The Laboratory Animal Science Association

Thank you for inviting comments on the ethics of research involving animals. The Laboratory Animal Science Association has examined the consultation paper and we are pleased to attach our comments.

Background information about the Laboratory Animal Science Association
The Laboratory Animal Science Association of the United Kingdom was founded in 1963 by a group of people from industry, universities, government ministries and representatives of the research councils. Their aim was to establish an organisation which provided information and a forum for ideas on the science of animals used in research. We keep our members informed about the latest developments in the three R's, and ensure that new developments such as improved procedures and techniques are circulated throughout the scientific community.

LASA realises that many ethical considerations are raised by the use of animals in research and it constantly reviews its policies on these issues. Members are encouraged to consider the ethics of what they do and not only is this topic included as standard in training courses but also the Association holds regular discussions with other interested scientific and welfare organisations.

Yours sincerely

Laboratory Animal Science Association

Q1. Research using animals clearly produces information unavailable by any other means and is transferable to man providing experiments are properly conducted and species choice is appropriate.

- In vivo experiments are largely concerned with integrative biology and investigate phenomena evident in whole organs or dependent on interactions between body systems.
    - Pharmacokinetics of pharmaceutical agents is ultimately only measurable in vivo although a considerable amount of information can be obtained in in vitro studies to inform the design of animal experiments.
    - Blood pressure is a multifactorial phenomenon, dependent on the combination of a number of factors such as cardiac output, vascular tone and peripheral resistance.
    - Long term effects of new therapeutic agents can only be investigated in whole animals. In vitro systems are by their nature short term and long term adaptive changes are not measurable. This an apply to therapeutic effects or toxicity.
    - The pharmaceutical industry uses preclinical models in the choice of candidates for evaluation in humans. Numerous examples of how animal models have predicted effects in humans have been published.
    - The predictive value of toxicological studies was examined in detail by the House of Lords enquiry. In general the data supports the view that animal studies are capable of demonstrating the toxicological potential of new agents (eg Olson et al, 2000, Regulatory Pharmacology and Toxicology 32; 56-67).
    - However there has been some discussion, among toxicologists questioning whether the full range of studies currently used (and demanded by regulatory bodies) before progression to studies in man is optimal (see eg Munro and Mehta, 1996, Clinical Pharmacology and Therapeutics , 59; 258-264).
    - Animal studies may also duplicate human conditions and allow insight into mechanism underlying diseases. One example is the role of high fat diets in inducing heart disease. It is often stated that animals do not suffer form the effects of over eating. However it has been shown that rats 'cafeteria' fed a highly caloric diet, become obese, develop symptoms of type II diabetes (including pancreatic changes) and hypertension much as observed in humans (eg Coatmellec-Taglioni G *et al* (2000). Hypertension in Cafeteria-fed rats: Alterations in renal α_2-adrenoceptor subtypes. Am J Hypertension, 13: 529-534.)

- Acceptability of animal experiments is dependent on a robust and rigorous cost benefit analysis of proposed studies. This should be structured so as to ensure that maximal data is obtained, that this data is relevant and necessary and that this is achieved with minimal possible harm to the animals.
- The majority of animals experience very low levels of suffering, often only involving transitory discomfort associated with administration of compounds, or in the case of GM animals no regulated procedures other than being born.
- Housing is increasingly being modified to meet behavioural and physiological needs.
- Rigorous cost benefit analysis can be used to ensure all steps are taken to minimise suffering.

Q2 GM animals do not essentially raise any new welfare issues. Manipulating genes should be considered no more unnatural than selective breeding which has been carried out for millennia, producing some very grossly distorted phenotypes. Similarly spontaneous mutations have produced large phenotype changes which may be deleterious to welfare and experimentally useful.

- The creation and use of GM animals should be subject to the same robust cost benefit analysis as any other experimental procedure
- Genetic models of long-term degenerative diseases should be adequately addressed by these processes and be regarded in the same way as (for example) a surgical model.
- Genetic modification does present some new challenges for the cost benefit analysis, largely due to the possibility of unexpected adverse effects and the possibility that phenotypic changes may only be apparent in response to an environmental or other stimulus. Measures to control unexpected effects can be built into Project Licences.

