

The **A P C**
Animal Procedures Committee

**FINAL REPORT OF THE CAMBRIDGE/BUAV
WORKING GROUP**

16 JUNE 2005

Executive summary

Under the heading of 'process and procedure' we make the following three proposals:

- That the APC should confine its attention to the prospective consideration of strategic issues, and not be drawn into retrospective judgements (13-16)
- That the APC, in its advisory capacity, should actively explore the feasibility of instituting some form, or forms, of complaints procedure (10-12, 17)
- That the APC, in furtherance of its advisory capacity, should consider the feasibility of regularising meetings of a bilateral nature with the key players involved in animal research, with the aim of keeping strategic issues under review (18).

Under 'issues of substance', we make one proposal:

- That the APC, possibly through its sub-committee on primate research, should consider initiating a case study of a key area of medical research such as Parkinson's Disease with a view to facilitating an overall strategic assessment of the role of animal research within the broader endeavour to alleviate human, and animal, suffering (26-27).

We also identify the following areas as fit subjects for further scrutiny:

- staffing issues: levels, training and competency(20-21)
- standards: the roles and responsibilities of the various bodies involved, for setting, reviewing and maintaining standards of animal welfare, and initiating improvements (23-25)
- the publicity issued by funding bodies and medical charities regarding the benefits of the research that they fund and, especially, the costs to the animals (28)
- a re-working of the labels used to indicate the severity of animal suffering so as to build a more detailed picture, and more generally agreed understanding, of what animal research involves (30-32)
- the sources of disagreement about the nature and degree of severity of suffering (33-34)
- the implications of food and water deprivation and deferral (35)
- the detection of suffering: what levels of detection should be in place in order to satisfy the requirements of the Act? (36-37).

Introduction

1. What follows is the final report of the 'Cambridge/BUAV' working group that was set up by the Animal Procedures Committee (APC) in June 2002:

“to assess the allegations of the British Union for the Abolition of Vivisection (BUAV) about the use of marmosets at Cambridge University in the light of the Chief Inspector’s report and the Home Office’s response, and to identify areas of discussion for the APC”;

and

“to consider the matters of whistle blowing by established members of staff and clandestine investigations by undercover activists”.

The membership of the group is as follows: Professor Holland (chair), Dr Jennings and Professor Atterwill. In April 2003, Dr Hubrecht was asked to join the group because of his expertise in primate behaviour and welfare.

2. The working group (WG) has held a number of meetings, both separately and with interested parties, and assembled a considerable amount of material, which is recorded in the various appendices. We also received input from the Inspectorate and from members of the full APC in response to an 'emerging findings' paper circulated previously. The issues arising out of our discussions appear to fall into two categories: (A) Issues of procedure and presentation, and (B) Issues of substance. Before reporting on the issues, it would be useful first to remind members of some of the background to this report.

3. In May 2002 the British Union for the Abolition of Vivisection (BUAV) issued a report making a series of allegations about work being carried out at Cambridge University. The work licensed included projects covering brain disturbance and repair, neurodegeneration and repair; and neural mechanisms underlying cognition and emotion. A BUAV undercover investigator had infiltrated the research unit and worked there undetected for several months. The allegations were the subject of a report on "Newsnight", and the BUAV sent copies of their report to all members of the Animal Procedures Committee (APC), also enclosing a short compilation of extensive video filming carried out by the undercover investigator. The then Home Office Minister, Bob Ainsworth, who had separately been sent the BUAV material, announced that he would ask the then Chief Inspector, Dr. Richmond, to look, not at all of the issues raised in the BUAV's report, but at those that were judged to be matters for ministerial concern. Dr. Richmond was, in particular, to review the relevant licensing decisions, the severity limits and bands assigned to the projects, and related compliance issues. He completed his report in October 2002. The Home Office Minister accepted the Chief Inspector's main findings and conclusions.

4. In pursuit of its task, the WG decided early on that it would be helpful to have face to face discussions with those centrally involved, namely the Cambridge Research Unit, the Chief Inspector, the bodies which funded the research and the BUAV. Accordingly:

- on 6 June 2003 the WG visited the Cambridge facility, where we met university staff, including researchers at the unit, the Certificate Holder, the Named Animal Care and Welfare Officer (NACWO) and animal technicians. We also viewed the animal accommodation where we saw both stock and experimental animals, and observed an animal performing behavioural testing tasks;
- on 27 August 2003 the WG had a meeting with the Chief Inspector (the notes from our meeting with the Chief Inspector are attached as Annex A);
- on 21 November 2003 the WG met with David Thomas (legal adviser to the BUAV), Sarah Kite of BUAV and their undercover investigator (the notes of our meeting with BUAV are attached as Annex B).
- on 27 January 2004 the WG met with Tony Peatfield and Vicky Robinson of the Medical Research Council (MRC) and MRC Centre for Best Practice in Animal Research (CBPAR) respectively (the notes of that meeting are attached as Annex C.)
- the WG was unable to arrange a similar meeting with the Wellcome Trust, co-funders of the research, but they kindly provided us with a written response to our questions, which is attached as Annex D
- while at Cambridge the WG also met with Professor David Morton, who had been interviewed on Newsnight on the day that news of the BUAV undercover investigation was first reported. Professor Morton subsequently viewed the official BUAV video for us and kindly provided us with his comments, which are attached as Annex E.

In all cases, save for the meetings with Professor Morton and the Cambridge researchers, the questions that the WG wished to ask were circulated in advance. However, it was not always possible to address all of the questions at the meeting. Indeed, we usually ended up with further questions that we would have liked to ask. We showed our report in draft form to each of the above-named organisations and individuals. Where applicable, each was also shown our note of the organisation's and individual's responses to our questions. We considered all the further comments we received, but did not in all cases accept the suggested amendments.

General observations

The BUAV report

5. In their investigation, the BUAV claims that there is strong evidence that the Home Secretary has acted unlawfully in the regulation of the research covered by their report. They do not claim that there were infringements by the licensees and animal technicians involved - it is the implementation of the Act itself that they say is at fault. The concerns expressed by the BUAV in this regard can be summarised into 10 key areas. Some of these issues are currently the subject of an application for judicial review brought by the BUAV against the Home Secretary:

- i) The cost/benefit assessment: how was the cost/benefit assessment originally applied and which factors were taken into account?
- ii) The severity banding: were moderate limits and bands appropriate in the majority of cases, and should these have been amended in the light of the actual marmoset suffering during the projects?
- iii) Licensable procedures: why were practices such as food and water restriction and confinement in test boxes not routinely considered as

- causing distress or suffering in the licences? Is it acceptable that marmosets only used in training, but who were confined in test boxes and water restricted, did not appear to have been counted in the statistical returns to the Home Office?
- iv) Husbandry and care: did the conditions in which the primates were kept reflect accepted best practice and did they fulfil the requirements in the Home Office Code of Practice (COP)?
 - v) Management of breeding colonies: were triplets managed in the most humane way? Should they be allowed to die, be hand reared or humanely killed?
 - vi) Surgery and anaesthesia: was the most appropriate anaesthetic regime followed, was anaesthesia always sufficiently maintained?
 - vii) Post-operative monitoring and care of marmosets: was this adequate, in particular for animals left overnight when sometimes there was apparently no staff cover?
 - viii) Food and water restriction and the provision of bland diets: was this necessary and was any associated suffering taken into account?
 - ix) Techniques - such as blood sampling, telemetry: were these adequate or were they poorly conducted, such that animals suffered unnecessarily?
 - x) Staffing issues: was there adequate animal technician staff cover (including "out of hours")? Was it sufficient to have only one full-time named vet responsible for all the animal units at the university? Were the responsibilities of the NACWO too widely spread?

The underlying principle behind the BUAV's argument is that the legislation has not been interpreted and implemented in the way they believe the ASPA and its COPs and guidelines should be. Hence the impact on the animals and their welfare had not been given due weight, and they had suffered unnecessarily. The validity and relevance of the scientific studies, and therefore the role of the funding bodies, is also strongly challenged.

The Chief Inspector's review

6. The Chief Inspector was asked by the Minister to review the severity limits and bands, consider if the licensing decisions were sound, and report on issues of compliance. It is our understanding that he undertook an extremely comprehensive review, going through all the relevant records and repeatedly visiting Cambridge University. His report provides background and explanation to many of the BUAV's points. He concluded that the severity bands for the three Cambridge project licences together with the severity limits for the component protocols, were properly assigned, and that all of the licensing decisions were sound and sustainable. The BUAV challenges his conclusion in their judicial review. The Chief Inspector found four instances of non-compliance during the period from 1998 to 2004 three of which involved technical irregularities, whilst one involved the breach of a severity limit, and therefore exceeded the permitted level of suffering. He goes on to make 5 recommendations:

- (i) Provide a forum for sharing ideas on best practice
- (ii) Seek further expert advice on the most appropriate anaesthetic regimen
- (iii) Revise guidance notes used by researchers

- (iv) Modify statistical returns to better reflect the uses ultimately made of the animals
- (v) Consider the use and effectiveness of the current severity limit and severity band labels.

The funding bodies' view

7. In response to the BUAV's critique, the MRC submitted the contested research to a further check, using a wider range of scientific peer reviewers than were originally consulted. In light of their reports, it concluded that the research had benefit and continued to be justified. It is worth noting that since the working group was set up there have been a number of changes involving the MRC and the ways in which it operates in respect of the animal research that it funds, many of them focused around the MRC CBPAR which was set up in 2000, and has recently been superseded by the National Centre for the 3 Rs – see for example Appendix C.

A Issues of Procedure and Process

8. The WG quickly determined that its primary purpose should be a prospective one - the identification of areas for discussion that the main APC might profitably take forward in furtherance of its statutory role – that of advising the Minister on the operation of the Act. Crucially, we did not feel that we were authorised to conduct, or re-open an investigation, nor to offer adjudication. Rather we were being asked to examine the BUAV's report – including the official BUAV video – and the Chief Inspector's review, and on that basis make recommendations to the main Committee of the APC regarding any lessons to be learned and any issues that it would be feasible, fruitful and appropriate for the APC to take forward. Nor did we see ourselves as authorised to speak on behalf of the APC, but merely as a sample of that body despatched, as it were, on a 'scouting' mission.

9. Nor do we feel qualified to prescribe how the issues might be taken forward, although we imagine that possible avenues would include:

- a) items for discussion at main meetings or annual conference;
- b) subjects for further study by sub-groups of APC, feeding into the future work programme;
- c) subjects for commissioned research;
- d) proposals to other bodies;
- e) subjects for mutual discussion with relevant bodies, e.g. animal facilities, funding bodies – including medical charities, animal welfare organisations, ERPs, the inspectorate, researchers in the field;
- f) standing 'liaison committees' with above relevant bodies;
- g) seeking legal opinion where appropriate.

10. In discussion arising from the attempt to clarify our own role, we touched on a number of points relevant to (a) the matters of whistle-blowing and

undercover investigations mentioned in our brief, and (b) the potential nature, role and value of having an 'independent element' in the investigation of complaints.

11. Regarding the former (a), an initial observation is that, although both may lead to 'exposés', whistle-blowing and undercover investigations are very different in kind. The first involves a bona fide employee who, for whatever reason, feels compelled to go outside the organisation employing them in order to draw attention to matters that concern them. An undercover investigator, on the other hand, enters an organisation surreptitiously and in order to draw attention to matters that concern them.

12. A further observation is that although both kinds of 'exposé' have sometimes been invaluable in revealing matters that need to be revealed, they have also had costs, such as the effect on the personal and professional lives of members of staff. We would presumably all prefer a world in which neither practice was in fact necessary. Since both, in different ways, make appeal to some kind of external or independent perspective, it would seem prudent, then, if we think it desirable to minimise the need for such exposés, to explore how far such a perspective might be built in to the existing system - the so-called 'independent element' (b) referred to above.

13. The independent and comprehensive adjudication of such exposés, once they have occurred, is a different matter entirely. In our judgement, in order to conduct such an adjudication one would necessarily require something approaching the legal trappings of a (possibly long drawn out) official inquiry. Not only are there intractable elements, but also various kinds of partiality and incompleteness of view that would need to be overcome.

14. Intractable elements include:

- perceived disputes of fact: e.g. in the present case, the number of unannounced visits, the numbers of animals that were singly housed;
- incompatibilities of agenda e.g. in the present case, between the research community and BUAV;
- contrasting perspectives e.g. on the standards of welfare it is reasonable to expect for laboratory animals.

15. Risks of partiality/incompleteness include:

- the use of uncorroborated evidence that might reflect lack of understanding or awareness
- the incompleteness of evidence e.g. regarding competence, attitude, colony management, health, telemetered animals, sampling techniques, home cage testing, and staffing levels
- the unavoidable reliance on single source contemporary records in ascertaining particular points.

We do not mean in any way to impugn any of these sources, merely to point out the lack of independent corroboration that might be thought a precondition for the formation of a robust and fair adjudication.

16. Accordingly, our first recommendation here so far as the APC itself is concerned is that it should eschew any active part in the investigation or adjudication of complaints, which in any case we would judge to be beyond its capabilities, and concentrate instead on issues of a strategic nature – in particular trying to ensure that processes are in place that minimise the need for such ‘exposés’ or, if they occur, trying to ensure that the processes to deal with them are adequate

17. Our second recommendation is that the APC, in its advisory capacity, should actively explore the feasibility of instituting some form, or forms, of external and independent appeals procedure. We say ‘forms’ since, in light of our initial observation above, it is possible that different processes might be appropriate for the whistle-blowing and undercover scenarios respectively. A possible model here might be the ‘ombudsman’ system, where a single individual is authorised and available to intervene at quite short notice.

