HOME OFFICE

Report of the ANIMAL PROCEDURES COMMITTEE for 1992

CM 2301 LONDON: HMSO

Report of the Animal Procedures Committee for 1992

Presented to Parliament by the Secretary of State for the Home Department by Command of Her Majesty.

September 1993

LONDON: HMSO

Contents

MEMBERSHIP OF THE ANIMAL PROCEDURES COMMITTEE AS AT 31 DECEMBER 1992

LORD NATHAN, MA HON LLD *Chairman*
PROFESSOR MICHAEL BALLS, MA DPHIL FIBIOL
MR EDWARD BERNARD, FIAT
PROFESSOR MARGARET BRAZIER, LLB
PROFESSOR BARRY BRIDGES, BSC MD
DR ROGER BRIMBLECOMBE, PHD DSC FRCPATH FIBIOL
PROFESSOR FIONA BROUGHTON PIPKIN, MA DPHIL
DR HENRY CARTER, CBE MRCVS
PROFESSOR ANTHONY DAYAN, MD FRCP FRCPATH FFPM FIBIOL
MR ROGER EWBANK, OBE MVSC FIBIOL MRCVS
MR CLIVE HOLLANDS
SIR ANDREW HUXLEY, OM FRS
DR SUSAN IVERSEN, MA PHD
DR BRIAN NEWBOULD, BPHARM FPS PHD MCPP
DR ONORA O'NEILL, MA PHD
PROFESSOR LORD SOULSBY, MA PHD DVSM AM DSC MRCVS
PROFESSOR MICHAEL SPYER, BSC PHD DSC
DR ANTHONY SUCKLING, BSC PHD
PROFESSOR PETER VENABLES, BA PHD HON DSC FBPSS

MR P R EDMUNDSON
MR I F ARCHBOLD
} *Secretaries*

ANNUAL REPORT OF THE ANIMAL PROCEDURES COMMITTEE FOR 1992

Submitted to the Rt Hon Michael Howard QC MP, Secretary of State for the Home Department, and to the Department of Health and Social Services, Northern Ireland; July 1993

1 Introduction

1.1 The Animals (Scientific Procedures) Act 1986 regulates *any experimental or other scientific procedure* applied to a vertebrate animal which may have the effect of causing that animal *pain, suffering, distress or lasting harm.* The Act and its main provisions are described in Appendix I.

Functions of the Committee

1.2 The Animal Procedures Committee is an independent statutory body, appointed under sections 19 and 20 of the Act. Under section 20(1) of the Act, the duty of the Committee is to advise the Home Secretary on matters concerned with the Act and his functions under it. The Home Secretary may refer matters to the Committee for consideration but the Committee is free to select subjects for study for itself. The annual reports of the Committee are laid before Parliament by the Home Secretary under section 20(5) of the Act.

Composition of the Committee

1.3 The intention of the Act is that the Committee should reflect a broad range of expertise from across the scientific community, as well as those whose principal concern is for animal welfare. The Committee is also required to have one member who is a lawyer and, since its inception, the Committee has also had at least one member without any scientific or animal welfare connection.

1.4 The membership of the Committee as at 31 December 1992 is shown on page iv. During the year Professor John Ledingham and Professor Thomas Pilkington left the Committee. Professor Ledingham was the first Chairman of the Committee's Research Sub-Committee and helped ensure that the Sub-Committee has been able to play its part in funding the search for alternatives to the use of living animals in biomedical research and safety testing. We should like to record our gratitude to both Professor Ledingham and Professor Pilkington for the contributions they made to the work of the Committee.

Business of the Committee

1.5 The Committee met on ten occasions during 1992, including four special meetings to discuss regulatory toxicity testing, cephalopods and non-human primates. One of these meetings was a visit to an establishment carrying out licensed work, including work on primates and on dogs, and regulatory toxicity testing. 1992 was the busiest year so far for the Committee, during which it commenced the detailed work on its review of regulatory toxicity testing, establishing a new sub-committee for the purpose, completed its consideration of whether cephalopods should be given protection under the 1986 Act (see Chapter 3), and commenced its review of non-human primates.

1.6 This level of activity illustrates the commitment of the Committee to ensure that many issues surrounding the use of living animals in scientific procedures are fully and properly considered. However, this inevitably places additional demands upon Committee members who give freely of their time to carry out the Committee's work and places additional burdens upon the Secretariat. We have commented in previous annual reports about our concern that the level of support provided by the Secretariat should be increased, for example, by freeing the existing staff of the Secretariat as much as possible from other duties within the Home Office. We were pleased to note that the Home Office is seeking to relieve the Secretary of duties not connected with

the work of the Committee and animal procedures more generally, so that more time can be devoted to the work of the Committee.

1.7 The Parliamentary Under Secretary of State at the Home Office with responsibility for animal experimentation, the hon. Charles Wardle Esq MP visited the Committee at one of its meetings. The Committee took the opportunity to discuss a range of issues with him and we are most grateful for the time he took to meet the Committee and discuss its work. The Committee explained that in view of its interest in non- human primates, it had been particularly concerned by allegations made by an anti-vivisection group in a report published in the summer of 1992 about the treatment of primates at a designated breeding and supplying establishment, and at a designated scientific procedure establishment, (see paragraphs 7.12–7.16). The Minister said that he fully shared the Committee's concern about the allegations made and had instructed the Inspectorate to carry out a thorough investigation.

1.8 The Committee discussed with the Minister some of the issues arising from the use of animals in regulatory toxicity testing, which its sub-committee was investigating. The Chairman explained that when action came to be taken as a result of the Regulatory Toxicity Testing Sub-Committee's work, the effectiveness of that action would depend, in part, upon cooperation between the Home Office and Government Departments with regulatory functions as well as the Foreign and Commonwealth Office, as significant progress was only likely to be achieved through concerted international action. We were encouraged that the Minister undertook to use his influence to ensure that any agreed recommendations are implemented. He did however rightly point out that there was a risk that if the United Kingdom, or the European Community, were unilaterally, to consider that particular restrictions on the use of animals in regulatory toxicity testing were justified, and if they sought to impose such restrictions unilaterally the effect might be simply to drive such testing to other countries where the laboratory animal legislation is less strict, or indeed non-existent, and where laboratory animals do not have the same protection in terms of their housing and care and use in procedures.

1.9 The Committee again took the opportunity of the Minister's visit to voice its concern about the level of funding available for the scheme to fund research into ways of reducing, refining or replacing the use of living animals in scientific procedures. We have previously made it clear that this budget needs to be properly safeguarded and increased. The Committee is pleased to note that Government was able to increase the budget for the scheme in 1992/93 and 1993/94. However, a continuing difficulty facing the Research Sub-Committee is the uncertainty about the level of funding which will be available from year to year. The long lead time between advertising for projects and the point at which a research project is started, with the intervening steps of considering shortlisting, assessing and selecting worthwhile projects, the recruitment of staff by the successful applicant and the purchase of the necessary equipment, often all to be undertaken before the start of the academic year, does not fit in well with the Government's timetable for determining the annual expenditure round. Forward planning, including arranging an advertising campaign, is difficult if the amount of money which will ultimately be available is not known. The Minister listened sympathetically to the Committee's concerns. He pointed out that while he could not offer a ready solution, as the problem of uncertainties about future financial provision which is common to all areas of Government activity, he undertook to consider whether there might be ways in which the particular problems facing the Committee's research budget could be alleviated.

Particular issues in 1992

1.10 1992 saw a number of campaigns by groups opposed to the use of living animals in scientific procedures. Most prominent among these campaigns were those by Advocates for Animals and the British Union for the Abolition of Vivisection about non-human primates. More detail of these campaigns is included in paragraphs 7.12 to 7.14.

1.11 Paragraph 1.14 of the Committee's Annual Report for 1991 noted that the fixed dose procedure (FDP), which does not rely on lethality as an end point and resulted

from a British initiative, was to be included in OECD guidelines in 1992 as an alternative to the LD50 test. It will undoubtedly take some time to see whether the inclusion of the fixed dose procedure in OECD guidelines will lead to fewer LD50 tests being carried out, as the FDP has not been included as a preferred alternative and data from LD50 testing may still be required by some regulatory authorities around the world.

1.12 The Committee has also noted a possible further obstacle to a reduction in LD50 testing. While the search for alternatives, not least to the LD50 test, is encouraging, one effect of the many programmes of research into alternatives is that, if further alternatives to the LD50 test are developed and satisfactorily validated they too may be included in OECD guidelines as alternatives to the LD50 test. However, while this might at first sight appear to be a welcome development, it could mean that the LD50 test will continue to be used. Faced with a range of alternatives to the LD50 test, which, like the fixed dose procedure, may be included in OECD guidelines but not be preferred alternatives, regulatory authorities may prefer to continue to expect data derived from the familiar LD50 test. At the same time, companies submitting animal test data to regulatory authorities may understandably choose to supply data which they can be reasonably sure the regulatory authorities will accept, i.e. data derived from LD50 tests. This again points to the need to ensure that the basis on which data derived from alternative tests will be accepted is agreed and widely understood, and that where regulatory authorities have indicated that they will accept data from alternative tests, pressure is brought to bear to ensure that in practice they do so. Individual states have a role to play in monitoring the extent to which regulatory authorities overseas are, in practice, willing to accept data from validated and accepted test methods which do not involve animal testing. We hope that the British Government for its part will use its influence to encourage the acceptance of data derived from alternative tests.

2 Operation of the Animals (Scientific Procedures) Act 1986

Numbers of certificate and licence holders

2.1 During 1992, 11 certificates of designation, 1257 project licences and 2844 personal licences were issued under the Act in Great Britain. Of the project licences, 546 were assessed as being of mild severity; 608 were assessed as being of moderate severity; and 33 were assessed as being of substantial severity. The remaining 70 project licences, where the work was with terminally anaesthetised or decerebrate animals, were unclassified.

2.2 In Northern Ireland, 2 certificates of designation were issued, together with 55 project licences and 69 personal licences. Of the project licences, 17 were assessed as being mild; 34 moderate; and 3 of substantial severity; with one unclassified.

2.3 On 31 December 1992, in Great Britain, there were 347 certificates of designation for scientific procedures establishments; 11 certificates of designation for establishments breeding and supplying animals for use in scientific procedures; 4419 project licences; and 17205 current personal licences.

2.4 As noted in the Committee's annual report for 1991, assessment of the severity banding of any project licence is prospective. It is an estimate of the overall level of suffering likely to occur. Further, it is necessary to distinguish between the overall severity assessment accorded to a project licence and the severity of an individual procedure.

2.5 **The severity assessment of an individual procedure** is defined in terms of the maximum harmful effect which that procedure is likely to cause. It presents an upper limit of what is allowed to be done to an animal or group of animals during that procedure and will be the subject of a condition on the project licence. It is possible that, in the event, none or only a very small proportion of the animals used in that procedure will actually experience severity approaching this limit. This assessment does not take into account the numbers of animals which might experience the maximum severity nor the length of time for which the animal might experience the severe effects. The project licence will normally authorise a range of procedures, each with its own severity limit, and could include any combination of unclassified, mild, moderate or substantial procedures.

2.6 **The overall severity assessment of the project** takes into account the likely adverse effects on all the animals to be used on all the procedures within the project, and therefore takes heed of the number of animals used in each of the procedures, the proportion of these animals which may be expected to be exposed to the upper limit of severity allowed in each procedure, and the duration of the adverse effects upon the animals. The severity assessment of a project licence is an overall assessment of the severity of the component procedures on the project licence. It follows therefore that, for example, a project assessed overall as being of mild or moderate severity may include one or more procedures assessed as being of substantial severity.

2.7 It is important to note that it does not follow that because an individual procedure or a project is assessed as being of substantial severity, substantial suffering **will** necessarily occur. All project and personal licences contain conditions requiring that pain and suffering be minimized and therefore the permitted severity should only be approached when absolutely necessary. In addition, a standard condition on all personal licences requires that any animal in severe pain or severe distress which cannot be alleviated must be humanely killed immediately.

