Professor Michael Balls- Chairman of FRAME Trustees, UK

[The following comments are those of the author, and should not be assumed to be necessarily representative of the views of FRAME as a whole.]

Question One:

1. My overall view is that causing suffering of any kind to laboratory animals is always regrettable, but that it can be justifiable in certain circumstances, where it has been shown, according to strict criteria, that there is a sufficient likelihood of achieving justifiable and worthwhile benefit to humans and other animals.

2. The first supplementary questions are not well phrased, as they demand *yes* or *no* answers, which cannot be given on any rational basis. The fact is that research involving animals *can sometimes* provide information that is not available from any other method. The point is *when*, and whether the information is of *sufficient necessity* to justify the use of the animals. Similarly, results from research on animals *can sometimes* be transferred to humans. The point is *in what circumstances*, *with what relevance* and *with what reliability*. A case-by-case approach is essential.

3. The acceptability of using animals depends on far more than the purpose of the research, especially when gaining more fundamental knowledge is the purpose. Merely to say that the purpose is to seek a cure for cancer or for Alzheimer's disease is not enough. The quality of the proposed research in the light of current knowledge and of other work in progress, the degree of likely suffering in relation to the likelihood of benefit, and the competence and experience of those involved, for example, are only some of the other factors that must be taken into account.

4. Indeed, this kind of consideration is specifically required by the *Animals (Scientific Procedures) Act 1986* (ASPA), as is justification of the choice of animal species to be used (with a requirement that these are the least sentient animals which can provide the results to be sought).

5. Considerable suffering is undoubtedly caused to laboratory animals, not least that which comes from being maintained in confined housing and being killed when no longer needed, in addition to that involved in actual scientific procedures. This especially applies to the higher primates. There is a huge literature on these issues.

6. The ASPA requires that likely suffering be estimated before a project is licensed, and that this suffering is weighed against the likely benefit from the research. This is good in principle, but its administration at present is biased

in favour of science and benefit, and against animals and suffering. For example, keeping a macaque monkey in a small cage, then restraining it in a chair with its head clamped rigid and electrodes into its brain for six hours a day, for five days a week, for up to 18 months, merely in the search for basic neurophysiological information, is classified as of *moderate* severity (on a scale involving *unclassified*, *mild*, *moderate* and *substantial*).

7. The Home Office already considers some procedures to cause too much suffering irrespective of their purpose, and so does not permit them. It would be useful to know what these procedures are, how many and which British scientists go abroad to use them in countries with less strict laws and regulations, and how often the Home Office refuses to licence a project or to approve a procedure protocol on the grounds that the likely suffering would be too great in relation to the likely benefit.

8. In my opinion, *all* maintenance of higher primates under laboratory conditions, and *all* procedures applied to them, inevitably involve levels of suffering which are unacceptable.

Question Two:

9. GM animals undoubtedly raise new and different issues, as has been discussed with authority in a number of reviews, not least those from FRAME (see *ATLA* **27**, Supplement 1, pp. 811-902, 1999), which have been consistently ignored by the Scientific Establishment in Britain (e.g. the Royal Society), as well as the Home Office. One issue is that the scientists creating GM animals are often ill-informed about the species concerned, but only know about molecular biology at the cell and gene levels.

10. All laboratory animals are unnatural, at least physiologically and behaviourally, if not genetically. GM animals can be created in ways which involve far too great a departure from their natural state. They can become mere objects carrying genes and genetic disorders, with little thought given to their own welfare or to the suffering caused to them.

11. One type of animal procedure which should not be permitted, involves the injection of male mice with potent chemical mutagens in order to cause mutations (see Jenkins *et al*., *ATLA* **29**, 63-68, 2001). This unscientific, shotgun approach, funded by the MRC in the UK, is not hypothesis driven, involves very large numbers of animals, and produces very little of value. It should be stopped forthwith. When FRAME took up this issue, we were subjected to a great deal of criticism and hostility from those involved in this work, but they refused to accept an invitation to justify their approach in *ATLA*. This led me to the conclusion that, being funded by the MRC, they didn't feel the need to have to justify their work more widely.