18. Our third recommendation arises from our experience of having met with most of the parties involved in the current episode. Although we cannot speak for the other parties concerned, we have ourselves found these meetings not simply useful for the task at hand, but illuminating in more general ways. They have also been ways in which the various parties could learn of the concerns, pre-occupations and interest of the APC. Our recommendation, therefore, is that meetings of this kind, aimed at keeping more strategic issues under review, might be established on a more regular basis.

B Issues of Substance

19. During our enquiries it was only to be expected that we should encounter differences of perception and moral conviction, some of which probably remain irresolvable. Not surprisingly, we have also found that different parties presented different factual information about the same issues as well as different *interpretations* of this factual information. We have already made it clear that resolving the many points of disagreement would have required a full and detailed investigation, such as the WG was not tasked to conduct. We were neither appropriately resourced nor qualified to carry such an investigation out, nor could we without access to all of the background information available to the Chief Inspector, the BUAV, the institution and the funders of the research, some of which would be confidential. In what follows, therefore, we focus exclusively on the generic issues raised by, but by no means peculiar to, the research conducted at Cambridge and the BUAV report, such as the classification of suffering, staff training, best practice, standards of husbandry and care etc. In particular, our comments should **not** be interpreted as implying any judgement on our part relating to this particular case. Nor does our coverage of these issues aim to be in any way comprehensive. As said before, we focus only on those aspects that it would be feasible, fruitful and appropriate for the APC to take forward. These issues as we see them fall into four areas: institutional; the funding and direction of research; regulatory; adverse effects and their detection.

Institutional Issues

20. Under the heading of 'institutional issues', the WG looked first at the area of staffing levels (both absolute numbers and availability) and also at staff training. What are, or should be the criteria for determining the correct concentration of staffing and the training they should receive? We note and fully appreciate the Chief Inspector's view that the attempt to determine staffing levels numerically is impractical. Conditions and management practices at different institutions vary enormously, and the species of animal involved and the nature of the research are also clearly important variables. His own approach is to focus on standards of performance: if the health and welfare of a colony is maintained, then the staffing levels are right (Review 5.A.9-19). This issue strikes us as one that might repay further scrutiny. For it seems in principle possible, at least, for health and welfare to be maintained but, for example, for there to be no time available for factoring additional activities such as the evaluation and provision of additional environmental enrichment. Is there perhaps a middle way, between the numerical approach and one that is focused solely on performance? There are likely to be at least norms for certain kinds of animal facility, permitting certain guiding principles to be drawn up, with departures from the norm requiring justification. There is also the question of how, from a management point of view, the 'correct' level of staffing is determined in the first place (see further paragraphs 36 and 37 below).

21. On the general issue of staff training, modular training is required for all licensees. Some animal technicians will undergo licensee training, but this is not essential unless they are undertaking procedures. In the latter case they may take the qualifications offered by the IAT, but again this is not essential; nor are they required to have specific training in the species they are caring for. This seems to us to be an omission. Furthermore, modular training is only an introduction. Additional training, both to develop expertise and competency, and contribute to the in-house 'culture of care' is also very important. The APC Education and Training sub-committee is currently reviewing the modular training system and will consider how best to address the provision of CPD. The training of animal carers and technicians who do not require a licence is another issue that the Sub-Committee intends to address, although we note that training is now a requirement for NACWOs.

22. The second issue we looked at was the importance of the effectiveness, or otherwise, of channels of communication both within and between the various institutions involved in animal research – the research facility, the funding bodies, the inspectorate and so forth. Communication is of course a challenge for all organisations, and not least for those involved in animal research due to the heterogeneity of the tasks involved. Researchers, animal care staff and vets have different priorities, as do funding bodies and universities. It involves among other things the establishing of chains of

command and responsibility, provision for the sharing and exchange of information, as well as provision for the voicing of concerns. It also involves making sure that everyone knows of this provision. We can, of course pass general comment, for example about the need for the channels of communication within organisations to encompass all relevant staff and all relevant issues, and for those between organisations to be effectively linked to those with the power and responsibility to act. But we are inclined to the view that effective communication, though of course hugely important, is very much a contextual matter – involving attitudes and habits both of individuals and institutions, also relations of trust, reciprocity and so forth – and hence very difficult to make general provision for.

23. Third, despite the fact that the term ‘best practice’ is widely used to describe current husbandry, care and procedures carried out under ASPA, we have found definitions of ‘best practice’ somewhat difficult to pin down. In particular we have struggled to understand how such a thing is identified, and who, or what, is the authority (source) that establishes its existence. The authority for best practice might be said to lie in ‘the agreement of experienced practitioners’, and in fact this was the approach taken in setting the standards in the 1995 Code of Practice for Housing and Care of Animals in Designated Breeding and Supplying Establishments. However, even among experienced practitioners there are different perspectives on what is best depending on context and feasibility as well as on knowledge of animal welfare and individual perspectives. We are aware that this is an issue to which experienced veterinarians, animal technicians and welfare organisations have been drawing attention for some years. Indeed we note that a recognition of ‘variations in standards’ in MRC units was one of the reasons why CBPAR was created (see MRC minutes Q 7). In any event, it strikes us that ‘best practice’ is bound to be a moving target, and that ‘good practice’ might be the more appropriate, and less misleading, term. This is not mere semantics since it could be argued that part of the impact of exposés generally is due to a perceived mismatch between the claims of the research community and ‘reality’, not simply with regard to animal husbandry but also more widely with regard to the effects of procedures and the benefits of research.

24. Last and perhaps the most significant set of issues under this heading, focuses around the question of (a) what are the incentives and triggers for the review, maintenance and improvement of standards; (b) wherein lies the responsibility for such initiatives; and (c) what are the mechanisms for putting them into effect. Many of the questions that we raised with the parties involved in this particular case were aimed at seeking general clarification in this area, but we remain very unclear whether we have got to the bottom of the matter in every case. The areas in question include: staffing levels; staff training; staff job satisfaction; husbandry/colony management; housing and environmental enrichment; surgical techniques including anaesthesia and pain management; and the 3Rs.

25. We encountered an associated lack of clarity regarding the precise roles and responsibilities of the various bodies involved e.g. ERPs, the Inspectorate, the universities and the funding bodies, with respect to the

above areas. We note that another of the stated reasons for the creation of CBPAR was a recognition that “the role of MRC with respect to animal welfare was not widely known” (see again MRC minutes Q 7). We note also that equally important to the clarification of roles is the mutual recognition of those roles, assuming they are clear, by the various parties concerned. Certainly we regard these as areas for further scrutiny and believe that the APC should seek to ensure that the initiatives of the MRC are followed through and emulated by all other funding bodies involved in animal research.

The Funding and Direction of Research

26. That primate research is an especially sensitive area has long been recognised on all sides, and the APC, for example, has a designated primates sub-committee. Even among those who believe in the value of animal research there are those who believe it should not extend to primates. There is also a lively debate among scientists themselves regarding the validity of this research as is evidenced by the extensively referenced research cited in the BUAV ‘Investigation’. Accordingly, the processes leading up to the granting of a licence for this kind of research are bound to attract the keenest attention. They involve a whole variety of factors, such as: the priorities assigned by the funding bodies, judgements about areas of potential ‘breakthrough’, questions about the scientific validity of the proposal, judgements about the availability of alternative approaches, and so forth. Over the whole process of applying for, and being granted, funding, we were struck by the weight that is attached, no doubt with justification, to the opinions of referees. This places all the more onus on the right referees being approached and their being asked the right questions, not only so far as the quality of research is concerned but also so far as the use of animals and animal welfare is concerned. We were also struck by the apparent absence of opportunities for developing an overall strategic assessment of the role of the animal research being proposed within the broader context of the medical research agenda. The Minister oversees the operation of the Act, and the APC advises the Minister. The funding bodies choose from amongst the proposals put to them, and the referees judge the quality of the proposals referred to them. The Inspectorate advises the Minister in the matter of weighing the costs and benefits of those proposals deemed fit for funding. No one, it seems is invited to look at the place of the animal research being proposed within the broader context of the medical research agenda.

27. Accordingly we propose that the APC attempt to facilitate such a strategic evaluation in respect of a specific and therefore manageable, but also ‘illustrative’ area, such as the attempt to find alleviations and remedies for Parkinson’s Disease. It might look at all aspects relevant to the question of how such research, insofar as it involves animals, comes to merit the licence to proceed, including such matters as how the funding bodies, including the medical charities, assess and monitor the work that they fund. It might also look at the role and value of retrospective assessment of licensed projects that have been completed. The ideal arrangement, in our view, but obviously this would need to be negotiated with the inspectorate and relevant funding

bodies, would be for the APC to play a co-ordinating role, possibly through its Primate Sub-Committee. The main reason is that we see this proposal, along with the various other suggestions made in this report, as aimed in part at enabling the APC to perform its role of advising the minister. The evaluation might usefully include a workshop or two, facilitated by the Home Office, at which key perspectives are represented.

28. A separate issue is whether funding bodies – and others, e.g. medical charities and the Home Office – are sufficiently explicit in their publicity about the costs to the animals. This speaks to the issue raised in paragraph 23 of how far the public is able to form an accurate view of the research that is conducted in their name. A society that endorses animal research in its legislation needs to be assured that it is justified in continuing to do so. For this to happen, public understanding of the nature of this research needs to be as comprehensive and accurate as is possible¹. This leads straight on to our next topic, that of regulatory provision.

Regulatory Issues

29. One of the major and recurring features of the material that the WG was asked to consider is the absence of a shared understanding of what the labels, mild, moderate and substantial mean in the classification of severity. In particular there seems to be a significant difference between the regulatory interpretation and how the “man in the street” might interpret such labels. We do not feel that it is appropriate for us to explore the labels issue in itself more deeply, since it is one that is being considered in a number of different fora (European Commission, Boyd Group and the RSPCA, and by the APC itself). We pause only to note this complication - that the issues involved are not straightforwardly factual, and therefore are unlikely to be just a matter of ‘public information’. The reason is that a person’s understanding of – say – ‘substantial’ is likely to be tied in both with that person’s personal experience, and with their view of the degree of justification required for this degree of severity to be acceptable – which involves evaluative judgements.

30. However, our reflections on the types of suffering or distress that animals undergo (those resulting from the surgery itself, the effects of lesions, food/water restriction, and so forth) do cause us to raise the question whether the unitary categorising of suffering/severity is appropriate for the purpose of enabling the public ‘to form an accurate view of the research that is conducted in their name’.

31. The Project licence application guidance notes state that:
“The estimation of the overall severity band should take into account the pain, suffering, distress or lasting harm likely to be caused by each of the protocols; their nature, duration and intensity; and the number of animals affected.

¹ We understand that the Wellcome Trust intends revising its website to take account of issues raised in this section. We also note that the Home Office has recently started publishing summaries of project licences on its website.

Overall severity thus has qualitative and quantitative aspects and does not simply equate to the severity of the single most severe protocol.”

Consider, too, that the APC has previously in its cost/benefit report included in the scope of costs considered by the Inspectorate in their assessment of applications such diverse items as: any material disturbance to the normal health, i.e. to the physical, mental and social well-being, of the animal; both immediate effects, e.g. transient discomfort from injections, and longer-term effects, e.g. the subsequent toxic effects of test materials; costs arising from both regulated scientific procedures and husbandry and care systems; all of the interventions applied to an animal or group of animals from the time they are issued from stock until they are killed or discharged from the controls of the Act; any expected adverse phenotypic expression; costs arising from both acts of commission, e.g. dosing or sampling, and omission, e.g. withholding food or water; and costs in terms of the biology, behaviour and life-style of the species concerned.

32. It is clear, then, that the costs to animals used in research are extremely diverse in nature. It is therefore reasonable to question whether it is appropriate to use for public information purposes severity bands and limits which aggregate such a variety of adverse effects that may be associated with any project. Hence the WG is minded to suggest that the APC consider the merits of separating out the various components used in arriving at the current severity bands and limits. The advantages would be at least twofold: i) affording a richer, and therefore more informative characterisation of divergences where they exist (e.g. there might be very minor surgery, but quite major disruption of social relations, and so forth); ii) affording an account that would more effectively map onto the ‘narrative’ approach to the weighing of costs and benefits that characterises the HOI approach: “costs considered are derived from detailed narrative descriptions of the nature, incidence and severity of the likely adverse effects (and the measures to be taken to prevent, identify and ameliorate the adverse effects” (CI’s Review 4.10)

Adverse effects and their detection

(a) Adverse effects

33. What poor welfare (especially suffering) is, and how it is detected, are questions of substance, and separate from, though connected with, the question of how the ‘severity’ of poor welfare is to be classified (ie the question of labelling). We have encountered different views about what suffering is, including views that are incompatible yet (probably) defensible. We might just let such differences lie. But an alternative approach would be to invite attempts to explain them, creating at least the possibility of dialogue. For they often appear to stem from difference of focus, different priorities and perspectives, different levels of understanding of animals and their needs and behaviours, and the use of different reference classes, as well as difference in prior experience.

