to nerve agents – see below] sheep dips and improving the protection against and treatment for nerve agent poisoning. The aim is to study the effects of multiple vaccines together with nerve agent pre-treatment as given to soldiers during the Gulf War.”

In our view no further licences should be granted for continuation of this research.

Internal Regulation and the Ethical Review Process at Porton Down

There is circumstantial evidence that the ethical review process is slovenly at this particular establishment. According to the *Fourth Report of the Animal Welfare Advisory Committee* the current system meets all the requirements for an effective ethical review. However, there is deliberately no external adviser. Such a person would be truly independent, whereas at present all involved in the ethical review process are from within DERA. This is not an acceptable situation.

The NAVS has seen details of the background to the ethical review process at DERA establishments, as set out in the *Fourth Report of the Animal Welfare Committee* and believes the process to be inadequate. The system consists of three committees and was set up to meet the specific needs of the Porton Down establishment. The committees consist of the Certificate Holder’s Committee, the Animal Care and Use Committee (involving the Named Animal Care and Welfare Officers who report to the certificate holders) and the Ethical Review of Project Licences group which consists of scientists and members of the Animal Care and Use Committee (who so far have merely observed and taken no part in discussion of the projects), plus anyone else “in the establishment” who wants to attend, and two internal scientists not involved in animal experiments.

AWAC send a written report on animal care and their use in research in DERA establishments, to the Chief Scientific Adviser at the Ministry of Defence at least once a year. Regulation is deemed the duty of the Home Office.. We would like to know how often Home Office Inspectors visit the establishment at Porton Down.

About sarin:

A colourless and odourless gas, twenty six times more deadly than cyanide gas. 0.01 milligram per kilogram of body weight, or a pinprick-size droplet, is enough to kill a human. It is a ‘nerve agent’. All nerve agents belong chemically to the organophosphorous group of compounds (OPs).

Nerve agents are so called because they affect the transmission of nerve impulses.

Nerve agents, such as sarin, have dominated chemical warfare since the Second World War.

Sarin is one of 2000 new OPs that were synthesised in the 1930s by the Germans.

Sarin is considered to be one of the three ‘classic’ OPs. The other two are tabun and soman.

Nerve agents were not employed in WW2 as the Germans were afraid of the superiority of American airpower – the gases would have devastated German cities if the allies were to retaliate with their own nerve agents.

Chemical and biological weaponry are considered the ‘future of modern warfare’ and millions of pounds are spent annually by governments of the world on research into new nerve gases and

biological weapons.

Iraq used OP nerve agents against Iran in the 1984-1988 Iran-Iraq war.

Sarin was released into the air at Khamisiyah, Iraq, when rockets were destroyed during the Gulf War.

Some troops were briefly exposed to low levels of sarin.⁹

1 Merck Index, 12th edition

2 PC Pearce et al. The effects of acutely administered low dose sarin on cognitive behaviour and the electroencephalogram in the common marmoset. *Journal of Psychopharmacology*, 1999; 13 (2): 128-135

3 Evans R. Gassed. Pubs: House of Stratus 2000

4 Carter GB. Chemical and Biological Defence at Porton Down 1916-2000. DERA. Pubs: The Stationery Office.

5 BMJ, 25 May 1996, vol. 312: 1313-4

6 Brimblecombe RW, CDE, Porton Down. In: Boyland E, Goulding R, eds. *Modern Trends in Toxicology*, vol 1. Butterworths, London, 1968: 157-8

7 National Anti-Vivisection Society (2000). 125 facts against vivisection.

8 Dawson GR et al. *Behavioural Pharmacology* 1992; 3: 285-97

9 <http://www.geocities.co/CapeCanaveral/Lab/7050/introduction.html>

<http://www.gulfink.o.../low-lv-chem.htm&qt=sari>

MUSTARD GAS EXPERIMENTS ON PIGS

Publication

Rice, P., *et al.* (2000). 'Dermabrasion – a novel concept in the surgical management of sulphur mustard injuries'. *Burns* 26: 34-40.

Summary & Background

At Porton Down, the skin of pigs was exposed to mustard gas in order to induce chemical burns. The affected areas of skin were then rubbed with abrasives (a process called dermabrasion) to determine whether this affected the healing process.

12 Yucatan miniature pigs and 6 Large White pigs were anaesthetised and an area of skin on their backs 875cm² was prepared by shaving. The open ends of four glass chambers containing sulphur mustard vapour (mustard gas) were placed on the prepared skin for 6 hours, in order to induce four patches of partial thickness burns. The animals were allowed to recover and left for 3-4 days, after which time they were anaesthetised again. Two of the four patches of burns on each pig were rubbed with an abrasive emery cloth soaked in liquid antiseptic, to remove the surface layers of the burned skin to the point of bleeding.