2.8 It is also worth noting that the use or non-use of anaesthetics is not a reliable indicator of severity. In the majority of procedures carried out, anaesthetics are not

used because the procedures themselves are so minor that the administration of the anaesthetic would cause more pain or suffering than the immediate effects of the procedure to be applied.

Annual statistics for 1991

2.9 The Committee wishes to see a continued decline in the use of animals in biomedical research and safety testing. It was therefore disappointing that the annual statistics for 1991, published in July 1992, showed a small increase (one percent) in the total number of procedures started during 1991, although the total was still lower than that for 1989. There were two main causes for the small increase. The first was the increased ability to modify genetic material, which has led to more work in many areas of biomedical science, for example, in providing models of human genetic diseases; further research into normal and abnormal embryonic development; and the production of therapeutic substances.

2.10 The second main cause was the implementation of new rules on the re-use of animals in scientific procedures. The Home Office *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986*, published in February 1990, contains a section explaining in simple terms the otherwise complex provisions of section 14 of the Act, which sets out the conditions under which protected animals may be re-used. It is clear that it took a little while for the clarification in the *Guidance* to take effect which has led to a change in recording practice, resulting in an increase in the number of procedures recorded.

2.11 It is worth noting, however, that despite the small increase in 1991, the long term trend in animal experimentation is still downward and that the total number of procedures started each year has declined by more than 40% over the past 15 years. While the Act has given further impetus to this downward trend, the increased activity in the modification of genetic material referred to in paragraph 2.9 above illustrates that, provided the research in question can be justified under the Act and other relevant considerations are satisfied, it will be permitted. It is worth noting that an overall increase in the use of animals as a result of increased research activity in particular areas of biomedical science is not inconstistent with minimising the use of animals in research and ensuring that they are used only where necessary in properly controlled work.

2.12 Despite the slight increase in the total number of animal procedures started during 1991 the Committee was pleased to note that there was another reduction in the use of animals in the safety testing of cosmetics, a reduction in the number of eye irritation tests carried out on rabbits, a notable drop in the use of higher order primates in particular and a reduction overall in the number of procedures started on all primates.

Re-use of animals

2.13 During 1992 the Committee gave initial consideration to whether there was a case for adjusting the rules on the re-use of animals. This consideration is at an early stage, but were any change to be recommended and adopted it would have implications for the severity assessment of project licences, which would need to include the effects of re-use on the animals concerned. The fundamental principle embodied in the 1986 Act is that the pain and suffering endured by any individual animal undergoing scientific procedures should be kept to the minimum consistent with the purpose of the procedure. This means that no animal should be subjected to pain or suffering through repeated use for different purposes. There is a view, however, that this is unnecessarily restrictive, in that there are situations in which an animal might be re-used without significantly increasing the overall suffering, (however assessed), in situations which at present would require the use of another animal. A change in the strict rules on re-use could thus reduce the overall number of animals used in scientific procedures. However, the Committee is aware that changes to the rules on re-use raises a number of fundamental questions which go to the heart of the purpose of the 1986 Act.

The general question of re-use is one to which the Committee hopes to return in due course.

Project licence applications for animal use in microsurgery training

2.14 Applications for the use of animals (terminally anaesthetised rats) for the acquisition of skills in microsurgery are routinely referred to the Committee for advice. Paragraph 2.28 of the Committee's annual report for 1991 noted that, following discussions with the Presidents of the Royal Colleges of Surgeons, the Home Office had concluded that the use of animals for the acquisition of skills in microsurgery was now justified only in the case of the acquisition of skills in microvascular surgery. As a result, the Home Office promulgated guidance for applicants for project licences for training in microvascular techniques. A copy of that guidance was included in Appendix III to the Committee's annual report for 1991.

2.15 During 1992 six applications for the use of animals in the acquisition of skills in microsurgery were referred to the Committee. All were concerned with the acquisition of skills in microvascular surgery and had been completed in accordance with the new guidance for applicants for project licences for training in microvascular techniques. The Committee recommended that the applications be approved.

Project licence applications involving the use of tobacco

2.16 In line with the normal practice whereby applications for the use of animals in research involving the use of tobacco are referred routinely to the Committee for advice by the Home Office, the Committee considered two such applications during 1992. Although both involved tobacco smoke, neither was concerned with the testing of tobacco or its products.

2.17 The first application was concerned with the development of *in vitro* methods to monitor the genetic damage caused by environmental pollutants in humans. These very sensitive methods rely on detecting specific patterns of DNA and chromosomal damage and, in order to characterise these patterns for occupational and other pollutants, it is necessary to identify and exclude those due to tobacco smoke. The project concerned a one-off *in vivo* study, to allow the calibration for *in vitro* studies of cells in culture, involving the exposure of unanaesthetised rats to cigarette smoke. The applicant considered animal work to be necessary to correlate changes in a full range of tissues with those seen in blood, as the latter are usually the only samples available for human work. The Committee considered that the project was well designed and that the research should give a useful result. It recommended the application be approved.

2.18 The second application involved the use of tobacco smoke as one experimental tool to study lung disease. As a progression from other studies conducted at the establishment, which indicated increased white blood cell sequestration in humans during acute cigarette smoking, the applicants sought authority to expose rats to cigarette smoke. Tobacco smoke studies were also to be performed on human volunteers and patients, and use of animals was sought only for those occasions when the required protocols could not be applied in these circumstances, not because the exposure requirements were extreme, but because the tissue could not be obtained during life. With the exception of the tobacco protocols, the Committee noted that the lung inflammation models were already well established and were known not to give rise to any detectable welfare problems during the timescales applicable to the study.

2.19 In considering the application the Committee had the benefit of a report from an external assessor to whom the Home Office had referred the application. The Committee noted that the programme of research had the potential to underpin new therapeutic strategies to limit damage in serious respiratory conditions and, after considering the application and the external assessor's comments, the Committee recommended that the application be approved, on condition that the rat model proposed should be validated before the applicant proceeded to more advanced studies.

3 Cephalopods

3.1 As reported in paragraph 2.19 of the Committee's Annual Report for 1991, the Committee was asked by the Home Office to consider whether there was a case for extending the controls of the 1986 Act to cephalopods (the octopus, squid, nautilus and cuttlefish). The Committee considered that it would assist its deliberations to have the advice of those with expert knowledge of cephalopods on the central question of whether cephalopods are sufficiently sentient to experience pain and suffering. During the course of 1992 the Committee held special meetings to which experts in the field of cephalopods where invited to give evidence to the Committee. Having considered this evidence and the issues raised the Chairman wrote to the Home Secretary as follows:

"Last year, your predecessor asked the Animal Procedures Committee to consider whether there is sufficient scientific evidence to suggest that cephalopods (the octopus, squid, cuttlefish and nautilus), are sufficiently sentient to merit being brought within the scope of the Animals (Scientific Procedures) Act 1986. I am writing to inform you of the Committee's deliberations.

At present the controls of the 1986 Act extend only to vertebrate species, although at the time of the passage of the legislation it was recognised that there was some doubt about whether cephalopods, which are invertebrates, should also receive the protection of the Act. At that time, it was decided that in view of the lack of definite scientific evidence available to suggest they can experience pain or suffering, cephalopods should not be brought within the scope of the legislation. However, the Government made it clear that, should the Animal Procedures Committee subsequently advise that cephalopods should be brought within the scope of the Act, then the Government would accept that advice.

After the matter was discussed by Parliament and before the matter was referred to the Committee by your predecessor, the question of whether cephalopods used in research should be protected by law has again been considered, perhaps most notably as part of the report of the Institute of Medical Ethics published in 1991. Also during this period the Universities Federation for Animal Welfare published its handbook on the Care and Management of Cephalopods in the Laboratory. Indeed it was following an approach by UFAW, that the matter was referred to the Committee for advice. In considering the issue, the Committee has had regard both to the report of the Institute of Medical Ethics and the UFAW handbook. However, in view of the importance of the issue, the Committee also decided to take evidence from experts in the field of research involving cephalopods, namely Professor Patrick Bateson, Professor Peter Boyle, and Dr Martin Wells, and we are grateful to them for their advice.

The Committee has concluded that the scientific evidence currently available is insufficient to suggest with any certainty that cephalopods can experience pain and suffering. It noted that little more is known now about their sentience than was known when the Act was passing through Parliament. However, a clear majority of the Committee believe that there is sufficient doubt about the sentient status of cephalopods, to give the benefit of that doubt to one species, Octopus vulgaris, *about which most is known and which is of particular concern.*

I would not be giving you a proper indication of the views of the Committee if I did not record that a minority of the Committee would like to see the benefit of the doubt given to all cephalopods, while others do not believe that the protection of the Act should be given to any cephalopods in view of the lack of convincing scientific evidence that they can experience pain and suffering. Nonetheless, as I

said, the majority view of the Committee is that Octopus vulgaris *should be brought within the controls of the Act. You may find it helpful to know of the various considerations which members of the Committee took into account in reaching their views. These are set out in the annex to this letter.*

I should say that I propose that this letter and the annex be published, as is customary, in the Committee's next annual report."

3.2 A copy of the annex mentioned in Lord Nathan's letter is included at Appendix II.

3.3 When the Parliamentary Under Secretary of State, the hon. Charles Wardle Esq MP visited the Committee, he informed it that the Home Secretary accepted the majority opinion of the Committee that the protection of the Act should be extended to *Octopus vulgaris*, a decision which was reported in a reply by Mr Wardle to a Parliamentary Question from Sir John Wheeler JP MP(Westminster North), as follows:

"The Government recently received the views of the Animal Procedures Committee. The Committee has concluded that there is not yet definite scientific evidence to suggest that cephalopods can experience pain or suffering. However, a majority of the Committee believes that there is sufficient doubt about one species of cephalopods, the common octopus or Octopus vulgaris, that the benefit of the doubt should be given to that species and that it should be protected by the 1986 Act.

The Government accepts the majority view of the Committee and agrees in principle that Octopus vulgaris should be included within the definition of "protected animal" for the purposes of the 1986 Act. Work is in hand to give effect to this change.

I have placed in the Library of the House a copy of the letter from Lord Nathan, chairman of the APC, to my right hon. and learned Friend the Home Secretary, giving details of the Committee's considerations."

3.4 This amendment to be made in the law represents a significant change, as the United Kingdom's controls will, for the first time, apply to animals which are not vertebrate. It is also confirmation that the Government is prepared to give due weight to animal welfare concerns in considering the scope of the Act.

4 Research to Reduce, Refine or Replace Animal Procedures

4.1 During 1992, the Committee's Research Sub-Committee met on five occasions. The Chairman was Sir Andrew Huxley, and the other Members of the Sub-Committee were Professor Anthony Dayan, Professor Fiona Broughton Pipkin and Mr Clive Hollands. As in previous years, a Home Office Inspector acted as adviser and the Home Office provided the Secretariat. The Sub-Committee particularly wishes to record its thanks to Dr Donald Straughan, OBE, the outgoing Home Office adviser, for his excellent work and support.

Budget for the scheme

4.2 Following an increase in the research budget to £215,000 for 1991/92, the budget was again increased well above inflation, to £253,000 in 1992/93. It was also decided by the Sub-Committee during 1992 that since research projects could not be financed until part-way through the academic year following the announcement of the Government's expenditure plans in the Autumn Statement, part payment of first year grants could properly be held back until the second year. By this means, it proved possible to fund some six new projects starting in 1992/93, as compared with an average of just four a year in 1990/91 and 1991/92. Details of the projects funded are given at paragraphs 4.6 to 4.11 below.

4.3 Nevertheless, the Committee remains concerned about the level of funding, particularly given the new requirement of most, although not all, universities and some other institutions, to charge overheads of at least 40% of the salary element of projects. Indeed, in view of this factor, and the fact that monies available for new projects in 1993/94 were less than the cost of highly recommended projects brought forward from the previous year but not yet funded, the Sub-Committee decided it would not be reasonable or economic to place advertisements in the scientific press inviting further applications for grants in 1993/94.