34. Thus, in the present case, what appear to be fundamental disagreements might be attributed to lesser differences of opinion regarding one or more of the following areas:

- i) The time-scale that it is appropriate to consider – the protocol itself, the whole lifetime experience of the animal, or something in between;
- ii) The comparative weight to be attached to short, medium and long-term consequences.
- iii) The significance (for the question of suffering) of major surgery;
- iv) The significance (for the question of suffering) of disruptions to the central nervous system, including the potential for psychological suffering;
- v) The significance of being subjected to risk of greater harm (as distinct from greater risk of harm), which major surgery/disruption of the central nervous system brings with it;
- vi) The meaning of 'normality'. There is an assumption within the research establishment that captivity is compatible with a reasonable level of welfare. This assumption is not shared by BUAV. For the latter, therefore, the return of a captive animal to relatively normal behaviours - 'the normal activities of daily living'- is of little significance. One question here is the extent to which animals might be subject to the 'institutionalisation' that humans exhibit when confined for long periods;
- vii) The significance of a return to normal behaviours, assuming that captivity is compatible with a reasonable level of welfare. There is a question about whether ability to cope, as evidenced by a willingness to eat and wash, demonstrates absence of misery.

Our sense is that the further exploration of any one of these issues could help to deepen our understanding of the nature of animal suffering.

35. On one particular point, the WG was agreed – that there is a need for more information on how to assess the potential costs to animals of food and water deferral and/or deprivation for varying periods. We understand that this issue was already being taken up by MRC CBPAR and now by the new NC3Rs.

(b) Detection and prevention of suffering

36. Under ASPA there is a requirement that severe pain or distress should be promptly alleviated. Severe pain or distress can only be promptly alleviated if it is promptly detected. This raises the question: what does it take to meet the requirement of prompt detection? The BUAV claims that, in the context of the Cambridge research, without 24-hour care, the provisions of the Act could not be met, as proven by the occasions when animals were discovered dead in the morning (BUAV minutes Q 1). Furthermore, this does not simply apply to the alleviation of severe suffering but to the minimising of all suffering. In his review the CI responds by saying that sufficient pain relief would be given to tide an animal over until the next observation. What we take the Chief Inspector to be saying in effect is that, depending on circumstances, (such as type and level of anaesthesia, the condition of the animal and the surgical procedure that it has experienced) the minimisation of post-operational suffering does not necessarily require constant care. (CI's Review 5.B.30). One issue for further scrutiny therefore seems to be: should we accept that

there are conflicting standards of evidence here, or simply conflicting expectations - and should we seek a resolution?

37. Under ASPA there is a requirement that severe pain or distress that is foreseeable should be prevented by euthanasia where appropriate. This raises a second question: under what circumstances can severe pain and distress be said to be foreseeable? Concerning deaths that occurred in the Parkinson's study (Chief Inspector's report 5.C.69), the Chief Inspector responds that the deaths 'could not have been foreseen'. In the 'Brain Disturbance and Repair' study, it is reported (5.C.39) that 4% of the animals died from causes connected with the study. There is no conflict here. One could foresee, perhaps, that a percentage of the animals are likely to die in the wake of major surgery without knowing in advance which particular animals will die. Unfortunately, the application of euthanasia requires knowledge of the particular. But given the ambiguity in the concept of a 'foreseeable' death, it seems appropriate to explore what other approaches might be available to prevent them.

A point in the interpretation of ASPA

38. On a separate point, the WG notes that on p.4 of their 'Investigation', the BUAV challenges the lawfulness of the Home Office approach on the grounds that it makes a practice of licensing research that is fundamental "and therefore, almost by definition, not 'likely' to lead to any benefit". The point is taken up again in BUAV minutes Q 30 through a distinction between research that is 'interesting' and research that is 'useful'. "Useful" means "has a practical application". Research which is "interesting" may be intellectually stimulating but have little or no practical application. We felt it would be helpful to attempt some clarification of this point.

39. One can of course challenge the claim that research that is fundamental is unlikely to lead to benefit, (where "benefit" is understood (narrowly) in terms of the relief of suffering). One can do this, for example, by insisting on a distinction between research that is 'likely' to lead to benefit, and research that might lead to 'immediate' benefit. Using this distinction, one can then argue that the more fundamental the research, because of the generality of its reach the more likely the benefit, even though less immediate. But there remains the question of whether the Act constrains us to this (narrow) interpretation of benefit.

40. (a) It is true, of course, that the mere increase of knowledge is not of itself sufficient justification for research. But this is no more true of knowledge than it is of the relief of suffering. Both will need to be 'weighed'. (b) It is also true that a mere increase in knowledge does not necessarily entail a benefit. Knowing that the number of letters in 'to' is one fifth of the number of letters in 'unleavened' may be of no benefit at all. It depends on the quality of the knowledge. (c) It is further true that a benefit is different from a purpose: aims are not the same as outcomes, and the Secretary of State must look to the latter. Whether your research is likely to advance knowledge is separate from

the question of whether it aims to do so, in just the same way as whether your research is likely to relieve suffering is separate from the question of whether it aims to do so. So the fact that “the advancement of knowledge in the biological and behavioural sciences” is listed separately as a permissible purpose under the Act, does not by itself *entail* that it is an allowable benefit under the Act.

41. But it does not follow from any of this that the increase of knowledge is *not* an allowable benefit in its own right under the Act. For in the first place it is hard to understand the point of listing the permissible purposes if it is not intended at least to define the range of benefits that may be weighed. And it is equally hard to understand the point of listing the advancement of knowledge in biological and behavioural sciences as a separate purpose if its outcome is not allowed to count as a stand-alone benefit. Moreover, if we reflect on the character of ‘fundamental knowledge’, we can see why it is so listed. Fundamental knowledge, typically, is knowledge that does not lead directly to a specifiable (medical) benefit. Rather, being fundamental, it is knowledge that forms the *necessary background* for the understanding that generates benefits that are as yet unspecifiable. So it can indeed be said to be likely to ‘lead to’ medical benefits – it is a *sine qua non* of those benefits - only we cannot in advance say precisely what those benefits are. Hence, even if one insists on defining benefit in narrow terms, as referring to a medical benefit such as the relief of suffering, one has every reason to allow fundamental knowledge to count as a benefit under the Act. Note, finally, that this point is quite different from, and must not be mistaken for, the appeal to ‘serendipity’ – the notion that any knowledge is a benefit because it might just quite by accident lead to a discovery that is medically beneficial. We think it unlikely that the Act is intended to countenance knowledge as a benefit on those grounds.

Brief summary of proposals

42. In sum, we came to the conclusion that we should focus exclusively on the generic issues raised by the material that we have studied (8).

Under the heading of ‘process and procedure’ we make the following three proposals:

- That the APC should confine its attention to the prospective consideration of strategic issues, and not be drawn into retrospective judgements (13-16)
- That the APC, in its advisory capacity, should actively explore the feasibility of instituting some form, or forms, of complaints procedure (10-12, 17)
- That the APC, in furtherance of its advisory capacity, should consider the feasibility of regularising meetings of a bilateral nature with the key players involved in animal research, with the aim of keeping strategic issues under review (18).

Under ‘issues of substance’, we make one proposal:

- That the APC, possibly through its sub-committee on primate research should consider initiating a case study of a key area of medical research such as Parkinson’s Disease with a view to

facilitating an overall strategic assessment of the role of animal research within the broader endeavour to alleviate human, and animal, suffering (26-27).

We also identify the following areas as fit subjects for further scrutiny:

- staffing issues: levels, training and competency(20-21)
- standards: the roles and responsibilities of the various bodies involved, for setting, reviewing and maintaining standards of animal welfare, and initiating improvements (23-25)
- the publicity issued by funding bodies and medical charities regarding the benefits of the research that they fund and, especially, the costs to the animals (28)
- a re-working of the labels used to indicate the severity of animal suffering so as to build a more detailed picture, and more generally agreed understanding, of what animal research involves (30-32)
- the sources of disagreement about the nature and degree of severity of suffering (33-34)
- the implications of food and water deprivation and deferral (35)
- the detection of suffering: what levels of detection should be in place in order to satisfy the requirements of the Act? (36-37).

ANNEX A

Issues raised in BUAV/Cambridge Marmosets meeting with the Chief Inspector

The meeting took place on Wednesday 27 August. In attendance, Dr Hubrecht, Professor Atterwill (Acting Chair), Dr Jennings and Professor Holland from the Working Group, Mr West and Mr Earle from the Secretariat and the Chief Inspector, Dr Richmond. The Working Group members prepared a set of questions (1-35) after having read the BUAV and Chief Inspector's reports and following a meeting the group had at Cambridge University. These questions were forwarded to Dr Richmond in advance of the meeting.

Please note: Where no answer is given or where the answer is incomplete this reflected that insufficient time was available for pursue these.

Issues about the severity limits and severity bands assigned to the Cambridge work, and about the licensing decisions

1. What was the justification for setting the severity limits at moderate, when the tests conducted at Cambridge University appear to be comparable to a recent urgent non-human primate application seen by the APC which involved MPTP administration?

Note: Presumably Appendix I para 15, p.79 is relevant, but the sub-group would welcome further elaboration.

MPTP is a neurotoxin, which severely disables and the animals never properly recover from this drug administration. The effects are both severely disabling and persistent, requiring long-term care to minimise the welfare costs. In contrast the animal models used in the Cambridge neuroscience programmes produce transient problems, requiring skilled post-operative care (and this is generally only required overnight or for a few days) and any residual neurological dysfunction is often intended to only be detectable on formal testing. It is often difficult to tell the difference between stock and stable post-operative animals.

2. When applying the cost/benefit assessment, how far did the applicant, and the Inspectorate, take into account housing and husbandry issues, including the potential for mental distress?

The research groups have previously evaluated and published studies on aspects of the care and accommodation studies used. The Inspectorate took account of the local provisions when the applications were assessed.

3. Was the procedure of food restriction not included within the licence, and if so, why not?

Food restriction was not included in the licence, as it was not considered in this context to cause pain, suffering, distress or lasting harm. My own observation of the feeding schedules and its effects on the study and non-study animals tended to confirm this conclusion. Restriction might not be the most appropriate term, as this was more of a rescheduling of feeding times.

4. Why was it considered acceptable to use food restriction as a training method?

This was considered to be an adjunct to the training and testing programme that did not of itself impose any significant additional welfare cost.

5. Other groups do not see a need to use water restriction to motivate marmosets, but instead use positive reinforcement such as banana milkshake. During our visit the licensees defended the use of water restriction and lack of use of in-cage testing on the basis that they were dealing with more relatively invasive disturbances to the brain than, other organisations' work and they were concerned to reduce variation. How did the Inspectorate judge whether water restriction was necessary in this case?

The Inspectorate judges its advice on a case-by-case basis, but will challenge any proposal for food or water restriction or deprivation. The Inspectorate look at national and international best practice, but the aim is always to minimise the amount of water restriction. In context water restriction was only used in specialist contexts where the applicants offered a sustainable case that the use of reward or dietary re-scheduling would not have the desired effect.

The Chief Inspector did not share the view that the non-use of home cage testing necessarily caused stress to the animals in this context. Indeed, significant stressors would have invalidated the scientific programme.

6. What was the maximum period of water restriction, was it really 22 hours?

Yes. The care staff were tasked to look for signs of abnormal behaviour and other possible indices of impaired welfare. There were no signs recorded to indicate that water deprivation caused stress to or welfare problems in the animals. The only signs of distress resulting from such practices occurred in another unit and resulted from water intoxication once the period of restriction ended.

7. The sections from 4.31 to 4.39 (Licensing Decisions) appear to yield the following sequence of statements:

- i) the model was suitable**
- ii) the purpose was permitted**

- iii) the objectives and benefits were clearly set out
- iv) the severity limits/bands were properly applied
- v) the costs were minimised

Therefore (vi) the licensing decision was sound.

The conclusion, as stated, cannot in any obvious way be generated by the premises. Can the CI elaborate on the further considerations that actually justify this conclusion?

All of the relevant information features on the form of application and the Inspectorate analysis. The Chief Inspector was confident that the Inspectorate had sufficient information to make its assessment to the Home Office and that there no new insights within the BUAV report, which would compromise the cost-benefit assessment.

8. Concerning section 5C, can all three projects really be thought necessary to generate the relevant insights into neural disturbance and degeneration? Is this a question that the inspectors ask?

The Inspectorate do not think that there was any duplication in UK primate research (there are similar programmes, but with acknowledged differences) and the improvements have had an accumulative effect in knowledge and treatments. The Inspectorate also have experts in neuroscience and the applicants were asked for literature to support their application. Understanding these processes and developing strategies for dealing with them in clinical practice will require many such projects.

9. The use of concepts such as 'normal activities of daily living' and 'special care' (4.5) to differentiate between e.g. moderate and substantial severity is of considerable interest. But are these concepts sufficiently well defined? What is *normal* daily activity? Is it just the ability to feed and groom? Is it the same for wild/captive/tamed/domesticated individuals of a species? What is *special care*?

The term first refers to what is needed to be able to function normally in the environment one finds oneself (it is a concept and term in routine use in rehabilitative medicine). Activities of daily living are context specific and depend on the activities that form part of their day to day tasks and the ability of the subject (e.g. for example, the ADLs of an 80 year old in sheltered housing differ from those of a 30-year-old fire-fighter). Special care refers, for example, minimising disturbance of the animals in the early post-operative period, hand feeding, hand grooming and other support provided by the scientific staff to minimise the welfare impact of the surgical interventions .

10. In general, how are criteria applied to distinguish between moderate and substantial bands? Could we discuss this in more depth, for example the sort of 'benchmarks' used for assessing limits and bands and how full lifetime experience is judged?