12. The overwhelming problem with the use of GM animals as models of human disease is that it is very rare for sufficient to be known about either the human disease or the purported human equivalent to permit an understanding of how good (or otherwise) such models really are. Given the development and availability of non-animal alternative methods, and of non-invasive methods which can ethically be applied directly to humans, this approach increasingly looks old-fashioned and is increasingly hard to justify on any rational, scientific grounds.

13. Attempts to "humanise" animals should be strictly controlled. They should also be looked on with suspicion from the scientific viewpoint. For example, the idea that the human immune system can be recreated in mice is naïve, since the immune system is also controlled by a complex of neuroendocrine factors which would be significantly different in mice and humans. The outcome would be the provision of information which would be misleading and/or could not be interpreted effectively.

14. Another specific example of naivety is the use of GM models for chemical carcinogenesis. The use of rats or mice in carcinogenicity testing might (only might) tell us something useful about the induction of cancer in rats and mice. It can tell us very little about risk to humans. The use of GM mice for this purpose merely adds another complication, to the benefit only of the developers of the technology and their employers. There is a further scandal here – some regulators now require a rat test, a mouse test *and* a GM mouse test for carcinogenicity, even though the GM mouse test has not been scientifically validated. Some experts believe that there is no evidence that the mouse test adds any useful information above that provided by the rat test, so it is very hard to see what a GM mouse test could add. The GM mouse test appears to be permitted in the UK, merely because the companies concerned threaten that they would otherwise take their operations abroad.

15. Finally, let me say that, in my opinion, the creation, breeding and use of GM non-human primates should be specifically prohibited.

Question Three:

16. I have appeared before the Committee to discuss alternatives, and I have provided a number of publications.

17. There should be more work specifically on alternatives, especially as bodies such as the MRC have hitherto been unwilling to support such efforts. This work should be funded by the Government, by the major funding bodies (MRC, Welcome Trust, Cancer Research UK, etc.), industry, and animal

welfare/antivivisection organisations (especially those with large incomes, e.g. the RSPCA, NAVS, BUAV).

18. Alternatives could be used more effectively in toxicity testing, potency testing and quality assurance testing, but there should also be a much more sincere and active effort in relation to finding replacement alternatives for use in fundamental biomedical research.

19. Scientists wanting to use animals currently have to do little more that to say that alternatives do not exist, before gaining permission to conduct animal procedures. Two current examples are of particular concern, namely, the testing of botulinum toxin (*ATLA* **31**, 381-391, 2003) and testing for diarrhetic shellfish poisoning toxins (Combes, *ATLA* **31**, in press, 2003). In both cases, animal tests of substantial severity are conducted, with little apparent effort by the companies involved or the Home Office to consider the alternative methods which are available.

20. With regard to the question of sharing information, my experience suggests that greater openness is usually a good thing, but that the unnecessary duplication of animal studies is not an enormous problem.

21. I have two concerns about the way that research involving in animals is reported in scientific journals. Firstly, as was found in an RSPCA/FRAME report on the use of primates in Great Britain (*ATLA* **17**, 335-400, 1990), it is often impossible to discern how many animals were used or what was done to them. Secondly, experiments are often so badly designed that excessive numbers of animals are used – and the data are often so poorly analysed that the conclusions drawn are erroneous. These issues have been discussed on many occcasions, notably by Dr Michael Festing, a FRAME Trustee. An *ATLA* supplement, based on a conference on reduction and experimental design, organised by the FRAME Reduction Committee, will be published early in 2004.

22. The potential of the alternative approaches mentioned (*in silico*, *in vitro*, etc.) is enormous and largely unrealised. Investment in these areas specifically to reduce, refine or replace animal experimentation is very low in Great Britain, largely perhaps because the Scientific Establishment would fear that it would weaken their oft-stated claim that animal experimentation will always be essential.