4.4 Whilst it is hoped to reinstate arrangements for advertising in the Autumn of 1993, it remains to be seen whether the level of financing available will make this viable, and the Committee's continuing concern in the matter has been conveyed to the Government.

4.5 In making its selection of projects for Home Office grants, the Sub-Committee has determined that it will give preference to projects most likely to result in early and substantial reduction in animal usage and to reducing the severity of procedures, rather than supporting fundamental investigative work. All projects selected for funding are first reviewed by an independent external assessor. All applicants for grants under the scheme are required to undertake that the results of any project funded will be published or otherwise be made generally available. This applies to all applicants, including those from the commerical sector where confidentiality might otherwise be an issue.

New research grants awarded during 1992

4.6 A grant was made to Dr Christine Nicol of the Department of Animal Husbandry, University of Bristol, who had proposed a project to define the most important behaviourial needs and housing preferences of laboratory rodents (primarily mice), to assess the extent to which standard laboratory accommodation meets these needs, and to suggest and evaluate caging modifications in terms of improved welfare, safety, cost-effectiveness and hygiene. Behavioural techniques are being used to assess the respective needs for different resources (eg cage space; density and design; bedding and substrate; co-housing; recreational facilities; and control of light and food). Obser-

vations will be made of behaviour (eg stereotype and aggressive behaviour) in different types of cage.

4.7 A grant was made to Dr A R Peters of Hoechst Animal Health, Milton Keynes, who had proposed developing further *in vitro* tests for assay of clostridial protective antigens (exotoxin and toxoid). If successful, this work will contribute directly to the replacement of laboratory animals in the routine testing of clostridial vaccines. It is intended to develop immunoassays using monoclonal antibodies to replace the present *in vivo* lethality assays in mice. *In vivo* assays are at present used at several stages in the manufacturing process for veterinary clostridial vaccines and in their final potency testing. The applicant's research group has recently successfully replaced the mouse assay by immunoassay for four of the clostridial components of the vaccine.

4.8 A grant was made to Dr D Sesardic of the National Institute for Biological Standards and Control, who intends to validate an alternative *in vivo* assay in mice for botulinum toxin type A using a non-lethal endpoint (local paralysis). The toxin is used therapeutically. At present, significant numbers of mice need to be used in lethality assays, particularly for potency determinations. A secondary and longer term objective is the development of sensitive *in vivo* assays for botulinum toxin. The applicant and her laboratory have an important role in checking potency assays performed by manufacturers and in advising regulatory agencies on the utility and acceptability of such assays and on possible alternative assays.

4.9 Dr P M Edwards of MAFF Central Veterinary Laboratory, is being funded to develop a tissue culture system to detect transmissible spongiform encephalopathy (TSE) infective agents (including BSE). The programme will take a number of years, but if successful will provide a short term assay to replace present tests. The latter involve the deliberate inoculation of significant numbers of animals (mice and other species), and may not produce an answer for several years. The project involves the use of advanced molecular biological techniques, and aims to accelerate the response of cultured cells to TSE agents and to increase their sensitivity.

4.10 A grant has been made to Dr A J Paine of the St Bartholomew's Hospital Medical College, to investigate the mechanisms underlying the well known loss of metabolising enzymes (of the cytochrome P450 super-family) in cell culture. These enzymes play a key role in metabolism and in determining toxicity, so their loss at present limits the use of cultured hepatocytes (liver cells) in toxicology. Molecular biological techniques will be employed to determine if the enzyme loss is related to one or more fundamental causal factors (for example, altered expression of specific transcription factors), and is amenable to correction.

4.11 Finally, a grant has been made to Dr Glynn Taylor of the University of Wales College of Cardiff, who hopes to develop and evaluate alternative animal models of inflammation (arthritis) for use in research with a novel drug delivery system. The alternatives proposed (rat air pouch and rabbit monoarticular arthritis) are of low severity, and have good prospects as replacements for rat adjuvant induced arthritis. The latter is regarded as a severe procedure. The proposed research is expected to be completed within a year, and seems likely to lead to some reduction in the use of rat adjuvant arthritis.

Completed research

4.12 Since the scheme was first introduced in 1988/89, some 9 projects have been completed. The projects are briefly summarised in paragraphs 4.13 to 4.29 below. In the opinion of the Committee, the potential benefits of the various projects in terms of reducing, refining and replacing animal procedures and in improving the welfare of laboratory animals demonstrates the value of the scheme.

Validation of an enucleated eye model

4.13 The purpose of this project, conducted by ICI Central Toxicology Laboratory, was to evaluate the enucleated eye test (EET), an *in vitro* pre-screening test, with a view to reducing the use of living animals in the evaluation of the ocular irritancy of

chemicals. Following a literature review, an inter-laboratory trial was established at three sites, using a wide range of chemicals of known *in vivo* irritancy, and two exposure protocols. A separate study evaluated a tiered *in vitro* test battery (K526 assay and the EET) as a pre-screen to the use of animals for safety assessment purposes.

4.14 In the first study consistency amongst the laboratories was good, with 22 of the 27 substances tested being rated within one *in vitro* category. Use of a 10 second exposure protocol allowed the moderate to severe irritants to be separated from the lesser irritants, and a 60 second exposure protocol allowed clearer discrimination between moderate and mild irritants. In the second study, the *in vitro* test battery predicted severe irritancy with high specificity and sensitivity, potentially allowing a reduction in the number of animals required and refinement of subsequent *in vivo* testing.

4.15 The enucleated eye test is currently being used in three major UK laboratories as part of their step-wise in-house screening of chemicals for ocular irritancy, and is also one of the tests forming part of the joint UK/EC validation study referred to at paragraphs 4.30 to 4.32 below.

Publications

E Whittle, D Basketter, M York, L Kelly, T Hall, J McCall, P Botham, D Esdaile and J Gardner (1992): Findings of an inter-laboratory trial of the enucleated eye method as an alternative eye irritation test. Toxicology Methods 2: 30–41.

J C McCall, P A Botham and R W Lewis (1992): Proceedings of the 3rd CESIO Surfactants Congress (London): 170–178.

Assay of pyrogens measuring cytokine production in vitro

4.16 This project was established at the National Institute for Biological Standards and Control to develop, as an alternative to the *in vivo* rabbit pyrogen test, a novel *in vitro* test to screen parenterally administered pharmaceutical products for pyrogenic contamination, based on the detection of Interleukin-6 (IL-6) in a monocyte culture system. This project formed part of a longer study funded by several sponsors, and a number of different objectives were pursued. The long term stability of the MONO MAC 6 cell line was investigated, the IL-6 immunoassay was improved, and the system was then applied in practical tests on batches of pharmaceutical materials.

4.17 Publication of the results attracted much attention, and production of the reagents is being scaled up, both to meet local demand, and also to provide reagents for other control authority laboratories in Europe and North America for validation and routine product screening. The NIBSC group are undertaking a project investigating the use of the test to screen other parenteral pharmaceutical products, including vaccines, though the development of a practical testing kit remains a long term aim.

Publications

Y S Taktak, S Selkirk, A F Bristow, A Carpenter, C Ball, B Rafferty and S Poole (1991): Assay of pyrogens by Interleukin-6 Release from monocyte cell lines. Journal of Pharmacy and Pharmacology 43: 578–582.

Alternative potency tests for acellular pertussis vaccines

4.18 The purpose of this project, conducted by the Public Health Laboratory Service, was to study the adherence of *B.pertussis*, the organism which causes whooping cough, to mammalian cell cultures, and the ability of immune serum to block the phenomenon. The intention was to consider if these phenomena could be exploited to produce a milder alternative to the mouse intracerebral challenge test and murine respiratory infection assay currently used in the potency testing of pertussis vaccines. The ability of *B.pertussis* to adhere to vero cells was studied, as was the ability of

immune serum from animals successfully vaccinated with various pertussis antigens to prevent adherence. This involved *in vivo* vaccination of mice, with the degree of protection being estimated *in vitro* using serum from the animals. The same range of antigens were evaluated for their ability to confer *in vivo* protection as demonstrated by the murine respiratory infection assay.

4.19 The study showed that the ability of several *B. pertussis* antigens to protect mice against lung colonization correlated with their ability to raise murine antibodies inhibiting the adhesion of the bacteria to vero cells. Further work demonstrated that bacterial fimbriae play a key role in adhesion of *B. pertussis* to the nasal mucosa of infant mice and to the tracheas of adult mice and baboons but *not* to vero cells. The similarity between protection against murine lung colonization and inhibition of adherence to vero cells suggests that this novel test system, or a similar system, could play a useful role in future vaccine potency testing, and, in addition to incorporating methodological advantages, would allow for fewer animals to be used.

4.20 Details of the test system have been published and groups involved in vaccine development as well as regulatory bodies are aware of its existence.

Publications

A Robinson & S G P Funnell (1992): Potency testing of acellular pertussis vaccines. Vaccine 10, 139–141. A Robinson et al (1990): Structure-function studies of B.Pertussis fimbriae: Proceedings of the 6th International Symposium on Pertussis, Publication Number (FDA) 90–1164 (1990), p.126. S G P Funnell & A Robinson (1991): Adhesion of B. Pertussis. Journal of Medical Microbiology, 35, 181–182.

Fish cell cultures for toxicity assessment

4.21 The purpose of this programme of work, which was carried out at the SOAFD Marine Laboratory, Aberdeen, was to develop the use of fish gill cell cultures for the *in vitro* toxicity assessment of water-borne toxicants. Cell lines which retained specialist gill cell functions would be more relevant in this field than the currently available cell cultures which have few tissue-specific functions, and might allow screening programmes not requiring the use of fish for LC50 studies. There were four components to the study, which began with attempts to obtain primary cultures from fish gill cells. It was intended to develop cell lines from such cultures, and to develop methods for monitoring cell injury and mortality in response to toxicants in those cell culture systems. Once these were established, the results were compared with established *in vivo* tests. The work confirmed the principle that cell lines which have retained gill cell function are suited to assessing water borne toxicants, but highlighted current technical limitations to the ability to generate continuous cell lines which preserve gill cell functions.

The use of in vitro assays for the potency testing of rabies vaccines

4.22 This project, which was conducted at the National Institute of Biological Standards and Control, was concerned with the evaluation of single radial immunodiffusion (SRD) *in vitro* assays of glycoprotein antigen for the standardisation of rabies vaccines, as a possible alternative to the *in vivo* NIH mouse protection test which requires both the use of animals and live virus. To this end, it was essential to show a correlation between vaccine efficacy, as measured by the current *in vivo* test, and its glycoprotein antigen content as determined by SRD. Studies were carried out to identify storage conditions and treatments which might result in a reduction in the mouse *in vivo* potency of a vaccine, but not its glycoprotein content. In addition, collaborative studies under the auspices of the World Health Organisation were undertaken to evaluate batches of rabies vaccines for human use by both *in vivo* and *in vitro* assays.

4.23 Although regulatory bodies have yet to accept this as an alternative assay method, it has the potential for more immediate use by individual manufacturers in assaying the consistency of production of successive vaccine batches.

Publications

Morag Ferguson and Alan Heath: Report of a Collaborative Study to Assess the Determination of Glycoprotein Antigen Content of Rabies Vaccines for Human Use. Biologicals (1992) 20, 143–154.

A replacement for the clostridium chauvoei vaccine potency test

4.24 The objective of this study, by Wellcome Research Laboratories, was to develop and validate a serological test for potency of *Cl. chauvoei* vaccines which would establish the identification and measurement of specific protective antibodies in vaccinated animals and might replace the guinea pig challenge model currently used. Hybridoma lines were developed to produce monoclonal antibodies (MCAbs) against antigens isolated from *Cl. chauvoei,* and ELISA assays were developed to confirm their specificity to this organism. The antibodies were screened for their ability to confer passive immunity to the organism in an animal model, and the relevant antigens were characterised. An assessment is under way of the relationship between the level of circulating antibodies to these antigens in vaccinated animals, and vaccine potency as established by the conventional challenge test.