The Large White pigs were killed in pairs at 1, 2 and 3 weeks after injury, and the Yucatan miniature pigs were killed at intervals throughout the eight weeks after injury. The sites of injury were then examined to calculate the area of new skin growth.

Further experiments were carried out on 2 domestic white pigs. Mustard gas burns were induced as before, and dermabrasion was performed using emery paper (as before) or a hand-held electric drill with either small sanding discs or grinding stones. In order to compare the methods, the rates of healing were compared at intervals after dermabrasion.

Importance of Objectives

Mustard gas was developed in 1917¹, and has been used on humans in conflicts around the world ever since. There has therefore been ample opportunity to study the effects of the gas and the treatment of the wounds in the unfortunate people exposed in the years since.

There are existing successful methods of treatment for mustard gas burns available, including enzymatically active dressings, surgical debridement and laser debridement.

This experiment refined an existing method of treatment. The results could have been predicted based on the knowledge that similar techniques of removal of surface skin have previously had success in the treatment of lesions, scars and thermal burns.

Probability of Achievement

The authors feel confident to state that: “*The use of porcine skin has proved to be an ideal model for human skin*”, despite the fact that:-

- they admit that there are differences in skin reactions to mustard gas and skin healing between many different species, and that the reasons for these species differences are unclear.
- they describe the skin reaction to mustard gas of pigs as “*intermediate*” between humans and rabbits or rodents, contradicting their later claim that porcine skin is an “*ideal*” model for human skin in such experiments.
- the results of this experiment show considerable differences within species, since although the healing of abraded sites in the Yucatan pigs is statistically significant, that in the Large White pigs is not.

This uncertainty and unpredictability make it impossible to claim that this study achieved anything, and any claims to the contrary can only be described as assumptions.

Cost to Animals

There is no mention of pain-relief being administered to the pigs. Mustard gas burns are known to cause “*excruciating pain*”, and:-

- it appears that the pigs had to endure the gas being administered without analgesia;
- it appears that the pigs had to endure the period after exposure to the gas, when burns had formed, without analgesia;
- the process of dermabrasion was undoubtedly extremely painful, but it appears that the pigs did not receive analgesia during or after the procedure.

One of the pigs was killed before the end of the experiment, as a consequence of infection of the burn site; this could indicate that the pigs received insufficient care during the study.

Conclusion

Using pigs as a model for human skin is both cruel, and provides unreliable results, due to both the experimental situation and species differences; furthermore, to develop treatments based upon laboratory experiments when there are already treatments available, cannot be justified under cost/benefit criteria.

References

1. *New Scientist* (1984) 22 March:15
2. Dr. Moonie. *Hansard*, Written Answers (2000), 16 November.

PERITONITIS EXPERIMENTS ON PIGS

Publication

Parker, Stephen, *et al.* 'Pentoxifylline fails to improve organ dysfunction and survival when used in the resuscitation of a porcine model of haemorrhage and abdominal sepsis'. *Resuscitation* (2000) 44:61-69

Summary/Background

At DERA, Porton Down, 10 female Large White pigs were bled 40% of their blood, then injected with faeces, left for 1 hour before being resuscitated then killed.

The pigs were starved for 12 hours, anaesthetised, then tubes were inserted into the vessels in their neck, into their bladder and down their throats. All 10 animals were then bled 40% of their blood volume (a haemorrhage). Following this, the pigs were given peritonitis (inflammation of the membrane lining the abdominal cavity), by the injection of pig faeces and bacteria. After 1 hour, the pigs were resuscitated by replacing the lost blood with a substitute. Over the next hour, half the animals were given a drug thought to adjust the immune response (a potential immunomodulatory agent, pentoxifylline), while the others were given balanced salt water. Animals were then left in this state for 24 hours, so researchers could assess survival time. It is unclear from the paper whether they were under anaesthesia for this entire period, during which 7 of the pigs died. The other 3 were killed with an anaesthetic overdose at 24 hours.

The ASPI Chief Inspector states that the licence application must consider the whole project, and not just the individual experiment when assessing cost/benefit. However, without freedom of information, this is extremely difficult to do, as the entire project is not described. This is possibly because this experiment may not be part of a wider project, and indeed at no point in this paper do the researchers mention any past or future experiments conducted by their research group which relate to this experiment.