The general principles are as set out in the Home Office Guidance, and each case is judged on its merits with the onus being on the researcher to minimise

the welfare costs. Thus many surgical procedures with optimal post-operative care will be accommodated within the moderate severity limit. However, If for some defensible reason aftercare were to be sub-optimal , than a substantial classification might be merited.

11. Why isn't brain damage sufficient to warrant a substantial rating?

Each case is judged on its merit depending on the effects it has on the welfare of the animals. "Brain damage" is a very broad term and might span outcomes varying from no more than post-operative discomfort, to devastating effects on normal daily activities. In the case of many of the animal models used in Cambridge after the immediate post-operative effects had worn off, the persistent alterations in behaviour and function were intended to be detectable only by testing, with little or no outward detectable signs.

12. If animals die from complications of the dosing regime (5.C.69), does this not reflect on the severity grading?

Based on the experience of others using the same regime in the same species for other purposes, significant adverse seriously compromising animal welfare were not expected: that was the basis for the original classification. The welfare problems encountered in practice were unexpected and incompatible with the severity band that had been assigned. The Home office was informed, and the use of this regimen was discontinued. It is still not clear why these problems were encountered on this study.

13. Training/testing resumes a week after surgery. Is this not too soon? How is this to be judged?

It depends on the procedure and its effect on the animal. The information available suggests that training and testing are only recommenced when the animal is considered to be a suitable experimental subject and is sufficiently recovered that the training and testing regimens do not cause additional welfare problems.

14. Could we clarify why putting a marmoset in a test box and performing a test is not a procedure?

The Inspectorate does not consider that this procedure caused pain, suffering distress or lasting harm. Indeed if the test system caused such problems, the test data would, in this context, be invalid.

15. Has the use of low light or infrared been considered for nighttime monitoring?

Post-operatively the incubator lights are kept on low, and this seems not to stress the animals and enable proper assessment of the condition of the

animals. Parts of the BUAV videotapes seem to show animals in the early post-operative period filmed at higher light intensities.

16. In the CI's report Section 4.10 it says the 'costs' were derived from "detailed narrative descriptions of the nature, incidence and severity of the likely adverse effects (and the measures to be taken to prevent, identify and ameliorate the adverse effects)". Is this in the original project licence and have we seen it? If so, it might be useful to have it to hand.

Yes it is in the original licence. Severity bands are labels, administrative devices, but detailed material from which they are devised (section 19b.vi of the project licence) is used for the cost-benefit assessment and to dictate the measures to be taken to make proper provision for the welfare of the animals. [One of the licence documents was available at this meeting.] The key parts of the project licence relate to section 18 which lists everything and 19(b)vi which gives a narrative description of the potential adverse effects and the endpoints to be applied .

Issues about compliance and 'best practice'

17. What was the number and ratio of announced vs. unannounced visits before, during and after the undercover investigations?

On average, this unit merits of the order of six site visits each year with two-thirds of these unannounced. While the investigation was being conducted, there were more visits by appointment to interview staff and scrutinise records. There have been more visits this year as part of the handover process with a different inspector taking a primary interest in the place and the programmes of work. .

18. Was the staff cover provided during the period of the undercover investigation really sufficient? How (i.e. on what basis) is such a judgement made? Were staffing levels observed during the CI's review the same as those which pertained during the period of the undercover investigation?

The Home Office does not specify staffing numbers, but rather concentrates on performance. Inspection reports do not record any problems with care and accommodation attributable to either the quality or quantity of staff. Staffing levels were very similar now compared to the time of the undercover investigation (even though there is one less person), as the investigator had taken periods of sick/compassionate leave. The numbers of marmosets now held in the unit are slightly fewer than those kept when the BUAV material was collected. .

19. Given that the number of operations performed late in the day, how is it possible in these cases to provide adequate post-operative care?

It is not clear where the concept of surgical procedures performed late in the day comes from. Only one (minor) operation took place as late as 5pm. More serious surgery was carried out early in the week and early in the day, reflecting best practice. The documentation maintained by the scientific staff tends to confirm that post-operative observations and treatments continued until the animals appeared to be stable and to require no additional observations or treatments before the morning. The records confirm that, when required, staff remained in the unit tending to post-operative animals until the early hours of the morning.

20. In some cases, e.g. 5.A.28 re cage size and stocking density, it appears that the research centre adopted minimum standards rather than best practice. Is this defensible? Indeed is the notion of minimum standards as distinct from best practice defensible at all, given that it seems to condone avoidable suffering?

For clarification, the report says that the research centre either met or exceeded and never provided less than minimum standards.

21. At several points in the CI's Report (e.g. 5A8, 5A32, 5A44, 6.1) it is claimed that researchers at Cambridge were following best practice:
(a) Where does the authority lie for what is considered best practice?
(b) To say that best practice is followed implies that it is known. Why then does the CI recommend a centre for sharing ideas on best practice (2.1)?

22. In Section 6.2. the Chief Inspector says examples of best practice are seen at Cambridge. It would help understand the benchmarks the HOI use if he could tell us what these are.

23. How did the Chief Inspector determine that the culture of care was appropriate prior to his investigation, rather than as detailed in the "notes on shaping document" (5C25)?

The notes on shaping document is dire and does not reflect the prevailing culture within the unit. Visits of inspection allow conclusions to be drawn from the attitude and performance of staff as well as documentary evidence. The Chief Inspector devoted a considerable proportion of his time on site speaking and with staff of all grades, and observing day to day working practices.

24. The statement at 5C50 that procedures were carried out competently jars slightly with paragraph 5C48 which states that some procedures were carried out without appropriate project license authority. Doesn't competence include insuring that license conditions are complied with?

As the context of the report makes clear, the issue in question was technical competence – that is the requisite surgical skills.

25. Does the Inspectorate keep records on enrichment and other environmental provisions at the sites that they license?

The Inspectorate already has a great deal of information and with more Inspectors they will be able to do more to codify and disseminate this knowledge.

26. One recommendation was to review the anaesthetic regimes and the CH told us they should have done this before. It is hard to understand why if some members of staff were concerned about this it could not just be done. Whose responsibility is it to insist on this sort of thing?

This centre has a very good contemporary analgesic regime that had evolved with time and was regularly reviewed by the attending veterinary surgeon. However, the anesthetic regimen, which had originally been implemented on the basis of expert advice, had not always kept pace with technical progress.

27. 5B 46 Re the review by the HOI of food management and water restriction schemes - has this been published and could we see and discuss?

The principles to consider will be published at the Home Office web-site – the background technical review will not be published unless and until it is peer reviewed.

General issues

28. Does the CI find there to be any significant differences between the standards of animal welfare achieved by academic and commercial establishments respectively?

There is not so much of a difference between standards; it is more differences in mindsets and resources.

29. How do standards of housing and husbandry at Cambridge, in all their different aspects, compare with those of other research establishments?

Cambridge has tried to improve the environment for the marmosets. A number of forms of 'enrichment' have been tried, and some attempt made to evaluate their impact. They also have a good record on minimising the social isolation of animals, with only 1% of marmosets single housed at any one time and then for welfare rather than scientific reasons. The line management of NVS and NACWO was outside of the scientists' responsibility (to remove or minimise potential conflicts of interest), which was an another example of good practice.

30. Does the nature of the species affect the way that the severity limits of different procedures are set, and if so, how does this apply in the case of primates?

Only if you believe that species suffer in different degrees. That general point apart, there is a general appreciation that non-human primates have a capacity to suffer that is probably not to be found lower down the phylogenetic scale.

31. At 4.14, the CI's Review states that "other forms of surgery intended to produce painful or distressing disorders that ... cannot or will not be relieved, can be regarded as .. substantial". Isn't this an incorrect rendering of the 'substantial' category, in light of Appendix 1.9, which rules out severe or enduring pain or distress?

32. Re Section 4.18 of the CI's report - is mental distress considered as a cost? It says the neurological effects are only demonstrable on formal testing but could that be because subtle indicators are just not being recognized (or looked for)?

No neurological sign should have gone unnoticed or unrecorded in this unit as the entire research output of this department is focused in the functional rather than the histological changes.

33. Similarly, in Section 5C 33 it states that if signs indicative of pain were detected and recorded analgesics were given. However, this critically depends on the ability of staff to recognise these. How does the inspectorate judge whether all signs are detected? Who states what these are likely to be?

Through observation of the animals and by checking the centre's records.

34. One would not expect the HOI to be expert in every field of science and therefore be able to assess benefit in the same way as peer review. The CI's report does not comment on the peer review process and states that a detailed analysis of the significance and impact of this work is beyond the scope of the review. It would be helpful to have a better understanding of how the peer review analysis relates to the HOI assessment, how is it factored in, how are the outcomes factored in to decisions about follow on work i.e. how does all this actually work in practice.

The Chief Inspector made some comments at the end of the meeting.

1. If the working group wishes to comment on food and water restriction regimes and whether these can be justified they may wish to seek independent expert advice.

2. He suggested reviewing the published papers by the Cambridge scientists should be a pre-requisite for any informed analysis of the costs and the benefits of the licensed studies.
3. The discussion of the BUAV report has to date centered on the costs of the research, so it would be reasonable to look at the benefits as well.
4. Members of the European Marmoset Research Group also viewed the facility recently. (N.B. the Home Office are corporate sponsors of the EMRG)
5. The funding bodies might a useful source of information on the strategic importance and quality of the research undertaken at this establishment.
6. He emphasised that the 3R's should be a team game and that care staff, scientists, inspectors etc. all have a role to play in refining procedures.

APC Secretariat
September 2003 (updated December 2003)

MEETING WITH THE BUAV ON 21 NOVEMBER 2003

In attendance, Alan Holland (Chair of the BUAV/Cambridge Marmosets WG), Richard West (Chair/APC Secretariat), Chris Atterwill (APC), Robert Hubrecht (APC), Maggy Jennings (APC), Gary Earle (APC Secretariat), Nadine Hall (APC Secretariat), David Thomas (BUAV), Sarah Kite (BUAV), Undercover Investigator (UI) (BUAV)

Note. Where nothing appears below a question, this is because it was not asked.

1. What staffing levels (of animal care staff) at the Cambridge unit would BUAV judge to be sufficient? What view does UI and/or BUAV take of the CI's approach to this question (5.A.9-19), based on performance, which appears to be: 'enough to ensure the well-being of the protected animals'?

The UI said that any reasonable person would not consider that three animal technicians were adequate for the duties expected to be carried out in an eight-hour day. On weekends, only one technician worked, usually for a three-hour period. Post-operative care was not provided 24 hours a day (or anything approaching it) and care over the Christmas period was insufficient. In the ten months that the UI worked in the facility, there were ten weeks when there were absences due to holidays or illnesses. During these 10 weeks there were only 2 animal technicians to look after the marmosets with no extra cover to replace the 3rd technician).

The UI noted that even a 30-second check of each of the 460 marmosets (including infants, sick and lesioned marmosets) would take 3.75 hours – 1.25 hours for each technician. This meant that particularly on weekends when only one technician was present, there was insufficient time to check the animals as well as feed them. The UI also noted that in the afternoon there was not sufficient time for a proper 2nd check of the animals when they were fed and watered as this was only supposed to take 30 minutes for 9 rooms which meant about just about 3 minutes in each room.

Of the 460 animals, 200 were experimental with the remainder as breeding stock.

David Thomas said that there was a legal duty under S6(6), S7(6) and S10(2) of the Act² to ensure any health problems were dealt with, including euthanasia

² These sections read as follows:-

S6(6) If it appears to any person specified in a certificate pursuant to subsection (5) above that the health or welfare of any such animal as is mentioned in that subsection gives rise to concern he shall –

(a) notify the person holding a personal licence who is in charge of the animal; or
(b) if there is no such person or it is impracticable to notify him, take steps to ensure that the animal is cared for and, if it is necessary for it to be killed, that it is killed by a method which is appropriate under Schedule 1 to this Act or approved by the Secretary of State.

where appropriate. The BUAV argued that without 24-hour care, the provisions of the Act were unable to be met – as proven when animals were discovered dead in the morning. The BUAV contends that this was foreseeable and therefore preventable.

The UI reported her concerns about staffing to the Senior Animal Technician (SAT). On the one hand, she was told that through experience her efficiency would increase, and the pressure of looking after over 150 animals, with various needs, would reduce over time. On the other hand, she said that the SAT also expressed unhappiness with the situation and passed on his concern to the NACWO. She also said that she had talked with the other technician about the situation and he was also unhappy with it. She said that while the researchers were at the facility, they also sometimes cared for some of the experimental animals, but this was without pattern and mainly the researchers did not attend the facility over the Christmas/New Year period.

2. Was UI given any training before, or during, the time she spent working at the facility?

UI completed the Module 1 course before beginning work at Cambridge. Modules 2 & 3 were completed during the course of employment. No specific training was provided on the operation of the unit or working with experimental animals, although the UI met and spoke to the researchers about their work. The UI's previous relevant experience included work with mice and at various animal rescues.

3. What were UI's 'duties', and those of her co-workers charged with caring for the animals? Was there sufficient time to perform those duties? Was the attitude of her co-workers in general a caring attitude?

The UI read out some notes she had made on the 14/8/01 of the tasks she was required to carry out: This went as follows:

"Now that X is away I have an even greater work-load. In summary, yesterday I swept, tidied and mopped 4 rooms. I cut up the 55 sandwiches for the day then fed, checked water and checked 5 rooms of marmosets. I collected and put the laundry on and then at 10 o'clock I shelled three trays of eggs, that I had boiled until 10.30am. The rest of the day I spent making 170 sandwiches, cutting up 4 carrots and then enough bananas to make 480 pieces, making up

S7(6) If it appears to any person specified in a certificate pursuant to subsection (5) above that the health or welfare of any such animal as is mentioned in that subsection gives rise to concern he shall take steps to ensure that it is cared for and, if it is necessary for it to be killed, that it is killed by a method appropriate under Schedule 1 to this Act or approved by the Secretary of State.