4.25 The emerging technology may have the potential to be developed to detect potentially subpotent batches of *Cl. chauvoei* during vaccine production. The work is expected to be published once the results have been formally evaluated.

Development of a recombinant vaccine against infectious bursal disease

4.26 This project, the result of a collaboration between the AFRC Institute for Animal Health and Pitman-Moore, was aimed at producing a recombinant vaccine against Infectious Bursal Disease Virus (IBDV) in chickens which would dispense with the current vaccine manufacturing requirement to use tissue from a large number of chickens deliberately infected with the virus. The aim was to engineer and evaluate the use of fowlpox virus expression of IBDV antigens as a recombinant vaccine. However, as recorded in paragraph 4.11 of the Committee's report for 1991, this work was overtaken by the development of other vaccines, calling into question the viability of the project and the Home Office withdrew funding after the first year.

Publications

C D Baylis, R W Peters, J K A Cook, R L Reece, K Howes, M Binns & M E G Boursnell (1991): A recombinant fowlpox virus that induces protection against mortality caused by the virus. Archives of Virology 120, 193–205.

Development of in vitro assays for neurovirulence testing of live polio vaccines

4.27 This study, conducted by the National Institute for Biological Standards and Control, was aimed at developing *in vitro* screening tests which might distinguish safe from unsafe vaccines on the basis of molecular differences in the genome of the safe attenuated forms and the unsafe "wild" varieties of the virus. The intention was to develop various methods of molecular analysis, based on known differences between the wild and attenuated strains and to measure the risk from wild type virus strains in batches of live polio vaccine. Taken to a successful conclusion, new methods could avoid the need to use several hundred non-human primates each year for *in vivo* screening of live polio vaccines.

4.28 Results suggest that *in vitro* methods have the potential to distinguish between wild and vaccine strains, even though none of the methods and reagents developed and evaluated to date have immediate practical application.

Housing and Care of Primates

4.29 This project, conducted with the joint support of the Bill Hiddleston Memorial Award Fund, Laboratory Animals Ltd, the Home Office, the RSPCA and Glaxo Group Research Limited, sought to assemble information from Brazil, the Philippines, the USA, the Netherlands and Scotland on the housing and care of primates, in the hope of contributing to the care of primates in the United Kingdom. The work, which is expected to be published shortly in "Laboratory Animals", provided useful insights into a number of aspects of primate husbandry, including housing conditions, captive breeding systems, dietary requirements, capture from the wild and supply and transportation.

Other work of the Research Sub-Committee

4.30 Progress has continued on setting in hand the joint UK/EC validation study of alternatives to the standard Draize eye test, as described in paragraphs 4.14 to 4.16 of the 1991 Annual Report. Joint finance is being made available by the European Commission, and, in terms of staff and resources, by the Home Office, the Fund for the Replacement of Animals in Medical Experiments (FRAME), the University of Nottingham, and participating laboratories in the UK (ICI, Unilever and Shell), other EC countries, the United States and Japan.

4.31 The Committee, which continues to give its full support to the project, was represented at the preparatory conference held at the Home Office in October 1992 by Sir Andrew Huxley, Professor Michael Balls and Professor Anthony Dayan. The meeting was part-financed from the Research Sub-Committee budget.

4.32 The Conference agreed to press forward with the validation study, and detailed preparations are now under way. The meeting brought together representatives from the European Commission, EC Member States, the OECD, and North America in discussions on the UK/EC proposal for an international study of nine potential alternatives to the Draize eye irritancy test. The study will involve forty laboratories in nine countries testing some sixty or seventy chemicals. A management team of four was established to organise the project and the cost of the study had been estimated at £1.4 million. The timetable for the study was that work would begin in March 1993, and it was intended that the preliminary analysis of the results would be available by the end of 1993. The final report would be produced by March 1994. The Committee is very encouraged by the progress which has been made and the level of co-operation shown by all those involved. The project is likely to be the best planned study ever undertaken into the subject.

5 Infringements

5.1 The Committee is continuing the practice established in previous annual reports of noting the number of infringements against the Act and licence conditions issued under it during the year. These statistics had previously been reported only in the annual volume of *Statistics of Scientific Procedures on Living Animals, Great Britain.*

Number of infringements

5.2 In 1992 there were 11 infringements resolved. In one case the personal and project licences were revoked by the Secretary of State. In one other case the project and personal licences were surrendered for revocation by the offenders before any action could be taken by the Home Office. A case is determined when the Home Office has considered all the relevant facts, is satisfied that a breach of the Act or of licence conditions has occurred, and has written to those concerned setting out what action it proposes to take. Some cases decided during the year will have been reported in the previous year and some cases reported towards the end of the year may not be determined as infringements until the following year. The time taken to determine a case depends upon its nature. In general, straightforward cases where it is clear that there has been an infringement, will be determined more quickly than more complex cases, for example, where there is a dispute about the scope of a project licence.

5.3 As in previous years, the nature of the infringements varied from the relatively minor and technical to the more serious. The range of action available to the Home Office in dealing with infringements is included in Appendix III.

5.4 A summary of each infringement where a decision has been taken is reported to the Committee in an anonymised form. The Committee has previously expressed its concern about the extent to which infringements have resulted from a lack of understanding by those involved in animal procedures of the system of controls established by the Act. While it is encouraging that, in general, infringements do not appear to be the result of deliberate disregard of the controls of the Act, the Committee finds that unfamiliarity with, or ignorance of, the system of controls are poor excuses for breaches of the controls which have been in operation for over six years. While not every person who infringes will have been involved in regulated animal research for that period, it should be clear by now that there is a strict system of controls on the use of animals in scientific procedures. The controls are designed to ensure that animal procedures are properly conducted, and although the sort of technical infringement which occurs from time to time only rarely has adverse implications for animal welfare, the Committee is increasingly of the view that those who inadvertently breach these controls should expect to be more harshly dealt with.

5.5 The Committee accepts that, in deciding what action should be taken in a particular case, the Home Secretary must judge each individual case on its merits and that his decision must be reasonable. Part of the test of reasonableness will inevitably include the consideration of how similar cases have been treated in the past. However, the Committee has made it clear to the Home Office that, within these constraints, it would hope that less weight will be placed on excuses of unfamiliarity with, or ignorance of, the controls.

5.6 During 1993 the Committee will be considering the Home Office's policy on handling infringements under the Act more generally, and the Committee will take that opportunity to re-emphasise its concern about the handling of inadvertent infringements.

5.7 Paragraph 3.9 to 3.11 of the Committee's annual report for 1991 reported the very serious case involving a series of infringements in an institution. The infringe-

ments included the performance of unauthorised surgical procedures on pigs, and instances of unauthorised re-use. As recorded in the annual report for 1991, the matter was referred to the prosecuting authorities who, in the event decided not to bring proceedings. Paragraph 3.11 recorded that the Home Secretary then decided that administrative action should be taken against the project licence holder and personal licensee involved in the case. The Home Secretary decided that, in view of the seriousness of the infringements, the licence of the personal licensee and the project licences of the project licence holder, together with his personal licence should be revoked. Under section 12 of the Act, where the Secretary of State proposes to revoke a licence, he is required to serve upon the licence holder a notice of his intention to do so. The Act gives a licence holder who has been so notified the right to make written and, if desired, oral representations to a person appointed for that purpose. In the case in question, the personal licensee accepted the Home Secretary's decision to revoke his personal licence. However the project licence holder decided to exercise his right under section 12 of the Act to make representations to a person appointed by the Home Secretary. At the time of writing, a legally qualified independent person had been appointed by the Home Secretary to consider the representations being made by the project licence holder against the Home Secretary's decision to revoke his project licences and his personal licence.

6 Education and Training of Project and Personal Licence Holders

6.1 . Paragraphs 2.20 to 2.25 of the Committee's annual report for 1991 drew attention to developments in the education and training of project and personal licence holders. The importance of pre-licensing training in fitting applicants for their future roles and responsibilities under the 1986 Act has long been recognised and many establishments already have formal training programmes. This is in line with the responsibility of holders of certificates of designation to take steps to provide such training as is necessary for all licensees carrying out regulated procedures. A result of the work which has already taken place is that there is a ready and increasing pool of expertise. The occurrence of inadvertent breaches of the controls on the use of animals in scientific procedures, referred to in paragraph 5.4 above, highlights the importance of proper training for those involved in such work.

6.2 The Home Office published a discussion document in 1991 on the appropriate education and training of those seeking licences under the 1986 Act. The proposals had been drafted by the Home Office Inspectorate and received a large measure of support. The Home Office subsequently issued a statement of policy to all certificate holders in which these original proposals for a modular training scheme remained essentially unchanged. A copy of the statement of policy is included in Appendix IV.

6.3 From 1 April 1994, applicants for personal licences will be required to have completed successfully an accredited training programme. In addition to this, from 1 April 1995, those project licence applicants seeking a project licence for the first time will require further pre-licensing training to be acquired from accredited training programmes. These proposals will ensure a greater consistency in the formal training of applicants for both personal and project licences. All training programmes for applicants for personal and project licences are to be accredited under a scheme recognised by the Home Office. Accreditation will be increasingly important given the diversity and increasing number of courses which are already available. Accreditation seeks to achieve common and high standards for licensee training and should facilitate free movement for licensees within the United Kingdom and Europe, as well as ensuring high standards in the use of animals for scientific procedures. The Committee welcomes the action being taken to introduce formal training requirements.

7 Non-Human Primates

7.1 The Committee's annual report for 1991 recorded the Committee's intention to undertake a review of the use of laboratory primates. The 1986 Act contains a provision requiring special justification for the use of primates in research reflecting concern about the need to use such animals in biomedical research and safety testing. The Committee itself has long had an interest in the use of primates in scientific procedures. Indeed all project licence applications involving procedures of substantial severity on non-human primates are referred as a matter of course to the Committee for advice. During 1992 no such applications were received.

7.2 The Committee's decision to review this area as part of its continuing interest in the subject of laboratory primates follows on from the Committee's consideration of the FRAME/CRAE proposals in their 1987 report, T*he use of Non-Human Primates as Laboratory Animals in Great Britain* and the then Home Secretary's response to them, and the RSPCA/FRAME report of 1990, *An RSPCA/FRAME Survey of the Use of Non-Human Primates as Laboratory Animals in Great Britain in 1984–1988.*

7.3 The Committee endorsed the concern for non-human primates which lay behind the preparation of the FRAME/CRAE report. The Committee considered that report at the time and recommended that the Home Office accept and implement the majority of the recommendations in the report and the then Home Secretary, accepted the Committee's recommendations.

7.4 As one of the first steps of the Committee's latest review, the Committee will be looking at current practice in the light of the Home Office's response to the 1987 report, and the concerns raised in the 1990 report, together with the *Guidance* on the operation of the 1986 Act in so far as it relates to primates. The Committee has also decided that it will examine current use of primates as part of the background to its work. The Committee will be paying particular attention to the way in which the benefits/suffering consideration of section 5(4) of the Act operates in relation to applications for project licences for work involving non-human primates. As part of this consideration the Committee is looking at whether it is desirable, and if so, whether it is possible within the legal framework of the Act to consider the cost or suffering side of the equation in the wider context to include, for example, the sourcing of the animals. The Committee also has it in mind to pay particular attention to procedures involving long periods of restraint. The Committee has established a small working group to take the review forward.

7.5 It is clear to the Committee that the review needs to be carried out in close consultation with the Inspectorate, which shares the aims of the Committee. The Committee has also requested that it should be made aware by the Home Office of all project licences which are issued for use of non-human primates. The small working group established by the Committee will, in the first instance, examine the project licence applications which have been granted and report to the Committee on a regular basis. The report will indicate the scale, species used, severity of the procedure, and the purpose and justification of the research.