This experiment should not have received a licence as it contravened all three sections of the cost benefit assessment (*1993 APC Report*, Appendix 2) in the following ways:

Importance of Objectives

Not potentially beneficial due to zero likelihood of success:

The researchers state that pentoxifylline was supposed to suppress a specific toxin-induced event (TNF- production), but that this had also failed in other pig sepsis experiments (3 referenced); they knew it was not going to work. Parker et al state that the probable reason for the failure of the drug was that the damage inflicted on the pigs by bleeding 40% of their blood and injecting them with faeces was so severe that the drug would never have worked, regardless of timing or dosage. The Chief Inspector's paper (*1997 APC Report, Chapter 2, Annex 1*) defines the first determinant of benefit as 'likelihood of success'. In this experiment the researchers knew and admit that the experiment could never have succeeded, and therefore any possible benefit is entirely absent. Referring to the cost/benefit analysis in the 1993 APC report appendix 2; if the probability of achievement is zero (as it is with certain failure), then regardless of the importance of the objectives, the product of the benefits will always be zero. The costs of the animals' lives therefore unquestionably outweigh the benefits.

Not an original experiment, therefore objectives have no importance:

Pentoxifylline has been tested in animals before for this specific purpose – its immunomodulatory properties – and has been found to be effective, but in this study it did not reduce toxin-induced effects. There was no significant difference in survival of the treated and untreated groups. In fact pentoxifylline increased the lactic acid levels (a natural acid, toxic at high levels) associated with septic shock, an event it was supposed to treat. This study found different results to other animal studies. In

their discussion of why pentoxifylline was unsuccessful in treating the pigs, the authors state that if a smaller dose had been given, some of its bad effects may have been reduced. The researchers must have known the appropriate dose before they began the experiments, had they referred to the literature; they reference at least 18 animal studies using pentoxifylline, many of which were conducted on pigs. They also state that human sepsis studies using the drug have been effective with considerably lower doses.

Furthermore, animals have been used to model sepsis and haemorrhage before, and have shown different and misleading results to clinical observations (based on a critical review by Deitch, 1998). There is no reason why, when sepsis and haemorrhage are induced together, the findings should somehow become relevant to humans.

The same authors (plus another) published a paper in the journal *Shock*, also this year, in which a similar experiment is described involving 17 white pigs, with peritonitis being bled 40% of their blood volume under terminal anaesthesia¹.

Probability of Achievement

Lack of any probability of achievement due to lack of scientific quality:

Culture-dish studies had already predicted probable causes of death. It is known from *in vitro* studies that pentoxifylline causes dilation of blood vessels and low blood pressure, which was the cause of death in some of the pigs.

Species differences for these drugs are known. For immune-response affecting drugs, in animal studies by other researchers, they were effective at reducing sepsis, in human patients they were not.

No human, animal or scientific benefits:

Pentoxifylline is already in use in human patients (for reasons other than the treatment of sepsis). Its safety in humans has therefore been established and it could have been used in direct clinical trials.

Cost to Animals

The animals suffered for longer than necessary; adverse effects were not minimised:

The pigs were kept alive after the surgery, with an average survival time of 11 hours for the control group and 16 hours for the treated group. But most notable physiological changes were seen in the first 6 hours, so data from beyond this time wasn't analysed; the pigs may have been suffering an average of 7.5 hours more for absolutely nothing. A stark contrast to the insistence in the Chief Inspector's paper that experiments are scrutinised to ensure costs cannot be further reduced.

Humane endpoints were not observed; 7 of the pigs died before the end of the experiment, during the 24 hours they were left after surgery. It is not clear whether they were under general anaesthetic or not.

Conclusion

The researchers have admitted repeatedly in this paper that they had indication that what they were doing to the pigs would fail, and that the drugs used have been tested in numerous previous studies in both humans and animals. The literature they cite also reveals contradictory results from human and animal studies. This experiment is not relevant to humans. It is not justified and a licence should not have been granted. Costs to the animals hugely outweigh any realistic perceived or expected benefit to humans.

1. Parker, S. J. *et al* (2000). *Shock* 13, 4: 291-6 (Medline abstract)

SEIZURES IN GUINEA PIGS

Publication

Bourne, James A., Fosbraey, Paul. 'Novel method of monitoring electroencephalography at the site of microdialysis during chemically evoked seizures in a freely moving animal'. *Journal of Neuroscience Methods* (2000) 99: 85-90

Summary & Background

At Porton Down, researchers monitored chemically evoked seizure activity in 6 guinea pigs by drilling into their skulls and inserting a probe in their brains. They were trying to develop a piece of equipment to monitor the brain of a freely moving animal for use during behavioural tests and epilepsy research etc.