Question Four:

23. Discussions about the moral status of animals are frustrating, because such discussions are always among humans and on human terms, since the animals themselves cannot take part.

24. Thus, whether or not animals have *rights* or a *moral status* which are in any way comparable with those of humans, is totally determined by ourselves. Thus, my own view is that the way we treat animals should primarily be seen as a question of *human responsibility* or *human stewardship*.

25. As a zoologist, I know very well that there are major differences between mosquitoes, mice and monkeys, but I was trained not to call *Amoeba* a primitive animal as it is highly suited to its lifestyle. Degree of sentience is a reasonable way of discriminating among animals when the question is how much suffering should be allowed to be caused to them in pursuit of a particular purpose. Hence, if fish, mice or monkeys will do, use fish. But, if only monkeys will do, use monkeys (although, as I myself would say, only if the suffering to be caused to them would be genuinely no more than mild, such as injecting a therapeutic dose of a medicine and collecting body fluids).

26. Causing suffering to animals to the benefit of humans is an example of human selfishness. That we are prepared to do this should not surprise us, since, day by day, we learn of unbelievable suffering caused by humans to other humans. The way we are prepared treat our own species should not be a justification for treating other species as badly.

27. The second group of questions here are particularly unhelpful. There is little point in referring to "animals" or "all animals" or using words such as "feel" with regard to pain. Adverse stimuli are detected by many living organisms, but, in higher animals, this information is processed and perceived as what we describe as pain. The parts of the brain associated with this perception are more highly developed in primates in other animals, which is a very good reason for not subjecting non-human primates to what would be likely to cause pain in humans.

28. Many schemes are available for scoring welfare and/or suffering in laboratory animals, and they can undoubtedly be useful. However, what is really needed is a commonsense approach. Nobody who has lived with dogs and cats can fail to know when they are suffering, whether or not we could quantify it or describe it perfectly. We must not let those who want to apply experimental procedures to animals get away with clever and pseudoscientific arguments about animal consciousness, ability to perceive pain, etc., as a means of escaping the need to justify what they want to do.

29. No, I don't think we should make animals suffer in order to know more about how they "experience the world" (whatever that may mean). The classic example here is bird migration. We don't understand how they manage it, but who would benefit if we removed parts of their brains or

sense organs to try to find out? Certainly not the birds. And how would it really benefit humans?

30. I support the prediction and weighing of likely benefit and suffering, as required under the ASPA (especially as this clause was inserted at the specific request of the BVA/CRAE/FRAME Alliance advisers, of whom I was one, during the passage of the Bill through Parliament). However, I am not satisfied with the way in which this requirement is being applied, as I said earlier.

31. The ways in which animals are used to provide food or clothing, or in sport, or are treated as pets, are nothing whatsoever to do with how we should approach the use of animals in biomedical research. It is very tiresome to have to listen so frequently to proponents of animal experimentation, when they ask how many chicken are eaten compared with the small numbers of cats, dogs, monkeys, etc, they want to use.

32. Similarly, the fact that rats and mice are treated as vermin in other circumstances does not justify subjecting them to unjustifiable suffering in laboratories.

33. The environments in which animals are kept are of great importance, and the whole lives of laboratory animals should be part of the suffering consideration, not just what happens to them in experimental procedures.

Question Five:

34. No, I think the current procedures for the assessment of animal welfare are not appropriate, and that they should be continuously reviewed and improved.

35. Welfare assessments should be conducted before, during *and* after procedures are applied.

36. Yes, the welfare of various types of animals and subtypes (e.g. in particular, GM animals) can be captured in guidelines and regulations.

37. Yes, licences should be required for the breeding of all GM animals.

38. No, the current regulations are not appropriate for the assessment of new types of GM animals.

39. The current systems for cost-benefit analysis are badly in need of improvement. Far, far too many projects are classed as of *moderate* severity, and only about 2% are classed as being of *substantial* severity.