The holding of larger primates

7.6 Paragraph 7.8 of the Committee's annual report for 1991 noted the particular concern which the Committee has felt for some time about the designs and sizes of cages in which larger non-human primates are kept. In 1989 the Committee were advised of the findings of a survey carried out by the Inspectorate during 1988 into the conditions under which larger primates were held for regulatory procedures. During

1992 the Inspectorate carried out a further review of establishments using larger primates which has enabled an assessment to be made of progress achieved in improving facilities since the earlier review.

7.7 Overall the review revealed a number of encouraging developments. There has been a move away from the use of wild-caught primates towards captive bred animals. In 1988, only 35% of the large primates held were captive bred. By 1992 this figure had risen to 80%. This is a welcome improvement although it has to be noted that a proportion of the captive bred animals will have been captive bred overseas in conditions which may well fall below standards required in this country. The Inspectorate's review has also revealed a significant change in practice in husbandry systems. It is now the norm for larger primates to be grouped or pair-housed, reserving single housing for those occasions when such housing is dictated by the needs of the procedure, for veterinary reasons, or because of demonstrated incompatibility between an individual and its mate or group. For this reason most establishments still retain a need to have some single housing. In 1988, 95% of establishments used single housing for large primates and 43% used it exclusively. By 1992, 77% of places used single housing but only 20% used it exclusively. In 1988, only 28% of the places regarded group or paired housing as the norm, while by 1992 this proportion had risen to 60%.

7.8 The Committee has been keen to see efforts made to improve the environmental enrichment of primates. The Inspectorate's review showed that there have been substantial improvements in the two forms of environmental enrichment which current opinion suggests are of most importance to captive primates. These are social contact with peers and the provision of foraging substrate. Social groupings and pairing increased from 54% of establishments in 1988 to 74% of establishments in 1992. The corresponding increase in the provision of foraging substrate was from 44% in 1988 to 74% in 1992. These improvements are encouraging, but the Committee expects that efforts will continue to increase the provision of environmental enrichment measures for all primates.

7.9 One area of continuing concern to the Inspectorate and the Committee is the cage sizes in single caging only situations for larger primates. Because 60% of establishments now use group or pair housing as their norm, the dimensions of single cages cannot accurately represent the situation concerning overall compliance with the Home Office *Code of Practice*. The dimensions of single caging do of course concern the individual animal so confined. Although single caging is quantitatively less important than in 1988, the Committee commends the Inspectorate's intention to investigate further those instances where the cages do not fully meet *Code of Practice* standards.

7.10 The Committee commends establishments holding larger primates for the improvements they have made, and the Inspectorate for the pressure for improvements which it has brought to bear.

7.11 The Inspectorate's review identified a number of areas where there is a need for further action. There remain particular problems which can arise with contract research establishments. There is a need for continued pressure on such establishments and their sponsors to introduce paired or group housing for primates involved in regulatory toxicology. Secondly, the Inspectorate intends to carry out further inquiries into the validity of the reasons behind the use of single caging by choice in a small number of establishments where the justification of this seems most open to question. It will also continue to encourage enlightened innovation in the provision of environmental enrichment. The Committee endorses these plans for further action by the Inspectorate.

Campaigns about laboratory primates

7.12 The whole issue of laboratory primates was brought into sharp focus at the end of 1991 and during 1992 by two campaigning organisations.

7.13 At the end of 1991, Advocates for Animals sent to the Home Office the first part of a three part report alleging that the controls on the use of living animals in research had not been properly applied in respect of the use of non-human primates. The report was based on a sample of 13 published medical research papers covering experimental work carried out on non-human primates published between 1987 and 1991, although

most of the research work had been carried out before the 1986 Act had come into force. The report asserted that much of the likely benefit was not sufficient to justify the use of primates; that the knowledge gained was insignificant; that some of the research undertaken duplicated other research; that some of the research was of poor quality and in some instances that the animals died after protracted illness. Part I of the report also made a number of recommendations concerning laboratory primates, and proposed changes to the operation of the 1986 Act. Parts II and III made available in 1992 followed a similar line to Part I. Part II contained criticisms of research describing 16 published papers and Part III criticised research in five published papers. The criticisms were considered thoroughly by the Home Office. Its investigations concluded that the allegations could not be substantiated and detailed responses were made to Advocates for Animals. The Committee was kept fully informed, and saw the full text of the criticisms made and the Home Office's response. The Committee did not consider that it was its role to comment on criticisms made of individual pieces of research although it did note that a published paper may not always contain all the detail necessary to enable a fully informed opinion on the value of the animal work to be made. Rather the Committee decided that the general questions raised by the report should be taken into account in its review of laboratory primate use, (see paragraphs 7.1 to 7.5 above).

7.14 Late in 1992, a two part campaign was also launched by the British Union for the Abolition of Vivisection. The first report concerned the international trade in primates for research and, *inter alia*, criticised the conditions in which primates are trapped, bred, transported and cared for during their journey from the place of capture to the laboratory. The report called for action by the Home Office and by the Department of the Environment, (which is the Department responsible for the Convention on the International Trade in Endangered Species). Although activities outside the United Kingdom are not strictly within the purview of the Committee it is not unreasonable that the Committee should have an interest in questions of the welfare of animals destined for laboratories in this country. The Committee had already identified the question of the sourcing of non-human primates as one matter which might be included in its review of non-human primates to which it had already given consideration before the BUAV campaign was launched.

7.15 The second of the two reports submitted by the BUAV was concerned with the care and treatment of primates in this country; the adequacy and enforcement of existing standards of primate housing and care; the licensing of scientific procedures involving primates; and the operation of the 1986 Act in respect to the special position accorded to primates in the Act. The second report contained very serious allegations against Shamrock (Great Britain) Ltd which operates as a primate breeding and supplying establishment, and Hazleton UK, designated under section 6 of the 1986 Act as a scientific procedure establishment. The BUAV also made available video material taken at the breeding and supplying establishment. The Committee was extremely concerned at the allegations made against the establishments. The Committee shared the understandable concern felt by many members of the public who saw the video material when it was broadcast on television. The Home Office also took the allegations very seriously and Home Office Ministers directed the Inspectorate to carry out an investigation. The Committee was kept fully informed of the Inspectorate's investigation, the thoroughness of which it fully commends, and had the opportunity to comment on its findings before the Inspectorate reported to Home Office Ministers. In the light of those findings the Home Office took firm action. In response to a Parliamentary Question from Sir John Wheeler JP MP (Westminster North) the hon. Charles Wardle Esq MP replied:

> *"The Home Office Animals (Scientific Procedures) Inspectorate has investigated the allegations contained in written and video material sent to the Home Office by the BUAV, in respect of the treatment of animals at Shamrock Farms and Hazleton UK. The results of that investigation have been reported to the Animal Procedures Committee (APC) and to me, and I have had the benefit of the APC's comments on those conclusions.*
>
> *The investigation found evidence of poor standards of care and handling at Shamrock Farms, and a lack of effective managerial control. Insufficient attention was paid to the maintenance of a regime in which animals are treated at all times*

with due dignity and respect, and in which the physical and emotional needs of the animals are given proper emphasis. My conclusion is that poor technique and over-forceful handling may have resulted in avoidable stress and possible suffering.

I have concluded that these findings represent a significant failure on the part of the Named-Day-to-Day Care Person at Shamrock, and I have directed that Shamrock's Certificate of Designation be amended to appoint a new person to that role.

Other measures are being taken in the light of the report:

i. I have concluded that new and existing staff at Shamrock should be trained in the wider ethical and legal issues associated with animal use: the nature and content of that training will be agreed between the management and the Home Office Inspectorate.

ii. Some aspects of the accommodation at both Shamrock and Hazleton fall short of desirable standards, and programmes of improvement and replacement of facilities have been developed or accelerated.

iii. Another member of staff at Shamrock will be excluded from duties involving any further animal contact until he has satisfactorily completed the retraining already mentioned.

I am satisfied that other allegations are misconceived, may be based on a misinterpretation of legitimate procedures or are incapable of being proved one way or the other. All staff in the two establishments have been made aware, however, of the importance of the proper treatment of animals in their care, and the seriousness with which alleged breaches will be regarded.

The response which is being made to problems uncovered as a result of these allegations is firm, fair and designed to deal effectively with public concerns. I recognise that the use of primates in research causes particular anxiety, and I am pleased that the APC is considering the general questions raised. I look forward to hearing their conclusions."

7.16 Criticisms made by the BUAV of specific programmes of research involving primates were still under consideration by the Home Office when the year ended.

8 Regulatory Toxicity Testing

8.1 Paragraph 5.4 of the Committee's annual report for 1991 recorded that the Committee had decided to appoint a sub-committee to consider the many issues arising from the use of living animals in regulatory toxicity testing. The paragraph also set out the sub-committee's remit. During 1992 the Regulatory Toxicity Sub-Committee met on 8 occasions including one visit to a contract research establishment. The Chair was Dr Onora O'Neill, and other members of the sub-committee were Professor Michael Balls, Professor Margaret Brazier, Professor Barry Bridges, Professor Anthony Dayan, Dr Brian Newbould and Dr Anthony Suckling. An Inspector acted as adviser and the Home Office provided the Secretariat.

8.2 The Sub-Committee decided that, in view of the complexity and technical nature of much of the subject matter, it should, as a first step, seek evidence from those with special knowledge in the field. The Sub-Committee invited a wide range of people to meet it and discuss general and some particular issues. In seeking this input, the Sub-Committee took evidence from academic toxicologists, those working in industry, UK regulators and those who co-ordinate or represent the United Kingdom Government's position in discussion with other countries and international organisations, animal welfare interests, and those with previous experience in the area of toxicity testing. The Sub-Committee is grateful to all of those who gave evidence which has provided useful background for the Sub-Committee's deliberations.

8.3 The Sub-Committee has considered a large amount of background material and listened to a range of views on the use of animals in regulatory toxicity testing. The Sub-Committee intends submitting its report to the main Committee during 1993.

9 The Use of Animals in The Safety Testing of Cosmetics

Developments in Europe

9.1 Previous annual reports of the Committee have contained detailed discussion of the use of living animals in the safety testing of cosmetics. Such use of animals remains a matter of public concern, even though the use of animals for this purpose is at its lowest level for very many years. Cosmetics testing which accounts for a fraction of one per cent of all animal testing in this country fell by some 40% during 1992. Over 80% of the testing was carried out on ingredients, and only one beauty preparation finished product was tested. Most testing was carried out for companies overseas, mainly in Europe.

9.2 The Committee notes that the United Kingdom has been a moving force in Europe in seeking the setting of targets for the phasing out of certain forms of animal testing. During 1992, the hon. Edward Leigh Esq MP, the then Minister for Consumer Affairs, called on industry to set 1998 as a target date after which it will no longer be necessary to use animals in skin and eye irritancy tests. (Although the Home Office is responsible for animal scientific procedures matters, the Department of Trade and Industry is responsible for consumer safety matters and discussions in Europe on the EC Cosmetics Directive.) The Government targeted these skin and eye irritancy tests because it is generally agreed that progress in finding replacements seems most likely to be reached in these areas.

9.3 In the Committee's last annual report we recorded our concern about the changes which had been proposed to the Sixth Amendment to the EC Cosmetics Directive 76/768/EEC, which has a number of purposes, but one effect of which would have been to increase the amount of cosmetics animal testing. As noted in paragraph 6.2 of the Committee's last annual report, the European Community was persuaded that it was not necessary to test existing cosmetic ingredients on animals unless toxicologists have particular concerns about them. The original proposals from the European Commission would have required the testing of existing cosmetic ingredients which would have led to a considerable increase in animal testing. In addition, it has been agreed that new ingredients will not have to be tested if this is unnecessary, for example, in the case of bland natural ingredients.

9.4 At the end of 1992, after protracted negotiations, the United Kingdom Government secured political agreement on a common position on the Sixth Council Amendment. The position adopted by the Consumer Affairs Council included a ban on the use of ingredients which have been tested on animals after 1 January 1998, although there is provision for the Commission to propose the postponement of the ban if validated alternative testing methods are not available by then.