Guinea pigs were injected with antibiotics, then rendered unconscious through an injection into their abdomen (intraperitoneal). The guinea pigs' heads were then placed in a stereotaxic device; a contraption used to restrain animals during intrusive procedures, and sliced open to reveal their skulls.

The scientists then drilled 2 holes in the guinea pigs' skulls and twisted in 3 mm screws until they were touching the outer membrane of the brain, where they were stuck in place with dental cement. Attached to the screws was a microcircuit board used to monitor the brain.

Once all the monitoring equipment was in place, holes were drilled into the guinea pigs' skulls again to insert the equipment to invoke seizures. A probe was inserted 4 mm into the animals' brains, again stuck with dental cement, with 2 electrode wires protruding another 2 mm deeper into the brain.

Another electrode was then placed under the skin in the guinea pigs' necks, and held in place with a plastic collar, for comparison of movement of the animals. The animals were apparently given no pain relief when they regained consciousness after this intrusive surgery.

For 7-9 days after the implantation of these devices, the guinea pigs were regularly hooked up to the machines to be used for the experiment to get them used to them. This was because previous studies using similar methods had shown the animals became stressed when this was done.

A transmitter was fitted to the guinea pigs' implants and the animals were placed in a cage and attached to a microdialysis machine for 2 hours before the experiment even began. This machine delivers artificial brain and spinal fluid into the animal's brain, and allows experimenters to analyse samples that are filtered out of the brain. The guinea pigs were injected with a chemical designed to induce fits, imitating those experienced by sufferers of epilepsy, then subjected to these fits and microdialysis for 3 hours.

The equipment was then removed from the animals' heads using acetone to dissolve the dental cement, so the electrodes could be used for insertion into another animal.

This experiment should not have received a licence as it contravened all three sections of the cost benefit assessment (1993 APC report, Appendix 2) in the following ways:

Importance of Objectives

The results have no human or scientific benefits, due to species differences:

Studies on human brain slices for epilepsy research use naturally epileptic tissue, and therefore have no problems with differences in experimentally invoked diseases, or with species differences³. The authors also mention other studies using depth electrodes to examine epileptic activity in humans, revealing that they were aware of viable alternatives to animal models of epilepsy. It is not necessary to test equipment to record seizures in animals, as there is no relevance of studying epilepsy models in non-human animals.

There were no expected direct benefits:

The aim of this experiment was simply to test equipment which could be used to monitor the brain of animals. These 6 animals were therefore never intended to make any contribution towards curing or diagnosing any human disease; they died simply as a prelude to future, equally irrelevant animal tests. Previous studies had already shown that animals are stressed by being connected to this kind of equipment, and yet this pointless study lasting over a week was still carried out by government researchers.

Probability of Achievement

Species differences lead to a lack of scientific validity:

These seizures were induced because the equipment being tested is intended to be used in animal models of human epilepsy. However, previous reports by the NAVS have shown that drugs effective in treating animal models of epilepsy may not work in human epilepsy, and/or may have unpredictable side effects. Rodent models used to test epilepsy drugs often show they are anticonvulsants, but in humans they are inactive¹.

Cost to Animals/Conclusion

Adverse effects were not minimised:

Completely unacceptable in this experiment is the lack of any mention of pain relief, either when the guinea pigs woke up after researchers had drilled into their heads, or at any time while they had the probes embedded in their brains. Surgery with significant post operative suffering (i.e. without postoperative analgesia) is classed as causing substantial pain – the most severe category of procedure allowed². The guinea pigs in this experiment not only had to suffer a lack of analgesia after surgery, but also chemically evoked seizures while they were conscious.

The intraperitoneal injection used before the surgery when the animals were still awake is a method not recommended by the Animal Procedures Committee; it is described as a 'potentially distressing procedure', and have in the past banned its use in particular experiments³.

Unnecessary stress:

The paper does not mention how many fits the animals experienced during the 3 hour experiment, or how long they lasted (although they appear to last at least 1 minute). This, combined with being connected to possibly noisy machines, would have been extremely frightening for the animals; guinea pigs have a 'well developed startle response that causes them to make sudden movements in response to unfamiliar sounds'⁴. Causing fits in these animals particularly cannot be justified. The researchers could still have found out whether the equipment worked without evoking any seizures in the animals, but by recording normal brain activity.