S10(2) The conditions of a personal licence shall include –

- (a) a condition to the effect that the holder shall take precautions to prevent or reduce to the minimum consistent with the purposes of the authorised procedures any pain, distress or discomfort to the animals to which those procedures may be applied; and
- (b) an inviolable termination condition, that is to say, a condition specifying circumstances in which a protected animal which is being or has been subjected to a regulated procedure must in every case be immediately killed by a method appropriate to the animal under Schedule 1 to this Act or by such other method as may be authorised by the licence.

3 clean cages for tomorrow, folding up and replacing the clean laundry, and finally feeding the 9 rooms with Y their afternoon food.

Today I collected and put in the laundry, cut up 55 sandwiches, fed and checked 5 rooms of marmosets. I cleaned and rinsed 10 pots that the pellets are put in from room 5. I took the pots out of the cages in room 1 to be soaked. I changed 6 cages from room 5 and then dismantled 4 of them to be ready to go through the cage wash. Then I cleaned the trays out of 2 rooms, swept the floors and tidied these rooms and 3 others. Later I cut up a box full of about 48 malt loaves, folded and replaced the laundry and took out the rubbish. Last thing Y and I fed the 9 rooms of marmosets their afternoon food.”

One of the APC members questioned the UI on how long it would take to check the marmosets and suggested that one could just check them quickly as a group. The UI pointed out that as marmosets are a prey species they may not usually show signs of illness/pain until they are very ill or suffering and so need to be checked on an individual basis as well as how they interact as a group.

The UI said that staff did not have the option to work extra hours and if anyone complained that there was not enough time, they were simply encouraged to pick up the pace. The UI often spent extra time in the unit during lunch breaks, monitoring the animals and making observations on the whiteboard.

The UI said that researchers very rarely provided assistance with regard to animal technician duties stating that their role involved research, not animal care. The UI did say that one of the researchers did help out on occasion when she realised that there was one technician short and there was too much to do, although this was not her job to do this. The UI said that the staff at the facility varied in their attitudes. Some had expressed dissatisfaction with the demands of the job and they had told her that they were so busy that they just did not have the time to do individual health checks on all of their experimental marmosets; some made an effort to care for the animals, while others, in her view, displayed an uncaring attitude to the marmosets.

4. We note that UI attempted to provide some enrichment of the marmosets’ environment. Was there any encouragement to her, or others, to do this? Did the UI feel able to make suggestions about enrichment?

The UI reported that when she joined the facility, the experimental cages had a wooden broom handle, nest box and a verandah. There was also a wooden shelf. The breeding cages sometimes had a nest box, a plastic container and piece of wood or branch. The UI made attempts, often at her own expense, to provide environmental enrichment – including placing more boxes/containers in the cages – resulting in increased playing/activity. Other staff tolerated these actions, but often joked/mockered the UI for doing this.

There was no encouragement for environmental enrichment and there was no money set aside for this. The SAT even boasted that the amount of money

spent on marmosets had increased by only 25% in six years, even though the number of animals kept had more than doubled.

5. The CI reports (5.A.14, 5.A.19) that during the period of his review all animal handling, husbandry and care tasks were performed to a high standard. Also that over the 2001/02 Christmas & New Year holiday period all essential animal care tasks were performed, and no significant welfare problems are recorded. We would appreciate UI's comment on these particular findings.

This is answered in issue 1.

6. Did the UI observe significant occurrences of stereotypic behaviours in the unit (CI's report 5.A.40)? If not, would UI/BUAV accept this as (some) evidence that conditions at the unit are generally reasonable?

Stereotypical behaviour (including back-flipping) was displayed mostly by experimental marmosets that had not yet undergone surgery. Experimental animals were housed in pairs, in half-size cages, for 1-2 years. Some animals were singly housed, as many as 21 at one point, for 3-4 months. These animals were split from their families due to fighting and were kept alone until they could be paired. The UI believed that more could have been done to pair single housed animals.

It was the responsibility of the SAT to manage the colony. The NACWO was not often around, usually only turning up when asked. In fact the UI mentioned that the SAT had told her how researchers actually joked about the NACWO not even being able to find the marmoset unit. The NVS has no responsibility for management and was there simply to deal with health problems. The UI reported the high levels of single-housing at the facility. One marmoset's cage-mate was put down and even 10 months later, she was single-housed. All the experimental animals were kept in half-cages, which restricted their movement. Many were kept in isolation and at one point, 21 (over 4%) of the 460 colony of marmosets were singly-housed. *(Note this is at odds with the CI's figure of 1%)* Work pressures often meant that this issue was not addressed.

7. CI (5.B.41) challenges UI's statement that altered food and water regimes cause stress. Any comment?

The UI claims that the SAT disagreed with food and water restrictions, stating that the process stressed the animals. The BUAV has tape evidence of his expression of concern. The UI said that she was told by the SAT that the NVS also disagreed with the practice and he said was going to raise this issue at the Ethical Review Process (the UI was unsure if this actually happened).

Around 60 pairs of marmosets were water and food deprived and those on food deprivation were usually present when the other animals were fed, causing them to scream and hang off their cages. When marmoset pairs on

water deprivation were finally provided with a drink, they were given only one bottle between them. They were very thirsty. No records were kept on the cages or elsewhere to show when they were last watered – the researchers managed the process themselves.

8. What key positive suggestions would BUAV make for improving the standards of accommodation and care at the Cambridge facility?

The BUAV said that the conditions at Cambridge breach the code of practice and did not meet best practice. Paradoxically, the proposal for the new Cambridge primate facility was state of the art. BUAV believe that it is inappropriate to use the term “normal behaviour” as no animal (particularly primates) kept in a laboratory environment is able to display normal behaviour, whether directly involved in a project or simply in a family unit.

9. Was there a mechanism at Cambridge for dealing with concerns about animal husbandry and care and levels of suffering that the investigator could use? Presumably the investigator communicated her concerns - what was the response?

There was no formal mechanism for dealing with problems. The UI approached the SAT whenever there were specific issues/concerns, particularly about the health of the animals. The UI also stated that she would always also tell the researcher in charge if the animal was experimental and would make a note on the whiteboard in the relevant room. The UI gave the meeting details about two particular occasions when she had raised specific health concerns with the SAT that elicited an unduly delayed response, which caused additional and unnecessary suffering for the animals concerned.

10. The BUAV record a number of concerns regarding the health and diet of animals in the colony, including injury, diarrhoea, dental problems and pneumonia. We note that the CI's report generally downplays these concerns (5.A.58-68). How do BUAV respond? Given that no population of animals anywhere (including humans) could be expected to have perfect health, what do BUAV regard as an appropriate reference point for comparison? Does BUAV perhaps believe that no captive colony of marmosets could have a satisfactory health and dietary regimen?

(NB said here or on a different occasion during the meeting) The UI said that the colony was generally unhealthy and there were no formal health check procedures.

11. We note that the marmosets are often seen on the video to blink and avert their eyes. Is it reasonable to infer that this was solely a response to the lighting necessary to make the recording, or is there any other reason?

The UI said that the video camera she used needed no additional lighting, so the animal's blinking shown on the video was not caused by that. The UI's view was that it appeared to be a side effect of surgery.

12. We note that some of the marmosets on the video have traces of saliva round their mouths. This might have a number of causes e.g. vomiting, the effects of the anaesthetic, etc. Can UI shed any light on the actual cause?

13. BUAV claim that the weakest of triplets were sometimes left to starve. We have been given to understand that, although this might occasionally and unavoidably have happened, the policy of the unit was either to hand feed, or humanely kill these animals. Can UI confirm whether this was the policy of the unit?

The UI stated that the infant mortality rate in 2001 was 41% and it was not always triplets that died. There seemed to be a general acceptance of infant mortality. The UI noted that the policy was to humanely kill infants that were not thriving, but this could not be done during night-time and it was difficult to determine which animal was not thriving. The UI also stated that the policy of the unit was specifically not to hand feed babies. Mr Thomas pointed out that the CI confirmed this in his report (para 5.A.5 et seq.)

14. Did the investigator observe the training sessions for marmosets and did she see 'punishment' training i.e. lowering the shutters onto animals' fingers?

The testing was carried out in separate rooms, and the UI was only occasionally allowed to view the procedures. However, she said that a researcher did comment that the marmosets sometimes got so tired by the procedures that they put their heads against the bars and got confused. *(Note: the reference to the "punishment" training sessions came from the researchers' own Shaping notes.)*

15. Does the investigator know why some marmosets were denied forage mix (Para. 102)?

Researchers often wanted to work on the weekends or wanted their marmosets hungry and ready to work on Monday mornings.

Forage mix was usually given to the animals on Friday afternoon. Some animals were denied forage mix, as part of the behavioural tests carried out by the researchers.

16. Did the investigator see the multiple injections reported in Para 90 and what is her view of the reaction of the animals? Did the investigator see the telemetred marmosets referred to the Para 97 and if so what was her view of the condition of the animals?

17. Would BUAV accept CI's view that venepuncture problems are 'not entirely preventable' (5.B.49)?

18. Potential shortcomings of anaesthetic regimens (CI 5.C.28-9). Would BUAV accept the view of the 'two experts' regarding the incident recorded on the video that the animal concerned was unlikely to have experienced pain?

19. In what way was the postoperative care given to brain damaged marmosets wholly inadequate (see bullet point 6, page 4 of the BUAV report). Could BUAV tell us what they would consider to be adequate care?

20. The BUAV list, and illustrate, several concerns over post-operative monitoring. The CI (5.B.30) identifies the principles of monitoring that were followed, and finds no evidence of significant welfare problems, or death, that would have been avoided by a more intensive regime (5.B.31). Would UI/BUAV care to comment?

The BUAV report gives examples of post-operative marmosets who were left unattended for 15 hours or more overnight who clearly suffered as a result. If a member of staff had attended to these animals at night then the suffering could have been alleviated earlier. The CI's position is unsustainable.

21. In his review (3.3), the CI states that the BUAV campaign video shows animals in the immediate and early-postoperative periods reflects a combination of early effects of surgery and post-operative medication shows extent of surgical exposure rather than magnitude of surgical procedure. Would UI like to comment on this statement?

BUAV said that the video portrayed a variety of marmosets in different stages, including immediate post-op to show the effects of surgery and the inadequate post-operative care. The UI said it appeared that the APC members did not see the worst of the animals' physical conditions during their visit in June. They did not know if they had visited all of the rooms. She questioned whether any immediate post-operative animals had been seen and added that the side effects of some procedures were greater than for others. Marmosets involved in the study for Parkinson's disease rotated constantly – the UI said that this was a permanent effect of the tests. The testing for these animals involved 30-60 minutes in an isolated and bare Perspex box.

She said that visits from the Home Office Inspectorate were always pre-announced, and time was spent by the facility staff to prepare that resulted in standards being raised compared to usual practice. This included the re-tagging of 20 marmosets on one occasion. On this occasion, the UI noted that the inspector only saw marmosets under one project licence, did not spend long in the rooms and had only visited three out of nine.

22. Would UI/BUAV elaborate on their view that only ‘minimum effort’ was made to make the cages interesting? Are the UI and/or BUAV familiar with the paper by staff based at the Cambridge facility on the use by marmosets of available cage space (Ely et al., CI’s report n.15), and do they have a view about the conclusions reached in that paper?

Research cages were furnished with a wooden perch, nest box and sometimes a verandah. Family cages had perches, platforms, nest box, verandah and the occasional plastic container. The environmental enrichment was generally only improved by the actions of the UI (see issue 4).

23. Does BUAV accept CI’s clarification regarding the reference to severe pain in the project licences, that this is intended not to provide for its occurrence but to provide for its alleviation (CI’s report 5.C.65)?

Mr Thomas saw a contradiction between the CI’s report and the Home Office guidance on protocol severity limits. The CI said in his report that the severity limit was used as the maximum level of suffering not to be exceeded. Home Office guidance says that severe pain was the upper limit of the expected adverse effect and the worst potential outcome for any animal subjected to the protocol. Mr Thomas said it should therefore be a prediction of the potential suffering, not a control mechanism.

24. On the key issue of the severity limits applied to these protocols, the CI appears to have been guided by consideration of how far the procedure permitted a return to ‘the normal activities of daily living’ and did not entail ‘extended periods of special care (e.g. 4.5)’. How does the BUAV view this proposed criterion for distinguishing between moderate and substantial severity?

Ms Kite thought that the CI’s criteria were misleading on a fundamental level. She said that when caged, animals cannot carry out normal activities of daily living. This is exacerbated after brain surgery and the subsequent lack of social interaction. She said that it was impossible for the marmosets to behave normally in an experimental environment. Mr Thomas thought that the CI, apart from conducting a retrospective review of the facts, adopted a mechanistic approach and always concluded that if there was no record or sign there was no suffering. Mr Thomas pointed to the fact that, according to the CI, 4% of the animals under one project were euthanased on welfare grounds as an example of high suffering levels. The APC working group members commented that the APC had accepted that work was required on severity bands/classification and had already agreed to look into the issue when current studies, by other organisations, had been completed.

25. The BUAV is clearly of the view that these protocols should have been classified as ‘substantial’. What are the key aspects of the procedures that lead them to this view?