9.5 At the same time work to make progress on validation of alternatives to certain animal tests is continuing. For example, as referred to in paragraphs 4.30—4.32, there is a joint EC validation study of alternatives to the Draize eye test, resulting from a UK initiative. The final report of the EC study is expected to be received and promulgated to regulatory bodies well in advance of the 1998 target date for the replacement of such tests.

Project licence application

9.6 All project licence applications involving the use of animals in the safety testing of cosmetics are referred to the Committee routinely for advice. During the year one application for renewed authority for the testing of cosmetics was referred to the Committee. The application was concerned with the testing of cosmetics ingredients

only and not finished products. The applicant wished to carry out animal work to provide toxicological data for the base set data for chemicals required by regulatory authorities for both the manufacture and transportation of new chemicals. The company in question had extensive experience and background data in the field of the development and testing of cosmetics enabling them to restrict animal testing to a small number of novel ingredients. The company expected that the number of new ingredients tested each year would be very low and anticipated that very few tests would be carried out over the five year life of the project licence. The Committee noted that the number of animals per procedure complied with the OECD guidelines for the testing of chemicals. Having considered the application carefully the Committee recommended that the application be approved.

10 Forward Look

10.1 The Committee intends to continue its increasingly pro-active approach to issues arising from the use of living animals in scientific procedures. Although some of its business results from matters referred to it by the Home Secretary, for example its work on cephalopods, the Committee is keen to continue examining issues of its own choosing. This fully accords with the functions of the Committee as set out in section 20(1) of the Act. The Committee is grateful to the Home Office and its Inspectorate for the assistance given to it.

Regulatory Toxicity Testing

10.2 During 1993, the Committee hopes to have received and considered the report by the Regulatory Toxicity Testing Sub-Committee. Depending upon any findings and recommendations made by the Sub-Committee and agreed by the Committee, recommendations will be made to the Home Secretary. We do not see this as the end of the process. As noted in Chapter 8, the issue of the use of living animals in regulatory toxicity testing is a complex one. The report of the Regulatory Toxicity Testing Sub-Committee will provide the foundation for further work in this area as the Committee monitors how any agreed recommendations are implemented. This is likely to be a continuing task for the Committee.

Non-Human Primates

10.3 As Chapter 7 on non-human primates makes clear, the Committee maintains its continuing interest in the operation of the special controls relating to the use of non-human primates in research, and the housing and care of laboratory non-human primates. It is likely that the Committee's investigation of these issues will develop into a rolling programme of review, with specific issues being examined by the Working Group on non-human primates which the Committee has established.

Animal Technicians

10.4 Chapter 6 of this report deals with developments in introducing requirements for formal training for project and personal licensees before licences are granted by the Home Office. However, there is another group of people who also play an important part in animal care and use. Clearly it is important that those who are in day to day contact with laboratory animals are fully competent to carry out their responsibilities in respect of the animals. Much work has already been done in this area by the Institute of Animal Technicians in the provision of appropriate syllabuses, examinations and qualifications. The Committee intends, in due course, to give consideration to whether, and if so what, measures might be taken to ensure that all designated establishments make full and appropriate use of training opportunities available and so ensure that all animal technicians are suitably trained for the duties allocated to them.

Appendix I

GENERAL SYSTEM OF CONTROL UNDER THE ANIMALS (SCIENTIFIC PROCEDURES) ACT 1986

Introduction

1. The Animals (Scientific Procedures) Act 1986, which came into force on 1 January 1987, replaced the controls which had operated under earlier legislation with a system of controls on scientific work on living animals which includes the need for both the researcher and the project to be separately licensed; a requirement that the likely adverse effects on the animals used should be weighed against the likely benefit of the research; stringent safeguards on pain and suffering; and general requirements to ensure the care and welfare of animals. With effect from 1 January 1990, establishments breeding and supplying animals commonly used in scientific procedures became regulated by section 7 of the Act. The United Kingdom legislation conforms with the Council of Europe Convention for the *Protection of Vertebrate Animals used for Experimental and other Scientific Purposes* and the European Community Directive 86/609/EEC of 24 November 1986 on the *Approximation of Laws Regulations and Administrative Provisions of the Member States regarding the Protection of animals used for Experimental and other Scientific Purposes.*

Scope of the Act

2. The Act provides for the licensing of experimental and other scientific procedures carried out on *protected animals*, which may cause *pain, suffering, distress or lasting harm*. Such work is referred to in the Act as a *regulated procedure*. This means that the Act controls the whole range of scientific procedures, from major surgery to the many thousands of scientific procedures which are minor and do not require anaesthesia, like the taking of a blood sample.

3. Protected animals are defined in the Act as all living vertebrate animals except man and the definition extends to foetal, larval or embryonic forms which have reached specified stages in their development. Under the Act an animal is regarded as "living" until the permanent cessation of circulation or complete destruction of its brain. It follows that procedures carried out on decerebrate animals are subject to the controls of the Act.

4. The Act extended controls to some scientific work not covered by earlier legislation. Such work includes, in particular, some breeding of animals with genetic defects; production of antisera and other blood products; the maintenance and passage of tumours and parasites; and the administration for a scientific purpose of an anaesthetic, analgesic, tranquilliser or other drug to dull perception. The humane killing of an animal for scientific purposes requires licence authority in certain circumstances.

5. The controls do not extend to procedures applied to animals in the course of recognised veterinary, agricultural or animal husbandry practice; procedures for identification of animals for scientific purposes, if this causes no more than momentary pain or distress and no lasting harm; or clinical tests on animals for evaluating a veterinary product under authority of an Animal Test Certificate, under the Medicines Act 1968.

Guidance, Codes of Practice and Annual Statistics

6. The Act requires the Home Secretary to publish and lay before Parliament guidance on the operation of the controls, codes of practice as to the care

and accommodation of animals and their use in scientific procedures, and annual statistics.

7. The *Code of Practice for the Housing and Care of Animals used in Scientific Procedures* (HC 107) was published in 1989 and the *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986* (HC 182) was published in 1990. The *Guidance* sets out in detail how the controls of the Act are applied. The *Statistics of Scientific Procedures, Great Britain, 1990* (Cm 1574) was published on 25 July 1991.

Project and personal licences

8. Two kinds of licence are required for all scientific work controlled by the Act. The procedures must be part of a programme of work authorised by a *project licence* and the person applying the regulated procedures must hold a *personal licence*. No work may be done unless the *procedure*, the *animals* used and the *place* where the work is done are specifically authorised in both project and personal licences.

9. A *project licence* is granted where the Home Secretary considers that the use of living animals in a programme of work for a purpose permitted by the Act is justified, and the methods proposed appropriate. In deciding whether and on what terms to authorise the project, the Home Secretary is required to weigh the likely adverse effects on the animals used against the benefit likely to accrue from the work. The Home Secretary must also be satisfied that the application has adequately considered the feasibility of using alternative methods not involving living animals. The holder of a project licence undertakes overall responsibility for the scientific direction and control of the work and the management of the project. The standard conditions applying to project licences are set out on page 49 of the *Guidance*. Someone may hold more than one project licence.

10. The *personal licence* is the Home Secretary's endorsement of the holder's competence and suitability to carry out specified procedures on specified animals. Applicants, who must be over 18, are required to give details of their qualifications, training and experience. Those who have not previously held a Home Office licence need the endorsement of a sponsor (normally someone in a senior position at the applicant's place of work). One or several personal licensees may work on any one project. The standard conditions applying to personal licences are set out on page 54 of the *Guidance*.

Certificate of Designation

11. Except where otherwise authorised in a project licence (e.g. for field work at a specified place and time), any place where work is carried out under the Act must be *designated* as a scientific procedure establishment. In addition, establishments which breed certain types of commonly-used animal—*mouse, rat, guinea-pig, hamster, rabbit, dog, cat* and *primate*—for use in scientific procedures (*breeding establishments*), and establishments which obtain such animals from elsewhere and supply them to laboratories (*supplying establishments*), must also be designated. Designated establishments are inspected by the Home Office Inspectorate, and are required, like scientific procedure establishments, to nominate a person to be responsible for the day-to-day care of animals, and a veterinary surgeon to advise on their health and welfare. The standard conditions applying to certificates of designation are set out on pages 45 and 47 of the *Guidance*.

Fees

12. Section 8 of the Act empowers the Home Secretary to charge fees to the holders of certificates of designated scientific procedure establishments and for each establishment breeding or supplying animals for use in scientific procedures. The fees for scientific procedure establishments are charged annually and consist of a flat rate annual fee relating to the establishment itself, and a fee for each personal licensee with primary availability at the establishment at any time in the preceding calendar year. (A personal licensee with primary availability at an establishment is considered to be based there.) The level of fees payable for 1992 for scientific procedure establishments was £110, and £99 for each personal licensee. For breeding and supplying establish-

ments with no personal licensees, the fee was £500. The fees are set to recover the full cost of the licensing system, including the cost of the Inspectorate, Home Office staff involved in the licensing system, and the cost of the APC Research Sub-Committee's budget.

Assessment of Applications

13. All applications for certificates of designation, project or personal licences are considered by the Home Office Inspectorate, who recommend whether and on what terms the application should be granted. The Home Secretary may also seek the opinion of an external assessor on part or all of an application, if he thinks it is necessary, for example because the area of research is highly specialised or the techniques involved novel. The assessor will be an expert from an appropriate branch of the biological sciences. The applicant is always informed if it is proposed to consult an assessor. The final decision about any application for authority under the Act rests with the Home Secretary.

14. Applications may also be referred for advice to the Animal Procedures Committee. Currently, all project licence applications involving a substantially severe procedure on a primate are referred to the Committee, together with project licence applications for work on cosmetics; for work on conscious animals involving tobacco products; and also for training in microsurgery.

Conditions of Licences and Certificates

15. The Home Secretary may include appropriate conditions in any personal licence, project licence, or certificate designating an establishment as a scientific procedure, breeding or supplying establishment. Certain conditions are referred to in the Act itself, in particular conditions in personal licences requiring precautions to be taken to prevent or minimise suffering by animals used in procedures, and requiring any animal in severe pain or severe distress which cannot be alleviated to be humanely killed immediately. Conditions are also included in all project licences regulating the source of animals used in work under the Act. Special restrictions apply to the sources of cats and dogs.

Representations against refusal of applications, etc

16. A person whose application for authority under the Act is refused, or whose licence or certificate is to be revoked or varied other than at the holder's own request, has the right to make representations to an independent legally qualified adviser appointed by the Home Secretary. The adviser will consider any representations made and the Home Secretary will take into account the adviser's recommendation. The procedures for making representations are set out on page 57 of the *Guidance*.

Additional Controls

17. The Act contains a number of additional controls. These include restrictions on the use of animals in more than one series of procedures; a requirement to kill an animal suffering at the conclusion of a series of procedures; and restrictions on the use of neuromuscular blocking agents. Other controls prevent the performance of procedures as an exhibition to the general public or for live showing on television; penalise the provision of false information in support of an application; and prohibit the improper disclosure of information obtained in confidence by a person exercising functions under the Act.

The Inspectorate

18. The Act gives statutory recognition to the Home Office Inspectorate and describes the Inspectors' duties. On 31 December 1992, there were 21 Inspectors all of whom hold either medical or veterinary qualifications. They are available to give advice and assistance to licensees and other personnel and have powers to require the destruction of an animal which they consider to be suffering excessively.

19. Inspectors consider in detail applications for licences and advise the Home Secretary how to ensure that only properly justified work is licensed. They carry out visits, mainly without notice, to establishments designated under the Act to ensure that its controls and the terms and conditions of licences issued under it are being observed (although increasingly they are being called upon to mount detailed retrospective investigations into allegations made by anti-vivisectionist organisations concerning animal handling or facilities at designated places, or the justification for animal work presented in published research papers).

Appendix II

ANNEX TO LORD NATHAN'S LETTER TO THE HOME SECRETARY ON CEPHALOPODS

The Committee noted that, in the past, cephalopods have been used mainly for the study of brain mechanisms, although it is understood that proportionately more work is now being done on understanding the life cycle and ecology of cephalopods, which does not on the whole involve experimenting on live animals.