1. *Labs Unlocked*. NAVS (1994):47

2. Animals (Scientific Procedures) Act 1986. House of Commons (1990)

3. Report of the Animal Procedures Committee for 1999. The Stationary Office (2000)

4. *Laboratory Animal Management – Rodents*. National Research Council, National Academy Press (1996)

FERRETS AND FOOD POISONING

Publication

Wright, Angela *et al.* 'Induction of emetic, pyrexia and behavioural effects of *Staphylococcus aureus* enterotoxin B in the ferret'. *Infection and Immunity* (Apr 2000), 68, 4: 2386-89.

Summary & Background

At Porton Down (joint project with St. George's Medical School), (at least) 19 adult female ferrets were dosed with a bacterial toxin which causes food poisoning, as a small animal model for the human symptoms, then watched for 3 hours while they retched, vomited and defecated.

Ferrets were anaesthetised, then had a device inserted under their skin to record body temperature. Two weeks later they were starved for 24 hours, then had a tube inserted into their stomachs through which they were given small, medium or large doses of an enterotoxin (a toxin specific to cells of the intestine which causes food poisoning) *S. aureus* enterotoxin B (SEB), or salt water. There is no mention of anaesthetic being used for this procedure. The observers then recorded the number of times the ferrets retched, vomited or defecated over 3 hours.

One animal given the medium dose retched 50 times and vomited 8 times in 3 hours. All the animals given the highest dose retched and vomited, and 60% of their defecations were diarrhoea and contained bile, similar to when ferrets have been exposed to full body radiation.

This experiment should not have received a licence as it contravened all three sections of the cost benefit assessment (*1993 APC report*, Appendix 2) in the following ways:

Importance of Objectives

Not original, relevant or current:

Data already available from human studies, and repetition of animal studies. The bacteria used in this study are a well known cause of food poisoning in humans. It is the second most common cause in the US, so clinical cases to study are likely to be easy to find; there is no need to involve the whole biology of another species to study an event occurring in so many humans every year. This said, the bacteria has still been tested previously in monkeys, rabbits, goats, cats, mice and ferrets as far back as 1964.

Probability of Achievement

Low scientific validity due to species differences:

Studies have reported that the amount of SEB which causes vomiting in monkeys is between 10 and 1000 times less than the largest dose used in this study. The authors report that the dose required to make ferrets vomit is higher than that required in primates, then go on to say that ferrets can be used as alternatives to primates to study this bacteria. If the doses used in ferrets are so different to those affecting primates, and hence those seen in human food poisoning, they are highly unlikely to be able to tell us anything about the biological effects of this bacteria. The authors also proposed that there are differences between humans and ferrets in the way SEB is broken down in the gut.

Choice of species:

It is very apparent that the ethical and scientific (or perhaps financial or practical) drawbacks to using primates in these sorts of studies are not solved by using ferrets, which are even further removed from human biology. Some emetic (vomiting-inducing) substances in humans cause contrasting responses in ferrets and vice versa. Thompson *et al* (1992) state that "*the significant emetic response of ferrets to M6G [a metabolite of morphine] is in contrast to the results obtained in a phase 1 study of M6G in human patients...no patients experienced nausea within this dose-range...¹*".

Costs to Animals/Conclusion

The animals' suffering is of the 'substantial' severity limit, and still the results gleaned no useful information due to species differences. Allowing a ferret to retch 50 times and vomit 8 times in 3 hours shows no attempt to avoid, minimise or terminate adverse effects.

1 Thompson et al (1992), British Journal Pharmacology 106:3-8

HERPES B EXPERIMENTS ON MACAQUE MONKEYS

Publication

Bennett AM, *et al.* 'Protection against herpes B virus infection in rabbits with a recombinant vaccinia virus expressing glycoprotein D'. *Journal of Medical Virology* (1999) 57: 47-56

Summary and Background

Herpes B virus is a hazard for vivisectioners experimenting with macaques in research laboratories. This is because a significant number of the macaques used in biomedical research are still wild caught and often infected with the virus. Scientists are trying to develop a herpes B virus vaccine for human use to protect monkey handlers.

At Porton Down, Bennett *et al* carried out an experiment using 17 New Zealand white female rabbits to test the potential of a herpes B virus vaccine. The rabbits were randomly divided into 4 groups. Group 1 (3 rabbits) and group 2 (2 rabbits) were given two different types of dummy vaccinations respectively as a control for the experiment. The rabbits in groups 3 and 4 (6 rabbits each) were given the test vaccine, and those in group 4 were also given a booster 4 weeks later. All vaccines were delivered by scratching the skin of the rabbits' upper back. The rabbits were then dosed with the herpes B virus 66 days after the initial vaccinations.