40. More emphasis should be placed on individual procedures/protocols and effects on individual animals, rather than on the project as a whole. At present, *substantial* protocols can be hidden with a *moderate* project. Also, some animals can suffer *substantially*, even if the average suffering in a particular case is *mild* or *moderate*. The Home Office Statistics on this issue are uninformative and useless.

41. The cost-benefit analysis should be continuous – before, during and after a project is licensed. There should certainly be a re-assessment, of both suffering and benefit, in the light of what happens during the lifetime of a project. Some use of laboratory animals appears to go on, project period after project period, whether or not it produces any identifiable benefit. The tracing of the functions of individual neurones in the macaque brain (in the kind of "moderate" project referred to above) is one such example. Also, when I once asked a Home Office Inspector about a project involving cats (a species supposedly given special protection under the ASPA), he said that the work was being done in cats, merely because it had always been done in cats. Rats would have done just as well, he said.

42. Claims are frequently made that progress in tackling serious diseases is dependent on the use of animal models. However, there is a great deal of evidence that there is relatively little reference in the clinical literature to work done on animals, and that those involved in, for example, neurophysiological work on the brains of higher primates, frequently quote their own work or that of similar research groups, whilst having little real effect on progress in understanding or treating the diseases their studies are purported to underpin (see Sauer, *ATLA* **31**, Supplement 2, 309-313, 2003). This issue deserves a thorough, objective and balanced investigation, free of the bias, for and against, which characterises so much of the discussion about animal experimentation.

42. Yes, there should be a way of publishing all results. The numbers of primates used in Great Britain are far less than the numbers referred to in publications, partly because most of the work conducted by industry is not published in the open literature, and partly because the results of unsuccessful experiments are usually not published at all.

43. I strongly believe that regulation in the UK should be strengthened, despite the threats regularly issued by companies and scientists that they will take their work abroad, if their freedom is further curtailed. I would go further and say that I consider it unethical and immoral for a British companies or scientists to do or fund work in another country which would not be permitted in the UK. We do not lower our employment standards merely

because there are lower standards elsewhere. Nor do we permit child abuse merely because sex tourists can readily find child prostitutes elsewhere.

Question Six:

44. It may surprise those who read the rest of my comments, when I say that I have few complaints about the information about research involving animals which is available to the general public.

45. The annual Home Office Statistics are, on the whole, excellent and useful, although there is room for improvement in certain areas (e.g. on severity banding, as suggested above). Also, the Home Office should provide information on what kinds of procedures are not permitted in the UK (whether or not they are permitted elsewhere) and on how many project licence applications and procedures protocols are rejected each year.

46. The best source of balanced information about research involving animals is (or at least, should be) the Animal Procedures Committee, of which I was a Founder Member, and which was set up to give the Home Secretary independent advice on the operation of the ASPA.

47. I do not think that medicines should be labelled to indicate whether or not they have been tested on animals, as this would lead to the kind of dishonesty which has been rife in the labelling of cosmetics (see *ATLA* **19**, 302-307, 1991).

48. Nor do I think that the individuals or institutions involved in particular projects should be identified, except in special circumstances (e.g. if an offence is committed under the terms of the ASPA or other legislation).

49. Most importantly, I think that the standard of debate about the scientific and ethical issues surrounding the use of laboratory animals is abysmally low, and that this is not helped by the media, which prefer entertaining confrontation to a constructive middle-ground approach, or by scientists who seek to dismiss all those who question their activities as antivivisectionist activists. I would like to think that the Nuffield Council will be able to make a positive contribution here.

50. In this context, the MORI poll referred to deserves close scrutiny, since it reveals more that the Coalition which commissioned it, or the MRC, which funded it, would have us believe (see *ATLA* **31**, 83-84, 2003, *attached*).

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[Professor Balls also submitted to the Council an article he had written, published in the ATLA 2003, entitled, *Animal Experimentation as Perceived by the Citizens of Britain and France*].