Most of what is known about cephalopods relates to the octopus, and to some extent the squid Loligo *and cuttlefish. Certainly almost everything that is known about the higher nervous activity in cephalopods is based upon one species,* Octopus vulgaris. *The octopus has a relatively large neurological mass and it has been suggested that this might indicate that there are homologies in the nervous systems of humans and cephalopods. However, the Committee noted that the evolutionary line that led to the relatively large nervous system of the octopus is very different from the evolutionary line that led to the human brain. A nervous system which has evolved to cope with the particular life-style of the octopus is not likely to have the same characteristics as the cautiously self-preservatory brain of a mammal. Cephalopods have evolved life-styles which are quite different from those of vertebrates. Cephalopods grow very quickly, breed once, lay hundreds of thousands of eggs and have lifespans of perhaps no more than a couple of years.*

Nonetheless, the octopus is certainly a remarkable animal. The octopus seems to have the ability to learn through, for example, a system of rewards for correct responses and the administration of adverse stimuli for incorrect responses. However, while the octopus can learn to identify and avoid potentially damaging situations, these reactions may prove no more than that the octopus is capable of learning by response.

On the central question of whether cephalopods can experience pain and suffering, the Committee noted that any consideration of the notion of pain is likely to raise questions of psychology and indeed philosophy. In everyday speech, "pain" is understood to mean that the subject is aware of the experience. The International Association for the Study of Pain define it as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage." However while it is not known whether cephalopods can experience pain as so described it is possible to set criteria that are based on modern methods of measuring behaviour and analysing the functional character of the nervous system. There are, for example, grounds for suspecting that an animal might feel something if it ceases activity that it habitually performs in conditions that might be supposed to produce pain; or if it learns to avoid such conditions; or if it has part of its central nervous system dedicated to the processing of information relevant to the avoidance of damage.

The Committee heard that an injured octopus can exhibit abnormal behaviour, but not in a conventional "vertebrate" sense. Complex surgical procedures can be carried out on Octopus vulgaris *and the animal appears not to notice; indeed it will feed or copulate within minutes of recovery from anaesthesia. Octopuses with damaged arms may often be apparently "cured" by cleanly cutting off the lesioned arm. This may be related to normal behaviour; a high proportion of octopuses caught have regenerating arms, perhaps due to predatory activity. However trawling by fishing boats sometimes produces animals with skins that are badly abraded, and such animals may not feed.*

While the Committee concluded that the scientific evidence currently available is not sufficient to suggest with any reasonable degree of certainty that cephalopods can experience pain or suffering in the way humans can, the Committee noted, the continuing change in understanding of, and perceptions of morality in relation to the animal kingdom. It is fair to say that there has been a perceptible change in approach to questions about the moral implications of the possibility of causing pain to animals. As far as cephalopods are concerned this is reflected to some extent by the fact that researchers using cephalopods have adopted an informal code of practice. This not only seems to illustrate a commendably responsible attitude to the use of animals in research, but adds weight to the view that those with special knowledge of cephalopods are sufficiently concerned that cephalopods may be able to experience pain that they have felt it necessary to adopt such a code. It was also noted that it is apparently common for researchers using cephalopods to anaesthetise the animals before using them in procedures. This is not only to facilitate their handling but also because, while it is not known whether cephalopods can experience pain or suffering, the researchers do not wish to take the risk of inflicting avoidable pain. The view that the benefit of the doubt should be given at least to the Octopus vulgaris *is supported by the views expressed in the report of the Institute of Medical Ethics which commented that while most invertebrates may not be able to experience pain, cephalopods and in particular the octopus, have much more complex nervous systems and behaviour and give cause for concern; that while the character of their bodies differs greatly from that of vertebrates, the general level of organisation suggests that cephalopods might well be able to experience pain; and that as there is no reason to assume that cephalopods are any less able to suffer than vertebrate fish and amphibia (protected by the Act), there may indeed be a case for extending legal protection to cover cephalopods. The Committee noted that most of what was known about cephalopods relates to the octopus, and that doubt about whether cephalopods can experience pain and suffering focuses mainly on that species. If additional material were to become available to suggest that the same concerns about the octopus apply to other species of cephalopod then those species can be given the protection of the Act at that stage. The view was noted that it might be inappropriate to extend the protection of the Act to species about which next to nothing is known including, for example, the nautilus generally considered to be no more than a living fossil. One point made by those members of the Committee who are not in favour of extending the controls of the Act to the* Octopus vulgaris *was that in the absence of definite scientific evidence about the ability of the octopus to feel pain, it would be difficult to establish the criteria to be used in considering whether other invertebrate species should be brought within the scope of the Act.*

Although not relevant to the main principles at issue, the Committee noted the fact that very few cephalopods are used in this country in research which would be controlled by the Act if Octopus vulgaris *were to be brought within its scope. The view of the Inspectorate was that the small additional licensing and inspection work needed would be unlikely to affect adversely the operation of the Act in relation to vertebrate species.*

The Committee also took legal advice on whether the law on cruelty to captive and domestic animals, the Protection of Animals Act 1911, applies to cephalopods. This is of significance for two reasons. If the Act does not apply to cephalopods there is no legal protection for cephalopods used in research. If the 1911 Act does apply, then it is in the interests of researchers using cephalopods in experimental work which might cause pain or suffering to have such work covered by the 1986 Act. The advice the Committee received on the question of whether the 1911 Act does or does not apply was that the legal position is uncertain especially when the provisions of the 1911 Act are read in conjunction with later related amending legislation. It is perhaps worth recording that the Committee is not aware of any research being carried out in the United Kingdom which would not be likely to be permitted under the 1986 Act.

Appendix III

CRIMINAL OFFENCES UNDER THE ACT

1. Licensees and holders of certificates of designation should appreciate that failures in the control of licences, in particular the conduct of unauthorised procedures in establishments, where they are attributable to poor management, can lead to the revocation of all or part of the certificate of designation. It is, therefore, most important that certificate holders appreciate that under the Act their duties are active and not purely formal, as they might have been under previous legislation.

2. The Act not only controls the way in which scientific procedures on living animals are regulated, but also provides some exemption from the Protection of Animals Act 1911 (1912 in Scotland) for licence holders who are performing authorised procedures under the 1986 Act. However, where unauthorised procedures are being conducted, this immunity is not conferred and it would be possible to bring charges under the 1911 or 1912 Acts.

3. The main criminal offences in the Act relating to the performance of animal procedures can be set out broadly as follows:

(i) An offence is committed by anybody who carries out a regulated procedure on a protected animal if:

(a) he does not hold a personal licence authorising him to carry out that procedure on that animal;

(b) the procedure or species of animal used is not authorised by a project licence; and

(c) the procedure is carried out somewhere other than a place authorised both in the personal licence and in the project licence (this is normally an establishment covered by a certificate of designation).

(d) The person who carries out the procedure is not guilty of the offence of acting without the authority of a project licence if he can show that he reasonably believed, after making due enquiry, that he had proper authority.

(ii) An offence is committed by any project licence holder who procures or knowingly permits anybody under his control to carry out a regulated procedure either not authorised by the project licence or outside the authority of that person's personal licence.

(iii) No offence under paragraph (i) above is committed by a personal licensee's assistant if the assistant carries out, under the personal licensee's direction and if they are authorised by the personal licence, subordinate duties permitted by the Home Secretary, examples of which are listed in Appendix VII of the *Guidance*. The personal licence must contain specific authorization for the use of assistants. A personal licensee cannot delegate the authority of his licence to anybody else, and anybody who carries out a procedure which somebody else, but not he, is allowed to do by a personal licence, commits the offence described in paragraph (i) above.

(iv) It is an offence to re-use an animal if the animal has previously been used in a series or combination of procedures carried out for a different purpose and one or more of those procedures consisted of giving the animal a general anaesthetic. Exceptions to this general rule are if the animal is under a general anaesthetic

throughout the further procedures and is not allowed to recover consciousness; or if the anaesthetic was given only for surgical preparation, or only to immobilise the animal. But in any such case, the re-use must have been authorised in advance. It is also an offence, except where specifically authorised, to re-use an animal if the animal has previously been used in a series of procedures for a different purpose, even when none of those procedures involved giving the animal a general anaesthetic. Paragraphs 4.21–4.29 of the *Guidance* set out the circumstances in which authority for re-use can be sought.

(v) The Act requires that an animal which has been used in a series of procedures carried out for any one purpose, and which at the conclusion of the series is suffering or is likely to suffer adverse effects, must immediately be killed or caused to be killed by the personal licensee, either by a Schedule 1 method of humane killing, or by some other method authorised in the personal licence of the person who carries out the killing. A personal licensee who does not comply with this requirement commits an offence.

(vi) It is an offence to use a neuromuscular blocking agent unless expressly authorised to do so by the personal and project licences under which the procedure is carried out, or to use a neuromuscular blocking agent instead of an anaesthetic. Should a neuromuscular blocking agent be used without authority the person who carried out the procedure is not guilty of the offence if he shows that he reasonably believed, after making due enquiry, that he had that authority.

(vii) If an Inspector considers that a protected animal is undergoing excessive suffering, it is an offence to fail to comply with the Inspector's requirement that the animal must immediately be killed either by a Schedule 1 method of humane killing or by another method authorised in the personal licence held by a personal licensee.

(viii) In addition, breaches of standard licence conditions 1 to 5 of a project licence (page 49 of the *Guidance*) and standard conditions 1 to 10 of a personal licence (page 54 of the *Guidance*) may also constitute criminal offences.

Prosecutions

4. In England and Wales, proceedings for an alleged offence under the Act can be brought only by or with the consent of the Director of Public Prosecutions. There is equivalent provision for Northern Ireland. In Scotland, only the Lord Advocate can undertake prosecutions.

Non-criminal sanctions

5. Where an infringement does not constitute a criminal offence or is not being referred for possible prosecution, there are nevertheless extensive administrative sanctions available to the Home Office. These have included:

(i) revocation of all or part of the certificate of designation;

(ii) revocation of the project and/or the personal licence(s);

(iii) immediate suspension of the licence for the protection of the animals;

(iv) imposition of special conditions on the certificate of designation or licence(s) in order to prevent a recurrence of the incident;

(v) replacement of the deputy project licence holder, named day-to-day care person or named veterinary surgeon;

(vi) imposition of a supervision requirement on a personal licensee;

(vii) disqualification from supervising other licensees or from sponsoring personal licence applications;

(viii) a letter of admonition.

6. In practice, the majority of infringements are breaches which have not resulted in

unnecessary suffering to animals. Should such an infringement constitute a criminal offence, it does not follow automatically that a prosecution would be in the public interest. For example, a personal licensee might apply procedures without project licence authority, believing such authority to exist after due inquiry or the project licence holder may have had the licence revoked at his request but have failed to inform the personal licensees working under it.

7. In such cases administrative action by the Home Office is usually considered the most appropriate and effective response. A minor breach of the Act which constitutes a criminal offence may nevertheless be referred to the Director of Public Prosecutions where, for example, it is but one of several indicating disregard for the Act on the part of an individual or the establishment.

8. Where it is clear, or indeed where there is doubt, that an offence has been committed involving more than a technical breach, consideration will always be given to referring the matter to the Director of Public Prosecutions. While a decision to refer a case to the Director is for the Home Office, a decision to prosecute is for the Director of Public Prosecutions alone, based on his judgement of the merits of the case, the evidence available and other relevant factors, including whether a prosecution would be in the public interest.

9. Whether or not an infringement is referred for prosecution, it should be appreciated that the imposition of the administrative sanctions described in paragraph 10.5 can have significant repercussions for those involved in an infringement and be both immediate and far-reaching. The revocation of a project licence will stop further scientific work on that project and the revocation of a personal licence will prevent the licensee performing any further scientific procedures on living animals.