The control rabbits (groups 1 and 2), which had received the dummy vaccines, contracted the herpes B virus and died 8 days later. One rabbit from group 4, which had received the test vaccine with booster, showed rear leg paralysis and died 22 days after receiving the virus. Unaccountably, one of the rabbits in group 3 suffered a broken spine 7 days after the initial vaccination and was therefore killed by laboratory workers immediately.

Blood samples were taken from all rabbits at various stages. Oral, vaginal, eye and inoculation site swabs were taken after death of the non-inoculated rabbits (group 1 and 2). Of the 10 rabbits which remained healthy 4 were autopsied and the nerve next to the inoculation site removed. This was to check for latent herpes B virus.

Importance of Objectives

The primary objective of this research is to protect monkey handlers from the herpes B virus. In this experiment, the development of a vaccine for human use has been the chosen method to meet this objective. The question therefore becomes, does the need for such a vaccine outweigh the cost to develop it. Points to consider are:

- Several approaches have been developed to control human infection with herpes B virus. Of these the most obvious is to not use imported or wild caught macaques for research, thereby completing eliminating the need for a vaccine to be developed. Secondly, guidelines for handling macaques have been published. If monkey handlers followed these more effectively the need for a vaccine could be reduced.

- Human treatment for herpes B virus is currently available. Early diagnosis is of paramount importance and anti-viral therapy reduces mortality by nearly 100 % if it is initiated prior to the onset of respiratory arrest. Long term suppressive treatment with acyclovir is then required to avoid reactivation of the latent virus.

A diagnosis method using monoclonal antibodies and PCR is currently being developed which should facilitate earlier and more specific diagnosis of clinical specimens from potentially infected monkey handlers.

Overall, the argument for the development of the vaccine is counterbalanced by more than one alternative strategy.

Probability of achievement

The researchers openly admit in the publication that the vaccine used on these rabbits could never be used in humans and they suggest that another strain of the vaccine suitable for humans as well as rabbits should be developed before further animal studies are carried out. This fact was known prior to carrying out the experiments, and prevents the results from being applicable to the overall objective.

The researchers quote: *“As herpes B virus does not occur naturally in humans, and the number of monkey handlers likely to be exposed to the disease is minimal, a phase II vaccine trial is likely to be prolonged and a phase III trial would probably never take place.”* In other words, the results of this experiment are unlikely to be taken any further towards developing a licensed vaccine for human use.

The planning of the experiment did not allow meaningful results to be achieved. Results from the 4 rabbits which were autopsied suggested that the vaccine had also protected against latent herpes B virus, i.e. a delayed reaction to the virus. But the scientists quote; *“... more extensive biopsy of similar specimens is needed to confirm this observation.”*

It is a well known fact that when herpes is transferred from one species to another a change in pathogenicity occurs (ability to cause disease). For example, it may completely fail to infect the new host or alternatively it may produce a dramatically lethal infection¹. Any results obtained from rabbits are unlikely to give a true representation of how the vaccine would affect the pathogenicity of the virus in humans.

Overall, the above points indicate that this experiment does not offer applicable advancement to meeting the project objective of developing human protection method against the herpes B virus.

Costs to Animals

17 rabbits suffered substantial procedures.

Conclusion

It would appear that the objective of this project may be met without the use of animals by the use of alternative strategies. Due to bad science and planning the particular experiment detailed here has not contributed to the success of this project. There can therefore be little argument that the benefits of this research do not outweigh the costs to the animals.

1. *The Lancet*, Vol 1, 22 March 1975: 667.

PSYCHOLOGICAL RESEARCH

BRAIN DAMAGE EXPERIMENTS ON CYNOMOLGUS MONKEYS

Publication:

Nixon, P. D., Passingham, R. E. The cerebellum and cognition: cerebellar lesions impair sequence learning but not conditional visuomotor learning in monkeys. *Neuropsychologia* (2000) 38: 1054-72.

Summary and Background

University of Oxford: 6 cynomolgus monkeys, plus 3 used in pilot study. This experiment involving brain surgery on monkeys was conducted to support what is already known from human patient studies, but results contradicted those from humans.

This experiment involved making 32 lesions in monkeys' brains during major surgery. When they had recovered from the operation, they were required to complete numerous repetitions of psychological tests.

A pilot study had been conducted earlier as part of a doctoral thesis using 3 cynomolgus monkeys. The monkeys were taught a task requiring both cognitive and motor functions (visuomotor task), then had lesions made into both the white and grey matter of the cerebellum of their brains using a radio-frequency probe. The animals were then retested on the task, and it was found that the monkey with the most complete lesions was unable to perform as required even after 2000 trials.