26. CI (5.C.90-94) report suggests that images shown to animals were not designed to elicit fear or alarm; that Rye was not blind; and that Turks was adequately attended. Any comment?

Researchers were presenting images to elicit a response from the marmosets. The UI said that members of staff were aware of the animals' fear of "the glove" and that particular image was purposely shown to the animal by one researcher to cause a dramatic response. Mr Thomas said that the BUAV disagreed with the licencees and CI's view that this was not stressful.

(Note: there was insufficient time to discuss Rye and Turks at the meeting.)

27. Some of the evidence in the BUAV report is based on what 'records showed' (e.g. para. 82). What sort of records are these and did the investigator also see the animals and effects reported?

28. We surmise that UI's undercover role might sometimes have put her into a situation where she felt unable to take action to alleviate perceived suffering. If so, how did she deal with such conflict, and how does she feel about it now?

(Note: said either here or on another occasion during the meeting) The UI said that she never allowed her role as an undercover investigator to mean that suffering which could otherwise have been avoided took place. She always put the animals' interests first.

29. What sense of responsibility did the UI feel toward her Cambridge University colleagues?

The BUAV declined to comment on this question as not being relevant to the Working Group's stated remit.

30. BUAV state on page 4) of their report that the research has been going on for a number of years with little apparent progress and that there is considerable doubt as to whether the availability of non-animal alternatives was properly explored by Cambridge University or the Home Office. What do they base these statements on?

Ms Kite advised that the BUAV had received expert advice that was not available at the meeting, but that further details would be forthcoming. According to the researchers' own published papers some research looked promising but often failed in clinical tests. BUAV believe the researchers should be able to prove what benefits had been derived from the projects. It was pointed out that there was a requirement for researchers to publish their work, so that it may be peer-reviewed. BUAV said that the fact that the research may have been peer-reviewed and published no doubt meant that it was scientifically interesting but did not necessarily mean that it was useful. The BUAV report contained detailed analysis of lack of benefit.

The BUAV also argued that lesion work was very problematic as it was not always possible to replicate lesions with sufficient precision in every experiment.

31. BUAV mention ‘numerous other undercover investigations and leaked information’ revealing serious inadequacies in the way the Home Office carries out its regulatory role. This is a very serious allegation. Could they let us have a list of all the investigations they are referring to?

(Note: the following details were provided subsequent to the meeting.)

These are the BUAV’s UK undercover investigations over the past few years.

Huntingdon Research Centre (now Huntingdon Life Sciences) (HLS) 1989
London Hospital Medical College 1991
Shamrock (GB) Ltd. 1992
Hazleton Research Laboratories (now Covance) 1992
Wickham Research Laboratories 1993
Harlan-Hillcrest 1999
The Wellcome/CRC Institute at the University of Cambridge 1992
The University of Cambridge 2001/2

Another recent example is the xenotransplantation research carried out at HLS for Immutran. Extensive documentation was leaked to “Uncaged” Campaigns in 2000. “Uncaged” has made numerous, substantiated allegations about the adequacy of the Home Office’s regulation of the research, most recently in a detailed submission to the Home Affairs Committee.

The UI said that there were no arrangements for whistle-blowing at Cambridge. Any concerns had to be fed through the SAT, but if he was unavailable then they would be raised with the NVS and NACWO.

32. On a point of clarification, BUAV (Investigation p.4) claims that ‘fundamental’ research is ‘almost by definition’ not likely to lead to benefit. On our interpretation of the ‘permissible purposes’, however (Guidance p.28), a gain in fundamental knowledge is regarded as itself a benefit, whether or not it leads to further benefits. Would BUAV care to comment?

Mr Thomas, for the BUAV, drew a distinction between “permissible purpose” and “benefit” and quoted a passage from the Chief Inspector’s cost:benefit note (1998). The tests in subsection (3) and (4) of the 1986 Act were cumulative – it was not sufficient to show that the research met one of the permissible purposes, such as the advancement of knowledge; it also had to be likely to produce a benefit for human health etc. Professor Holland offered a different view. He said that the advancement of knowledge and understand

was in itself a benefit and met the requirements of A(SP)A. A failure for a drug test did not mean there was no benefit attached to the research.

APC Secretariat
November 2003

Issues for discussion with MRC, Tuesday 27 January 2004. Held at Room 512, Allington Towers.

Present: Richard West (Chair, APC Secretariat); Alan Holland, Christopher Atterwill, Robert Hubrecht, Maggy Jennings (All APC); Gary Earle (APC Secretariat); Vicky Robinson and Tony Peatfield (Both MRC).

The meeting began at 10.27. Richard West welcomed all to the meeting. Alan Holland explained the work of the Working Group to the MRC representatives. The group then discussed the list of issues that had been sent to the MRC representatives on Monday 26 January.

A. Questions specific to the Cambridge projects

Husbandry

1. What is the MRC's view of the standards of husbandry (e.g. cage size and design, environmental enrichment) at Cambridge, both before and after publication of the BUAV report. Is this an issue that would have been considered when these projects were funded?

The cage size, design and environmental enrichment met legally required minimum standards. The MRC recognised that the two-tiered caging and the level of environmental enrichment were not examples of best practice, but that the standards of husbandry have improved since the expose. The MRC rarely inspects husbandry standards outside of its own facilities and only when the investment is considerable. Ultimately, the legal responsibility for the facilities lies with the Certificate Holder.

2. With the setting up of CBPAR we understand the MRC has set out expected standards for husbandry and care of primates. Are these publicly available and could the APC have a copy? How does the MRC see them – as the minimum required, or as 'best practice'? Will these standards be mandatory for grant holders?

This has become a priority for the MRC. Guidelines on best practice in the accommodation and care of primates used in scientific procedures have been written by CBPAR following discussions with stakeholders and have received approval from the MRC council. They will be published very shortly. Future funding of projects involving primates will be dependent on the establishment meeting these guidelines. Dr Robinson said that she would provide copies of the guidelines to the Working Group members. The guidelines will also be published on the MRC's website³. The MRC said that giving guidelines for

³ Now available: see <http://www.mrc.ac.uk/pdf-primate-best-practice.pdf>

best practice for primates was a start. There may be guidelines on other species.

Procedures

3. Could any of the ‘models’ or procedures used be further refined and are more refined models used elsewhere?

Vicky Robinson and Tony Peatfield said they were not expert in this area. Expert comment is sought through review by referees and Research Boards. All grant applications are peer reviewed and suggested refinement is often made at this stage. The “peers” offer suggestions on all of the 3Rs, not only refinement. There may be advantages in adopting different procedures, but a new technique might involve using more animals and add to the “costs” of the experiment. The Cambridge scientists have refined some of their techniques throughout the project, including anaesthesia, analgesia and post-operative procedures.

The MRC has recently instituted a mid-term check of projects involving primates, to audit and ensure that. Their use is still necessary and justifiable. This addresses the ever-increasing and changing levels of scientific knowledge. The MRC would also expect that the ERP would review the anaesthetic, analgesia and post-operative regimes as part of the implementation of the best practice primate guidelines and these are reported to the MRC Council through CBPAR.

4. How did the MRC respond to the BUAV’s concerns about conduct of procedures (e.g. anaesthesia, blood sampling, restraint, behavioural testing) in these projects?

The MRC has funded a review by Professor Flecknell of the anaesthetic regime used by the research groups at Cambridge that are the subject of the BUAV’s allegations. The MRC will give further consideration to behavioural testing. They were uncertain whether the criticisms from the BUAV on blood sampling and restraint were representative of the standards at Cambridge University.

5. More generally, is the competence and/or ‘attitude’ of grant applicants considered by the MRC in its grant awarding process? If so, how?

It is very difficult to measure an individual’s attitude, but this might be considered at the peer review stage. The culture of the establishment is often well known and informs the MRC at the grant review stage. Details of all funded projects are published on the MRC website (accessible through: <http://www.mrc.ac.uk/index/current-research/current-overview.htm>).

Any project that promotes the 3R’s can be eligible for additional MRC funding, including resources for meetings or equipment.

Benefits

6. What benefits have this research programme delivered? Why and how are these important and are they considered to be essential? What is the MRC's view of the criticism made by the BUAV of the validity, relevance and necessity of the research?

The MRC's primary role is to consider whether the programme will address important scientific issues and lead to advances in human health. To date, there have been clear, if not well publicised benefits, from the Cambridge University project. The stroke work resulted in the development of drugs which have reached Phase III clinical trials at Astra Zeneca. There have also been useful data recorded from the Parkinsons Disease project. The MRC encourages organisations that it funds to publish such successes. Whenever possible, the MRC reports on positive research through its website and annual reports. The MRC also funds non-animal and non-invasive alternatives, which over time will significantly reduce animal use.

The MRC agreed with the Working Group's views that negative data can be of great benefit and should be reported whenever possible; also that alliances with commercial organisations need to be closely monitored.

B More general issues

7. Have any changes been made in MRC policy and procedures as a result of the BUAV report. Did the MRC consider these were issues that needed to be addressed and what were these. "How will it pass on any lessons learnt to other funding bodies?"

The changes in MRC policy on primates are mainly a reflection of the work of CBPAR, which was created before the BUAV expose. It is difficult to answer whether the BUAV expose led to a hastening of changes in MRC policy but it clearly had an effect and galvanised CBPAR into producing the primate guidelines. CBPAR was created in 1999 as a result of three concerns 1. A recognition that MRC's contribution to the 3Rs was not widely known. 2. A recognition of variations in standards at some establishments and 3. A recognition that there had been an increase in mouse use in genetics and physiology.

8. How does the funding review process within the MRC operate? How are ethical issues (for example use of primates; impact of research on animals) addressed? Is this kind of information, i.e. on the process, made public?

The process for funding projects is public, published on the MRC website and in the MRC's ethics booklet. There are as many ethical issues associated

with humans as with animals. All issues of important ethical consequence are considered by the main Council.

9. How does the MRC see its role in balancing conflicting public demands e.g. to develop cures for disease versus reducing animal use and suffering.

The two are not mutually exclusive. The MRC's mission is to support research aimed at improving human health (the benefits), but also by creating and adopting procedures that lead to a reduction in the costs to the animals. The MRC recognised that more could be done to publicise its processes, including the use of referees to evaluate projects. The comments of referees are summarised and brought to the relevant MRC Research Board. The benefits to animals from advances in veterinary medicine could also be more widely publicised.

10. Does the MRC consider the costs of maintaining adequate numbers of animal care staff in the funding allocated to projects?

Where the MRC controls the organisation, ie its own Institutes and Units, they ensure that there is sufficient funding to cover all staff costs. In academic institutions, the MRC reimburses the costs of all the staff directly employed on the grant, plus 46% of all salary costs on the grants that it funds, as a contribution to "indirect" costs. The Universities fund the remainder of the staff costs associated with the project. The MRC do not police the establishments they fund, but act when they know that standards, including staff levels, fall below an acceptable level. However, it is the legal responsibility of the Certificate Holder to ensure that there is sufficiently trained and competent staff for each project.

11. In particular, does the MRC undertake its own welfare assessment? For example, might it ever reject a proposal on the grounds that, though promising a considerable contribution to knowledge and/or human welfare, it comes at too high a cost (to the animals)?

The MRC does reject grant applications on the basis of expected costs to the animals. This is often through consultation with referees and particularly where primates are involved. CBPAR reviews all grant applications involving the use of primates.

[12. Would it *consider* undertaking such assessment, or does it consider that this is entirely a matter for the inspectorate and/or the local ethical review process?

[Already covered in 11].

13. Does the MRC undertake ongoing and/or retrospective assessments of the projects that it funds? Are these ever of the form 'is it/was it worth the cost to the animals?'

Full reviews are held at the grant renewal stage. For programmes involving primates a further check is carried out at their mid-point normally 2.5 years.

14. How does the MRC see its role and responsibilities in regard to the welfare of the animals involved in the projects that it funds, or does it consider that these are entirely a matter for the Inspectorate and/or the local ethical review process?

The MRC takes responsibility for animal welfare at its own units and institutions. Naturally, the MRC has less authority where only grant support is given. However, grant holders are required to comply with MRC policies on the use of animals in research.

15. In particular, does the MRC have a (share in) responsibility for ensuring that the number and severity of the procedures is kept to the minimum that is compatible with securing the desired results?

The MRC has a share in the responsibility for the numbers and severity of procedures, particularly at the application stage, and asks questions where appropriate. However, on a day-to-day basis, once the project is started, adherence to the legal requirements is mainly the role of the Inspectorate and regulators.

16. Does the MRC have a (share in) responsibility for ensuring that 'adverse effects' on the animals is kept to a minimum? Might this extend to some responsibility for the welfare of the animals overall?

[This was answered in response to earlier questions.]

17. Pursuing this latter thought, does the MRC consider, or might they consider:

- i) e.g. stipulating environmental enrichment as a condition of funding;**
- ii) e.g. earmarking funds for environmental enrichment;**
- or iii) e.g. offering incentives for environmental enrichment?**

Cambridge University grantholders have published papers on environmental enrichment using verandahs and reviewing cage heights. The MRC makes funding available for 3R's research through CBPAR. On average, CBPAR currently spends around £150,000 per project per year and spends around £1m annually. The Cambridge University group recently received £10,000 from MRC to investigate new marmoset cage designs.

18. Given that there is a general responsibility, under the Act, not simply to ensure that the cost to the animals is justified in light of the likely benefits, but to ensure that the balance of benefit over cost is maximised (which entails both maximising benefit and minimising cost), how is the latter to be achieved?