Appendix IV

EDUCATION AND TRAINING OF PERSONNEL UNDER THE ANIMALS (SCIENTIFIC PROCEDURES) ACT 1986

Home Office Statement of Policy on Education and Training

Introduction

The Home Office published a discussion document in 1991 on the appropriate education and training of those seeking licences under the Animals (Scientific Procedures) Act 1986. The proposals received a very large measure of support and the Home Office is now in a position to set out its policy. It has not proved necessary to make substantial changes to the proposals set out in the discussion document. The present paper also advises on the training of those with administrative duties under the Act and of those performing non-regulated procedures on animals within designated establishments. The Animals (Scientific Procedures) Act, 1986 imposes clear responsibilities on persons with specific roles in relation to the care and use of animals in laboratories. These are elaborated further in the Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 (HMSO, 1990: HC 182). As the roles differ, it follows that the education and training required before assuming these responsibilities will differ:

> Personal licence holders are responsible for the welfare of animals on which they carry out regulated procedures; applicants will be granted licences only if adequately trained to take on this responsibility, usually under supervision;
>
> Project licences will be issued only to persons properly able to direct a programme of work that is well-justified and takes account of all reasonable possibilities for reduction, refinement and replacement;
>
> Holders of Certificates of Designation have responsibility not only for ensuring that the fabric and staffing of designated places are maintained to appropriate standards but also for ensuring that reasonable steps are taken to prevent unauthorised procedures being carried out and that adequate training facilities are available for all animal users.

Considerable progress has been made over recent years in providing appropriate training for those involved in research with animals. In the United Kingdom great importance has been placed on 'on-the-job' training under the close supervision of those already expert in the field. The policy set out below in no way detracts from the need to maintain quality training and guidance after the issue of licences. Rather, it is intended to establish a sound foundation upon which such training can be more effectively built.

Training should be relevant to applicants' individual requirements and be provided at a time when animal work is being planned. Thus, programmes need to reflect the local needs of institutions and should be available at frequencies sufficient to meet the demands of the participants.

Effective assessment at the conclusion of the programme is required since it is the acquisition of knowledge and skills which matters and not simply attendance at a course.

Personal licence applicants

Applicants for Personal Licence after 1 April, 1994 will be required to have successfully completed an accredited training programme comprising the subjects described in Modules 1 to 3 in Appendix A and also those in Module 4 where appropriate to the techniques included in the licence application. Very limited exemptions from these requirements may be considered by the Home Office (see Appendix B).

The training requirements of former personal licensees who are applying for reinstatement of their licences will be determined by many factors including previous formal training and length of time away from use of animals in procedures. In general, anyone applying for a licence more than 5 years after relinquishing the previous licence should expect to undergo the full training programme. Where less than 5 years has elapsed the training requirements should be discussed with the Inspector.

Personal licensees seeking extension of authority from minor surgical procedures to major surgical procedures will be expected to complete Module 4 of the programme before application for such amendment.

Personal licensees seeking significant amendments to the species authorised on the licence which involve additional skills (eg extension from rodents to dogs or to farm animals) will be expected to undergo additional practical training as provided by the relevant parts of Modules 2, 3 and/or 4 before application for such amendment.

Project licence applicants

New applicants for Project Licences after 1 April, 1995 will be required to have successfully completed at least modules 1, 2 and 5 described in Appendix A and also Modules 3 and 4 when appropriate to the procedures to be carried out in the project. In most cases, project licence applicants will have held or still hold Personal Licences and therefore will only need to complete Module 5 prior to application for a project licence. There is merit in personal licence holders who are likely to become project licence holders or deputies later in their career completing Module 5 at an early stage, perhaps with a refresher course before application.

It is unlikely that persons who have never been personal licensees or who have very limited experience of animal science or animal welfare will be considered to have sufficient appropriate experience to hold a Project Licence.

Accreditation

All training programmes for applicants for personal and project licences (as described in Appendix A) should be accredited under a scheme recognised by the Home Office. Accreditation seeks to achieve common and high standards for licensee training which will facilitate free movement of licensees within UK and Europe as well as ensuring high standards in the use of animals for scientific procedures.

The *Accreditation Scheme for training programmes for personnel working under the Animals (Scientific Procedures) Act 1986*, operated by the Institute of Biology, is currently recognised for this purpose.

Other Education and Training expectations

Certificate Holders and administrative staff involved with the Animals (Scientific Procedures) Act, 1986 need to be familiar with the legal framework within which they carry out their duties. They should also have some awareness of the ethical issues involved in the use of animals for scientific purposes. Such personnel would derive considerable benefit from completing Module 1.

Appropriate training in more advanced techniques is strongly recommended when seeking major extensions to licence authorities. The Home Office Inspector should be consulted about the need for further training in these circumstances.

Certificate Holders of Designated Establishments should consider setting up mechanisms for updating licensees on a regular basis on developments, for example, in

laboratory animal science, animal welfare, anaesthesia, the law and ethics. Methods of Reduction, Refinement and Replacement can also be addressed within such a system.

Certificate Holders should note carefully their responsibility under the conditions of the Certificate to ensure that a person competent to kill animals humanely is available. Those involved in killing animals by methods listed in Schedule 1 of the Act and others carrying out non-regulated procedures using live animals need to be aware of the ethical issues involved in the use of animals for scientific purposes. They need also to be familiar with good husbandry and handling practices and with local arrangements for matters such as security, animal acquisition, disposal and safety. Certificate holders could largely meet their responsibilities in these matters by requiring such personnel to complete Modules 1 and 2.

Further Information

The syllabus set out below in Appendix A is not exhaustive and course organisers should feel able to include any other topics which they consider relevant in the particular circumstances. The elements of each module are those which the Home Office believe to be necessary for the proper instruction of those who will be responsible for using animals in scientific procedures. The modular and practical nature of the training programme allows considerable flexibility in the planning of courses and training can be achieved in a variety of ways, via lectures, tutorials and discussions, videos, films and reading. Formal courses may be a convenient way of achieving the necessary objectives, but may not provide the flexibility necessary in some situations.

The importance of practical experience within the training programme needs to be emphasised. As this experience precedes the granting of a licence, it must be limited to basic handling, husbandry and non-regulated procedures.

Organisers of training programmes may wish to consult the Named Veterinary Surgeon and Named Person in charge of Day-to-Day Care in the Establishment during the development of their programmes. Home Office Inspectors are available to offer any further advice required.

Module 1

Elements

1. **Historical background**
   Legislation and attitudes to animals and animal welfare in the United Kingdom.

2. **An introduction to ethical aspects of the use of animals in scientific procedures.**

3. **The Animals (Scientific Procedures) Act 1986**
   The Certificate of Designation
   The Project Licence
   The Personal Licence
   Schedule 1
   Schedule 2
   Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986
   Home Office Code of Practice for the Housing and Care of Animals used in Scientific Procedures
   Other codes of Practice and Guidelines

4. **Other relevant legislation**

Module 2

Elements

1. **Recognition of wellbeing, pain, suffering or distress**
   in the relevant species

2. **Handling and restraint**
   of the the relevant species

3. **Humane methods of killing**
   appropriate to the relevant species

4. **Local procedures**
   Security
   Administration
   Supply of animals
   Disposal of animals

5. **Personal Health and Safety**

Module 3

Elements

1. **Biology and husbandry**
   of the relevant species

2. **Common diseases and recognition**
   in the relevant species

3. **Health monitoring and disease prevention or control**
   General principles
   Principles of gnotobiology
   Local practices and procedures

4. **Introduction to anaesthesia and analgesia**
   in the relevant species

5. **Conduct of minor procedures**
   in the relevant species
   Common methods of dosing
   Common methods of sampling
   Minor procedures not requiring sedation, analgesia or general anaesthesia
   Other minor procedures involving sedation, analgesia or brief general anaesthesia

Module 4

Elements

1. **Surgical anaesthesia and analgesia**
   in the relevant species

2. **Conduct of surgical procedures**
   Principles of surgery
   Common surgical procedures
   Post-surgical care and monitoring

Module 5

1. **Ethical aspects of the use of live animals**

2. **Analysis of the literature**
   Critical appraisal
   Literature searches

3. **Alternatives**
   Refinement
   Reduction
   Replacement

4. **Project design**
   Plan of work
   Good laboratory practice
   Appropriate laboratory methods
   Selection of appropriate animal models
   Appropriate statistical methods

5. **Project licence management**
   Responsibilities
   Supervision of personnel and programme of work
   Record keeping requirements
   Annual return of procedures

6. **Legal aspects—the European and wider international context**

Appendix B

Exemptions from mandatory training requirements

All exemptions are discretionary on a case-by-case basis and should be discussed with the Inspector before application for a licence is made. The following examples indicate the types of circumstances in which exemptions will be considered.

Personal licence applicants

Exemption from all training requirements will be considered only for those persons with formal training in laboratory animal science, for example holders of the Certificate or Diploma in Laboratory Animal Science of the Royal College of Veterinary Surgeons, the MSc in Laboratory Animal Science of the University of London or the Associateship or Fellowship of the Institute of Animal Technology.

Completion of Module 1 only will be considered:

—for applicants for personal licences valid only for practical work on a microsurgery training course, the licence to be surrendered immediately upon completion of the course. The contents of this module may be incorporated into the microsurgery training course itself;

—for veterinary surgeons with practical experience of the relevant species;

—for animal technicians highly experienced with the relevant species;

—for holders of qualifications in laboratory science from outside the UK. They will be expected to complete Module 1 to ensure familiarity with UK law.

Completion of Modules 1 and 2 only will be considered:

—for applicants for very limited species and techniques (eg one species, oral dosing only);

—for undergraduates who will be under close supervision and with limited authorities; the contents of these modules may be integrated into the undergraduate course

—for experienced overseas researchers.

Completion of Modules 1 and 3 only will be considered:

—for applicants with extensive experience of the relevant species.

Project licence Applicants

Project licence applicants who already hold a project licence will not normally be expected to undertake further training.

Order Form

A number of publications relating to the Animals (Scientific Procedures) Act 1986 are published by HMSO. To obtain any of these, please send a photocopy of this form to the addresses shown below or telephone the numbers given.

	No.	Cost
Code of Practice for the Housing and Care of animals used in Scientific Procedures 1989; HC 107; price £4.50		
Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 1990; HC 182; price £7.20		
ANNUAL PUBLICATIONS: *Report of the Animals Procedures Committee:* 1987; HC 36; price £4.80		
1988; HC 458; price £3.20		
1989; HC 581; price £6.00		
1990; Cm 1646; price £6.60		
1991; Cm 2048; price £8.80		
Statistics of Scientific Procedures on Living Animals, Great Britain 1987; Cm 515; price £6.50		
1988; Cm 743; price £7.50		
1989; Cm 1152; price £8.50		
1990; Cm 1574; price £9.45		
1991; Cm 2023; price £9.60		
TOTAL		

Printed in the United Kingdom for HMSO
Dd 5061091 9/93 C11 3398 4235 255829 Job No. 933964

HMSO publications are available from:

HMSO Publications Centre
(Mail, fax and telephone orders only)
PO Box 276, London SW8 5DT
Telephone orders 071-873 9090
General enquiries 071-873 0011
(queuing system in operation for both numbers)
Fax orders 071-873 8200

HMSO Bookshops
49 High Holborn, London, WC1V 6HB
071-873 0011 Fax 071-873 8200 (Counter service only)
258 Broad Street, Birmingham, B1 2HE
021-643 3740 Fax 021-643 6510
33 Wine Street, Bristol, BS1 2BQ
(0272) 264306 Fax 0272 294515
9–21 Princess Street, Manchester, M60 8AS
061-834 7201 Fax 061-833 0634
16 Arthur Street, Belfast, BT1 4GD
(0232) 238451 Fax 0232 235401
71 Lothian Road, Edinburgh, EH3 9AZ
031-228 4181 Fax 031-229 2734

HMSO's Accredited Agents
(see Yellow Pages)

and through good booksellers

ISBN 0-10-123012-5

9 780101 230124