Q3 Alternatives to animal experiments provide an important and integral part of the research process. As the House of Lords recognised, the majority of alternative methods have been developed as part of ongoing research into biological systems- not by 'alternatives specialists'.

- Undoubtedly more funding for alternatives would be useful; this must however be applied in the context of advances in biology.
- Industry spends large amounts of money on alternatives research, integrated with other research (a figure of £300M has recently been quoted). More funding may be available from this source; however government and research council funding should also be identified.
- Greater strides could be made by using alternatives more effectively in toxicology and safety studies. Validation is a key

problem here and Government funding would usefully be applied to validation. Progress here is also impeded by regulatory issues, another area in which government can play a key role.

Duplication

- It is unlikely that true duplication (the same agents being tested in identical experiments) is at all common
- Parallel programmes of research in academia and industry undoubtedly exist. This is essential for progress since differing approaches often ensure rapid advances.
- Much data is shared; data is published either in journals or as part of patents and scientists participate in conferences.

Publication

- Accounts of experimental details in papers are often limited by journal editors and pressure on space.

Q4 It is generally accepted by the public at large that animals do not have equal moral status to humans. They do not have responsibilities or life plans in any way similar to humans.

- Society does make distinctions between species and their moral status. The welfare of eg primates is viewed very differently from that of mammals such as mice and even more differently to the respect accorded to invertebrates. [Contrast the casual destruction of pests such as slugs in gardens to the care given to laboratory animals].
- It is difficult to truly assess the suffering of animals however:
  - It is accepted that animals experience pain (eg they react as humans do in nociceptive tests)
  - A measure of distress and/or suffering can be derived from the disruption of normal behaviours for a number of species
- Invasive models to assess the nature of animals' experiences may be difficult to justify in a rigorous cost benefit analysis; behavioural studies may be more appropriate.
- Can we justify making animals suffer? This returns to the question of rigorous cost benefit analysis combined with an acceptance of differing moral status. In addition, justification for the use of animals brings a responsibility to carry out experiments in such a way as to minimise harm to animals.

Q5. There is a strong framework of regulations, training requirements and culture of care protecting animals in the UK.

Legislation

- Local ethical review is conducted in all establishments

- There is an active community of professionals involved in animal care who share good practice
- Welfare assessments are, rightly, carried out at all stages of a project, before, during and at the completion.
- GM animals are correctly included in the regulatory framework when new strains are being produced. The current framework if rigorously applied is adequate for the review of GM animals.
- There may be scope for releasing some GM animals from these controls if the strain is shown to be free from adverse effects (they would subsequently be bred in the same way as any other laboratory strain). However it must be established that the genetic abnormality is unlikely to be expressed in offspring resulting from crosses with other GM animals

Cost Benefit analysis

- Current provisions are robust and effective when appropriately applied.
- This analysis should be in advance of starting work but kept under review throughout
- Retrospective analysis of the value of research can be valuable and can provide useful data to inform evaluation of future programmes.
- Publication of data may be similarly useful; however considerable thought should be given to what would be useful and to agree a 'scale' for assessment of costs to the animals.

Additional legislation

- Will almost certainly drive research abroad; this may be manifested as a reluctance to invest further if it is perceived that the risks associated with a tough regulatory environment slow the progress of projects. There has been much publicity recently about the export of the "animals" component of collaborative academic research projects to countries with less rigid legislation.

Q6 The balance of information available to the public is probably inadequate to allow real judgements on the benefits derived from research involving animals

- There is a huge body of information from campaign groups opposed to animal work, much of it claiming support from published data. These claims rarely withstand close scrutiny, published work is selectively quoted and statements paraphrased so that their meaning is changed.
- Scientists publish their work in professional journals. This requires the context and background to be fully understood. The language used is often not accessible to the general public.
- In addition there is an understandable reluctance by many scientists to talk publicly about experiments involving animals since some scientists have been targeted by activists following such disclosure.

- Scientists' primary role is the conduct of research, leaving little time for public information programmes.
- Trust should be placed in those with first hand experience of the scientific questions being discussed. The media could play a more helpful role in questioning the qualifications, experience and motivation of those making public statements.
- Medicines should be labelled to indicate the use of animals in their development. This would encourage a more realistic assessment amongst the public of the real impact of any ban on, or restriction of animal studies. A simple statement would suffice.