In the 1st main experiment, 6 monkeys were put in wheeled cages of less than 0.2m³ (56x59x49cm) with bars and perspex placed so they could stick only one hand through to reach a joystick. The monkeys were made to associate 2 visual cues with moving a joystick in a certain direction by using food pellet rewards. The trials were continued until the monkey gave at least 500 correct responses to the cues. This drawn out activity was only the pretask training; after this the monkeys were made to do 100 correct repetitions daily on the same task. If the animal made a mistake, the same cue was presented repeatedly until they responded correctly. This training was continued for between 2400 and 5700 trials (until the individual achieved a 90% success rate). Immediately after this, the monkeys were trained on another task for experiment 2 which took 4 months to learn, then tested another 200 times on the first task.

The next stage of the experiment involved brain surgery on 3 healthy animals so that the researchers could compare how the monkeys with multiple lesions in their brains performed on the tasks compared to those without lesions. The researchers state that the monkeys were sedated, but give no mention of doses or drugs used to onset anaesthesia. They go on to say that deep anaesthesia was maintained using sodium thiopentone at a 5% concentration in 0.25ml doses. This is a very short-acting anaesthetic sometimes used to induce anaesthesia with a different drug¹. It is not recommended specifically for maintenance of anaesthesia, and an extremely low dose was used.

Once inside the monkey's skull, a section of the dura (membrane enveloping the brain) was cut and pulled back. A needle was then inserted through deeper dura into the cerebellum and a solution of an acid injected into the monkey's brain to destroy nerve tissue at 16 different places on 1 side of the brain. 5 days later, the same 3 monkeys were put through the same operation on the other side of their brain, involving another 16 injections of the toxin. After the injections, the dura was sewn back and the bone flap and soft tissues fixed down with stitches.

The operative animals were then given a 3 week recovery period before the researchers had to assess whether they could still move their arms enough to be able to do the visuomotor tasks, due to the severity of the damage they had caused. All 6 monkeys were then made to do another 10 days

retesting of the same task once again, before being retested for experiment 2 over 1000 trials. After this, the 3 monkeys that had not been operated on performed another experiment in which they were trained on a similar task as before, then given the same brain lesions as the other 3 monkeys and retested on 100 correct trials a day. Finally, all 6 monkeys were killed under anaesthetic by replacing their blood with a preservative solution before removing their entire brains for study.

Importance of Objectives

Unoriginal and irrelevant to humans:

The purpose of this experiment is to repeat studies done on humans, for application to human patients, in monkeys. This is a common example of needless repetition of irrelevant, pointless, unscientific research. They attempt to show whether the cerebellum is involved in cognitive as well as motor functions, but the researchers themselves state; *“The present decade has seen a striking increase in the number of studies that suggest that the cerebellum contributes to cognitive performance. These claims have been based almost entirely on evidence from human subjects.”* This study is in no way justified in terms of scientific quality, nor was it the best method for application to human patients. A licence should not have been granted.

Lack of any potential benefits for humans or other animals:

The researchers mention that the problem with human studies is that the brain damage is not usually confined to the cerebellum and this is why they feel the need to use artificially mutilated monkeys' brains to study the behavioural effects of damage to this region. This is in itself a contradiction; if there are rarely humans with damage specifically confined to the cerebellum, and none alive and available for studying behavioural effects, then this is not a situation which needs to be studied. If there are living victims of accidents or diseases which do have this specific damage, then they could be studied instead to gain relevant useful results from which can be gained reliable solutions, without the vast differences between the brains of humans and monkeys ever being a problem. In fact there are a number of studies cited in the paper which do just this; for example, Drepper *et al* (1999) studied isolated cerebellar degenerative disease in humans using an associative learning task very similar to the one used on the monkeys.²

Probability of Achievement

No scientific validity; unnecessary animal use:

The number of repetitions the monkeys were made to do on the same tasks seems highly excessive. The training alone for the experiments took 2400-5700 trials for the first task and 4 months of trials for the second task. The monkeys took this long to learn the tasks, even before the lesions, implying that it was not a suitable task. The humans in the Drepper *et al* experiment certainly did not take anywhere near this long to learn the task, even with lesions in their cerebellum, emphasising again the differences between human brains and the monkey's brains. The use of monkeys as a model for this human condition has no scientific validity.

Consideration of alternatives

These injuries can be studied, and information gained, from direct observation of the patient using techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET) and functional MRI (fMRI). Animal use is unnecessary and irrelevant for the study of human brain trauma.