[This was answered elsewhere, mainly in answer 9.]

The meeting was closed at 12.03pm.

Tony Peatfield advised that he would let the Working Group know about the renewal date for the Cambridge Project.

BUAV/Cambridge Marmoset Working Group
February 2004

The Wellcome Trust: Response to questions from the Home Office Animal Procedures Committee

General statement

The Wellcome Trust considers that research using animals has made an important contribution to advances in medicine and surgery, which have brought major improvements in the health of human beings and animals.

Much basic research on physiological, pathological, and therapeutic processes still requires the use of animals in experiments. Such research has provided and continues to provide the essential foundation for improvements in medical and veterinary knowledge, education and practice.

Research using animals will continue to be essential for the conquest of many unsolved medical problems, such as cardiovascular disease, stroke, AIDS, other infectious diseases, cancer, and genetic, developmental, neurological and psychiatric conditions.

Therefore, the Wellcome Trust supports biomedical and veterinary research provided that:

- it fully complies with Home Office regulations;
- it has approval from a local ethics committee;
- it has been successfully independently peer reviewed; and
- consideration has been given to the refinement, reduction and replacement ('3Rs') of the animals in the experiment and no viable alternatives exist.

Our full position statement is published on our website at: <http://www.wellcome.ac.uk/en/1/awtvispolani.html>.

B. Questions specific to the Cambridge projects

Husbandry

1. What is the Wellcome Trust's view of the standards of husbandry (e.g. cage size and design, environmental enrichment) at Cambridge, both before and after publication of the BUAV report. Is this an issue that would have been considered when these projects were funded?

The Wellcome Trust believes that the Home Office regulations provides an adequate basis on which to set standards of care and welfare for primates used in research. When the Trust reviews an application for funding research involving the use of animals it takes into consideration the requirements of the Home Office, approval from a local ethics review committee, the quality of the

science and whether due consideration has been given to the 3Rs. There was no difference in the procedure with regard to this application.

In relation to this particular BUAV report, the Trust's understanding is that there was a subsequent investigation by the Home Office Chief Inspector. The conclusions of that report found that the severity limits had been correctly assigned and that the marmoset facility "meets, and in some respects exceeds, the standards of housing and care set out in the relevant Home Office Codes of Practice, and that some examples of best practice are to be found there".

As such, the Trust did not feel it was appropriate or necessary for it to reassess its own support for this research.

2. Does the Wellcome Trust have expected standards for husbandry and care of primates.

All research involving primates has to abide by Home Office regulations and the Trust would not, and could not fund research which did not have Home Office animal licences covering the research facility, the researchers themselves and the specific research project.

Procedures

3. Could any of the 'models' or procedures used be further refined and are more refined models used elsewhere?

As stated above, the Trust funded this project subject to Home Office approval, review by a local ethics committee and scientific review by seven national and international referees and an independent panel of scientific experts. As with all peer reviewed medical research funding, the comments made by peer reviewers are kept confidential. However, we can say that certain questions were raised about the scientific protocol in this instance which resulted in a refinement of the procedure. In fact it is quite common in a number of the research applications the Trust receives, not just those involving the use of animals, that the peer review process results in suggested changes and improvements to the research protocol. When there are recommendations these are fed back to applicants and the required changes become a condition of any award.

4. How did the Wellcome Trust respond to the BUAV's concerns about conduct of procedures (e.g. anaesthesia, blood sampling, restraint, behavioural testing) in these projects?

The then Director of the Wellcome Trust, Dr Mike Dexter responded to a letter from Ms Michelle Thew, Chief Executive of the BUAV on 27 June 2002. This letter restated the Wellcome Trusts policy on the use of animals in research as outlined in the opening statement of this response.

5. More generally, is the competence and/or 'attitude' of grant applicants considered by the Wellcome Trust in its grant awarding process? If so, how?

It is the Wellcome Trust's view that research undertaken with animals in the UK is conducted within a framework that provides some of the most stringent licensing conditions in the world. The Trust is satisfied that compliance with UK legislation meets the highest ethical standards and therefore considers any additional stipulation demanded by funding organisations would be excessively onerous. The competence of the individual Scientist is dealt with as part of the overall assessment of the application for funding.

Benefits

6. What benefits have this research programme delivered? Why and how are these important and are they considered to be essential? What is the Wellcome Trust's view of the criticism made by the BUAV of the validity, relevance and necessity of the research?

The research programme grant in question has not yet reached completion. However, it was funded on the grounds that the research will further essential human knowledge on the neuropsychological and neurochemical basis of the decision-making process which would be of direct relevance to patients suffering from brain damage or neurodegenerative diseases. The research has the potential to lead to novel pharmacotherapies or other treatments to alleviate human suffering. These arguments were accepted and supported by the referees and the grant awarding panel and would have been made in the context of the historical contribution the use of marmosets have made in this area and the reputation of the scientists as world class leaders in their field.

B More general issues

7. Have any changes been made in Wellcome Trust policy and procedures as a result of the BUAV report. Did the Wellcome Trust consider these were issues that needed to be addressed and what were these? Also, how will it pass on any lessons learnt to other funding bodies.

The Trust has not made any changes to its policy and procedures as a result of the BUAV report for the reasons set out in the answer to question 1. However, the Trust does have an internal standing committee which meets regularly to discuss changes in practice and to keep our policy under continuous review. Our procedures are evaluated to ensure they meet current practice amongst all grant-funding agencies supporting research involving animals. In addition, there is Trust representation on appropriate external bodies to maintain our awareness. These include the Boyd Group, the FRAME Reduction Committee and the AMRC Animals in Research Committee.

8. How does the funding review process within the Wellcome Trust operate? How are ethical issues (for example use of primates; impact of research on animals) addressed? Is this kind of information, i.e. on the process, made public?

In completing the application forms, the applicant provides specific information relating to the proposed research. In the case of an application to fund a research project involving the use of animals, no grant will be made unless the conditions outlined in the general statement above are complied with. In addition, on the application form, the applicant must provide a justification for the use of animals and in particular, the species and number requested. Applicants must also provide information on the current status of project and personal licences. The Trust's Grant Application form and Notes to Grant Applicants are on the Trust website⁴.

In determining whether or not to fund a grant application the Trust seeks comments on the proposed research (including procedures) from external referees. These comments, which are often quite detailed, are considered alongside the application itself by the relevant scientific funding panel which is composed of experts in the relevant scientific field. In the case of grant applications involving the use of animals, the panel is asked specifically to consider and comment on whether the use of animals (including the species and level of use) is appropriate and justified. This information is minuted and forms part of the internal record of the process.

9. How does the Wellcome Trust see its role in balancing conflicting public demands e.g. to develop cures for disease versus reducing animal use and suffering.

The Trust is very much aware of the need for continued dialogue to balance the justified needs of medical research to improve human and animal health with the concerns of the general public regarding animal welfare. As part of furthering the Trust's charitable objects, the Trust has a responsibility to ensure that the biomedical research community is able to operate in an environment which fosters and promotes all research which will improve human and animal health. As part of this, the Trust recognises the importance of facilitating discussions and maintaining a sense of balance about the use of animals in medical research.

Two recent examples of such facilitation are given below:

1. The Boyd Group sponsored a roundtable discussion on the use of severity limits involving NVS (Named Veterinary Surgeon) and NACWO (Named Animal Care and Welfare Officer) representatives which was hosted at the Trust on 7 October 2003.

⁴ http://www.wellcome.ac.uk/doc_WTD004053.html

2. The Dr Hadwen Trust / Lord Dowding Fund / National Human Tissue Bank sponsored a meeting on the use of animals in sepsis research which was hosted at the Trust on 25 January 2004.

In addition, the Trust believes that school children should be given the opportunity to discuss controversial issues in biomedical science, including the use of animals in research, in a fair and balanced way. In support of this aim the Trust commissioned some research by an interdisciplinary team from the Institute of Education at the University of London. They sought to uncover how, and in which curriculum subjects, controversies arising from biomedical science are tackled in schools and colleges in England and Wales. The aims of the research were to highlight good practice, identify institutional obstacles, find ways of enhancing young people's experience of science education and prepare them to engage confidently with the issues that they are likely to face in the future.

A report of the research published in 2001 and entitled "Valuable Lessons"⁵ explores how teachers approach controversial topics raised by science in their lessons. Its key findings and recommendations led to a 'stakeholder' conference examining how to put theory into practice and the findings of that conference were made available to the whole teaching community.

The Trust considers that a continued dialogue with the public on the use of animals in research is healthy and that the research community should explain the methods and aims of research. MORI public attitude studies conducted in 1999, 2000 and 2002 indicate that public trust with regard to animal experiments increased between 1999 and 2002 and that there is a link between levels of public trust and openness from the scientific community. However, we also believe that openness needs to be balanced against the need to protect researchers from violence and intimidation from animal rights extremists.

10. Does the Wellcome Trust consider the costs of maintaining adequate numbers of animal care staff in the funding allocated to projects?

The costs associated with animal housing and maintenance are supported through grants and are assessed alongside all other budget requests in the course of the scientific panel meeting which makes the funding decision.

11. In particular, does the Wellcome Trust undertake its own welfare assessment? For example, might it ever reject a proposal on the grounds that, though promising a considerable contribution to knowledge and/or human welfare, it comes at too high a cost (to the animals)?

The Trust believes that its grant funding system previously outlined gives a sound basis for the consideration of ultimate benefit from the use of animals in

⁵ Valuable Lessons Engaging with the social context of science in schools. Full report available at www.wellcome.ac.uk/en/1/pinpubacteduisc.html

research. If the research outputs are borderline or negligible or the use of animals unjustified this is revealed during the process and the proposal will be rejected with appropriate feedback on the reasons for failure to the applicants.

12. Would it consider undertaking such assessment, or does it consider that this is entirely a matter for the Inspectorate and/or the local ethical review process?

All the Trust's processes and procedures are reviewed on a regular basis. At present, the current procedures for assessing grant applications to fund research involving the use of animals are seen as sufficiently robust.

The Trust feels that to require an assessment and review process, additional to that already undertaken by the Home Office and the local Ethical Review Committees would be complicated, onerous and potentially costly. The Trust would be strongly opposed to such measures. The Trust does however, visit Trust funded scientists on regular occasions, thus providing an opportunity to informally monitor and assess work and give feedback if required

13. Does the Wellcome Trust undertake ongoing and/or retrospective assessments of the projects that it funds? Are these ever of the form 'is it/was it worth the cost to the animals?'

The Wellcome Trust does undertake retrospective assessment of the research it funds and the Trust's grant conditions require Trust-funded researchers to submit a final report on the project funded by the grant. Such assessments do not specifically examine this point on a case by case basis.

14. How does the Wellcome Trust see its role and responsibilities in regard to the welfare of the animals involved in the projects that it funds, or does it consider that these are entirely a matter for the inspectorate and/or the local ethical review process?

As stated previously, the Trust as a key funder of biomedical research is committed to the principles of the 3Rs and has developed a range of measures (principally through grant awarding procedures) intended to ensure that proper account is taken of all possibilities for the application of the 3Rs so that high standards of research accommodation and welfare can be achieved.

15. In particular, does the Wellcome Trust have a (share in) responsibility for ensuring that the number and severity of the procedures is kept to the minimum that is compatible with securing the desired results?

The Trust, through the grant funding process outlined in the answer to question 8 above takes steps to ensure that the principles of the 3Rs have been actively considered in the research it funds. However, the Trust also believes that 3Rs work is best conducted and developed by the researchers themselves.

16. Does the Wellcome Trust have a (share in) responsibility for ensuring that 'adverse effects' on the animals is kept to a minimum? Might this extend to some responsibility for the welfare of the animals overall?

Please refer to the answer given for question 15.

17. Pursuing this latter thought, does the Wellcome Trust consider, or might they consider:

- i) e.g. stipulating environmental enrichment as a condition of funding;**
- ii) e.g. earmarking funds for environmental enrichment; or**
- iii) e.g. offering incentives for environmental enrichment?**

Environmental enrichment is part of the recommended approach to primate husbandry and maintenance as part of the MRC Primate Guidelines from the Centre for Best Practice for Animals in Research and the Trust is currently considering whether to adopt these. As part of this process the Trust conducted a consultation exercise with its grant holders and the findings of that consultation is being prepared for consideration by the Trust's senior management team.

18. Given that there is a general responsibility, under the Act, not simply to ensure that the cost to the animals is justified in light of the likely benefits, but to ensure that the balance of benefit over cost is maximised (which entails both maximising benefit and minimising cost), how is the latter to be achieved?

This is to be achieved by ensuring, through the Trust's grant funding processes, that researchers have given active consideration of the most up-to-date approaches in the 3Rs. Stringent peer review of grant applications ensures that applicants are mindful of this.

The Trust is also involved in a number of external groups where these issues are discussed.

The Wellcome Trust

March 2004

Report to the APC on the BUAV video “Witness the cutting edge of British Medical research”.

From: David B. Morton

1. I have been asked for my comments on the above video to help the APC’s enquiry into the use of marmosets at Cambridge University. This video was very different from the footage I saw before commenting on the NewsNight programme some months ago. At that time I viewed a variety of clips for over an hour and I was also told of other instances of concern such death rates, post operative care, strategy for analgesia.