Cost to Animals

Severe procedures conducted on primates, with no evidence of minimisation or early termination:

A pilot study was carried out to investigate how deep the lesions needed to be in the monkeys' brains. This used 3 different monkeys performing the same tasks as the main study. One of these animals had

lesions so broad that he had considerable difficulty after the brain surgery even moving his arm enough to make the movements required to complete the task, but he was still made to do 2000 repetitions.

Conclusion

Nine monkeys were given brain surgery and made to perform thousands of repetitive trials to model a human injury. The results are not relevant and alternative studies on human patients could have been performed. Therefore benefits in no way outweigh costs and a licence should not have been granted.

1. Anaesthesia and Analgesia in Laboratory Animals. Eds. Kohn, D.F. *et al* (1997) Academic Press

2. Drepper, J., Timmann, D., Kolb, F.P. & Diener, H.C. Non-motor associative learning in patients with isolated degenerative cerebellar disease. *Brain* 1999, 122, (pt.1), 87-97

NAVS RESPONSE TO APC COST/BENEFIT CONSULTATION

ANNEX 2: ETHICAL CONSIDERATIONS

Just as humans have a moral worth as well as a physical one, so do animals. Unless animals are regarded by the APC as having moral worth, it would make no sense to say that we must include their deaths and suffering on the scales of cost and benefit. Since the 'cost to the animals in suffering' is included as the one and only cost when calculating the justification assessment, we can assume that the APC accepts the moral worth of animals.

When calculating the justification assessment, we can take three factors into account which cover the moral asymmetries we are presented with:

Definite harms vs. possible benefits

Inflicting suffering on animals is definite, while preventing the suffering of humans is merely possible. Animal experiments therefore sacrifice good in the mere hope that some other good will possibly be achieved. The probability of benefits to humans must be greater than the certain suffering of the animals for the benefits of the experiment to outweigh the costs. But the probability of success of the experiment is likely unknown, otherwise there would be no need for the experiment. So therefore the probability of benefit to humans is also unknown. The probability of suffering of animals however, is certain. If the probability of these adverse effects is certain, and the probability of a benefit to humans less than certain, it follows that the costs always outweigh the benefits.

Those that suffer vs. those that benefit

The species reaping the benefits of the experimentation are generally not the same species as those paying the costs. This is in direct conflict with the moral assumption against inflicting suffering on one creature in order to benefit another. It is an example of 'speciesism' i.e. putting members of your own species before those of others simply because they are your own species, and for no other reason. But as argued above, the APC have accepted that animals have a moral worth, and therefore it is not logical to disregard other species' welfare in this way for the benefit of one species in particular. We assume that humans should not be forced to sacrifice their lives in medical experiments for the benefit of other humans, and in the same way, why should we expect animals to do this for the benefit of humans.

Of course, researchers could simply reject these moral claims, but there are consequences:

If they claim we should pursue any activity which yields greater good, it follows that we should perform non-consensual experiments on humans if they yield greater good for a far larger number of humans.

Calculating the costs

When determining the gains relative to the costs, we must include not only the direct costs to the animals, but also the costs to humans of misleading experiments. The preoccupation with misleading animal models undoubtedly delays scientific discoveries, and any delay means that the number of people who died in the mean time have been sacrificed, along with the animals. Animal models also

directly cause deaths; drugs tested on animals are sometimes lethal to humans. We must also include possible costs; deadly diseases may be transferred to humans through our use of animals – these are future effects of animal experimentation.

Those who support animal experimentation without question appear to believe that regardless of their success or failure, animal experiments advance our understanding; they believe that all animal experiments produce absolute facts. The truth is that these ‘facts’ are not as incontrovertible as they appear, and certainly, not as they are sold to a concerned public. In reality, they produce information about other species, in a specific set of circumstances, in a laboratory. What works in a laboratory can be quite different outside. What works in one species, can have another effect in another species.

Alternatives

Supporters of vivisection must demonstrate that the practice of animal experimentation yields greater benefits than any alternative practices – otherwise benefits do not outweigh costs. Crucial to the calculation of costs is the possible benefits animal experimentation could achieve relative to those of non-animal methods. It is any increase in benefits relative to what alternative methods would have yielded had the money and time been invested in these that we must consider. This of course is unknown as investment in alternatives where animal methods are established is minimal. No-one can be sufficiently confident of the benefits of animal methods relative to non-animal as they simply have not been systematically tried. Cost benefit assessments of animal methods must demonstrate that their methods outweigh the costs relative to alternative methods, and including the moral costs¹.

¹ Based on ‘Utilizing Animals’. Hugh LaFollette & Niall Shanks, J. Applied Philosophy (1995) 13-25

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