2. I have taken the view that details of what can be seen and heard on the video might provide some factual basis on which to make judgements on the severity in the project licences. The following comments are based on an assessment of the adverse effects shown by the marmosets not only by myself, but also by others who have considerable experience in breeding and keeping marmosets. I have deliberately not addressed the potential benefits of the work as I do not see that as my brief. I concentrate on the adverse effects as that is what I have commented upon before. The scientific objectives of the work seem laudable and supportable but I would like to see some of the comments of the researchers on the ‘lack of success’ challenge by those doing the work. My concern is more with the way the work was carried out, not that it should not have been done at all (although that may still be a debatable point). One of my concerns is that there is no peer review by the funding body of the detailed way in which work is done, and it has a public responsibility to do so. The funding body and the institution should not simply leave it to the Home Office as they may not have the expertise. On the other hand, there may be significant national expertise that could be approached by the national funding body. In my opinion, this video provides strong evidence for that view. There is also an issue of whether there should be regional/national primate centre(s) where such work can be carried out under ideal conditions and with resources to maximise benefit through a whole range of scientific measures, lacking in this work. Maximising benefit is a refinement that is often overlooked. In other words it is a factor in addition to minimising harms and enhancing animal welfare.

3. I take it that I do not need to re-iterate my views that assessment of psychological/mental and physiological distress, as opposed to overt pain, is an important and under-estimated factor in the assessment of harms done in research projects. I have written extensively on these issues in various book chapters and other publications (see reference list at end). In brief, several forms of adverse effects can be recognised in animals including pain, physiological ‘dystress’, and mental distress. Pain needs little explanation in its causation based on human experiences, and may be assessed for example from an animal’s behaviour and its response to analgesia. Physiological dystress is, by and large, intrinsic and is internally driven by homeostatic neuroendocrine mechanisms and can result in changes to the

hypothalamic, pituitary adrenal cortex axis, and the sympathetic adrenal medulla axis. Psychological distress is more directly related to an animal's environment, which may be barren and impoverished, or other extrinsic factors such as tethering, social separation, or being able to see or smell food but unable to get to it when hungry. Moreover, animals have to be seen as a whole and not as fragmented physiological parts. Thus an animal in pain will also show neuroendocrine responses that can lead to an increased heart rate, and increased corticosteroid levels, for example on the approach of someone who has caused that animal pain in the past such as a vet diagnosing a fracture. Such animals may well show other behaviours related to mental distress such as cowering, vocalisation, even aggression. There is always some species specific element, as well as some individual responses. Other clinical signs of physiological distress might include salivation when experiencing nausea, borborygmi (intestinal rumbling noises) in hunger and gut infections, and for animals kept in impoverished environments, behaviours related to mental distress including stereotypies, and compulsive behaviours such as self-mutilations.

4. In making an assessment of the level of severity, the type of adverse effect and the type of response by an animal have to be considered as well as the intensity and duration of the adverse effect. This raises the practical problem of when an animal is in substantial pain for a few seconds. Does that contravene a severity limit of substantial? What about if the period is 5 minutes or 5 hours, or 5 days after the judgment? Does it depend on the length of time an animal is expected to survive after a procedure? If it is a 100 day survival model, how does the 5 seconds rate as opposed to 5 minutes or 5 hours etc? One has to remember that to the animal itself it makes no difference as it is unable to comprehend what is likely to happen in the future? The same argument applies to substantial distress (is there such a thing?). How does one apply this philosophy to physiological states such as hunger in animals, and whether there is such an emotion in animals that naturally eat continually compared with those that feed once a day or once a week? What about stereotypic behaviours which may occupy 20-70% of an animal's waking time? And what about mental distress such as a lack of, or perhaps an inability to carry out, social behaviours and interactions through being in isolation, or being in groups thereby unable to keep up with the 'herd'?

Video commentary

5. I will list the clinical and behavioural signs seen in the video, with approximate timings (as measured on my video recorder). The caveat to my comments is that the video does not tell us what goes on the rest of the time, and gives no indication of what has been given to the animals, or what has actually been done to them, or what action has been taken by others. Nevertheless, the signs shown by the animals were often outside those normally seen for the species and have to be taken at face value, even if they were only exhibited for a short time.

The importance of recognising normal behaviour

6. Normal behaviour was well illustrated at the beginning of the video in [captive animals](#) (00.89 – 1.28). This forms the benchmark from which deviations from normality should be judged. I find that sometimes people ‘discount’ some observed adverse signs in animals on the basis of: “Well what do you expect after an operation or procedure like that?” This is not the point, in my view. I use ‘normality’ as the basis for deciding the level of severity i.e. the degree to which an animal has changed after the procedure compared with before. If one does not use that pre-procedural behaviour as a benchmark, what other basis can be used?

Husbandry

7. Single housing of marmosets is very stressful as they naturally live in family groups. Keeping them at ground level was also unnatural as they normally escape threats by climbing vertically and the size of the enclosure would drastically restrict their flight distance. The bare tails seen in some of the animals could indicate excessive grooming brought on by the adverse husbandry and boredom resulting in the development of an obsessive compulsive behavioural disorder. Our opinion was that the housing itself imposed moderate distress severity on the animals, and if singly housed this would increase the severity of the distress to substantial (1.79, 2.38) and this is before anything else is done to the animals.

Poor husbandry may decrease model sensitivity

8. It is interesting to look at development of the brain in other species that have been kept in ‘poor’ barren unstimulating conditions where both brain structure and the ability to problem solve or complete tasks have been reduced and impaired. These conditions could mask the diversity of behaviours and that in turn would make these animals a less sensitive model for the human conditions being studied. A behavioural deficit after stroke for example would be more likely to be found when the animals are kept under better conditions that promote behavioural diversity and reduce stereotypy. Thus the science could be improved by better welfare due to better husbandry

Neonatal deaths

9. Neonatal marmosets were apparently allowed to die of starvation (2.95) and, if true, will cause those animals to suffer distress and mental distress from the inner drive and a need to suckle. Young animals have well developed nervous systems, although not fully mature, and it is likely that this drive will be strong. It is also likely they feel nociceptive noxious stimuli more than older animals. However, it is not easy to hand rear animals that are not being cared for by the family group (as happens with triplets and quadruplets), and to intervene too early might prejudice the survival of other neonates. My criticisms here might rest more with the system of breeding but no information is available on that. It may be more humane to identify such abandoned animals as early as possible and to humanely kill them rather than leave them to die.

Hunger and thirst

10. On a similar theme, I would have liked some reassurance that the paradigm to make the marmosets work in the tests was the least harmful way

of making them work. Hunger and thirst are very strong evolutionary motivators and so the associated distress may be significant (3.50). One could also view tests with a positive reward system as being a positive enrichment for the animal. It is the negative operant conditioning paradigm that is of concern, unless it is unavoidable and then that has to be added to the cost of the experimental work to the animals that I would rate as 'moderate'. As marmosets have a relatively high metabolic rate and feed continually during their waking hours to deprive them of both food and water 22/24 would cause considerable distress that should be classified as substantial in our opinion. We assume that food is normally readily available to them during the day? Moreover, if deprived animals were kept in the same room as other animals given food and water, the sight and smell of food in other cages would only add to the mental distress being experienced.

Fear

11. There was a good example of fear (mental distress) in the video in response to a picture of a 'forest' (raised blood pressure, retreating to the back of the cage) and trying to escape by biting at the air holes in a later clip. (4.10, 9.30)

12. It wasn't clear why the training boxes had to be so small? (4.40)

Anaesthesia

13. It did not appear that they were monitoring the anaesthetic level carefully enough so that animals were inadequately anaesthetised for the level of surgical intervention. If they died then that is more likely to be due to either a surgical accident or an overdose of anaesthetic. Death under anaesthesia is not necessarily a welfare issue except that another animal may have to be bred, used and kept in the poor conditions of husbandry. Did they have an intravenous line in, if so why was not an infusion of anaesthetic used? Did they give pre-emptive analgesia, either an opioid or a non-steroidal? Had a good case been made for not using either or both of those strategies, and in the absence of firm data, was the animal or the science given the benefit of the doubt? Primates are good at covering up overt signs of pain, and that is probably why they may suddenly come to light under anaesthesia, they are conscious and stay still until they are really 'hurt'. There was some suggestion that students were given the responsibility for monitoring anaesthesia and that the monitoring apparatus was not functioning properly. If so the surgery should not have gone ahead. How was competence monitored for these persons and what records were kept of the progress of a new licensee? What training programme was in place?

Surgery

14. Scraping the periosteum (skull connective tissue) is painful in animals (sometimes requiring the use of local anaesthesia to supplement the general anaesthesia), and a high level of analgesia may be needed at the time and afterwards. I would have liked some details on the time it took for the animals to return to normal eating habits and to regain their normal bodyweight. The video would appear to have been incorrect in the order of removal of muscle and periosteum and sawing to remove the skull cap. I would hope that the type of saw would be one that oscillated rather than reciprocating, as the latter

would cause a serious rise in temperature that itself would have potentially longer term neurosensitisation.

Post-operative care

15. I agree that this is major surgery and I would have thought that these animals were given good analgesic cover for a sufficient period, saline post-operatively until they were drinking normally, an appetising diet if necessary with medication, and checked last thing at night (6.20). It might have been possible for them to be with another animal (also just operated?) though there is always an objection that one animal may remove the sutures of another. This can be overcome by using subcuticular sutures, but it is not clear what happened longer term after the stitches had been removed and whether this precluded the use of a 'buddy'.

16. There would also be a serious concern over the frequency of observation of these animals and the numbers found dead. What steps were taken to monitor their health, for example using weighing platforms; staff being given time to observe behaviours? The workload on the staff appears to have been very high - 3 technicians for 400-500 animals, and is inadequate to include all the husbandry, post-operative care and monitoring, and record keeping. It would be interesting to see their score sheets?

Photophobia and blepharospasm and grimacing

17. Animals appeared to be responding adversely to light through closing their eyes, screwing up their eyelids and trying to take avoiding action, e.g. lowering head. This could have been due to shining a bright light on their faces, or going from dark to light without a period of adjustment. It is also seen in eye diseases due to retinal sensitivities, and MAY reflect a general sensitivity of the brain as in a headache (00.40, 8.93, 10.20). The grimacing was not normal and may indicate substantial pain. Marmosets like other primates do not normally show signs of pain and therefore it must be quite severe for them to do so.

Inability to climb

18. One marmoset was seen attempting to climb a branch rather unsuccessfully. A failure to do this would frustrate the animal (multiple attempts to climb) and would seriously hinder an animal's attempt to flee a threatening situation, possibly from those with whom it associated its condition. If the animal was in a group, such a handicap may well frustrate it through not being able to play and interact normally with others. This might be rated as a substantial mental harm.

Fitting

19. It is not known whether this is painful or causes mental distress in animals as it may be difficult to determine the degree of consciousness. If the animals are conscious then it must be disorientating at the very least. If, however, muscle spasms occur this could produce post-spasm discomfort. (00.58, 6.72)

Vocalisation

20. On several occasions the animals vocalised perhaps to communicate with others and this looks to be normal but perhaps the type of quality and the duration of the vocalisation is important (6.45, 9.40).

Salivating and vomiting

21. In some of the clips it looks as if the animal's mouth was covered in saliva suggesting to was unable to swallow (6.64) and in others in the behaviour cage it looked as if they were vomiting and were nauseous (9.20). Again a very unpleasant and distressful state and equivalent to moderate/substantial harm depending on its duration.

Social withdrawal and unable to carry out normal behaviours

22. The animals look as if they were withdrawn from a normal animal that would be inquisitive and moving rapidly around the cage (6.85, 7.00). Moreover some animals were unable to climb, an activity that they presumably were able to perform before the procedure. This could lead to frustration, and injury through dropping off the pole (8.32) and would lead to a substantial deviation from normality and, dependent on its duration, there is also the possibility that an animal may harm itself by repeatedly dropping onto the floor and bruising itself.

Depression

23. On occasions animals looked depressed (e.g. 6.86, 9.57). They were not looking inquisitive and alert, the shape and position of the lower lips, and the eyelid aperture looks partially narrowed and curled up making the animal appear very miserable. Again indicative of substantial discomfort and distress.

Circling

24. May well be accompanied by disturbances of the inner ear or one side of the brain affected. If it was the inner ear this is an area known for inducing a feeling of nausea. Possibly also some distress if the animal is trying to get to food for example and cannot reach it and steady itself to eat (8.80, 9.05)?

Assessment of behaviour

25. I disagree with Gill Langley's commentary that the assessment of behaviour is subjective. It needn't be as it can clearly be quantified in both form and duration. However, its interpretation certainly can be subjective, and in many ways (subtle emotions) it has to be so. (9.62)

Staffing levels

26. These seem woefully inadequate and it must have been hard on the staff to cope with this workload as well as the type of work. Animal technicians go into this line of work because they like animals, and the stress on the staff should not be underestimated. Was the staff given every encouragement to care for the animals and to implement enrichment systems and to provide advice during the study without hindrance or humiliation? Were they adequately resourced for out of hours monitoring work?

I hope you find these comments helpful. The above judgments are based on my extensive experience in a range of vertebrate species as well as the experience of others with whom I work. My/our categorisation of the degree of suffering will no doubt be disputed, but detractors really have to justify their potential underestimate of the degree of suffering given the evolutionary background of the species concerned and our experience in zoos and farms. The situation with psychological distress is very different from the situation with pain, as with pain the evolutionary background between species is very similar.

A handwritten signature in black ink that reads "David B. Morton". The signature is written in a cursive style and is positioned above a long, horizontal, slightly curved line that serves as a decorative underline.

David B. Morton
8th November 2003

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